

## REVIEW

# A case for preconceptual education programs for women: Integrative review

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## ABSTRACT

Exposure to environmental factors before conception or in the very early stage of the embryonic period, can cause permanent changes in an individual life that can result in the development of chronic illness later in life or be transferred to progeny and hence future generations. Diverse effects of poor diet, alcohol, tobacco consumption, infectious diseases, obesity, anxiety, and depression in pregnancy and fetal origin of adult diseases all are well documented and known. Many of these are preventable or can be modified or treated. The general provision of prepregnancy interventions, however, are neglected by current health system policy. According to the World Health Organization (WHO), 50% of pregnancies worldwide are unintentional. The consequences of this is that embryo exposure to the teratogens can occur weeks before the pregnancy has been detected. Most women modify their risky behavior, such as smoking cessation, reducing alcohol consumption and even alter their lifestyle to a healthier one, such as consuming folic acid and multivitamins, when they learn about their pregnancy, typically around 8-10 weeks of gestational age. By this time, however, women have missed the opportunity of providing a healthy uterine environment for their fetus through the critical stage of the embryonic period. Preconception care is a relatively new concept and provides a unique opportunity to improve maternal health and pregnancy outcomes before pregnancy, through pregnancy, and after birth. Despite the general acknowledgment of the potential valuable impact of preconception care, there are various impediments to implementation of preconception care as part of routine practice in the health system.

**Key Words:** Pre-conceptual, Pre-conceptual care, Preconception counseling, Barriers for preconception, Healthy pregnancy behaviors

## 1. INTRODUCTION

Exposure to adverse environmental factors in the very early stage of fetal development could have life span consequences and induce fetal origin adult disease, such as cardiovascular, neurological, and metabolic disorders in later life.<sup>[1-5]</sup> This is because environmental factors have the potential to alter epigenetic modification through DNA methylation, histone modification and producing of non-coding RNA.<sup>[1,2,4]</sup> Epigenetic alteration prior to, or at conception and during the embryonic period can impact on the relatively large number

of cells, including germline and embryonic precursors of gametes. Consequently, there is a potential for intergenerational transmission of these alterations.<sup>[4]</sup>

Epigenetic modifications during the embryonic period has the potential to alter epigenome, which is irreversible due to epigenome ultra-sensitivity.<sup>[2]</sup> According to the developmental plasticity theory and predictive adaptive response (PDR), the current environmental information is a predictor of the future health for the fetus. The fetus, therefore, attempts to alter the function of the biological system to fit into the

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predicted environment when there is a mismatch between early life environment and later life circumstance. This can result in the development of fetal origin adult disease in later life.<sup>[1-3,6]</sup>

Maternal prepregnancy issues such as obesity, stress, various infections, poor diet, exposure to tobacco, alcohol consumption, certain medications and environmental teratogens are potential hazards to alter the fetal environment and induce a permanent malfunction in the fetal biological systems. These modifications can cause several metabolic and neurological disorders in infants including childhood obesity, attention deficit hyperactivity disorder (ADHD), schizophrenia, autism and low IQ.<sup>[2,7]</sup> There are, therefore, a number of issues that can potentially have an effect on the developing fetus, some of which can be prevented or treated. The aim of this integrative review is, therefore, to provide evidence in support of preconceptional care and the impediments to implementation of such care.

