

## Insights into the association between smoking and obesity: the 2014 Indonesian Family Life Survey

Yusuf Syaeful Nawawi,<sup>1</sup> Afsheen Hasan,<sup>2</sup> Liza Salawati,<sup>3</sup> Husnah,<sup>3,4</sup> Widiastuti<sup>1</sup>



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### Authors' affiliations:

<sup>1</sup>Department of Radiology, Faculty of Medicine, Dr. Moewardi Hospital, Universitas Sebelas Maret, Surakarta, Indonesia, <sup>2</sup>Department of Biostatistics and Epidemiology, The University of Oklahoma Health Sciences Center, Oklahoma City, United States of America, <sup>3</sup>Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia, <sup>4</sup>Department of Nutrition, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

### Corresponding author:

Yusuf Syaeful Nawawi  
 Department of Radiology, Dr. Moewardi Hospital, Jalan Kolonel Sutarto No. 132, Jebres, Surakarta, Central Java 57126, Indonesia  
 Tel/Fax: +62-271-634634/  
 +62-271-637412  
**E-mail:** yusufnawawi@unsyiah.ac.id;  
 yusuf\_radiologi20181@student.uns.ac.id

### ABSTRACT

**BACKGROUND** Various findings on the relationship between smoking and obesity have been demonstrated. This study aimed to investigate the association between smoking behavior and obesity in the Indonesian adult population.

**METHODS** A cross-sectional analysis was conducted using data from the 2014 Indonesian Family Life Survey. A body mass index of  $\geq 25$  kg/m<sup>2</sup> was employed to define obesity. Smoking behavior was assessed in terms of smoking status and its attributes. The potential confounders of gender, age, education, residential environment, economic status, physical activity, and education level were adjusted using logistic regression.

**RESULTS** Study subjects were 28,949 adults aged  $\geq 20$  years. Current smoking was a protective factor of obesity (adjusted odds ratio [aOR] = 0.53; 95% confidence interval [CI] = 0.48–0.58), whereas previous smoking habit showed no association with obesity (aOR = 0.96; 95% CI = 0.84–1.09). The risk of current smokers having obesity was lower than that of nonsmokers as smoking duration increased (aOR = 0.46–0.63). By contrast, the risk of obesity was relatively higher among former smokers than current smokers as the duration of quitting increased (aOR = 1.46–2.20). Heavy smokers had a higher risk of obesity than light smokers among former (aOR = 1.85; 95% CI = 1.27–2.67) and current smokers (aOR = 1.38; 95% CI = 1.23–1.65).

**CONCLUSIONS** Overall, smoking negatively affected obesity among the Indonesian adult population. By contrast, quitting smoking was associated with an increased risk of obesity. Thus, weight management along with smoking cessation intervention should be prescribed.

**KEYWORDS** Indonesian Family Life Survey 2014, obesity, smoking

Tobacco smoking has been known as a major risk factor of chronic noncommunicable diseases (NCDs), which contributes to more than 7 million deaths annually worldwide.<sup>1</sup> Despite the rising public awareness of the hazards of smoking, many people experience difficulty in avoiding initiation and quitting smoking. Smoking has become a part of social culture in some communities. It does not only have an addictive effect, but it is also believed to suppress an appetite, thus preventing a body weight gain.<sup>2</sup>

Indonesia is one of the highest-burden of smoking countries worldwide. The estimate projection of prevalence of Indonesian adult male smokers is increased from 56.2% in 2000 to 87.2% in 2025,<sup>3</sup> as opposed to decrease of the number of smokers elsewhere.<sup>4</sup> This situation is worsened with the growing burden of obesity. Ministry of Health of the Republic of Indonesia reported 35.4% of Indonesian adults are overweight and obese, based on 2018 Indonesia National Health survey.<sup>5</sup> Tobacco smoking, coupled

with obesity, present as major public health challenges contributing in an even higher risk of all-cause, cancer, and cardiovascular disease mortality.<sup>6-8</sup>

