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TOBACCO CESSATION GUIDELINES FOR HIGH-RISK POPULATIONS

ATHENS 2017

EDITOR

PANAGIOTIS BEHRAKIS

CO – EDITORS

CONSTANTINE VARDAVAS

SOPHIA PAPADAKIS

Co-funded by
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PANAGIOTIS K. BEHRAKIS, MD, PhD, FCCP

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Chair, Scientific Committee, ENSP

Director, Institute of Public Health, the American College of Greece

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Scientific Coordinator, TOB.g Project

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Scientific Expert, TOB.g Project

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COORDINATING COMPETENT BODIES
Hellenic Center for Disease Control & Prevention
European Network for Smoking and Tobacco Prevention
CMT Prooptiki
Anlet Med S.R.L.
TobaccoFree Research Institute Ireland LBG

EXTERNAL REVIEWERS

PREGNANCY AND POST-PARTUM PERIOD
Francisco Rodríguez Lozano, DMD
President European Network for Smoking and Tobacco Prevention
Email: frguez@infomed.es

ADOLESCENTS
Scott Leatherdale, PhD
Associate Professor, CIHR-PHAC Chair in Applied Public Health Research
School of Public Health and Health Systems, University of Waterloo, Waterloo, Ontario, Canada
Email: sleather@uwaterloo.ca

Nicholas Chadi, MDCM, FRCPC, FAAP
Division of Adolescent Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada
Email: nicholas.chadi@umontreal.ca

DIABETES
Manfred Neuberger, M.D.
Professoreof Environmental Health
Institute of Environmental, Health, Medical University Vienna
Austrian Academy of Science, C. Climate & Air Quality Vienna, Austria
Email: manfred.neuberger@meduniwien.ac.at

COPD
Taylor Hays, MD
Professor of Medicine, Vanderbilt University
Associate Director, Nicotine Dependence Centre, Mayo Clinic, Rochester, New York, USA
Email: hays.taylor@mayo.edu

CARDIOVASCULAR
Andrew Pipe, MD, CM, FRCPC
Chief, Division of Prevention and Rehabilitation, University of Ottawa Heart Institute,
Professor, Faculty of Medicine, University of Ottawa, Ottawa, Canada
Email: Apipe@ottawaheart.ca

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Panagiotis K. Behrakis, MD, PhD, FCCP
Principal Investigator, TOB.g Project
Chair, Scientific Committee, ENSP
Director, Institute of Public Health, the American College of Greece
Member of the BoR, the American College of Chest Physicians

FOREWORD

SMOKING IS A DISEASE. It is the biggest epidemic of all time. To tackle the problem, the Global Community has created the Framework Convention on Tobacco Control (FCTC), the largest global Treaty of WHO. In addition, the European Union has adopted two clear and strict directives regulating tobacco products licensing and use (Tobacco Products Directives I and II).

However, the solution to the problem remains challenging as we confront a severe addiction. Nicotine, the main ingredient of tobacco products, is considered to be the third most addictive substance after heroin and cocaine. Complex and not fully elucidated destructive neurobiological and behavioral mechanisms compose the personality of the typical addicted smoker who desires but fails to quit.

The medical practice of smoking cessation requires specialized knowledge. Almost all organizations dealing with tobacco control have issued relevant guidelines. Quite distinctively, the European Network for Smoking and Tobacco Prevention has issued first and second editions of a general cessation guideline readily available in many European languages.

Generalization and simplicity are imperative for success in preventive medicine. However, medical science of the twenty-first century is systematically moving toward more individualized therapeutic approaches. In other words, “One key cannot open all doors”. The “TOB.g project” and ultimately this book represent the first innovative action towards the scientific application of this principle in tobacco cessation.

Aim of the project is to provide an individualized approach to smoking cessation within five clearly distinctive subpopulations of smokers, who obviously cannot continue to be treated as a single entity. Teenagers, cardiovascular patients, pregnant women, patients with diabetes or chronic obstructive pulmonary disease belong to clearly distinct groups and reasonably require a tailored approach to treatment.

The course to successful cessation is a long and arduous one. This book represents the first step toward a new consideration, a new direction and a new path, leading to a more efficient approach to a major Public Health concern.

The entire project has evolved from the general scopes of the ENSP and in accordance with Article 14 of the FCTC.

Panagiotis K. Behrakis, MD, PhD, FCCP

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1.

SMOKING CESSATION DURING PREGNANCY AND THE POSTPARTUM PERIOD

AUTHORS

Victoria G. Vivilaki, RM, PgCert, MMedSc, PhD,
Assistant Professor of Midwifery Department, TEI Athens, Greece

Andriani N. Loukopoulou, RN, MSc, PhD,
General Oncological Hospital of Kifisia, Athens, Greece

About this Guideline

This special chapter of the European Tobacco Treatment Guideline is intended to summarize evidence regarding the health risk associated with tobacco use and second-hand smoke exposure during pregnancy and the postpartum period as well as effective approaches to supporting cessation and preventing relapse.

Within the chapter clinical practice recommendations are presented for health care professionals working with woman during the pre-natal and postpartum periods. The GRADE evidence grading system has been used to rate the quality of evidence supporting each recommendation. GRADE uses 4 evidence grading categories: 'high', 'moderate', 'low', 'very low' (see table below). The evidence grading scale reflects the type, quality and quantity of available evidence supporting the guideline recommendation. The level of evidence grading appears in brackets at the end of each recommendation statement.

GRADE - Evidence Grading Categories:

CODE	QUALITY OF EVIDENCE	DEFINITION
A	High	– Further research is very unlikely to change our confidence in the estimate of effect. – Several high-quality studies with consistent results. – In special cases: one large, high-quality multi-center trial
B	Moderate	– Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. – One high-quality study. – Several studies with some limitations.
C	Low	– Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. – One or more studies with severe limitations.
D	Very Low	– Any estimate of effect is very uncertain. – Expert opinion. – No direct research evidence. – One or more studies with very severe limitations.

EXECUTIVE SUMMARY

SMOKING CESSATION DURING PREGNANCY AND THE POSTPARTUM PERIOD

Health Effects of Smoking in Pregnancy

Maternal tobacco use and exposure to second-hand smoke during pregnancy imposes a significant risk to the unborn foetus and new born. Maternal smoking has been associated with a number of adverse pregnancy outcomes.[1] Tobacco use during pregnancy is in fact the most preventable cause of adverse pregnancy outcomes. Perinatal mortality rates are 150 per cent greater when the mother is a smoker, and smoking is estimated to be responsible for 15 per cent of all cases of premature birth.[1-3]

The adverse effects of tobacco use and second-hand smoke exposure have also been shown to extend into childhood and are associated with increased risk of congenital malformation, sudden infant death syndrome, genetic-related hereditary diseases, perinatal mortality and morbidity, short stature, cognitive delays, and neurologic disorders.[4-10] Exhibit 1 presents a summary of the known health effects of tobacco use during pregnancy.

EXHIBIT 1:
Health effects of maternal smoking on the foetus, new born, and children

IMPACT PERIOD	HEALTH EFFECT
Antenatal Impact	– Placental abnormalities – Ectopic pregnancy – Placental detachment – Placenta praevia – Pre-eclampsia – Still birth – Spontaneous miscarriage – Premature rupture of membranes
Impact Postnatal	– Increased perinatal mortality – Premature birth (twice as great) – Intra-uterine growth retardation – Low birth weight infant 150-250 grams smaller – Sudden Infant Death Syndrome (SIDS) – Birth Defects
Impact in child's later life	– Type 2 Diabetes – Obesity – Hypertension – Reduced High Density Lipoprotein cholesterol – Increased hospitalization – Bronchial asthma, lower respiratory infection, decreased lung function – Conduct disorder, Attention Deficit Disorder and hyperactivity – Impaired academic performance – Significant increase in psychiatric disorders

Second-hand Smoke Exposure

Second-hand smoke (SHS) exposure during pregnancy is associated with multiple health risks to the unborn foetus. This includes a significantly increased risk of preterm birth, broncho-pulmonary dysplasia, congenital malformation, and wheezing/asthma etc.[6, 11-13] Specifically, pregnant women who are exposed to SHS are 23% more likely to experience stillbirth and 13% more likely give birth to a child with a congenital malformation.[14, 15]

100% smoke-free environments should be a priority during pregnancy for all women, including non-smokers. Smoke-free environments should be maintained during the post-natal period for new borns and children.

Tobacco Use in Pregnancy

Despite the magnitude of the risks associated with tobacco use during pregnancy, an estimated 6-19% of woman in Europe will continue to smoke during pregnancy and a large portion of woman who quit will return to smoking following pregnancy.[16] Quitting smoking can be extremely difficult and few recognize that due to both physiological and other factors that it can be even more difficult for pregnant woman to quit smoking. For example rates of nicotine metabolism during pregnancy increase 60-140% and contributing to greater nicotine withdrawal and difficulty with quitting.[17]

Pregnant smokers fall into three groups:

- Those who quit spontaneously when they found out they were pregnant.
- Those who cut back on smoking when they found out they were pregnant.
- Those who continue to smoke during pregnancy.

Smoking Cessation Interventions in Pregnancy

There is no safe level of smoking in pregnancy and women should be advised to quit smoking completely. More specifically, it was found that the relative risk of ectopic pregnancy increased to 1.6 times that of non-smoking women for those who smoked from 1-5 cigarettes daily, and to 2.3 times for women who smoked 11-20 cigarettes daily.[18] The greatest gain in health benefits comes from full cessation during pregnancy rather than reducing smoking.[19, 20] Furthermore, women should be encouraged to quit smoking before becoming pregnant to ensure optimal pregnancy outcomes. Importantly, serious adverse effects of smoking are reversible if smoking is stopped early in pregnancy. Evidence has shown that women who quit smoking during the first trimester of pregnancy give birth to infants of similar weight to those that never smoked.[21, 22]

Increased concern of expectant parents about the risks of smoking on pregnancy outcomes and the health of their new born creates a "teachable moment" where expectant mother's may have increased receptivity to quitting smoking.[23] The same is true for expectant fathers and other members of the family.

