Acta Obstetricia et Gynecologica. 2010; 89: 454–464

informa
healthcare

ACTA OVERVIEW

Non-cigarette tobacco use among women and adverse pregnancy outcomes

LUCINDA J. ENGLAND[1], SHIN Y. KIM[1], SCOTT L TOMAR[2], CECILY S RAY[3], PRAKASH C. GUPTA[3], THOMAS EISSENBERG[4], SVEN CNATTINGIUS[5], JOHN T. BERNERT[6], ALAN THEVENET N. TITA[7], DEBORAH M. WINN[8], MIRJANA V. DJORDJEVIC[8], MATS LAMBE[9], DAVID STAMILIO[10], TSUNGAI CHIPATO[11,12] & JORGE E. TOLOSA[12,13]

[1]*Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA,* [2]*Department of Community Dentistry and Behavioral Science, University of Florida College of Dentistry, Gainesville, Florida, USA,* [3]*Healis-Sekhsaria Institute for Public Health, Navi Mumbai, India,* [4]*Department of Psychology and Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, Virginia,* [5]*Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden,* [6]*Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA,* [7]*Center for Women's Reproductive Health, Department of Obstetrics and Gynecology, University of Alabama at Birmingham, Birmingham, Alabama, USA,* [8]*Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland, USA,* [9]*Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden,* [10]*Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis University, St. Louis, Missouri, USA,* [11]*Department of Obstetrics and Gynecology, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe,* [12]*Global Network for Perinatal and Reproductive Health, Portland, Oregon, USA, and* [13]*Department of Obstetrics and Gynecology, Oregon Health and Science University, Portland, Oregon, USA*

Abstract

Although cigarette smoking remains the most prevalent form of tobacco use in girls and in women of reproductive age globally, use of non-cigarette forms of tobacco is prevalent or gaining in popularity in many parts of the world, especially in low- and middle-income countries. Sparse but growing evidence suggests that the use of some non-cigarette tobacco products during pregnancy increases the risk of adverse pregnancy outcomes. In this paper we review the literature on the prevalence of non-cigarette tobacco product use in pregnant women and in women of reproductive age in high-, middle-, and low-income countries and the evidence that maternal use of these products during pregnancy has adverse health effects. In addition, we communicate findings from an international group of perinatal and tobacco experts that was convened to establish research priorities concerning the use of non-cigarette tobacco products during pregnancy. The working group concluded that attempts to develop a public health response to non-cigarette tobacco use in women are hindered by a lack of data on the epidemiology of use in many parts of the world and by our limited understanding of the type and magnitude of the health effects of these products. We highlight research gaps and provide recommendations for a global research agenda.

Key words: *Global, smokeless, tobacco, waterpipe, pregnancy*

Correspondence: Lucinda J England, Centers for Disease Control and Prevention, 4770 Buford Highway NE, MS K-23 Atlanta, Georgia, 30030, USA. E-mail: lbe9@cdc.gov

(Received 13 November 2009; accepted 5 January 2010).

ISSN 0001-6349 print/ISSN 1600-0412 online
DOI: 10.3109/00016341003605719

Introduction

Cigarette smoking is the most common form of tobacco use worldwide and results from the Global Youth Tobacco Survey suggest that the gap in cigarette smoking between boys and girls is closing (1). Smoking among girls and women of reproductive age is of particular concern because of the many adverse effects of maternal smoking on pregnancy and infant health outcomes, including increased risk of fetal growth restriction, preterm birth, stillbirth, perinatal death, sudden infant death syndrome, and placental abnormalities (2–4).

The use of non-cigarette forms of tobacco is prevalent or gaining in popularity in many parts of the world, including many low- and middle-income countries (LMICs) (1,5). Non-cigarette tobacco products are often less expensive than manufactured cigarettes, and may be viewed by some as a safer alternative to smoking (6–10). In some areas, use of non-cigarette tobacco products is a socially acceptable cultural norm. However, use of non-cigarette tobacco products can result in nicotine addiction, a particular concern for products with high nicotine content (11). Use of some smokeless tobacco products has been associated with increased risk of oral and pancreatic cancer, and cardiovascular disease (5,12,13). There is also evidence suggesting that the use of smokeless tobacco products during pregnancy may increase the risk of adverse pregnancy outcomes (5).

A meeting of international perinatal and tobacco experts was convened in September 2008 by the Global Network for Perinatal and Reproductive Health (www.gnprh.org), the Centers for Disease Control and Prevention of the United States, and the National Cancer Institute of the United States, to evaluate available literature and to identify research priorities concerning the use of tobacco during pregnancy in LMICs. In this review, we examine the literature related to prevalence of use and pregnancy-related health effects of non-cigarette tobacco products in LMICs and high-income countries (HICs). We then highlight research gaps and make recommendations for a global research agenda. Because of differences in the types of products used, the patterns of use, and women's health status, LMICs and HICs are discussed separately.

Prevalence of non-cigarette use among women

There are three major types of non-cigarette tobacco products: smokeless tobacco, cigars and pipes, and waterpipes. Using cigars, pipes, and waterpipes involves heating or burning the tobacco, whereas using smokeless tobacco does not.

Smokeless tobacco in LMICs

Oral smokeless tobacco products are used in many parts of the world, while nasal use of smokeless tobacco is rare (5). A list of commonly used smokeless tobacco products and their definitions can be found in Table 1. The composition and properties of these products vary widely (5).

There are few published prevalence studies of smokeless tobacco use in pregnant women. In a recent multicenter, cross-sectional study of a convenience sample of pregnant women in nine developing nations, face-to-face surveys were administered to 7961 pregnant women between October 2004 and September 2005 (14). The prevalence of reported current use of non-cigarette tobacco products among pregnant women was 6% in the Democratic Republic of the Congo (DRC), 33.5% in Orissa, India, and 4.9% in Karnataka, India. Pregnant women in the DRC reported using snuff or chewing tobacco and women in India reported using chewing tobacco, tobacco tooth powder, or both. The prevalence of ever having used non-cigarette products in all other countries surveyed was $< 5\%$.

