Effects of Smoking vs. Nicotine Replacement Therapy during Pregnancy on Childhood Health

Outcomes: An Integrative Literature Review

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Abstract

**PICOT:** In pregnant women does the use of nicotine replacement therapy compared to smoking during pregnancy reduce the risk of future childhood health concerns?

**Methods:** A search was conducted on healthcare literature databases (Alt HealthWatch, AMED, CINAHL, and Medline). The initial search yielded 940 results related to the topic. Initial review narrowed the search to 25 articles. Articles were excluded if published before 2008. After reviewing the full articles and evaluating effectiveness of the studies, 12 studies met the criteria. These 12 articles focused on the effects of smoking and childhood outcomes, NRT, and success of NRT.

**Findings:** The articles concluded that NRT may aid in positive health outcomes since it excludes the risk factors associated with carbon monoxide and other carcinogens found in cigarettes. The NRT still delivers significant levels of nicotine exposure to the fetus and leads to pregnancy complications ending in low birth weight and preterm birth.

**Recommendations:** Further studies should be conducted on the effects of nicotine and NRT especially on birth outcomes and future childhood health concerns.

**Key words:** pregnancy, maternal smoking, nicotine replacement therapy, nicotine, childhood health concerns, childhood obesity
Effects of Smoking vs. Nicotine Replacement Therapy during Pregnancy on Childhood Health Outcomes: An Integrative Literature Review

Smoking during pregnancy is a worldwide issue. However, little is known about whether new forms of Nicotine Replacement Therapy (NRT) are safe for the fetus. According to the North Carolina Department of Health and Human Services (NCDHHS), approximately 10.6% of women smoke while they are pregnant (NC DHHS, 2013). Smoking during pregnancy can lead to many complications such as premature birth, low birth-weight, and stillbirth. Complications due to maternal smoking include Sudden Infant Death Syndrome (SIDS), poor lung development, obesity, and respiratory infections (CDC, 2011). The costs of the required neonatal care for these issues are estimated to be more than $350 million per year. Furthermore, smoking while pregnant may lead to growth retardation as well as increased risk of childhood obesity. Carbon monoxide and nicotine interfere with fetal oxygen supply. This nicotine easily crosses the placenta (NIH National Institute on Drug Abuse, 2014).

**Background**

**PICO Question**

The purpose of this review is to examine whether NRT reduces the risk of childhood health concerns as opposed to cigarettes. The PICO question is as follows: In pregnant women (P) does the use of Nicotine replacement therapy (I) compared to smoking (C) during pregnancy reduce the risk of future childhood health concerns (O)?

**What is already known about this topic:**

- Smoking during pregnancy can lead to premature birth and low birth weight (LBW) (Coleman, Chamberlain, Cooper, Leondardi-Bee, 2010).
• Nicotine use during pregnancy causes decreased blood perfusion to the fetus leading to increased fetal heart rate (Gaither, Brunner, Thompson, Huet-Hudeson, 2008).

• Cessation of smoking during pregnancy is the most effective defense to prevent smoking related birth defects, preterm labor and future childhood health concerns (Wang, Mamudu, Wu, 2012).

What this topic adds:

• Knowledge of the effects of NRT use during pregnancy

• Risk factors at birth related to maternal smoking that influence future childhood health concerns.

• Maternal smoking behavior during pregnancy that determines the likelihood of future childhood health concerns.

RN Interview

Two current certified Obstetric Registered Nurses were interviewed for the study. The initial RN interviewed works on a Labor and Delivery care unit. Questions asked were, “What types of Nicotine Replacement Therapy do they see used by pregnant smokers? What effects do the women and baby present during pregnancy and after birth?” The RN talked about the clinical effects often seen on the fetus. She stated that nicotine causes increased fetal heart rate related to the decreased blood flow to the placenta, due to the overall maternal systemic vasoconstriction. The increased fetal heart rate is seen on the fetal heart monitor. Mothers who use NRT during pregnancy most often use the patch form. These patients will wear a patch on admission due to restrictions on leaving and entering the care unit once admitted. Often these patients will remove the NRT patch and leave the unit without RN knowledge to smoke a cigarette. Once the patient returns to the unit, she will put the patch back on. This combination of
cigarette acquired nicotine and NRT causes extreme, prolonged elevations in the fetal heart rate. This elevated exposure to nicotine can lead to many infant complications. The interviewed RN stated that it is difficult to evaluate the effects of NRT treatment on these patients and the fetus. This difficulty is due to patients often starting the NRT treatment in the last days of pregnancy, usually improperly.

