Determinants of depressive symptoms increase in older persons during the COVID-19 pandemic: evidence from Czech cohort study using repeated assessments

Andrea Dalecká,1 Hynek Pikhart,1,2 Anna Bartošková,1 Naděžda Čapková,3 Martin Bobák1,2

ABSTRACT
Background Numerous studies reported higher levels of mental health issues during the COVID-19 pandemic but only a minority used repeated measurements. We investigated change in depressive symptoms in the Czech ageing cohort and the impact of pre-existing and COVID-19-related stressors.

Methods We used data on 2853 participants (mean age 73.4 years) from the Czech part of the prospective Health, Alcohol and Psychosocial Factors in Eastern Europe cohort that participated in postal questionnaire surveys before (September 2017–June 2018) and during the pandemic (October 2020–April 2021). Participants reported their depressive symptoms using the Centre for Epidemiological Studies-Depression Scale including 10 (CES-D-10) tool. A principal component analysis (PCA) was used to create representative components of the pandemic-related stressors. The impact of the stressors on change in depressive symptoms was tested using multivariable linear regression, after adjustment for age and potential confounders.

Results Three patterns of the pandemic-related stressors (‘financial stressors’, ‘social and perception stressors’ and ‘death and hospitalisation stressors’) were extracted from the PCA. The mean CES-D-10 score increased from 4.90 to 5.37 (<0.001). In fully adjusted models, significantly larger increases in depression score were reported by older people (β=0.052, p=0.006), those with poor self-rated health (β=0.170, p<0.001), those who experienced death or hospitalisation of a close person (β=0.064, p<0.001), social deprivation (β=0.057, p<0.001), delays in healthcare (β=0.048, p=0.005) and those who suffered from COVID-19 (β=0.045, p=0.008).

Conclusion This study confirms an increase in depressive symptoms in older persons during the pandemic and identified several pandemic-related risk factors suggesting that public health policies should address this vulnerable group by adopting the preventing strategies.

WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ There is growing evidence that the COVID-19 pandemic contributed to deterioration in mental health. A sizeable literature has looked at the predictors of depression symptoms worsening, however, less is known about the effect of the pre-existing and pandemic-related stressors on depression in older populations.

WHAT THIS STUDY ADDS
⇒ This study revealed the significant increase in depression symptoms during the COVID-19 pandemic compared with prepandemic time using repeated measurements. Larger increases in depression score in older persons were associated with higher age, poor self-rated health, social deprivation, delays in healthcare, suffering from COVID-19 and experiencing death or hospitalisation of a close person.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
⇒ This study provides evidence of the susceptibility of the older individuals to mental distress suggesting that pandemic emergency policies should address this vulnerable population group in future threats.

INTRODUCTION
Mental disorders including depression are recognised as the leading causes of disease burden. Soon after WHO declared COVID-19 as a pandemic, concerns were raised about its impact on mental health. There is growing evidence that the COVID-19 pandemic resulted in deterioration in mental health, possibly mediated by health concerns and changes in daily life related to long-lasting quarantine measures. Early studies of general population samples and specific subpopulations, such as health workers and college students revealed a substantial increase in the prevalence of depression in these groups. However, the impact of the COVID-19 pandemic on mental health in older population remains inconclusive. It has been reported that older population is less likely to report worsening in mental health compared with younger adults, perhaps linked to the assumption that older individuals may be more resilient and cope more successfully with challenging life events. However, much of the evidence related to COVID-19 is based on cross-sectional data that lack repeated measures of mental health before and during the pandemic.
Several factors that may negatively affect the mental health of the ageing population during the pandemic were distinguished. First, older persons are physically most vulnerable to severe and fatal courses of COVID-19 disease that might lead to a higher perceived threat of getting infected. A few studies reported that epidemic risk perception has been associated with both depression and anxiety. Second, older adults are at greater risk of being socially isolated compared with younger adults under normal circumstances. In order to reduce the transmission of the virus, control measures were introduced to reduce face-to-face interactions with other people. Thus, the retirement home residents were not allowed to accept the visitors and older persons were advised to stay at home. These conditions inevitably contributed to social isolation (‘cocooning’) for many older people that might magnify loneliness and aggravate mental well-being and depression. Another potential contributing factor is experiencing personal loss due to the pandemic. During the pandemic, people could experience bereavement related to losing a beloved spouse or family member. In previous studies, mental health problems were identified as the most adverse consequence of bereavement. In addition, these pandemic-related factors, numerous individual and social predictors of worsened mental health were investigated in older persons. Generally, poor self-rated health, social isolation and increased difficulty in mobility belong among the most substantial predictors of depression in the elderly population.