The continuously increasing prevalence of obesity and smoking has raised considerable concern among Indonesian health policy makers. Both risk factors have been known as major risk factors of numerous NCDs in Indonesia, leading to disease epidemiology transition and significant financial burden.<sup>9,10</sup> The Indonesian government has continuously taken efforts to reduce the rate of increase in NCDs. The latest national program, namely, “Healthy Life Society Movement” (*Gerakan Masyarakat Hidup Sehat*), which was launched in 2016, devoted serious efforts to suppressing the prevalence of unhealthy behaviors causing NCDs at household and community levels.<sup>11</sup>

Previous studies have elucidated the relationship between smoking behavior and obesity and arguably demonstrated that smoking is related to a low body mass index (BMI),<sup>12-14</sup> which has been confirmed in other studies with robust design.<sup>15,16</sup> However, most studies have been conducted on non-Asian populations. Despite the nationwide increasing trend of obesity and smoking behavior, studies exploring a similar issue in the Indonesian population are limited. This study aimed to investigate the association between smoking behavior and obesity in the Indonesian population by utilizing national representative data from publicly available datasets from the Indonesian Family Life Survey (IFLS).

## METHODS

### Survey dataset

Secondary data from a publicly available dataset of the fifth wave of the IFLS (IFLS5) were subjected to a cross-sectional analysis. The IFLS is a longitudinal survey of households involving questionnaires and anthropometric measurements. The first wave of the survey was performed in 1993, and IFLS5 was conducted in 2014. In the 2014 IFLS wave, samples were obtained from a previous examination.<sup>16</sup> The 2014 IFLS sampling scheme was stratified based on approximately 83% of the Indonesian population or provinces and rural/urban locations, which represented 27 provinces (based on the number of administrative provincial division regions of Indonesia in 1993). Thirteen provinces were selected based on the heterogeneity of the communities in these

provinces and composed of four main islands in Indonesia (Sumatera, Java, Kalimantan, and Sulawesi). Within each of the 13 provinces, enumeration areas were randomly chosen from a national representative sample frame used in the 1993 *Survei Kesehatan Nasional* or National Health Survey, a socioeconomic survey of about 60,000 households. In the IFLS, 321 enumeration areas in the 13 provinces were randomly selected. The field teams oversampling urban enumeration areas and enumeration areas in smaller provinces to facilitate urban-rural and Javanese–non-Javanese comparisons. Within selected enumeration area, 20 households from each urban areas and 30 households from each rural area were randomly selected.<sup>17</sup> The IFLS complete data and guidelines are publicly available on the RAND Corporation website (<https://www.rand.org/labor/FLS/IFLS/ifls5.html>).

### Measures

The completed data of subjects aged 20 years or older for individuals and households were combined from the publicly available dataset of the 2014 IFLS. For our analysis, we defined obesity by employing cut-off of BMI >25 kg/m<sup>2</sup> for the Asian population.<sup>18</sup> The following sociodemographic information was extracted: area of residence (i.e., urban and rural); the highest level of attained education (grouped as not attending school, elementary school or equivalent; middle school or equivalent, high school or equivalent, college and universities or above, and others, including purely religious school and special school); and monthly household expenditure (cost of food items [e.g., rice, meat, fish, vegetables, cooking oil, and granulated sugar] and non-food items [e.g., kerosene]). Per capita monthly expenditure was categorized into quintile, i.e., five equal groups based on the distribution of per capita monthly expenditure (Q1 as the group with the lowest expenditure to Q5 as the group with the highest expenditure).