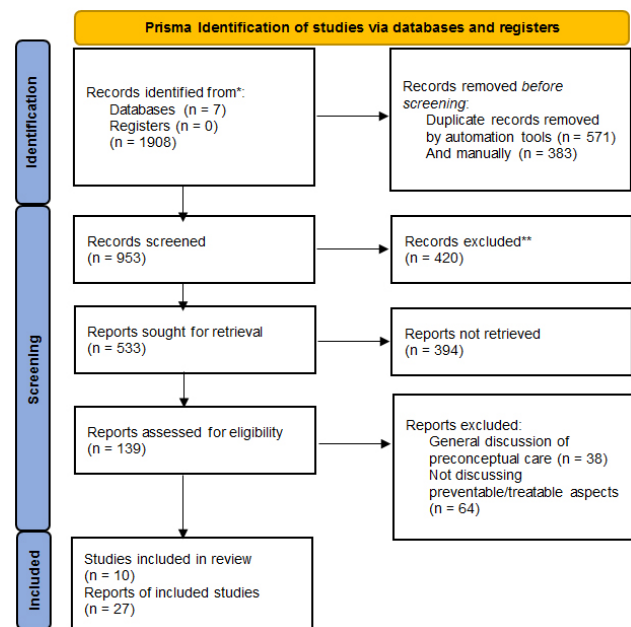
## 2. METHODS AND SEARCH STRATEGY

A theoretical integrative review process was utilized for this paper as it facilitates a comprehensive understanding of this topic by including discussion articles as well as research papers. The literature was gathered using the five step framework outlined by Arksey and O'Malley,<sup>[8]</sup> and more recently Levac et al.'s<sup>[9]</sup> method of synthesising health evidence. To facilitate an integrative review of the literature on this topic, literature was identified from multiple sources, including CINAHL, Cochrane Library, Medline, Pubmed, Science Direct, Scopus, Google Scholar for articles published between 2008 to 2019. The keywords used were preconception, preconception care, preconception counseling, pregnancy, early life intervention, and risky behavior during pregnancy. The search strategy was pursued by assessment of the bibliographies of the relevant articles manually to recognize additional relevant literature not found in the original electronic search. All articles were retrieved for currency and relevance to the topic, in peer reviewed journals and in English and reviewed by the two supervisors. This resulted in 37 articles that provided evidence either in support of preconceptional care or the identification of preventable or treatable environmental factors that could potentially affect the fetus. A content analysis of this literature is presented here. The PRISMA flow diagram below (see Figure 1) shows the results of the search strategy.

## 3. MATERNAL PRE-PREGNANCY TOBACCO AND ALCOHOL CONSUMPTION

Fetal exposure to tobacco and alcohol are two main preventable risk factors than can result in critical adverse effects

on the fetus. Tobacco is one of the leading teratogens with resultant severe adverse impacts on human embryo. Maternal active, or second-hand smoking, is associated with the deposition of thousands of detrimental chemicals in the fetal body.<sup>[10]</sup> This includes nicotine, and carbon monoxide which can have a considerable adverse impact on the developing fetus and placentation process. Tobacco use in early pregnancy is associated with a thickening of trophoblast basement membrane, increased collagen level in mesenchymal villous and reduced vascularization in the placenta. This explains the substantial incidence of fetal growth restriction and miscarriage in pregnancies with maternal active or passive smoking.<sup>[11]</sup> Smoking in early pregnancy, particularly around implantation time, may also intensify the risk of ectopic pregnancy, placenta previa, placenta accreta and fetal orofacial clefts.<sup>[11]</sup> Furthermore, smoking during pregnancy is associated with low birth weight, prematurity in the infant and respiratory conditions such as asthma in children.<sup>[12]</sup> In addition, maternal smoking during pregnancy can be associated with a four-fold increase in the risk of childhood cancer.<sup>[13]</sup>



**Figure 1.** PRISMA flow diagram of literature search

Several studies indicated that successful smoking cessation through pregnancy is not readily attainable. Through preconception care intervention and behavioral therapy in conjunction with nicotine replacement therapy, however, parents are more likely to successfully decrease or cease tobacco smoking and prevent fetal exposure to 4,800 toxicants existing in a cigarette.<sup>[14]</sup>

Alcohol is a well-known teratogen that is capable of inducing an extensive range of developmental abnormalities.<sup>[15,16]</sup> Preimplantation alcohol exposure may induce low placenta and fetal weight.<sup>[16-18]</sup> Alcohol consumption during pregnancy increases the risk of adverse pregnancy outcomes such as fetal growth restriction, neurological disorders, miscarriage, prematurity, birth defects, morphological anomalies and fetal alcohol spectrum disorder.<sup>[16-18]</sup> Fetal alcohol spectrum disorder is a neurodevelopmental disorder associated with in utero alcohol exposure resulting in a wide range of life long neurocognitive difficulties. This includes impairment in learning, memory, intellectual ability, executive functions, and social skills.<sup>[15,16]</sup> This spectrum disorder is more prevalent than any other neurodevelopmental disorder, such as autism spectrum, and is often under recognised and under diagnosed.<sup>[15,16]</sup> The available body of evidence is signifying that there is no safe level of alcohol consumption during pregnancy. Hence, it is strongly recommended that women entirely abstain from ingesting alcohol throughout pregnancy.<sup>[15,19]</sup>