As previously mentioned, longitudinal studies with prepanademic measures of mental health are encouraged, as they allow to assess the changes according to a clear temporal sequence. Several longitudinal studies have recently reported no or a little deterioration in mental health and well-being during the COVID-19 pandemic among older people in the UK, Netherlands, and Sweden. By contrast, a multicountry longitudinal study reported a substantial worsening in mental health in all 26 included European countries. Notably, most of these studies were conducted in the early months of the pandemic, showing the only short-term effect of the pandemic control measures.

To address the inconsistence evidence, we investigated: (1) changes in depression symptoms between the prepanemic and pandemic periods in a cohort of older individuals with repeated measurements; (2) the impact of individual factors on changes in depression symptoms and (3) whether COVID-19-related stressors (e.g., limiting social contacts; a significant decrease of your household’s income) were associated with changes in depression symptoms.

MEthODS
We used data from the Czech arm of the HAPIEE (Health, Alcohol and Psychosocial factors In Eastern Europe) study; the protocol and baseline characteristics have been reported previously. In brief, the HAPIEE study is an ongoing prospective cohort study designed to examine the impact of socioeconomic and psychosocial conditions on non-communicable diseases in Central and Eastern Europe. Four cohorts in Russia, Poland, the Czech Republic and Lithuania were established from 2002 to 2005 and consisted of a random sample of men and women aged 45–69 at baseline selected from population registers. Only the Czech cohort collected information on depressive symptoms, including the pandemic period. The Czech subcohort includes participants recruited in seven cities (Havlíkov, Karviná, Hradec Králové, Liberec, Jihlava, Kroměříž and Ústí and Liben). From an original cohort sample of 8856 respondents, 3190 individuals participated in postal questionnaire surveys in September 2017 to June 2018 (before the pandemic) and in October 2020 to April 2021 (during the pandemic). Persons with missing data on the depression score (n=177), with missing data on prevalent depression in the previous wave (n=41) and with missing data on prepanemic-related stressors from wave 2 (n=119) were excluded. This resulted in an analytical sample of 2853 participants.

Measures
Depression
Participants reported their depressive symptoms using the Centre for Epidemiological Studies-Depression Scale including 10 items (CESD-10) rated from 0=rarely/never to 3=most/all of the time. The items included the following statements regarding the respondent’s feelings during the last week: ‘I felt depressed’, ‘I felt all was an effort’, ‘My sleep was restless’, ‘I was happy’, ‘I felt lonely’, ‘People were unfriendly’, ‘I enjoyed life’, ‘I felt sad’, ‘I felt people disliked me’, ‘I could not get going’. A total score was calculated as the sum of all items after reversing the positive mood items. The score ranged from 0 to 30 in maximum, higher scores represented greater degrees of depressed mood.

Next, the change in symptoms was calculated by subtracting the depression score measured during the pandemic from the score measured in a prepanemic wave. The positive value of the change, therefore, indicates an increase in depression symptoms while the negative value of the change indicates a decrease in depression symptoms. Finally, the binary variable of the CESD-10 score was defined to enable to adjust for the pre-existing depression before the pandemic. Any score equal to or above 10 was considered as being depressed.

Pandemic-related stressors
We defined 13 pandemic-related stressors, representing the situations that participants might experience (yes/no) during the first year of the COVID-19 pandemic. The questionnaire included the following items: loss of job or paid work, job loss in family, a significant decrease of your household’s income, inability to pay bills, lack of money for food, lack of medication, delays in healthcare, limited social contacts, limited leisure activities, concerns about COVID-19, hospitalisation of close person (due to COVID-19 or other disease), death of close person (due to COVID-19 or other disease) and suffering from COVID-19.