Health professionals have an important role to play in supporting cessation among pregnant women as well as other members of the family. Given the significant health risks imposed to the unborn foetus and new borns as a result of tobacco use, it is critical for health professionals working with pregnant woman, including family physicians, midwives, obstetricians and gynaecologist, and nurses, be familiar with the latest evidence and be comfortable intervening and supporting women with achieving cessation.

The "5 As" (Ask, Advise, Assess, Assist, Arrange) can be used as a clinical model for supporting cessation among pregnant woman (See Exhibit 2). As part of the 5 As model, all pregnant women should have both their smoking status and second-hand smoke exposure assessed as part of routine examinations. Pregnant woman often do not disclose their smoking status, likely due to the social stigma of tobacco use during pregnancy. Honest disclosure of smoking status can be increased by as much as 40% by using multiple-choice questions instead of a simple yes/no question.[24-26] Validation of tobacco use exposure with carbon monoxide testing is recommended. Non-judgmental advice to quit and support with quitting should be pro-actively offered to pregnant woman and providers should arrange follow-up with patients.[24-26]

Counselling Interventions

Intensive counselling is often required to support cessation among pregnant women who are unable to quit on their own. Intensive counselling has been shown to significantly increase smoking cessation among pregnant woman compared with usual care (30 studies; average risk ratio (RR) 1.44, 95% confidence interval (CI) 1.19 to 1.73).[27] In most studies an intensive intervention lasting more than 15 minutes was found to be more effective than the shorter and less individualized interventions (18 studies; average RR 1.25, 95% CI 1.07 to 1.47). Referral to specialized smoking cessation services, when available, is recommended.

Internet-based interventions, financial incentives, or interventions involving the spouse or peers are promising intervention strategies being explored to support cessation among pregnant smokers however, more research is required to better understand their value.

Quit Smoking Medications

While nicotine replacement therapy (NRT) is considered a first-line quit smoking therapy in adult populations, the use of NRT during pregnancy has been an area of controversy in international clinical practice guidelines. A 2015 Cochrane review found no evidence that the use of NRT for smoking cessation in pregnancy had either a

beneficial or harmful effect on birth outcomes.[28] This review however also did not find evidence to support increased rates of cessation among pregnant women who used NRT for smoking cessation compared to controls.[28] Poor compliance with NRT treatment is commonly reported among those studies conducted to date and limits our ability to accurately understand the efficacy of NRT among pregnant women. Despite limitations of the evidence, the potential risk from the use of NRT is considered magnitudes less than continued tobacco use and as such the risk benefits of using NRT should be discussed with woman who are unable to quit on their own. Given the lack of efficacy data, NRT should be considered a second-line therapy. Adequate dosing and duration of NRT is likely to improve outcomes.

The use of varenicline or bupropion is not recommended during pregnancy due to a lack of research regarding safety and efficacy.[28]

Post-Partum Relapse Rates

Postpartum relapse rates are extremely high (29-85%) among women who are successful with quitting during pregnancy. Many woman who quit smoking during pregnancy, do so with the intention of resuming smoking after birth. Stress, post-natal depression, concerns about weight gain and having a smoking partner, lower socio-economic status are also known to be contribute to relapse. Supporting maintenance of cessation following pregnancy is an important secondary target for intervention.[29, 30] It is recommended that clinicians address plans for continued cessation following pregnancy early in the quitting process and that counselling support extend into the postpartum period.

EXHIBIT 2: 5 AS TOBACCO TREATMENT PROTOCOL

PREGNANT & POSTPARTUM WOMAN

Summary of Key Recommendations for Health Professionals:

- There is no safe level of smoking in pregnancy and women should be advised to quit smoking completely (Level of Evidence A).
- Pregnant women should quit smoking as early as possible during the first trimester of pregnancy and stay smoke-free after birth (Level of Evidence A).
- Health professionals should inform expectant parents about the health risks of second-hand as well as third-hand smoke to the mother, foetus, and new born (Level of Evidence D).
- Health professionals should advise pregnant women to maintain 100% smoke-free environments by banning smoking in their homes and cars and avoiding settings in which there may be exposure to second-hand smoke (Level of Evidence A).
- All health professionals working with pregnant women including family physicians, midwives, obstetricians and gynecologist, and nurses should be familiar with the latest evidence and be comfortable intervening and supporting women with achieving cessation (Level of Evidence A).
- The "5 As" (Ask, Advise, Assess, Assist, Arrange) can be used as a clinical model for supporting cessation among pregnant women (Level of Evidence B).
- All pregnant women should have both their smoking status and second-hand smoke exposure assessed as part of routine examinations (Level of Evidence A).
- Health professionals should deliver strong non-judgmental advice to quit to all women who smoke and assist tobacco users with cessation, which includes follow-up throughout the duration of the pregnancy and early postpartum period (Level of Evidence A).
- Women unable to quit smoking should receive intensive counselling and support with quitting as early as possible in their pregnancy (Level of Evidence A).
- Counselling interventions are effective in increasing quit rates and significantly reducing low birth weight, increasing mean birth weight, and reducing neonatal intensive care admissions (Level of Evidence A).
- When available women unable to quit should be referred to specialized cessation support. Health professionals should follow-up to ensure treatment is undertaken (Level of Evidence A).
- The use of nicotine replacement therapy (NRT) is preferred to continued smoking during pregnancy. Evidence in terms of its effectiveness among pregnant women is however mixed. As such, NRT can be considered a second-line therapy for pregnant women who are unable to for quit with counselling support alone (Level of Evidence B).
- Due to a lack of research bupropion and varenicline are not recommended for smoking cessation during pregnancy (Level of Evidence – n/a).
- Parents should be encouraged to remain smoke-free in the postpartum period. A pregnant woman's social support network, including her spouse and close family should be involved in supporting smoke-free environments in spaces shared by the new born (Level of Evidence D).
- Postpartum care should address relapse prevention for both parents before hospital discharge and during post-natal home visits (Level of Evidence A).
- Parents, who continue to smoke at the time their babies are admitted to neonatal intensive care units (NCIU), should be referred to local smoking cessation programs (Level of Evidence C).

1.0
TOBACCO USE AND CESSATION IN PREGNANCY

1.1 Prevalence of tobacco use during pregnancy

Addressing tobacco use and second-hand smoke (SHS) exposure during pregnancy is a significant public health priority.[13]

A large proportion of women will stop smoking during pregnancy. Data suggest that up to 49% of women who smoked before pregnancy 'spontaneously quit' before their first antenatal visit.[27, 31, 32] The perceptions of pregnant smokers regarding the health risks of personal tobacco use and exposure to passive smoking have been identified as important factors influencing their decision to quit.[15, 33]

According to the European Perinatal Health Report on smoking during pregnancy in Europe, in most countries more than 10% of pregnant women continue to smoke during pregnancy (See **Table 1**).[7, 16] The prevalence of smoking during pregnancy varies from country to country. European countries with the highest proportion of tobacco users during pregnancy are: France (17.7%), Scotland (19%), Wales (16%), Northern Ireland (15%) and Spain (Catalonia – 14.4%).[16]

A second study involving 15 European countries (n=8,344) in 2011/12 found 35.3% of woman smoked before pregnancy.[34] This study found 26.2% of women continued smoking during pregnancy with 11.4% of report-

ed smoking more than ten cigarettes per day. This study also documented a large variation among the 15 European countries in prevalence of tobacco use.[34]

Specific sub-groups of women are more likely to continue to use tobacco during pregnancy. Single women, teenagers and those in the lowest socio-economic brackets, and suffering from depression or other mental health illnesses are more likely to smoke during pregnancy.[35] An estimated 50% of individuals who smoke during pregnancy have a mental health illness.[36]

1.2 Postpartum relapse rates

During the first 12 months of the postpartum period there is a very high risk of relapse to smoking by women who stopped during pregnancy or an increase in the number of cigarettes smoked by those who reduced smoking significantly during pregnancy.[37] Data suggests that between 29% and 85% of women who quit smoking relapse postpartum.[29, 30]

The specific events, factors, or decisions that precipitate a woman's resolution to quit are not necessarily the same as those that trigger a woman to smoke again.[30] Among woman who quit smoking during pregnancy who received intervention for smoking cessation, between 6.2% and 37.2% remained smoke-free.[30] Importantly, there is an association between tobacco use and decisions related to breastfeeding. Mothers who smoke tobacco after delivery are more than twice as likely not to be breastfeeding postpartum.[38-40] The value of breastfeeding for all infants, especially for premature infants, has been well established.[41, 42] As such, supporting a mother's efforts to remain smoke-free during postpartum period may be an important factor to prolong the duration of breastfeeding.

TABLE 1:
Percentage of women who report tobacco use during pregnancy in Europe and internationally

		DEFINITION OF PERIOD		PERIOD 1			PERIOD 2		
Country/ coverage	Source	Period 1	Period 2	All stated N	Not stated N	Smokers %	All stated N	Not stated N	Smokers %
Belgium									
Czech Republic	1		During				114407	0	6.2
Denmark	1		During				60947	1256	12.8
Germany	1		During				625615	0	8.5
Estonia	1	1st Trim	During	15111	535	9.1	15111	535	7.8
Ireland									
Greece									
Spain									
ES: Catalonia	7	Before	3rd Trim	NA	NA	26.7	NA	NA	14.4
ES: Valencia	6	1st Trim		4629	53	15.8			
France	1	Before	3rd Trim	13933	748	30.6	14087	594	17.1
Italy									
Cyprus	1	1st Trim		8312	43	11.5			
Latvia	1			19003	0	10.4			
Lithuania	1	Before	During	30568	0	7.0	30568	0	4.5
Luxembourg	1		3rd Trim				6370	70	12.5
Hungary									
Malta	1	1st Trim		3952	0	8.2			
Netherlands	4	1st Trim	>1st Trim	1441	7	10.5	1441	7	6.2
Austria									