#### 4. MATERNAL NUTRITION STATUS THROUGH PRECONCEPTION PERIOD

Nutritional evaluation and recommendations are fundamental constituents in preconception counseling. Following a healthy and balanced diet, consumption of an adequate amount of vitamins and mineral supplements and folic acid, such as specific preconception or pregnancy multivitamins, may reduce the incidence of congenital neurological disorders and birth defects such as neural tube defects and orofacial clefts remarkably. Furthermore, a balanced diet could improve pregnancy outcomes predominantly for the women and fetus.<sup>[2,20,21]</sup>

Of greater concern is the impact of a maternal diet with excessive saturated fatty acids, and high level of glucose. These are elements that potentially can increase the risk of neonatal large for gestational age and possibility of developing childhood obesity, adulthood obesity, hyperlipidemia, hyperglycemia, and cardiovascular disease later on in life.<sup>[22,23]</sup> Maternal pregravid obesity, therefore, could generate fetal origins of adult diseases such as cardiovascular disease, type 2 diabetes, renal diseases, and metabolic disorders which could effect the quality of life of the offspring in later life.<sup>[2,20]</sup> This is because maternal pregravid obesity and exposure to obesogenic factors could induce an epigenetic alteration in a developing embryo. Epigenetic alteration processes such as DNA methylation and histone modification alleviate gene transcription modulation and modify the phenotype of the developing embryo irreversible.<sup>[1,2,4]</sup> These processes can affect the developing embryo in early life and

also have an effect on gene expression and phenotype outcomes lasting for a lifetime.<sup>[1,2,24]</sup> Furthermore, maternal prepravid high BMI and excessive gestational weight gain are independent factors from each other, and might induce a high birth weight infant (large for gestational age) and can cause an intergenerational cycle of obesity, due to the epigenetic modification that converts the phenotype over time.<sup>[1,2,23,24]</sup> In addition, data suggests that maternal prepravid obesity escalates adiposity in the offspring and maternal high free fatty acid and glucose concentration can alter appetite control, neuroendocrine action, and energy metabolism in the developing fetus.<sup>[1,2,24]</sup> There is also strong evidence that neonatal low birth weight and fetal growth restriction are associated with increasing risk of childhood obesity. These have the potential to increase the risk of coronary heart disease, type 2 diabetes, stroke, osteoporosis, high blood pressure and metabolic disorders later on in adult life.<sup>[1,23]</sup>

The other side to this is the risks for the women. It is estimated that about two-third of women of childbearing age are overweight or obese, worldwide.<sup>[1,23,25]</sup> There is evidence to indicate that obstetrical complications are three times greater in obese pregnant women compared with women who have a healthy BMI. For instance, maternal prepravid high BMI and excessive gestational weight gain (GWG) could induce serious pregnancy complications such as preeclampsia,<sup>[23]</sup> fetal insulin resistance,<sup>[1]</sup> and hypertensive in pregnancy.<sup>[1,2,4]</sup> Hypertensive diseases of pregnancy, particularly, severe preeclampsia, and eclampsia, may in turn increase low birth weight infants.<sup>[1,2,4,23]</sup>

There is also a risk of labour issues including failed induction, fetal distress and increased caesarean sections with maternal obesity. For the neonate whose mother was obese, they are at increased risk of prematurity, congenital abnormalities such as neuro tube defects and stillbirth.<sup>[23]</sup> Maternal preconception obesity is also the strongest risk factor for excessive gestational weight gain and postpartum weight retention.<sup>[1]</sup> According to Skouteris et al.<sup>[23]</sup> 25% of women retain at least 5 kg of pregnant weight gain for at least 12 months. This is a strong predictor of maternal overweight long term and development of associated conditions such as type 2 diabetes and cardiovascular disease.

#### 5. MATERNAL PRE-PREGNANCY INFECTION DISEASES

Various infections during pregnancy may increase the risk of congenital malformations, neurological damage or perinatal death. For instance, maternal viral or bacterial infectious diseases during pregnancy such as influenza, Herpes simplex virus, rubella, urinary tract infection and also sexually

transmitted diseases have the potential to increase the risk of schizophrenia and mental illness in the offspring.<sup>[2,7]</sup> There is also evidence to suggest that maternal viral infections in the first trimester can increase the risk of autism in offspring. These studies indicated that maternal treatment, or at least control of infectious diseases prior the pregnancy, may reduce the risk of neuropsychiatric disorders like schizophrenia (30%) and autism significantly.<sup>[7,26]</sup> Prevention and preconception screening for infectious diseases provides an opportunity to improve maternal health and prevent transmission of infectious diseases before the adverse events arise.<sup>[26]</sup>

