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ORIGINAL RESEARCH ARTICLE

Symptomatic SARS-CoV-2 Episodes and Health-Related Quality of Life

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Abstract

Background Understanding the physical and mental health needs of the population through evidence-based research is a priority for informing health policy. During the COVID-19 pandemic, population wellbeing dramatically dropped. The relationship between experiences of symptomatic illness episodes and health-related quality of life has been less documented.

Objective This study analysed the association between symptomatic COVID-19 illness and health-related quality of life.

Methods The analyses drew from a cross-sectional analysis of data from a national digital symptoms' surveillance survey conducted in the UK in 2020. We identified illness episodes using symptoms and test results data and we analysed validated health-related quality of life outcomes including health utility scores (indexed on a 0–1 cardinal scale) and visual analogue scale (VAS) scores (0–100 scale) generated by the EuroQoL's EQ-5D-5L measure. The econometric model controlled for respondents' demographic and socioeconomic characteristics, comorbidities, social isolation measures, and regional and time fixed effects.

Results The results showed that the experience of common SARS-CoV-2 symptoms was significantly associated with poorer health-related quality of life across all EQ-5D-5L dimensions of mobility, self-care, usual activities, pain/discomfort and anxiety/depression, a decrement in utility score of − 0.13 and a decrement in the EQ-VAS score of − 15. The findings were robust to sensitivity analyses and restrictive test results-based definitions.

Conclusion This evidence-based study highlights the need for targeting of interventions and services towards those experiencing symptomatic episodes during future waves of the pandemic and helps to quantify the benefits of SARS-CoV-2 treatment in terms of health-related quality of life.

JEL Classification C1 · I1 · I14 · I310

Key Points for Decision Makers

Survey results show that respondents that experienced common SARS-CoV-2 symptoms during 2020 reported poorer health-related quality of life such as mobility, self-care, the ability to conduct usual activities, pain/discomfort and anxiety/depression.

This evidence-based study highlights the need for targeting interventions and services towards those experiencing symptomatic episodes during future waves of the pandemic and helps to quantify the benefits of SARS-CoV-2 treatment.

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1 Introduction

Understanding the physical and mental health needs of the population during the Coronavirus disease 2019 (COVID-19) pandemic through evidence-based research represents an immediate priority for informing public health strategies. Quantifying people's self-perception or subjective judgement of importance of their health status, including their health-related quality of life (HRQoL), can help to identify and measure the impact of COVID-19 illness on people's lives and inform decisions around the benefits of treatment.

The published literature reports that, during the pandemic, HRQoL deteriorated in substantial ways across the general population [1–5]. However, there is less evidence about HRQoL among people that experienced COVID-19 illness symptoms.

The EuroQoL's EQ-5D-5L is extensively employed as a measure of health, allowing for the monitoring of health status and changes therein over time and across population groups [6], and is preferred for economic evaluation purposes in many jurisdictions [7]. The EQ-5D-5L is accompanied by a preference-based value set, which produces an overall index when applied to the multidimensional health states generated by the descriptive system. The literature often refers to HRQoL measures accompanied by preference-based value sets, such as the EQ-5D-5L, as multi-attribute utility instruments. The value sets accompanying these measures use stated preference methods, including standard gamble (SG) and time trade-off (TTO), to trade-off between a health state and mortality risk or life expectancy, respectively [8]. A key advantage of these methods is their ability to yield values that are anchored on a scale in which a value of zero corresponds to being dead and a value of one corresponds to full health. These attributes are essential for the use of values for estimating quality-adjusted life years (QALYs) in-utility analysis. Hence, the results of this analysis, which focuses on the impacts on EQ-5D-5L outcomes among people that experienced COVID-19 illness symptoms, can inform comparative studies and can support considerations around the utility and benefits of interventions that address and mitigate common COVID-19 symptomatic episodes.

