Reducing Tobacco Use Among Women of Childbearing Age: Contributions of Tobacco Regulatory Science and Tobacco Control

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Abstract

Tobacco use has unique, adverse health consequences for reproductive-aged women, particularly should these women become pregnant. Thus, successful efforts to reduce tobacco use among this population have strong potential to improve public health and reduce health disparities. The present review examines contributions to reducing tobacco use among women of childbearing age spanning the domains of tobacco regulatory science and tobacco control from the passage of the Family Smoking Prevention and Tobacco Control Act in 2009 through September 2019. In the domain of tobacco regulatory science, such efforts include research conducted by various National Institutes of Health/Food and Drug Administration (FDA)-supported Tobacco Centers of Regulatory Science, epidemiological surveillance studies, as well as studies examining the potential impact of tobacco regulatory policies currently under consideration by the FDA (e.g., reduced nicotine content cigarettes, health warning labels). Tobacco control efforts within this same 10-year timeframe include developments in pharmacological and psychosocial approaches to promoting tobacco cessation, mHealth interventions, and tobacco control policy. Emerging issues pertinent to ongoing efforts to reduce tobacco use within the domains of both tobacco regulatory science and tobacco control are also reviewed, including e-cigarettes, comorbid health conditions, course of tobacco and other drugs of abuse, and obstacles to the dissemination and implementation of evidence-based treatment and policy. Although the past decade has seen numerous important contributions to reducing tobacco use among reproductive-aged women within both domains, existing obstacles must be surmounted to continue reducing tobacco use and protecting health among this population.

Keywords

women of reproductive age; tobacco regulatory science; tobacco control; cigarette smoking; e-cigarettes

Although recent estimates of cigarette smoking prevalence among U.S. adults published by the Centers for Disease Control and Prevention (CDC) indicate a 67% decrease in smoking

since 1965 (Wang et al., 2018), this decline been unevenly distributed, with smoking prevalence remaining stable or increasing over time among specific subgroups (e.g., economically disadvantaged women; Higgins & Chilcoat, 2009; Kurti et al., 2017). For example, prevalence of cigarette smoking during pregnancy has remained stable at ~13% over the past decade (Kurti et al., 2017), and the 20.1% smoking prevalence among nonpregnant women of childbearing age (ages 15–44) (Lopez et al., 2018) is higher than the current national average of 14% (Wang et al., 2018). These trends are concerning, as tobacco use is associated with substantial adverse health outcomes that are unique to women. For example, female smokers of childbearing age are at increased risk for conception delay and infertility (Centers for Disease Control and Prevention, 2010; U.S. Department of Health and Human Services, National Institutes of Health, 2004), and women who smoke during pregnancy are more likely to experience pregnancy complications, fetal growth restriction, premature delivery, and sudden infant death syndrome than nonsmokers (Cnattingius, 2004; Dietz et al., 2010; Pauly & Slotkin, 2008). As nearly half (~45%) of pregnancies in the general U.S. population are unintended (Finer & Zolna, 2016), nonpregnant women of childbearing age are also vulnerable to experiencing these adverse health effects given their relatively high likelihood of experiencing an unintended pregnancy. Importantly, women who do not plan their pregnancies are less likely to engage in health-promoting behaviors during the preconception and perinatal periods (e.g., initiating prenatal care, taking prenatal vitamins, quitting cigarette smoking) versus women with intended pregnancies (Cheng et al., 2016; Dott et al., 2010; Rassi, Wattimena, & Black, 2013). Following childbirth, postpartum smoking increases risk for ear and respiratory infections among infants and children (U.S. Department of Health and Human Services, National Institutes of Health, 2014). As cigarette smoking among women of reproductive age has become increasingly concentrated among women who are young, socioeconomically disadvantaged, and more nicotine dependent (Higgins & Chilcoat, 2009; Kandel, Griesler, & Schaffran, 2009), efforts to decrease tobacco use spanning the domains of tobacco regulatory science and tobacco control are critical to protecting maternal and infant health and reducing health disparities.

The opportunity for developing and deploying ambitious, far-reaching, multipronged approaches to reducing tobacco use among women of reproductive age has been made more feasible with legislation passed within the past decade. For example, passage of the Family Smoking Prevention and Tobacco Control Act in 2009 gave the U.S. Food and Drug Administration (FDA) regulatory authority over the manufacture, distribution, and marketing of tobacco products with the overarching aim of protecting the U.S. public from the adverse health impacts of tobacco use (Family Smoking Prevention and Tobacco Control Act, H.R. 1256, United States Congress, 2010). To inform FDA regulation of tobacco products nationwide, 14 Tobacco Centers of Regulatory Science (TCORS) were established at U.S. universities and medical institutions in 2013 (U.S. Department of Health and Human Services, National Institutes of Health, 2013). In addition to legislation that provides opportunities to reduce tobacco use among reproductive-aged women via tobacco regulatory policy, separate legislation passed within the past decade provides opportunities within the domain of tobacco control. For example, in 2010, the Affordable Care Act required coverage of tobacco cessation in all nongrand-fathered private plans and for pregnant women on Medicaid (American Lung Association, 2017), with the objective being to expand access to

tobacco cessation treatment among vulnerable populations including reproductive-aged women. Although both legislative actions are reflective of a broader context that is conducive to moving the needle in a positive direction regarding tobacco use among women of reproductive age, numerous obstacles remain. For example, it is unclear whether increases in the number and variety of tobacco products over the past decade, and particularly as this pertains to electronic nicotine delivery systems (ENDS), will facilitate or undermine efforts to quit using combusted tobacco among childbearing-aged women (Kurti, Bunn, Tang, et al., 2019). In addition, barriers such as time and lack of training in tobacco counseling continue to limit adherence to current best practice guidelines for promoting smoking cessation among health care providers (Flemming et al., 2016) and implementing evidence-based approaches to reducing tobacco use as part of routine care remains immensely difficult (Fiore, Keller, & Curry, 2007).

The present review examines tobacco regulatory policy and tobacco control efforts to reduce tobacco use among women of reproductive age spanning the time from 2009 through September 2019 when the review was completed. This timeframe was selected because 2009 is the year in which congress passed the Family Smoking Prevention and Tobacco Control Act. As the present review represents a narrative summary of the literature on these topics, it did not require approval by the University of Vermont Institutional Review Board.

The subsequent review first examines contributions to reducing tobacco use among reproductive-aged women in the area of tobacco regulatory science, followed by a section on contributions in the domain of tobacco control. These sections are followed by a third section which explores current issues and challenges to achieving ongoing progress in both domains (e.g., ENDS use, presence of multiple comorbidities or co-occurring vulnerabilities to tobacco use, co-use of tobacco and other substances). Finally, the review concludes by synthesizing the various contributions made within both the tobacco regulatory science and tobacco control domains, and providing several recommendations for future research, treatment, and policy that may further reduce tobacco use and protect the health of both childbearing-aged women and their offspring.