		DEFINITION OF PERIOD		PERIOD 1			PERIOD 2		
Country/ coverage	Source	Period 1	Period 2	All stated N	Not stated N	Smokers %	All stated N	Not stated N	Smokers %
Poland	3	Before	3rd Trim	2765	128	24.6	2697	196	12.3
Portugal									
Romania									
Slovenia	1	1st Trim		22000	0	11.0			
Slovakia									
Finland	1	1st Trim	>1st Trim	59120	1301	15.5	59.120	1301	10.0
Sweden	1	1st Trim	3rd Trim	110212	3276	6.5	108843	4645	4.9
United Kingdom	1	Before or during	During	15315	NA	26.0	15315	0	12.0
UK: England	1	Before or during	During	7139	NA	26.0	7139	0	12.0
UK: Wales	1	Before or during	During	2571	NA	33.0	2571	0	16.0
UK: Scotland	12		During				53087	3442	19.0
UK: Northern Ireland	1	Before or during	During	2592	NA	28	2592	0	15.0
Iceland									
Norway	1	1st Trim	3rd Trim	52501	9038	18.6	51100	10439	7.6
Switzerland									

Source: Euro-Peristat project with SCPE and EUROCAT. European Perinatal Health Report. The health and care of pregnant women and babies in 2010. May 2013. Available www.europeristat.com [13]

2.0
HEALTH EFFECTS OF SMOKING DURING PREGNANCY AND POSTPARTUM PERIOD

2.1 The health effects of smoking on the foetus

When a pregnant woman smokes, the foetus inherently becomes a passive smoker. Tobacco use in pregnancy has significant and well established, adverse effects on the health and growth of the foetus.[1, 43] **Table 2** presents a summary of the known risk of tobacco use during pregnancy to the foetus and new born. Importantly, perinatal mortality rates are 150% greater when the mother is a smoker,[2] and data suggest that smoking is responsible for 15% of all cases of premature birth.[3] A meta-analysis of eight studies indicated that abruption placentae is greatly increased among pregnant smokers with an odds ratio (OR) of 1.62 [95% CI 0.46 to 1.77] compared to non-smokers.44 Smoking was also found to be one of the most important causes of premature rupture of membranes (PRM), with an OR of 1.81 [95% CI 1.36 to 2.26] based on pooled data for six studies.[44]

According to a US cohort study, which was based on the data from medical records of births, there is a dose-related association between the number of cigarettes smoked on a daily basis and the occurrence of placenta praevia; the increase in relative risk for placenta praevia associated with smoking was 4.4% for singleton births and 2.7% for twin births.[45]

Research has shown that perinatal mortality is increased among the offspring of pregnant smokers regardless of the number of cigarettes daily smoked.[20, 46-49] More specifically, it was found that the relative risk of ectopic pregnancy increased to 1.6 times that of non-smoking women for those who smoked from 1-5 cigarettes daily, and to 2.3 times for women who smoked 11-20 cigarettes daily.[18] The greatest gain in health benefits comes from full cessation during pregnancy rather than reducing smoking.[47, 50]

2.2 The effects of maternal smoking on the health of infants and children

Tobacco smoking during pregnancy is associated with significantly increased risk of intrauterine growth retardation, preterm birth, low birth weight, miscarriage, stillbirth, congenital malformation, sudden infant death

syndrome, genetic-related hereditary diseases, perinatal mortality and morbidity, short stature, cognitive delays, and neurologic disorders.[4-7, 9, 10, 51] Exposure of the foetus to maternal smoking may also effect fetal birth weight, fetal growth such as height, head perimeter, perimeter of thorax and shoulders and affect the growth of the lungs and brain, with possible effects that could continue into later life.[52-55] Active maternal smoking during pregnancy can also effect the development of other diseases in infancy such as Sudden Infant Death Syndrome (SIDS),[56,57] infant respiratory function[58-60] and the development of asthma in childhood.[61] Maternal smoking is also an important risk factor associated with the incidence of asthmatic bronchitis during the first year of life.[62]

Multiple epidemiologic studies argue that exposure to cigarette smoke during pregnancy can affect the fetal nervous system and could lead to behavioural disturbance in the infant, the child, or even the young adult. 63,64 Tobacco use during pregnancy is associated with the development of attention deficit disorders in children 65 and a higher risk of hyperactivity with more specific learning difficulties 66 and distractibility.[67] Even though the relative risk of autism occurrence is low at a rate of around 1/1,000 births,[68] an association with maternal daily smoking in early pregnancy has been documented in national observational study in Sweden.[69]

TABLE 2: Health effects of maternal smoking on the fertility, foetus, new born, and children

IMPACT PERIOD	HEALTH EFFECT
Fertility	Delayed conception (average 2 months)
	Infertility females (60% increase)
	Infertility males
	Reduced odds of conception with reproductive assistance
Antenatal Impact	Placental abnormalities
	Ectopic pregnancy (OR 2.5)
	Placental detachment
	Placenta praevia (OR 2.1)
	Pre-eclampsia (OR 0.51)
	Still birth (OR 1.1-3.2)
	Spontaneous miscarriage (OR 1.8)
	Premature rupture of membranes (OR 1.8)

IMPACT PERIOD	HEALTH EFFECT
Impact Postnatal	Increased perinatal mortality (150%)
	Premature birth (twice as great)
	Intra-uterine growth retardation
	Low birth weight infant 150-250 grams smaller
	Sudden Infant Death Syndrome (SIDS), OR 2.25
	Birth Defects
Impact in child's later life	Type 2 Diabetes (OR 1.1)
	Obesity (OR 1.52)
	Hypertension (1.5-5.4 mm HG increase)
	Reduced High Density Lipoprotein cholesterol (0.014 mmol/L decrease)
	Increased hospitalization
	Bronchial asthma, lower respiratory infection, decreased lung function
	Conduct disorder, Attention Deficit Disorder and hyperactivity
	Impaired academic performance
	Significant increase in psychiatric disorders

Maternal smoking during pregnancy can influence the future fertility of male infants.[70] Data found, the more the mother smokes during pregnancy, the greater the adverse effect in the reduction of volume and concentration of sperm.[70]

Additionally various studies have claimed that when the mother smokes during pregnancy, the occurrence rate of congenital abnormalities increases, particularly the occurrence of cleft palate and cleft lip.[71] According to an observational study of 1,974 children by Wisborg et al., investigated the relationship between smoking during pregnancy and the hospitalization of infants younger than 8 months, and found that children of mothers who smoked[15] or more cigarettes daily had twice the risk of hospitalization than those whose mothers had never smoked.[72] According to the findings of a population-based retrospective cohort study conducted in the State

of Ohio USA, which used birth records from 2006 to 2012, smoking of any duration in pregnancy is associated with increased Fetal Growth Restriction Risk.[73]

RECOMMENDATIONS:

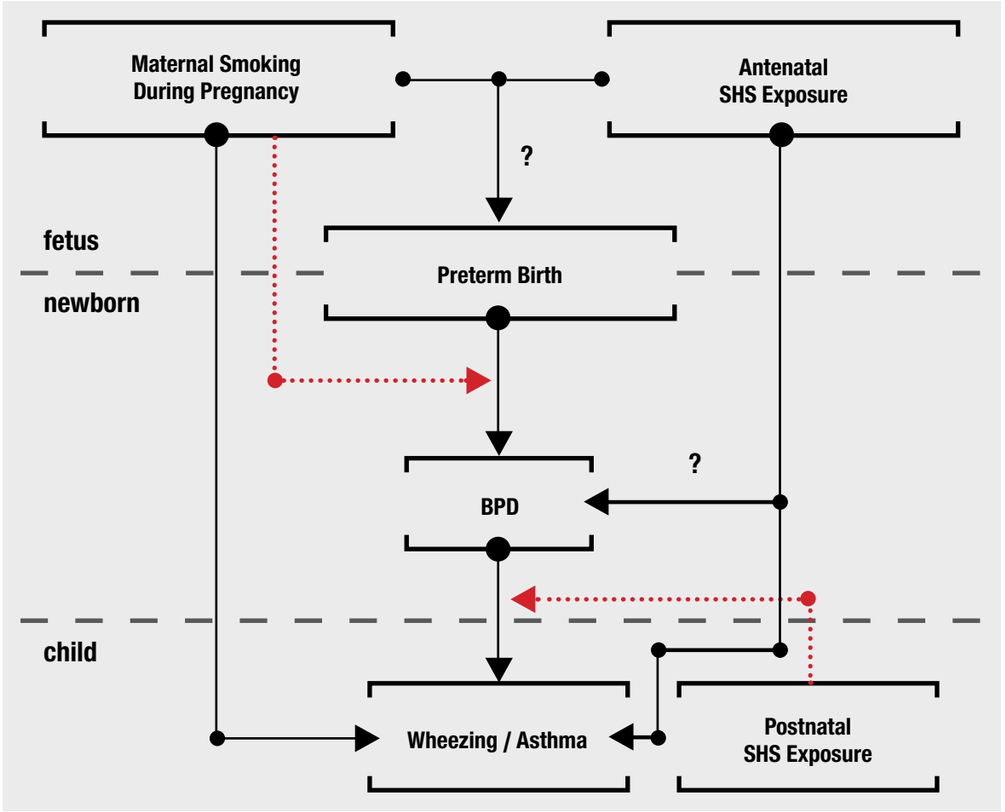
- There is no safe level of smoking in pregnancy and women should be advised to quit smoking completely (Level of Evidence A).

