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Prenatal tobacco prevention and cessation interventions for women in low- and middle-income countries

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Abstract

Although the prevalence of tobacco use is decreasing in many high-income countries, it is increasing in many low- and middle-income countries. The health and economic burden of increasing tobacco use and dependence is predictable and will have devastating effects in countries with limited resources, particularly for vulnerable populations such as pregnant women. We sought to review effective tobacco prevention and intervention strategies for decreasing tobacco use and secondhand smoke exposure before and during pregnancy in high-, middle-, and low-income countries. We reviewed several types of interventions, including population-level efforts (increasing tobacco prices, implementing tobacco control policies), community interventions, clinical interventions, and pharmacological treatments.

A second purpose of this report is to present findings of an international expert working group that was convened to review the evidence and to establish research priorities in the following areas: (a) preventing the uptake and reducing tobacco use among girls and women of reproductive age; and (b) reducing tobacco use and secondhand smoke exposure among pregnant women. The working group considered the evidence on existing interventions in terms of burden of disease, intervention impact, intervention costs, feasibility of integration into existing services, uniqueness of the contribution, and overall feasibility. Finally, we present the working group's recommendations for intervention research priorities.

Key words: *Global, tobacco, perinatal and reproductive health*

Introduction

Currently, an estimated 5.4 million people worldwide die each year from tobacco use (1). In the course of the next 30 years, tobacco-related deaths are expected to increase to 8 million each year; 80% of these deaths are projected to occur in low- and middle-income countries (LMICs). While far more men than women

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use tobacco in LMICs, surveillance data from the Global Youth Tobacco Surveys suggest that the difference between the two sexes is narrowing (2). Women and their offspring face additional health risks if women smoke cigarettes during pregnancy, as smoking by pregnant women increases the risk of low birthweight, prematurity, placenta previa, placental abruption, preterm premature rupture of membranes, and sudden infant death syndrome (SIDS) (3). The risks of maternal smokeless tobacco use (e.g. snuff or chewing tobacco) are less studied, but the available evidence shows an increased risk of stillbirth, low birthweight, prematurity, and infant death (4,5). Waterpipe smoking may increase the risk of delivering a low birthweight infant as well as other pregnancy complications (6,7). Secondhand smoke (SHS) exposure to infants causes increased risk of SIDS and lower respiratory illness (8). Current efforts to address the overall globalization of tobacco focus on tobacco use among all populations. In 2003 the World Health Assembly adopted the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) in response to the globalization of the tobacco epidemic (9). The FCTC's goal is to protect the health of citizens and many of its 38 articles address health-related topics such as safeguarding of public health policies with respect to tobacco control from commercial and other vested interests of the tobacco industry; protection from exposure to tobacco smoke; packaging and labeling of tobacco products; and tobacco advertising, promotion, and sponsorship. The WHO published its first 'Report on the Global Tobacco Epidemic', in 2008, which presented the 'MPOWER' framework for tobacco control (1). This framework calls for monitoring of the tobacco epidemic; offering assistance to quit; protecting nonsmokers from exposure to SHS; warning smokers of the health effects of smoking; enforcing advertising bans; and raising taxes on tobacco products. While the MPOWER framework does not directly address pregnant women, many of its strategies will reduce prenatal tobacco exposure. Pregnant women, nonetheless, are a special population with some unique needs regarding tobacco control.

Although tobacco use is decreasing in most high-income countries, it is on the rise in many LMICs among girls and women of reproductive age. The prevalence of cigarette smoking among girls aged 13–15 ranged from 2% in Southeast Asia and the Eastern Mediterranean region to 17% in Europe (Figure 1) (2). The prevalence of other tobacco use [e.g. pipes, waterpipes, smokeless tobacco, and bidis (thin, hand-rolled cigarettes)] among girls was generally higher than that of cigarette use in several regions and ranged from 6% in the Western Pacific region to 11% in Africa (2). A potential high concordance of tobacco use in pregnant and nonpregnant women in LMICs highlights the need for prevention and cessation interventions to target both pregnant and reproductive age women.