Tobacco Regulatory Science

As noted above, the 2009 Family Smoking Prevention and Tobacco Control Act permits the FDA to regulate the manufacture, distribution, and marketing of tobacco products (Family Smoking Prevention and Tobacco Control Act, H.R. 1256, United States Congress, 2010), and research to inform FDA on nationwide tobacco product regulation is underway at 14 TCORS across the United States (U.S. Department of Health and Human Services, National Institutes of Health, 2013). Following the completion of the initial 5 years of TCORS support, several reviews were published highlighting research conducted in the domain of tobacco regulatory science between 2013 when TCORS funding began through 2018 (Higgins, Kurti, Palmer, et al., 2019; Perry et al., 2019). One of these reviews included a section that focused explicitly on women of reproductive age (Higgins, Kurti, Palmer, et al., 2019), however the need to address multiple populations in that same review (e.g., racial/ethnic minorities, rural populations, those with serious mental illness) prohibited an in-depth examination of tobacco regulatory science research on reproductive-aged women

specifically. That in-depth examination is accomplished in the present review. In addition, as the inclusion of only TCORS-supported studies in Higgins, Kurti, Palmer, et al. (2019) may have excluded relevant studies on the potential impact of tobacco regulatory policies on women of childbearing age, research not associated with any TCORS is also included in the present review.

Tobacco regulatory science studies that either include or focus directly on women of childbearing age have used a variety of research methods to answer questions with implications for tobacco regulatory policy. These methods include leveraging U.S. national data sets to provide information on prevalence, predictors, and trajectories of tobacco use among reproductive-aged women; clinical trials; and human laboratory studies utilizing procedures derived from behavioral pharmacology to examine the reinforcing value of cigarettes varying in nicotine content. In the following, I review epidemiological studies intended to inform FDA about tobacco use patterns among reproductive-aged women, as well as clinical trials and human laboratory studies that examined potential impacts of specific regulatory policies currently under consideration by the FDA.

Epidemiological Studies

Several TCORS-supported empirical studies have leveraged U.S. nationally representative data to provide basic information on prevalence and patterns of use of a range of commercially available tobacco products among women of reproductive age (Higgins, Redner, et al., 2017; Kurti et al., 2017; Kurti, Bunn, et al., 2018; Kurti, Redner, et al., 2018; Lopez et al., 2018; Nighbor et al., 2018). Two of these studies represent parallel investigations of prevalence and correlates of using various tobacco products among nonpregnant women of reproductive age (Lopez et al., 2018) and pregnant women (Kurti et al., 2017) who completed Wave 1 of the Population Assessment of Tobacco and Health (PATH) study (2013–2014). In both populations, prevalence of using noncigarette tobacco products (e.g., e-cigarette, hookah, any cigar) was higher among women who also smoked conventional tobacco cigarettes relative to overall prevalence. As an example, overall prevalence of e-cigarette use among nonpregnant women was 5.5%, whereas prevalence among nonpregnant women who smoked cigarettes was 22.5% (Lopez et al., 2018). Similarly, among pregnant women, overall prevalence of e-cigarette use was 4.9% versus 28.5% among pregnant women who smoked cigarettes (Kurti et al., 2017). These findings were suggestive of substantial dual and poly tobacco use among reproductive-aged women, however patterns of single versus multiple tobacco product use were not explicitly examined in either report. Thus, a subsequent study was conducted to examine this question, and the longitudinal nature of PATH was leveraged to also assess changes in tobacco use over time and when punctuated by pregnancy (Kurti, Bunn, et al., 2018). As this second report was purely descriptive, a third study was conducted to examine the influence of pregnancy versus other respondent characteristics on longitudinal transitions in tobacco use, specifically as these characteristics relate to quitting tobacco (Kurti, Redner, et al., 2018).

Key overarching findings revealed by the latter two studies above (Kurti, Bunn, et al., 2018; Kurti, Redner, et al., 2018) include the following: First, regardless of pregnancy status, the most common form of tobacco use among reproductive-aged women was using cigarettes

alone, followed by dual use of cigarettes plus e-cigarettes. The vast majority of additional poly use patterns also included conventional cigarettes. Second, regardless of pregnancy status, the most common transition among women using cigarettes alone was to continue using cigarettes exclusively. For women using cigarettes plus other tobacco products, the predominant transition was to discard the alternative tobacco product(s) and continue smoking cigarettes over time. Third, quit rates associated with entering pregnancy were substantially lower for conventional cigarettes (53.4%) relative to e-cigarettes (81.3%), cigars (88.0%), and hookah (98.3%). Finally, pregnancy was independently associated with increased odds of quitting each of the former tobacco products minus cigars, and multiple logistic regression analyses revealed that pregnancy was more strongly associated with quitting these products than other respondent characteristics.

In addition to the above, two additional reports used U.S. nationally representative data to examine the impact of smoking higher-nicotine/tar-yield (regular full-flavor) cigarettes on nicotine dependence and quitting smoking during pregnancy (Higgins, Redner, et al., 2017), and disparities in smoking among reproductive-aged women associated with residing in urban versus rural areas (Nighbor et al., 2018). The former report found that smoking full flavor cigarettes relative to lower estimated yield cigarettes was associated with increased odds of continuing to smoke during pregnancy. This association remained significant even after controlling for demographic, socioeconomic, and psychosocial characteristics, thereby implicating full-flavor cigarettes directly in undermining quit attempts among this population. The latter report on disparities in smoking associated with urban-rural status found that regardless of pregnancy status, smoking prevalence and nicotine dependence were higher among rural relative to urban residents. In addition, this report also found lower nonpregnant-to-pregnant reductions in odds of smoking among rural relative to urban women, potentially suggesting disparities in pregnancy-related smoking cessation.

Collectively, the above studies that have leveraged U.S. nationally representative data to examine prevalence, correlates, and longitudinal transitions in tobacco use among women of childbearing age have made numerous worthwhile contributions. First, the updated prevalence estimates reported in this work highlight the extent to which conventional tobacco cigarettes remain the predominant and most persistent pattern of tobacco use. Although use of numerous alternative tobacco products is also quite prevalent, it occurs most commonly among women already smoking conventional cigarettes. The above studies also raise questions about how alarmed researchers, clinicians, and policymakers should be about dual and poly tobacco use (Sung, Wang, Yao, Lightwood, & Max, 2018), as patterns of multiple product use appeared to be less stable than exclusive use of one product, and particularly when that one product used is tobacco cigarettes (Kurti, Bunn, et al., 2018; Kurti, Redner, et al., 2018). Finally, study findings revealing significant, independent associations between various risk factors and cigarette use after adjusting for the presence of others (Higgins, Redner, et al., 2017; Nighbor et al., 2018) are suggestive of a process whereby additional risk factors have cumulative effects on vulnerability to tobacco use (Higgins et al., 2016), including during pregnancy. Thus, researchers, clinicians, and policymakers must ensure that the emergence of novel tobacco products does not detract from a focus on conventional cigarettes, as the decreases in cigarette smoking observed among the general U.S. population are not being matched among subpopulations such as

reproductive-aged women (Wang et al., 2018). The reports reviewed above provide compelling evidence that use of conventional tobacco cigarettes remains a significant problem among women of childbearing age, thereby continuing to pose serious threats to women's health and exert multigenerational adverse health impacts.

Research Examining the Impact of Potential Regulatory Policies

Although the epidemiological studies reviewed above provide the basic information necessary to conduct evidence-based regulation, they do not address the potential impacts of any specific policies currently under consideration by the FDA. Thus, the present section reviews several studies that used varying methods to examine the potential impact of regulatory policies that the FDA may implement in the near future. Briefly, these policies include reducing the nicotine content in commercially available cigarettes, requiring specific warning labels on cigarette packaging and advertising, and banning the production of menthol cigarettes and flavored e-cigarettes. Exemplars of research supported by TCORS, FDA Center Tobacco Products, or other funding mechanisms conducted to inform the FDA about the potential outcomes of particular regulatory policies are provided below.

