

Risk and Protective Factors of Depression in the General Population during the COVID-19 Epidemic in Korea

Sung-Wan Kim (✉ swkim@chonnam.ac.kr)

Chonnam National University Medical School

In-Hoo Park

Gwangju Mental Health Commission

Mina Kim

Gwangju Mental Health Commission

A-La Park

London School of Economics and Political Science

Min Jhon

Chonnam National University Medical School

Ju-Wan Kim

Chonnam National University Medical School

Hee-Ju Kang

Chonnam National University Medical School

Seunghyong Ryu

Chonnam National University Medical School

Ju-Yeon Lee

Chonnam National University Medical School

Jae-Min Kim

Chonnam National University Medical School

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Abstract

Background: The risk of depression has risen in the general population during the COVID-19 epidemic. This study was conducted to explore risk and protective factors associated with depression among the general population uninfected by COVID-19.

Methods: A cross-sectional study was conducted with 1,500 representative South Korean citizens aged 19–65 years through an anonymous online survey. Depression was defined as a Patient Health Questionnaire-10 score of 10 or higher. Other questionnaires included one measuring psycho-behavioural and social changes, and stress, due to COVID-19, a six-item version of the Gratitude Questionnaire (GQ-6), and a three-item version of the UCLA loneliness scale.

Results: Of the 1492 participants not infected by COVID-19, 312 (20.9%) exhibited depression. Multiple logistic regression analysis revealed that depression was positively associated with COVID-19-related stress and psycho-behavioural variables such as disturbances in eating and sleeping, younger age, smoking, underlying mental illness, and loneliness scale scores. In contrast, exercise three or more times per week and GQ-6 scale scores were inversely associated with depression.

Conclusion: During the COVID-19 pandemic, maintaining daily routines including eating, sleeping, and regular exercise and focusing on gratitude may be important for the prevention of depression. In addition, more attention should be paid to vulnerable populations, including young people, those with mental illnesses, and smokers, who might be more susceptible to depression.

Background

The Corona Virus Disease 2019 (COVID-19) pandemic has drastically changed our society and infiltrated every aspect of our daily lives [1]. Long-lasting social distancing and shrinkage of economic activity tend to lead to depression [2]. The risk of depression has risen in the general population as well as in those with COVID-19 infection [3]. Most people have been affected by the psychosocial changes associated with the pandemic regardless of their viral infection status [4]. Uncontrolled depression can increase functional impairment and the risk of suicide. Thus, the higher prevalence of depression during this pandemic may be a crucial component of the increased socioeconomic burden imposed by COVID-19.

Insufficient information has been available with regard to various psychosocial factors associated with depression among the general population relevant to COVID-19 pandemic societies. This study aimed to investigate risk and protective factors associated with depression in the general population uninfected by COVID-19.

Methods

Study design and participants

This was an online-based cross-sectional study that was part of a survey on the psychosocial effects of COVID-19 in the general population. Details of the data collection method were described previously [5]. Briefly, between April 24 and May 5 of 2020, the third month of the COVID-19 outbreak in South Korea, we conducted an anonymous online survey with a total of 1,500 residents aged 19–65 years from three metropolitan areas according to prevalence of COVID-19. The online survey was conducted via a service provider (Macromill Embrain). In this study, data from 1,492 respondents without a history of COVID-19 infection (excluding eight confirmed cases of COVID-19) were used. The study was approved by the Chonnam National University Hospital Institutional Review Board (CNUH-2020-092). Electronic informed consent was obtained from each participant prior to starting the investigation.

Outcome measures

Demographic variables included sex, age, marital status (married or not), residential location, religious identity, education level, medical insurance (Medicaid or Medicare), employment status (unemployed or temporarily employed vs. employed, student, or homemaker), frequency of exercise (three times or more per week before and during the COVID-19 pandemic, respectively), and smoking status. Clinical characteristics included underlying physical or mental illness (defined as currently taking medication for a condition), quarantine experience, and COVID-19 testing.

Depression was measured using the Patient Health Questionnaire-9 (PHQ-9) [6, 7]. A cutoff score of ≥ 10 , was used as an indicator of clinically relevant symptoms of depression in this study [8]. Gratitude and loneliness as indices of psychological status were measured using a six-item version of the Gratitude Questionnaire (GQ-6) [9, 10] and the three-item UCLA Loneliness Scale [11].

