Correlation between Passive Cigarette Smoke Exposure on Low Birth Weight: Meta-Analysis

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ABSTRACT

Background: Low birth weight (LBW) is defined as a newborn baby weighing less than 2500 grams. Low birth weight is a serious condition in developing countries. The impact of cigarette smoke on pregnant women who are exposed to cigarette smoke is at a higher risk of complications, such as miscarriage, premature birth, or babies born with low weight. This study aims to analyze the relationship between exposure to secondhand smoke and low birth weight.

Subjects and Method: This research is a systematic review and meta-analysis by systematically reviewing primary articles from Pubmed, Google Scholar, Scient Direct and Springerlink by selecting articles published in 2012-2022. The articles searched using PICO were P: Pregnant women, I: exposed to cigarette smoke, C: not exposed to cigarette smoke, O: low birth weight. Keywords "Exposure to smoking pregnant women" OR "Expectant mother" OR "Pregnancy women" OR "Exposed to cigarettes" OR "Secondhand smoke exposure" OR "Cigarette smoke exposure" AND "Low birth weight" OR "Low weight babies" AND “Case control” AND “Adjusted odds ratio”. Articles used PRISMA flow diagrams and analyzed using Review Manager 5.3.

Results: There were nine articles analyzed consisting of Nepal, Morocco, Ethiopia, Sierra Leone, India, Indonesia and China. Meta-analysis showed that cigarette smoke exposure increased the risk of low birth weight and was statistically significant (aOR = 2.19; 95% CI = 1.58 to 3.03; p < 0.001).

Conclusion: Exposure to cigarette smoke increases the risk of weight gain in LBW infants by 2.19 times compared to not exposed to cigarette smoke.

Keywords: Exposure to cigarette smoke, low birth weight, meta-analysis.

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BACKGROUND

Low birth weight babies have limitations stating that the baby is born with a low weight, namely babies born weighing <2,500 grams (Anil et al., 2020)

Related to this, to be able to weigh with certainty the weight of a newborn, the baby will be weighed within the first hour after birth (Sugiarti et al., 2021).

Body weight is the most important determinant of a baby’s survival, health, growth and development. There are many factors associated with low birth weight, including socio-demographic, genetic factors, nutrition and exposure to cigarette smoke. Cigarette smoke has an impact during pregnancy which causes the risk of low birth weight birth (Adah et al., 2014).
Based on UNICEF data, it was found that globally the number of births in the world is approximately 27.1%, while for each country there are also some inequalities related to this LBW problem. For Latin America, the Caribbean and Western Europe, there was no significant change in the prevalence of low birth weight between 2000 and 2015, while in North America there was a statistically significant, albeit small increase over the same period 7.3% (7.2–7.5) in in 2000 and 7.9% (7.8-8.0) in 2015 (Blencowe et al., 2019).

In Indonesia, low birth weight (LBW) has problems and polemics related to this LBW problem because it was recorded that as of 2019 it was recorded that as many as 111,827 babies or 3.4% of children born had low birth weight (LBW). Meanwhile, in 2018 it was also recorded that there were 6.2% of babies born with low weight (Kemenkes RI, 2020).

Meanwhile, the percentage of mothers who gave birth to live births with a weight less than 2,500 grams fluctuated. In the year of 2020, the percentage shows a figure of 11.37%, not much different in 2019 at 11.32%. When viewed by area type, mothers in rural areas who gave birth to live-born children in the last 2 (two) years, where the last live-born child was born with a weight less than 2,500 grams had a higher percentage than mothers in urban areas, namely 13.24 percent compared to 9.85 percent (BPS, 2020).

Smoking is a stupid habit that is not commendable and self-defeating for the habit of smoking frequently. Smoking makes a person look not fresh, unhealthy and wrinkled (Sodik, 2018). Pregnant women who are exposed to cigarette smoke have a negative impact on the fetus they contain. Cigarettes are one of the products that are often used by adults but of course have a negative impact on health. Cigarettes are a product made from tobacco that will be burned and smoked. Cigarettes are made from several similar plants, including the Nicotina tabacum and Nicotiana rustica plants (Wandita, 2020).