Low nicotine content cigarettes.—One authority granted to the FDA by the 2009 Tobacco Control Act is to reduce although not eliminate nicotine levels in cigarettes if doing so protects public health (Family Smoking Prevention and Tobacco Control Act, H.R. 1256, United States Congress, 2010). This authority creates the opportunity to eventually require that nicotine exposure levels from cigarettes fall below the threshold necessary to produce nicotine dependence, thereby making it easier for current smokers to quit and preventing the development of dependence among those newly initiated to cigarette smoking (Benowitz & Henningfield, 1994; Donny et al., 2015). The public health benefits of implementing such a policy have been examined under both acute (Donny, Houtsmuller, & Stitzer, 2007; Higgins, Heil, Sigmon, Tidey, Gaalema, Stitzer, et al., 2017) and extended exposure conditions (Benowitz et al., 2007; Donny et al., 2015; Hatsukami et al., 2010, 2018; Tidey et al., 2017), including among women of childbearing age.

Two empirical studies are available documenting subjective and behavioral responses to cigarettes varying in nicotine content among socioeconomically disadvantaged women of childbearing age (Higgins, Heil, Sigmon, Tidey, Gaalema, Hughes, et al., 2017; Higgins, Heil, Sigmon, Tidey, Gaalema, Stitzer, et al., 2017). These multisite, double-blind, within-participant laboratory assessments exposed participants to cigarettes with varying nicotine doses (0.4, 2.3, 5.2, and 15.8 mg/g of tobacco) across 14 outpatient sessions. Participants completed concurrent choice testing and validated measures of subjective effects at each visit to assess the addiction potential of the cigarettes. Results of both the initial pilot (Higgins, Heil, Sigmon, Tidey, Gaalema, Stitzer, et al., 2017) and the study proper (Higgins, Heil, Sigmon, Tidey, Gaalema, Hughes, et al., 2017) revealed that women chose the 0.4-mg/g dose less than the 15.8-mg/g dose in concurrent choice testing, although preference for higher over lower nicotine content cigarettes was reversed upon increasing the response cost (i.e., button presses) required to earn the higher dose. All doses reduced symptoms of nicotine withdrawal. These findings were robust, persisting across three diverse populations (i.e., socioeconomically disadvantaged women of reproductive age, individuals with

affective disorders, individuals with opioid use disorder), with follow-up secondary data analyses indicating that nicotine dependence severity did not moderate effects of nicotine content on the subjective and behavioral outcomes above (Higgins et al., 2018).

These findings indicating that reducing the nicotine content in cigarettes produced reductions in the reinforcing effects of smoking without causing excessive withdrawal, craving, or compensatory smoking are consistent with effects of reduced nicotine content cigarettes observed among the general population of adult smokers (Donny et al., 2015), and contribute additional support to the possibility that a national nicotine reduction policy may decrease the addiction potential of cigarettes. In addition, the observation that manipulating response cost shifted preference for the higher nicotine content cigarettes also has tobacco regulatory implications, for example suggesting that preference in naturalistic settings could be shifted by restricting sale of higher nicotine content cigarettes to specialized stores while permitting sales of low nicotine content cigarettes at common retail outlets. Additional studies examining effects of reduced nicotine content cigarettes among the aforementioned populations under extended exposure conditions, as well as studies on effects of low nicotine content cigarettes among pregnant women, are currently underway.

Health warning labels.—In addition to mandating a national nicotine reduction policy, the 2009 Family Smoking Prevention and Tobacco Control Act also gave the FDA regulatory authority to establish rules for larger and more prominent warning labels, including graphics, on cigarette packaging and advertising. One TCORS-supported study examined response to various health warning labels (HWLs) among a U.S. national sample of reproductive-aged women, including pregnant women, and whether HWL responses were associated with knowledge of health effects and harm perceptions of tobacco use (Mead et al., 2019). Results indicated that pregnant and nonpregnant women were equally likely to report seeing HWLs and foregoing smoking because of the HWLs. However, pregnant women were less likely to have knowledge of fetal harm and endorse being likely to quit because of HWLs. In both groups of women, foregoing cigarettes and endorsing a higher likelihood of quitting due to HWLs were associated with increased perceived harm and knowledge of smoking adverse health impacts. These data confirm the need for more effective HWLs to increase knowledge and deter reproductive-aged women from smoking cigarettes, especially pregnant women. In terms of how HWLs could be made more effective, some research suggests that pregnancy-related pictorial HWLs that include testimonials and pictures of real babies may be particularly effective among both pregnant and nonpregnant women of childbearing age (Berg et al., 2011; Hammond, Reid, Driezen, & Boudreau, 2013; Kollath-Cattano, Osman, & Thrasher, 2017; Levis et al., 2014), with the potential to reduce prenatal smoking and hospital costs by up to $100.2 million per year in the United States (Tauras, Peck, Cheng, & Chaloupka, 2017).

Other policies under consideration.—As mentioned above, the FDA also has the regulatory authority to ban the use of menthol in tobacco cigarettes, and to ban all characterizing flavors in e-cigarettes. Although there is a gap in research examining the potential effects of such policies among women of childbearing age specifically, there is strong evidence that menthol cigarettes and other flavored tobacco products are used at

disproportionately higher rates among subpopulations including reproductive-aged women, thereby suggesting that removing menthol cigarettes from the market may reduce smoking-attributable disease and death among at least some portion of this population (Lester & Gagosian, 2017; Schroth, Villanti, Kurti, & Delnevo, 2019; Wailoo, 2019). Although little research exists on the contribution of flavored e-cigarettes to long term, harmful tobacco use trajectories among women of childbearing age, the FDA's plan to restrict sales of flavored e-cigarette cartridges (American Association for Cancer Research, 2019; Jackler, VanWinkle, Bumanlag, & Ramamurthi, 2018) may combat initiation of nicotine product use among youth, including underage girls.

Tobacco Control

Although there is no equivalent to the 2009 Family Smoking Prevention and Tobacco Control Act in the domain of tobacco control, the past decade has nonetheless seen important contributions in terms of tobacco control efforts targeting women of reproductive age. After a brief review of current best practice guidelines for promoting tobacco use cessation, the present section reviews these contributions as they pertain to (a) pharmacological and (b) behavioral/psychosocial approaches to reducing tobacco use; (c) emerging eHealth/mHealth tobacco cessation interventions; and (d) tobacco control policy.

Current Guidelines and Recommendations for Health Care Providers

The U.S. Preventive Services Task Force (USPSTF) recommends that health care providers ask all of their pregnant patients about tobacco use and offer augmented, pregnancy-specific treatment for tobacco dependence services (U.S. Preventive Services Task Force, 2015). In addition, the American College of Obstetricians and Gynecologists (ACOG; Committee on Underserved Women & Committee on Obstetric Practice, 2017) and the Association of Women's Health, Obstetric, and Neonatal Nurses (AWHONN; Association of Women's Health, Obstetric & Neonatal Nurses, 2017) recommend that providers complete brief, evidence-based smoking cessation interventions based on the 5 A's (Ask, Advise, Assess, Assist, Arrange). Unfortunately, adherence to these guidelines is quite low given the high stakes involved when treating pregnant women who identify as current cigarette smokers. Indeed, many providers complete only the first two steps of the 5 A's without assessing, assisting, or arranging treatment for tobacco dependence services (Tong, Strouse, Hall, Kovac, & Schroeder, 2010), and only about half of providers report screening for any type of noncombustible tobacco use (England et al., 2014), even though e-cigarette use may signal interest in quitting smoking and openness to using other quit methods (Ghosh & Drummond, 2017; Kalkhoran, Grana, Neilands, & Ling, 2015). Although a review of barriers that limit provider adherence to current clinical practice guidelines is beyond the scope of this review, increased efforts are clearly needed to circumvent barriers in the health care setting so that reproductive-aged women reliably receive the brief, evidence-based interventions currently recommended by USPSTF, ACOG, and AWHONN.