2.3 Second-hand smoke exposure

Second-hand smoke (SHS) exposure can affect the health of mother and foetus of both smoking and non-smoking women.[7, 13] SHS exposure during pregnancy is associated with multiple health concerns in the perinatal period (**Figure 1**) including an increased risk of preterm birth, bronchopulmonary dysplasia, congenital malformations, and wheezing/asthma etc.[6, 11-13] Pregnant women who are exposed to SHS are 23% more likely to experience stillbirth and 13% more likely give birth to a child with a congenital malformations.[15, 56]

Among non-smoking women and women who manage to quit smoking or cut down the amount of smoking in pregnancy, exposure to SHS from their partners and other family members, or social environments is common in many EU countries.[4, 12,74] The two most prominent factors affecting the exposure of women to passive smoking is dining at restaurants and having a partner who smoked. Maintaining a smoke-free environment should be a priority for all parents.[11]

FIGURE 1: Impact of tobacco smoke exposure on preterm birth and its respiratory complications



Source: Wagijo, et al. (2015) Reducing tobacco smoking and smoke exposure to prevent preterm birth and its complications. Paediatr. Respir. Rev., http://dx.doi.org/10.1016/j.prrv.2015.09.00213

2.4 Third-hand smoke exposure

Third-hand smoke (THS) has been more recently brought to the forefront and has particular implications during pregnancy and the postpartum period. THS is the residual tobacco smoke pollutants that remain on surfaces and in dust after tobacco has been smoked.[179] Studies show that THS clings to hair, skin, clothes, furniture, drapes, walls, bedding, carpets, dust, vehicles and other surfaces, even long after smoking has stopped and is resistant to normal cleaning.[179] It is understood that THS reacts with oxidants and other compounds to yield secondary pollutants.[75] Research has found that THS contains cancer-causing substances, posing a potential health hazard to non-smokers who are exposed to it. However, human exposure to THS has not yet been thoroughly studied.[179,180] Multiple groups are presently studying the health risks to humans of THS in order to fill this evidence gap. THS is particularly relevant to health of infants and children who typically spend more time indoors and have age-specific behaviours that may increase their exposure to the potential health hazards of THS.[179,180] Presently there is very little awareness among the general public about the health risks of THS and its danger to human health.[180]

RECOMMENDATIONS:

- Parents should be informed about the health risks of second-hand as well as third-hand smoke to the mother, foetus, and new-born (Level of Evidence D).
- Health professionals should advise pregnant women to maintain 100% smoke-free environments by banning smoking in their homes and cars and avoiding settings in which there may be exposure to second-hand smoke (Level of Evidence A).

2.5 Health Benefits of Smoking Cessation during Pregnancy

There is good evidence that stopping smoking as early as possible during pregnancy can reduce health risks.[76,77] Women who quit smoking prior to the first 3-4 months of pregnancy, give birth to infants of similar weight to those that never smoked.[21, 22] McCowan et al. (2009) in a prospective cohort study indicated that the serious adverse effects of smoking may be reversible if smoking cessation occurs early in pregnancy.[78] Among women who quit smoking before 15 weeks of gestation, the rate of spontaneous preterm birth and small for gestational age infants did not differ from non-smokers.[78] A large Finnish population-based cohort study of 1,164,953 singleton pregnancies from 1991 to 2010 found that quitting smoking in the first trimester of pregnancy reduces obstetric risks like prematurity, stillbirth, low birth weight and small for gestational age newborns at levels close to those of non-smokers.[79] But the use of tobacco in early pregnancy increased the prevalence of admission to neonatal intensive care unit at 19% and the prevalence of major congenital abnormalities by 22% with compared

non-smokers.[79] The adjusted odds ratio (OR) [95% CI] of smoking cessation after the first trimester of pregnancy was 1.2 [1.1-1.2] and 1.3 [1.2-1.3] and after the second trimester of pregnancy was 1.7 [1.6-1.8] and 1.8 [1.7-2.0], respectively, for Fetal Growth Restriction less than the 10th and fifth percentiles. While, the highest Fetal Growth Restriction Risks were for those who smoked throughout pregnancy (adjusted OR [95% CI] 2.2 [2.2-2.3] and 2.4 [2.4-2.5]).[73]

A recent systematic review carried out by Lumley et al. (2009) indicated that interventions for smoking cessation increase the mean birth weight of infants by 33 g (95% CI 11 g to 55 g) and simultaneously reduce preterm birth (pooled RR 0.84, 95% CI 0.72 to 0.98) in pregnant women who quit smoking.[80] These children growing up are more likely to have a reduced need for health care, suffer less from chronic diseases and in general benefit the health care system.[81,82]

It has been estimated that the potential neonatal cost savings that could be accrued from maternal smoking cessation during pregnancy were estimated at $881 per maternal smoker.[83] More over the health benefits for women who quit smoking are direct and last for their whole lifetime.[84] Consequently, the minimal cost invested in successful smoking cessation programmes during pregnancy and large health gains mean these interventions are highly cost-effective.[85]

RECOMMENDATIONS:

- Pregnant women should quit smoking as early as possible during the first trimester of pregnancy and stay smoke-free after birth (Level of Evidence A).

3.0
FACTORS ASSOCIATED WITH PERINATAL SMOKING CESSATION

3.1 Nicotine Metabolism during pregnancy and breastfeeding

During pregnancy the rate of nicotine metabolism may increase in a woman by an estimated 60%.17 The increased rates of nicotine metabolism during pregnancy may make it more difficult for a woman to quit smoking. Likewise the use of nicotine replacement therapy (NRT) to support cessation may require adjusted dosing to account for this increase in metabolism. At the present time there is no data about nicotine metabolism among breastfeeding woman.

3.2 Maternal Stress and Mental Health Disorders

Women who smoke during pregnancy report higher levels of perceived stress, depression, neuroticism, and negative paternal support.[86] Maternal stress, may therefore, inhibit smoking cessation during pregnancy and promote relapse after pregnancy in women who have achieved abstinence.[87] Women reporting depressive symptomatology are up to four times more likely to smoke during pregnancy than non-depressed women.[27] The use of smoking "to cope with emotions or problems" more than doubles the odds of continued smoking in pregnancy.[88] Despite these strong associations, there is limited information available about the effects of smoking and interventions in pregnant women with psychological symptoms, as they are often excluded from trials.[27] The stigmatization of smokers has been an unintended consequence and may further increase stress among pregnant women who smoke.[89] After the infant is born, postpartum stress, infant irritability, and breastfeeding failure all may contribute to continued smoking.[90]

Compared to women who continue to smoke during pregnancy and those who quit, Lopez et al. (2011) found that pregnant smokers are more likely to have current and lifetime PTSD diagnoses, have more instances

of previous abuse trauma, and are more likely to endorse having used tobacco to "cope with emotions or problems."[88] Studies with pregnant survivors of sexual abuse trauma 91 and with pregnant women with PTSD 92 find associations of abuse history and PTSD with smoking during pregnancy..

Additional factors which are known to be associated with perinatal smoking include: health inequalities, lifestyle choices, drug dependence and addiction.[93]

3.3 Partner/Significant Others Tobacco Use

Partners play an important role in influencing women's smoking behaviour in the perinatal period, either as barriers or facilitators to quitting.[94] A partner who continues using tobacco throughout a woman's pregnancy is a significant predictor of the current smoking status of the pregnant woman.[4, 6, 12 5,8,25,95] Women who do not quit smoking during their pregnancy typically come from families with smokers, had partners who smoked, or lived with relatives who smoked.[4, 96]

4.0
THE ROLE OF HEALTH PROFESSIONALS

Smoking cessation is considered the "gold standard" of preventive intervention and has a powerful effect in reducing morbidity, mortality and quality of life of all tobacco users.[97] The severity of the health risk imposed to the unborn foetus and new born mean that it is even more important that health professionals working with pregnant woman including family physicians, midwives, obstetricians and gynaecologist, and nurses be familiar with the latest evidence and be comfortable intervening and supporting woman with achieving cessation. Likewise, eliminating or minimizing second-hand smoke exposure, should be aggressively addressed by all health professionals working with pregnant woman.

The increasing awareness of expectant parents about the risks of smoking on pregnancy outcomes and the health of their new born makes pregnancy a "teachable moment" in which an expectant mother's receptivity toward smoking cessation messages is increased and as such offers an important opportunity for smoking cessation.[98]

The **"5 As"** (**Ask, Advise, Asses, Assist, Arrange**) is a widely accepted model for delivering tobacco treatment in clinical settings and is appropriate for use among pregnant tobacco users (see **Figure 2**). The American College of Obstetricians and Gynaecologists recommends the "5 As" model as the intervention of choice for smoking cessation for pregnant smokers as the intervention model is both evidence-based, short and easy to use.[182] The **"5 As"** model recommends smokers are first **asked** about their smoking status at every visit and recorded in the medical record. If they have already quit smoking before or just after they found out they were pregnant, they are congratulated about their success in quitting and encouraged to stay smoke free. If they are currently smoking, brief and personal **advice** about smoking cessation and how it affects not only the foetus but also themselves should be delivered alongside an offer of support with quitting. Pregnant smokers' willingness to quit smoking within a month is then **assessed**. If pregnant women express the willingness to quit smoking, they receive **assistance** with quitting. Assistance includes the provision of self-help material, behavioural counselling, and as appropriate pharmacotherapy. Follow-up visits are **arranged** to support cessation among women making a quit attempt or a referral is made to a specialized quit smoking service.[84] Women who do not express a willingness to quit should receive intervention to examine barriers and concerns regarding quitting and follow-up should be scheduled. Setting incremental goals such as reduction of tobacco use may be appropriate among woman unwilling to quit. Referral to more intensive counselling services is recommended for woman unwilling or unable to quit.

FIGURE 2: The 5As Model for Smoking Cessation in Pregnancy and the Post-Partum Period

4.1 Midwives

Smoking cessation should be considered throughout the spectrum of care of a pregnant woman from the first visit and follow-up visits as well as following childbirth. All midwives should receive training in smoking cessation and should address tobacco use with all pregnant women as a standard practice of care. Midwives are uniquely positioned to deliver education and counselling that is more patient-centered during the antenatal and postnatal period in both clinical and community settings.[99] Midwives should provide women with evidence-based information about the risks of smoking to mother and foetus, including smoking by partners or family members.[77] At the initial and follow-up appointments midwives should record smoking status of the mother, partner and family members and use carbon monoxide (CO) breath test to validate self-reports and offer support with quitting including referral to available community-based smoking cessation services. At follow-up appointments midwives should check if referral was taken-up and provide alternatives to support cessation.

