Lifestyle Changes and Psychological Well-Being in Older Adults During COVID-19 Pandemic

Matteo Tosato, MD, PhD[a],*, Francesca Ciciarello, MD[a],
Maria Beatrice Zazzara, MD[a], Delfina Janiri, MD[a],
Cristina Pais, MD[a], Stefano Cacciatore, MD[a],
Rossella Montenero, MD[a], Maria Sandrina Leone, MD[a],
Enea Chisci, MD[a], Anna Picca, PhD[a], Vincenzo Galluzzo, MD[a],
Hélio José Coelho-Junior, PhD[b], Riccardo Calvani, PhD[a],
Emanuele Marzetti, MD, PhD[a,b], Francesco Landi, MD, PhD[a,b], on
behalf of Gemelli Against COVID-19 Post-Acute Care Team

KEYWORDS

- Older adults • COVID-19 • Frailty • Quality of life • Mobility disorders

KEY POINTS

- Emergency restrictions aimed at reducing contagion elicited lifestyle modification.
- The impact of nonpharmacologic interventions against COVID-19 pandemic was particularly significant in older adults.
- Main consequences of restrictions in older persons were lifestyle modifications, reduced quality of life, and overall well-being, worsening in mobility and depression.

INTRODUCTION

The advent of the COVID-19 pandemic disrupted our habits and lives. The updated numbers of infections and deaths in the world's population are staggering. To date, pandemic figures reached more than 500 million cases and more than 6,000,000 deaths.[1] The risk factors for developing more severe forms of the disease are advanced age, obesity, multimorbidity, immunodeficiency, and preexisting disorders affecting lung, heart, liver, and the kidneys.[2] In particular, advanced age (85+ years) is

the most significant independent risk factor associated with intensive care unit admission and in-hospital mortality.[3]

National health systems, even those of the most developed countries, were severely challenged by COVID-19 pandemic and urged emergency political decisions aimed at containing contagion and its burdensome consequences. Large-scale nonpharmaceutical interventions were put in place, including social distancing, school closures, isolation of symptomatic people and their contacts, and generalized lockdowns.[4] Restrictive measures had a large effect in reducing SARS-CoV-2 transmission but, at the same time, heavily affected the daily life of a large share of people, including more vulnerable people.[5] Older adults, especially when multimorbid and frail, were asked to comply even more strictly with those restrictions. Despite the fact that public health measures protected thousands of older adults from the negative COVID-19 health outcomes, unintended detrimental consequences were experienced by the older age classes.[6] Notably, social isolation and reduced physical activity are well-acknowledged risk factors for negative health outcomes in the elderly population. Specifically, social isolation is associated with reduced quality of life, reduced muscle mass, cognitive function, multimorbidity, and disability.[7–9] Physical inactivity has a significant impact on health, quality of life, cognitive impairment, falls, depression, disability, hospitalization, and mortality.[10]

Moreover, study coming from previous coronavirus pandemics demonstrated impaired quality of life, depression, and psychological discomfort.[11]

In light of this evidence, several concerns exist regarding the long-term outcomes of restrictions placed on the elderly population. The aim of this study was to evaluate the impact of public health measures to mitigate COVID-19 pandemic on subjects older than 80 years, who have not suffered COVID-19, in terms of quality of life, changes in their daily habits, and psychological discomfort.

EVALUATION

We conducted an observational study in community dwellers aged 80+ years consecutively referring to the vaccination center against Sars-CoV-2 at Fondazione Policlinico Universitario Agostino Gemelli IRCCS of Rome, Italy. Participants were asked to complete a dedicated questionnaire. The questionnaire was composed of 4 sections. In the first section, demographic, anthropometric, and clinical information were collected, including age, gender, education, body height and weight, diseases, and drug therapy, together with data regarding changes in individual daily habits (such as perturbations of previous usual activities, attendance to places of worship or senior centers, physical activity routines, access to health care services). The second section evaluated the quality of life at the time of the assessment compared with the prepandemic time using a visual analogue scale (0–100). Mobility difficulty and depression status were also compared across the same timeframe. The third section assessed subjective psychological well-being using the 5-item World Health Organization Well-Being Index (WHO-5).[12,13] WHO-5 consists of 5 questions assessing the subjective well-being of the participants. The items are on a 5-point Likert scale ranging from 0 "at no time" to 5 "all of the time." The final score is calculated by summing the single items and ranges from 0 to 25, with 0 representing the worst imaginable well-being and 25 representing the best imaginable well-being. The WHO-5 is among the most widely used questionnaires assessing subjective psychological well-being, and it has showed a good internal and external validity in elderly population. A significant worsening in the quality of life was defined as a loss of at least 5 points in the visual analogue scale and/or a WHO score less than or equal to 15.