Pharmacological Interventions

Regarding pharmacological approaches to promoting smoking cessation, current USPSTF recommendations for nonpregnant adults include pharmacotherapy interventions such as

nicotine replacement therapy (NRT), bupropion hydrochloride sustained-release (bupropion SR), and varenicline, either with or without behavioral counseling; using two types of NRT rather than one; and using NRT plus bupropion over bupropion alone (Siu & the U.S. Preventive Services Task Force, 2015). For pregnant women, the USPSTF concluded that because of limited and conflicting evidence, lack of evidence on other forms of pharmacotherapy, and unclear balance of benefits versus harms, the current evidence on pharmacotherapy for smoking cessation in pregnant women is insufficient (Siu & the U.S. Preventive Services Task Force, 2015). This same incomplete grade provided by the USPSTF in 2015 was also provided in the USPSTF's earlier report in 2009 (U.S. Preventive Services Task Force, 2009). That being said, research examining effects of NRT among pregnant women has demonstrated that adherence to NRT predicts smoking cessation (Fish et al., 2009; Vaz et al., 2016), although promoting adherence in these reports was challenging and consequently adherence was generally low (e.g., 29% in Fish et al., 2009). Low adherence to NRT among pregnant women was also reported in Coleman et al. (2012; 7.2%), and presumably contributed to the nonsignificant differences in quit rates between NRT- and placebo-treated women. Thus, the overall health benefits of pharmacotherapy-based approaches to promoting smoking cessation during pregnancy have remained unclear for approximately the past decade.

Although the most recent USPSTF report did not find any studies on bupropion or varenicline in pregnancy, several studies examining this question were published following the release of the USPSTF report in 2015. The first systematic review investigating the safety of bupropion and varenicline in pregnancy was published in 2018 and contained 18 studies (Turner, Jones, Vaz, & Coleman, 2019). The authors concluded that although there was no evidence that either bupropion or varenicline were harmful to pregnant women, the studies reviewed were generally of poor quality and failed to provide strong evidence supporting the safety of these medications. More research, particularly in the form of randomized controlled clinical trials, is needed to elucidate whether these pharmacological approaches to promoting smoking cessation are safe and effective among pregnant women.

Behavioral and Psychosocial Interventions

Although few interventions are designed specifically to target nonpregnant women of reproductive age, the same is not so for pregnant women. Indeed, sufficient behavioral and psychosocial approaches to promoting smoking cessation during pregnancy have been used to permit a series of meta-analyses on this topic (Chamberlain et al., 2013; Lumley et al., 2009). In these meta-analyses including over 77 controlled clinical trials and 77,000 women, financial incentives-based interventions were found to produce the largest effect size of any psychosocial or pharmacological approach to promoting smoking cessation during pregnancy, producing increases in cessation rates of 24% above control levels versus the 6% increase in cessation rates produced by other approaches. Figure 1 shows a plot of individual trial and overall effect sizes and 95% confidence intervals (CIs) for achieving late-pregnancy smoking abstinence in eight randomized clinical trials involving 1,297 women treated with financial incentives contingent on biochemically verified abstinence or a control condition (Cahill, Hartmann-Boyce, & Perera, 2015). Financial incentives increased the odds of antepartum abstinence 3.79-fold above control levels (95% CIs [2.74, 5.25]), with odds for

abstaining at the longest follow-up assessment increased by 3.60 (95% CIs [2.39, 5.43]; not shown).

Researchers at the University of Vermont have conducted a series of randomized controlled clinical trials examining the effectiveness of financial incentives contingent on the submission of breath and urine specimens indicating smoking abstinence versus a submission-contingent control condition where incentives were provided regardless of smoking status (Heil et al., 2008; Higgins et al., 2004, 2012). Across trials, late pregnancy smoking abstinence rates have been nearly fivefold higher among the contingent incentives condition versus the controls (34.1% vs. 7.4%), with treatment effects remaining discernible at a final 24-weeks postpartum assessment (14.1% vs. 1.2%), 12 weeks after incentives were discontinued. Contingent incentives were also associated with higher mean birth weights among infants, and a lower proportion of low birth weight infants and neonatal intensive care unit admissions, relative to controls. Ongoing studies are underway at the University of Vermont examining the comparative effectiveness of financial incentives versus standard of care for promoting smoking cessation during pregnancy, as well as a national study examining the feasibility, acceptability, and effectiveness of a smartphone-based financial incentives intervention for promoting smoking abstinence among pregnant women. Although there are numerous challenges to integrating this evidence-based approach into routine prenatal care in the United States, one U.S. study demonstrated the feasibility of incorporating incentives into prenatal visits at four federally qualified health centers in rural New Hampshire (Olson, Boardman, & Johnson, 2019). In addition, research conducted in the United Kingdom has demonstrated the effectiveness of the financial incentives intervention developed at the University of Vermont when delivered by clinicians in a clinical rather than research setting (Ierfino et al., 2015), as well as providing evidence supporting the cost-effectiveness of this approach (Boyd, Briggs, Bauld, Sinclair, & Tappin, 2016).

As noted in a recent review on the underutilization of financial incentives for promoting behavior change (Higgins, Kurti, & Davis, 2019), the challenge now is building on the above efforts to make this evidence-based treatment widely available and easily accessible. For example, researchers at the University of Vermont are currently engaged in discussions with Medicaid officials in Vermont regarding the possibility of moving incentives for smoking cessation into routine care for pregnant and newly postpartum women. Although these dissemination and implementation efforts present considerable challenges, surmounting these challenges is likely to offer considerable opportunities to impact public health.

The Emerging Field of Mobile Health (mHealth)

As with many other fields of study, mHealth approaches to promoting behavior change continue to grow in the tobacco field. Although much of this work focuses on reducing tobacco use among the general population, one recent report found that a U.S. national sample of both nonpregnant women of childbearing age and pregnant women who smoked used various digital forms (e.g., social media, text messaging, smartphone apps) at similar rates as both their nonsmoking counterparts and the general U.S. population (Kurti, Bunn, Nighbor, et al., 2019). These findings provide support for the potential utility of leveraging

technology to deploy tobacco prevention, education, and treatment efforts to reduce tobacco use among reproductive-aged women. To date, only a few text programs and even fewer apps have been designed specifically for pregnant women (Griffiths, Brown, Fulton, Tombor, & Naughton, 2016), however the field may see continued proliferation of such efforts in coming years given their broader reach, as well as the modest benefits and high treatment acceptability that have been reported in some studies (Pollak et al., 2013). The availability of funding to support mHealth efforts to reduce tobacco use may also grow increasingly favorable. For example, both private employers and the Center for Medicare and Medicaid Services recently reported significant increases in funding for telehealth services (Castellucci, 2017), and the 21st Century Cures Act mandated the use of technology in health care services and called for more research on connecting rural patients with health care providers (Privacy & Data Security, 2017). Considered together, all of the above point to ample opportunities to capitalize on technological advances to provide reproductive-aged women with smoking cessation resources and support.