In a cohort study of 1593 South African women with singleton live births in the greater Johannesburg-Soweto area in 1990, 7.5% of women overall reported using snuff during pregnancy (15). Snuff products in South Africa consist of ground tobacco leaves, frequently combined with additives (5,16), and snuff use was seen primarily among black women. In a prospective cohort study of 1,217 pregnant women from eight selected geographic areas in Mumbai, India, 16.9% reported using smokeless tobacco, and 80% of these smokeless tobacco users used mishri (17).

A number of additional studies report the prevalence of smokeless tobacco use in girls and women in general. Some of the largest of these were conducted in India. For example, the Third National Family Health Survey in India collected information on both smoking and smokeless tobacco use in girls and women in 2005–2006. In a nationally representative sample of 124,385 women age 15–49 years, approximately 10% of rural women and 6% of urban women reported using some type of chewed or smokeless tobacco product (paan masala, gutkha, or other chewed tobacco) in the preceding 24 hours (18). However, the prevalence of smokeless tobacco use varied greatly between states. In a WHO study conducted in Karnataka and Uttar Pradesh, India, the overall prevalence of current smokeless tobacco use

Table 1. Smokeless tobacco products and description.

Name	Product description
Chimó	Made of tobacco leaf, sodium bicarbonate, brown sugar, ashes from the Mamon tree, and flavoring A small amount is placed between the lip or cheek and the gum and left there for some time, usually 30 minutes. The mixture and saliva are spit out
Creamy snuff	Made from finely ground tobacco, clove oil, glycerin, spearmint, menthol, and camphor Used for cleaning teeth
Dry snuff	Made from fire-cured and fermented tobacco, then processed into a powdered form. In India, made from roasted tobacco, then powdered Held between the lip and gum or cheek or inhaled into the nostrils, may be applied to teeth and gums
Gudhaku	Made of powdered tobacco and molasses Applied to the teeth and gums with the finger
Gul	Made of tobacco powder, molasses, other ingredients Used for cleaning teeth, applied to gums
Gutkha	Made of areca nut, catechu, tobacco, lime, saffron, and flavoring Held in the mouth, sucked and chewed. Saliva is generally spit out, but sometimes swallowed
Iqmik	Made of tobacco and punk ash The users may pre-chew the Iqmik and place in small container for later use Held in mouth and chewed
Khaini	Made from dried or fermented tobacco, slaked lime paste, sometimes areca nut Held in mouth for 10–15 minutes and sucked from time to time
Loose leaf chew	Made of loose tobacco leaves, sweetener, and/or licorice Placed between the cheek and lower lip; it is either chewed or held in place. Saliva is spit out or swallowed
Maras	Made from tobacco, ash of wood (particularly oak, walnut or grapevine), and water for humidification A small amount is applied between the lower labial mucosa and gingiva for 4–5 minutes
Mawa	Made from tobacco, slaked lime, and areca nut Placed in mouth and chewed for 10–20 minutes
Mishri (masheri, misheri)	Made from roasted tobacco which is then powdered Applied to teeth and gums often for the purpose of teeth cleaning
Moist plug	Made of enriched tobacco leaves, fine tobacco, sweetener, and/or licorice Chewed or held between the cheek and lower lip. Saliva is spit or swallowed
Moist snuff	Made from air- or fire-cured tobacco, contains up to 50% moisture Placed and held between the lip and cheek or gum. Saliva may be swallowed or spit out
Nass (naswar, niswar)	Made from tobacco, ash, cotton or sesame oil, water, and sometimes gum Held in mouth for 10–15 minutes
Pan masala	Made from tobacco, area nuts, slaked lime, and betel leaf condiments Placed in mouth (usually between the gum and cheek) and sucked and chewed
Plug (chew)	Made of enriched tobacco leaves, fine tobacco, sweetener, and/or licorice Chewed or held between the cheek and lower lip. Saliva is spit or swallowed
Qiwam (kimam)	Made from tobacco, spices, and additives, such as musk. Place in mouth and chewed.
Red tooth powder	Made from tobacco Used for cleaning teeth
Shammah	Made of powdered tobacco, lime, ash, black pepper, oils and flavorings Placed in the buccal or lower labial vestibule of the mouth
Snus (snuff)	Made from tobacco, water, sodium carbonate, sodium chloride, moisturizer, flavoring, and nicotine Placed between the gum and upper lip
Toombak	Made from tobacco and sodium bicarbonate Rolled into a ball, it is held between the gum and the lip or cheek, or under the tongue on the floor of the mouth. Sucked slowly for 10–15 minutes
Twist roll (chew)	Made of enriched tobacco leaves, fine tobacco, sweetener, and/or licorice Chewed or held between the cheek and lower lip. Saliva is spit or swallowed
Zarda	Made from tobacco, lime spices, vegetable dyes, and areca nut Chewed or used as an ingredient for betel quid

Note: Adapted from Smokeless Tobacco Fact Sheet, Stockholm, Sweden, 2002 and from IARC monograph volume 89, Smokeless tobacco and some tobacco-specific *N*-nitrosamines (5,16).

was 14.4 and 6.6%, respectively (19). In a large national survey conducted in South Africa in 1998, 10.2% of women reported using smokeless tobacco (20). Data on the prevalence of smokeless tobacco use in these and other countries are reviewed in detail elsewhere (5). High prevalence of smokeless tobacco usage has also been reported in parts of Bangladesh, Malaysia, and Nepal (5).