2 Data and methods

2.1 Survey and Study Participants

This study relied on primary data from a digital symptoms' surveillance survey that a digital health service provider company, EMIS Health, designed in collaboration with researchers at the University of Oxford and the Royal College of General Practitioner's Research and Surveillance Centre [9]. EMIS provides digital health technology services for more than 10,000 organisations in the UK, including primary care and community pharmacies, hospices, specialist services, secondary health and community care, with a nationwide reach. The version of the survey that was relevant to this study was run between 27 July and 31 December 2020, collecting data from over 10,000 respondents across the UK, of which 8113 had valid entries. The survey recruited participants aged 16 years and above via the EMIS-run Patient Access website and a digital primary health care service app that people use to obtain health-related information and to book general practice visits. EMIS Health obtained explicit consent from each survey participant (or their guardian, if below age 18 years) and provided de-identified data to the research team. The distribution of survey responses over time was primarily related to the position of the survey link in the Patient Access website and mobile app web interfaces and advertisement outreach by Patient Access and EMIS. The cross-sectional data included information on basic demographic characteristics (age, gender, ethnicity), cohabitation (binary for presence or absence of cohabitants), employment status, postcodes (first two to four digits), underlying health conditions and comorbidities, smoking behaviour (yes, no, past smoker), COVID-19-related self-reported ongoing and past illness status and COVID-19 testing data (date, type, and result), as well as specific symptoms that respondents selected from a predefined list. The survey included a HRQoL module with two components, based on the EuroQoL framework: the EQ-5D-5L descriptive system and its Visual Analogue Scale (EQ VAS), as described in Sect. 2.3.

2.2 COVID-19 Illness State Measures

To define COVID-19-related illness states, this study used information on (a) specific symptoms and (b) COVID-19 test results within the 14 day period prior to completion of the survey. It derived two sets of explanatory variables that classified respondents into two groups: those with ongoing illness and those who never experienced illness symptoms after the pandemic onset. The survey asked participants to report symptoms from a predefined list. The research team identified symptomatic COVID-19 ('ongoing illness (symptoms)') from anosmia (loss of smell/taste) in combination with either high fever, a new continuous cough or feeling breathless. This classification followed definitions of COVID-19 symptoms prevalence from the medical literature [10, 11]. Individuals reporting no symptoms during and before the survey were classified

as 'never ill'. To improve the robustness of the explanatory variable's definition, we excluded from the study population all respondents that did not present symptoms as they were taking the survey but had experienced them in the past, following the pandemic onset.

The second definition used COVID-19 PCR/lateral flow testing information (date and results). With this data, we generated a binary variable equal to zero for respondents with a negative test in a window of 14 days before the survey and no symptoms, and equal to one for those with positive results and high fever/new-continuous cough/breathlessness. The 14 day time-window corresponds to the incubation period for the development of COVID-19 symptoms [12]. We used this test-verified variable for a sensitivity check. Due to limited availability of tests during the early period of the pandemic, this analysis excluded 94.1% of the surveyed population without test-confirmed status.

2.3 Outcome Measures: HRQoL

To measure HRQoL, this study used EuroQoL's EQ-5D-5L. The EQ-5D-5L is a generic, multi-attribute, preference-based measure [7] used by decision-making bodies such as the National Institute for Health and Care Excellence (NICE) in England and Wales for cost-effectiveness comparative purposes [13] and health technology assessments. The EQ-5D-5L consists of two principal measurement components. The first is a descriptive system, which elicits self-assessed health status on the day of completion across five dimensions (5D): mobility, self-care, usual activities, pain/discomfort and anxiety/depression. For each dimension, respondents can choose one of five severity levels (5L): no problems, slight problems, moderate problems, severe problems and extreme problems, respectively. The 5L responses were converted into health utilities based on the UK tariff for the EQ-5D-3L descriptive system [14] using the van Hout and Hernandaez-Alarva crosswalk algorithms in line with current NICE recommendations [15, 16]. The health utility scores are indexed at zero (dead) and one (perfect health) with negative values indicating health states worse than dead. The second measurement component of the EQ-5D-5L consists of a visual analogue scale (VAS) ranging from 100 (best imaginable health state) to 0 (worst imaginable health state), which provides an indication of the respondent's own assessment of their health status on the day of survey completion.

We expected that individuals with COVID-19 symptoms will have a lower HRQoL compared with healthy participants. This hypothesis is based on previous studies that have shown that individuals with COVID-19 often experience a range of symptoms that can have a negative impact on their physical and mental wellbeing. These symptoms can include fever, cough, shortness of breath, fatigue, muscle aches and loss of taste or smell. We expected lower scores on measures of HRQoL, such as the utility and VAS scores, among respondents with COVID-19 symptoms. We calculated the expected effect size based on estimates from previous studies and used this to determine the sample size needed for our study.[1]