Finally, the last section assessed psychological distress related to the restrictions put in place to counteract the Sars CoV2 pandemic, through Kessler 10 Psychological Distress Scale (K10).[14] K10 is a 10-item questionnaire providing a global measure of distress based on questions about anxiety and depressive symptoms experienced in the last 4 week. Items are rated using a 5-point Likert scale ranging from 1 (never) to 5 (always). Score may range from 10 to 50. Low scores indicate low levels of psychological distress, whereas high scores indicate high levels of psychological distress. Consistently with previous validation studies[15,16] we adopted the cut-off score of greater than 19 to detect the likelihood of presence of psychological distress. The K-10 can be used with confidence in general-purpose health surveys and when assessing psychological distress in old-age communities.

At the end of the questionnaire, the study personnel assessed the frailty status of the study participants using the Clinical Frailty Status.[17]

The only exclusion criterion was the unwillingness to participate.

Statistical Analyses

Study participants were categorized into 2 groups: individuals who had changed lifestyle during the COVID-19 pandemic and individuals who reported no change. The 2 groups were compared on demographic and key clinical characteristics, quality of life, and psychological distress. Continuous variables were expressed as mean, and categorical variables were expressed as frequencies by absolute value and percentage of the total. Differences in proportions and means between the 2 groups were assessed using Fisher exact test and t-test statistics, respectively. The level of statistical significance was set at $P>.05$. Factors significantly associated with lifestyle change in bivariate analyses, together with age and sex, subsequently underwent a multivariate logistic regression to generate odds atios (ORs) and their 95% confidence intervals, with lifestyle change as dependent outcome measure. We examined possible multicollinearity between variables of interest by ensuring that the variance inflation factor indicator obtained from linear regression analysis was less than 4. We used the statistical routines of SPSS Statistics 24.0 for Windows (IBM Co., Armonk, New York, USA).

DISCUSSION

We collected data from 504 participants; main characteristics are summarized in Table 1. Briefly, mean age of our population was 83.2 years, and 56% were women. More common diseases were hypertension (55%), arrhythmia (16%), diabetes (15%), ischemic heart disease (11%), any cancer (10%), and osteoarthritis (10%). Mean number of diseases was 2.1 and mean number of drugs 3.6. Most of the participants had taken flu vaccination (85%), whereas only 36% had taken pneumococcal vaccination. Around 78% of participants performed routine blood check in the previous year, and 64% were visited by general practitioners. The mean score of clinical frailty scale was 3.5 ± 1.3.

We stratified our study sample into 2 groups, based on their self-reported change in daily routines. In the whole study sample, 284 older adults (56.3%) reported substantial lifestyle changes following COVID-19 pandemic and 220 individuals (43, 7%) preserved their prepandemic habitual activities. The 2 groups differed by age ($P = .02$), education ($P = .01$), and clinical frailty scale ($P<.01$). Specifically, study participants reporting lifestyle changes were younger, with higher level of education and a lower score at the clinical frailty scale. Furthermore, in the same group, a higher percentage of individuals reported a worsening in the quality of life compared with prepandemic time (Table 2). Multivariate logistic regression identified the worsening at the visual

Table 1
General and clinical characteristics of study population according to lifestyle change during COVID-19 pandemic era

