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Modifiable risk factors for stillbirth: a literature review

A stillbirth is defined as an infant born weighing 500grammes and/or more or at a gestational age of 24 weeks who shows no signs of life. Having a stillborn baby has a wide range of consequences that can affect parents, family and the healthcare professionals involved. Several risk factors have been associated with an increased risk of stillbirth: including maternal medical factors, maternal characteristics, fetal factors, sociodemographic factors and behavioral factors. The aim of this work is to review the literature on risk factors that have a behavioral component. The main behaviors modulating the risk of stillbirth that have been more widely studied in the literature include use of substances (smoking, alcohol, illicit drugs and medical drugs), weight management, attendance at antenatal care and sleeping position. There is evidence in the literature that supports that all those behaviors have an impact on the risk of stillbirth, especially in the cases of smoking and drugs consumption during the pregnancy. Hence, more research is needed to establish interventions targeting these behaviors as preventive measures to reduce the risk of adverse obstetric outcomes.

Keywords: stillbirth; modifiable risk factors; pregnant women; health behavior

Introduction

The loss of an unborn child is one of the most devastating life events that parents can face during their lifetime. Having a stillborn baby in a family has a wide range of consequences that can affect the parents, the rest of the family, and even the healthcare professionals involved.

According to the Irish Stillbirth Registration Act (1994), a stillbirth is defined as an infant born weighing 500grammes or more or at a gestational age of at least 24 weeks who shows no signs of life. However, stillbirth is defined differently around the world depending on weeks of gestation and weight; there is no globally accepted definition of stillbirth versus second trimester miscarriage (see Supplementary Table 1). Therefore, the challenge of comparing birth rates and associated risk factors is greater (Page and Silver, 2017; Tavares et al., 2016).

Stillbirths are associated with 2.6 million deaths each year all over the world (De Bernis et al., 2016). Although rates of stillbirth for high-income countries are lower than in middle or low-income countries, 1 in 200 babies will be stillborn and this rate has remained steady since 2000 (*Late Intrauterine Fetal Death and Stillbirth Green-top Guideline No. 55*, 2010). According to the last report published by the National Perinatal Epidemiology Centre in 2016, the rate of stillbirth at >24 weeks gestation or a birthweight of >500grammes was 3.9 per 1,000 births in Ireland (Manning et al., 2018).

There is a wide range of risk factors that have been studied in relation to stillbirth, including maternal medical factors, maternal characteristics, fetal factors, sociodemographic factors and behavioral factors. The purpose of this review is to focus on behavioral factors as they consist of different habits, lifestyles or choices that women make; these are smoking , alcohol and drug consumption, weight management, attendance at antenatal care and sleeping positions. Establishing which risk factors are modifiable and understanding how they can be

changed can help develop prevention strategies to empower women to reduce their own risks of experiencing a stillbirth. This review also gives an overview of some of the evidence available and highlights areas of controversy, serving as a tool for researchers to understand where to focus their efforts (see Table 1). Although this area has been a matter of concern for some time among healthcare professionals, the well-informed groups are very specialized. This review can serve as an informative document for a wider audience, including practitioners in primary care and pregnant women themselves.

To conduct this review, a non-systematic search was performed using different databases such as Pubmed and Google scholar. Relevant articles regarding the different selected risk factors were reviewed and organized using Mendeley, however, the search progressed as the work was being completed. Although there were no timing restrictions, most recent publications were prioritized. The review is organized by sections, each one corresponding to one of the above mentioned risk factors. Each section aims to give an overview of the evidence in relation to specific risk factors for stillbirth. Evidence regarding early miscarriage or other types of perinatal loss are not included, as it is not within the scope of this review.