There are also a number of infections that could significantly increase newborn morbidity and mortality if they occur during pregnancy. One of these is rubella that if contracted during early pregnancy can cause congenital rubella syndrome as a result of inhibited cell division in embryonic eyes, ear, heart and brain. If this infection is contracted after the first trimester, the most common defect is deafness.<sup>[26]</sup> All women in the childbearing age should be screened for rubella immunity, and vaccinations should be offered to all non-pregnant women who are not entirely immune. Women who receive rubella vaccination should be counselled regarding when to conceive and that a reliable form of contraception be used for the next three months to prevent infection.<sup>[26]</sup> Vaccination during pregnancy is contraindicated because of the risk of the vaccine being teratogenic.<sup>[26]</sup>

Hepatitis B virus is a potentially serious infection that can affect the liver. The aim of Hepatitis B screening antenatally and use of maternal vaccination is to prevent vertical transmission. This then eliminates the risk of perinatal infection and sequelae, including hepatic failure, liver carcinoma and death. In addition, vertical transmission to the fetus may result in an infant who will be a chronic carrier.<sup>[26]</sup>

Listeria if contracted during pregnancy can result in congenital infection with severe consequences, such as miscarriage, amnionitis, preterm labour, fetal distress and stillbirth. Listeriosis is a foodborne infection caused by Gram-positive bacterium *Listeria Monocytogenes*.<sup>[26]</sup> Women need to avoid food such as fresh soft cheese made from unpasteurized milk, delicatessen meats, hot dogs, pate and left over foods to prevent an infection during the first trimester of pregnancy.<sup>[26]</sup>

Toxoplasmosis is found in dog and cat faeces and uncooked meat. During pregnancy a toxoplasmosis infection could cause congenital infection through transplacental transmission. Fetal toxoplasmosis could increase the risk of hepatosplenomegaly, stillbirth and severe neurological disorders such as microcephaly, and hydrocephaly.<sup>[26]</sup> Women need to cook meat to a sufficient temperature, wash fruit and vegetables, wash hands thoroughly afterwards, and stay away from

cat litter to prevent infection.<sup>[26]</sup>

Cytomegalovirus (CMV) is another infectious maternal disease that could cause congenital infection through transplacental transmission of the virus. This virus is the most common cause of intrauterine viral infection and sensory neural deafness. Maternal primary or secondary infection could cause congenital CMV. Fetal CMV infection could increase the risk of fetal growth restriction, microcephaly, hepatosplenomegaly, petechiae, jaundice chorioretinitis, thrombocytopenia and anaemia.<sup>[26]</sup> If a neonate is born with CMV symptoms the prognosis is usually poor.<sup>[26]</sup> The other risks if CMV is contracted during pregnancy are miscarriage, and stillbirth. Prevention is key and involves washing hands after touching any infant utensils or toys and cleaning surfaces, not sharing cups, toothbrushes and not putting infant pacifier into the mouth.<sup>[26]</sup>

Sexually transmitted infections (STI) are significant health issues globally. The infectious diseases such as syphilis, gonorrhoea, Human Papillomavirus (HPV), chlamydia, herpes simplex and human immunodeficiency virus (HIV) during pregnancy could increase the incidence of significant congenital anomalies and adverse pregnancy outcomes.<sup>[26]</sup> This includes ectopic pregnancy, miscarriage, low birth weight, stillbirth, and of course perinatal infection. HIV can be transmitted to the fetus/baby from the mother but the risk can be reduced if the infection is diagnosed prior to birth. For the neonate HIV can lead to AIDS.<sup>[26]</sup>

COVID-19 infection if contracted in pregnancy and women develop pneumonia, can result in preterm birth and fetal growth restriction. There is also evidence of increased risk of caesarean section birth and preterm birth. Though preterm birth is believed to be more iatrogenic where clinical staff deliberately birthed the neonate for maternal indications. There is no evidence of vertical transmission of COVID-19.<sup>[27-29]</sup>