Tobacco Control Policy

In addition to improving provider adherence to current clinical practice guidelines and expanding access to evidence-based cessation services, additional means of reducing tobacco use among women of childbearing age involve advocating for the implementation of effective tobacco control policies. Several exemplars of such policies are described briefly below.

Removing barriers to Medicaid coverage of tobacco cessation treatment.—Although Medicaid recipients smoke at much higher rates than individuals with private health insurance (Jamal et al., 2018), most states have limited coverage for evidence-based tobacco cessation treatment, thereby contributing to the problem of economic disparities in accessing cessation services. As economically disadvantaged women of reproductive age represent a subpopulation in which cigarette smoking prevalence has not matched the promising trends observed among the general U.S. population, advocating for policy-level changes to remove barriers to Medicaid coverage of tobacco cessation treatment may represent an important step toward achieving comparable gains among this population as observed among U.S. adults overall.

Smoke-free legislation.—Research suggests that smoke-free laws are associated with decreases in preterm birth and small for gestational age (Faber et al., 2017; Peelen et al., 2016), and increases in gestational length (Hajdu & Hajdu, 2018). A 2014 literature review using 11 studies using interrupted time-series designs corroborated this evidence in reporting that smoke-free legislation was associated with small decreases in preterm birth, although there were no obvious effects on birth weight (Been et al., 2014). Advocating for the implementation and/or enforcement of smoke-free legislation may represent worthwhile pursuits in the domain of tobacco control, as smoke-free laws appear to make small, independent contributions to protecting fetal health.

Licensing and zoning regulations.—Tobacco retailer density has been shown to be positively associated with increased smoking prevalence and cigarette intake, low life

expectancy, and high mortality among the general population (Chuang, Cubbin, Ahn, & Winkleby, 2005). In a recent study focused on pregnant women specifically, researchers examined the association between changes in rates of smoking during pregnancy and corporate-policy change in TRD within six U.S. states that declined to adopt the Affordable Care Act Medicaid Expansion in 2014, thereby limiting access to smoking cessation services among these states' low-income populations (Hall et al., 2019). The specific corporate-policy change in TRD examined in this report was the beginning of tobacco product sales at Family Dollar and Dollar General stores. Results of this study indicated that experiencing high TRD change mitigated decreases in prevalence of smoking during pregnancy, even after controlling for rurality, socioeconomic status, and ongoing tobacco control efforts. The finding that high TRD may be inhibiting progress in smoking reduction during pregnancy suggests that states should potentially consider licensing and zoning as lasting strategies to reduce TRD.

Related Research and Challenges in a Changing Tobacco Landscape

Factors like the passage of the 2009 Family Smoking Prevention and Tobacco Control Act and the growth of mHealth interventions for reducing tobacco use represent just two examples of a tobacco landscape in flux. As noted previously, it will also be important for researchers, clinicians, and policymakers to continue keeping pace with the rapid proliferation of alternative tobacco products observed within the past decade (Cantrell et al., 2018) without allowing their examinations of these novel products to detract from a focus on conventional cigarettes, which remain the most prevalent, toxic, and dependence-producing form of tobacco use. Moreover, it may also prove fruitful to view today's changing tobacco landscape in its broader context—a context in which an opioid epidemic continues to wreak havoc on U.S. public health and U.S. states are increasingly legalizing marijuana for medical and recreational uses. How tobacco use is impacted within this larger context is unclear but worth considering as tobacco use initiation and the development of dependence may be impacted by these broader contextual factors, and tobacco use may predispose individuals to using other substances.

The following section addresses the above, as well as other timely and relevant issues pertaining to conducting research in the fields of both tobacco regulatory science and tobacco control. Although not an exhaustive review of current issues and challenges, considering the issues below when deploying tobacco regulatory and tobacco control strategies to decrease tobacco use may increase the likelihood of achieving meaningful behavior change.

ENDS

Although parallel examinations of tobacco use prevalence among U.S. national samples of nonpregnant (Lopez et al., 2018) and pregnant women were described earlier in this review, the most recent estimates of ENDS prevalence in a national sample comes from National Health Interview Survey data collected between 2014 and 2017 (Boozang, Bachrach, & Detty, 2014). This report found similar rates of ENDS use among nonpregnant (3.6%) and pregnant women (3.3%). Moreover, consistent with the epidemiological studies described

above (Gentry, Forouhi, & Notley, 2019; Kurti et al., 2017; Kurti, Bunn, et al., 2018; Kurti, Redner, et al., 2018; Lopez et al., 2018), prevalence of ENDS use was substantially higher among current cigarette smokers in both nonpregnant (13.0%) and pregnant women (38.9%), and relative to overall prevalence. It is important that those in the tobacco field are aware and keep abreast of basic information surrounding the prevalence of ENDS use among this population. Regarding the question of whether ENDS offer reproductive-aged women any benefits in reducing or quitting conventional cigarette smoking, a recent systematic review reported that very few studies examined the effectiveness of ENDS for smoking cessation among specific subgroups, including reproductive-aged women (Gentry et al., 2019). Thus, it remains generally unclear whether ENDS are a barrier, facilitator, or have no impact on women's ability to achieve tobacco use cessation.

With respect to tobacco regulatory science implications surrounding women of childbearing age, the FDA must weigh mixed findings regarding the ability of ENDS to reduce toxicant exposures if completely substituted for cigarettes (National Academies of Sciences, Engineering, and Medicine, 2018) with findings suggesting that only a minority of reproductive-aged women using combusted tobacco products transition to using ENDS alone or no tobacco over time (Kurti, Bunn, et al., 2018). Future research that delineates those variables associated with continued use of cigarettes or other combusted products, versus transitioning to ENDS or quitting tobacco, will provide valuable insights to policymakers at the FDA, who extended their authority to regulate ENDS in 2016 and await research that informs regulatory policy surrounding these products.

Regarding tobacco control, ACOG recommends that health care providers include ENDS in smoking screening questions (Bhatnagar et al., 2014; Committee on Health Care for Underserved Women, 2011), a recommendation to which adherence as noted above is quite low (England et al., 2014). Research indicating that many women of childbearing age perceive ENDS as safer than cigarettes (Wagner, Camerota, & Propper, 2017) and use ENDS to reduce or quit smoking (England et al., 2016), sometimes over evidence-based treatment like NRT (Oncken et al., 2017), supports the importance of screening for ENDS use as it may signal interest in quitting smoking. Such findings also suggest that randomized controlled trials examining whether ENDS can promote smoking cessation among women of childbearing age may also be worthwhile. Research examining effects of ENDS use during pregnancy will also be important, as there is currently a lack of consensus in health care messaging surrounding this question, thus women report receiving inconsistent advice on the safety of using ENDS during pregnancy (Fallin, Miller, Assef, & Ashford, 2016). Finally, additional research is needed on tobacco control policies surrounding ENDS use among reproductive-aged women. For example, in contrast to smoke-free legislation which has been shown to reduce cigarette smoking among women of reproductive age (Been et al., 2014; Faber et al., 2017; Hajdu & Hajdu, 2018; Peelen et al., 2016), simulation models anticipate that comprehensive indoor vaping restrictions may have the opposite effect, potentially increasing prenatal smoking up to 2% due to advancing misperceptions about ENDS being equally or more dangerous than cigarettes (Cooper & Pesko, 2017).