In West Scotland the development of a home-based midwifery intervention program to support young pregnant smokers to quit was a feasible approach to engaging young pregnant smokers to help them quit.[100] Local community-based midwives were found to be very willing to support this approach. [101]

4.2 Nurses

Nurses have an important role to play in smoking cessation in all health care settings.[102] There are an estimated 17 million nurses worldwide, who encounter smokers daily in their clinical routines.[103] Nurses are at the forefront of primary health care and well placed to advise all groups of tobacco users and provide cessation counselling.[104,105] A meta-analysis by Gaffney et al. included 64 published studies (1988-2009 reported a statistically significant effectiveness of nursing interventions in smoking cessation during pregnancy (OR = 1.14, 95% CI = 01.08 - 01.02).[106] Also, according to a systematic review published by Rice et al (2013), which included 35 research studies with more than 17,000 participants that compared a nursing intervention to usual care or control group, demonstrated that nursing intervention increased the likelihood of smoking cessation (RR 1.29; 95%CI 1.20 to 1.39). These results demonstrate the benefits of smoking cessation advice and counselling provided by nurses, especially by those whose main role was health promotion or smoking cessation.[107]

4.3 Primary health care – General Practice, Obstetricians & Gynaecologists

Smoking cessation in primary health care / general practice should be considered for the full spectrum of pregnancy from pre-conception visit to at least 1 year postpartum. The family planning process is a useful time to address cessation among both men and woman who are planning a pregnancy and for infertile couples who

smoke, because they could quit smoking before pregnancy. The "5 As" model should be used to guide treatment delivery. All primary care providers should be prepared to provide counselling support to expectant woman and their partners and as appropriate be knowledgeable about specialized cessation support services for smoking cessation that pregnant woman who smoke can be referred to for more intensive support. The flowchart with the procedures for smoking cessation during pregnancy at primary health care is illustrated in **Figure 4**. **Table 3** summarizes opportunities for intervention for young women smokers (15-45 years old) created by the World Health Organization.[108]

TABLE 3: Opportunities for intervention for female tobacco users ages 15-45 years

SMOKING STATUS	RECOMMENDED INTERVENTIONS
Smokers (age 15-45)	– Use policy and interventions to promote pre-pregnancy quitting.
Early pregnancy smokers	– Promote early first-trimester cessation. – Offer cessation help (5As) in obstetric care.
Early pregnancy quitters	– Provide support to maintain cessation during pregnancy and postpartum. – Promote spouse and family quitting and exposure reduction. – Shift motivation to include mother not just baby.
Late pregnancy quitters	– Provide intensive interventions to promote cessation. – Support reduction even late in pregnancy. – Involve the family in protecting the foetus and preparing for the baby.
Pregnancy quitters	– Engage family and spouse smokers to quit. – Offer relapse prevention individually postpartum.

SMOKING STATUS	RECOMMENDED INTERVENTIONS
Continuing smokers	– Prevent return to pre-pregnancy levels. – Provide interventions during paediatric visits. – Promote smoke-free home policies. ‘
Postpartum relapsers	– Support a new quit attempt and learn from past quit experience. – Promote smoke-free home policies.

Source: Adapted from Samet J M, & Yoon S Y. (2010). Gender, women, and the tobacco epidemic. Geneva, World Health Organization.[108]

4.4 Specialized Smoking Cessation Services

Specialised smoking cessation programs and services can offer more intensive counselling and support that is tailored to the needs of women who continue smoking during pregnancy, however the availability of such services as well as referral rates from health providers has been poor.[109] Major barriers of pregnant women to access such services include transportation difficulties and problems with childcare for other children, lack of time and a belief that they would not be helped but such services.[99] According to a large (n=52,370) observational study conducted in Scotland in 2005/6, 25% of pregnant women reported being current smokers at the maternity booking and 24% (3,133/13,266) were referred to specialised cessation services.[110] Fifty-eight percent of all pregnant smokers were referred to cessation support services, 11.5% were engaged in specialized services, 11% of women set a quit date and 3.5% had quit four weeks later.[110] Among woman who were ready to quit smoking, 19% engaged in service delivery, 15% set a quit date and 4.3% had quit four weeks later.[110]

RECOMMENDATIONS:

- All health professionals working with pregnant women including family physicians, midwives, obstetricians and gynecologist, and nurses should be familiar with the latest evidence and be comfortable intervening and supporting women with achieving cessation (Level of Evidence A).
- The “5 As” (Ask, Advise, Assess, Assist, Arrange) can be used as a clinical model for supporting cessation among pregnant women (Level of Evidence B).
- Health professionals should deliver strong non-judgmental advice to quit to all women who smoke and assist tobacco users with cessation, which includes follow-up throughout the duration of the pregnancy and early postpartum period (Level of Evidence A).
- Women unable to quit smoking should receive intensive counselling and support with quitting as early as possible in their pregnancy (Level of Evidence B).
- When available women unable to quit should be referred to specialized cessation support. Health professionals should follow-up to ensure treatment is undertaken (Level of Evidence D).

5.0
ASSESSMENT OF NICOTINE USE IN PREGNANCY

The appropriate screening for tobacco exposure during pregnancy is critical. Health professionals should ensure at minimum all pregnant women are screened for:

- Second-hand smoke exposure (SHS);
- Personal tobacco use at present and prior to pregnancy (using biochemical validation when possible).

Additionally among women who report current or past tobacco use the following should be assessed:

- Nicotine Dependence (optional);
- Readiness/Motivation to Quit;

We outline here available tools for the assessment of tobacco use exposure as well as tools for the assessment of pregnant tobacco users in order to guide intervention delivery.

5.1 Assessment of Second-hand Smoke Exposure

The World Health Organization (WHO) recommends that health professionals should assess exposure to during pregnancy.[111] **Figure 3** provides a summary of recommended questions for the assessment of SHS exposure that health professionals should ask expectant parents during perinatal period. Health professionals should promote SHS avoidance behaviours and implement strategies to reduce second-hand smoke exposure in the home, car, work and social activities recognizing that smoke-free workplace legislation increases the likelihood that people (both smokers and non-smokers) will voluntarily make their homes and cars smoke-free.[111] Lee et al 2012 found most pregnant women felt powerless and lacked self-efficacy to stop others from smoking in their presence.[112]

FIGURE 3: Recommended questions for screening for second-hand smoke (SHS) exposure during pregnancy

PARTNER/SIGNIFICANT OTHERS

1. Does your partner/spouse smoke? Do they smoke in your presence?
2. Do other significant others who you have routine contact with smoke in your presence?

HOME

3. Is there a total smoke-free ban in the home?
   - Are there any exceptions to that rule?
   - Is smoking allowed in specific rooms in the home that is used by the pregnant woman?
   - Is smoking limited to part of the house where the pregnant woman rarely goes?

CAR

4. Is there a total car-smoking ban?
   - Are there any exceptions to that rule? (e.g. smoking with open window during driving)

WORK AND SOCIAL

5. Is there a smoking ban in your work place?
6. Are you exposed to smoke in your workplace?
7. Do you attempt to go places for social activities (cafes, restaurants, bars, events) where there is a smoking ban?
8. How frequently would you say you are you in places where people are smoking?

5.2 Biochemical Validation of Smoking Cessation

Research has found a high rate of misreporting of smoking status among pregnant women.[80] Walsh found the rate of false declaration of abstinence from smoking was 48% of pregnant women sampled.[113] As such, biochemical validation of smoking status is recommended for all pregnant women.[114] There are a variety of methods, which can be used, for biochemical validation including: cotinine levels in salivary samples or in urine samples, expired carbon monoxide, or by hair analysis to detect nicotine and cotinine. We briefly review each method and its relevance among pregnant woman here.

5.2.1 Expired Carbon Monoxide (CO)

Expired CO is a convenient, low-cost measurement, providing immediate results for the evaluation of smoking status. Its short half-life (3-6 hours) can lead to false negatives, as it is not able to detect tobacco use among individuals who have abstained from smoking for several hours.[115,116]

Overview of CO-Testing

- Ask about smoking status and exposure to second-hand smoke.
- Explain what the CO test is and that she will be able to see a physical measure of her smoking and her exposure to other people's smoking.
- In order to interpret the CO reading correctly ask if she is a light or infrequent smoker, how many cigarettes she has smoked on the test day and when she smoked her last cigarette.
- The best cut-off point to separate smoker and non-smoker is 7 ppm.[117]

5.2.2 Nicotine

Nicotine has a half-life of only 2-3 hours in the blood, due to its short half-life, nicotine levels can only inform us about recent exposure to tobacco smoke.[118]

5.2.3 Cotinine

Cotinine is the major metabolite of nicotine and the biomarker that determines the exposure to smoke for a longer time, because compared with the half-life of nicotine (2-3hours), it has a longer half-life (15-19 hours) in different body fluids (plasma, urine and saliva).[118] Therefore, cotinine is the biomarker of choice for both active and passive smoking exposure. [118] Because of its longer half-life, cotinine levels accumulate during the day. Furthermore, cotinine is eliminated over a longer time period than nicotine, which leads to relatively stable levels of cotinine throughout the day. [118]

However, the concentration of cotinine in the body fluids of pregnant women differs from that of the normal adult population.[119-121] Rebagliato et al. found significant differences between prenatal and postnatal cotinine concentrations in smokers after controlled smoking consumption.[119] The researchers conclude that the metabolism and distribution of nicotine and cotinine during pregnancy is modified, with higher rates of clearance of cotinine compared with those of non-pregnant smokers.[121]

A new method of biochemical validation uses hair analysis; depending on the length of the hair, this method provides information about the smoking status during the last six months, as hair grows approximately 1 cm per month.[122] Klein et al analysed hair samples from the scalps of 28 pregnant women, who reported that they smoked the same amount during all three trimesters of pregnancy, to find that indeed there is an increase in nicotine metabolism in pregnancy.[123] However, cotinine remained steady throughout pregnancy in the analysis. Therefore, the levels of cotinine should be examined as they provide a more reliable history of exposure to active smoking. On the other hand, a decreased concentration of nicotine should be treated with caution, taking into account the increase in its metabolism.