Covariates
Age was considered as a continuous variable, while sex was defined as a binary variable for men and women. The highest achieved level of education was grouped into three categories (primary/vocational, secondary and university). Social relations were approximated by asking the participants whether they live alone or not (yes/no). Economic activity was assessed by the actual employment status (still working/non-working). Health status was measured by a question on self-rated health categorised into three groups (very poor/poor, average and good/very good).

Statistical analysis
First, we described the changes in depression scores by socio-demographic determinants and pandemic-related stressors using means and SDs. Second, we tested whether mean score of depression changed from before to during the COVID-19 pandemic using a non-parametric Wilcoxon signed-rank test (since depression scores were not normally distributed), and we also tested whether there are differences between groups (based on sex, education, etc) in mean differences of depression
symptoms using Mann-Whitney test and Kruskal-Wallis test with a Bonferroni test to correct for multiple comparisons. The prevalence of the stressors is presented individually for each specific stressor.

We used a principal component analysis (PCA) to identify representative components of the pandemic-related stressors. All of the above-listed stressful events were included into the PCA as potential indicators of pandemic-related stressors. Components were defined based on eigenvalues >1.0, scree plot and meaningful interpretation of the components. We used the Kaiser-Meyer-Olkin measure and Bartlett’s test of sphericity to test the appropriateness of using PCA on our data. The significance level of the Bartlett’s test (<0.05) and the value of the Kaiser-Meyer-Olkin test over 0.5 were considered acceptable. To characterise each stressor component, we considered factor loadings with absolute value >0.5. The Oblimin rotation was applied as there was a reasonable assumption that the indices were correlated. Factor scores for each of the stress patterns were assigned to all participants; with the higher factor scores indicating higher levels of stressful occasions Thus, the factor scores provide an additional (quantitative) value of the predictor compared with binary variables (stressors present/absent).

Third, we tested the differences between groups in change in depression symptoms using t-test and one-way ANOVA as the differences in scores followed a normal distribution. Fourth, we examined the association between sociodemographic determinants and change in depression symptoms scores using multiple linear regression. Finally, we examined the association between the pandemic-related stress factor scores and change in depression symptoms, again using multiple linear regression. Standardised β were calculated using the following models: model 1 adjusted for age; model 2 adjusted for sex, age, education, living alone, self-rated health, employment status and being depressed before the pandemic. These covariates were selected as potential confounders based on the previous research. P values less than 0.05 were considered statistically significant. All statistical analyses were conducted in IBM SPSS, V.26.

As a sensitivity analysis, we repeated the same analysis on persons who participated in postal questionnaires not only in 2020–2021 and 2017 but also in previous waves in 2012, 2013 and 2015 to examine long-term changes through repeated measures (n=2334). The change in depression was calculated by subtracting the depression score measured during the pandemic from the average of scores measured in three prepandemic waves.

RESULTS
Demographics of the sample
The analytical sample consisted of 2853 participants, among whom 1688 (59%) were women and 1165 (41%) were men, with a mean age of 73.4 (range, 60.6–88.2; SD, 6.75) in the pandemic wave. Descriptive characteristics of the study subjects are shown in table 1. Most participants (44 %) completed secondary education, followed by those who completed primary or vocational education (37%) and who had obtained an university degree (19%). Most participants were non-working pensioners (86%). Married participants or those who were in partnership represented 63% of the population sample and most of the participants did not live alone (71%). During the COVID-19 pandemic, almost half of the sample (46%) reported ‘very good’ or ‘good’ health.