The second interview was conducted with a Newborn Intensive Care Unit (NICU) RN. She was asked the same questions as the previous RN. She stated that in the NICU the effects of nicotine use are seen frequently on the infants. The RN stated that most newborns whose mothers smoke are born small for gestational age (SGA), have low birth weights and have increased heart rate for prolonged periods. These infants often have nicotine withdraw in the NICU. This withdraw is due to an addiction, caused by nicotine crossing the placenta to the fetus in utero. The nurse also stated that many nicotine using mothers often abuse other illicit substances along with high-risk lifestyles. Many of these mothers are non-compliant with NRT. Both nurses concurred that a key issue with NRT treatment is lack of adherence to the regime by the mothers.

**Methods**

**Aim of the Study**

The aim of this review was to evaluate the effectiveness of NRT compared to smoking while pregnant on respiratory complications and obesity as specific childhood health concerns.

**Search Strategy**

A search was conducted on healthcare literature databases (Alt HealthWatch, AMED, CINAHL, and Medline). Keywords used were Pregnancy, Maternal Smoking, Nicotine Replacement Therapy, Nicotine, Childhood Health Concerns, Childhood Obesity.
Findings

Search Results

The initial search with keywords yielded 940 results related to the topic (Figure 1). Initial review narrowed the search to 25 articles. Exclusion criteria were applied to the remaining articles. Articles were excluded if published prior to 2008, used a non-human test population, or had a small or inadequate sample size. After reviewing the full articles and evaluating effectiveness of the studies, 12 studies met the criteria. These 12 articles are used. Papers included in this review met the following inclusion criteria: articles published between 2008 and 2014, focused on fetal health concerns, childhood health concerns, NRT use and maternal smoking effects during pregnancy.

Article Synthesis & Critique

Each article was reviewed and synthesized as shown on Table 2.

Risks related to maternal smoking during pregnancy. Babies who were subject to smoking by the mother during pregnancy and were carried by obese mothers were found to be born with low birth weight and were small for gestational age (SGA). These babies were then found to have rapid weight gain during their first year of life. This rapid weight gain continued to affect the infant’s metabolism and lipoprotein storage. Followed from birth until age eight, these children had an increase in total-to-HDL cholesterol ratio. These children also had a significantly increased BMI level ($P<.0001$) compared to their counterparts. Clinically this adds perspective to the rapid obesity rise in children.

The limitations and weaknesses of this study were that the blood samples obtained were not drawn during a fasted state for the child. The child could have eaten anytime before the study, causing an alteration to the consistent cholesterol levels in their blood. Despite the
limitation and weakness, the study conducted used a large sample size with defined circumstances for each individual factor examined (Bekkers et al., 2011).

**Risks of maternal NRT use during pregnancy.** Gaither et al. investigated whether NRT was associated with adverse pregnancy outcomes. They used logistic regression to obtain odds ratios (10%) and 95% confidence intervals to identify factors. They discovered that of the women who were prescribed or recommended NRT during pregnancy, 13.05% had low birth weight infants while only 9.26% participants dropped out due to adverse side effects of NRT. Their findings did not prove that using NRT while pregnant is safer than smoking. Similar results were seen with preterm birth. In this study, 17.54% of women using NRT, 10% of smokers, and 9.42% of nonsmokers had preterm births. Women using NRT had twice the risk of low birth weight babies compared to nonsmokers. Smokers had 1.31 times the risk. The results were from self-reports from the mothers. The study stated that the negative test results may have been related to frequency of maternal smoking, poor adherence to NRT, pre-existing health concerns, or use of NRT in addition to smoking. These variables as well as pre-pregnancy BMI and maternal weight gain were factors that were not originally accounted for during this study (Gaither et al.).

In utero, the fetus receives nicotine from the NRT. Nicotine passes across the placenta and accumulates in the placental tissue and amniotic fluid. The fetus cannot metabolize the nicotine as efficiently as the mother can. Nicotine buildup causes decreased oxygen to the fetus and impaired fetal growth. The maternal body can sense the impaired fetal growth and may see the baby as nonviable, which can contribute to the low birth weight and preterm delivery.

Limitations of this study were that NRT was used incorrectly or not at all, self-report was incorrect, and unknown factors of NRT itself. This study concluded that further studies on
adverse effects of NRT should be conducted. Also, greater emphasis should be placed on smoking cessation during the pre-conception time to avoid complications from smoking altogether (Gaither et al.).

The benefits of NRT on birth outcomes. A randomized control trial by Oncken et al. looked at the effects of NRT on birth outcomes. The study found that newborns whose mothers used nicotine gum and attended individualized behavioral counseling were found to have increased birth weight ($P<.001$) and increased gestational age compared to the placebo group ($P<.014$). The mothers using NRT compared to the placebo group had relatively even quit rates that were found non-significant. The team of researchers also found that different concentrations of the components of cigarettes were less concentrated in the NRT group compared to the placebo group. Clinically this study compares the use of NRT to no NRT intervention for the well-being of the fetus. The concept of replacing cigarettes that contain multiple carcinogens with a nicotine only component is seen by this study as an aid in fetal weight and gestational age at birth; a factor that can determine future health concerns.

