

# Areca Nut Chewing as a Modifiable Risk Factor for Maternal Anemia, Prematurity and Fetal Low Birth Weight: A Cross Sectional Study in Teluk Wondama, West Papua

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**Introduction:** Maternal anemia remains a major global public health problem, affecting over 40% of pregnancies and contributing to maternal morbidity, perinatal mortality and impaired child development. Areca nut (*Areca Catechu*) chewing is a common cultural practice in South and Southeast Asia including Papua, Indonesia, and has been hypothesized to exacerbate anemia, yet evidence in pregnancy is limited. This study aimed to investigate the association between areca nut chewing with maternal anemia, low birth weight and prematurity.

**Methods:** A cross-sectional study was conducted among 263 pregnant women attending antenatal care at Dr. Albert H Torey District General Hospital, West Papua, Indonesia, between September 2024 and September 2025. Areca nut chewing was recorded during routine antenatal care and subsequently extracted from medical records. Maternal anemia was defined as hemoglobin <11 g/dl, low birth weight as <2500 gr and prematurity as delivery before 37 weeks. Associations were analyzed using Chi-square and multivariate logistic regression tests (ORs 95% CI, significant if p value <0.05), adjusted for potential confounders.

**Results:** The prevalence of maternal anemia occurred in 65.4% of participants, low birth weight in 43.3% and prematurity in 41.4%. Areca nut chewing was strongly associated with maternal anemia (OR = 11.4; 95% CI: 4.38–29.65), low birth weight (OR = 10.89; 95% CI: 5.69–20.84) and prematurity (OR = 10.67; 95% CI: 5.50–20.68) (all p <0.001).

**Conclusion:** Areca nut chewing during pregnancy significantly increases the risk of maternal anemia, low birth weight and preterm birth. Highlighting the need for culturally sensitive preventive interventions.

**Keywords:** areca catechu, fetal low birth weight, maternal anemia, prematurity, pregnancy

## Introduction

Anemia in pregnancy is a major global health concern, affecting approximately 37% of pregnant women and 30% non-pregnant women aged 15–49 years worldwide and is more pronounced in developing regions such as South Asia and Sub-Saharan Africa (WHO, 2021).<sup>1–3</sup> In Indonesia, especially in Papua Health Service, profile maternal anemia remains high at 31.3–46% for past decade was associated with increased maternal morbidity and adverse perinatal outcomes including preterm delivery, low birth weight and perinatal mortality.<sup>1,4</sup> In Papua and across many Asia Pacific populations, *Areca Catechu* chewing is a long-standing cultural practice among both men and women, including pregnant women.<sup>4</sup> The habit carries social and traditional significance, symbolizing identity, community belonging and cultural continuity, while also being perceived to relieve nausea, suppress appetite, enhance alertness and freshen the mouth. Numerous research indicates that areca nut consumption exacerbates gingival inflammation, impairs the immunological response, influences osteoblasts, and exhibits cytotoxic effects on periodontal fibroblasts.<sup>1,2</sup>

Numerous bioactive compounds have been identified in areca nut, including alkaloids, polyphenols, polysaccharides, fatty acids, arginine, arecoline, and aminobutyric acid, which demonstrate diverse bioactive functions such as antibacterial, antiparasitic, antiviral, antioxidant, anti-inflammatory, and antitumor effects.<sup>1,5</sup> The nut contains tannins which can inhibit non-heme iron absorption in the small intestine; arecoline is alkaloid (1–2%) that induces oxidative stress and appetite suppression and polyphenols (5–40%) which interfere with micronutrient metabolism.<sup>6,7</sup> A cohort study in Papua reported higher risk of anemia among pregnant women who chewed areca nut.<sup>1,4</sup> A study in Jayapura also found a negative correlation between areca nut chewing frequency and hemoglobin levels.<sup>1</sup> However, evidence from local settings remains limited. Therefore, this study aimed to analyze the association between Areca nut chewing with both maternal anemia, prematurity and low birth weight in local populations remains limited among pregnant women in Teluk Wondama, West Papua. By identifying areca nut chewing as a modifiable risk factor, this study contributes to the evidence base needed for culturally tailored maternal health interventions.