## 6. MATERNAL MENTAL HEALTH

There is evidence indicating that women of reproductive age are at a higher risk of stress, anxiety and depression.<sup>[30]</sup> Through a population base study, it has been revealed that more than 13% of women in the childbearing age suffered from a mental health disorder.<sup>[30,31]</sup> Poor maternal mental health status during the preconceptional period is the most significant risk factor to intensify antenatal and postnatal depression<sup>[30]</sup> and for adverse pregnancy outcomes such as low birth weight, fetal growth restriction, operative births and stillbirth.<sup>[30,31]</sup> It is estimated that one in ten women suffer from antenatal or postnatal depression.<sup>[30]</sup> Maternal antenatal and postnatal depression could also increase the risk of suicide and infanticide.<sup>[30]</sup> Furthermore, maternal depres-

sion could have long-term implications on child neurodevelopment due to the resultant poor attachment and bonding between the mother and infant.<sup>[30]</sup> In addition, a history of postnatal depression could increase the risk of depression during the antenatal and postnatal period in subsequent pregnancies.<sup>[30]</sup>

Maternal psychological stress, anxiety, socioeconomic adversity and intimate partner violence may all increase the incidence of preterm labour.<sup>[30,31]</sup> The preterm labour could be the result of uterine hyperactivity in response to excess cortisol that is secreted from maternal adrenal gland resulting in the women going into labour early.<sup>[30,31]</sup> Poor preconception mental health is a relatively modifiable risk factor that could be treated through counselling, mindfulness, yoga, medication, and exercise.<sup>[30,31]</sup> Preconception care could, therefore, create a unique opportunity to intervene and enhance future pregnancy outcomes.

Furthermore, stress during pregnancy releases cortisol and is shown to lead to a higher risk of infants having malnutrition, neurological disabilities, low body weight and insecure attachment. This in turn is shown to impact negatively on neurobehavioural and cognitive development of the child.<sup>[30]</sup>

## 7. OTHER RISK FACTORS

There are a number of other risk factors that has the potential to affect the developing fetus. For instance, maternal chronic disease can play a critical role in preconception care. Chronic disorders such as pre-existing hypertension, pre-existing diabetics (type 1 and 2), thyroid dysfunction, cardiac disease, epilepsy, and rheumatoid arthritis may have an adverse effect on pregnancy outcomes.<sup>[32]</sup> In addition, some medications that the women is taking for these disorders may have a life changing influence on offspring and can cause birth defects such as anti-convulsion medicine, antidepressants, and anti acne drugs.<sup>[33]</sup> Women with chronic disorders such as these, therefore, would benefit from having their medications reviewed and trying as much as possible to maximise their health prior to conception in order to decrease adverse events occurring.<sup>[32]</sup>

It is evident from what has been written above, that the first eight weeks of life (embryonic period) plays a crucial role in human development. It is estimated, however, that more than fifty percent of pregnancies worldwide are unplanned.<sup>[17,32]</sup> Consequently, embryo exposure to the teratogens can occur weeks before pregnancy has been detected. In addition, despite advances in accessing antenatal care and improvements in the care provided, there has been no reduction in the incidence of congenital anomalies, preterm birth and maternal mortality rates observed in many countries. This

indicates the inadequacy of relying on antenatal care to improve pregnancy outcomes.<sup>[34]</sup> Most women modify their risky behavior, such as smoking cessation, reducing alcohol consumption and even alter their lifestyle to a healthier one, such as consuming folic acid and multivitamins, when they learn about their pregnancy, typically around 8-10 weeks of gestational age. By this time, however, women have missed the opportunity of providing a healthy uterine environment for their fetus through the critical stage of the embryonic period.

## 8. PRECONCEPTION CARE

Early life intervention can have a significant impact on alleviating the risk of adverse pregnancy outcomes. Most of teratogens and risk factors can be identified and treated during the preconception period, and therefore, may reduce neonatal and maternal mortality and morbidity rates.<sup>[1,4,34]</sup> The main aim of preconception care is to identify and modify potential risk factors that can lead to adverse pregnancy outcomes. There is evidence to suggest that any intervention for improving the pregnancy outcome before conception and overall education of childbearing age women regarding healthy lifestyle behaviors can be very effective.<sup>[34,35]</sup> Women during the preconception period are usually more motivated for lifestyle modification, and probably this span of life is an excellent opportunity for alteration of lifestyle generally with implementation of regular exercise on a daily base and a healthy nutritional intake.<sup>[5,36]</sup>

It would appear, therefore, that implementation of a sensible lifespan reproductive plan for everyone in the childbearing age, with the provision of practical recommendation and education of utilization of an effective contraception method to establish their desirable family planning, has a positive impact on general public health. In general, unplanned pregnancies have the potential to be complicated with maternal preexistent health issues such as hypertension, dental disease, infections, nutritional status, overweight and obesity, asthma, tobacco smoking, alcohol consumption, cardiac diseases, and mental health disorders.<sup>[34,35]</sup> Through preconception counseling, women have an opportunity for the provision of health evaluation and receive inspirational education to utilize these recommendations in everyday life.