Smokeless tobacco in HICs

There are few studies in HICs of the prevalence of smokeless tobacco use in pregnant women and in women of reproductive age, but data suggest that use in these populations is generally rare. Oral snuff has been regulated in the European Union since 2001 and is banned in all member states except Sweden, where use of moist snuff is widespread. Smokeless tobacco use in girls and/or women in Finland and Norway is estimated to be less than 2%, but use appears to be increasing among Swedish women, in whom overall prevalence of current daily snuff use increased from 0.6% in 1988–1989 to 4% in 2007. The increase was most pronounced among young women age 16–24 years, whose snuff use increased from 1.2% in 1988–1989 to 6.3% in 2007 (21). Based on data from the population-based Medical Birth Register, the prevalence of snuff use in early pregnancy in Swedish women was estimated to be 1.4% in 2006. However, large regional variation exists, with a reported prevalence of 6.9% of pregnant women in northern Sweden (22).

In Canada, 2% of women age 15 and older reported ever trying smokeless products (chewing tobacco, pinch, or snuff) in 1999–2003 (23), but higher prevalence of use has been reported for some native populations and among athletes (5). In the United States, less than 0.5% of women reported past-month smokeless tobacco use in a national survey conducted in 2003–2005 (24). However, as in Canada, the prevalence of smokeless tobacco use is substantially higher in some subpopulations, such as in Lumbee Indian (25), Navajo (26) and Alaska Native communities. In parts of western Alaska, data from the Special Supplemental Nutrition Program for Women, Infants, and Children and from the Pregnancy Risk Assessment Monitoring System show that use of chew tobacco in pregnant Alaska Native women exceeds 50% (27,28).

Non-cigarette tobacco products that are heated or burned in LMICs

Studies examining the prevalence of use of combustible non-cigarette tobacco products, such as cigars or pipes, in pregnant or reproductive age women are scarce, but a small number of descriptive studies have been published. For example, in a cross-sectional study of Chutta (a homemade cigar) use in four villages in the district of Andhra Pradesh in India, 41.2% of women reported that they reverse smoked a chutta (placed the burning end into the oral cavity), and 3.2% reported that they smoked chutta in a conventional way (29). In a small descriptive study conducted in a village in Indonesia, 36% of women aged 14–20, 96% aged 21–40, and 100% aged ≥ 41 years old reported that they smoked cigars (30).

Tobacco smoking using a waterpipe, also know as shisha, hookah, narghile, hubble bubble, and other names that vary by region, is a practice in which smoke from tobacco that has been heated (usually with burning charcoal) passes through a device and into water before it is inhaled through a flexible pipe (31). Waterpipe smoking is most common in North Africa, the Eastern Mediterranean Region, and the South-East Asia Region (31) and the practice is believed to result in high levels of exposure to carbon monoxide (32). Two studies in Lebanon examined the prevalence of waterpipe use in pregnant women. The first was a cohort study of consecutive singleton newborns delivered in 2000–2003 in the greater Beirut area. Of 8,592 women, 5.4% of women reported smoking a waterpipe during pregnancy (33). In a cohort study of women in Lebanon who delivered in nine selected hospitals in Beirut or Bekaa in 1997–1998, 6.1% of women reported smoking waterpipes during pregnancy (34). In a national survey in Kuwait, 69% of women reported ever using a waterpipe (35), and in a study of students at Beirut University, 23% of women reported current waterpipe use (36).

Non-cigarette tobacco products that are heated or burned in HICs

There is limited information on the prevalence of use of combustible non-cigarette tobacco products among women of reproductive age. Results from the 2006 National Youth Tobacco Survey showed that 7.2% of high school girls in the United States reported that they smoked a cigar in the 30 days preceding the survey, and 1.8% reported that they smoked a pipe (37). Data for United States adults in the National Survey on Drug Use and Health indicate that 5.1% of women aged 18–25 years smoked a cigar in the past month in 2007, but the prevalence was just 1.2% among women aged 26 years and older (38).

We were unable to find any population-based prevalence estimates of waterpipe smoking in any HICs, but a few studies on waterpipe smoking have been conducted on some college campuses in the United States. Prevalence estimates for past-month use ranged from 10 to 20% (39,40). In only one study was the prevalence reported by gender. In this case, past-month waterpipe smoking was more prevalent than past-month cigarette smoking among women at the University of Florida (11.6 vs. 6.9%, respectively) (41).

Health effects of using non-cigarette tobacco products during pregnancy

Smokeless tobacco in LMICs

Several studies of smokeless tobacco and fetal growth have been conducted in LMICs. In a study of 70 smokeless tobacco users (tobacco leaves, tobacco leaves with lime, zarda, ingested tobacco leaves, or tooth powder) and 70 non-users in Jabalpur, India (matched on maternal age, socio-economic status, literacy, parity, birth interval, height, weight, gestational age, and infant sex), researchers found that infants of smokeless tobacco users had a significant reduction in birthweight (395 g) and in height (0.5 cm) compared with infants of non-users (42). The authors found no evidence of a dose-response relation between tobacco exposure and birthweight; however, the sample size was small. It is not clear whether residual confounding by gestational age at delivery might have contributed to birthweight differences. In a cohort of 1,217 women in Mumbai, India, researchers found an 87 g birthweight deficit in smokeless tobacco users (mainly mishri) compared with non-users ($p = 0.02$), after adjusting for maternal age, education, socio-economic status, maternal weight, anemia, antenatal care, and gestational age at delivery (17). Finally, in a study of 1,593 women in South Africa, the authors found a non-significant birthweight deficit in snuff users of 29 g compared with non-users. There was no increase among snuff users in the proportion of newborns born small for gestational age (15).

In the previously described cohort of 1,217 pregnant women in Mumbai, India, smokeless tobacco users delivered 6.2 days earlier on average than non-users ($p < 0.001$) (17). In addition, smokeless tobacco use was associated with preterm delivery, even after adjustment for multiple confounders including age, education, socio-economic status, and anemia (AOR = 1.5, $p = 0.05$), although results were not significant after adjustment for maternal weight and antenatal care utilization. Associations between smokeless tobacco use and increased preterm delivery at < 32 and < 28 weeks' gestation remained significant after adjustment for relevant confounders (AOR = 4.9, 95% CI 2.1–11.8; AOR = 8.0, 95% CI 2.6–27.2, respectively). There was a dose-response relation between smokeless tobacco use and gestational age; light smokeless tobacco users and heavy smokeless tobacco users delivered 4.9 and 8.9 days earlier than non-users, respectively. In the previously described cohort of 1593 women in South Africa, smokeless tobacco users had a slightly reduced gestational age at delivery compared with tobacco non-users in unadjusted analysis (37.9 vs. 38.3 weeks, $p = 0.003$), but there was no increase in preterm delivery defined as < 36 weeks' gestation (1.7 vs. 2.4%, $p = 0.63$) (15).