Table 1 Descriptive characteristics of the study sample and changes in depression symptoms scores before and during COVID-19 pandemic (N=2853)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N  (%)</th>
<th>Change in depression score Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td>2853  (100)</td>
<td>0.46 (4.56)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>1165 (40.8)</td>
<td>0.36 (4.52)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>1688 (59.2)</td>
<td>0.52 (4.59)</td>
</tr>
<tr>
<td>Age</td>
<td>≤65 years</td>
<td>492 (17.2)</td>
<td>0.04 (4.64)</td>
</tr>
<tr>
<td></td>
<td>66–75 years</td>
<td>1281 (44.9)</td>
<td>0.24 (4.46)</td>
</tr>
<tr>
<td></td>
<td>≥76 years</td>
<td>1080 (37.9)</td>
<td>0.91 (4.62)</td>
</tr>
<tr>
<td>Education</td>
<td>Primary, vocational</td>
<td>1049 (36.8)</td>
<td>0.37 (4.75)</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>1266 (44.4)</td>
<td>0.54 (4.50)</td>
</tr>
<tr>
<td></td>
<td>University</td>
<td>538 (18.9)</td>
<td>0.46 (4.34)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married/partnership</td>
<td>1808 (63.4)</td>
<td>0.46 (4.54)</td>
</tr>
<tr>
<td></td>
<td>Si/Div/Sep/Wid</td>
<td>1042 (36.6)</td>
<td>0.48 (4.61)</td>
</tr>
<tr>
<td>Living alone</td>
<td>No</td>
<td>2010 (70.5)</td>
<td>0.37 (4.59)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>843 (29.5)</td>
<td>0.68 (4.50)</td>
</tr>
<tr>
<td>Self-rated health</td>
<td>Very good or good</td>
<td>1312 (46.0)</td>
<td>0.34 (3.97)</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td>1260 (44.2)</td>
<td>0.47 (4.77)</td>
</tr>
<tr>
<td></td>
<td>Poor or very poor</td>
<td>281 (9.8)</td>
<td>0.98 (5.97)</td>
</tr>
<tr>
<td>Employment status</td>
<td>Still working</td>
<td>389 (13.6)</td>
<td>0.55 (4.63)</td>
</tr>
<tr>
<td></td>
<td>Non-working</td>
<td>2464 (86.4)</td>
<td>−0.09 (4.07)</td>
</tr>
<tr>
<td>Depression before pandemic</td>
<td>No</td>
<td>2158 (90.2)</td>
<td>0.66 (4.18)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>234 (9.8)</td>
<td>−0.91 (6.48)</td>
</tr>
</tbody>
</table>

Pandemic-related stressors
The proportions of participants who experienced pandemic-related stressors are shown in table 2. Limitation of contacts with relatives and friends reported 67% of people, followed by experiencing limited leisure activities (50%). Concerns about being infected by COVID-19 were experienced by 49%. Hospitalisation and/or loss (death) of a close person reported 10% and 9%, respectively, and 9% suffered from COVID-19.

Three types of the pandemic-related stressors were extracted from the data using PCA and were labelled as ‘financial stressors’, ‘social and perception stressors’ and ‘death and hospitalisation stressors’. The principal components explained 33.8% (eigenvalue 3.72), 16.2% (eigenvalue 1.79) and 10.8% (eigenvalue 1.18) of the total variation, respectively. ‘Delays in healthcare’ and ‘suffering from COVID-19’ were excluded from the PCA because of their low factor loadings on the extracted patterns. Bartlett’s test of sphericity was significant (<0.001) and the Kaiser-Meyer-Olkin test measured a value of 0.829 that indicate substantial correlation within the individual components of the pandemic-related stressors suggesting the data are appropriate for the factor analysis. The variable loadings are presented in online supplemental table 2.

Depressive symptoms scores before and during COVID-19
The mean CESD-10 score increased from 4.90 to 5.37 (p<0.001) (online supplemental table 1). The distribution of depression symptoms within demographic categories was consistent with patterns observed before COVID-19. For example, before and during the pandemic, women reported significantly higher depression scores than men (before: 5.09 vs 4.65; and during: 5.62 vs 5.01 for women vs for men, respectively). Married participants or those who were in partnership reported


J Epidemiol Community Health: first published as 10.1136/jech-2022-219412 on 22 November 2022. Downloaded from http://jech.bmj.com/ on September 14, 2023 by guest. Protected by copyright.
lower depression scores than those who were single, divorced, separated or widowed (before: 4.60 vs 5.51; and during: 5.06 vs 6.11 for those living with somebody vs those living alone, respectively) (online supplemental table 1).