Characteristics	Total Sample (n = 504)	Lifestyle Change		p
		NO (n = 220)	YES (n = 284)	
Age (y)	83.2 ± 5.1	83.8 ± 4.5	82.8 ± 5.5	*0.02*
Gender				
Male	221 (44)	104 (47)	117 (41)	0.10
Female	283 (56)	116 (53)	167 (59)	
Education (y)	11.4 ± 5.3	10.7 ± 6.0	11.8 ± 4.7	*0.01*
Hypertension	276 (55)	117 (53)	159 (56)	0.28
Ischemic heart disease	55 (11)	26 (12)	29 (10)	0.34
Arrhythmia	80 (16)	32 (15)	48 (17)	0.27
Diabetes	75 (15)	36 (16)	39 (14)	0.24
Renal failure	14 (3)	6 (3)	8 (3)	0.58
COPD	33 (7)	18 (8)	15 (5)	0.13
Cancer	49 (10)	17 (8)	32 (11)	0.11
Osteoarthritis	41 (8)	18 (8)	23 (8)	0.55
Number of diseases	2.1 ± 1.4	2.3 ± 1.5	2.1 ± 1.2	0.12
Number of drugs	3.6 ± 2.8	3.8 ± 2.9	3.5 ± 2.6	0.20
Flu vaccination	427 (85)	189 (86)	238 (84)	0.30
Pneumococcal vaccination	183 (36)	78 (36)	105 (37)	0.39
Routine blood check	397 (78)	166 (76)	231 (81)	0.07
General practitioner visit	321 (64)	131 (60)	190 (67)	0.05
Clinical frailty scale	3.5 ± 1.3	3.7 ± 1.3	3.3 ± 1.3	*<0.01*

Data are given as number (percent) for gender, diseases, flu and pneumococcal vaccination, blood check, and general practitioner visit; for all the other variables, means ± SD are reported.

analogue scale as a specific risk factor for lifestyle change (OR = 2.03; $P<.001$), whereas clinical frailty score was associated with the preservation of prepandemic activities (OR = 0.78; P = .001) (**Table 3**).

In **Fig. 1** we reported the usual activities interrupted because of the pandemic. The most affected habitual routine was the visit to relatives and friends (reported by 46.5% of study participants), followed by physical activity (45.8%), participation to religious services (19.7%), cinema and theater show attendance (18.1%), shopping (12.7%), travel (7.7%), and work activities (6.1%).

As for the mobility status, the percentage of the study participants reporting no difficulty in mobility reduced from 57.4% in the prepandemic phase to 43.2%. People reporting moderate difficulty increased from 37% to 44.7%, whereas older adults reporting severe difficulty increased from 5.6% to 12.1% (**Fig. 2**).

A similar trend was observed for the depression status. Indeed, at the time of evaluation only 43.9% reported no depression compared with 76.3% in the prepandemic time, 50.3% reported moderate depression (vs 22% pre-COVID-19 time), and 5.8% reported severe depression (vs 1.7%) (**Fig. 3**).

Older adults, in particular the multimorbid and frail older population, were the most heavily affected population segment in terms of negative health outcomes and mortality during COVID-19 pandemic.[18] The latest Italian report estimated that around 85%

Table 2
Quality of life and psychological well-being of study population according to lifestyle change during COVID-19 pandemic era*

Characteristics	Total Sample (n = 504)	Lifestyle Change		p
		NO (n = 220)	YES (n = 284)	
Self-rated health (visual analogue scale)				
VAS pre-COVID-19	76.5 ± 16.9	75.8 ± 18.3	77.0 ± 15.8	0.42
VAS COVID-19 era	69.6 ± 19.2	70.7 ± 19.8	68.7 ± 18.8	0.25
Worsened EQ-VAS	217 (43)	75 (35)	142 (65)	*<0.001*
WHO-5: The 5-item World Health Organization Well-Being Index				
WHO-5	15.8 ± 5.2	16.3 ± 5.4	15.4 ± 5.0	0.07
WHO-5 ≤15	229 (45)	87 (39)	142 (50)	*0.01*
K10 test—Kessler Psychological Distress Scale				
K10 test	16.0 ± 4.8	15.7 ± 4.9	16.2 ± 4.8	0.23
K10 test more than 19	116 (23)	46 (21)	70 (25)	0.19

Worsened quality of life: greater than 5 points lost at VAS.
WHO-5: The World Health Organisation—Five Well-Being Index (ranging from 0 to 25, with 0 representing the worst imaginable well-being and 25 representing the best imaginable well-being).
K10 test: Kessler Psychological Distress Scale (ranging from 0 to 50, with 0 representing the better result and 50 representing the worsen result).