In the cohort of 1217 pregnant women in Mumbai, India, the cumulative incidence rate of stillbirth was significantly higher among smokeless tobacco users than among non-users (8.9 vs. 3.1%) with an adjusted proportional hazard ratio of 2.6 (95% CI = 2.4–4.8). Variables included in adjusted models were maternal age, parity, education, socio-economic status, working status, number of antenatal visits, number of tetanus toxoid doses received, place of delivery, previous stillbirth, and previous cesarean section (43). In an earlier study of women in Pune, India an increased incidence of stillbirth in users of chew tobacco compared with non-users was found (5.0 vs. 1.7%), but statistical testing was not performed and potential confounders were not taken into account (44).

Smokeless tobacco use was found to be associated with anemia (Hb < 10 g/dl) in the Mumbai, India, cohort (45). The association remained significant following adjustment for maternal age, parity, education, socio-economic status/type of residence, underweight status, vegetarian status, and trimester at first antenatal visit (AOR = 1.7, 95% CI 1.2–2.5).

In a study in Karachi, Pakistan of 80 term placentas (40 from tobacco non-users and 40 from snuff users), snuff users had evidence of increased degenerative placental changes compared with non-users (46). Samples from snuff users had significantly higher numbers of chorionic villi with excessive collagen, higher incidence of apoptosis in parenchymal cells, higher density of syncytial knots, and thicker subtrophoblastic basement membrane. Such changes could be associated with increased risk of adverse birth outcomes such as fetal growth restriction. An increase in placental weight in smokeless tobacco users compared with tobacco non-users in Jabalpur, India, has also been described (47,48), but the clinical relevance of this finding is unclear.

We were unable to find any studies of neurobehavioral outcomes conducted in LMICs.

Smokeless tobacco in HICs

In a retrospective cohort study of 789 snuff users, over 11,000 smokers, and over 11,000 tobacco non-users in Sweden, snuff use was associated with a 39 g birthweight deficit (95% CI 6–72 g) compared with non-users (49). Results were adjusted for maternal age, parity, body mass index, height, gestational age at delivery, and infant sex. When analysis was restricted

to women who used smokeless tobacco throughout pregnancy, the birthweight deficit in smokeless tobacco users was 93 g after adjustment (95% CI = 38–147 g). Smokeless tobacco use was not significantly associated with small-for-gestational age deliveries (defined as a birthweight of >2 SD below the mean for gestational age) (AOR = 1.25, 95% CI 0.72–2.17).

In the previously mentioned study of births in Sweden, snuff users had a significantly elevated risk of preterm delivery compared with non-users, even after adjustment for maternal age, body mass index, height, parity, and infant sex (AOR = 1.98; 95% CI 1.46–2.68) (49). The risk for preterm delivery was comparable to that found in women who smoked ≥ 10 cigarettes/day during pregnancy. In addition, snuff users were at increased risk of preeclampsia compared with non-users (AOR = 1.58, 95% CI 1.9–2.27), in contrast to cigarette smokers who were at decreased risk (AOR = 0.63, 95% CI 0.53–0.75).

We were unable to find any studies of stillbirths, anemia, or placental morphology conducted in HICs.

Neurobehavioral outcomes associated with Iqmik, a homemade mixture of leaf tobacco and ash, were assessed in a pilot study of 41 pregnant Alaska Native women (50). Compared with women who used no tobacco products, women who used Iqmik had significantly higher levels of nicotine and cotinine (a major metabolite of nicotine), both in umbilical cord blood, and higher levels of cotinine in maternal blood. No significant differences between Iqmik users and non-users were found for mean gestational age, birthweight or head circumference. However, neonates born to mothers who used Iqmik during pregnancy had a significant increase in the number of neurobehavioral signs as assessed by the Lipsitz score, compared with infants born to mothers who did not use tobacco.

Non-cigarette tobacco products that are heated or burned in LMICs

In a study of 106 waterpipe users and 512 non-users in Lebanon, waterpipe smoking was not associated with a significant reduction in infant birthweight. In models adjusting for previous low birthweight, second hand smoke exposure, maternal age, delivery hospital, and gestational age, the mean birthweight for waterpipe users was 40 g less than for non-users, but this finding was not significant (51). The mean birthweight of infants born to women who smoked >1 waterpipe per day was 110 g less than those born to non-users, but this finding also was not significant. Infants born to waterpipe users were not at significantly increased risk for low birthweight, even after adjustment for a history of low birthweight, second hand smoke exposure, maternal age, hospital location and gestational age (AOR = 2.17, 95% CI 0.74–6.33). Waterpipe smoking was not significantly associated with low Apgar scores or infant malformations, but was associated with infant respiratory distress (AOR = 3.65, 95% CI 1.52, 8.75).

In a more recent study of waterpipe users in Lebanon, waterpipe use was not associated with increased risk of preterm delivery, reduced gestational age, antepartum or intrapartum bleeding, hypertensive disorders of pregnancy, low Apgar scores, or neonatal intensive care unit admissions compared with non-users (33). Smoking more than one waterpipe a day was associated with a significant increase in risk for delivering a low birthweight infant after adjustment for maternal and paternal education, maternal age, parity, working status, various pregnancy complications, and second hand smoke exposure (AOR = 2.4, 95% CI 1.2, 5.0). However, waterpipe smoking overall was not associated with a significant reduction in mean infant birthweight. The mean birthweight of infants born to women who smoked >1 waterpipe/day was 57 g less than those born to non-users, but this difference was not significant.