The limitations of this study were the small sample size. The strengths of this study were the aspect of providing not only physical NRT replacement but providing mental and behavioral counseling as well (Oncken et al., 2008).

Coleman et al. wanted to determine the efficacy and safety of NRT use during pregnancy. They conducted 5 trials and the pooled risk ratio (RR) was 1.63 (0.83, 1.65) with a 95% confidence interval (CI). They determined that efficacy estimates varied with trial design (placebo/ non-placebo). Five of the seven safety outcomes were more positive with babies born to women who used NRT. However, none of the differences between trials reached statistical significance. Birth outcomes were more desirable in regards to birth weight among infants born
to women who used NRT while pregnant. Adherence to NRT was low, but there was some evidence for safety and effectiveness of NRT for smoking cessation during pregnancy (Coleman et al.)

**Summary of Critique & Synthesis**

Table 2 summarizes the finding in each one of the articles used in this paper.

**Discussion**

**IOWA Model**

The Iowa Model of Evidence-Based Practice to Promote Quality Care (Titler et al., 2001) was used to provide direction for this study. Problem focused and knowledge focused triggers were identified. The effects of smoking and NRT on childhood health outcomes were identified as a priority for nursing. A team was formed and relevant literature and research was assembled. Each relevant article was critiqued and synthesized for use in practice. Following the critique and synthesis, it was discovered that there is not an adequate research base.

**Study Limitations**

The limitations to this study were the lack of primary literature within the past five years (2008-2014). The lack of studies done on the effects of NRT on the fetus and future health concerns was another limitation. Lastly, the effects of nicotine on the development of the fetus and risk for childhood health concerns related to birth outcomes.

**Recommendations**

Based on the evidence reported in the literature, NRT as a single solution is not an effective method for smoking cessation. Women seeking smoking cessation before or during pregnancy need more intensive behavioral support in addition to NRT to prove more effective. Combination NRT was also shown to improve quit rates. However, NRT still delivers nicotine to
the fetus and can cause complications. Complete smoking cessation would be most beneficial to fetal and maternal health. There was inadequate research on the future health of children born to mothers who smoked during pregnancy. There was also very little research done on NRT itself and the effects it has on the fetus. Further studies should be conducted on the effects of nicotine and NRT especially on birth outcomes and future childhood health concerns.
References


Figure 1 - Search Strategy Methods

Database Search
- Alt HealthWatch: 1
- AMED: 2
- CINAHL: 855
- Medline: 82
  n=940

Removal of Duplicates

Removal based on title and abstract

Total
n=25

Screening of full articles

Reasons for Exclusion
- Non-human test population
- Year of publication prior to 2008
- Small sample size