A questionnaire developed and validated by the authors was used to identify psychological and behavioural changes and distress due to the spread of COVID-19 [5]. All items in the questionnaire were rated using a five-point Likert scale. The COVID-19-related questionnaire included five factors: fear of COVID-19 infection (seven items), difficulties related to outside activities (four items), disturbances in eating and sleeping (three items), stigma of COVID-19 (three items), and fear of blame for COVID-19 infection (two items). In addition, six items related to stress associated with the COVID-19 pandemic, including economic stress and difficulty with obtaining daily necessities, were included. Scores on all subfactors of the questionnaire are presented as mean values (total scores divided by number of items).

Statistical analysis

Differences in sociodemographic, clinical, and psychosocial characteristics for those with depression measured by PHQ-9 were analysed using the chi-square test for categorical variables and independent *t*-tests for continuous variables. A multivariate logistic regression analysis was used to identify factors independently associated with depression after adjusting for variables that were statistically significant in the univariate analyses. SPSS for Windows software was used to perform the statistical tests. All statistical tests were two-tailed, and *p*-values < 0.05 were considered significant.

Results

Among 1,500 members of the general population, eight people (0.5%) had been infected by COVID-19. The prevalence of depression, indicated by PHQ-9 scores ≥ 10 , was 21.1% in the total population (316 of 1,500 people) and 20.9% without COVID-19 (312 of 1,492). Half of infected people (four of eight) exhibited depression, but this incidence was not significant ($p = 0.066$).

Table 1 shows comparisons of sociodemographic factors and scores on clinical scales with or without depression in the general population uninfected by COVID-19. Unmarried people, smokers, people on psychiatric medication, and unemployed or temporarily employed people were significantly more likely to exhibit depression. Those with depression were significantly younger than those without. In contrast, people who were currently exercising at least three times weekly were significantly less likely to exhibit depression. However, the frequency of exercise before the pandemic was not significantly associated with depression. There was no significant difference in depression according to sex, religion, region, or presence of a physical illness treated by medication.

Table 1

Comparisons of sociodemographic factors and clinical scales according to the presence of depression

| | Total | Depression (+) | Depression (-) | Statistics | P value |
|--|-------------|------------------|-------------------|-------------------|-----------------|
| | (N = 1492) | (N = 312, 20.9%) | (N = 1180, 79.1%) | | |
| Sex, n (%), Female | 748 (50.1) | 158 (21.1) | 590 (78.9) | $\chi^2 = 0.041$ | .840 |
| Age, mean (SD), years | 40.3 (11.8) | 37.5 (11.2) | 41.0 (11.9) | t = 4.654 | <.001 |
| Region, n (%) | | | | | |
| , Gwangju | 499 (33.4) | 112 (18.2) | 388 (81.8) | $\chi^2 = 3.257$ | .196 |
| , Daegu | 493 (33.0) | 109 (22.1) | 384 (77.9) | | |
| , Capital area | 500 (33.5) | 91 (22.4) | 408 (77.6) | | |
| Marital status, n (%), Unmarried | 755 (50.6) | 199 (26.4) | 556 (73.6) | $\chi^2 = 27.411$ | <.001 |
| Education, n (%), High school graduate/dropout or less | 255 (17.1) | 62 (24.3) | 193 (75.7) | $\chi^2 = 2.153$ | .142 |
| Occupational type, n (%), Unemployed or temporary workers | 305 (20.4) | 93 (30.5) | 212 (69.5) | $\chi^2 = 21.275$ | <.001 |
| Medical security, n (%), Medicaid | 69 (4.6) | 20 (29.0) | 49 (71.0) | $\chi^2 = 2.852$ | .091 |
| Religious status, n (%), yes | 580 (38.9) | 110 (19.0) | 470 (81.0) | $\chi^2 = 2.173$ | .140 |
| Smoking status, n (%), yes | 318 (21.3) | 88 (27.7) | 230 (72.3) | $\chi^2 = 11.171$ | .001 |
| Underlying mental illness, n (%), yes | 67 (4.5) | 27 (40.3) | 40 (59.7) | $\chi^2 = 15.942$ | <.001 |
| Underlying physical illness, n (%), yes | 398 (26.7) | 77 (19.3) | 321 (80.7) | $\chi^2 = 0.804$ | .370 |
| Quarantine experience, n (%), yes | 33 (2.2) | 11 (33.3) | 22 (66.7) | $\chi^2 = 3.148$ | .076 |
| Frequency of exercise | | | | | |
| three times or more per week before COVID-19 pandemic, n (%) | 891 (59.7) | 191 (21.4) | 700 (78.6) | $\chi^2 = 0.369$ | .544 |