**Risk factors associated with depressive symptom changes**

Higher levels of depressive symptoms were observed in all demographic groups during COVID-19 compared with the prepandemic period, apart from those who were still working or who had the CESD score ≥10 before the pandemic. The largest increases in depression score were reported in the oldest age group (mean change of 0.91; p<0.001) and in people with poor or very poor health (mean change of 0.98; p<0.005) (table 1, figure 1). In addition, a substantial increase in depression scores was found in people who experienced death or hospitalisation of a close person (mean change of 1.43; p<0.001 and 0.98; p<0.001, respectively) and in people who suffered from COVID-19 (mean change of 0.93; p<0.005) (table 2, figure 2).

Results from linear regression analysis, using pandemic stressors as latent continuous measures, are presented in table 3. The most substantial elevation of depression score was observed in individuals who experienced hospitalisation or death of a close person (β=0.064; p<0.001), followed by people who experienced social isolation (limitation of contacts with relatives and friends, restrictions on leisure activities) and who were concerned about COVID-19 (β=0.057; p<0.001). In addition, those who stated that COVID-19 impacted delays in healthcare and those who suffered from COVID-19 also reported a significantly larger increase in depression score (β=0.048; p=0.005 and β=0.045; p=0.008, respectively). The associations remained statistically significant after adjusting for potential covariates. However, being delayed in healthcare was not significantly associated in the age-adjusted model (table 3).

In addition, older people were associated with significantly higher CESD score change compared with younger individuals in both models. Those who reported average self-rated health (β=0.073; p<0.001) and those who reported poor or very poor self-rated health (β=0.170; p<0.001) had significantly higher CESD scores during the pandemic compared with the youngest age group and those who reported good or very good self-rated health in the fully adjusted model but not in the age-adjusted model. By contrast, individuals who suffered from depression before the COVID-19 pandemic were more likely to report significantly lower depression scores than during the pandemic in age-adjusted as well as in the fully adjusted model (β=−0.444; p<0.001) (table 3).

Sensitivity analysis revealed similar results, although, several significant associations were not replicated. For example, the higher change in depression score was no longer predicted by average or poor/very poor self-rated health nor by suffering from COVID-19 (online supplemental table 3).

**DISCUSSION**

To date, relatively few longitudinal studies examined mental health changes in ageing populations. Significant increases in...
depression symptoms in older persons, compared with pre-pandemic levels, were reported in the UK, German and Finish cohorts. In line with these results, our findings provide evidence for a substantial deterioration in depression symptoms from autumn 2020 to early 2021 compared with the prepandemic period (2017) using a representative sample of the older Czech population. The largest increases in symptoms were observed among the oldest participants, people with poor or very poor health, people who experienced hospitalisation and/or death of close persons and people who suffered from COVID-19.

We aimed to determine the impact of the pre-existing and pandemic-related stressors on depression symptoms using repeated measures. We found that the magnitude of mental health changes varied by sociodemographic characteristics. Contrary to previous European research suggesting that older adults cope with the COVID-19 crisis better than younger individuals, our study showed that changes in depression scores were strongly associated with age; the highest depression changes were observed in the oldest age group (≥76 years) of the participants compared with younger individuals. This could be explained by the exacerbated fear of becoming severely ill or dying for COVID-19 with increasing age. On the other hand, the inconsistency of findings in previous studies might also be explained by the fact that depression outcomes among population are predicted by the scale of sociodemographic indicators that vary substantially between countries and might have a positive or negative impact on depression inequalities by age. In addition, the policy responses to the COVID-19 crisis also differed between the countries, as did the enforcement and adherence to these measures. Therefore, it might be hypothesised that the preventive measures adopted in different countries could unequally affect different age groups. We did not unequivocally confirm the previous assumption that women are more likely to experience worsened depression symptoms than men.

A consistent finding is that people with fair or poor overall health before the pandemic were substantially more likely to report larger changes in depression symptoms from before the pandemic. Again, the result might suggest a relationship between COVID-19 comorbidities and increased fear of the severe health implications during COVID-19 disease. This assumption is supported by the finding that increased depression symptoms were observed in persons who were more concerned about being infected by COVID-19. The positive association between COVID-19 risk perception and fear of COVID-19 was observed in the existing literature. Not surprisingly, persons who were diagnosed with COVID-19 disease were also more likely to experience a decline in mental health, which is aligned with findings from previous studies.