The lifestyle risk factors included in this study were current smoking behavior and physical activity level. The subjects were classified as nonsmokers, current smokers, and former smokers based on their smoking behavior. Current smokers were asked about the duration of smoking from the age that they started smoking regularly until the time of assessment/survey and the average number of cigarettes consumed per day. Former smokers were asked about the duration of their previous smoking period, the age when they

ceased smoking, and the average number of cigarettes consumed per day. The status of smoking exposure was classified as light ( $\leq 10$  cigarettes daily), moderate ( $\leq 20$  cigarettes daily), and heavy ( $> 20$  cigarettes daily) smokers.<sup>12,19</sup> Physical activity was based on the metabolic equivalent of task-minutes and further classified as low, moderate, and high physical activity levels.<sup>20</sup>

### Ethical consideration

The IFLS survey and its procedures were reviewed and approved by the Institutional Review Boards in the USA (at RAND) and in Indonesia (Ethics Committees of Universitas Gadjah Mada, Yogyakarta, and earlier at Universitas Indonesia, Jakarta). Written informed consent was obtained from all the participants. This particular study involved only a secondary analysis; thus, no new ethical clearance was required.

### Statistical analysis

All statistical analyses were conducted using SPSS version 23 (IBM Corp., USA). For all analyses, two-tailed  $p < 0.05$  indicated statistical significance. Results were weighted to represent the Indonesian population by using the calculated weights to account for the complex survey design, nonresponse rate, and

post-stratification. The general characteristics of the subjects with and without obesity were compared descriptively. Logistic regression was performed to test trends across variables. Multivariate logistic regression analysis was conducted to assess the associations of obesity status and smoking behavior, and adjustments were made for the potential confounding effects of age, gender, education level, economic status, residential environment, and physical activity. Crude and adjusted odds ratios were presented. Stratified analysis was carried out based on gender, age, and economic status by adjusting for other potential confounders to assess the association of obesity and smoking behavior.

## RESULTS

As shown in Table 1, 28,949 adults were included in the analysis, and the number of males was slightly higher than that of females (50.4% versus 49.6%). The prevalence of obesity in females was higher than in males. The prevalence of obesity was the highest in individuals aged 40–49 years. The prevalence of obesity increased with high educational level and economic status. The rate of obesity of nonsmoking individuals living in urban areas was significantly

**Table 1.** Characteristics of the subjects

Variable	Nonobese group, n (%)	Obese group, n (%)
Gender		
Male	11,163 (76.6)	3,414 (23.4)
Female	8,315 (57.9)	6,057 (42.1)
Age group (years)		
20–29	5,556 (76.6)	1,698 (23.4)
30–39	4,482 (63.4)	2,587 (36.6)
40–49	3,593 (57.3)	2,680 (42.7)
50–59	2,810 (62.9)	1,659 (37.1)
$\geq 60$	3,036 (78.2)	848 (21.8)
Education		
No school	1,441 (79.7)	368 (20.3)
Elementary	7,284 (68.6)	3,329 (31.4)
Middle	3,502 (66.5)	1,763 (33.5)
High	5,173 (66.7)	2,584 (33.3)
College and university	2,077 (59.3)	1,428 (40.7)
Residential environment		
Urban	9,689 (63.2)	5,644 (36.8)
Rural	9,788 (71.9)	3,828 (28.1)