2.4 Other Covariates and Empirical Specification

To investigate the relationship between COVID-19-related illness states and HRQoL, first, we estimated and compared proportions of respondents who reported having any issue (i.e. EQ-5D-5L levels 2–5) as opposed to no issues (EQ-5D-5L level 1) between those with ongoing symptomatic illness and those who did not experience it, for each of the EQ-5D-5L dimensions. Next, we estimated multivariable Tobit regressions of the EQ-5D-5L utility and VAS scores, controlling for additional individual, geographical and time-specific variables and modifiers. The EQ-5D-5L health utility score is upper bounded at the utility score corresponding to health state 11111 (i.e. no problems in all five dimensions) and lower bounded in correspondence to 55555 (extreme issues in all five dimensions) and the EQ VAS is bounded between 0 and 100. Multivariable Tobit regressions reflect the censored nature of the utility and VAS score distributions [30]. The regression estimations draw from the following model, in which 'i' represents individual respondents as unit of analysis:

$$\begin{aligned} Y_i =& \alpha_i + \beta \text{Age}_i + \gamma \text{Gender}_i + \delta \text{EthnGroup} \\ &+ \zeta \text{Comorbidity}_i + \lambda \text{HRisk}_i + \xi \text{Socio}X_i \\ &+ \sigma \text{Smoke}_i + \kappa \text{COVID19}_i + \vartheta \text{Lockdown} + \eta \text{Reg}_i + \varepsilon_i. \end{aligned}$$

The outcome measures, defined at the individual level, included, alternatively, (1) the EQ-5D-5L health utility score or (2) the EQ-VAS score. The main explanatory variables of interest consisted of the classification of ongoing COVID-19 illness status, defined using information on symptoms (and, alternatively, on test results, for a sensitivity analysis).

Additional covariates included gender (female = 1), ethnic group (white = 0, other groups = 1), containment policies ('Lockdown' = 1 for periods of lockdown under government-specified Tier 3 (very high alert) and Tier 4 (stay at home) restrictions (e.g. no mixing of households; hospitality closure; highly restricted travel) , versus no

[1] To better understand the statistical relevance of the reported difference in HRQoL between healthy participants and those with COVID, we conducted power calculations using an alpha level of 0.05, a sample size of 4786 in group 1 and 830 in group 2, and an expected effect size of 0.15; the study would have a power of approximately 80.2%. This suggests that the study has a high probability of detecting a statistically significant difference between the two groups.

lockdown = 0 [17]), and comorbidities ('Comorbidity' = 1 if the respondent had any comorbid or chronic health condition, including a lung disease, e.g. asthma or chronic obstructive pulmonary disease (COPD), heart disease, chronic kidney disease, liver disease, conditions of the nervous system such as Parkinson's or multiple sclerosis, diabetes, spleen issues, a weakened immune system, or serious overweight with a body mass index (BMI) greater or equal than 40). 'HRisk' (dichotomous) indicated the presence of any highly risky pre-existing health condition (organ transplant, pregnancy with heart disease, lung cancer and ongoing radiotherapy, blood or bone marrow cancer, ongoing chemo/immunotherapy, medications that weaken the immune system, sickle cell disease, cystic fibrosis, severe asthma/COPD, motor neuron disease, or whether the National Healthcare Service indicated that a respondent had to shield/self-isolate). The regression included a vector ('SocioX') of socio-economic covariates such as employment status, household income, and cohabitation—binary (see Table 1 for detailed categories). All regressions also included indicators for smoking behaviour (yes, no, past), age group (16–34, 35–49, 50–64 and 65+ years) and regional fixed effects. Each covariate included a category identifying missing data.

For a sensitivity analysis, we repeated the estimations by applying the following modifications to the main model: excluding observations with a missing covariate, keeping only the explanatory variable as a regressor, including month-specific dummy variables while excluding lockdown and social restriction measures, and excluding survey weights. Further, we replicated the main regression model while restricting the sample to respondents that had validated test results within the previous 14 days, while still having/not having symptoms.

3 Results

Table 1 summarises the descriptive statistics of the study population and the categories that compose the covariates included in the analyses. All the variables were drawn from the survey, except for the lockdown/social isolation measure, which we derived from official sources [18, 19] by cross-mapping local policies with the region and time of survey completion for each respondent. We recovered regions of residence from postcode identifiers provided in the survey.

Figure 1 displays the proportion of respondents that reported having any issue (i.e. EQ-5D-5L levels 2–5) as opposed to no issues (EQ-5D-5L level 1) for each of the five dimensions of the EQ-5D-5L measure, plotted separately for respondents that were never ill with COVID-19 symptoms and those with an ongoing symptomatic illness. This figure shows significantly higher proportions of respondents with

Table 1 Descriptive statistics: participant characteristics of the study population

