Social isolation and risk of fatal cardiovascular events

Since the start of the COVID-19 pandemic in March, 2020, in-person contact with family members, friends, and colleagues has been heavily restricted. These mitigation measures can worsen pre-existing social isolation.[1] In this phase of widespread insecurity, evidence on the prevalence and cardiovascular consequences of social isolation represents an important guideline for estimating the health consequences of COVID-19. Despite continuous therapeutic progress, coronary heart disease and stroke remain the leading causes of death globally.[2] Social isolation has previously been associated with increased risk of coronary heart disease and stroke events,[3,4] however, the impact of isolation on coronary heart disease and stroke survival remains unclear.

In *The Lancet Public Health*, Robert Smith and colleagues[5] have attempted to address this knowledge gap through a combined analysis of data from 481946 participants included in the Million Women Study and 456612 participants from UK Biobank Study without previous coronary heart disease or stroke. In this large dataset, 42402 first coronary heart disease events (1834 fatal events) and 19999 first stroke events (529 fatal events) occurred during a mean follow-up of 7 years (SD 2). In the Million Women Study and UK Biobank social isolation was assessed quantitatively via a summary index of the number of people living together in a household and the frequency of contact with family, friends, and groups. Based on this index, participants were categorised into least isolated (379031 [40%] of 938558 participants), moderately isolated (429541 [46%]), and most isolated (129986 [14%]) groups, with the least isolated group defined as the reference group. Consistent with previous literature,[3,4,6] individuals in the most isolated group reported more pronounced health-risk behaviours, such as smoking and physical inactivity, and were more likely to be obese, in poor health (self-rated), and live in more deprived areas (based on the Townsend Deprivation index) than the least isolated group. Multivariable Cox regression analyses controlling for health behaviours and established cardiovascular risk factors (age, sex, region of recruitment, deprivation, smoking, alcohol intake, physical activity, body-mass index, and self-rated health) identified no significant overall association between social isolation (most isolated *vs* least isolated) and

non-fatal coronary heart disease (combined risk ratio [RR] for both studies 1·01 [95% CI 0·98–1·04]) and non-fatal stroke (1·13 [1·08–1·18]). In contrast, there were clear associations with fatal coronary heart disease (1·86 [1·63–2·12]) and fatal stroke (1·91 [1·48–2·46]).

When different types of social isolation were analysed separately, associations were stronger for participants living alone than not alone (RR 1·60 [95% CI 1·46–1·75] for fatal coronary heart disease and stroke combined) and for participants with few versus more social contacts (1·27 [1·16–1·38]). Results did not differ significantly between the two studies, or by self-rated health, sex, or cardiovascular risk profile. Considering that fatal events were defined as death due to first coronary heart disease or stroke event without previous hospital admission, the association observed between social isolation and fatal events, but not with non-fatal events, could imply that this association is mediated by the absence of another person who can assist in seeking health-care following a cardiovascular event. This interpretation is supported by the stronger effect of living alone than having few social contacts.

Considering the large sample size of this combined analysis, this observation provides strong rationale for future intervention studies, in which the potential benefits of personal emergency alarms and internet-based surveillance in reducing fatal coronary heart disease and stroke events are assessed. To date, a variety of methods for evaluating social relationships have been used in the literature. One limitation of the study by Smith and colleagues[5] is the authors were only able to evaluate the consequences of having few contacts, but not of an excess of contacts, which can also be stressful. Furthermore, the quality of social contacts[6] was not assessed. The social isolation index used in the Million Women Study included questions about email, phone, and in person contacts, whereas the UK Biobank study only included questions on in-person contact. To achieve better comparability, future studies should seek consensus on how different aspects of social relationships can best be assessed. In-person contacts and virtual contacts should be differentiated in future studies, considering that virtual contacts such as video conferences have predominated social interactions during the COVID-19 pandemic. In the context of psychiatric

disorders, it has already been shown that in-person social contacts protect against mood disorders, but this has not been observed for online contacts.[7] For the assessment of health consequences, the differentiation between contacts with family versus friends and other groups also requires attention in future studies.

Social contacts have largely been restricted to household members during COVID-19 lockdowns. For the outcome of all-cause mortality, it has been shown that support from family members was more beneficial than support from friends.[8] Smith and colleagues suggested that the absence of another person who could assist with health-care seeking during acute events might explain the association between social isolation and fatal cardiovascular disease.[5] Such findings contradict the results of the REGARDS cohort study, which showed that having contact with family or friends in the past months—but not having anyone to care for you if you become ill or disabled—was significantly associated with incident fatal coronary heart disease.[9] Smith and colleagues observed little effect modification of social isolation-related health consequences by sex, however, it has previously been shown that men who live alone have a significantly higher long-term mortality risk following acute myocardial infarction than women.[10] In addition to sex, social determinants, character traits, previous experiences, and genetic factors can modify the cardiovascular impact of social isolation.[3]

The COVID-19 pandemic has highlighted the need to develop of a more comprehensive view of the health consequences of social isolation. The analysis by Smith and colleagues[5] provides an important contribution to this task. With a better understanding of social isolation, and a focus on internet-based surveillance and tele-medicine interventions, prevention of the devastating, and specifically fatal, health effects of such isolation might be possible.

We declare no competing interests.

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