Table continued on next page

**Table 1.** (continued)

Variable	Nonobese group, n (%)	Obese group, n (%)
Household expenditure* (N = 28,622)		
Q1	4,044 (75.8)	1,294 (24.2)
Q2	4,158 (69.6)	1,816 (30.4)
Q3	3,917 (66.8)	1,951 (33.2)
Q4	3,653 (64.8)	1,982 (35.2)
Q5	3,453 (59.5)	2,354 (40.5)
Physical activity (N = 27,673)		
Low	7,524 (65.2)	4,011 (34.8)
Moderate	4,092 (61.8)	2,529 (38.2)
High	6,818 (71.6)	2,699 (28.4)
Smoking status		
Nonsmoker	10,058 (59.1)	6,958 (40.9)
Former smoker	1,042 (68.4)	482 (31.6)
Current smoker	8,378 (80.5)	2,031 (19.5)
Duration of smoking of current smokers (years) (N = 10,151)		
≤10	2,333 (83.1)	474 (16.9)
11–20	2,265 (78.7)	612 (21.3)
21–30	1,564 (75.1)	519 (24.9)
≥30	1,989 (83.4)	395 (16.6)
Number of cigarettes used by current smokers (per day consumption) (N = 10,231)		
<10	2,961 (80.9)	697 (19.1)
10–20	4,513 (81.5)	1,022 (18.5)
>20	759 (73.1)	279 (26.9)
Duration of smoking of former smokers (years) (N = 1,424)		
≤10	358 (68.8)	162 (31.2)
11–20	210 (63.8)	119 (36.2)
21–30	149 (64.8)	81 (35.2)
≥30	248 (71.9)	97 (28.1)
Number of cigarettes used by former smokers (per day consumption) (N = 1,483)		
<10	409 (71.3)	165 (28.7)
10–20	483 (70.6)	201 (29.4)
>20	114 (50.7)	111 (49.3)
Duration of quitting of former smokers (year) (N = 1,244)		
≤10	507 (68.0)	239 (32.0)
11–20	201 (70.8)	83 (29.2)
21–30	90 (68.7)	41 (31.3)
>30	54 (65.1)	29 (34.9)

\*Per capita monthly expenditure was categorized into quintile, i.e., five equal groups based on the distribution of per capita monthly expenditure (Q<sub>1</sub> as the group with the lowest expenditure and Q<sub>5</sub> as the group with the highest expenditure)

high. In terms of smoking status, 17,016 were nonsmokers, 1,524 were former smokers, and 10,409 were current smokers. The highest average BMI (mean [standard deviation (SD)] = 24.33 [4.71])

**Table 2.** Risk factors associated with obesity

Variable	OR (95% CI)	aOR (95% CI)*
<b>Gender</b>		
Male	1.00	1.00
Female	2.38 (2.26–2.51)	1.72 (1.58–1.86)
<b>Age group (years)</b>		
20–29	1.00	1.00
30–39	1.89 (1.76–2.03)	2.04 (1.89–2.20)
40–49	2.44 (2.27–2.63)	2.75 (2.54–2.98)
50–59	1.93 (1.78–2.10)	2.37 (2.16–2.60)
≥60	0.91 (0.83–1.00)	1.28 (1.15–1.43)
<b>Education</b>		
No school	1.00	1.00
Elementary	1.79 (1.58–2.02)	1.66 (1.45–1.91)
Middle	1.97 (1.73–2.24)	1.99 (1.71–2.32)
High	1.96 (1.73–2.21)	1.90 (1.64–2.21)
College and university	2.69 (2.36–3.08)	2.28 (1.94–2.67)
<b>Residential environment</b>		
Urban	1.00	1.00
Rural	0.67 (0.64–0.71)	0.74 (0.70–0.78)
<b>Household expenditure<sup>†</sup></b>		
Q1	1.00	1.00
Q2	1.37 (1.26–1.48)	1.27 (1.16–1.39)
Q3	1.56 (1.43–1.69)	1.40 (1.28–1.53)
Q4	1.70 (1.56–1.84)	1.49 (1.36–1.62)
Q5	2.13 (1.96–2.31)	1.81 (1.65–1.97)
<b>Physical activity</b>		
Low	1.00	1.00
Moderate	1.69 (1.09–1.23)	1.12 (1.05–1.20)
High	0.74 (0.70–0.79)	0.90 (0.84–0.95)
<b>Smoking status</b>		
Nonsmoker	1.00	1.00
Former smoker	0.67 (0.60–0.75)	0.96 (0.84–1.09)
Current smoker	0.35 (0.33–0.37)	0.53 (0.48–0.58)

OR=odds ratio; aOR=adjusted odds ratio; CI=confidence interval  
 \*aOR for gender, age, expenditure, education, residential environment, expenditure, and physical activity as appropriate;  
<sup>†</sup>per capita monthly expenditure was categorized into quintile, i.e., five equal groups based on the distribution of per capita monthly expenditure (Q1 as the group with the lowest expenditure and Q5 as the group with the highest expenditure)