Discussion

There is a paucity of information on the global prevalence of use of non-cigarette tobacco products in pregnant women and women of reproductive age. The limited data available from surveys and small studies suggest that in some areas, prevalence of use is very high, especially in India and South Africa. In many instances, such as in western Alaska, this phenomenon appears to be highly localized.

In contrast to the number of studies of the health effects of cigarette smoking (52), few studies have addressed the health effects of non-cigarette tobacco use during pregnancy. However, the available data suggest that the use of non-cigarette tobacco products may adversely affect pregnancy outcomes. Studies from both LMICs and HICs support that different smokeless tobacco products have modest effects on fetal growth and increase risk of preterm delivery. Data from two studies suggest that smokeless tobacco use also may be associated with increased risk for stillbirth, and associations between smokeless tobacco products and other outcomes such as anemia and abnormal placental pathology have also been reported. It is unknown what mechanism might result in increased risk of anemia in smokeless tobacco users, and it is uncertain if the relation is causal. It

is also unclear whether effects of smokeless tobacco use on placental morphology contribute to adverse birth outcomes, but an etiological pathway between tobacco-related placental degenerative changes and adverse pregnancy outcomes is biologically plausible.

Evidence for causality in the relation between smokeless tobacco and adverse pregnancy outcomes will be strengthened if additional research demonstrates consistency across studies, by showing improvement in pregnancy outcomes after tobacco cessation (as through a randomized cessation trial), and through additional animal research. There are very few studies of pregnancy outcomes in waterpipe smokers and existing data are limited due to small sample sizes. More research is needed before conclusions can be drawn regarding health effects of smoking waterpipes during pregnancy.

Studying health effects of various forms of tobacco use on pregnancy outcomes is extremely challenging for several reasons. For example, products can vary greatly with respect to nicotine content and bioavailability, nicotine delivery, presence of additives, toxin levels, and/or portion size, and all of these factors could potentially contribute to health outcomes. This product variability can make it difficult to generalize findings across different populations. In addition, product type and timing of exposure can vary between women, making it challenging to identify cohorts of women with uniform type, intensity, and duration of tobacco exposure during pregnancy. Furthermore, many adverse pregnancy outcomes are relatively rare, making it difficult to find populations with sufficient sample size to detect significant differences between exposure groups. Finally, stigmatization around tobacco use during pregnancy may discourage women in many cultures from disclosing their tobacco use to providers and/or research staff, resulting in exposure misclassification. These factors together can make conducting studies of tobacco and reproductive health outcomes resource- and labor-intensive.

Despite the paucity of data on pregnancy outcomes associated with use of non-cigarette tobacco products in pregnant women, it is important to keep in mind that all tobacco products contain nicotine. Data on the adverse effects of nicotine on the developing fetus are sufficient to have resulted in the classification of nicotine as a developmental toxin by the California Environmental Protection Agency (Cal/EPA) (53). The use of any products containing nicotine likely will have adverse effects of fetal neurological development. Animal and human data support that prenatal nicotine exposure may contribute to associations between maternal smoking and perinatal mortality, decreased infant arousal, cognitive defects, and sudden infant death syndrome. These concerns should be kept in mind even while studies of pregnancy outcomes in non-cigarette tobacco users are lacking.

Recommendations from the expert working group

Surveillance

The working group convened in September 2008 recommends that existing surveillance systems be modified, or new systems be developed where necessary, to monitor trends in the use of non-cigarette tobacco products in women of reproductive age and pregnant women living in countries where these products are used. When new surveillance programs are developed, they should be designed to allow a timely response to new or emerging threats, such as changes in who is using non-cigarette tobacco products, changes in how these products are being used, or the appearance or introduction of new products. Based on surveillance findings, more specific surveillance studies can be developed to gather detailed information about tobacco use practices.

Additionally, surveillance programs should also be developed in order to monitor tobacco industry activities targeting young women in LMICs. Information from these surveillance activities can be used to help guide decisions around where and how to conduct surveillance of tobacco use practices in women.

Health outcomes

Continuing evaluation of suspected or potential associations between tobacco exposure and reproductive health outcomes will be necessary in order to develop accurate estimates of the burden of disease related to use of non-cigarette tobacco products. When developing research priorities for studying health outcomes, the working group considered the following factors:

(1) Feasibility of conducting the research, including consideration of the size of the population exposed, research costs, and incidence of the outcome of interest.
(2) The extent to which use of the product is established in the population of interest (well-established practices should take priority over 'fad' practices, all else being equal).
(3) The severity and public health burden of the health outcomes of interest.
(4) The potential for the research to affect local or national policy.
(5) Whether there is previous demonstration of an association between a particular outcome and cigarette smoking.

(6) Whether there is previous demonstration of an association between a particular outcome and use of non-cigarette tobacco products.
(7) Whether there is biologic plausibility underlying the potential relation between the exposure and the outcome of interest.
(8) The ability to measure the exposure accurately.

The working group recommends that the following health outcomes receive the highest priority: preterm delivery, fetal growth, preeclampsia/gestational hypertension, stillbirth, early pregnancy loss, and placental abruption. Areas felt to be important but of lower priority included placental morphology/histology, fertility, maternal anemia, birth defects with consideration of gene-environment interactions, neonatal complications, sudden infant death syndrome, and cognitive development. Other areas for consideration included chronic maternal medical conditions such as cancer and asthma, long-term outcomes in offspring such as obesity, postpartum complications such as complications from cesarean section (such as postoperative infections) and infant sex ratio.

In conducting studies of health outcomes in users of non-cigarette tobacco products, the working group recommended the following approach:

(1) All studies should control for suspected confounders.
(2) All studies should address the potential for exposure measurement error, especially underreporting of tobacco use, and use biomarkers to assess exposure whenever possible.
(3) Studies should include a smoking group whenever possible, as well as a non-exposed control group.
(4) Temporal relations between tobacco exposure and the outcomes of interest should be clearly established.