Bold values denote statistical significance at the p < 0.05 level.

| | Total (N = 1492) | Depression (+) (N = 312, 20.9%) | Depression (-) (N = 1180, 79.1%) | Statistics | P value |
|--|---------------------|--|---|-------------------|-----------------|
| three times or more per week during COVID-19 pandemic, n (%) | 464 (31.1) | 71 (15.3) | 393 (84.7) | $\chi^2 = 12.814$ | <.001 |
| COVID-19-related questionnaire | | | | | |
| Stress associated with the COVID-19 pandemic | 18.2 (4.6) | 20.2 (4.5) | 17.7 (4.5) | t = -8.754 | <.001 |
| Fear of COVID-19 infection | 3.8 (0.7) | 3.9 (0.8) | 3.8 (0.7) | t = -2.764 | .006 |
| Difficulty in outside activities | 4.2 (0.6) | 4.3 (0.6) | 4.2 (0.6) | t = -0.619 | .536 |
| Disturbance in eating and sleeping | 2.8 (0.9) | 3.3 (0.9) | 2.7 (0.9) | t = -9.845 | <.001 |
| Stigma of COVID-19 | 2.9 (0.8) | 3.0 (0.8) | 2.8 (0.8) | t = -4.383 | <.001 |
| Fear of blame for COVID-19 infection | 3.6 (1.0) | 3.7 (0.1) | 3.5 (1.0) | t = -3.049 | .002 |
| Psychiatric scales | | | | | |
| UCLA loneliness scale-3 | 5.2 (1.7) | 6.7 (1.7) | 4.8 (1.5) | t = -17.959 | <.001 |
| Gratitude questionnaire-6 | 30.2 (6.1) | 26.9 (6.2) | 31.0 (5.7) | t = 10.970 | <.001 |
| Bold values denote statistical significance at the p < 0.05 level. | | | | | |

The loneliness scale scores were significantly higher, and the GQ-6 scores significantly lower, in people with depression than in those without. Of the items used to assess COVID-19 distress, scores for fear of infection, disturbance in eating and sleeping, stigma of COVID-19, fear of blame for COVID-19 infection, and stress associated with COVID-19 were significantly higher in people with depression.

Table 2 shows the results of the logistic regression analysis of factors associated with depression. Higher scores on the loneliness scale, younger age, current smoking, and current psychiatric treatment were significantly associated with increased risks of depression. Of the questions specifically asking about COVID-19-related distress, disturbances in eating and sleeping and the level of stress due to COVID-19 were significantly associated with increased risks of depression. In contrast, exercising three times or more per week during the COVID-19 pandemic and scores on the GQ-6 were significantly inversely associated with depression.

Table 2
Logistic regression analysis to detect factors associated with depression