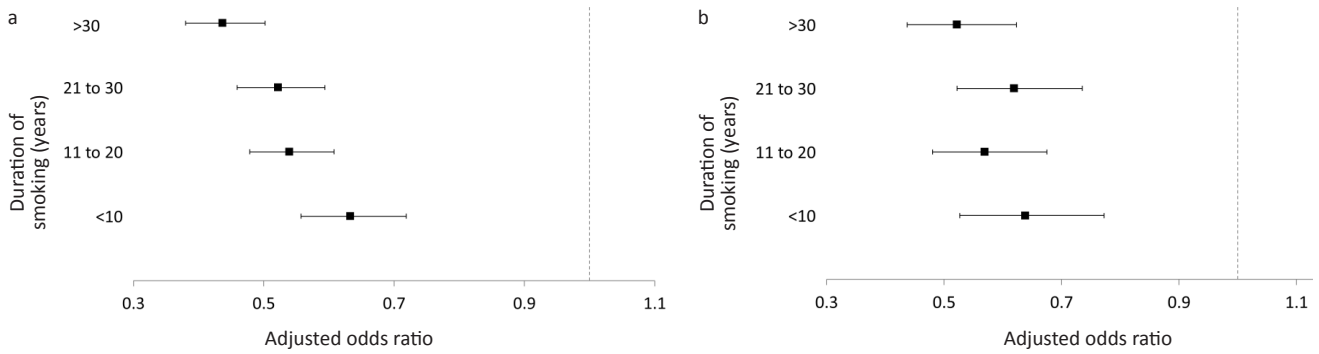
was observed in nonsmokers, followed by former smokers (mean [SD] = 23.30 [4.45]) and current smokers (mean [SD] = 22.06 [3.74]). The rate of the current smoking behavior of men was significantly higher than women.

The risk factors potentially associated with obesity in the present study are shown in Table 2. Even after adjustments for other factors were made, the results revealed that females were more likely to have obesity than males. The risk of obesity increased gradually with age, and the highest risk was observed among individuals aged 40–49 years. However, this risk decreased among individuals aged 60 years and older. The results also showed a positive dose-response relationship of smoking and obesity with education and economic status. Subjects living in rural areas, those who have a high intensity of physical activity, and those who are current cigarette smokers were less likely to have obesity.

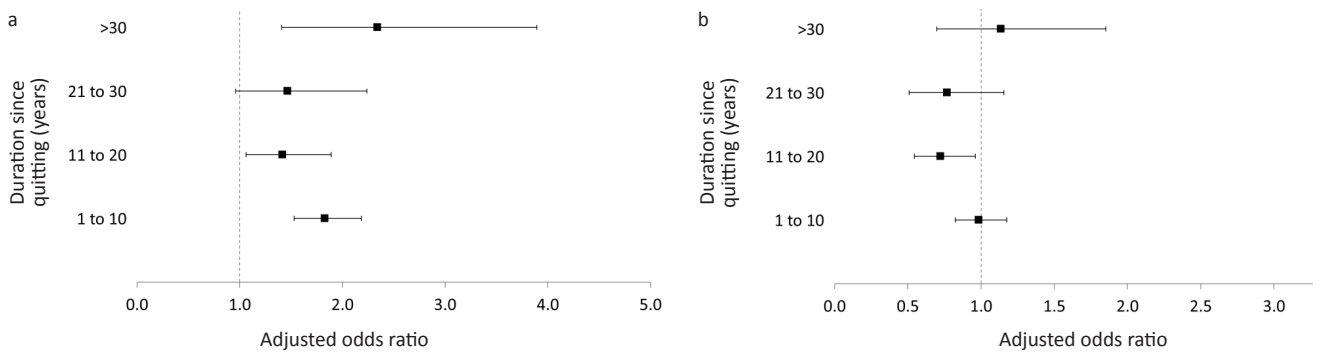
**Table 3.** Stratified analysis of smoking status by gender, age group, and household expenditure