## Methods

This study employs an analytical cross-sectional design using secondary data obtained from maternal and neonatal medical records at Dr. Albert H Torey District General Hospital, West Papua, Indonesia, between September 2024 and September 2025. The records included routinely collected information from antenatal care visits, delivery and neonatal outcomes. Data on sociodemographic characteristics, areca nut chewing habits, iron supplementation adherence and nutritional status were recorded during routine antenatal care using structured clinical forms and subsequently extracted from medical records for analysis. No additional interviews were conducted specifically for this study. We conducted a power analysis utilizing SPSS to ascertain the requisite sample size for attaining a statistical power of 0.80 at a significance level of 0.05. This power analysis was conducted based on the expected effect size and the type of statistical Chi-Square test used. Sampling selection of 159 women areca nut chewers (cases) and 104 women non-areca nut chewers (controls) based on the following inclusion criteria: pregnancy patient aged 18–40 years with singleton pregnancies who agreed to participate and provided informed consent. Exclusion criteria included women with a known history of chronic hematological disorders such as thalassemia, chronic kidney disease or other systemic illnesses that could affect hemoglobin levels as well as women who had received blood transfusions within the last three months or presented with severe obstetric complications requiring urgent intervention.

The primary outcome variable was maternal anemia defined according to the World Health Organization as a hemoglobin level <11 g/dl. The main independent variable was *Areca Catechu sp* nut chewing, categorized into frequent use ( $\geq 2x/day$ ) and infrequent or non use ( $<2x/day$ ). Covariates assessed included maternal age, parity, nutritional status, measured by mid upper arm circumference (MUAC) and adherence to iron supplementation. Hemoglobin concentrations were measured using a standardized hematology analyzer by clinical pathology specialist and trained laboratory personnel following standard operating procedures.

Data were obtained from medical records encompassing: demographic details (age, BMI, educational attainment, and marital status), reproductive history (number of pregnancies, parity, and abortions), medical history (anemia diagnosis verified by hematological examination and other hematological disorders influencing hemoglobin levels), lifestyle factors (smoking status and contraceptive usage), and areca nut chewing practices. Bivariate and multivariate logistic regression analyses were conducted, using an odds ratio and a 95% confidence interval. Variables were considered statistically significant if  $p < 0.05$  in the multivariate analysis. We followed the methodological framework previously described by Disastra et al, 2024 to ensure consistency in the analytical process and enhance comparability with prior studies.<sup>8</sup>

## Definition Operation

Maternal anemia was defined according to the World Health Organization criteria as a hemoglobin concentration <11 g/dl during pregnancy.<sup>3,9</sup> Hemoglobin levels were measured using standardized hematology analyser operated by trained laboratory personnel and pathology clinic specialist.

*Areca Catechu* nut chewing was defined as the habitual consumption of Areca nut during pregnancy was categorized into frequent chewers  $>2x/day$  and infrequent or non use if  $<2x/day$ .

Maternal age was classified into two groups: <25 years, 25–35 years and >35 years. Parity was defined as the number of previous pregnancies as the previous pregnancies that reached at least 20 weeks of gestation categorized as primigravida if in their first pregnancy and multigravida if two or more pregnancies. Nutritional status was assessed using mid-upper arm circumference (MUAC), measured in centimeters with a non-stretchable measuring tape; values <23.5 cm were categorized as undernutrition while values >23.5 cm were considered normal nutritional status. Iron supplementation adherence was defined as the regular intake of iron or iron-folic acid tablets provided through antenatal care services, with adherence classified as good if the mother had taken at least four tablets in the previous seven days and poor if fewer than four tablets were taken.

Data were analyzed using IBM SPSS Statistics Version 26 (for Windows). Descriptive statistics summarized demographic and clinical characteristics. Chi-square testing was conducted to assess the association between areca nut chewing with maternal anemia, low birth weight and prematurity events. Confounding variables were identified through statistical testing (Chi-square, *T*-tests) and prior literature on areca nut chewing and maternal anemia. Variables that were significantly associated with both the exposure (areca nut chewing) and the outcome (maternal anemia, low birth weight and prematurity) in the preliminary analysis were considered as potential confounders. We controlled for age, body mass index (BMI), parity, and smoking status as confounders based on their established associations with both areca nut chewing and maternal anemia, as well as their significant impact on the relationship between these two variables in multivariable regression analysis. By controlling for these variables, we aimed to isolate the true relationship between areca nut chewing and maternal anemia while minimizing the influence of confounders. For all variables with a 95% confidence interval, and the results were considered statistically significant with a  $p < 0.05$  for all analyzed variables.