Prevention and cessation programs for pregnant women have been studied extensively in high-income

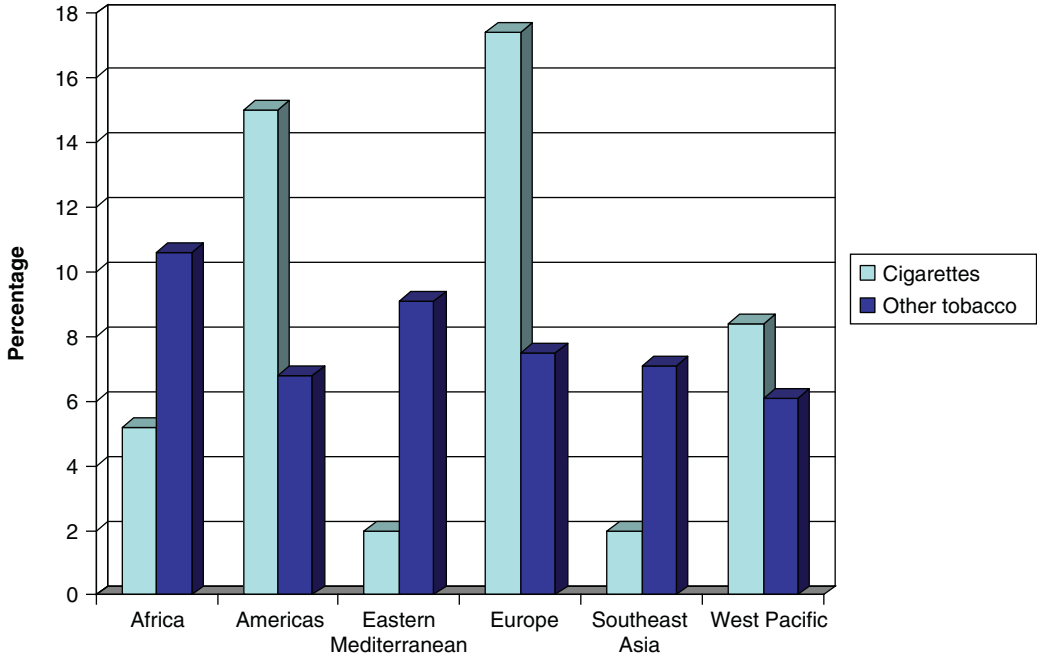

Figure 1. Self-reported tobacco use among girls aged 13–15 years by WHO region: Global Youth Tobacco Survey, 2000–2007.

countries; however, few studies testing interventions have been conducted in LMICs. We sought to provide a comprehensive review of interventions to decrease tobacco exposure before and during pregnancy in high-, middle-, and low-income countries and to discuss relevant considerations for adopting and evaluating interventions in LMICs. We also present findings of an international expert working group that was convened to review the evidence and to establish research priorities.

Material and methods

We conducted a search of peer-reviewed articles on interventions (ranging from clinical to population-level) in the databases of Pubmed, the Cochrane Library, Global Health, and the WHO regional libraries of Latin America, Africa, the Eastern Mediterranean region, and South East Asia. We searched for articles from January 1975 to June 2009 using several keywords and keyword combinations (e.g. pregnancy, smoking cessation, tobacco, smokeless tobacco, environmental tobacco smoke, tobacco smoke pollution, waterpipe). We reviewed articles with English- or Spanish-language abstracts. When possible, we limited our searches to randomized-controlled trials. We used existing meta-analyses or consensus opinions assessing interventions for tobacco prevention, cessation, or reduced tobacco exposure. We also queried via email tobacco control professionals who are members of the Society for Research on Nicotine and Tobacco and GLOBALink to find additional completed or ongoing studies of interventions tested in LMICs. Countries were categorized as low-, middle-, or high-income using the World Bank's July 2009 economy classification, which is based on the gross national income per capita (10). Our search yielded 417 articles. We excluded articles that did not assess clinical or population-level interventions. Of the 44 articles that met our inclusion criteria, 18 were meta-analyses or systematic reviews, and 26 were individual studies; 11 studies were conducted in LMICs (11–21).