Product and biological specimen storage

The working group recommends that a repository or network of repositories for biological specimens and tobacco product samples be established. Standardized materials and protocols for sample collection, handling, and storage should be developed for international use.

Exposure measurement

The working group recommends that a group of core laboratories be identified to conduct analyses of biological specimens and product samples. Participating facilities would assist medical and epidemiologic researchers in addressing the following goals:

(1) To test various local and commercial products for nicotine, carcinogens, heavy metal, and other toxic compounds and to identify the most common constituents across products.
(2) To monitor commercial products for changes in nicotine, carcinogen, and heavy metal content, as well as other toxic compounds.
(3) To assess exposure of non-cigarette tobacco product users to nicotine, carcinogens, heavy metals, and other toxic compounds.
(4) To better understand metabolism during pregnancy of nicotine and other components found in tobacco products.
(5) To study dose-response relations between health outcomes and levels of exposure.
(6) To identify specific agents (such as nicotine and carbon monoxide) responsible for particular adverse health outcomes.

To accomplish these, the working group recommends:

(1) Creation of a global list of laboratories available to conduct analysis of product and biological samples.
(2) Development of standardized control materials and an interlaboratory validation program.
(3) Further consideration of a common matrix to assess exposure (such as hair or urine) which would allow comparison of exposure levels across populations.

Social and cultural factors influencing tobacco use practices

The working group recommends that research should be conducted in local communities to help improve our understanding of social and cultural factors associated with non-cigarette tobacco product use. Qualitative work would address local attitudes and perceptions about tobacco and its harmful effects, particularly with respect to pregnancy. Other areas of interest include the role of family members in influencing decisions around tobacco use, and knowledge, attitudes and practices of health care providers regarding tobacco use during pregnancy.

Tobacco cessation

The working group recognizes that established cessation interventions for smokers have not been well

studied in users of other products, and may not be effective in different cultural settings. The working group recommends that cessation interventions should be developed for and tested in communities where non-cigarette tobacco products are used. The cost-effectiveness of such interventions should be established.

Other areas

The working group recommends that the following areas should also be considered for study: (i) non-health related effects of non-cigarette tobacco product use on society, such as the effects of family on economic status; (ii) effects of concomitant use of tobacco and other substances such as alcohol, areca/betel quid, khat, and caffeine and (iii) the health effects of reverse smoking.

Conclusions

The use of non-cigarette products is an understudied public health threat. Of particular concern are signs of increasing efforts by the tobacco industry to market smokeless tobacco products to young adults, including women of childbearing age (54). However, the burden of non-cigarette tobacco-related disease is not yet well-characterized. Our ability to develop an appropriate public health response is limited by a lack of data on the epidemiology of use in many parts of the world, and our limited understanding of the type and magnitude of the health effects of these products. Surveillance systems are needed which are designed to allow tobacco control experts to rapidly recognize increases in tobacco use, including non-cigarette product use. More information is needed regarding the health effects of various non-cigarette tobacco products, and local informational campaigns need to be developed to inform providers and women about the risks. Cessation interventions need to be developed, and they will likely need to be tailored to the specific product and cultural setting.

Acknowledgements

The authors would like to acknowledge the members of the Epidemiology of non-cigarette products used during pregnancy working group: Scott Tomar DrPH, DMD, MPH, University of Florida College of Dentistry (group leader), Prakash Gupta, PhD, Healis-Sekhsaria Institute for Public Health, Mumbai, India (group leader); Thomas J. Bernert, PhD, Centers for Disease Control and Prevention; Tsungai Chipato, Sven Cnattingius, Karolinska Institute; M. V. Djordjevic, PhD, National Cancer Institute; Thomas Eissenberg, PhD, Virginia Commonwealth University; Mats Lambe, MD, PhD, MPH, Karolinska Institute; David Stamilio, MD, MSCE, Washington University School of Medicine; Alan Thevenet N. Tita, MD, PhD, University of Alabama at Birmingham and Deborah M. Winn, PhD, National Cancer Institute; members of the steering committee: Jorge E Tolosa, MD, MSCE, Oregon Health and Science University, USA; Michele H. Bloch, MD, PhD, National Cancer Institute, USA; Patricia M. Dietz, DrPH, MPH, Lucinda J. England, MD, MSPH, Shin Y. Kim, MPH, Van T. Tong, MPH, Centers for Disease Control and Prevention; and Terry Njoroge, MPH, Centers for Disease Control and Prevention for her contribution to the literature reviews.

Participants of the expert meeting entitled 'Tobacco exposure during pregnancy in low- and middle-income countries: Establishing research priorities' held September 8–10, 2008: Bernardo Agudelo-Jaramillo, Erik Augustson, Cathy Backinger, Dilyara Barzani, José Belizán, Vincenzo Berghella, John Bernert, Michele Bloch, Neal Brandes, F. Carol Bruce, Tsungai Chipato, Sven Cnattingius, Patricia Dietz, M. V. Djordjevic, Thomas Eissenberg, Lucinda England, Ellen Feighery, Mario Festin, Christine Galavotti, Lorrie Gavin, Robert Goldenberg, Lorraine Greaves, Prakash Gupta, Paul Holmes, Carys Horgan, Ann Jensby, Annette Kaufman, Shin Kim, Priyadarshini Koduri, Michael S. Kramer, Mats Lambe, Harry Lando, Xingzhu Liu, Ann Malarcher, Elizabeth McClure, Mario Merialdi, Suneeta Mittal, Patricia Dolan Mullen, Katherine Murphy, Mimi Nichter, Thomas Novotny, Cheryl Oncken, Michael Paglia, Karen Parker, Alexandra Parks, Zhaoxia Ren, Jonathan Samet, Susan Sanders, Isabel Scarinci, David Stamilio, Mary Ellen Stanton, Alan Tita, Jorge Tolosa, Scott Tomar, Van Tong, Sheela Shenoy Trivikram, Deborah Winn, and Linda Wright.