This study was submitted to and approved by the Ethics and Research Committee of the Development and Research Department at Dr. Alberth H Torey District General Hospital, Raisei Wasior West Papua in accordance with ethical approval for research protocol 12/2003 No. 445.1/1188/EAFR/RSUD-AHT-TW/IX/2025 research permit on September 11<sup>th</sup> 2025. As this study used secondary anonymized data from medical records collected as part of routine clinical care, informed consent had been obtained at the time of clinical registration. All medical record data were used exclusively for the purposes of this research and will not be shared with any parties outside the researchers and research supervisors. The data are intended solely for academic purposes.

## Results

According to [Table 1](#), a total of 263 pregnant women were enrolled in this study. The majority of participants were aged between 25 years and 35 years (42.2%), followed by those aged below 25 years (32.7%) and above 35 years (25.1%). Most respondents were multiparous (72.6%), while 27.4% were primiparous. The prevalence of areca nut chewing was notably high with 60.5% of women reporting habitual use during pregnancy. With respect to nutritional status, more than half of the participants (54.8%) had a normal body mass index (BMI) between 18.5 kg/m<sup>2</sup> and 24.9 kg/m<sup>2</sup>, whereas 16% were classified as obese (BMI >30 kg/m<sup>2</sup>). Based on mid upper arm circumference (MUAC), 55.1% of participants had measurement ranging from 23.5 cm to 28 cm and 5.7% were identified as undernourished (MUAC <23.5 cm). A high prevalence of maternal anemia was observed in the study population, affecting 65.4% of the women. Furthermore, 43.3% of neonates were classified as having low birth weight (<2500 gr) and 41.4% of deliveries were preterm, defined as gestational age <37 weeks.

The bivariate analysis demonstrated statistically significant associations between areca nut chewing and several maternal and neonatal outcomes. According to [Table 2](#), pregnant women who reported areca nut use had a substantially greater risk of developing maternal anemia (OR: 11.4; 95% CI: 4.38–29.65  $p < 0.001$ ), compared to non chewers. Areca nut chewing was strongly associated with an increased risk of low birth weight, with affected mothers being approximately 11 times more likely to deliver infants weighing less than 2500 grams (OR: 10.89; 95% CI: 5.69–20.89;  $p < 0.001$ ). Areca nut chewing demonstrated a significant relationship with premature birth, as chewers were over 10 times more likely to experience prematurity (OR: 10.67; 95% CI: 5.50–20.68;  $p < 0.001$ ). These findings collectively indicate that areca nut chewing during pregnancy is a major modifiable behavioral risk factor contributing to maternal anemia, preterm delivery and low birth weight in this population.

**Table 1** Variable Description, Sample and Data Characteristics

Analyzed Variable	Areca Nut Chewers (n:159 = 100%)	Non Areca Nut Chewers (n:104 = 100%)	p-value (sig 2 sided)
<b>N</b>	159	104	
<b>Age</b>			0.960
≤ 24 years	52 (32.7)	34 (32.69)	
25–34 years	68 (42.7)	43 (41.3)	
≥35 years	39 (24.5)	27 (25.9)	
<b>BMI</b>			0.017
Underweight (<18.5 kgBB/m <sup>2</sup> )	13 (8.17)	2 (1.92)	
Normoweight (18.5–24.9 kgBB/m <sup>2</sup> )	93 (58.4)	51 (49.03)	
Overweight (25–29.9 kgBB/m <sup>2</sup> )	34 (21.38)	28 (26.92)	
Obese (>30 kgBB/m <sup>2</sup> )	19 (11.94)	23 (22.11)	
<b>Obstetric Status</b>			0.016
Primipara (1)	35 (22.01)	37 (35.57)	
Multipara			
2	38 (23.89)	31 (29.80)	
3	30 (18.86)	12 (11.5)	
4	23 (14.46)	13 (12.5)	
≥5	33 (20.75)	11 (10.57)	
<b>Education Level</b>			0.031
Elementary school	19 (11.94)	7 (6.73)	
Junior High School	48 (30.18)	16 (15.38)	
Senior High School	66 (41.50)	45 (43.26)	
Diploma	8 (5.03)	24 (23.07)	
Bachelor degree	2 (1.25)	2 (1.92)	
Magister degree	0 (0)	4 (3.84)	
None	16 (10.06)	6 (5.76)	
<b>MUAC</b>			0.008
<23.5 cm	13 (8.17)	2 (1.92)	
>23.5–28 cm	94 (59.11)	51 (49.03)	
>28 cm	52 (31.44)	51 (49.03)	
<b>Iron supplementation adherence</b>			0.012
Yes (≥ 4 tablets/week)	16 (10.06)	22 (21.15)	
No	143 (89.93)	82 (78.84)	
<b>Smoking status</b>			0.030
Yes	7 (4.40)	0 (0)	
No	152 (95.59)	104 (100)	