Results

Time periods for interventions to reduce tobacco exposure

A range of clinical and population-level interventions have been used to decrease maternal tobacco exposure, including interventions that can be instituted in adolescence to prevent tobacco initiation, before pregnancy or during pregnancy to increase cessation. Table 1 shows interventions targeting each of these time windows that have been shown to be effective based on systematic reviews, some of which include meta-analyses. The majority of reviews focused on interventions targeting cigarette smoking (22–28), with some targeting smokeless tobacco use (chewing tobacco or snuff) (22,29). We found no

Table 1. Effective interventions to decrease initiation and increase cessation of tobacco use, by time period.

	Initiation (at any time)	Cessation before pregnancy	Cessation during pregnancy
Increasing unit price for tobacco products	X[a]	X[a]	
Advertising bans in most or all available media	X[b]		
Mass media combined with other interventions (e.g. in schools)	X[a,b]	X[a,b]	
Reducing client expense for cessation therapies		X[a]	
Systems interventions (screening systems, provider training, coverage of treatment)		X[c]	
Clinical interventions (e.g. physician or nurse advice, or counseling)		X[c]	X[c,d]
Pharmacotherapy		X[c,e,f]	X[d]
Relapse prevention[g]			

[a]Hopkins et al. (24).
[b]National Cancer Institute (23).
[c]Fiore et al. (22).
[d]Lumley et al. (27).
[e]Hughes et al. (26) and Stead et al. (28).
[f]Pharmacotherapy has been shown to be effective for reducing cigarette use [Fiore et al. (22)], but not smokeless tobacco use in non-pregnant users [Ebbert et al. (29)].
[g]Hajek et al. (25).

interventions on other forms of smoked or smokeless tobacco, and a Cochrane review found no interventions targeting waterpipe use (30).

Population-level interventions/tobacco control

Interventions to prevent initiation or increase cessation of tobacco use among women of reproductive age can be implemented at the population (national or smaller geo-political areas) or individual levels. This section provides a summary of effective interventions that are implemented outside of the clinical setting.

Increasing tobacco price. Article 6 of the WHO FCTC requires countries to implement "tax policies, and where appropriate, price policies ... aimed at reducing tobacco consumption" (9). Interventions that increase the price of tobacco products reduce tobacco consumption in both high-income countries and LMICs (24,31,32). In high-income countries, where the majority of studies have been conducted, a 10% increase in cigarette prices would result in a 2.5–5% reduction in demand for cigarettes (32). A review examining price increases in LMICs indicates that a sustained 10% increase in cigarette prices would reduce cigarette consumption from 4 to 14% (31), suggesting that price increases have a greater impact in LMICs than in high-income countries.

Several studies have evaluated the impact of increasing cigarette prices on use by pregnant smokers. One study found that a price increase of USD $0.55 per pack would reduce maternal smoking by 3% points, a 22% reduction in prevalence (33), and another found that a 10% increase in cigarette taxes would increase the probability of a woman quitting by 10% (34). Additionally, a study examining the impact of increased cigarette prices (from the US Master Settlement Agreement) found that prenatal smoking did decline, but after adjustment for secular trends, by less than half than what was predicted by previous studies (35). Although most studies show that increases in tobacco taxes decrease smoking rates in pregnancy, we did not find either a meta-analysis or a consensus opinion from an expert panel confirming effectiveness of this intervention during pregnancy. In one US study, higher cigarette prices through taxation and smoking bans and tobacco use restrictions in work places, child care centers, and restaurants were associated with a reduction in deaths due to SIDS; a 10% increase in cigarette taxes was estimated to reduce deaths due to SIDS by a range of 1.6−1.8% (36).