of deaths occurred in people aged 70 years or older.[19] However, people in the oldest age groups were also the most affected by the emergency restrictive measures put in place to contain contagion due to their intrinsic vulnerability.[20] Indeed, social distancing, loneliness, and difficulty in accessing care caused by the anti-COVID-19 public health measures may have further increased the risk for several negative outcomes, including reduction of quality of life, cognitive impairment, falls, depression, disability.[21]

Studies on the topic showed conflicting results. A study conducted in individuals aged 50+ years from Italy, Spain, and France reported that about 50% of participants felt sad or depressed more often than usual during the lockdown.[22] Similarly, in Australian older adults receiving home- and community-based services, quality of life significantly worsened during the pandemic compared with the previous year.[23]

Table 3
Multivariate logistic regression (NO lifestyle change vs YES lifestyle change)

|	OR [95% CI]	Wald	p
Gender	1.27 [0.87–1.86]	1.59	0.20
Age	0.98 [0.94–1.02]	0.90	0.34
Education	1.03 [0.99–1.06]	3.14	0.07
Heart failure	0.45 [0.20–1.05]	3.35	0.06
Clinical frailty scale	0.78 [0.67–0.91]	10.15	**0.001**
Worsened EQ-VAS	2.03 [1.38–3.00]	12.89	**<0.001**
WHO-5 ≤15	1.46 [0.98–2.16]	3.56	0.06

Significant results in bold.
Abbreviations: CI, confidence interval; OR, odds ratio; p, statistical significance.
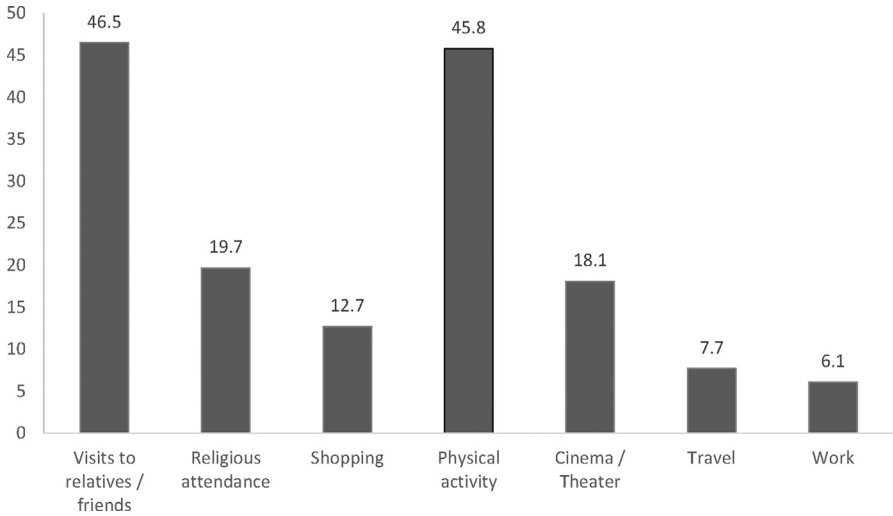
Fig. 1. Usual activities interrupted during pandemic.

In community-dwelling older adults from United States, a higher rate of depression and loneliness was reported following the onset of the pandemic.[24] In middle-aged and older adults from the Canadian Longitudinal Study on Aging the odds of depressive symptoms doubled during the pandemic compared with the prepandemic period.[25]