Variable	Former smoker, aOR* (95% CI) (N = 1,524)	Current smoker, aOR* (95% CI) (N = 10,409)
<b>Gender</b>		
Male	1.02 (0.88–1.19)	0.56 (0.51–0.62)
Female	0.68 (0.461–1.02)	0.71 (0.57–0.88)
<b>Age (years)</b>		
20–29	0.96 (0.67–1.39)	0.51 (0.42–0.61)
30–39	1.02 (0.76–1.36)	0.55 (0.47–0.66)
40–49	0.86 (0.65–1.15)	0.54 (0.46–0.64)
50–59	1.17 (0.87–1.57)	0.55 (0.44–0.67)
≥60	0.80 (0.58–1.11)	0.44 (0.33–0.58)
<b>Household expenditure<sup>†</sup></b>		
Q1	0.86 (0.59–1.25)	0.50 (0.40–0.63)
Q2	1.01 (0.74–1.38)	0.53 (0.44–0.65)
Q3	0.92 (0.67–1.26)	0.51 (0.42–0.62)
Q4	0.77 (0.57–1.03)	0.47 (0.39–0.57)
Q5	1.15 (0.89–1.49)	0.61 (0.52–0.73)

aOR=adjusted odds ratio; the reference of the calculation of ORs was compared with that of the nonsmoker group (n = 17,016)  
 \*aOR for gender, age, expenditure, education, residential environment, expenditure, and physical activity; <sup>†</sup>per capita monthly expenditure was categorized into quintile, i.e., five equal groups based on the distribution of per capita monthly expenditure (Q1 as the group with the lowest expenditure and Q5 as the group with the highest expenditure)



**Figure 1.** Forest plot of the adjusted odds ratio (aOR) of obesity and smoking duration of current smokers and former smokers. (a) comparison between current smokers and nonsmokers; (b) comparison between current smokers and former smokers. aORs were adjusted for gender, age, expenditure, residential environment, and physical activity as appropriate



**Figure 2.** Forest plot of the adjusted odds ratio (aOR) of obesity and duration of quitting among former smokers. (a) comparison between former smokers and current smokers; (b) comparison between former smokers and nonsmokers. aORs were adjusted for gender, age, expenditure, residential environment, and physical activity as appropriate

The stratification of the smoking status based on gender, age, and economic status revealed differential results (Table 3). The risk of obesity was consistently lower among current smokers than nonsmokers across all stratified subgroups. The risk of obesity was found similar between former smokers and nonsmokers in all subgroups.

The risk of obesity among current smokers was significantly lower than nonsmokers and former smokers. This finding was consistent in all the smoking durations of current smokers (Figure 1). By contrast, the risk of obesity of former smokers was significantly higher than current smokers in all durations except those in individuals aged 21–30 years, which showed no difference from that of nonsmokers in all durations of smoking cessation (Figure 2). The risk of obesity was significantly higher in former and current smokers who consumed more than 20 cigarettes per day, but the risk of obesity was higher in former smokers than current smokers. However, the risk of obesity of the group with moderate consumption per day was not different from the reference group (Figure 3).

## DISCUSSION

This study presented the overall prevalence of obesity of 32.7% in Indonesian adults (42.1% in females versus 23.4% in males). These values, despite its lower rates, are comparable to the report from the 2018 Indonesia National Health Survey, which found 35.4% of overall prevalence of obesity in adults aged >18 years (44.4% in females versus 26.6% in males), when the similar cut-off of obesity was employed.<sup>5</sup> Regardless the different sampling methods and analysis among these studies, these findings describe the progression of obesity rates in Indonesian adult population during recent years which deserves considerable attention. Indonesia undergoes a rapid and profound nutrition transition and has constantly rising obesity rates. Poverty and food insecurity, especially in early ages, indirectly contribute to obesity-related problems.<sup>21</sup> Our results were consistent with those of other studies on obesity in the Indonesian population, whose prevalence rates of obesity are more pronounced in adult females, those who live in urban areas, and those

who have higher income and education than in groups with opposing characteristics.<sup>21,22</sup> Therefore, the trend of increasing obesity is not confined in urban areas or affluent households because a similar trend is also observed in rural areas and low-income segments.<sup>21</sup>