5.3 Fagerström Test For Nicotine Dependence (FTND)

The Fagerström Test For Nicotine Dependence (FTND) is a brief and widely used 6-item questionnaire used to evaluate the level of nicotine dependence among tobacco users (See **Figure 4**).[124] The FTND measures both behavioural and physiological aspects of addiction (e.g. the rate of smoking, smoking in the morning, and difficulty in abstaining from smoking).[125,126] The FTND score is calculated based on the ranking of responses on a scale from 0-10. Score of 7 to 10 indicates the maximum nicotine dependence, 4-6 moderate dependence and less than 4 indicates minimal dependence.[124]

FTND can be used to determine the appropriate initial dosing of nicotine replacement therapies and can potentially predict the need for more intensive cessation support.[124] Berlin et al 2015 examined the FTND in a sample of pregnant smokers (n=476). Results demonstrate that the Cronbach's alpha coefficient for the FTND was 0.55 and that FTND was associated with saliva cotinine concentration, but failed to anticipate smoking status two weeks after smoking cessation.[127] A recent systematic review of Yang and Hall (2016) that included fifty-five studies provides an analysis of nicotine dependence measures used for smoking cessation perinatally and their psychometric properties. The majority of the studies had used the FTND, however this review demonstrated that FTND might not be the best way for measuring nicotine dependence in this specific population suggesting future research to assess its reliability during pregnancy and postpartum period.[128]

FIGURE 4: Fagerström Test for Nicotine Dependence (FTND)

1.	How soon after you wake up do you smoke your first cigarette?	
	Within 5 minutes	3 points
	5 to 30 minutes	2 points
	31 to 60 minutes	1 point
	After 60 minutes	0 points
2.	Do you find it difficult not to smoke in places where you shouldn't, such as in church or school, in a movie, at the library, on a bus, in court or in a hospital?	
	Yes	1 point
	No	0 points
3.	Which cigarette would you most hate to give up, which cigarette do you treasure the most?	
	The first one in the morning	1 point
	Any other one	0 points
4.	How many cigarettes do you smoke each day?	
	10 or fewer	0 points
	11 to 20	1 point
	21 to 30	2 points
	31 or more	3 points
5.	Do you smoke more during the first few hours after waking up than during the rest of the day?	
	Yes	1 point
	No	0 points
6.	Do you still smoke if you are so sick that you are in bed most of the day, or if you have a cold or the flu and have trouble breathing?	
	Yes	1 point
	No	0 points

SCORING: 7 to 10 points = highly dependent
4 to 6 = moderately dependent | less than 4 points = minimally dependent

Source: Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119–27. [129]

5.4 Assessment of Motivation to Quit

Motivation / readiness to quit smoking should be assessed in all pregnant tobacco users. Tools such the readiness to quit ladder (see Figure 5) which asks pregnant smokers to assess their readiness to quit on a scale for 1 to 10 are a useful tool for understanding readiness to quit and tailoring interventions based on the current readiness of the tobacco user (See section 6.2 Stages of Change).

FIGURE 5: Readiness to Quit Ladder

10	I have quit smoking.
9	I have quit smoking, but I still worry about slipping back, so I need to keep working on living smoke free.
8	I still smoke, but I have begun to change, like cutting back on the number of cigarettes I smoke. I am ready to set a quit date.
7	I definitely plan to quit smoking in the next 30 days.
6	I definitely plan to quit smoking in the next 6 months.
5	I often think about quitting smoking, but I have no plans to quit.
4	I sometimes think about quitting smoking, but I have no plans to quit.
3	I rarely think about quitting smoking, and I have no plans to quit.
2	I never think about quitting smoking, and I have no plans to quit.
1	I have decided not to quit smoking for my lifetime. I have no interest in quitting.

Source: Abrams DB, Niaura R, Brown RA, Emmons KM, Goldstein MG, Monti PM. The Tobacco Treatment Handbook: A Guide to Best Practices. New York: Guilford Press, 2003 (page 33). Adapted by the Center For Tobacco Independence.[130]

RECOMMENDATIONS:

- All pregnant women should have both their smoking status and second-hand smoke exposure assessed as part of routine examinations (Level of Evidence A).
- It is recommended that tobacco use be biochemically assessed at antenatal and postnatal visits to determine smoking status (Level of Evidence A).
- When available, the use of urine or saliva cotinine tests is recommended, as they are more accurate than CO tests and detect tobacco exposure over the past few days rather than few hours (Level of Evidence A).

6.0
COUNSELLING INTERVENTIONS FOR SMOKING CESSATION DURING PREGNANCY

Counselling interventions for smoking cessation during pregnancy can serve to enhance motivation to quit, guide to problem solving and increase coping skills.[131] The 2016 ENSP Guidelines for Treatment of Tobacco Dependence identifies three categories of behavioral counselling interventions: psychological support for smoking cessation, cognitive-behavioral therapy (CBT) and motivational interviewing (MI). All three intervention approaches have common elements, to treat psychological and behavioral dependence of tobacco users.

A variety of formats have been tested for delivering non-pharmacologic smoking cessation treatments including: individual counselling, proactive telephone counselling, group counselling, web-based, and self-help in the general population. Counselling interventions, which may be used during pregnancy, are summarized in **Figure 6**.

FIGURE 6: Examples of Individual psychosocial interventions to support cessation during pregnancy

- > Individual behavioural counselling
- > Motivational interviewing
- > Stage-based interventions,
- > Telephone counselling
- > Mobile phone-based interventions
- > Internet-based interventions
- > Incentives
- > Health professional advice
- > Enhancing partner support
- > Training health professionals in smoking cessation
- > Relapse prevention

Source: Chamberlain C, et. al. Psychosocial interventions for supporting women to stop smoking in pregnancy. Cochrane Database of Systematic Reviews 2017. No.: CD001055.[27]

6.1 Cognitive Behavioural Interventions

Cognitive behavioural interventions are a well-accepted counselling model and have been widely used in smoking cessation in both the general population and among pregnant woman.[27] Cognitive behavioural interventions aim to change an individuals' tobacco use by changing habitual ways of thinking and feelings about smoking and oneself and provides encouragement and advice on ways of minimizing and managing the desire to smoke. Cognitive behavioural interventions have been used to support cessation in pregnant smokers with positive results.[114,132-134]

A 2017 Cochrane review by Chamberlain found high quality evidence that among pregnant woman who smoke, counselling significantly increased smoking cessation in late pregnancy compared with usual care (30 studies; average risk ratio (RR) 1.44, 95% confidence interval (CI) 1.19 to 1.73), and less intensive interventions (18 studies; average RR 1.25, 95% CI 1.07 to 1.47).[27] The effect on smoking abstinence was further broken down

by time point postpartum. A significant effect was found at zero to five months postpartum (11 studies; average RR 1.59, 95% CI 1.26 to 2.01), a borderline effect at six to 11 months (6 studies; average RR 1.33, 95% CI 1.00 to 1.77), and a significant effect at 12 to 17 months (2 studies, average RR 2.20, 95% CI 1.23 to 3.96).27 High-quality evidence was found which indicates that women who received psychosocial interventions had a 17% reduction in infants born with low birth weight, a significantly higher mean birth weight (mean difference (MD) 55.60 grams, 95% CI 29.82 to 81.38 grams higher) and a 22% reduction in neonatal intensive care admissions.[16] The difference in preterm births and stillbirths was unclear.

In most studies an intensive intervention lasting more than 15 minutes was found to be more effective than the shorter and less individualized interventions, which are described in some studies as "low intensive intervention" and in others as "usual care" (<5 minutes).[114,134,135] Perhaps this is also due to the fact that some studies included communication for a period of time after childbirth and final biochemical measurement after 2-6 months.[136,137] A systematic review and meta-analysis by Melvin et al. examined the most effective counselling interventions for smoking cessation during pregnancy and also found that more intensive intervention is more effective.[84] Authors propose that the duration of this intervention be about 15 minutes, that counselling use cognitive behavioural approaches and be accompanied by printed material.[84]

RECOMMENDATIONS:

- Counselling-based interventions are effective in supporting cessation among pregnant women (Level of Evidence A).
- Counselling interventions are effective in significantly reducing low birth weight, increasing mean birth weight, and reducing neonatal intensive care admissions (Level of Evidence A). The effect of counselling intervention on pre-term births and stillbirths is unclear (Level of Evidence C).
- Intensive cognitive behavioural interventions are more effective in supporting cessation among pregnant women (Level of Evidence A).

6.2 The "Stages of Change"- Transtheoretical Model

The well-known "stages of change" proposed by Prochaska and DiClemente transtheoretical model have also been used to deliver counselling based interventions.[138] According to this model a person may go through five stages of change, when trying to change their behaviours and it is recommended that intervention strategies be tailored to the stage in which each smoker finds herself (See **Table 4**).[138] The first stage that is "pre-contemplation" in which there is indifference about smoking cessation and tobacco user's may show resistance with recognizing the problem behaviour.[138] At the second stage, that is named "contemplation", the health professional investigates whether there is a concern about smoking cessation that needs to be strengthened. The basic characteristic of someone at the contemplation

stage is that the person at this stage is seriously thinking about resolving the problem.[139] The third stage is the stage of "planning and preparation" that indicates that there is a desire to quit smoking in the next 30 days.[117] The fourth stage is called "action" because during this stage the decision for smoking cessation is implemented. At this fourth stage smoking cessation is a fact and efforts are made to prevent smoking relapse.[138] The final stage is called "maintenance" because its objective is the maintenance of abstinence from smoking without the occurrence of relapse.

TABLE 4: The "Stages of Change" and associated intervention strategies

STAGE OF CHANGE	DESCRIPTION
1. Pre-contemplation	no intention to quit
2. Contemplation	thinking about quitting
3. Planning and preparation	planning to quit in the next 30 days
4. Action	successful quitting for up to 6 months
5. Maintenance	smoke-free for more than six months

Source: European Smoking Cessation Guidelines: The authoritative guide to a comprehensive understanding of the implications and implementation of treatments and strategies to treat tobacco dependence. Revised 1st edition. October 2012 pp49.[117]

The "stages of change" counselling strategy for smoking cessation has been used to investigate the effectiveness of brief intervention (10-15 minutes) for smoking cessation in pregnancy provided by hospital staff in routine conditions.[136] Pregnant women who did not want to stop received brief intervention in order to be motivated. Those who wanted to quit smoking received support. At the same time, those who had already quit smoking received an intervention to help them avoid smoking relapse. The intervention was not found to be effective in increasing cessation.[136]

An RCT by Lawrence et al. compared the effectiveness of interventions based on the "stages of change" with those provided with standard care. This survey involved 918 pregnant women, who were divided into three groups.[140] The first group received routine care, the second group received self-help manuals based on the transtheoretical model of "stages of change", while the third group received the same intervention as the second group along with a computer-based educational program with personalized advice on smoking cessation. Ten days after child birth, 3.5% of the first group, 4.7% of the second group and 8.1% of the third group had stopped smoking.[140] The combination of educational methods in the intervention proved to be most effective.

Despite the popularity of the stages of change model there is no strong evidence to support its use.