Table 1. Summary of the evidence exposed in this

Associated with stillbirth/ Not recommended	**No association/ Recommended**	**Conflicting evidence**
Smoking Active smoking Passive smoking Ever smoking Highest influence in first trimester Higher amounts increase the risk **Alcohol and illicit drug use** High amounts increase the risk	**Prescription drugs** Prescription nausea medication Prescription pain medication **Herbal and dietary supplements** Iron folic acid **Sleep position** Sleeping on the left side Maternal snoring	**Alcohol and illicit drug use** Small amounts of alcohol **Prescription drugs** Acetaminophen Aspirin Antihistamines Selective Serotonin Reuptake Inhibitors **Herbal and dietary supplements**

Use of any illicit drugs **Prescription drugs** Migraine medication on second trimester. Ultrasound exposure on first and second trimester Naproxen **BMI** Unbalanced energy and protein dietary supplementation BMI over 25 Severity of overweight increases the risk **Sleep position** Sleeping on the back Sleeping on the right side Supine sleep position Not getting up to the toilet or just getting up once during the last night of pregnancy Regular daytime sleep **Attendance to antenatal care** Attending 50% less than the recommended visits. Decrease in the number of visits increases the risk	Daytime sleepiness **Attendance to antenatal care** At least four antenatal visits during pregnancy	Herbal remedies (ginger, cranberry, raspberry, chamomile, peppermint) Vitamin C Vitamin D **Attendance to antenatal care** Gestational age at first booking **Sleep position** Sleeping less than 6h per night

Smoking

Smoking is one of the risk factors associated with stillbirth that has been widely studied and has been associated with an increased risk of stillbirth (see Table 2). Hyland et al. found suffering a stillbirth is 1.44 times more likely for women who were ever-smokers than for women who were never-smokers. Furthermore, these authors also concluded that never-smoking women exposed to passive smoking showed a 22% increase in the odds of experiencing a stillbirth compared to never-smoking women not exposed to passive smoking

(Hyland et al., 2014). A meta-analysis conducted by Marufu et al., (2015) found that smoking during pregnancy was associated with a 47% increase in the odds of stillbirth. Accordingly, The Lancet published a different meta-analysis showing that smoking during pregnancy was associated with a 36% increase in the odds of stillbirth and this risk was bigger in smoking pregnant women of 40 years or older (Flenady et al., 2011).

Varner et al. conducted a study to explore the effects of the dose used on the risk of stillbirth. They concluded after their case-control study that increasing amounts of self-reported smoking were associated with an increase in the incidence of stillbirth, being 1.77 times more likely for women who reported smoking 1 to 9 cigarettes per day and 2.17 times more likely for women who reported smoking more than 10 cigarettes per day. (Varner et al., 2014).

Some researchers have tried to study the effect of time of smoking exposure on stillbirth. Dodds and colleages concluded in their study that the effect of smoking on stillbirth was similar in women who quit smoking before 16 weeks of pregnancy and women who continued to smoke after 16 weeks (Dodds et al., 2006). The authors reported that these findings give support to the hypothesis that the first trimester of a pregnancy might be the more susceptible to the influence of smoking in regards to stillbirth, and that cessation pre-pregnancy would be ideal.

Table 2. Characteristics and results from the studies related to smoking

Author	Type of study and population	Objectives	Main outcomes	Results
Hyland et al. (2014)	Cross sectional study 80762 women	Study association between tobacco exposure and pregnancy outcomes	Ever active smokers	OR 1.44 (95% CI 1.20 to 1.73)
			Never active smoker exposed to passive smoking	OR 1.22 (95% CI 1.02 to 1.47)
Marufu et al. (2015)	Meta-analysis including 34 studies	Study the association between maternal smoking and risk of stillbirth	Smoking during pregnancy	OR 1.47, (95% CI 1.37 – 1.57, p<0.0001)
Flenady et al. (2011)	Meta-analysis including 96 studies	Identify priority areas of stillbirth prevention	Smoking during pregnancy	aOR 1.36 (95%CI 1.27–1.46)
Varner et al. (2014)	Case control study 663 stillbirths 1932 live births	Compare illicit drug use and smoking in pregnancies with and without stillbirth	Smoking 1-9 cigarettes a day	OR1.77 (95% CI 1.13 – 2.80)
			Smoking ≥10 cigarettes a day	OR 2.17 (95%CI 1.25 – 3.78)
Dodds et al., (2006)	Population based case control study 105 stillbirth cases and 389 live-births	Identify risk factors for stillbirth and explore possible causes based on time of exposure	Quitting before 16 weeks of pregnancy	HR 2.6, 95%CI 1.5 – 5.8
			Quitting after 16 weeks of pregnancy	HR 2.2, 95%CI 1.2 – 4.1