However, an online survey involving 825 US adults aged 60 years and older revealed that confinement/restrictions, although listed among the most stressful events of the pandemic, were not associated with negative indicators of psychological well-being.[26] Moreover, a longitudinal study conducted in Sweden concluded that COVID-19 had only minimal effects on well-being in older adults.[27] Notably, in the early pandemic phase, many Swedish older adults rated their well-being as
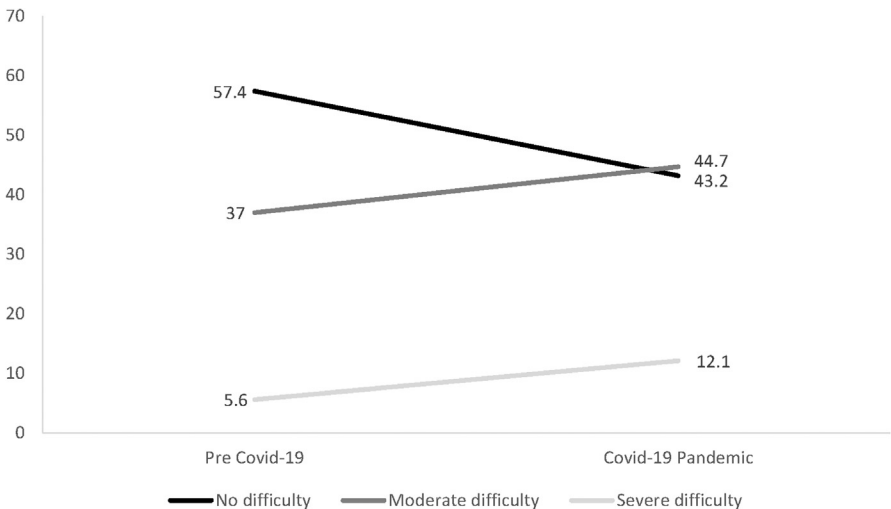
Fig. 2. Self-report difficulty in mobility before and during COVID-19 pandemic.
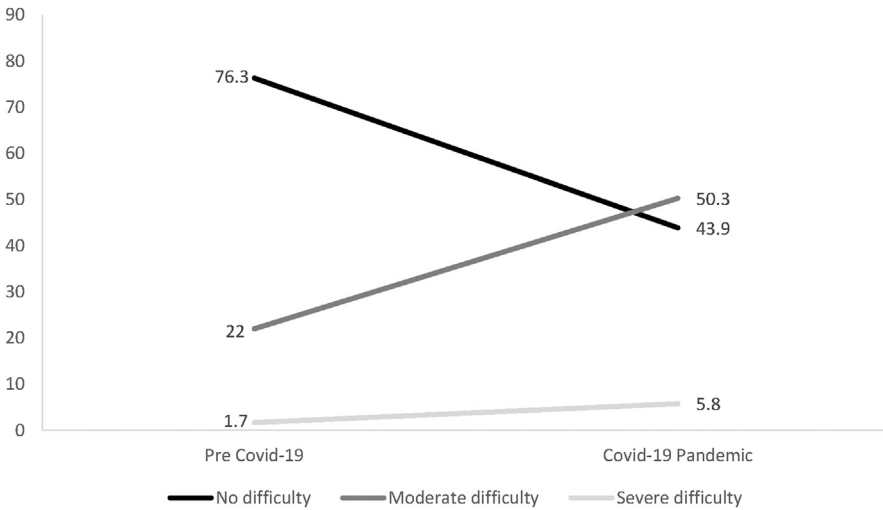
Fig. 3. Self-report depression status before and during COVID-19 pandemic.

high as or even higher than previous years. Data collected from more than 36,000 English adults of the UCL COVID-19 Social Study showed that anxiety and depressive symptoms increased during the early stages of lockdown, but with a fast improvement within a few weeks.[28]

Finally, in 720 people from the Fifth National Survey on Quality of Life in Older Adults in Chile, Herrera and colleagues found no changes in self-rated health in older adults during the pandemic, although some health indicators, including depression and anxiety, worsened.[29]

Collectively, those findings highlighted a huge heterogeneity of responses to pandemic public health measures in older adults and suggested that many older individuals may have substantial adaptive capacity and resilience.

Our results showed a significant impact of restrictive measures in community-dwelling older adults aged older than 80 years who have not contracted SARS-CoV-2 infection. Specifically, of the 504 subjects interviewed, 284 (56%) reported substantial lifestyle modifications. The main activities interrupted were visits to relatives (46%), physical activity (45.8%), attending religious services (19.7%), and cinema/theater (18.1%). Notably, although 57.4% of participants reported having no difficulty in terms of mobility before the pandemic, this percentage dropped alarmingly to 43.2%. The same pattern was observed in those who had moderate difficulty (that increased from 37% to 44.7%) and those who had severe difficulty (from 5.6% to 12.1%) increased. Mobility is critical for living independently. Older adults who lose their mobility have poorer quality of life and higher risk of several medium- to long-term negative outcomes including falls, cognitive impairment, disability, disease, hospitalization, and death.[30–32]

In this context, the increase in mobility difficulty reported by our participants is quite concerning for the overall impact this may have from both health and socioeconomic perspectives. Not surprisingly, we also found a similar trend in depression figures, with the percentage of study participants reporting no depressive symptoms that dropped from 76.3% in the pre-COVID era to 43.9%. A concomitant increase was found for moderate and severe depression.