Variable	*N*	%
COVID-19 illness status		
No illness	4786	85.23
Current illness symptoms	830	14.77
Age, years		
16–34	1669	29.72
35–49	1330	23.69
50–64	1331	23.70
65+	1285	22.89
Age missing	0	0
Gender		
Male	2720	48.43
Female	2896	51.57
Gender missing	0	0
Ethnicity		
White	5203	92.64
Other Ethnic Group	413	7.36
Missing	0	0
Employment status		
Not employed	1172	20.86
Self-employed	194	3.46
Employed part-time	373	6.65
Employed full-time	2230	39.71
Retired	1515	26.98
Student—not employed	131	2.34
Annual income (GBP)		
Less than 5200	156	2.78
5200 to less than 18,200	619	11.03
18,200 to less than 31,200	1092	19.45
31,200 to less than 52,000	1269	22.59
52,000 to less than 100,000	1259	22.42
100,000 or more	388	6.90
Missing	833	14.82
Cohabiting		
Yes	4561	81.21
No	1055	18.79
Has comorbidity		
No comorbidity	3557	63.34
Has comorbidity	1987	35.39
Missing	71	1.26
Risky health condition		
No risky condition	4665	83.07
Risky condition	497	8.85
Missing	454	8.08
Smoking behaviour		
Smoker	535	9.53
Non-smoker	3637	64.77
Past smoker	1444	25.70
Mobility restrictions		
No restrictions	5121	91.19

Table 1 (continued)

Variable	*N*	%
Lockdown or Tier 3/4	495	8.81
Region		
Scotland	173	3.08
Northern Ireland	60	1.06
North East	231	4.12
North West	1059	18.86
East Midlands	367	6.53
West Midlands	671	11.95
Wales	83	1.48
South West	442	7.88
South East	1360	24.21
Greater London	1057	18.81
Missing region	113	2.01
Month		
July	1	0.01
August	41	0.73
September	621	11.06
October	4238	75.47
November	448	7.97
December	267	4.76

Descriptive statistics of the study population from the UK COVID-19 symptoms tracker survey data (July–December 2020). Sample size: 5616. Observations are weighted using estimated probability weights at the age-gender level

issues among those who had an ongoing illness episode in each of the five EQ-5D-5L dimensions. *P*-values from two-sample tests of proportion were equal to zero for all dimensions, suggesting that the null hypothesis that the proportion of respondents with functional limitations is the same for the two groups could be rejected.

Figure 2 reports the coefficients of the multivariable Tobit regression for the HRQoL outcomes, with 95% confidence intervals. Ongoing symptomatic COVID-19 illness was associated with a lower EQ-5D-5L health utility score (− 0.131) and EQ-VAS score (− 15.314). The coefficients were significant at the 1% level in all the regressions. For completeness, we report the results also in Table 2 and the full set of coefficients in Table A1 in the Appendix. Figure 2 also displays the coefficients for the additional covariates included in the analysis. All else equal, better HRQoL outcomes were estimated for older respondents (age > 65 years), non-white individuals, those with a household income between 52,000 and 100,000 GBP, and non-smokers, in comparison to those in their respective reference groups. Poorer HRQoL outcomes were estimated among those with a comorbidity or highly risky underlying health condition, current smokers, people not cohabiting and those in the lowest household income group, in comparison to their respective reference groups, and amongst the non-employed versus all other categories of employment status except for non-employed students.

Table 2 reports the main regression coefficients together with the results of several sensitivity analyses. Column 1 displays the results of the main model estimation (Tobit) for comparison. Column 2 reports Ordinary Least Squares (OLS) estimation results for the EQ-5D-5L health utility score for comparison purposes, which mirrored the Tobit results. Column 3 reports the coefficients for the estimation based on test results and symptoms. The coefficients of − 0.143 and − 17.07 on the health utility scale and EQ-VAS score, respectively, were similar in magnitude to the main estimation model and still significant at the 1% level, despite a smaller sample size. The table also reports the results of the other sensitivity checks: (i) excluding probability weights, (ii) excluding all covariates other than the main explanatory variable, (iii) including monthly dummy variables while excluding the lockdown variable and (iv) excluding all respondents for which a covariate was missing. The results were consistent and robust across all estimations, supporting the validity of the analyses and findings.

4 Discussion

This study showed that experiencing COVID-19 symptomatic illness episodes (with anosmia and high fever, new continuous cough or breathlessness) was associated with significantly poorer health-related quality of life outcomes. The coefficients exceed minimally important differences in utility scores for evaluative purposes [20]. Thanks to a large sample size and extensive set of controls, this study allowed us to compare individuals with the same gender, in the same age group, with the sample employment status and household income, with/without baseline risky health conditions and comorbidities, and subject to the same regional and social distancing features that the literature indicated as significant predictors of poorer HRQoL during the COVID-19 pandemic (e.g. [21, 22]). Further, the analyses used a validated measure of preference-based HRQoL outcomes, which is the preferred tool for cost–utility analyses of health care interventions in many jurisdictions.