| Variable | Wald | OR | 95% CI | <i>P</i> value |
|--|---------|-------|-------------|-----------------|
| Age | 4.294 | 0.983 | 0.967–0.999 | .038 |
| Marital status, Unmarried | 1.201 | 1.241 | 0.843–1.828 | .273 |
| Occupational type, Unemployed or temporary workers | 0.291 | 1.104 | 0.771–1.580 | .589 |
| Smokers, yes | 4.319 | 1.439 | 1.021–2.028 | .038 |
| Underlying mental illness, yes | 4.363 | 1.950 | 1.042–3.648 | .037 |
| Exercise, three times or more per week during COVID-19 pandemic | 5.171 | 0.672 | 0.477–0.947 | .023 |
| Stress associated with the COVID-19 pandemic, score | 11.442 | 1.077 | 1.032–1.125 | .001 |
| Fear of COVID-19 infection, score | 3.335 | 0.781 | 0.599–1.018 | .068 |
| Disturbance in eating and sleeping, score | 21.072 | 1.558 | 1.289–1.883 | <.001 |
| Stigma of COVID-19, score | 0.962 | 1.105 | 0.905–1.349 | .327 |
| Fear of blame for COVID-19, score | 0.005 | 0.994 | 0.831–1.188 | .945 |
| UCLA loneliness scale-3, score | 110.950 | 1.646 | 1.500–1.806 | <.001 |
| Gratitude questionnaire-6, score | 27.295 | 0.933 | 0.908–0.957 | <.001 |
| Bold values denote statistical significance at the $p < 0.05$ level. | | | | |
| Abbreviations: CI, confidence interval; OR, odds ratio | | | | |

Discussion

Our study results showed that during the COVID-19 pandemic, about one in five members of the general population who were not infected had clinically significant depression. Thus, the prevalence of depression was rather high. The risk of depression was increased in people suffering from loneliness and COVID-19-related stress, people who experienced psycho-behavioural changes such as disturbances in

eating and sleeping, smokers, people with underlying mental illness, and those who were younger. However, regular exercise and attitudes of gratitude were inversely associated with depression. Our study demonstrated that psychosocial changes and COVID-19-related stress increased the risk of depression and suggested that maintaining life routines such as regular exercise, eating, and sleeping and positive mind may be helpful in preventing depression during these COVID-19 times.

The prevalence of depression (21%) found in this study was similar to that of previous reports about depression prevalence (PHQ-9 \geq 10) during the COVID-19 pandemic in the US, Europe, and Asian countries (14.4–27.8%) [2, 12, 13]. According to the 2019 Korea Community Health Survey, the prevalence of depression in Korea, using the PHQ-9, was only 4.3% in 2018 [14]. Although there are limitations to comparing subjects and methods directly across studies, our results, showing an approximately fivefold increase in the prevalence of depression, suggest that psychosocial changes induced by the COVID-19 pandemic increased the risk of depression. The development of psychosocial strategies for the prevention of depression is urgently needed. For this, we should first understand the pathogenesis of, and factors associated with depression in COVID-19 pandemic societies.

In this study, the stress associated with psychosocial changes due to COVID-19 was significantly associated with increased risks of depression. In development of COVID-19 vaccines, social distancing and restricted economic activities are likely to continue. However, disturbances of sleep and eating patterns related to COVID-19, which were also significantly associated with increased risks of depression, might be more easily modified at a personal level. While a causal relationship is unclear, the inverse relationship between regular exercise during the pandemic and depression suggests that maintaining healthy lifestyles like regular exercise, eating habits, and sleep patterns daily may be important tools for preventing depression in the COVID-19 era [15] by improving mental and physical health.

Loneliness was strongly associated with the risk of depression in this study. Although social distancing is effective in preventing the coronavirus spread, it can cause loneliness due to emotional disconnection [13]. Despite long-lasting and inevitable social distancing policies, social and emotional interactions may reduce impacts of loneliness on depression.

Gratitude was inversely associated with depression. Gratitude has been reported as a protective factor against depressive symptoms following traumatic events [16]. At societal levels, gratitude is also important in forming and maintaining social relationships and encouraging people to be more prosocial [17]. Our results suggest that, during this COVID-19 pandemic, people are experiencing social isolation and loneliness, gratitude can be a psychological antidote to depression by reinforcing social bonds as well as positive mood. A recent study showed that positive attitudes reduced the negative effects of COVID-19 on mental health among Wuhan college students [18]. Although the COVID-19 pandemic and associated societal changes are drastically influencing our lives, positive attitudes and a sense of gratitude are likely to be helpful in preventing depression.