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Alcohol and illicit drug use

Alcohol and illicit drug abuse have also been studied in association with the risk of stillbirth (see table 3). Ethanol is the most commonly abused substance during pregnancy and it is a recognized public health problem (Doherty et al., 2019). Globally, about 10% of women consume alcohol during their pregnancy (Popova et al., 2017). Aliyu et al. (2008) concluded in their study that more than 3% (N = 120) of cases of stillbirth were associated with mothers that consumed alcohol during pregnancy, with a stillbirth rate of 8.3 per 1000 births versus a rate of 5.3 per 1000 births in the abstinent reference group.

Some researchers have tried to establish a correlation between the amount of drinks consumed and the risk of stillbirth by studying the maximum amount considered safe. Henderson et al. (2007) found in their systematic review and meta-analysis that most of the studies relating alcohol consumption with stillbirth were subject to recall bias; only one article was except from bias as it measured alcohol consumption with a validated questionnaire. These authors concluded that low-moderate levels of consumption were associated with slightly higher rate of stillbirth, but the association was not statistically significant. Similarly, Andersen et al. (2012) found that the adjusted risk of stillbirth was higher as the amount of drinks consumed per week increased, however, their results were not statistically significant.

Illicit drug consumption also has an impact on pregnancy outcomes (see Table 3). The drugs that have been more commonly found to be used during pregnancy besides tobacco and ethanol are cocaine, amphetamines, opioids, marijuana, hallucinogens and toluene-based solvents (Popova et al., 2017). Varner and colleagues concluded in their study that a positive toxicology test for any drug increased the risk of stillbirth almost a 94%, and this risk was more than 3 times higher in women who also reported having used illicit drugs. The most common drug that these authors found was Tetrahydrocannabinolic Acid (THCA), which is the active

component of cannabis, and was significantly associated with a 2.34 times higher risk of stillbirth (Varner et al., 2014).

Table 3. Characteristics and results from the studies about alcohol consumption.

Author	Type of study and population	Objectives	Main outcomes	Results
Aliyu et al. (2008)	Retrospective study 65000 pregnancies	Study the association between maternal alcohol consumption and early stillbirth	Alcohol consumption during pregnancy	aHR 1.4 (95%CI 1.2-1.7)
Andersen et al. (2012)	Cohort study 92719 participants	Assess the risk of fetal death according to maternal alcohol consumption	½ to 1 drink per week	HR 0.90 (95%CI 0.73-1.12)
			2 to 3½ drinks per week	HR 0.88 (95%CI 0.63-1.24)
			4 or more drinks	HR 1.20(95%CI 0.76-2.18)
Varner et al. (2014)	Case control study 663 stillbirths 1932 live births	Compare illicit drug use and smoking in pregnancies with and without stillbirth	Positive toxicology test	OR 1.94 (95%CI 1.16-3.27)
			Women who reported using illicit drugs	OR 3.30 (95% CI 1.54 - 7.03)
			Consuming cannabis	OR 2.34 (95% CI 1.13 - 4.81)

Use of medical drugs and supplements

Prescription and over-the-counter drugs

Some authors have also studied the effects of using medically prescribed drugs, over-the-counter drugs and food or herbal supplements on the outcomes of pregnancy (see Table 4).

A study conducted in Europe, North and South America and Australia reported that almost 80% of pregnant women used at least one drug during their pregnancy, and around 60-70% have reported using at least one over-the-counter medication (Lupattelli et al., 2014). Some of the most commonly drugs used by pregnant women are antihistamines, decongestants, expectorants and antitussives, analgesics and antipyretics, topical creams, antacids and antidiarrheal agents (Mølgaard-Nielsen et al., 2016).