These results strengthen previous findings, which indicate an overall deterioration in health-related quality of life during the pandemic compared with population norms [1–5]. The findings with regard to the observed differences in anxiety and depression levels are similar to those reported in previous studies examining the impact of a symptomatic COVID-19 infection on HRQoL [23–25]. While previous studies compared differences in function by EQ-5D dimension before and during the COVID-19 pandemic, observing a significant deterioration specifically

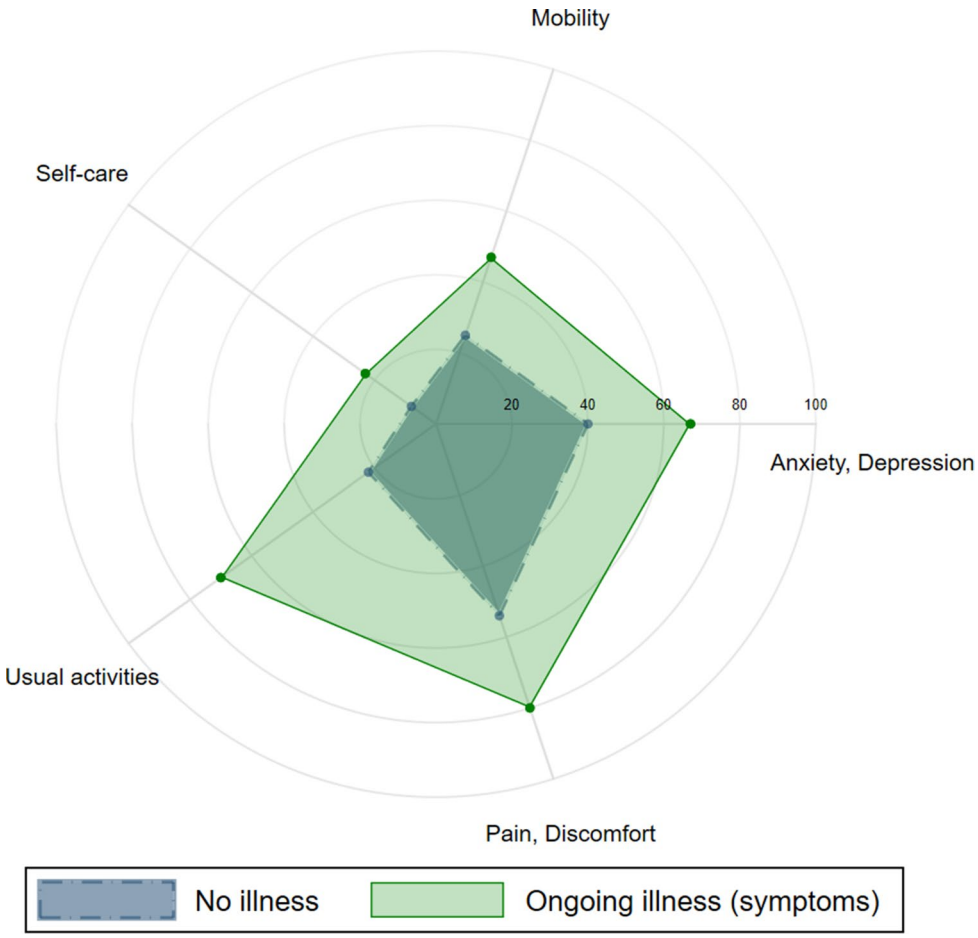

Fig. 1 Proportion (%) of respondents reporting any issues in each EQ-5D dimension by COVID-19-related illness state (symptoms based). Source: authors' estimations from the EMIS COVID-19 Symptoms Surveillance Survey, Version 2 (July-December 2020). 'No illness' identifies respondents that never experienced COVID-19 related illness since the pandemic onset. 'Ongoing illness with SARS-CoV-2 common symptoms' identifies respondents that reported ongoing compatible symptoms (anosmia and either cough, high fever or feeling breathless). The figure reports the percentage of respondents that reported any issues in each EQ-5D domain by study population group. *P*-values from two-sample tests of proportion were equal to zero for all dimensions

in anxiety and depression [1, 4, 5], this study went further and showed that COVID-19 symptomatic illness episodes were associated with significantly lower functional levels in each of the five EQ-5D-5L dimensions, including aspects of physical health, mobility, and daily activities. The average EQ-5D-5L dimension responses among individuals with active Covid-19 infections were similar to those found in a previous US study that examined mean dimension scores within 3 days of a positive test [23].