Socially and mentally vulnerable populations, such as the unemployed or temporary workers as well as people with underlying psychiatric illnesses, were more likely to have current significant depressive

symptoms, although employment status was no longer significant in the adjusted analysis. The younger generation tended to be at greater risks of depression. Generally, the prevalence of depression is higher in middle aged and elderly people [19]. However, many recent studies have found that young people were more vulnerable to mental health problems during the COVID-19 pandemic era [13, 20, 21]. Current drastic social changes may have greater impacts on the younger generation, whose psychological resilience and established social base may be inadequate for this situation. They may experience greater fear and worry about their future while living in this socioeconomically unstable society. In addition, young people are at greater risks for emerging psychiatric problems. Taken together, these results indicate that populations who are psychosocially vulnerable may be more severely affected by the distress associated with COVID-19. Therefore, we should observe these vulnerable populations carefully to facilitate early detection of mental health problems and to provide more active support.

Cigarette smoking is reportedly associated with increased risks of depression [22]. Recent studies investigating factors associated with depression also showed that smoking was associated with depression during the COVID-19 pandemic [23]. Both the biological impacts of smoking on neurotransmitters and vascular health [24] and the psychosocial influence of this respiratory pandemic on smokers should be considered as factors in the pathogenesis of depression in smokers.

This study has several limitations. First, we should be careful in applying our results to other populations affected by COVID-19. Second, causal relationships are uncertain because this study was cross-sectional. Longitudinal studies are needed to investigate the risks and protective factors of depression associated with the COVID-19 pandemic. Finally, results via an online survey method may differ from those acquired through face-to-face surveys, and there is a potential for selection bias. Therefore, caution is required when comparing the results of online and face-to-face surveys.

Conclusions

Findings of the factors associated with increased risks of depression in the general population during the COVID-19 pandemic offer important clinical implications for the general population as well as for researchers. We should pay more attention to the younger people, smokers, and people with mental health problems who might be at higher risks of depression. Psychological support for the loneliness and distress due to psychosocial changes related to COVID-19 are required to prevent depression. Furthermore, maintaining daily routines, including eating, sleeping, and exercise, and having a sense of gratitude could be recommended to the general population for preventing depression. Additional studies investigating the effectiveness of psychosocial strategies to prevent depression should be conducted.

Declarations

Acknowledgements

Not applicable.

Ethics approval and consent to participate

The study was approved by the Research Ethics Review Committee of Chonnam National University Hospital (approval number CNUH-2020-092). All participants were over 18 years old and electronic informed consent was obtained from each participant prior to starting the investigation. When participants checked consent, this survey was conducted. All methods were performed in accordance with the guidelines and regulations set by the University Institutional Review Board.

Consent for publication

Not applicable

Competing interests

The authors declare no conflicts of interest.

Author Contributions

SWK, MJ, JWK, and JYL were involved in the conception and design of the study. SWK, MK, IHP, SR, and JMK were involved in the analysis and interpretation of data. SWK drafted the manuscript and ALP, HJK, and JMK reviewed and critically revised the draft. All authors read and approved the final manuscript.

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Availability of data and materials

The dataset supporting the conclusions of this article is available on request from the first author.

References

1. Kim SW, Su KP. Using psychoneuroimmunity against COVID-19. *Brain Behav Immun* 2020;87:4-5. <https://doi.org/10.1016/j.bbi.2020.03.025>.
2. Choi EPH, Hui BPH, Wan EYF. Depression and anxiety in Hong Kong during COVID-19. *Int J Environ Res Public Health* 2020;17:3740. <https://doi.org/10.3390/ijerph17103740>.