**Note:** Multivariate logistic regression was used for adjusted analyses.

In addition, areca nut chewing was significantly associated with lower MUAC values ( $x: 9.75$ ;  $p=0.008$ ) and reduced neonatal APGAR scores ( $x=33.70$ ;  $p<0.001$ ), suggesting adverse maternal nutritional status and compromised neonatal vitality among habitual chewers. In bivariate analysis, Areca nut chewing, maternal age, parity, MUAC and iron supplementation adherence were significantly associated with maternal anemia ( $p<0.05$ ). After adjusting for potential confounders in multivariate logistic regression, frequent areca nut chewing remained strongly associated with anemia. Other significant predictors included undernutrition (MUAC <23.5 mm, adjusted OR 1.87; 95% CI: 1.12–3.12) and poor iron supplementation adherence (adjusted OR 2.13; 95% CI: 1.34–3.40). Maternal age and parity were not significant predictors in the adjusted model. Data adjustment for age, BMI, smoking status and number of previous pregnancies were made and analyzed using Chi-Square statistics concerning the association between both groups.

**Table 2** Association Between Areca Nut Chewing and Maternal Anemia Between the Two Groups

Variable	Areca Nut Chewing		OR (95% CI)	P value
	>2x/day (%)	<2x/day or Non Use (%)		
<b>Maternal anemia</b>			11.4 (4.38–29.65)	<0.001
Anemia	153 (88.95)	19 (11.04)		
Non anemia	6 (6.59)	85 (93.40)		
<b>Birth weight</b>			10.89 (5.69–20.84)	<0.001
Low birth weight	100 (87.72)	14 (12.28)		
Normal	59 (39.59)	90 (60.41)		
<b>Prematurity</b>			10.67 (5.50–20.68)	<0.001
Premature	96 (88.08)	13 (11.92)		
Mature	63 (40.9)	91 (59.1)		

**Note:** If the chi-square condition is not satisfied, the p-value for categorical data is determined using the Fisher's exact tests. P value <0.05 for statistically significant.

## Discussion

This study demonstrated a strong and statistically significant association between areca nut chewing with both adverse maternal and neonatal outcomes, specifically maternal anemia, preterm delivery and low birth weight among pregnant women in Teluk Wondama, West Papua. The prevalence of maternal anemia (65.4%) is higher than the global estimate of 40% and reflects the continued burden of maternal anemia in low resource setting (WHO, 2021) and exceeds national estimates reported from basic health research Indonesia (48.9%).<sup>3,7,9</sup> Our findings align with previous studies conducted in Jayapura, Papua New Guinea, Bangladesh and Srilanka, which also reported higher anemia prevalence and lower hemoglobin levels among areca nut chewers.<sup>1,2,5</sup> The biological plausibility of this association is supported by the known constituents of areca nut.<sup>5,6</sup> Tannins inhibit non heme iron absorption, while polyphenols interfere with the metabolism of essential micronutrients.<sup>6,10,11</sup> Numerous polyphenols in Areca nut have demonstrated genotoxicity, likely due to the generation of reactive oxygen species (ROS) in the saliva of chewers, leading to oxidative stress or degradation that the cell cannot adequately counteract. This results in detrimental effects, including oxidative and chromosomal DNA damage, which may play a role in various stages of the carcinogenic process in the oral mucosa.<sup>2,12</sup> Additionally, arecoline is a major alkaloid that induces oxidative stress and suppresses appetite, potentially reducing dietary intake and bioavailability of iron.<sup>1,7,9</sup> These mechanisms together contribute to iron deficiency and subsequently increase the risk of anemia.<sup>7,13</sup> Areca nut use in our study was 60.5%, comparable to data from Jayapura where more than half of pregnant women reported chewing (35%) but lower than the prevalence reported in Madang, Papua New Guinea (94%), suggesting that Teluk Wondama lies within a high use corridor of the Southwest Pacific.<sup>14,15</sup>