In addition, our data showed that people who most likely made lifestyle changes were younger, with higher education status and better Clinical Frailty Scale scores. As expected, the reduction in quality of life, as well as the reduced psychosocial well-being, was more evident in subjects who modified their lifestyles.

SUMMARY

Restrictive measures aimed at containing COVID-19 pandemic had a significant impact on lifestyle habits, quality of life, psychosocial well-being, and mobility in individuals older than 80 years who have not contracted SARS-CoV-2 infection. A comprehensive multidimensional assessment should be routinely implemented to determine and manage the potential negative consequences of public health measures on overall health status and quality of life of older adults.

CLINICS CARE POINTS

- Restrictive measures to contain COVID-19 pandemic caused substantial lifestyle modifications, reduced quality of life and psychosocial well-being, and increased mobility deficits in older adults.
- People who most likely made lifestyle changes were younger, with higher education status and better Clinical Frailty Scale scores.
- The reduction in quality of life and psychosocial well-being was more evident in subjects who modified their lifestyles.
- Approaches based on multidimensional assessments should be implemented to minimize the negative health outcomes in this vulnerable population segment.

ACKNOWLEDGMENTS

Pediatric team: Buonsenso Danilo, Valentini Piero, Sinatti Dario, De Rose Gabriella. • *Pneumology team:* Richeldi Luca, Lombardi Francesco, Calabrese Angelo, Varone Francesco, Leone Paolo Maria, Siciliano Matteo, Corbo Giuseppe Maria, Montemurro Giuliano, Calvello Mariarosaria, Intini Enrica, Simonetti Jacopo, Pasciuto Giuliana, Adiletta Veronica, Sofia Carmelo, Licata Maria Angela. • *Psychiatric team:* Sani Gabriele, Delfina Janiri, Simonetti Alessio, Modica Marco, Montanari Silvia, Catinari Antonello, Terenzi Beatrice. • *Radiology team:* Natale Luigi, Larici Anna Rita, Marano Riccardo, Pirronti Tommaso, Infante Amato. • *Rheumatology team:* Paglionico Annamaria, Petricca Luca, Tolusso Barbara, Alivernini Stefano, Di Mario Clara. • *Vascular team:* Santoliquido Angelo, Santoro Luca, Nesci Antonio, Di Giorgio Angela, D'Alessandro Alessia.

DISCLOSURE

No conflict of interest to disclosure.

REFERENCES

1. WHO coronavirus (COVID-19) Dashboard | WHO coronavirus (COVID-19) Dashboard with vaccination data. Available at: https://covid19.who.int/. Accessed May 2, 2022.
2. Wolff D, Nee S, Hickey NS, et al. Risk factors for Covid-19 severity and fatality: a structured literature review. Infection 2021;49(1):15–28.
3. Kim L, Garg S, O'Halloran A, et al. Risk factors for intensive care unit admission and in-hospital mortality among hospitalized adults identified through the US coronavirus disease 2019 (COVID-19)-Associated hospitalization surveillance network (COVID-NET). Clin Infect Dis 2021;72(9):E206–14.
4. Flaxman S, Mishra S, Gandy A, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature 2020;584(7820): 257–61.
5. Gashaw T, Hagos B, Sisay M. Expected impacts of COVID-19: considering resource-limited countries and vulnerable population. Front Public Health 2021; 9. https://doi.org/10.3389/FPUBH.2021.614789.
6. Falvo I, Zufferey MC, Albanese E, et al. Lived experiences of older adults during the first COVID-19 lockdown: a qualitative study. PLoS One 2021;16(6). https://doi.org/10.1371/JOURNAL.PONE.0252101.
7. Loyola WS, Camillo CA, Torres CV, et al. Effects of an exercise model based on functional circuits in an older population with different levels of social participation. Geriatr Gerontol Int 2018;18(2):216–23.
8. Douglas H, Georgiou A, Westbrook J. Social participation as an indicator of successful aging: an overview of concepts and their associations with health. Aust Health Rev 2017;41(4):455–62.
9. Lindsay Smith G, Banting L, Eime R, et al. The association between social support and physical activity in older adults: a systematic review. Int J Behav Nutr Phys Act 2017;14(1). https://doi.org/10.1186/S12966-017-0509-8.
10. Ozemek C, Lavie CJ, Rognmo Ø. Global physical activity levels - need for intervention. Prog Cardiovasc Dis 2019;62(2):102–7.
11. Lee AM, Wong JGWS, McAlonan GM, et al. Stress and psychological distress among SARS survivors 1 year after the outbreak. Can J Psychiatry 2007;52(4): 233–40.
12. Topp CW, Østergaard SD, Søndergaard S, et al. The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom 2015;84(3):167–76.