Antihistamines and antiemetics are principally used during pregnancy for the treatment of nausea and vomiting and approximately 15% of pregnant women use them (Li et al., 2013). Following a meta-analysis, Etwel et al. concluded that the risk of stillbirth was not higher for women who had used HI antihistaminic agents during the first trimester. However, the authors did not rule out a possible association between both factors due to a lack of information on the cause of death of the stillborn infants (Etwel et al., 2017).

Other common drugs used during pregnancy are analgesics such as acetaminophen (paracetamol), ibuprofen, naproxen and others. More than 60% of women use acetaminophen during pregnancy, and around half of them do so in the first trimester (Nakhai-Pour et al., 2011).. However, some studies have associated the use of ibuprofen, aspirin, and naproxen with a higher risk of spontaneous miscarriage and other fetal anomalies, especially when used around the time of conception (Hernandez et al., 2012).

According to a study conducted in Canada, around 18% of pregnant women had used psychotropic drugs (antidepressants, anxiolytic/sedative-hypnotics, antiepileptics, antipsychotics, lithium) before, during or after pregnancy, and this tendency has increased significantly over the years. Depression is one of the most common conditions with a prevalence among 7% to 19% in developed countries (Leong et al., 2017).

A population-based cohort study in all Nordic countries first showed that the likelihood of experiencing a stillbirth for women who had been exposed to Selective Serotonin Reuptake Inhibitors (SSRIs) was 25% higher than those who had not. However, when adjusting the data for maternal characteristics, country and year of birth, exposure to SSRIs was no longer significantly associated with higher risk of stillbirth. The authors concluded that the higher rates of stillbirth were likely to be related to the severity of the psychiatric diseases and other risk factors rather than to the exposure to the SSRIs themselves (Stephansson et al., 2013).

Table 4. Characteristics and results from the studies about prescription drugs and over-the-counter drugs.

Author	**Type of study and population**	**Objectives**	**Main outcomes**	**Results**
Pastore et al., (1999)	Case control study 332 stillbirths and infants deaths within 24h after birth 357 control livebirths	Study the association between stillbirth and 14 medical exposures	Migraine medication 2nd trimester	aRR 1.6 (95% CI 1.1-2.3)
Etwel et al. (2017)	Systematic review and meta-analysis 37 studies included	Determine whether exposure to antihistaminic during the first trimester is associated with negative obstetrics outcomes	Stillbirth	OR 1.23 (95%CI 0.48-3.18)
Stephansson et al., (2013)	Population based cohort study 1633877 singleton births, 6054 stillbirths; 3609, neonatal deaths; and 1578 post-neonatal deaths	Study the influence of exposure to SSRIs on the risk of stillbirth	Exposure to SSRI	aOR 1.17 (95%CI 0.96-1.41, P=0.12)

Herbal and Dietary Supplements

Herbal remedies are also widely used during pregnancy for different purposes such as palliating morning sickness, urinary tract infections, nausea or vomiting and hence some authors have tried to establish their safety during pregnancy (see table 5). The amount of pregnant women using herbal supplements ranges from 7% to 55% depending on different geographical, social and cultural settings and ethnic groups (John and Shantakumari, 2015).

Smeriglio and colleagues wrote a review to establish the most used herbal remedies during pregnancy and their potential side effects. The authors concluded that few clinical trials have been performed to assess the safety and efficacy of these remedies. According to the findings of these authors, the most common herbs used during pregnancy are ginger, cranberry, raspberry, chamomile, peppermint and Echinacea (Smeriglio et al., 2014). Although some of these herbs have been classified as safe by the European Medicines Agency, not enough data about their use in pregnancy and lactation is available and they cannot replace medical treatments (Holst et al., 2010). Some of the studies included in their review criticise the use of herbal medicines to treat conditions such as urinary tract infection, as this infection, without the appropriate treatment, could lead to bigger complications and adverse pregnancy outcomes such as stillbirth.