Experimental investigations have demonstrated the detrimental effects of Areca nut on human embryos and pregnant women, revealing the presence of the alkaloid arecoline in the biological matrices of neonates born to mothers exposed to arecoline during gestation.<sup>16,17</sup> Its cytotoxic and carcinogenic effects have been identified in meconium, cord samples, and urine.<sup>16,18</sup> Arecoline has been shown to relax human umbilical vessels in a dose-dependent manner, inhibiting endothelial cell proliferation and arresting the cell cycle due to DNA damage through the induction of sister chromatid exchange (SCE), thereby resulting in adverse pregnancy outcomes among pregnant women by increasing DNA susceptibility to damage.<sup>16,17</sup> Arecoline may directly stimulate the central nervous system, facilitating quick transit over the blood–brain barrier, accelerating heart rate, and enhancing blood flow in the carotid arteries, while concurrently reducing diastolic blood pressure through a peripheral cholinergic impact.<sup>10,16,19</sup> Lower maternal-fetal blood flows could result from this, which could negatively affect birth weight.<sup>19</sup>

Numerous studies indicate that Areca nut consumption during pregnancy adversely affects birth outcomes, resulting in low birth weight, reduced birth length, and preterm delivery.<sup>2,9,16</sup> A 2019 systematic review of four studies, including a total of 3570 pregnant women in the analysis found that prenatal areca exposure was significantly associated with increased odds of low birth weight (pooled OR 1.75; 95% CI 1.35–2.27) whereas although the point estimate for preterm

birth trended upward, the association was non statistically significant (OR 1.20; 95% CI 0.95–1.62) with no observed heterogeneity ( $I^2 = 0\%$ ) for both outcomes.<sup>6,10</sup> In a large cohort of Taiwanese aboriginal women (n: 1264), maternal betel quid chewing during pregnancy was associated with lower mean birth weight (−89.5 gr) and shorter birth length (−0.43 cm) and with higher odds of low birth weight (adjusted OR 2.40; 95% CI 1.21–4.80) and term low birth weight (AOR 3.67; 95% CI 1.70–7.96), preterm birth was more frequent among chewers (11.4% vs 8.3%) although this difference did not reach statistical significance and an adjusted estimate was not reported.<sup>19,20</sup> In Madang province, Papua New Guinea, areca chewing in pregnancy was near universal (94%) and heavy chewing was linked with a 238 gr reduction in birthweight, suggesting potential nutritional and haematologic pathways of harm during gestation.<sup>4</sup> Chewing was commonly motivated by perceived relief of morning sickness and other culturally embedded reasons and most women perceived no fetal risk.<sup>1,4</sup> In line with previous findings, our study found that frequent areca nut chewing was independently associated with low birth weight.<sup>19</sup> After adjustment for maternal age and parity, neither factor remained statistically significant, suggesting that the observed association may be driven primarily by behavioral or nutritional factors rather than maternal obstetric history. Interestingly, frequent chewing in our study also showed a strong independent association with preterm delivery.<sup>18</sup> In this high prevalence setting, our relatively large sample reduced uncertainty and revealed a statistically significant, independent association with preterm delivery, aligning with the previously upward point estimates.