6.3 Evidence for Various Intervention Approaches

6.3.1 Individual interventions

Individual counselling interventions demonstrated a significant effect compared with usual care condition (27 studies; (RR) 1.44, 95% (CI) 1.19 to 1.75).27 Previous Cochrane reviews have also indicated the potential for individual interventions during pregnancy to have a moderate but significant effect on reducing smoking in pregnancy, preterm births and infants' low birth weight.[80]

RECOMMENDATION:

- Person-to-person psychosocial interventions that exceed minimal advice to quit should be offered to pregnant smokers (Level of Evidence A).

6.3.2 Social Support and Group Interventions

Social support interventions appeared effective when provided by peers (five studies; RR 1.49, 95% CI 1.01 to 2.19).[27] Group interventions may include health education information about the risks of smoking and advice to quit, and support or advice about how to make this change.[27] During the group interventions the mother may be provided with feedback about foetal health status or measurement of tobacco smoke exposure to reinforce behaviour change.[27] This includes ultrasound monitoring and CO or urine cotinine measurements, with results fed back to the mother.[27] Finally, group intervention may also include exercise, weight control, alternative therapies etc.[27]

RECOMMENDATION:

- Group based interventions of sufficient intensity have a modest but positive effect in increasing smoking abstinence among pregnant women (Level of Evidence B).

6.3.3 Partner-based interventions

Partner-based interventions for smoking cessation have not been well evaluated but may be useful in particular when both partners are tobacco users.[27] One randomized controlled trial has evaluated couple-based support intervention to assist women's smoking cessation during pregnancy increased women's abstinence rates during and after pregnancy compared to usual care and a previously evaluated woman-only intervention.[141] Although the couple-based intervention did not significantly improve abstinence rates over usual care, the results

suggest the feasibility of couple-based interventions and further research is required to understand the value of partner-based therapy. [141]

RECOMMENDATIONS:

- There is very limited research regarding partners-based interventions to support smoking cessation and additional research is required to better understand the value of such interventions (Level of Evidence C).

6.3.4 Quitlines

Smoking Cessation quitlines offer telephone-based advice and counselling from trained smoking cessation specialists. These services can be offered when available to support cessation among pregnant woman. A meta-analysis of seventy-seven trials found in the general population of tobacco users that proactive telephone counselling of three or more calls to be more effective than a minimal intervention/brief advice.[142] Quitlines in the USA as well as the United Kingdom, offer a pregnancy tailored quit smoking protocol in which trained staff deliver counselling to support prenatal smoking cessation and postpartum relapse.[183] Bombard et al. (2013) examined the characteristics, service utilization and the self-reported quit rates among 1,718 pregnant and 24,321 non-pregnant smokers, who enrolled in quitline services from 2006 to 2008 in 10 states in USA.[143] Seven months after enrolment in quit-line services the self-reported quit rates were 26.4% for pregnant women and 22.6% for non-pregnant women.[143] In many countries, health care systems and health professionals have become partners with quitlines and refer patients regularly. Engaging health professionals in referring their patients to smoking cessation to quitline services, is a form of complementary service delivery in which health professionals identify and advise patients to quit smoking and refer patients for more intensive counselling to the quitlines.[144] Some health professionals might be more willing to refer to quitlines following a proactive enrolment model, where the patients' (who agree to be contacted by a counsellor) are referred to the quitline, who initiates contact with the patient.[145]

RECOMMENDATIONS:

- A tailored quit smoking protocol for prenatal smoking cessation and postpartum relapse delivered by trained counsellors, should be offered by all quit-lines services (Level of Evidence D).
- Proactive telephone counselling of 3 or more calls may be more effective than a minimal intervention (Level of Evidence B).

6.3.5 Incentives

The use of incentives to encourage smoking cessation among pregnant woman has been examined in recent literature. A recent review by the Cochrane Collaboration identified high quality evidence that incentive-based intervention were effective compared to non-contingent incentives (4 studies; RR 2.36, 95% CI 1.36 - 4.09).[27] An earlier meta-analysis by Higgins 2010 identified three trials (n=166) in which pregnant tobacco users were randomized to receive vouchers for retail goods based on abstinence from smoking compared to controls (no incentive).[146] The vouchers began at $6.25 and increased to a maximum of $45. The incentive group had significantly greater rates of smoking abstinence in late pregnancy (34.1% vs. 7.4%, $P < 0.001$), higher mean birth weight (3295 g vs. 3093 g, $p = 0.03$) and fewer babies with a birth weight< 2500 g (5.9% vs. 18.5%, $p = 0.02$). Interestingly, the effect on smoking abstinence was no longer significant when the vouchers were discontinued postpartum. In a small study, Donatelle et al. (2000) found similar rates of smoking abstinence in late pregnancy and increased rates of abstinence two months postpartum when both the patient and a "social supporter" received vouchers as an incentive to smoking abstinence compared to controls.[147]

The use of incentives to support cessation is a promising intervention strategy for supporting cessation among the population of pregnant smokers. Further research is needed to increase the strength and generalizability of this evidence.

RECOMMENDATIONS:

- The use of incentives is a promising intervention strategy for supporting smoking cessation among pregnant smokers however more research is required to strengthen this recommendation (Level of Evidence B).

6.3.6 Health Education and Self- help manuals

Self-help materials have been shown to be effective in a number of RCTs involving pregnant woman.[133,148] Self-help materials are defined as structured materials (printed or audio-visual) that assist the individual in making an attempt to quit and sustaining abstinence without significant assistance from health professionals.[149] In most studies a self-help manual is an informative booklet; after it has been presented and explained, the pregnant woman takes it with her and can read it as many times as she wishes and refer to it whenever necessary. A self-help manual is not limited to information about the effects of smoking on the foetus, the potential complications during pregnancy and adverse outcomes in childbirth, but also includes the effects of smoking on women's health in order to prevent a smoking relapse postpartum.

According to Chamberlain et al., the provision of self-help materials in pregnant women offered a modest but significant effect (RR 1.21, 95% CI 1.05 to 1.39), materials that were tailored for pregnant women were more effective than general materials (RR 1.31, 95% CI 1.20 to 1.42).[27]

RECOMMENDATIONS:

- The provision of self-help manual can have a modest but significant effect for supporting smoking cessation in pregnancy (Level of Evidence A).
- Information in the self-help manual should include the health effects of smoking on the foetus, the potential complications during pregnancy and adverse outcomes in childbirth, but also include the effects of smoking on women's health in order to prevent a smoking relapse postpartum and strategies to support cessation.

6.3.7 Internet-based Interventions

The use of the Internet in smoking cessation is a new and promising category of smoking cessation interventions and given the high rates of Internet use among pregnant woman may offer significant reach.[150] Online smoking cessation interventions seem to be suitable for pregnant smokers, because they offer non-judgmental and flexible help that is valued by pregnant smokers[151], and can be offered remotely.[152] Internet-based smoking cessation interventions offer the available treatment and close monitoring of behaviour and progress that might be especially helpful for smoking cessation for pregnant women.[153]

A new internet-based intervention focusing on smoking cessation in pregnancy named 'MumsQuit' deliveres fully automated cessation support.[154] In a pilot RCT evaluation, pregnant adult smokers (n=200) were randomized to either the "MumsQuit" intervention or a website that provided only information. The study found that participants in the 'MumsQuit' group logged in more often (3.5 vs. 1.3, $p<0.001$), viewed more pages (67.4 vs. 5.7, $p < 0.001$) and spent more time browsing the specific website (21.3 min vs. 1.0 min, $p < 0.001$) than the control group.[154]

A systematic review of Civljak et al. (2013) examined the effectiveness of Internet-based interventions for smoking cessation in the general adult population and found that some Internet-based interventions, especially those that are tailored and provide repeated automated contacts with the users can be effective in supporting cessation.[155] However these trials did not demonstrate consistent effects and did not specifically examine interventions for pregnant woman.[155] As such, future research is needed about the effectiveness of online smoking cessation interventions in pregnancy.

RECOMMENDATIONS:

- Internet-based Interventions for pregnant smokers are useful as they are flexible and non-judgmental, but their effectiveness has not been well documented at present (Level of evidence C).

6.4 Relapse Prevention in the Postpartum Period

Mothers who quit smoking during pregnancy remain at high risk for smoking relapse during the postpartum period. Women that have had a smoke free pregnancy should be offered help to remain smoke free after birth.[76,77] Counselling interventions used during pregnancy may not be the most effective in the postpartum period.[156,157] Culturally appropriate smoking cessation interventions should be a high priority. [92,99]

Postpartum cessation intervention strategies tested to date have documented great variation in terms of success and a broad range of relapse rates.[158] Research shows that reasons for continued cessation are related to the baby, whereas disadvantages for stopping are related to the mother.[158]

The postpartum hospitalization presents a widow of opportunity ("teachable moment") to screen and support the early identification of both mothers and fathers who currently smoke and recent quitters who may be at risk of relapse and connect them with tobacco treatment services in both the health care setting and the community. Research has found the majority of parents accepted tobacco treatment services during the hospital stay.[90]

RECOMMENDATIONS

- Parents should be encouraged to remain smoke-free in the postpartum period. Postpartum care should address relapse prevention in addition to cessation strategies for both parents before hospital discharge and during post-natal home visits (Level of Evidence A).
- Parents, who continue to smoke at the time their babies are admitted to neonatal intensive care units (NCIU), should be referred to local smoking cessation programs (Level of Evidence C).
- There is a need for more research on prevention of postpartum smoking relapse for both parents.

6.5 Interventions for reducing Second-hand Smoke (SHS) Exposure

While evidence remains scarce there have been some recent studies that report on interventions to reduce SHS among pregnant woman. According to a multi-component intervention, SHS reduction during pregnancy may reduce the risk of preterm birth.[159] A RCT by Blaakman et al (2015) found motivational interviewing was effective in reducing SHS exposure at home (home/car smoking bans and reduction in infant contact with smokers) after discharge from the NICU, however the effects of the intervention were only significant in the short-term (up to eight months post-discharge).[160]

Interventions to reduce perinatal SHS exposure needs to be tailored to the specific community settings, social support networks, and cultural assets of families within the European Union. Community-based interventions like home visits during perinatal period may be helpful in reducing SHS perinatal exposure especially for the high-risk groups like premature infants. 160 Policy-based interventions like smoke-free legislation or tobacco taxation are associated with reduced SHS exposure.[161,162]

RECOMMENDATIONS

- Health care professionals should assist with addressing SHS exposure during perinatal period by enforcing home smoking bans and reducing contact with smokers especially for infants (Level of Evidence A).
- Pregnant women's social support network, including her spouse and close family should be involved in supporting smoke-free environments in spaces shared by the new born (Level of Evidence D).