The use of daily multiple micronutrients on the risk of stillbirth has also been studied. Smith et al. (2017) conducted a meta-analysis including 17 randomized controlled trials on the effects of maternal multiple micronutrients supplementations on stillbirth (and other birth outcomes, in low-income and middle-income countries. The authors compared the use of micronutrient supplements containing iron-folic acid against using iron-folic acid only. The results show that the use of micronutrient supplements did not increase the risk of stillbirth (see Table 5).

Table 5. Characteristics and results from the studies about herbal and alimentary supplements.

Author	Type of study and population	Objectives	Main outcomes	Results
Holst et al. (2010)	Literature review	Review the literature on safety and efficacy of the most common used herbal remedies	Safety of different herbal remedies	Not enough data on efficacy of herbal remedies during pregnancy and lactation
Smith et al. (2017)	Meta-analysis 31 Randomised control trials	Identify modifiers on the effect of micronutrient supplements on stillbirth and other birth outcomes	Odds for stillbirth	RR 0.92 (95%CI 0.86-0.99)

The World Health Organization recommends balanced energy and protein dietary supplementation for pregnant women in undernourished populations to reduce the risk of stillbirth in their "WHO recommendations on antenatal care for positive pregnancy experience" report. Use of daily oral iron and folic acid with 30mg to 60mg of elemental iron[b] and 400 g (0.4 mg) of folic acid[c] to prevent maternal anemia, puerperal sepsis and low birthweight is also recommended. On the other hand, the WHO recommends against using zinc supplements, multiple micronutrient supplements, vitamin B6 (pyridoxine) supplements, Vitamin E and C supplements and Vitamin D supplements (World Health Organization, 2016). However, there are discrepancies among the recommendations made by the different health authorities regarding this issue (see table 6).

Table 6. Comparison of the recommendations of four different health authorities.

	Recommended	**Not recommended**
World Health Organization	• Folic acid supplements	• Zinc supplements • Micronutrients supplements • Vitamin B6 • Vitamin E • Vitamin C • Vitamin D
National Institute of Health and Care Excellence (NICE)	• Folic acid • Vitamin C • Vitamin D	• Vitamin A • Iron Supplements
Royal College of Obstetricians and Gynaecologists, London, UK	• Folic acid • Vitamin C • Vitamin D	• Vitamin A • Vitamin E • Vitamin B (other than folic acid)
The American College of Obstetricians and Gynecologists	• Folic acid • Vitamin A • Vitamin C • Vitamin D • Iron	• N/A

Maternal weight

According to the World Health Organization, obesity has almost tripled since 1975. In 2016, 39% of adults were overweight, and 13% were obese (World Health Organization, 2018). Although, the prevalence of overweight and obesity during pregnancy is very hard to establish, an increasing trend similar to the one in the general population has been observed (Huda et al., 2010).

Obesity during pregnancy can cause gestational diabetes and gestational hypertensive disorders, two conditions that have been associated with stillbirth, but obesity is also considered an independent risk factor for stillbirth (see Table 7) (Lawn et al., 2016). However, most women who try to conceive are not aware of these risks (Poston et al., 2016).

Chu et al. (2007) found in their systematic review and meta-analysis that overweight women were 47% more likely to experience a stillbirth than normal weight women, whereas in the case of obese women, the risk of stillbirth was 2.07 times higher compared with the normal weight group.

When examining the risk of stillbirth Yao et al. (2018) found that the hazard ratio (HR) increased significantly as overweight increased in severity but also as the pregnancy progressed (see table 7). The same authors concluded in previous work that almost 20% of the stillbirths included in their study were associated with obesity (Yao et al., 2014).