Though reduced tobacco expenditures may release household income for other essential expenditures (e.g. food, healthcare), it is unclear what effect taxation has on households with continued smokers, specifically low-income households. In the United Kingdom, spending on tobacco is proportionally higher among low-income women than among high-income women, and qualitative data show that these mothers considered tobacco an essential expenditure compared with food (37). However, a Chinese study showed that the relative financial burden from additional taxation on cigarettes is lower among low-income households than among high-income ones (38). Studies in Indonesia and Bangladesh have shown that having a smoker in the household diverts household income from food to tobacco, putting infants and children at greater risk of chronic malnutrition and death (39–41). Much work is currently in progress examining the impact of tobacco prices in LMICs; however, further research is needed to better understand positive and negative impacts, especially among households with pregnant women and infants. This research needs to carefully consider country-specific differences in tobacco products, prices, and approaches to taxation.

Advertising bans. A review of studies examining tobacco-advertising bans in different countries concluded that comprehensive bans reduce tobacco consumption (23). Partial bans, such as those limiting content or media venues, were not effective as these allowed advertising to be shifted to another media. Countries that restrict all advertising of tobacco products will effectively reduce tobacco consumption. The WHO FCTC calls for restriction on all advertising, promotions, and sponsorships (9).

Mass media campaigns combined with other interventions. A recent US National Cancer Institute monograph concluded that mass media campaigns (through television, radio, print, and billboards) designed to discourage tobacco use can change youth attitudes about tobacco use, curb smoking initiation, and encourage adult smoking cessation, and that the effect is greater when campaigns are combined with school- and/or community-based programming (23). Similarly, another review found that mass media campaigns reduce initiation among youth and, when combined with other interventions (e.g. tobacco tax increases), increase cessation and reduce tobacco consumption at the population level (24).

Mass media interventions have also been effective in decreasing tobacco use in LMICs. Media combined with household interviews, clinical oral exams, and personal cessation advice have been effective in reducing tobacco use (smokeless tobacco and

cigarette smoking) in large cohort studies conducted in several communities in India (13,17,18).

Warning labels. Today, most countries require tobacco product manufacturers to place warning labels on tobacco packages, because they are an effective way to warn smokers about the health hazards of tobacco use, and serve as a first step toward quitting (42). However, the impact of warning labels depends upon many factors, including their size, comprehensiveness, visibility, and whether they are printed in the local language (1). Large graphic (pictorial) warning labels, which are especially effective, were first introduced by Canada in 2000, and have now been implemented in more than 20 countries (43,44). The fact that the cost of the warning labels are borne by tobacco manufacturers makes them especially attractive to LMICs.

Recognizing their importance, Article 11 of the WHO FCTC requires parties to the treaty to implement "health warnings describing the harmful effects of tobacco use" ; detailed guidelines for governments to implement effective warning labels were adopted by the third session of the conference of the parties (9). Additionally, WHO has called on governments to require that all tobacco packages include pictorial warnings (45).

Clinical interventions

In high-income countries, clinical interventions have been found to be effective in helping both non-pregnant and pregnant smokers quit. In one meta-analysis, physician advice to quit increased long-term cigarette abstinence rates to 10.2% (95% CI 8.5–12.0) compared to no-advice abstinence rates of 7.9% among non-pregnant women (22). Although this increase in abstinence rates might seem low, physician advice to quit is a low-intensity and low-cost intervention that could have considerable population-level impact. Clinics that incorporate a systems approach to tobacco treatment (i.e. clinician training and reminder systems) significantly increase the rate at which clinicians intervene with their patients who smoke (22). The '5 As' model (ask, advise, assess, assist, arrange follow-up) has been shown to be effective in increasing quit rates when implemented in primary care settings in the US. (46). The '2 As and an R' model (i.e. ask, advise, and refer) has also been recommended as a practical tobacco treatment strategy for busy clinics (47). Clinical/behavioral interventions that are effective in clinical trials include practical problem solving (general skills training) and providing smokers with support during treatment. Practical counseling (104 studies) was associated with abstinence rates of 16.2% (95% CI 14.0–18.5), and intra-treatment social support (50 studies) had abstinence rates of 14.4% (95% CI 12.3–16.5), compared to a rate of 11.2% for no counseling (22).