Comorbid Conditions and Multiple Vulnerabilities

As cigarette smoking continues to decrease at the level of national prevalence while becoming increasingly concentrated among more disadvantaged groups (Graham, Inskip, Francis, & Harman, 2006), it is perhaps unsurprising that women who are current smokers increasingly exhibit multiple comorbid conditions. For example, disproportionate numbers of reproductive-aged women who smoke have psychiatric disorders or other substance use issues relative to their nonsmoking counterparts (Smith, Mazure, & McKee, 2014). Similarly, a higher proportion of pregnant women who smoke are young and have lower educational attainment relative pregnant nonsmokers (Chen et al., 2018; National Academies of Sciences, Engineering, and Medicine, 2018; Nguyen et al., 2018). Researchers, clinicians, and policymakers must be thoughtful and diligent about addressing the presence of multiple risk factors among women of childbearing age, as these characteristics may pose obstacles to both reaching and engaging these women in cessation support services, as well as successfully promoting smoking abstinence.

In addition to providing women with co-occurring vulnerabilities with access to intensive, evidence-based tobacco cessation treatment, efforts must also be made to address competing needs in the lives of these women so that they can fully engage in the treatments that are made available to them (Levinson et al., 2015). Although mHealth interventions may help surmount geographical barriers to accessing tobacco cessation treatment, it is worth noting that socioeconomic barriers in access to varying digital forms (e.g., smartphone ownership) are still present, with nonpregnant and pregnant smokers both endorsing less access relative to their nonsmoking counterparts, although digital form utilization among these women was still quite high (Kurti, Bunn, Nighbor, et al., 2019). Nonetheless, it will be important for those developing technology-based smoking cessation services to devise explicit plans for engaging smokers who remain in the minority without access to various digital platforms (e.g., directing them to locations in their community that offer free computer and Internet access (McInnes, Li, & Hogan, 2013), or programs that distribute free mobile phones to low-income persons; Komando, 2012).

Co-Use of Tobacco and Other Drugs of Abuse

Although tobacco use may accompany use of a variety of other substances, co-use of tobacco and marijuana, as well as tobacco and opioids, are reviewed as exemplars of poly substance use involving tobacco. The importance of these two substances is highlighted subsequently. It is also worth nothing that in a study of pregnant women enrolled in smoking cessation treatment, the most common additional substances detected in their urine specimens were marijuana (90% of positive specimens) and opioids (18%; Gaalema, Higgins, Pepin, Heil, & Bernstein, 2013), with few specimens containing cocaine or benzodiazepines (<6%). Although research on co-use of tobacco and these latter substances is not discussed in the present review, the importance of screening and intervening on smoking among women with any comorbid substance use disorder should not be understated, as many abused drugs are known to increase smoking rates (e.g., cocaine,Roll, Higgins, & Tidey, 1997; alcohol, Griffiths, Bigelow, & Liebson, 1976) and undermine quit attempts (Richter, Ahluwalia, Mosier, Nazir, & Ahluwalia, 2002; Stapleton, Keaney, & Sutherland, 2009).

Marijuana.—As U.S. states increasingly legalize marijuana, prevalence of marijuana use continues to grow among both nonpregnant women of childbearing age and pregnant women. For example, one recent study reported 62% increases in marijuana use among a U.S. national sample of pregnant women between 2002 and 2014 (Brown et al., 2017). Although overall prevalence of marijuana use among pregnant women in this report was nonetheless quite low (3.85%), other research indicates that marijuana use is more prevalent among women already smoking conventional tobacco cigarettes, with co-use of tobacco and marijuana during pregnancy continuing to trend upward (Young-Wolff et al., 2017). Although research on the adverse health impacts of co-using tobacco plus marijuana during pregnancy are limited, one recent study reported that co-using both substances was associated with significantly higher odds of infants having a small head circumference relative to using tobacco or marijuana alone (Coleman-Cowger, Oga, Peters, & Mark, 2018). In addition, much like offspring prenatally exposed to tobacco are more likely to become cigarette smokers (De Genna, Goldschmidt, Day, & Cornelius, 2016; Goldschmidt, Cornelius, & Day, 2012), offspring prenatally exposed to marijuana are more likely to use both combustible cigarettes and cannabis (Sonon, Richardson, Cornelius, Kim, & Day, 2015; Sonon, Richardson, Cornelius, Kim, & Day, 2016). Studies also suggest that regardless of pregnancy status, co-use of tobacco and marijuana is associated with increased nicotine dependence and greater difficulty quitting both substances relative to using either tobacco or marijuana alone (Coleman-Cowger, Schauer, & Peters, 2017; Vogel, Rubinstein, Prochaska, & Ramo, 2018), and at least one study demonstrated that marijuana increased difficulty quitting smoking during pregnancy (Haskins, Bertone-Johnson, Pekow, Carbone, & Chasan-Taber, 2010). Whether the availability of increasingly more potent cannabis (Dujourdy & Besacier, 2017) further increases the likelihood of adverse health impacts of co-use remains to be seen and should be carefully monitored. Researchers, clinicians, and policymakers should also continue monitoring other emerging trends in marijuana and tobacco co-use among reproductive-aged women (e.g., stuffing cigars or little cigars with cannabis to smoke blunts; Krauss, Rajbhandari, Sowles, Spitznagel, & Cavazos-Rehg, 2017). Staying abreast of such trends will permit researchers and clinicians to ask women appropriate questions about co-use, thereby permitting accurate surveillance and revealing opportunities to intervene and reduce co-use behaviors.

Opiates.—Whereas ~20% of nonpregnant women of childbearing age smoke in the United States (Lopez et al., 2018), and ~13% of pregnant women (Kurti et al., 2017), smoking prevalence is much higher among those with comorbid opioid dependence. More specifically, research indicates that over 90% of opioid-maintained patients smoke cigarettes (Chisolm et al., 2013; Nahvi, Richter, Li, Modali, & Arnsten, 2006), with similar rates reported among opioid-dependent pregnant patients (Chisolm, Brigham, Tuten, Strain, & Jones, 2010; Jones et al., 2009). Importantly, both of the main medications used to treat opioid dependence (i.e., buprenorphine and methadone) may increase difficulty quitting smoking (Elkader, Brands, Selby, & Sproule, 2009; Mutschler, Stephen, Teoh, Mendelson, & Mello, 2002), leaving pregnant women in particular vulnerable to adverse impacts of smoking on fetal and infant health even as they reduce their likelihood of adverse outcomes associated with illicit opioid use. Indeed, one study reported that pregnant women receiving either buprenorphine or methadone continued smoking at similar rates over the course of

their pregnancies (Chisolm et al., 2013), and in a second study zero of 22 pregnant women receiving opioid replacement therapy quit smoking despite reporting a desire to do so (Fallin et al., 2016).

Whether the greater difficulties quitting smoking among opioid-versus nonopioid-dependent pregnant women are attributable to factors such as a higher experience of trauma (Peirce, Kolodner, Brooner, & Kidorf, 2012), co-occurring mood and anxiety disorders (Conway, Compton, Stinson, & Grant, 2006), or to health care providers prioritizing discussions about illicit rather than licit substance use (Bailey & Jones Cole, 2009), remains to be determined. Nonetheless, the need for highly tailored tobacco treatment programs for pregnant women with comorbid opioid dependence is quite clear. Unfortunately, a recent review of the literature identified only three interventions testing smoking cessation interventions among pregnant patients receiving Opioid Maintenance Therapy (Akerman et al., 2015). Of these three interventions, financial incentives was the only effective intervention, with 31% of women receiving incentives achieving smoking abstinence by week 12 of the study versus 0% of women receiving usual care (Tuten, Fitzsimons, Chisolm, Nuzzo, & Jones, 2012).