Exposure to cigarette smoke is one of the factors causing low birth weight, in this case caused by chemicals in cigarettes. Cigarette smoke contains lead, which affects the health of the mother and baby when exposed to pregnant women (Regulation of the Government of the Republic of Indonesia Number 109, 2012).

Based on this background, a comprehensive study is needed from various primary studies regarding the relationship between exposure to secondhand smoke and low birth weight babies. This study aims to analyze the relationship between exposure to secondhand smoke and low birth weight.

**SUBJECTS AND METHOD**

1. **Study Design**
   This research is a systematic review and meta-analysis. The articles used in this study were obtained from several database sources, namely Pubmed, Google Scholar, Science Direct and Springerlink between 2013 and 2022. The selection of articles was carried out using PRISMA flow diagrams. Keywords to search for articles are as follows Keywords “Exposure to smoking pregnant women” OR "Expectant mother" OR "Pregnancy women" OR "Exposed to cigarettes" OR "Secondhand smoke exposure" OR "Cigarette smoke exposure" AND "Low birth weight" OR "Low weight babies" AND "Case control" AND "Adjusted odds ratio”.

2. **Inclusion Criteria**
   The inclusion criteria in this research article are: full-text articles using a case-control study design, research subjects are pregnant women with low birth weight babies, the size of the relationship uses AOR, the intervention given is exposure to cigarette smoke,
the outcome of the study is low birth weight babies.

3. Exclusion Criteria
The exclusion criteria in this research article are: Articles published in languages other than English and Indonesian, articles before 2012, articles are not free access and do not use multivariate.

4. Operational Definition of Variables
Article searches conducted using PICO were: P: Pregnant women, I: exposed to cigarette smoke, C: not exposed to cigarette smoke, O: low birth weight babies.

**Exposure to Cigarette Smoke** is contact with cigarette smoke during pregnancy that comes from the environment. Instrument used questionnaire and measurement scale was categorical.

**Low Birth Weight** is the baby's weight was weighed after 1 hour after birth and weighed < 2,500 grams.

Instrument: register book

5. Instrument
Assessment of the quality of this study using the Critical Appraisal of a Case-Control Study published by the Center for Evidence-Based Management (CEBM).

6. Data Analysis
Data processing was carried out using Review Manager (RevMan 5.3) by calculating effect size and heterogeneity to determine the combined research model and form the final result of the meta-analysis.

RESULTS
Research from primary studies related to the relationship between exposure to second-hand smoke and low birth weight babies consists of 9 articles consisting of countries: China, Nepal, Morocco, Ethiopia, Sierra Leone, India, Indonesia.

**Figure 1. PRISMA flow diagram**
Table 1 Research on the quality of case control research studies "The relationship of exposure to passive cigarette smoke to low-birth-weight infants" using the Critical Appraisal Skills Program for Case Control Study.

<table>
<thead>
<tr>
<th>No</th>
<th>Questions</th>
<th>Anil et al., 2020</th>
<th>Benkaddour et al., 2016</th>
<th>Dendir et al., 2017</th>
<th>Kargbo et al., 2021</th>
<th>Khattar et al., 2012</th>
<th>Lestari et al., 2015</th>
<th>Mingude et al., 2020</th>
<th>Owa, 2019</th>
<th>Xi et al., 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Does the study address clearly focused questions/problems?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Is the research method (research design) appropriate to answer the research question</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Is the case taken acceptable?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>Is the selection of controls acceptable?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Are the results accurately measured to minimize bias?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Apart from the experimental intervention, were the groups treated same?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Have the authors taken into account potential confounding factors in the design or in the analysis?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>How big is the treatment effect?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>How precise is the estimate of the influencing treatment?</td>
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<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>Are the results reliable?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>11</td>
<td>Are the results applicable to the local population?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>Are the results of this study consistent with the available evidence?</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