Two meta-analyses have shown that behavioral strategies increase quit rates in pregnant smokers by an additional 6% over those in control groups (22,27). A Cochrane review included randomized and quasi-randomized trials (72 studies; approximately 25,000 pregnant smokers) (27). The relative risk for continuing to smoke with a behavioral intervention versus control was 0.94 (95% CI 0.93–0.96). Although smoking cessation interventions appear to have a modest effect on quit rates, the impact on infant outcomes is significant. Treatment interventions compared to control conditions reduced the risk of delivering a low-birthweight infant (RR 0.83, 95% CI 0.73–0.95) and having a preterm delivery (RR 0.86, 95% CI 0.74–0.98). Moreover, there were sufficient studies in the meta-analysis to examine the potential effectiveness of different types of behavioral interventions. As shown in Table 2, cognitive behavioral strategies were the most commonly utilized intervention, and resulted in consistently enhanced quit rates. Contingency management interventions (i.e. reward type interventions in which participants receive incentives to quit) have achieved the largest increase in quit rates during pregnancy; however, to date, there are only four studies of this type of intervention, all conducted in high-income countries. Although cognitive behavioral strategies are effective in both non-pregnant and pregnant smokers, contingency management, which is not consistently effective in non-pregnant smokers (22), appears to be effective for cessation during pregnancy (27). Given the limited number of studies, this type of behavioral treatment needs further evaluation.

Two studies included in the meta-analysis were conducted in LMICs. A randomized-controlled trial

Table 2. Effects of interventions on smoking rates during pregnancy.

Intervention	Number of studies	Relative risk (95% CI)
Cognitive behavior strategies	30	0.95 (0.93, 0.97)
Stages of change	11	0.99 (0.97, 1.00)
Feedback	4	0.92 (0.84, 1.02)
Rewards (financial or material)	4	0.76 (0.71, 0.81)
Pharmacotherapy	5	0.95 (0.92, 0.98)

Data based on studies presented in a meta-analysis by Lumley et al. (27).

conducted in four Latin American cities (Rosario, Argentina; Pelotas, Brazil; Havana, Cuba; and Mexico City, Mexico) examined the impact of a multi-component home-based health education and psychosocial support intervention targeting pregnant women (included education about prenatal smoking) on knowledge uptake, health behavior change, and perinatal outcomes (14). Smoking cessation rates did not increase in the intervention group compared to the control group; approximately 20% of women in both groups smoked at study entry and at the end of pregnancy.

In a cluster-randomized trial in the Lodz district of Poland, the intervention group ($n = 205$) received four midwife visits during pregnancy and one after delivery (20). The control group ($n = 181$) received standard written information about the fetal health risks of maternal smoking. The odds of cessation were significantly higher in the intervention than in the control group (OR 2.5, 95% CI 1.8–3.7). We did not find any other studies examining interventions to decrease tobacco use during pregnancy in LMICs.

Pharmacotherapy

Pharmacotherapy is an integral component of the treatment of cigarette use and dependence among non-pregnant women and men in many high-income countries. Combination of counseling and medication is more effective than either component alone (22). To date, seven treatments have been shown to increase short- and long-term quit rates relative to placebo, including five nicotine replacement therapy (NRT) modalities (gum, patch, nasal spray, inhaler, and lozenge), bupropion sustained-release (SR), and varenicline (22). Bupropion is a non-nicotine smoking cessation medication (also used for the treatment of depression) that may be effective for smoking cessation by increasing brain levels of dopamine, norepinephrine, and serotonin (48). It is associated with a rare risk of seizures, and is contraindicated in persons with a seizure disorder, or who have anorexia nervosa or bulimia, or are taking monoamine oxidase inhibitors (48). Varenicline is a nicotinic receptor partial agonist specific for the alpha 4 beta 2 receptor (49). Pharmacotherapy is recommended for cigarette smokers making a quit attempt if they smoke at least 10 cigarettes per day, are at least 18 years of age, and are not pregnant (22). A course of pharmacotherapy typically ranges from six weeks to six months (22) and rates of success vary with the pharmacotherapy type, patient withdrawal symptoms, side effect profile, and perceived helpfulness. Although pharmacotherapies are generally considered safe and effective for smoking cessation, there have been reports of rare serious neuropsychiatric symptoms (i.e. changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide) with varenicline and bupropion SR (50).