Consistent with those findings, we also observed markedly higher odds of worse APGAR score among chewers. The most plausible pathways are maternal anemia as mediator (via reduced iron bioavailability), which is associated with lower 1 and 5 minutes APGAR score in contemporary synthesis. APGAR is not a direct measure of asphyxia, but lower scores correlate with umbilical artery blood gas indices, particularly pH, lactate, and  $PCO_2$ .<sup>21</sup> Population data show that lower umbilical artery pH tracks higher neonatal morbidity.<sup>20,21</sup> On the mother side, by reducing maternal oxygen carrying capacity, anemia plausibly lowers transplacental oxygen delivery, predisposing to fetal hypoxemia and metabolic acidosis (low umbilical artery pH) and thus to depressed APGAR scores.<sup>18,20</sup> A recent systematic review and meta analysis found significantly increased odds of low APGAR at 1 and 5 minutes among anemic mothers compared with non anemic mothers, supporting anemia as a biologically and clinically credible mediator between areca exposure and depressed neonatal condition.<sup>21,22</sup> Also, fetoplacental vascular effects of arecoline (umbilical vasorelaxation/endothelial inhibition) that may increase susceptibility to intrapartum depression.<sup>16,17</sup>

Areca nut chewing was associated with a shift toward worse MUAC. Two complementary pathways could plausibly link antenatal chewing to poorer MUAC.<sup>1</sup> First, appetite and intake displacement. Pregnant chewers frequently report using areca to relieve morning sickness (the postponing meals) and perceive the habit as suppressing hunger, both of which can reduce net energy intake.<sup>16,19</sup> Second, oral morbidity that constrains diet. Chronic chewing is associated with periodontal and mucosal pathology (e.g periodontal disease, oral submucous fibrosis), conditions that can impair mastication and limit diet variety (particularly harder, fibrous foods) thereby depressing protein and micronutrient density during pregnancy.<sup>6,10,22</sup>

Undernutrition as indicated by MUAC <23.5 cm also significantly predicted maternal anemia in our study, consistent with prior research showing that poor maternal nutritional reserves compromise hemoglobin synthesis and erythropoiesis.<sup>1</sup> Similarly, poor adherence to iron supplementation doubled the risk of anemia, in agreement with evidence that regular intake of iron folic acid tablets significantly reduces anemia in pregnancy.<sup>5,7</sup> Interestingly, maternal age and parity were not significant predictors after adjustment, suggesting that in this population, lifestyle and nutritional factors, particularly areca nut chewing, play a more dominant role influencing hemoglobin levels. This differs from studies in other regions where younger maternal age and higher parity were consistently associated with anemia risk.

The cultural acceptance of areca nut chewing in Papua presents a major public health challenge. Community-based interventions to reduce areca nut consumption, coupled with nutritional education and reinforcement of iron supplementation adherence, may be effective strategies for anemia prevention. Further research is needed to explore dose responsive effects, longitudinal outcomes and possible interventions targeting behavior change.

This study has several limitations, including an inability to establish causality, potential recall bias in self-reported chewing frequency, selection bias due to reliance on medical records from a single institution, which may restrict the generalizability of the findings, and confounding factors, as adjustments were made but unmeasured variables (genetic

and detailed lifestyle factors) were not assessed. However, the intensity of the link and its coherence with current data reinforce the robustness of the findings.

## Conclusion

This study demonstrates a significant association between frequent areca nut chewing during pregnancy associated with maternal anemia, prematurity and fetal low birth weight. This effect persisted even after adjusting for nutritional status and iron supplementation adherence. Public health strategies addressing cultural practices, maternal nutrition and adherence to supplementation are essential to reduce anemia burden in population.

## Abbreviation

APGAR, Appearance, Pulse, Grimace, Activity, Respiration; BMI, Body Mass Index; CI, Confidence Interval; DNA, Deoxyribonucleic Acid; FBW, Fetal Birth Weight; IBM SPSS, International Business Machines Statistical Package for the Social Sciences; MUAC, Mid Upper Arm Circumference; OR, Odds Ratio; pH, Potential of Hydrogen (concentration of hydrogen ions H<sup>+</sup>); PCO<sub>2</sub>, Partial Pressure of Carbon dioxide; ROS, Reactive Oxygen Species; SCE, Sister Chromatid Exchange; WHO, The World Health Organization.

## Data Sharing Statement

The datasets used and/or analyzed the current study are available from the corresponding author on reasonable request.

## Ethical Compliance

This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

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This paper has been uploaded to [www.authorea.com](http://www.authorea.com) as a preprint: <https://www.authorea.com/users/992968/articles/1354665-areca-nut-chewing-as-a-modifiable-risk-factor-for-maternal-anemia-prematurity-and-fetal-low-birth-weight-a-cross-sectional-study-in-teluk-wondama-west-papua>

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no potential conflicts of interest in this work.

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