13. Staehr Johansen K. The use of wellbeing measures in primary health care/The DepCare Project. World Health Organization, Regional Office for Europe: Well-Being Measures in Primary Health Care/The DepCare Project. Published online 1998:target 12, E60246.

14. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002;32(6):959–76.

15. Kessler RC, Barker PR, Colpe LJ, et al. Screening for serious mental illness in the general population. Arch Gen Psychiatry 2003;60(2):184–9.

16. Andrews G, Slade T. Interpreting scores on the Kessler psychological distress scale (K10). Aust N Z J Public Health 2001;25(6):494–7.

17. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173(5):489–95.

18. Variation in the COVID-19 infection-fatality ratio by age, time, and geography during the pre-vaccine era: a systematic analysis. Lancet 2022;399(10334):1469–88.

19. COVID-19 integrated surveillance: key national data. Available at: https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-integrated-surveillance-data. Accessed May 2, 2022.

20. Manca R, de Marco M, Venneri A. The impact of COVID-19 infection and enforced prolonged social isolation on neuropsychiatric symptoms in older adults with and without Dementia: a review. Front Psychiatry 2020;11. https://doi.org/10.3389/FPSYT.2020.585540.

21. Cacioppo JT, Cacioppo S. Older adults reporting social isolation or loneliness show poorer cognitive function 4 years later. Evid Based Nurs 2014;17(2):59–60.

22. Arpino B, Pasqualini M, Bordone V, et al. Older people's nonphysical contacts and depression during the COVID-19 lockdown. Gerontologist 2021;61(2):176–86.

23. Siette J, Dodds L, Seaman K, et al. The impact of COVID-19 on the quality of life of older adults receiving community-based aged care. Australas J Ageing 2021;40(1):84–9.

24. Krendl AC, Perry BL. The impact of sheltering in place during the COVID-19 pandemic on older adults' social and mental well-being. J Gerontol B Psychol Sci Soc Sci 2021;76(2):E53–8.

25. Raina P, Wolfson C, Griffith L, et al. A longitudinal analysis of the impact of the COVID-19 pandemic on the mental health of middle-aged and older adults from the Canadian Longitudinal Study on Aging. Nat Aging 2021;1(12):1137–47.

26. Whitehead BR, Torossian E. Older adults' experience of the COVID-19 pandemic: a mixed-methods analysis of stresses and joys. Gerontologist 2021;61(1):36–47.

27. Kivi M, Hansson I, Bjälkebring P. Up and about: older adults' well-being during the COVID-19 pandemic in a Swedish longitudinal study. J Gerontol B Psychol Sci Soc Sci 2021;76(2):E4–9.

28. Fancourt D, Steptoe A, Bu F. Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England: a longitudinal observational study. Lancet Psychiatry 2021;8(2):141–9.

29. Herrera MS, Elgueta R, Fernández MB, et al. A longitudinal study monitoring the quality of life in a national cohort of older adults in Chile before and during the COVID-19 outbreak. BMC Geriatr 2021;21(1). https://doi.org/10.1186/S12877-021-02110-3.

30. Rasch EK, Magder L, Hochberg MC, et al. Health of community-dwelling adults with mobility limitations in the United States: incidence of secondary health conditions. Part II. Arch Phys Med Rehabil 2008;89(2):219–30.

31. Freiberger E, Sieber CC, Kob R. Mobility in older community-dwelling persons: a narrative review. Front Physiol 2020;11. https://doi.org/10.3389/FPHYS.2020.00881.
32. Jain P, Bellettiere J, Glass N, et al. The relationship of accelerometer-assessed standing time with and without ambulation and mortality: the WHI OPACH study. J Gerontol A Biol Sci Med Sci 2021;76(1):77–84.