Table 7. Characteristics and results from the studies about overweight and obesity.**Author**	**Type of study and population**	**Objectives**	**Main outcome**	**Results**	
Chu et al. (2007)	Meta-analysis 6 studies	Summarize the available epidemiological evidence on the relationship between weight and stillbirth	Overweight group	OR 1.47 (95%CI 1.08-1.94)	
			Obese group	OR 2.07 (95%CI 1.59-2.74)	
Yao et al. (2018)	Retrospective cohort study 3279846 births included	Examine the risk of stillbirth with increasing obesity severity and progression of the pregnancy	Overweight group	33-36 weeks	HR 1.41 (95%CI 1.24-1.59)
				37-39 weeks	HR 1.36 (95%CI 1.19 – 1.54)
				40-42 weeks	HR 1.42 (95%CI 1.08-1.86)
			Class I Obesity	33-36 weeks	HR 1.52 (95%CI 1.31-1.75)
				37-39 weeks	HR 1.76 (95%CI 1.52-2.04)
				40-42 weeks	HR 1.95 (95%CI 1.43-2.66)
			Class II Obesity	33-36 weeks	HR 1.62 (95%CI 1.35-1.96)
				37-39 weeks	HR 2.36 (95%CI 1.98-2.82)
				40-42 weeks	HR 2.15 (95%CI 1.41-3.29)
			Class III Obesity	33-36 weeks	HR 1.61 (95%CI1.28-2.03)
				37-39 weeks	HR 2.26 (95%CI 1.80-2.83)
				40-42 weeks	HR 2.53 (95%CI 1.50-4.27)

Sleeping habits

One of the maternal everyday habits that have been investigated for having an effect on the risk of stillbirth are the sleeping practices of pregnant women (see Table 8). Stacey and Thompson (2011) conducted a prospective population-based control-study in New Zealand assessing maternal snoring, daytime sleepiness, and sleep position at the time of going to sleep and on waking (left side, right side, back or other) and the risk of late stillbirth. Snoring, daytime sleepiness and hours of sleep were not associated with higher risk of stillbirth when adjusting for co-founders. However, women who slept during the day regularly had 2.04 times higher risk of having a stillborn baby. Further, not getting up or getting up just once to the toilet during the last night of pregnancy increased the risk of stillbirth 2.42 times

The researchers also found differences in the risk of late stillbirth depending on the maternal sleep position both at time of going to sleep and at time of waking up, especially during the last night of the pregnancy, but also during the preceding month. The risk was higher for those women who did not go to sleep nor woke up on their left side and the authors determined sleeping on the back the least safe position (Stacey and Thompson, 2011). Similar results were found in a different study where the authors also concluded that the risk was higher for term compared to preterm stillbirths (McCowan et al., 2017). This is in concordance with the results from other studies that concluded that women who had a late stillbirth were 2.3 times more likely to have reported a supine sleeping position on the night before their stillbirth (Heazell et al., 2018; Platts et al., 2014)

Warland et al. (2018) undertook a systematic review and meta-analysis exploring the association between maternal sleep during pregnancy and poor fetal outcomes. The authors looked at four different areas of maternal sleeping: disordered breathing, sleep duration, sleep quality and sleep position. According to the authors, all these aspects of maternal sleeping can

be associated with different fetal outcomes such as fetal growth and preterm birth. However, with regard to stillbirth, studies showed that women who sleep less than 6 hours or more than 8 hours per night in late pregnancy have more than an 80% increase in the odds of experiencing a stillbirth (see table X). Furthermore, in accordance with Stacey and Thompson, the attributable risk of supine going-to-sleep position in the studies they included in their meta-analysis ranged between 4 and 37%.

One hypothesis that explains these results associates the mother's sleeping position with cardiac outputs and fetal oxygenation. The pressured exerted by the enlarged uterus over the vena cava and the aorta when lying in a supine or right lateral position could produce a decrease in uterine blood flow and subsequently lead to fetal hypoxia (Jeffreys et al., 2006; McCowan et al., 2017).

Table 8. Characteristics and results from the studies about sleep habits.