| Total of Score | 24 | 24 | 24 | 23 | 24 | 24 | 24 | 23 | 24 | 23 |

Note 2= Yes, 1= Can’t tell, 0= No
### Table 2. Description of the primary studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Primary Study</th>
<th>Country</th>
<th>Study Design</th>
<th>Sample</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anil et al., (2020)</td>
<td>Nepal</td>
<td>Case-control</td>
<td>Case: 123, Control: 246</td>
<td>Pregnant women aged 20-30 years</td>
<td>Exposure to cigarette smoke in the house</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Benkaddour et al., (2016)</td>
<td>Morocco</td>
<td>Case-control retrospektif</td>
<td>Case: 144, Control: 144</td>
<td>Pregnant mother</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Dendir et al., (2017)</td>
<td>Ethiopia</td>
<td>Case-control</td>
<td>Case: 112, Control: 235</td>
<td>Pregnant women aged 15-30 years</td>
<td>Exposure to cigarette smoke in the house</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Kargbo et al., (2021)</td>
<td>Sierra Leone</td>
<td>Case-control</td>
<td>Case: 146, Control: 438</td>
<td>Pregnant women with an average age of 24 years</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Khattar et al., (2013)</td>
<td>India</td>
<td>Case-control</td>
<td>Case: 100, Control: 200</td>
<td>Pregnant women (primigravida)</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Lestari et al., (2015)</td>
<td>Indonesia</td>
<td>Case-control</td>
<td>Case: 58, Control: 58</td>
<td>Pregnant women aged 20-35 years</td>
<td>Exposure to cigarette smoke in the house</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Mingude et al., (2020)</td>
<td>Ethiopia</td>
<td>Case-control retrospektif</td>
<td>Case: 60, Control: 240</td>
<td>Pregnant women with an average age of 28 years</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Owa. (2019)</td>
<td>Indonesia</td>
<td>Case-control</td>
<td>Case: 78, Control: 78</td>
<td>Pregnant women aged 20-35 years</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Xi et al., (2020)</td>
<td>China</td>
<td>Case-control retrospektif</td>
<td>Case: 289, Control: 1381</td>
<td>Pregnant women aged 18-35 years</td>
<td>Exposure to environmental cigarette smoke</td>
<td>Not exposed to cigarette smoke</td>
<td>Low birth weight</td>
</tr>
</tbody>
</table>
The article search process was carried out through several journal databases including Pubmed, Google Scholar, Science Direct and Springerlink. The article search process can be seen in the PRISMA flow diagram in Figure 1. Research related to the relationship between cigarette smoke exposure and low birth weight consists of 9 articles from the initial search process yielding 1,100 articles, after the process of deleting published articles, 746 articles were obtained with 53 of them fulfilling conditions for further full-text review. A total of 9 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis.

The following reasons are given for full-text articles that meet the exclusion criteria:
1. The article does not meet the criteria for the PICO formulation.
2. The population in the article is not pregnant women.
3. The article does not include the adjusted Odds Ratio value.
4. Articles published in languages other than English and Indonesian.
5. Articles that did not perform multivariate analysis.

**Quality Rating**

Quality assessment in this study used the Critical Appraisal of a Case-Control Study published by the Center for Evidenced-Based Management (CEBM).

The assessment criteria consist of 12 criteria, with a score of 2 = if the answer is yes, 1 = if the answer is not known, 0 = if the answer is no. This research assessment will use the Critical Appraisal of a Case-Control Study. The eleven questions that will be used are as follows:
1. Does the study address clearly focused questions/problems?
2. Is the research method (research design) appropriate to answer the research question?
3. Is the case taken acceptable?
4. Is the selection of controls acceptable?
5. Are the results measured accurately to minimize bias?
6. Apart from the experimental intervention, were the groups treated the same?
7. Has the author taken into account potential confounding factors in the design or in the analysis?
8. How big is the treatment effect?
9. How precise is the estimate of his influencing treatment?
10. Are the results reliable?
11. Are the results applicable to the local population?
12. Are the results of this study consistent with the available evidence?