Pharmacotherapies are not routinely recommended as first line treatment for smoking during pregnancy because safety and efficacy have not been established for any individual pharmacotherapy (22,51). Animal studies have shown that nicotine reduces uteroplacental blood flow, and has adverse effects on the developing nervous and pulmonary system (22,52). Although the risks of nicotine in human pregnancy are not fully known, based on the adverse effects of nicotine in animal studies, it seems prudent to minimize the amount of nicotine exposure with NRT if used during pregnancy (53). Consequently, given the similar efficacy rates among various NRTs, intermittent replacement therapies (gum or nasal spray) may be preferable to a continuous nicotine delivery system because they typically deliver an overall lower dose with a less constant duration of exposure. The preliminary safety of bupropion has been examined primarily in observational studies among pregnant women using this medication for depression or for smoking cessation. Bupropion SR does not appear to increase the risk of congenital malformations (54,55). We did not find any human studies of the effects of varenicline use during pregnancy.

Randomized prospective studies have evaluated the potential utility of pharmacotherapy (nicotine gum, transdermal nicotine system, nicotine lozenge, bupropion SR) for smoking cessation during pregnancy (56–62). In one meta-analysis, nicotine replacement was found to have an effect on end of pregnancy quit rates comparable to cognitive behavioral strategies (27). In Table 3, we review studies with a sample size of at least 150, the minimum number to detect differences in both quit rates and birth outcomes, and further sub-divide studies based on NRT type and on whether it was an efficacy or an effectiveness study. Two placebo-controlled studies suggest that NRT does not increase cessation rates, but may increase birthweight (60,62). Open-label studies have shown that NRT increases quit rates during pregnancy (56,61). One study raised concerns about safety (61); however, baseline differences in race and history of previous adverse pregnancy outcome between groups may explain the higher serious adverse event rate in the NRT group versus the control group (63). Large placebo-controlled studies examining the potential safety, tolerability, or efficacy of bupropion SR or varenicline for smoking cessation during pregnancy have not been conducted (54,55,59). More research is needed to better understand the risk and

Table 3. Studies assessing effectiveness and/or safety of pharmacotherapy use during pregnancy.

Study	Design	Sample size	Study treatment	Findings
Wisborg K et al., 2000 (62)	Randomized placebo-controlled	250	TNS vs. placebo	No effect on cessation, birthweight greater in intervention group
Oncken C et al., 2008 (60)	Randomized placebo-controlled	194	2 mg nicotine gum vs. placebo	No effect on cessation, birthweight greater in intervention group; risk of PTD reduced in NRT group
Hegaard HK et al., 2003 (56)	Randomized open label	647 (NRT given to heavier smokers only)	Choice of NRT (gum, TNS, both); part of a multi-modal intervention	Increased cessation rates in intervention group; birthweight similar between two groups
Pollak KI et al., 2007 (61)	Randomized open label	181	Choice of NRT (gum, TNS, or lozenge)	Increased quit rates in NRT group; serious adverse events (mainly PTD rate) greater in NRT group

Note: NRT, nicotine replacement therapy; PTD, preterm delivery; TNS, transdermal nicotine system.

benefit profile of each individual pharmacotherapy for smoking cessation during pregnancy. The risk/benefit profiles of an individual pharmacotherapy cannot necessarily be extrapolated to one another even within the same class (i.e. gum effects may differ from patch due to dose and mode of delivery). Another important consideration is that lack of availability and cost considerations may prohibit the use of pharmacotherapies as an integral cessation component in many LMICs.