Author	**Type of study and population**	**Objective**	**Main outcomes**	**Results**	
Stacey et al. (2011)	Population based control study 155 late stillbirths 310 controls	Determine whether certain sleeping habits are associated with stillbirth	Snoring	aOR 1.12 (95%CI 0.75-1.67)	
			Daytime sleepiness	Epworth sleepiness score 5.9(4.1) for cases and 5.6(3.8) for controls (P=0.51)	
			Hours of sleep	Less than 6h	aOR 1.81, (95% CI 1.14 to 2.88)
				More than 8h	(aOR 1.83 95%CI 1.14-2.94)
			Regular daytime sleep	aOR2.04 (95%CI 1.26 – 3.30)	
			Getting up one or zero times last night of pregnancy	aOR 2.42(95%CI 1.46 – 4.00)	

			Right side sleeping position	aOR 1.74(95%CI 0.98-3.01)	
			Back side sleeping position	aOR 2.54 (1.04 – 6.18)	
McCowan et al. (2017)	Multicentre case-control study 164 late stillbirths 569 controls	Test the hypothesis that maternal non-left and supine going-to-sleep position is a risk factors for stillbirth	Stillbirth at term	aOR 10.26 (3.00 to 35.04	
			Stillbirths pre-term	aOR 3.12 (0.97 to 10.05)	
Warland et al., (2018)	Systematic review and meta-analysis	Summarize current literature on maternal sleep including sleep disordered breathing, sleep quality, sleep duration and supine sleep position	Less than 6h sleep per night	aOR 1.81 (95%CI 1.14 – 2.88)	
			More than 8h sleep per night	aOR 1.83 (95%CI 1.14 – 2.94)	
			Sleep position	Heazell et al. (2018)	aOR 2.31 (95%CI 1.04-5.11)
				McCowan et al. (2017)	aOR 3.67 (95%CI 1.74 – 7.78)
				Owusu et al. (2013)	aOR 8.0 (95%CI 1.5-43.2)
				Gordon et al. (2015)	aOR 6.26 (1.2 – 34.0)
				Lakshmi et al., (2017)	aOR 2.95 (95%CI 1.5-5.8)

Attendance at antenatal care

The World Health Organization currently advises women to attend at least four antenatal visits during their pregnancy (World Health Organization, 2016), when there are no complications. Antenatal care gives healthcare professionals an opportunity to educate women and offer health information, and it is also an opportunity for them to monitor the development of the pregnancy (Tunçalp et al., 2017).

Stacey et al. (2012) conducted a study to examine the role of antenatal care in the prevention of stillbirth in high-income countries. The authors compared cases of women who experienced a late stillbirth with ongoing pregnancies at the same gestational week in which the stillbirth occurred. The authors concluded that gestational age at booking with a prenatal care provider was not associated with higher risk of late stillbirth (see Table 9). However, women who attended less than 50% of the recommended visits, were almost 3 times more likely to suffer a late stillbirth; the authors also found a significant relationship between the decrease in the number of visits attended and the increase in the risk of stillbirth. The researchers also concluded that small-for-gestational-age fetuses were almost 10 times more likely to be stillborn if they were not identified prior to birth than those who had been identified. This means that identifying small-for-gestational-age fetuses could reduce the risk of stillbirth, reinforcing the importance of regular antenatal care attendance (Stacey et al., 2012).

Table 9. Characteristics and results from the studies about antenatal care.

Author	**Type of study and population**	**Objective**	**Main outcomes**	**Results**	
Stacey et al. (2012)	Cohort study 215 stillbirth cases 310 control	Asses the relationship between antenatal care and risk of stillbirth	Gestation age at booking	10-20 weeks gestation	aOR 0.78 (95%CI 0.46-1.30)
				More than 20 weeks gestation	aOR 0.63 (95%CI 0.28-1.39)
			Attending less than 50% of recommended visits	aOR 2.68 (95%CI 1.04 – 6.90)	