Postponing medical appointments for COVID-19-related reasons in older people was observed in the previous European study. Our results showed that those who experienced delays in healthcare due to the pandemic reported higher depression change from before the pandemic, suggesting that disruption of healthcare services during the pandemic contributed to deteriorating mental health. By contrast, our results did not reveal any association between financial stressors and depression symptoms despite the fact financial stress has been suggested as an important determinant of depression during the pandemic. It should be noted that the prevalence of financial stressors in the participants was very low (5.7%). It might be only hypothesised whether older people used their retirement savings and assets that could postpone their financial crisis. Follow-up observation would be beneficial to examine whether this stressor pronounced later during the pandemic. Lastly, social isolation and loneliness are well-documented determinants of poor mental and physical

Figure 2 Changes in depression score (95% CI) between before and during pandemic by pandemic-related stressors. (A) financial stressors; (B) social and perception stressors, death and hospitalisation stressors. Differences between groups tested using t-test, presented via p values on right. Differences between repeated measures (before and during depression scores) tested using Wilcoxon test, Presented as *p≤0.05, **p≤0.001.

Note: Decrease of income corresponds to a significant decrease of your household’s income.
Our study has several major strengths. The HAPIEE study is well-established longitudinal cohort recruited in a representative sample of older individuals living in the Czech Republic. Data were collected via a postal questionnaire so that participants who were unable to access the internet were not excluded. In addition, depression symptoms were measured before the vaccination was available, which could cause much higher stress and anxiety. In addition, our study provides several potential pandemic-related risk factors of depressive symptoms (eg, social isolation, financial distress, death or hospitalisation of a close person) while current literature highlighted also the importance of personality characteristics and lifestyle (eg, sleep quality, physical activity etc) that might play an important role in mental health changes.2 7 31

Lastly, reverse causation bias, a pervasive issue in observational studies, might occur. Because the pandemic-related stressors were asked only during the pandemic, it may be a case that increased depression symptoms drove elevated social isolation. However, this bias was mitigated by adjusting the models for pre-existing stressors measured before the pandemic.

CONCLUSION

This longitudinal study confirms an important increase in depressive symptoms during the COVID-19 pandemic and identified several pandemic-related risk factors for mental health worsening. The observed rise in depression symptoms and many of the identified factors might be prevented or mitigated. We found that individuals who experienced social isolation (‘cocooning’) were in a higher risk of mental health deterioration, which highlights the importance of considering social support as part of the governmental response to the pandemic. Better accessibility and increased expenditure to prevention and treatment of mental health issues may be needed in future crises. This study provides evidence of the susceptibility of the older individuals to mental distress suggesting that pandemic emergency policies should address this vulnerable population group.

Acknowledgements We are most grateful for all the participants involved in the HAPIEE project and the study members who participated in data collection. Authors thank the RECETOX Research Infrastructure (No LM2018121) financed by the Ministry of Education, Youth and Sports, and the Operational Programme Research, Development and Education (the CETOCOEN EXCELLENCE project No. C2 02.1.1.0/0.0/0.0/17_043/0009632) for supportive background. This output was supported by the NPO "Systemic Risk Institute" number UX22NPOS101, funded by European Union - Next Generation EU (Ministry of Education, Youth and Sports, NPO: EXCELES).

Contributors AD, MB and HP conceived and designed the cohort study. AD and AB proposed the methodological design of this work. AD analysed the data and wrote the first draft of the manuscript. MB, HP and NC contributed on designing of the overall research study. All authors provided critical revisions. All authors read and approved the submitted manuscript. AD is a guarantor of this work.

Funding This work has received funding from the European Union’s Horizon 2020 Research and Innovation Programme under grant agreement No 857487, No 857560 and No 857340.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The HAPIEE study was approved by the University College London ethics committee, the University College Hospital ethics committee (99/0081) and local ethics committees in each participating centre. All methods were performed in accordance with the relevant guidelines and regulations. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines,
REFERENCES