Relapse prevention

Unfortunately, the majority of women who are able to quit smoking during pregnancy relapse after delivery. A Cochrane review of 54 interventions to prevent relapse concluded that there was "insufficient evidence to support the use of any specific behavioral intervention" to avoid relapse (25). Extended use of varenicline may help some smokers, and more research is needed to explore the benefit of extended use of NRT for relapse prevention (25). Of the 14 studies focused on pregnant and postpartum ex-smokers, all of which tested behavioral relapse-prevention interventions, pooled results of 8 failed to find any significant benefit at the end of pregnancy, and 12 failed to find any benefit at follow-up during the postpartum period (25). Testing of alternative approaches for effective relapse prevention is needed.

Secondhand smoke exposure

In many LMICs, women (including those who are pregnant) have low cigarette smoking rates, but face significant exposure to SHS at home due to high smoking rates among men (64). Studies in high-income countries have shown that policies that completely eliminate smoking in workplaces and public places significantly decrease SHS exposure and improve other health outcomes (65,66). Increasingly, jurisdictions are banning smoking in indoor workplaces and in public places. Moreover, the WHO FCTC requires participating countries to implement measures to protect the public from indoor SHS exposure in workplaces and public places, but these measures do not extend to homes (9).

A Chinese study examined the effect of physician advice to pregnant women to encourage their husbands to quit smoking in order to limit their SHS exposure; the intervention included educational materials on simple strategies to help husbands quit and brief reminders at subsequent visits (19). Women receiving this advice reported more quit attempts, a reduction in cigarettes smoked per day, and a higher seven-day abstinence rate among their husbands at the end of treatment. Further research is needed to determine effective, culturally acceptable interventions to eliminate SHS exposure among pregnant women, infants, and children in LMICs.

Finally, a Cochrane review found that 11 of 36 identified studies showed a statistically significant effect of decreasing children's SHS exposure in the intervention versus control groups; 4 of these studies provided intensive clinical counseling to parental smokers (67). Of the 36 studies, 5 were conducted in LMICs (4 in China and 1 in Turkey) (11,12,15,16,21). Of these 5, 1 was conducted in a community setting and 4 in pediatric healthcare settings. In 2 of the 4 studies, the parental cessation intervention was significantly effective, but 1 of these 2 studies did not biochemically validate quit status. The review concluded that the current evidence "does not determine which interventions are most effective for decreasing parental smoking and preventing exposure to tobacco smoke in childhood".

Discussion

As noted earlier, research and implementation of effective strategies for pregnant women in LMICs must occur in context with the global tobacco control efforts of the FCTC and MPOWER strategies. Though the goal of our expert working group was to set research recommendations, the authors acknowledge that with the rising global tobacco epidemic in LMICs, particularly among women, we are in a time for action, not just research. These actions must be built on a solid science base. Therefore, a parallel strategy of quickly developing effective interventions, while simultaneously evaluating their effectiveness, should be set up as quickly as possible. This research agenda also aligns with the Millennium Development Goals to reduce child mortality and improve maternal health (68).

Considerations for tobacco interventions in LMICs

Few LMICs have data, especially population-based ones, on the prevalence of tobacco use and SHS exposure among pregnant women. Addressing these gaps will help identify the areas where interventions are most urgently needed. Current tobacco control initiatives should be assessed within a country before introducing new interventions, to avoid overlap and to ensure a comprehensive tobacco control strategy. Discussions with clinicians, local health officials, and community members may help determine what interventions would be culturally acceptable and feasible, and healthcare delivery systems should be examined to determine whether interventions can be integrated into existing frameworks. For example, two studies in LMICs have incorporated smoking cessation interventions (e.g. health education and counseling) into existing healthcare services for pregnant women (14,20).

Research and implementation capacity in the area of tobacco and pregnancy needs to be developed and enhanced in LMICs. Traditionally, maternal and child health and reproductive health practitioners have not been trained in delivering tobacco prevention and cessation interventions. Efforts should be made to partner when possible with other tobacco control initiatives within LMICs, such as the Bloomberg Initiative to reduce tobacco use, which has provided various capacity building opportunities and led to a substantial enhancement in the number of individuals in tobacco control. These programs, or similar ones, could be expanded or adapted to treat pregnant tobacco users.