3. Kim JW, Stewart R, Kang SJ, Jung SI, Kim SW, Kim JM. Telephone based Interventions for Psychological Problems in Hospital Isolated Patients with COVID-19. *Clin Psychopharmacol Neurosci* 2020;18(4):616-620. doi:10.9758/cpn.2020.18.4.616.
4. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun* 2020;89:531-542. <https://doi.org/10.1016/j.bbi.2020.05.048>.
5. Kim M, Park IH, Kang YS, Kim H, Jhon M, Kim JW, Ryu S, Lee JY, Kim JM, Lee J, Kim SW. Comparison of Psychosocial Distress in Areas With Different COVID-19 Prevalence in Korea. *Front Psychiatry* 2020;11:593105. <https://doi.org/10.3389/fpsy.2020.593105>.
6. Spitzer RL, Kroenke K, Williams JB, Group PHQPCS. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *JAMA* 1999;282:1737-1744.
7. Han C, Jo SA, Kwak JH, Pae CU, Steffens D, Jo I, Park MH. Validation of the Patient Health Questionnaire-9 Korean version in the elderly population: the Ansan Geriatric study. *Compr Psychiatry* 2008;49:218-223. doi:10.1016/j.comppsy.2007.08.006
8. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606-613.
9. McCullough ME, Emmons RA, Tsang JA. The grateful disposition: A conceptual and empirical topography. *J Pers Soc Psychol.* 2002;82:112-127. <https://doi.org/10.1037//0022-3514.82.1.112>.
10. Kwon SJ, Kim KH, Lee HS. Validation of the Korean version of gratitude questionnaire. *Korean J Health Psychol.* 2006;11:177-190.
11. Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: Results from two population-based studies. *Res Aging* 2004;26:655-672. <https://doi.org/10.1177/0164027504268574>.
12. Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of depression symptoms in US adults before and during the COVID-19 pandemic. *JAMA Netw. Open* 2020;3:e2019686. <https://doi.org/10.1001/jamanetworkopen.2020.19686>.
13. Palgi Y, Shrira A, Ring L, Bodner E, Avidor S, Bergman Y, Cohen-Fridel S, Keisari S, Hoffman Y. The loneliness pandemic: Loneliness and other concomitants of depression, anxiety and their comorbidity during the COVID-19 outbreak. *J Affect Disord* 2020;275:109-111. <https://doi.org/10.1016/j.jad.2020.06.036>
14. Korea Centers for Disease Control and Prevention. Korea Health Statistics 2018: Korea National Health and Nutrition Examination Survey (KNHANES Ⅴ-3). Ministry of Health and Welfare, Sejong, Korea; 2019.
15. Jiménez-Pavón D, Carbonell-Baeza A, Lavie CJ. Physical exercise as therapy to fight against the mental and physical consequences of COVID-19 quarantine: Special focus in older people. *Prog Cardiovasc Dis.* 2020;63:386-388. <https://doi.org/10.1016/j.pcad.2020.03.009>
16. Van Dusen JP, Tiamiyu MF, Kashdan TB, Elhai JD. Gratitude, depression and PTSD: Assessment of structural relationships. *Psychiatry Res* 2015;230:867-870.

<http://dx.doi.org/10.1016/j.psychres.2015.11.036>.

17. Bartlett MY, Condon P, Cruz J, Baumann J, Desteno D. Gratitude: Prompting behaviours that build relationships. *Cogn Emot*. 2012;26:2-13. <https://doi.org/10.1080/02699931.2011.561297>.
18. Yang D, Tu CC, Dai X. The effect of the 2019 novel coronavirus pandemic on college students in Wuhan. *Psychol Trauma*. 2020;12:S6-S14. <http://dx.doi.org/10.1037/tra0000930>.
19. Alexopoulos GS. Depression in the elderly. *Lancet*. 2005;65:1961-1970.
20. Ahmed MZ, Ahmed O, Aibao Z, Hanbin S, Siyu L, Ahmad A. Epidemic of COVID-19 in China and associated Psychological Problems. *Asian J Psychiatr*. 2020;51: 102092. doi: 10.1016/j.ajp.2020.102092
21. Salari N, Hosseinian-Far A, Jalali R, Vaisi-Raygani A, Rasoulpoor S, Mohammadi M, Rasoulpoor S, Khaledi-Paveh B. Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. *Global Health*. 2020;16:1-11. <https://doi.org/10.1186/s12992-020-00589-w>.
22. Fluharty M, Taylor AE, Grabski M, Munafò MR. The association of cigarette smoking with depression and anxiety: a systematic review. *Nicotine Tob Res*. 2016;19:3-13. <https://doi.org/10.1093/ntr/ntw140>.
23. Ren Y, Qian W, Li Z, Liu Z, Zhou Y, Wang R, Qi L, Yang J, Song X, Zeng L. Public mental health under the long-term influence of COVID-19 in China: Geographical and temporal distribution. *J Affect Disord*. 2020;277:893-900. <https://doi.org/10.1016/j.jad.2020.08.045>.
24. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. *J Am Coll Cardiol*. 2004;43:1731-1737. <https://doi.org/10.1016/j.jacc.2003.12.047>.