## 9. BARRIERS TO IMPLEMENTATION OF PRECONCEPTION CARE

There is evidence that preconception care can have a positive effect on maternal and neonatal health.<sup>[35]</sup> However, health care professionals rarely has any opportunity to deliver preconception care to the target population. Future mothers do not usually seek pre-pregnancy advice, and most of the

insurance companies do not reimburse for it.<sup>[37]</sup> Currently, pre-conceptual care is undertaken through the general practitioner on an informal basis, and often antidotally, that is advising women to change medications if she wants to get pregnant. A qualitative Australian research study<sup>[37]</sup> has revealed that there are several impediments for delivery of preconception care counseling through general practitioners in Australia. Principally, a time restriction is reported as a major obstacle to the delivery of preconception care through a general practitioner. In addition, primary care providers believe that there are numerous preventive care issues which are more threatening than preconception care. This is a reflection of the lack of health professional awareness about the importance of preconception care and the consequences if not addressed. Furthermore, lack of resources for primary care providers and target populations was mentioned as additional barriers.<sup>[37]</sup>

Financial barriers have been suggested as impediments that have a powerful influence for prevention of preconception care practice.<sup>[35,37]</sup> Women have to pay to attend any preconceptional sessions. Therefore, modifying public health cover system, for instance by allocation of an extended time frame for delivery of preconception care, modifying health cover insurance policy and also the direct delivery of preconception screening and intervention through public health system can assist with this limitation.<sup>[35,37]</sup>

The lack of sufficient volume of clinical controlled trials in preconception care could be viewed as another impediment to implementation of routine preconception care in clinical practice.<sup>[1,37]</sup> Strong evidence from clinical trials can manifest the effectiveness of preconception care, and its efficacious impact on maternal and offspring health and pregnancy outcomes to persuade health policy planners to facilitate implementation of preconception care. Furthermore, a manifestation of how routine practice of preconception care can be cost effective, ultimately can impress executing preconception care policy in the health system.<sup>[35,37]</sup> Evidence-based studies can convince decision makers and insurance companies that preventive strategies, such as preconception care can effectively reduce maternal and neonatal mortality and morbidity and be cost effective. Sadly, there are only a limited number of clinical controlled trials in the area of preconception care.<sup>[35,37]</sup> The implications accentuate the researchers role, therefore, to conduct sufficient evidence based research to demonstrate efficacious of effective preconception care to promote women's health and improve pregnancy outcomes.

Lack of consumers awareness of existence and potentially need for preconception care and counseling service has also been identified as a barrier for implementation of preconception care practice.<sup>[35,37]</sup>

The main challenge for the delivery of preconception care, however, is the necessity to modify unhealthy lifestyle and transform attitudes and behaviors of targeted people at least a few months before pregnancy.<sup>[1,38]</sup> Preconception care policy needs to be considered in promoting public consciousness regarding reproductive health and parturition risks.<sup>[39]</sup> There has been suggestions that age appropriate education as part of curricula in school health programs can be a useful tool. Also engaging with media partners to cooperate in delivering the message that having a lifespan reproductive plan can help reduce potential adverse events during childbearing.

Insufficiency of primary care provider education regarding pre-pregnancy risk assessment have been reported in several studies as major barriers to preconception care delivery.<sup>[34,35,37]</sup> There is a need, therefore, for developing and implementing preconception care content in specific courses at undergraduate and postgraduate levels which would be a useful tool for improvement of health professionals skills for delivery of preconception care for the public. It has been recommended that consolidation and dissemination of current guidelines can be an effective technique for implementation of preconception care practice.<sup>[37]</sup>

## 10. CONCLUSION

Despite substantial evidence of efficacy of preconception care strategy to improve maternal and neonatal health and reduce adverse pregnancy outcomes; there is a considerable gap between implementation of preconception care as a routine clinical practice. A few barriers were identified, but still, there is a need for more evidence-based research to address issues and limitations in this area. There is a need to provide education to healthcare practitioners and identify best practice and the most effective means of providing integrated preconception services.

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## CONFLICTS OF INTEREST DISCLOSURE

The authors declare that there are no conflicts of interest with the work in this article.

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