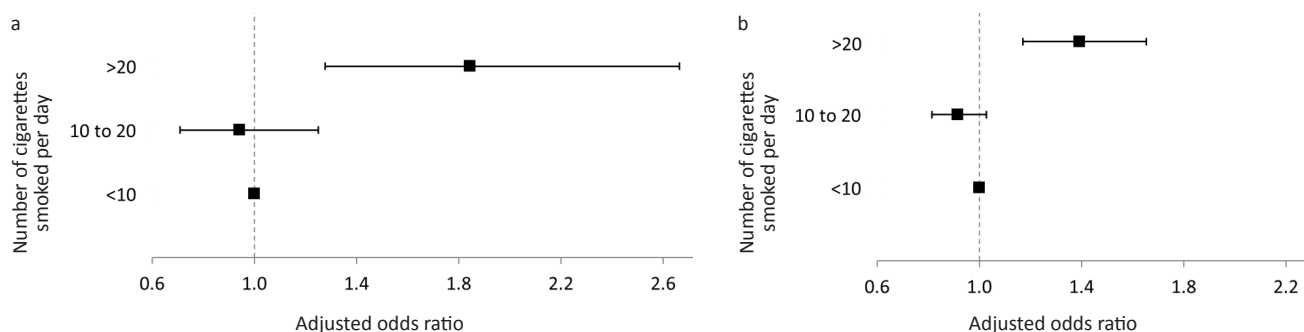
A negative relationship between obesity and currently active smoking behavior was shown by our data analysis, revealing that the body weight of current smokers was lower than nonsmokers and former smokers. Consistent with the results of numerous observational studies on Asian populations in Thailand,<sup>12</sup> Japan,<sup>23</sup> Western populations in the United States,<sup>24,25</sup> and the United Kingdom,<sup>13</sup> our finding demonstrated that active smoking was related to a low BMI. Smoking likely reduces body weight by increasing the metabolic rate, decreasing metabolic efficiency, and decreasing caloric absorption via a reduced appetite.<sup>2</sup> A consistent negative association of the current smoking behavior and risk of obesity was also demonstrated after gender stratification in males and females. However, previous studies revealed that the relationship between gender with smoking affects obesity.<sup>23,25</sup> The underlying mechanism possibly involves the anti-estrogenic effect of smoking and gender-related hormonal responses to smoking; these responses include different androgenic and estrogenic activities between males and females.<sup>26</sup>

The comparison of the duration of smoking among current smokers suggested a negative dose-response effect on obesity; that is, the longer duration of smoking was associated with a lower risk of obesity among current smokers than among nonsmokers and former smokers. Our results also suggested an inverse effect of current smoking behavior on obesity, but this effect should be further discussed because

numerous studies have found inconsistent results related to the duration of smoking. Previous studies also reported varying findings possibly because of inter-racial differences. For example, Dare et al<sup>13</sup> found no association between the duration of smoking and obesity among the British population. Albanes et al<sup>24</sup> indicated that BMI tends to decrease as the duration of smoking prolongs irrespective of the intensity of smoking among the American population. Watanabe et al<sup>23</sup> observed a similar negative association only in certain subsets of smokers, particularly among those who have been smoking for more than 35 years compared with nonsmokers in a Japanese population. Conversely, current smokers who have been smoking for more than 20 years are more likely to be overweight in the Scottish population.<sup>14</sup>