Dissemination and Implementation

One final issue relevant to discussions about reducing tobacco use among women of reproductive age involves the dissemination and implementation of evidence-based tobacco control and tobacco regulatory policy strategies outside a research context. With respect to tobacco control, barriers to implementing the highly efficacious financial incentives-based approach to reducing cigarette smoking during pregnancy include theoretical and philosophical objections to this approach (Krauss et al., 2017), as well as a lack of funding to support dissemination and implementation efforts. Although the passage of the Affordable Care Act has led to Medicaid playing a growing role in funding treatment for substance use disorders (Boozang et al., 2014), there is substantial room for improvement surrounding the incorporation of incentives into routine care for promoting smoking cessation during pregnancy, and Medicaid funding will be essential for accomplishing this (Higgins, Kurti, & Davis, 2019).

To disseminate new knowledge and novel findings about evidence-based tobacco cessation treatments for women of childbearing age, researchers and clinicians alike should attend national conferences targeting maternal-child health care providers. At present, a recent review of abstracts presented at the Society for Maternal-Fetal Medicine and ACOG annual meetings indicated that just 0.48% and 0.47% were focused on smoking, respectively (Fallin-Bennett, Scott, Fallin-Bennett, & Ashford, 2019). This is clearly a missed opportunity to educate health care providers on innovative and efficacious approaches to treating tobacco use and dependence among women of childbearing age. It may also be worthwhile to expand training in the area of women and addiction more generally, as there are currently limited opportunities for the next generation of researchers to develop niches in this area, and few funding opportunities related specifically to this topic (Meyer, Isaacs, El-Shahawy, Burlew, & Wechsberg, 2019), thereby limiting the number of both early- and mid-level investigators dedicated to alleviating the burden of substance use and dependence, including tobacco use, among reproductive-aged women.

Conclusion

The present review summarizes efforts to reduce tobacco use among women of childbearing age that span the domains of tobacco regulatory science and tobacco control. Important efforts have been made in both domains over the past decade that run the gamut from human laboratory studies examining acute effects of cigarettes varying in nicotine content to epidemiological studies that provide basic information on prevalence of using various commercially available tobacco products among reproductive-aged women. Although many research questions remain unanswered, the efforts reviewed above have collectively generated a rich knowledge base regarding tobacco use among the present population of interest, as well as illuminating important directions for future research, treatment, and policy. Several overarching themes reflected in this review are addressed below.

First, one of the most significant findings to emerge from the various TCORS-supported epidemiological studies reviewed above (Kurti et al., 2017; Kurti, Bunn, et al., 2018; Kurti, Redner, et al., 2018; Lopez et al., 2018) is the extent to which conventional cigarette smoking remains disproportionately more prevalent and persistent than other patterns of tobacco use among reproductive-aged women. Taken together, the findings that (a) a majority of poly tobacco use patterns included conventional cigarettes, (b) longitudinal transitions in tobacco use among poly users typically involved discarding noncigarette tobacco products over time while continuing to smoke cigarettes, and (c) pregnancy-related quit rates were substantially lower for cigarettes than other tobacco products illustrate the powerfully addictive nature of cigarettes relative to other tobacco products. Although these findings should not be interpreted as suggesting that poly tobacco use is an over-blown concern—indeed such use may be associated with equal or greater mortality risk than using cigarettes alone (Choi, Inoue-Choi, McNeel, & Freedman, 2019)—they do serve as an important reminder to tobacco researchers, clinicians, and policymakers that continued dedication to tobacco reduction efforts that explicitly target conventional cigarette use may be imperative to protecting health among women of reproductive age. The fact that a majority of studies included in the present review focus on cigarettes despite surges in the number of alternative tobacco products that have become available over the past 10 years (Cantrell et al., 2018) is promising: It suggests that those working in various capacities in the tobacco field share a common understanding of where the most significant concerns surrounding tobacco use among reproductive-aged women exist, which is without a doubt their persistent use of conventional tobacco cigarettes.

Second, there is a growing body of research that continues to bring important information to bear on tobacco regulatory policies that may reduce tobacco use among specific populations including women of reproductive age. Perhaps the most comprehensive example of this research are the various examinations of reduced nicotine content cigarettes. These studies provide compelling evidence that reduced nicotine content cigarettes may decrease dependence and permit smoking cessation among both the general population of U.S. smokers (Donny et al., 2015; Tidey et al., 2017), and among various unique subpopulations (Higgins, Heil, Sigmon, Tidey, Gaalema, Hughes, et al., 2017; Higgins, Heil, Sigmon, Tidey, Gaalema, Stitzer, et al., 2017; Higgins et al., 2018). The fact that reduced nicotine content cigarettes produced similar effects across both acute and extended exposure conditions, and

across populations, lend support to the robustness and generality of these effects. Although additional studies on reduced nicotine content cigarettes are still underway, it is safe to say that consensus is emerging that implementing a national nicotine reduction policy like that initially proposed in 1994 has strong potential to facilitate tobacco reduction and cessation including among vulnerable populations (Benowitz & Henningfield, 1994). Coupling a national nicotine reduction policy with complementary policies that increase access to acceptable alternative sources of nicotine (e.g., noncombusted tobacco products) may enhance the acceptability of nicotine reduction in tobacco and accelerate migration away from cigarettes (Benowitz & Henningfield, 2018). Indeed, this is precisely the plan for tobacco regulation released by the FDA in July 2017, which included a rule to reduce nicotine to nonaddictive levels, as well as plans to make medicinal and noncombustible nicotine products more available (Gottlieb & Zeller, 2017). It will be interesting to observe whether comparable, systematic lines of research examining the potential impact of other regulatory policies currently under consideration by the FDA (e.g., eliminating characterizing flavors in alternative tobacco products) follow a similar path as that of research concerning a national nicotine reduction policy.

Third, the present narrative review highlights a constellation of tobacco control efforts that should be made to reduce tobacco use among childbearing-aged women. These efforts range from less intensive strategies such as improving provider adherence to current clinical practice guidelines, to more challenging efforts such as incorporating evidence-based interventions into routine clinical care. Both avenues to impacting tobacco use among this population should be pursued, as female smokers today increasingly represent a hardened population of "hardcore" users (Smith, Rose, Mazure, Giovino, & McKee, 2014) who would likely benefit from multipronged tobacco control efforts. In addition, there is no reason that various tobacco control efforts cannot be pursued concurrently. More specifically, although systemic, administrative, and financial barriers must be overcome to deliver financial incentives as part of routine prenatal care (Higgins, Kurti, & Davis, 2019), there are fewer barriers to increasing provider adherence to current best practice guidelines. Thus, efforts to accomplish this latter goal should begin immediately. Although effects of brief smoking cessation counseling such as the 5 As produce relatively modest improvements in perinatal smoking cessation relative to more intensive efforts (Chamberlain et al., 2013), observing the periodic benefits of this "light touch" approach may provide the needed motivation for continuing to persist at more daunting and obstacle-ridden efforts such as modifying the standard of routine clinical care and advocating for the implementation of effective tobacco control policies.