Disclosure of interest: Ms. Kim, Ms. Ray, and Drs. England, Gupta, Eissenberg, Cnattingius, Bernert, Tita, Winn, Djordjevic, Lambe, Stamilio, Chipato, and Tolosa report no conflicts of interest. Dr. Tomar has served as an expert witness for plaintiffs in lawsuits brought against manufacturers of smokeless tobacco products and cigarettes. The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Warren CW, Jones NR, Peruga A, Chauvin J, Baptiste J-P, Costa de Silva V, et al. Global youth tobacco surveillance, 2000–2007. MMWR Surveill Summ. 2008;57:1–21.
2. Cnattingius S. The epidemiology of smoking during pregnancy: smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res. 2004;6: S125–40.
3. US Department of Health and Human Services. The Health consequences of smoking: a report of the surgeon general. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.
4. Rogers J. Tobacco and pregnancy. Reprod Toxicol. 2009; 28:152–60.
5. International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans: smokeless tobacco and some tobacco-specific N-nitrosamines. Lyon, France: IARC, 2007.
6. Anwar S, Williams SA, Scott-Smith J, Sage H, Baweja S, Singal M, et al. A comparison of attitudes and practices of gutka users and non-users in Chitrakoot, India: a pilot. Prim Dent Care. 2005;12:5–10.
7. Chaturvedi P, Chaturvedi U, Sanyai B. Prevalence of tobacco consumption in schoolchildren in rural India–an epidemic of tobaccogenic cancers looming ahead in the Third World. J Cancer Educ. 2002;17:6.
8. Renner CC, Patten CA, Enoch C, Petraitis J, Offord KP, Angstman S, et al. Focus groups of Y-K Delta Alaska Natives: attitudes toward tobacco use and tobacco dependence interventions. Prev Med. 2004;38:421–31.
9. Maziak W, Ward KD, Afifi Soweid RA, Eissenberg T. Tobacco smoking using a waterpipe: a re-emerging strain in a global epidemic. Tob Control. 2004;13:327–33.
10. Overland S, Hetland J, Aaro LE. Relative harm of snus and cigarettes: what do Norwegian adolescents say? Tob Control. 2008;17:422–5.
11. Djordjevic MV, Doran K. Nicotine content and delivery across tobacco products. Handb Exp Pharmacol. 2009;192: 61–82.
12. Boffetta P, Straif. Use of smokeless tobacco and risk of myocardial infarction and stroke: systematic review with meta-analysis. BMJ. 2009;339:b3060.
13. Boffetta P, Hecht S, Gray N, Gupta P, Straif K. Smokeless tobacco and cancer. Lancet Oncol. 2008;9:667–75.
14. Bloch M, Althabe F, Onyamboko M, Kaseba-Sata C, Castilla EE, Freire S, et al. Tobacco use and secondhand smoke exposure during pregnancy: an investigative survey of women in 9 developing nations. Am J Public Health. 2008; 98:1833–40.
15. Steyn K, de Wet T, Saloojee Y, Nel H, Yach D. The influence of maternal cigarette smoking, snuff use and passive smoking on pregnancy outcomes: the Birth To Ten Study. Paediatr Perinat Epidemiol. 2006;20:90–9.
16. National Cancer Institute, Centers for Disease Control and Prevention. Smokeless tobacco fact sheets. Prepared for: 3rd International Conference on Smokeless tobacco: advancing Science and Protecting Public Health;2002 Sep 22–5; Stockholm, Sweden.
17. Gupta PC, Sreevidya S. Smokeless tobacco use, birth weight, and gestational age: population based, prospective cohort study of 1217 women in Mumbai, India. BMJ. 2004; 328:1538.
18. International Institute for Population Sciences and Macro International. National Family Health Survey (NFHS-3), 2005–06, India: key findings. Mumbai: IIPS, 2007.
19. Chaudhry K, Prabhakar AK, Prabhakaran PS, Prased A, Singh K, Singh A. Prevalence of tobacco use in Karnataka and Uttar Pradesh in India. Final report of the study by the Indian Council of Medical Research and WHO South East Asian Regional Office, New Delhi, 2001.
20. Steyn K, Bradshaw D, Norman R, Laubscher R, Saloojee Y. Tobacco use in South Africans during 1998: the first demographic and health survey. J Cardiovasc Risk. 2002;9:161–70.
21. Statistics Sweden. Stockholm (Sweden): Statistics Sweden; 2009. Available online at: http://www.scb.se/Pages/TableAndChart____145246.aspx. (accessed November 13, 2009).
22. Tobaksvanor bland gravida och spädbarnsföräldrar 2006. Tobacco habits among pregnant women and infants parents in 2006. Stockholm, Sweden: Socialstyrelsen, 2008. Available online at: http://www.socialstyrelsen.se/publikationer2008/2008-125-18. (accessed November 13, 2009).
23. The Ontario Tobacco Research Unit. OTRU update: what population surveys say about smokeless tobacco use. October 2006. Available online at: http://www.otru.org/pdf/updates/update_oct2006.pdf. (accessed November 13, 2009).
24. Timberlake DS, Huh J. Demographic profiles of smokeless tobacco users in the U.S. Am J Prev Med. 2009;37:29–34.
25. Spangler JG, Michielutte R, Bell RA, Knick S, Dignan MB, Summerson JH. Dual tobacco use among Native American adults in southeastern North Carolina. Prev Med. 2001; 32:521–8.
26. Strauss KF, Mokdad A, Ballew C, Mendlein JM, Will JC, Goldberg HI, et al. The health of Navajo women: findings from the Navajo Health and Nutrition Survey, 1991–1992. J Nutr. 1997;127:2128S.
27. Patten CA, Renner CC, Decker PA, O'Campo E, Larsen K, Enoch C, et al. Tobacco use and cessation among pregnant Alaska Natives from Western Alaska enrolled in the WIC program, 2001–2002. Matern Child Health J. 2008;12:30–6.
28. Kim SY, England L, Dietz PM, Morrow B, Perham-Hester KA. Prenatal cigarette smoking and smokeless tobacco use among Alaska native and white women in Alaska, 1996–2003. Matern Child Health J. 2009;13:652–9.
29. van der Eb MM, Leyten EM, Gavarasana S, Vandenbroucke JP, Kahn PM, Cleton FJ. Reverse smoking as a risk factor for palatal cancer: a cross-sectional study in rural Andhra Pradesh, India. Int J Cancer. 1993;54:754–8.
30. Alexander J, Alexander P. Gender differences in tobacco use and the commodification of tobacco in Central Borneo. Soc Sci Med. 1994;38:603–8.
31. WHO Study Group on Tobacco Product Regulation. Advisory note: waterpipe tobacco smoking: health effects, research needs and recommended actions by regulators. Geneva: World Health Organization, 2005.
32. Maziak W, Rastam S, Ibrahim I, Ward KD, Shihadeh A, Eissenberg T. CO exposure, puff topography, and subjective effects in waterpipe tobacco smokers. Nicotine Tob Res. 2009;11:806–11.
33. Tamim H, Yunis KA, Chemaitelly H, Alameh M, Nassar AH. Effect of narghile and cigarette smoking on newborn birthweight. BJOG. 2008;115:91–7.
34. Bachir R, Chaaya M. Maternal smoking: determinants and associated morbidity in two areas in Lebanon. Matern Child Health J. 2008;12:298–307.
35. Memon A. Epidemiology of smoking among Kuwaiti adults: prevalence, characteristics, and attitudes. Bull World Health Organ. 2000;78:1306–15.