Total Remaining
n=12
Table 2: Synthesis of Articles

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample Size, Study design, purpose and setting</th>
<th>Level of Evidence</th>
<th>Factors that may lead to NRT being protective in fetal development and health future concerns</th>
<th>Factors of smoking that lead to future childhood concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behl, 2013</td>
<td>A primary literature search of PubMed concluded 101 articles: 83 human and 18 animal studies, that focused on the associations between maternal smoking or nicotine exposure during pregnancy and childhood obesity or metabolic disorders at any age.</td>
<td>4</td>
<td>N/A</td>
<td>Childhood overweight/obesity and maternal smoking is an early life proof-of-concept that early life exposure to environmental toxins can be a risk factor towards childhood obesity.</td>
</tr>
<tr>
<td>Bekkers, 2011</td>
<td>751 children participants of the Prevention and Incidence of Asthma and Mite Allergy birth cohort study were reevaluated through a parental questionnaire at the children’s age of 3 and 12 months, and yearly up until 8 years of age. The questionnaire were accompanied by a hospital based medical physical examination to determine early life determinants of total and HDL Cholesterol levels. The determinants examined were as follows: breastfeeding, birth weight, infant weight gain, maternal overweight before pregnancy, gestational diabetes and maternal smoking during pregnancy, while currently taking into account the child’s current BMI.</td>
<td>4</td>
<td>N/A</td>
<td>Children whose mothers were overweight, smoking during pregnancy and children who gained weight rapidly during infancy had higher total-to-HDL cholesterol levels at age 8 years than those of their counterparts.</td>
</tr>
<tr>
<td>Brose, 2013</td>
<td>Routinely collected data from 3,880 pregnant smokers stopping in one of the 44 Stop Smoking Services in England was analyzed in this cohort study. Measured in 4-week quit rates and confirmed by carbon monoxide levels &lt;10 ppm. This study assessed the association of single NRT and combination NRT with quit rates among pregnant smokers.</td>
<td>4</td>
<td>Combination of nicotine patch and a faster acting form showed a benefit for smoking cessation during pregnancy. The damage caused by smoking is greater than the use of NRT. NRT gives the nicotine without carbon monoxide and other toxins that come from cigarette use.</td>
<td>Combination NRT does expose the fetus to higher levels of nicotine.</td>
</tr>
<tr>
<td>Coleman, 2010</td>
<td>This systematic review and meta-analysis examines the</td>
<td>1</td>
<td>NRT would be more effective combined with</td>
<td>Nicotine exposure is related to LBW, preterm</td>
</tr>
<tr>
<td>Study</td>
<td>Methods</td>
<td>Findings</td>
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<td>Cooper, 2014</td>
<td>1050 women who attended ultrasonography appointments at seven hospital antenatal clinics in the Midlands and North-west England of whom 1034 births resulted were evaluated in a double-blind, randomised, placebo-controlled trial. The effects of nicotine replacement therapy versus a placebo on maternal effects of smoking sensation, the cost-effectiveness, issues affecting birth outcomes and breathing issues in the children at 2yrs of age was examined.</td>
<td>Woman found it difficult to adhere to NRT without a level of support or counseling. There was no significant difference between NRT group and NRT placebo group for breathing issues at 2yrs of age. NRT lead to more premature births compared to the placebo group. NRT was more expensive to distribute than the placebo group.</td>
<td></td>
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<tr>
<td>Gaither, 2008</td>
<td>This Cohort study of 5,716 pregnant smokers analyzed whether NRT was associated with any adverse pregnancy outcomes. Smoking and NRT referral was self-reported and information of birth outcomes was obtained by birth certificates.</td>
<td>It is possible that the heavier smokers did not use the NRT consistently or used them in addition to smoking. Nicotine can freely pass through the placenta and the fetus is not able to efficiently metabolize the nicotine, causing nicotine levels to accumulate in the tissues and amniotic fluid. This build-up causes a decrease in oxygen to the fetus, causing impaired growth leading to a probable cause of preterm delivery.</td>
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<td>Fish, 2009</td>
<td>Data came from counseling audio recordings and telephone surveys of 104 women examining the association of NRT, and smoking cessation of women enrolled in Baby Step, an open-label randomized controlled trial testing cognitive-behavioral therapy (CBT) verses CBT plus NRT.</td>
<td>NRT adherence is low among pregnant smokers, but adherence was a predictor of cessation.</td>
<td></td>
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</tr>
<tr>
<td>Forinash, 2010</td>
<td>Four literature studies evaluated the outcomes in women using NRT during pregnancy.</td>
<td>Behavior modification therapy should be used as the first method for smoking cessation. If failure occurs NRT should</td>
<td></td>
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<tr>
<td>Study Authors, Year</td>
<td>Description</td>
<td>Number of Studies</td>
<td>N/A</td>
<td>Notes</td>
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<td>Ino, 2010</td>
<td>17 papers were analyzed and used in this systematic review to look at the effects of maternal smoking during pregnancy and childhood obesity.</td>
<td>1</td>
<td>N/A</td>
<td>Maternal smoking during pregnancy is clearly indicated to cause childhood obesity and metabolic syndrome.</td>
</tr>
<tr>
<td>Oncken, 2008</td>
<td>Analysis of 194 women at 26 weeks gestation or less smoking during pregnancy and the effectiveness of smoking cessation with the use of NRT of 2mg nicotine gum in a randomized, double blind, placebo-controlled clinical trial. The women were enrolled at Hospitals in CT and MA.</td>
<td>1</td>
<td>The nicotine gum did not increase the quit rate compared to the placebo group, but the babies born to the NRT group had increased birth weight and more appropriate size for gestational age.</td>
<td>N/A</td>
</tr>
<tr>
<td>Wang, 2012</td>
<td>This study looked at the effect of smoking cessation one year prior to pregnancy in 5416 women.</td>
<td>2</td>
<td>N/A</td>
<td>Cessation should be targeted at mothers at least one year prior to pregnancy.</td>
</tr>
<tr>
<td>Weng, 2012</td>
<td>30 articles were analyzed in this study. Objective of the study was to identify predictable risk factors during infancy.</td>
<td>1</td>
<td>N/A</td>
<td>Several risk factors for obesity and metabolic development can be positively identified at birth, one of which is smoking.</td>
</tr>
</tbody>
</table>