The next step is to calculate the overall effect of combining the data. Data analysis was carried out using Review Manager 5.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anil et al. 2020</td>
<td>0.3365</td>
<td>0.2855</td>
<td>14.3%</td>
<td>1.40 [0.80, 2.45]</td>
<td></td>
</tr>
<tr>
<td>Benkaddour et al. 2016</td>
<td>0.571</td>
<td>0.1899</td>
<td>18.7%</td>
<td>1.77 [1.22, 2.57]</td>
<td></td>
</tr>
<tr>
<td>Dondir et al. 2017</td>
<td>0.6206</td>
<td>0.2774</td>
<td>14.6%</td>
<td>1.86 [1.08, 3.20]</td>
<td></td>
</tr>
<tr>
<td>Kargbo et al. 2021</td>
<td>1.4725</td>
<td>0.4132</td>
<td>9.8%</td>
<td>4.36 [1.94, 9.30]</td>
<td></td>
</tr>
<tr>
<td>Khatir et al. 2012</td>
<td>1.5418</td>
<td>0.703</td>
<td>4.6%</td>
<td>4.42 [1.18, 16.72]</td>
<td></td>
</tr>
<tr>
<td>Lestar et al. 2015</td>
<td>2.0109</td>
<td>0.6597</td>
<td>5.1%</td>
<td>7.47 [2.05, 27.22]</td>
<td></td>
</tr>
<tr>
<td>Mingude et al. 2020</td>
<td>1.5359</td>
<td>0.6139</td>
<td>5.7%</td>
<td>4.73 [1.42, 15.75]</td>
<td></td>
</tr>
<tr>
<td>Owa et al. 2019</td>
<td>0.5655</td>
<td>0.5027</td>
<td>6.6%</td>
<td>2.60 [0.88, 7.46]</td>
<td></td>
</tr>
<tr>
<td>Xi et al. 2020</td>
<td>0.3365</td>
<td>0.1468</td>
<td>20.7%</td>
<td>1.40 [1.05, 1.87]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>100.0%</td>
<td>2.19 [1.58, 3.33]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.11; Chi² = 17.76, df = 8 (P = 0.02); I² = 55%
Test for overall effect: Z = 4.71 (P < 0.00001)

**Figure 3. Forest plot of the relationship between exposure to secondhand smoke and low birth weight**

The forest plot in Figure 3 shows that there is a relationship between exposure to secondhand smoke and the risk of low birth weight. Pregnant women who were exposed to cigarette smoke from the environment had a risk of giving birth to children with low birth weight 2.19 times compared to those not exposed to cigarette smoke and the relationship was statistically significant (aOR = 2.19; 95% CI = 1.58 to 3.03; p < 0.001). The results of this meta-analysis showed a fairly high heterogeneity of the effect estimates between the primary studies in this meta-analysis with I²= 55%. So the overall effect synthesis of the primary studies in this meta-analysis was carried out using a random effects model approach.

**Figure 4 Funnel plot of the relationship between exposure to secondhand smoke and low birth weight infants**
The funnel plot in Figure 4 is more on the right of the vertical line of the average effect estimate than on the left of the funnel plot, so the funnel plot indicates publication bias. Because the distribution of the estimated effects in the funnel plot tends to be to the right of the estimated mean vertical, which is in the direction of the average diamond, which is also to the right of the vertical line. So this publication bias overestimates the true effect (overestimate).

DISCUSSION

Systematic studies and meta-analyses raise the title of the relationship between cigarette smoke exposure and low birth weight. This study discusses low birth weight babies which is considered important because the rate of low birth weight babies is still quite high both in Indonesia and in the world.

Indirect cigarette exposure can increase the risk of giving birth to babies with low birth weight. Some of the compounds found in cigarette smoke can cross the placenta. For example, nicotine in the blood of women who are exposed to secondhand smoke can indirectly reduce fetal blood flow and adversely affect the lungs, fetal heart, central nervous system, and digestive system. Carbon monoxide can also cause low birth weight. One of the causes is a decrease in oxygen supply to the fetus, which causes fetal hypoxia (Eftekhari et al., 2016).

Tobacco use, both active and passive, increases the levels of carbon monoxide and nicotine in the blood of the mother and fetus. Nicotine reduces blood flow to the maternal-placental circulation, which increases the risk of Intrauterine growth restriction (IUGR). There is a clear relationship between the number of cigarettes smoked or exposure to cigarettes and the occurrence of low birth weight (<2500 g). Women who smoke during pregnancy are more likely to experience ectopic pregnancy, placental abruption and infant death (Hamulka et al., 2018).