In addition, this study examined the relationship among demographic, socioeconomic and clinical characteristics and health utility scores, demonstrating that certain characteristics of individuals are significantly associated with lower health-related quality of life, all else being equal. For instance, poorer HRQoL outcomes were estimated among individuals with one or more comorbidities or risky underlying health conditions, with similar findings reported in previous studies that highlight the disproportionate physical and mental health burden of patients with pre-existing health conditions during the pandemic compared with individuals without concomitant conditions [1, 3]. Similarly, health risk behaviours, such as smoking, were associated with a decrease in preference-based HRQoL outcomes.

Individuals in the lowest household income group and those without employment experienced worse HRQoL outcomes compared with individuals in their respective reference groups. The role of socioeconomic hardship has been assessed in a number of studies, substantiating this study's findings that lower income and unemployment, as well as loss of job, income or economic decline during the pandemic decrease HRQoL [3, 26–28]. Notably, better HRQoL outcomes were estimated among individuals aged 64 years or older compared with those aged 16–30 years. Comparable findings were observed in a US population health survey assessing the effects of COVID-19 on population HRQoL, noting that uncertainties regarding the future, particularly education, employment and career prospects, combined with social distancing during a critical life stage for relationship and network development, are likely contributing factors to anxiety and a decline in mental health [3].

Even though COVID-19 causes respiratory symptoms similar to seasonal influenza and has been regarded as an influenza-like illness (ILI), it is distinct from other ILIs