Fourth, much of the research included in the present review focuses on pregnant women specifically as opposed to all reproductive-aged women regardless of pregnancy status. Although pregnancy may represent a unique "window of opportunity" for promoting healthy behavior change (Thomas et al., 2017), it would be preferable to address tobacco use well before a woman becomes pregnant, as the likelihood of delivering a baby with equally low risk for adverse birth outcomes as a never-smoker may disappear if women continue smoking beyond the first trimester (Pineles, Hsu, Park, & Samet, 2016). In addition to efforts targeting tobacco use among reproductive-aged women, one additional approach to reducing smoke-exposed pregnancies involves circumventing pregnancy in the first place by

increasing contraceptive access and use among women of reproductive age. Methods to accomplish this have been successfully used among women receiving opioid maintenance therapy (Heil et al., 2016) and are likely translatable to smokers. As half of all U.S. pregnancies are unintended (Finer & Zolna, 2011), and unwanted pregnancy is a significant, independent predictor of continuing to smoke during pregnancy (Salimi, Terplan, Cheng, & Chisolm, 2015), applying comparable methods to reduce unplanned pregnancies among female smokers of reproductive age merits consideration. Moreover, obstetrics and gynecology (OB/GYN) physicians may be more comfortable with such an approach, as they receive substantially more training surrounding contraceptive counseling relative to smoking cessation counseling. Indeed, one U.S. study reported that 77% of practicing OB/GYN's received no formal training in smoking cessation, with 85% of these physicians endorsing that the techniques they use in practice were self-taught (Nims, Jordan, Price, Dake, & Khubchandani, 2019).

Finally, it was mentioned previously that women represent a subpopulation in which evidence supports a progressive hardening of current smokers (Smith, Rose, et al., 2014). In simpler terms, women smoking today increasingly have multiple comorbid risk factors (e.g., younger age, less education, lower income), making them potentially harder to reach and more difficult to treat. The impact of progressive hardening among female smokers is that disparities exist not only between smokers and their nonsmoking counterparts, but also between current smokers in need of tobacco cessation support services and the people serving them. It will be important to protect against failures and disconnect in understanding the needs, challenges, and barriers faced by women of reproductive age struggling with tobacco use. One approach to ensuring that newly developed resources and interventions to support tobacco cessation are responsive to women's needs is to involve them in their development. This can be accomplished via community-based participatory research (Leung, Yen, & Minkler, 2004), following the dictum "nothing about us without us" (Bell & Salmon, 2011), and by obtaining support from agencies such as the Patient-Centered Outcomes Research Institute whose overarching mission is "engaging communities in defining healthcare needs and in receiving the benefits of research" (Nease et al., 2018). In addition to engaging reproductive-aged women themselves in the development of resources to promote tobacco cessation, it may also be important to establish collaborations that facilitate the integration of intensive, cross-disciplinary services capable of addressing the multitude of stigma, financial, childcare, and transportation issues experienced by reproductive-aged women with co-occurring vulnerabilities (Meyer et al., 2019; Smith, Rose, et al., 2014).

The present narrative review has summarized numerous invaluable contributions regarding tobacco regulatory science and tobacco control efforts to reduce tobacco use among women of reproductive age. These contributions provide important information for researchers, clinicians, and policymakers alike, in addition to revealing existing gaps in knowledge and important directions for future research, treatment, and policy. Although women of childbearing age who use tobacco represent a considerably and perhaps increasingly challenging population in which to effect behavior change, ongoing dedication to such efforts are imperative, and success will yield a most rewarding outcome. Specifically, leveraging diverse expertise to develop and implement innovative, effective, multipronged

strategies to reducing tobacco use within the domains of both tobacco regulatory science and tobacco control offers the opportunity to exert profound, multigenerational impacts on improving public health and reducing health disparities.

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Public Health Significance

Tobacco use is associated with adverse health outcomes that are unique to women, including conception delay, infertility, pregnancy complications, and premature birth. The present narrative review examines tobacco regulatory policy and tobacco control efforts to reduce tobacco use among women of reproductive age within the past decade. Although women who use tobacco represent a challenging population in which to effect behavior change, ongoing dedication to developing innovative, effective, multipronged strategies to reducing tobacco use among this population offers the opportunity to exert profound, multigenerational impacts on improving public health and reducing health disparities.
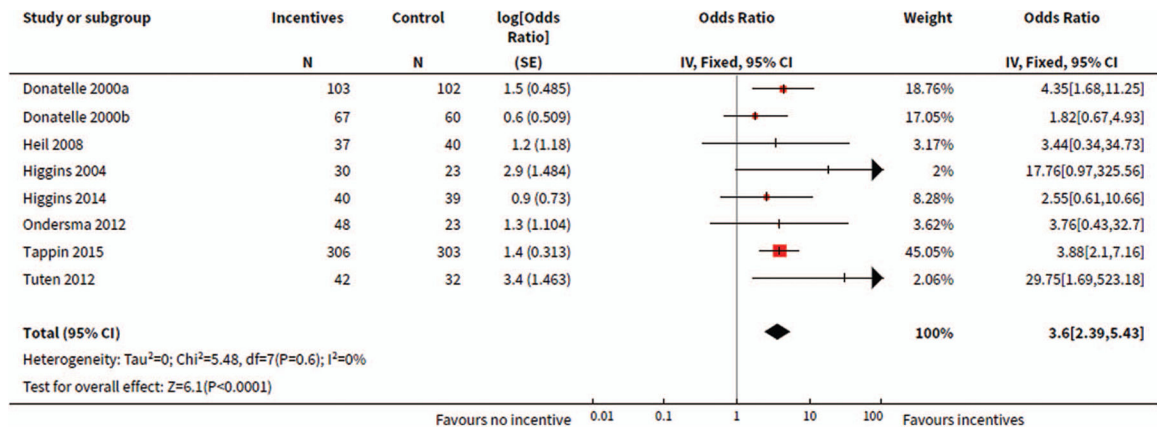
Study or subgroup	Incentives	Control	log[Odds Ratio]	Odds Ratio	Weight	Odds Ratio
	N	N	(SE)	IV, Fixed, 95% CI		IV, Fixed, 95% CI
Donatelle 2000a	103	102	1.5 (0.485)		18.76%	4.35[1.68,11.25]
Donatelle 2000b	67	60	0.6 (0.509)		17.05%	1.82[0.67,4.93]
Heil 2008	37	40	1.2 (1.18)		3.17%	3.44[0.34,34.73]
Higgins 2004	30	23	2.9 (1.484)		2%	17.76[0.97,325.56]
Higgins 2014	40	39	0.9 (0.73)		8.28%	2.55[0.61,10.66]
Ondersma 2012	48	23	1.3 (1.104)		3.62%	3.76[0.43,32.7]
Tappin 2015	306	303	1.4 (0.313)		45.05%	3.88[2.1,7.16]
Tuten 2012	42	32	3.4 (1.463)		2.06%	29.75[1.69,523.18]
Total (95% CI)					100%	3.6[2.39,5.43]
Heterogeneity: Tau²=0; Chi²=5.48, df=7(P=0.6); I²=0%						
Test for overall effect: Z=6.1(P<0.0001)						

Favours no incentive   0.01   0.1   1   10   100   Favours incentives

Figure 1.
Odds of smoking cessation during late pregnancy in individual clinical trials that met criteria for inclusion in the meta-analysis, and for all trials considered together. Adapted from "Incentives for smoking cessation," by K. Cahill, J. Hartmann-Boyce, and R. Perera, 2015, *Cochrane Database of Systematic Reviews, 18*, p. 18. Copyright 2015 by The Cochrane Collaboration.