One of the environmental factors is exposure to cigarette smoke. Several international studies "Smoking during pregnancy and harm reduction in birth weight" state that there is a relationship between smoking during pregnancy and low birth weight in infants, smoking intensity is one of the references that can cause babies to be born to have low weight. The high prevalence of smoking that exists during pregnancy shows that it has a significant effect on low birth weight in infants so that a policy to reduce cigarette smoke is needed (Kataoka et al., 2018).

Exposure to tobacco at an early age can contribute to stunting and stunt growth in children. The fetus in the mother's womb is exposed to cigarette smoke, there is an increased risk of premature birth and low birth weight and a twofold risk for sudden infant death syndrome (Ayu et al., 2020).

This causes long-term impacts and will increase the risk of chronic diseases such as heart disease in children as adults. Judging from the risk that arises because the fetus lacks nutrition, these nutrients are only distributed to several organs such as the brain and heart but are not channeled to other organs, so of course other organs become victims (Gebregziabher et al., 2017).

Several studies have shown a relationship between cigarette smoke exposure to low birth weight babies, one of which is a study (Lestari et al., 2015) entitled "Exposure to Cigarette Smoke in Pregnant Women in the Household to the Risk of Increased Incidence of Low Birth Weight Babies in Gianyar Regency" with 116 subjects, consisting of 58 cases and 58 controls, stated that exposure to husband's cigarette smoke increased the incidence of low birth
weight babies compared to pregnant women who were not exposed (aOR = 7.47; 95% CI = 2.05 to 27.17).

A similar study (Wang et al., 2020) in China stated that children experienced low birth weight babies when pregnant women were exposed to cigarette smoke (aOR= 2.42; 95% CI= 1.95 to 3.00). The mechanism underlying the occurrence of LBW is because cigarettes contain nicotine and other harmful substances in cigarettes causing uteroplacental decline which causes maternal weight loss, the impact on the fetus of short stature and decreased birth weight.

Research says that the bad effect of cigarette smoke is causing interference with the placenta. The placenta expands the area inside the uterus to meet the oxygen and nutritional needs of the fetus. This results in the thinning of the placental layer and the possibility of a lower position of the placenta or commonly known as placenta previa. In pregnancy, the placenta will function as a respiratory, metabolic, nutritional, endocrine, storage, transportation and expenditure tool from the mother’s body to the fetus’s body or vice versa. If one or more of the above functions are disturbed, the fetus and placenta will have problems (Mawaddah et al., 2021).

The results of this study are in line with research conducted (Owili et al., 2018) in Africa that exposure to cigarette smoke during pregnancy increases the risk of low birth weight in male infants (aOR= 1.08; 95% CI= 1.02 to 1.14). As well as the increased risk of miscarriage, low baby weight and baby’s respiratory tract disorders. Research conducted (Putri et al., 2018) states that pregnant women who smoke passively have a 7.06 times chance of giving birth to babies with low birth weight compared to pregnant women who are not passive smokers.

Exposure to cigarette smoke for pregnant women comes from husbands who are active smokers. Mothers who are exposed to secondhand smoke are more likely to experience disturbances in their pregnancies due to the higher chemical content of passive smokers than active smokers. Studies show that cigarette smoke is left in a room, the toxins contained from cigarette smoke stick to clothes, furniture that is around it for days and weeks after being used to smoke. When the door or window or fan is turned on, the toxins from cigarette smoke return to the surrounding air. So if you are exposed to cigarette smoke, you will experience problems during pregnancy (Husaini, 2017).

AUTHORS CONTRIBUTIONS
Winei Handriani is the main researcher who selects the topic, searches for and collects research data. Uki Retno Budihastuti and Eti Poncorini Pamungkasari analyzed data and reviewed research documents.

FUNDING AND SPONSORSHIP
This study is self-funded.

CONFLICT OF INTEREST
There is no conflict of interest in this study.

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