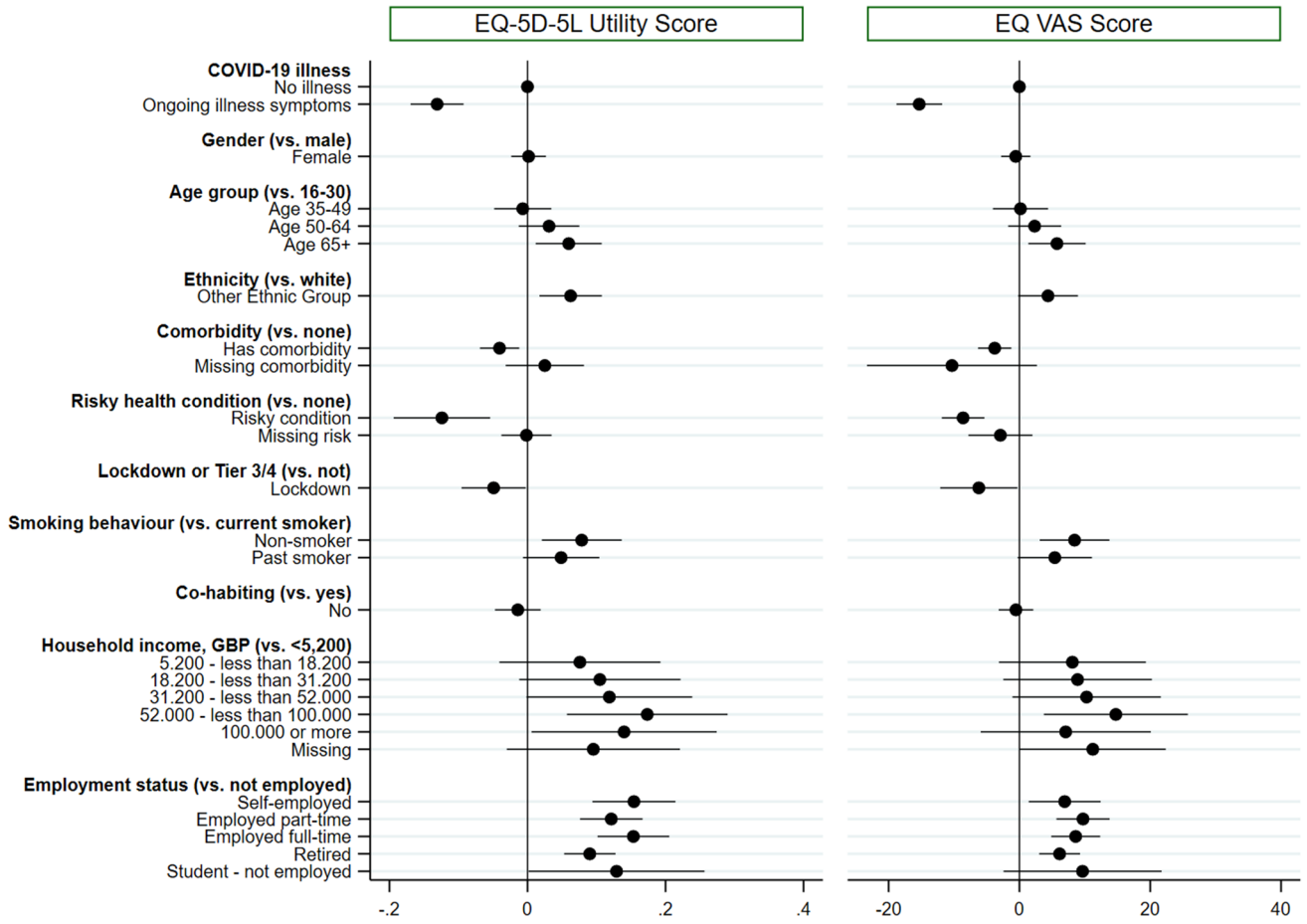

Fig. 2 COVID-19 ongoing symptomatic illness and HRQoL: Tobit regression coefficients. Authors' estimations from the COVID-19 symptoms tracker survey, Version 2 (July–December 2020). Multivariable Tobit regression coefficients with 95% confidence intervals. Sample size: 5616. 'Ongoing illness symptoms' identifies respondents with COVID-19 compatible symptoms. 'No illness' is the reference category. Additional covariates: region fixed effects and a constant. Outcomes are EuroQoL's EQ-5D-5l Health utility and Visual Analogue Scale scores. Estimates applied age–gender-specific survey weights. Standard errors are heteroskedasticity-robust

due to its higher risk of severe illness and death [29]. Previous studies estimating the costs and HRQoL outcomes associated with non-COVID-19 ILIs showed that patients seeking medical care reported a significantly higher cost and poorer HRQoL than community patients [30]; therefore, additional costs and deterioration of HRQoL is to be expected in COVID-19 patients. Furthermore, COVID-19 has a relatively longer incubation and infectious period compared with other ILIs, which consequently requires a longer isolation duration to decrease the risks of spreading the infection [31, 32]. A study conducted in Japan showed that the longer isolation period of COVID-19 compared with other ILIs is associated with a larger disease burden and therefore a poorer HRQoL among individuals infected with COVID-19 compared with those infected with other ILIs [33]. Given the higher deterioration in HRQoL among COVID-19 patients compared with those infected with other ILIs, particular focus should be paid to interventions and services that alleviate COVID-19 symptoms and support individual's health-related quality of life during illness episodes. However, to date, economic evaluations of COVID-19 treatments have not used EQ-5D-5L utility values derived from individuals with active COVID-19 infections. Therefore, the results and values produced in this study may be helpful to future research and economic evaluations.

The data utilised in this study present a potential 'collider bias' limitation [34]. This is due to a sampling design that relied on voluntary survey participation: survey participation may depend on unobservable factors that correlate with the outcomes and for which we had no information (e.g. [35]). This may have affected the representativeness of our study population. In particular, the survey did not fully represent the UK general population in terms of income, gender, age

Table 2 COVID-19 illness state and HRQoL outcomes: main results and sensitivity analyses

	(1) Tobit	(2) OLS	(3) Tobit	(4) Tobit	(5) Tobit	(6) Tobit	(7) Tobit
Panel A	Outcome: EQ-5D-5L utility score						
Reference: no illness							
Ongoing illness (symptoms)	− 0.131*** (0.020)	− 0.131*** (0.020)		− 0.129*** (0.011)	− 0.167*** (0.019)	− 0.133*** (0.020)	− 0.122*** (0.018)
Ongoing illness (test + symptoms)			− 0.143*** (0.037)				
N	5616	5616	352	5616	5616	5616	4266
Median of dep. var.	0.820	0.820	0.770	0.829	0.820	0.820	0.829
IQR of dep. var.	0.285	0.285	0.221	0.266	0.285	0.285	0.272
Panel B	Outcome: EQ-VAS score						
Reference: no illness							
Ongoing illness (symptoms)	− 15.314*** (1.780)	− 14.997 (1.785)		− 15.400*** (1.089)	− 19.330*** (1.958)	− 15.580*** (1.764)	− 13.846*** (1.935)
Ongoing illness (test + symptoms)			− 17.074*** (3.685)				
N	5616		352	5616	5616	5616	4266
Median of dep. var.	80	80	70	80	80	80	80
IQR of dep. var.	30	30	40	25	30	30	30
Other covariates	Yes	Yes	Yes	Yes	No	Month FE	No missing
Survey weights	Yes	Yes	Yes	No	Yes	Yes	Yes