Conclusion

Risk factors are crucial in prediction and prevention of stillbirth and raising awareness about them is essential to ensure women are making informed decisions. Smoking, substance

abuse, non-attendance to antenatal care, and sleeping positions have been established as behavioral risk factors for stillbirth and should be taken into consideration in every pregnancy. Behavioral risk factors can be reduced or eliminated through antenatal interventions as a preventive measure before pregnancy, or if necessary, can also be addressed in ongoing pregnancies (Page and Silver, 2017). A study published in the Lancet showed that some behavioral risks associated with stillbirth such as smoking, substance abuse and maternal obesity, were underestimated by healthcare professionals, and also the authors identified a lack of awareness among the wider community (De Bernis et al., 2016). This work summarizes the information regarding the risk factors that can be modified by the mothers, giving healthcare practitioners an opportunity to empower women.

Some of the results included in this review are contradictory, especially the older studies, and should be considered with caution. Some of the limitations found when revising the literature had to do with the difficulties in establishing proper comparisons due to differences in the definitions of stillbirth used. Further, different studies use various methodologies and measure different outcomes.

Another limitation of this review is related to several ethical issues to consider when conducting clinical research with pregnant women. Traditionally pregnant women have been excluded from research as this population are considered vulnerable that need to be protected from the potential risks of participating in research (Blehar et al., 2013). Hence, given pregnant women's exclusion from research trials, there is a paucity of studies which are eligible for inclusion in a systematic review on behavior change interventions targeting these risk factors,

Despite the difficulties mentioned above, it seems clear that there is evidence in the literature supporting the fact that certain maternal behaviors have an impact on the risk of stillbirth.

Smoking and abuse of illicit drugs seem to have the highest impact. In the case of medication and herbal or food supplements, the evidence is not clear, but there is a wide consensus in the literature that more clinical trials are needed to establish the safety and efficiency of their use during pregnancy. Maternal weight is another factor that needs to be taken into consideration when a woman is planning a pregnancy. As seen in the literature, it is not only an independent risk factor, but it can also lead to other risks such as gestational hypertension or diabetes (Bogaerts et al., 2014). With regard to maternal sleeping habits, it seems that avoiding sleeping on the right side might be a simple measure to reduce the risk of stillbirth, being possibly the most easily modifiable behavior among the different ones included in this review. On the other hand, it seems clear that attendance to antenatal care visit is very relevant in the prevention of stillbirth, as it is the only way healthcare practitioners can monitor pregnancies to detect other risk factors and diagnose pregnancy complications.

Despite some reviews and trials being currently conducted, not enough data is available on the efficacy of the preventive interventions established in regards with stillbirth specifically, with this research focusing mostly on sleep position. More research is needed in this area to establish the efficiency of interventions targeting these behaviors among pregnant women as preventive measures with the aim of reducing the risk of stillbirth and other adverse obstetric outcomes.

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Supplementary materials

Agency	Definition
Irish Stillbirth Registration Act	Infant born weighing **500grammes or more** or at a gestational age of at least **24 weeks** who shows no signs of life
MBRRACE-UK Perinatal Mortality Surveillance Report	Baby delivered at or after **24+0 weeks** gestational age showing no signs of life
Wold health organization (for international comparison)	Baby born with no signs of life at or after **28 weeks'** gestation or weighing at least **1000g** or being 35cm length
International classification of diseases 10th edition (WHO)	Fetus that has suffered intrauterine or intrapartum death after **24 weeks** gestation
International classification of diseases 11th edition (WHO)	Early stillbirth is defined as an early fetal death after **22 weeks** gestation and a birthweight of **500gm** or more
European Medicine Agency	Death of a fetus after **22 weeks** of gestation
Centers for Disease control and prevention (USA)	Loss of a baby after **20 weeks** of pregnancy or weighting 350gr.
Australian Institute of Health and Welfare	The birth of a baby who is **20 or more completed weeks** of gestation or of 400 grams or more birthweight who is expelled or extracted from his or her mother and shows no signs of life such as a heartbeat, voluntary muscle movement or pulsation of the umbilical cord

Supplementary table 1. Definitions of stillbirth