7.0
QUIT SMOKING MEDICATIONS

First-line quit smoking medications for the general population of smokers include nicotine replacement therapy (NRT), bupropion and varenicline. These medications are widely and effectively used outside of pregnancy. However, there is less evidence in terms of their efficacy and enough safety when used by pregnant smokers in order to help them quit smoking.[28] Summarized here are evidence and recommendations for each of the three first-line therapies for woman during pregnancy and the postpartum period.

7.1 Nicotine Replacement Therapy (NRT)

NRT is used to assist with reducing cravings and withdrawal symptoms related to quitting. NRT dosing is gradually reduced over time. NRT is available in the form of a long-acting patch, and short-acting gum, inhaler, spray and lozenge. NRT has been shown to double quit rates in the general population of tobacco users and triple quit rates when two forms of NRT are used in combination.[164]

Efficacy of NRT in pregnancy

Evidence on the effectiveness of NRT in helping women to quit smoking during pregnancy is mixed. The 2015 Cochrane Review by Coleman identified eight studies (2199 participants), which tested the efficacy of NRT among pregnant woman.[28] The pooled analysis found the use of NRT in combination with behavioural support was effective in supporting abstinence in pregnancy (RR 1.41, 95% CI 1.03 to 1.93). However a lower RR was found when only the higher quality of placebo-controlled trials were analysed (RR 1.28, 95% CI 0.99 to 1.66, five studies, 1926 women).[28] Four RCTs, which used NRT patches for smoking cessation in pregnancy for limited hours and behavioural counselling versus placebo NRT patches or only cognitive behavioural counselling, did not find a statistically significant effect on smoking abstinence.[28] The review also examined the use of NRT on maintenance of cessation after birth. A comparison of NRT placebo or non-placebo controlled trials did not find a significant effect of NRT when used alone for smoking cessation six months after childbirth

(RR for cessation with NRT versus placebo 1.15, 95% CI 0.75 to 1.77).[28] Importantly very low adherence to NRT was reported among trials of pregnant woman, which may limit our understanding of the effects of this therapy in this population.[28]

Safety of NRT in pregnancy

The 2015 review by Coleman found no evidence that the use of NRT for smoking cessation in pregnancy had either a beneficial or harmful effect on birth outcomes.[28] This review included six randomized studies that enrolled 2,068 women. The review found that there were no statistically significant differences between NRT or control groups in rates of miscarriage (RR 1.47,95% CI 0.45 to 4.77, four studies, 1782 Women), still birth RR 1.24, 95% CI 0.54 to 2.84, four studies, 1777 women), premature birth (RR 0.87, 95% CI 0.67 to 1.14, six studies, 2048 women), low birth weight (RR 0.74, 95% CI 0.41 to 1.34, six trials, 2037 women), admissions to neonatal intensive care (RR 0.90, 95% CI, 0.64 to 1.27, four studies, 1756 women), or neonatal death (RR 0.66, 95% CI 0.17, 2.62, four studies, 1746 women).[28]

A double-blind study by Oncken and colleagues (2008) found beneficial birth outcomes in the NRT group. Infants of nicotine gum group had greater birth weight than the control group (3287 g and 2950 g, respectively p<.0001) and gestational age was also increased at NRT group than control group 38.9 week and 38.0 week respectively (p=.014).[184] Considering the increased morbidity and mortality, which is associated with low birth weight, these birth outcomes are clinically significant. The above results are consistent with Wisborg et al. (2000) clinical trial about nicotine patches for pregnant smokers.[185] This trial reported a higher mean birth weight (by 186 g 95% CI 35, 336 g) in the NRT group compared with the placebo group.

One of the most recent and largest studies that has been published to date about the use of NRT and the major congenital anomalies (MCA) in offspring involved 192,498 children from the UK. [163] The study found no statistically significant increased risks in the most system-specific MCAs associated with maternal NRT prescribed during pregnancy, except for respiratory anomalies (OR: 4.65 [99% CI: 1.76–12.25].

Risk Benefit to NRT Use

When determining the appropriateness of using NRT for cessation among pregnant women, clinician's should consider both the risks and benefits. While the use of NRT exposes pregnant women to small doses of nicotine, active smoking exposes woman not only to nicotine, but also to numerous other chemicals that are harmful to both the woman and her foetus.[164]

Table 5 provides a summary of international guideline recommendations regarding the use of NRT to support cessation during pregnancy. The general consensus at the present time is that NRT is preferred to continued smoking if the pregnant smoker is unable to quit. Given the absence of clear data to indicate the efficacy of

NRT in supporting cessation among pregnant women it is not recommended as a first line pharmacotherapy.[165] The American College of Obstetricians and Gynaecologists has recommended that the use of NRT during pregnancy should be made after careful assessment and monitoring, and provided that a pregnant woman is determined to quit smoking.[186]

Pregnant smokers should be informed about the risks of continued smoking during pregnancy, as well as the potential risks of using NRT and a decision made in terms of use of NRT based on the risk-benefit.[29] This recommendation is based on the understanding the NRT use is inherently less dangerous than the continuation of cigarette smoking.[166,167]

Given the lack of definite safety and efficacy data, many guidelines have advised limiting the duration of patch use (i.e. 16 hours versus 24 hours) or to use intermittent dosing forms of NRT (i.e. gum, lozenge, spray or inhaler).[18,19,19,29] While this is a logical approach to reducing levels of nicotine, trials, which have tested the use of NRT for limited hours, found no effect on cessation rates.[17] Given that during pregnancy women metabolize nicotine faster, it is unclear whether lower and/or intermittent doses of NRT are effective.[168]

Further research is needed on NRT efficacy and safety, ideally from placebo-controlled RCTs.[17]

RECOMMENDATIONS

- The use of Nicotine replacement therapy (NRT) is preferred to continued smoking during pregnancy. Evidence in terms of its effectiveness among pregnant women is however mixed. As such, NRT can be considered a second-line therapy for pregnant women who are unable to for quit with counselling support alone (Level of Evidence B). The risk and benefits of using NRT should be discussed with pregnant smokers.

TABLE 5: Summary of international clinical practice guidelines regarding the use of nicotine replacement therapy (NRT) during pregnancy and the postpartum period

SOURCE	RECOMMENDATIONS
American College of Obstetricians and Gynaecologists Committee, Opinion No. 471. Smoking cessation during pregnancy. (2010)[186]	"The use of nicotine replacement therapies should be undertaken with close supervision and after careful consideration and discussion with the patient of the known risks. If nicotine replacement is used, it should be with the clear resolve of the patient to quit smoking."
New Zealand Ministry of Health Background and Recommendation of the New Zealand Guidelines for Helping People to Stop Smoking. Providing stop-smoking support to pregnant and breastfeeding women (2014)[76]	Indicates that pregnant or breastfeeding women can use NRT.
US Clinical Practice Guidelines U.S. Department of Health and Human Services. Treating Tobacco Use and Dependence (2008)[164]	"Although the use of NRT exposes pregnant women to nicotine, smoking exposes them to nicotine plus numerous other chemicals that are injurious to the woman and foetus"
CAN-ADAPTT Canadian Smoking Cessation Guideline Version 2.0: Specific Populations: Pregnant and Breastfeeding Women (2011)[169]	"If counselling is found ineffective, intermittent dosing nicotine replacement therapies are preferred over continuous dosing of the patch after a risk-benefit analysis."
UK NICE public health guidance 26 (2010) Quitting smoking in pregnancy and following childbirth (2010)[77]	"There is mixed evidence on the effectiveness of NRT in helping women to stop smoking during pregnancy. Use only if smoking cessation without NRT fails."

7.2 Bupropion

Bupropion is a non-nicotine therapy for smoking cessation available in tablet form, by prescription only. Bupropion has been found to mimic the effect of cigarette-derived nicotine by inhibiting the re-uptake of noradrenaline and dopamine and is thought to reduce nicotine withdrawal also by this mechanism.

There is very limited information regarding the safety and efficacy of bupropion among pregnant women.[17,170,170] There has been only one RCT published about the use of bupropion for smoking cessation during pregnancy, which due to recruitment challenges randomized only 11 pregnant women.[171] Two prospective studies have been published looking at the use of bupropion in pregnancy. A small prospective controlled observational study (n=44) of pregnant smokers who received bupropion and a control group found that 45% of women in the bupropion group quit smoking compared to 14% in the control group (p=0.047).[172] A second prospective comparative study examined pregnancy outcomes among women exposed to bupropion during pregnancy.[173] No statistically significant differences were found between the examined end points of the exposed and non-exposed groups. However, higher rates of spontaneous abortions were documented in the bupropion group (p=0.009). These findings are similar to the safety data available for the use of antidepressants during pregnancy. Further research in this area is needed to better understand the role of bupropion as a cessation aid during pregnancy. At the time of this guidelines preparation there were two trials of bupropion in pregnancy currently under way.[174,175]

RECOMMENDATION

- Bupropion is not recommended for smoking cessation during pregnancy (Level of Evidence C).

7.3 Varenicline

Varenicline is a tablet-based medication that acts on the nicotine receptors in the brain. Varenicline is a partial agonist, offering a two-pronged approach to treating nicotine addiction by reducing the symptoms of nicotine withdrawal, while simultaneously reducing some of its rewarding effects of nicotine use.[176] The medication is typically taken by prescription for 12-26 weeks. While Varenicline is a first line quit smoking medication for the general population of tobacco users, there are currently no trials that report on the safety or efficacy of varenicline use during pregnancy.[17,20,177]

One clinical trial is currently under way to assess the safety of varenicline in pregnancy and to identify the risks of major malformations and other undesirable pregnancy outcomes; this study had not been completed at the time of this guideline's preparation.[176] Further research in this area is needed.

RECOMMENDATION

- Varenicline is not recommended for smoking cessation during pregnancy (Level of Evidence - None).

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