Recommendations from the expert working group

A working group of international perinatal and tobacco control experts was convened to review the summary of the literature search and to establish research priorities in the following areas: (i) preventing the uptake and reducing tobacco use among girls and women of reproductive age; and (ii) reducing tobacco use and SHS exposure among pregnant women. To identify research priorities, the working group considered the research evidence in terms of burden of disease, intervention impact, intervention costs, feasibility of integration into existing services, uniqueness of the contribution, and overall feasibility. The group acknowledged that interventions tested in high-income countries may not be directly transferable to LMICs because of important differences (e.g. smoker demographics, general awareness of tobacco harms, healthcare systems); however, the evidence-base provides an important starting point for research and interventions in LMICs.

Given that population-level efforts (e.g. increasing tobacco taxes, prohibiting smoking in public places) have been shown to have consistent effects on decreasing the prevalence of tobacco use, the working group recommended giving high priority to the following research topics in countries where tobacco use is becoming more prevalent among women of reproductive age or where a high percentage of women are exposed to SHS.

Key research priorities

- Evaluating the impact of tobacco control policy efforts on reducing tobacco use and SHS exposure among pregnant and reproductive age women. Tobacco control policies include increasing tobacco taxes, adopting and implementing laws to eliminate smoking in public places, requiring health warning messages on tobacco products, and banning marketing of tobacco products. All of these policies are required of nations that ratify the FCTC.
- Developing and evaluating culturally adapted interventions that involve brief healthcare provider advice to quit tobacco use and reduce SHS exposure by pregnant smokers and evaluating whether psychosocial support, pharmacotherapy, incentives, and addressing other unhealthy behaviors can provide additional benefits. Use of non-traditional healthcare providers, such as lay health workers, should also be explored given access to healthcare systems is often limited in LMICs.

- Evaluating the concurrent implementation of population-level (e.g. tax increases, smoking bans) and clinical interventions for cessation among pregnant and reproductive age women.

The working group determined that the safety and efficacy of pharmacotherapies during pregnancy should be assessed in LMICs where pharmacotherapy is in routine use among non-pregnant smokers.

The working group recommended that reproductive health outcomes, such as birthweight, gestational age, placenta previa and abruption, and perinatal and infant morbidity and mortality, should be evaluated to assess intervention impact. The working group recommended validating maternal smoking rates with biochemical measurements (i.e. cotinine or exhaled carbon monoxide measurements) in clinical studies (69) as high rates of nondisclosure have been consistently documented in high-income countries (70). Studies without biochemical verification may be excluded from meta-analyses because of the risk of bias (27). Measures of quit rates and relapse after delivery should be assessed for pregnancy-based interventions. More research is needed on interventions for the postpartum period as an opportunity to reduce relapse and increase life-long cessation. Also, cost-effectiveness studies would provide evidence to policy-makers that replication and support of these programs is a wise use of scarce financial resources.

Finally, some consideration needs to be given to who should fund interventions to decrease tobacco use and exposure among pregnant women. Although substantial funds have been allotted to improve maternal and child health globally, very little has been directed towards decreasing tobacco use and exposure during pregnancy. Research and interventions should be a key priority for funding agencies interested in reducing the economic and health effects of tobacco, and for funding agencies for which improving maternal and child health is a priority.

Conclusion

In summary, tobacco use is increasing in many LMICs. In order to prevent high levels of tobacco use among women in LMICs (similar to many high-income countries), research is needed to test and measure the impact of interventions to prevent tobacco uptake and to aid in cessation in this population. Given the particular risks for adverse effects on pregnancy and birth outcomes of tobacco use and SHS exposure, efforts should be targeted specifically to pregnant women. Studies from high-income countries suggest that the rate of infant mortality is 40% higher among pregnant cigarette smokers (71). In LMICs where infant mortality rates are already high, increased tobacco use could cause devastating harm. In India, where women's smokeless tobacco use is common, there is already a three-fold increased risk of stillbirth and a two- to three-fold increased risk of having a low birthweight infant among smokeless tobacco users (72). Implementation of interventions to prevent or limit prenatal tobacco exposure and measurement of the net health benefit of such interventions on perinatal outcomes should be a high priority.

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