36. Tamim H, Terro A, Kassem H, Ghazi A, Khamis TA, Hay MM, et al. Tobacco use by university students, Lebanon, 2001. Addiction. 2003;98:933–9.
37. US Department of Health and Human Services. 2006 National Youth Tobacco Survey and Key Prevalence Indicators: Table 1: percentage of students in middle school (grades 6–8) who were current users of any tobacco product, by product type, sex, and race/ethnicity–United States, 2004 and 2006. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. Available online at: http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/pdfs/indicators.pdf. (accessed November 13, 2009).
38. US Department of Health and Human Services. 2007 National Survey on Drug Use & Health: Detailed Tables. Tobacco Product and Alcohol Use Tables—2.1 to 2.84 (Prevalence Estimates). Rockville, MD: US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Office of Applied Statistics. Available online at: http://www.oas.samhsa.gov/NSDUH/2k7NSDUH/tabs/LOTSect2pe.htm. (accessed November 13, 2009).
39. Eissenberg T, Ward KD, Smith-Simone S, Maziak W. Waterpipe tobacco smoking on a U.S. college campus: prevalence and correlates. J Adolesc Health. 2008;42:526–9.
40. Primack BA, Sidani J, Agarwal AA, Shadel WG, Donny EC, Eissenberg TE. Prevalence of and associations with waterpipe tobacco smoking among U.S. university students. Ann Behav Med. 2008;36:81–6.
41. University of Florida Healthy Gators 2010 Coalition. Healthy Gators Student Survey Report 2008. Gainesville, FL: University of Florida. Available online at: http://healthygators.hhp.ufl.edu/docs/Student%20Survey/2008%20HG%20Survey%20Report%20Public%203-23-09.pdf. (accessed November 13, 2009).
42. Verma RC, Chansoriya M, Kaul KK. Effect of tobacco chewing by mothers on fetal outcome. Indian Pediatr. 1983;20:105–11.
43. Gupta PC, Subramoney S. Smokeless tobacco use and risk of stillbirth: a cohort study in Mumbai, India. Epidemiology. 2006;17:47–51.
44. Krishna K. Tobacco chewing in pregnancy. Br J Obstet Gynaecol. 1978;85:726–8.
45. Subramoney S, Gupta PC. Anemia in pregnant women who use smokeless tobacco. Nicotine Tob Res. 2008;10:917–20.
46. Ashfaq M, Channa MA, Malik MA, Khan D. Morphological changes in human placenta of wet snuff users. J Ayub Med Coll Abbottabad. 2008;20:110–3.
47. Agrawal P, Chansoriya M, Kaul KK. Effect of tobacco chewing by mothers on placental morphology. Indian Pediatr. 1983;20:561–5.
48. Krishnamurthy S. Strength of association of increased placental weight and smokeless tobacco use in pregnancy. Indian J Pediatr. 1991;58:863–5.
49. England LJ, Levine RJ, Mills JL, Klebanoff MA, Yu KF, Cnattingius S. Adverse pregnancy outcomes in snuff users. Am J Obstet Gynecol. 2003;189:939–43.
50. Hurt RD, Renner CC, Patten CA, Ebbert JO, Offord KP, Schroeder DR, et al. Iqmik–a form of smokeless tobacco used by pregnant Alaska natives: nicotine exposure in their neonates. J Matern Fetal Neonatal Med. 2005;17:281–9.
51. Nuwayhid IA, Yamout B, Azar G, Kambris MA. Narghile (hubble-bubble) smoking, low birth weight, and other pregnancy outcomes. Am J Epidemiol. 1998;148:375–83.
52. US Department of Health and Human Services. The Health Consequences of Smoking: a Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.
53. State of California. Safe Drinking Water and Toxic Enforcement Act of 1986: chemicals Known to the State to Cause Cancer or Reproductive Toxicity: September 11, 2009. Sacramento, CA: State of California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, 2009. Available online at: http://www.oehha.org/prop65/prop65_list/files/P65single091009.pdf. (accessed November 13, 2009).
54. Lambe M. Swedish snus for tobacco harm reduction. Lancet. 2007;370:1206–7.