Different smoking levels were also compared in our study. The risk of obesity was significantly higher and more pronounced in current and former smokers who smoke heavily than in current and former smokers who smoke lightly, particularly after adjustments were made for the duration of smoking. Kim et al<sup>19</sup> and Saarni et al<sup>27</sup> suggested the metabolic consequences of smoking by demonstrating that different fat distributions may occur at various smoking degrees. For instance, the abdominal and visceral adiposity of heavy smokers is likely higher than that of light smokers. Similar results were demonstrated in previous studies on the effect of different degrees of current smoking behavior on overall obesity.<sup>19,23,28–30</sup>

The effect of quitting smoking on BMI differs among studies. Our finding suggested that the longer duration of quitting was associated with the higher risk of obesity among former smokers than current smokers. Heavy smokers who quit smoking had



**Figure 3.** Association between the number of cigarettes smoked per day and the risk of obesity among (a) former and (b) current smokers. Adjusted odds ratios (aORs) were adjusted for gender, age, expenditure, residential environment, physical activity, and smoking duration as appropriate

a higher risk of obesity than that of currently active ones after adjustments to the duration of smoking were made. Nevertheless, the risk of obesity between former smokers and nonsmokers did not differ. After stratification based on the duration of quitting was performed, the risk of obesity was higher among those who quit smoking for more than 30 years than among nonsmokers. Dare et al<sup>13</sup> found that the risk of obesity among individuals who quit smoking even after more than 30 years is higher than among current smokers. Courtemanche et al<sup>16</sup> conducted a randomized trial on smoking cessation treatment and demonstrated the short- and long-term weight gain effects of quitting smoking. They observed an increase of 1.5–1.7 BMI units in the short run and a slightly larger increase of 1.8–1.9 BMI units in the long run. Sohn<sup>15</sup> longitudinally analyzed IFLS data by controlling time-varying covariates, i.e., invariant individual heterogeneity, and demonstrated a relatively slight increase in weight gain among former smokers and weight loss among current smokers.

The strength of this study was a national representative sample with relatively detailed smoking histories to establish the association between smoking behavior and obesity. Our findings corroborated the perception that current smokers were less likely to have obesity than nonsmokers. Nevertheless, as demonstrated by other previous studies, the association of smoking and obesity is complex. The drawback of this study was the inherent issue of observational study design to explore association. Particularly, our cross-sectional design did not allow us to establish any definitive temporal associations for identifying clear causal relationships. Thus, reverse causation might occur.

Other identified limitations included the following: reliance on secondary data obtained from self-reported measures of smoking habits but no measurement of the potential degree of the passive smoke exposure of individuals who never smoked; exclusion of the role of dietary habits into our analysis despite the major role of dietary habit in obesity; and the low number of research subjects, particularly in several subgroups (e.g., former smokers and female smokers), which might contribute to insufficient statistical power to our analysis. This approach also has less bias than other methods of handling missing data. A considerable amount of information, particularly smoking behavior, was missing, so the

author performed pairwise deletion by including complete data points.<sup>31</sup> Lastly, utilizing the overall BMI as a measure of the risk of obesity has been debated. Some studies have argued that overall BMI is inaccurate and may lead to a wider margin of error in measurement.<sup>23</sup> Other measures, e.g., body fat, have been introduced as a more accurate measure of the risk of obesity, but they are unavailable in the IFLS5 database. Previous studies also utilized abdominal obesity and body shape, which are also more accurate than other measures.<sup>19,27</sup>

In conclusion, smoking behavior negatively affected obesity in Indonesian adult population. The body weight of current smokers was likely lower than former smokers and nonsmokers. The risk of obesity of heavy smokers was higher than light smokers. The risk of obesity among the participants who quit smoking, particularly those with a history of heavy smoking, was also higher than current smokers. Thus, weight management, along with smoking cessation interventions, should be recommended.

#### Conflict of Interest

Afsheen Hasan receives grants from the University of Oklahoma Health Sciences Center to work on a collaborative project with Cancer Research UK, University of Strathclyde, and University College London. Other authors have nothing to disclose.

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