Authors' estimations from the COVID-19 symptoms tracker survey (July–December 2020). 'Ongoing illness (symptoms)' identifies respondents with COVID-19 compatible symptoms [anosmia and either cough, high fever,' or breathlessness (= 1) versus those that did not experience an illness episode (= 0)]. Respondents that had symptoms in the past are excluded for robustness. Column 1 reports the results of the main regression model using survey weights computed from population statistics by gender and age. Additional covariates: gender, age group, ethnicity, comorbidity, highly risky health condition, smoking habit, cohabitation, household income, employment status, lockdown or Tier 3-4 and region fixed effects, with missing categories as separate covariate. Column 2 reports the results of an OLS regression. Column 3 uses a definition of COVID-19 based on having received a positive test result within 14 days and presenting COVID-19 symptoms (as in 'Ongoing illness'). The reference category in column 3 includes respondents with no COVID-19 symptoms combined with a negative test result. Column 4 does not apply probability weights. Column 5 excludes all covariates but the main explanatory variable. Column 6 includes all usual covariates and also month-specific dummy variables while excluding mobility and social restriction measures. Column 7 excludes all observations for which a covariate is missing. Parentheses report heteroskedasticity-robust standard errors

Statistical significance levels: 10 (*), 5 (**), 1 (***) per cent

and ethnicity. Nonetheless, targeted voluntary recruitment and snowball sampling are widely utilised methodologies in the field, with extensive application in the literature (see, e.g. [36–38]). To further improve the representativeness of the study population, we computed and applied probability weights based on population age–gender cell counts for the UK based on official national statistics [28]. Based on published research by the Office for National Statistics for England and Wales, the estimated percentage of the population testing positive for the coronavirus (COVID-19) on nose and throat swabs between 20 September and 31 October 2020 was similar across the age groups 25–34 years, 35–49 years, 50–69 years and 70+ years [39]. Comparatively higher rates were observed in younger age groups (school years 7–11, and school year 12 to age 24 years). In the case of COVID-19-related sex differences, earlier global data

from April 2020 indicate that men and women were equally likely to acquire COVID-19 [40]. However, a higher prevalence of SARS-CoV-2 infection and incidence of COVID-19 disease was reported in non-white ethnic minorities in the first 6 months of the pandemic in 2020 [41]. Therefore, while COVID-19 incidence appeared to be similar across sex and age groups in 2020 ([39, 40], ethnic minority groups had a higher incidence rate [41], which may not be captured in this study population. Another element to consider when interpreting the results of this study is that, during the COVID-19 pandemic, HRQoL deteriorated in the entire population, including individuals who did not experience illness symptoms [1–5]. Hence, our estimated effects based on comparisons between respondents with ongoing COVID-19 symptoms and respondents without an ongoing symptomatic COVID-19 experience may be underestimated with respect to comparisons outside pandemic times. The difference in terms of HRQoL may be smaller with respect to a comparison between COVID-19 symptomatic and 'healthy' individuals in other times. Previous research findings suggest that the COVID-19 pandemic may have impacted not only self-assessed health status but also how the UK population values health in general [42], which may also have affected the magnitude of the effects derived in this study. Further, the mental health and HRQoL consequences of COVID-19 as well as of the overall pandemic may have been different throughout time, and survey responses may reflect the respondents' mental health at a specific point in time. To address this, we included month-specific fixed effects. Finally, the probability of recruiting many participants who were hospitalised with COVID-19 was low, especially among those in intensive care. While this will be a small proportion of people with COVID-19, it is worth highlighting that this study does not reflect the outcomes of those who experienced the biggest impact from the disease in terms of HRQoL.

5 Conclusions

This study showed that experiences of COVID-19 symptomatic episodes were associated with poorer health-related quality of life, measured using the validated EuroQoL EQ-5D-5L instrument. Building on these findings, future research could focus on specific population groups with lower baseline HRQoL and higher exposure to COVID-19 infection risk. Further research should also focus on post-COVID-19 stages and long COVID symptomatic experiences. Respiratory diseases and seasonal coronaviruses significantly affect the worldwide population every year. This paper highlights the need to devote attention and resources to support individuals' health-related quality of life during illness episodes. The literature has shown that perceptions of poor health-related quality of life and wellbeing present substantial individual and societal costs. Poorer health-related quality of life and wellbeing are, in turn, associated with lower productivity and community engagement, slower recovery from physical conditions, a weaker immune system and higher health risks [43]. Building preparedness and developing resilience strategies can help communities and health care systems better manage the health-related quality of life toll of COVID-19, seasonal influenza and respiratory diseases. The findings of our study contribute to identifying critical priorities for health and social care policy planning agendas.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40258-023-00810-y.

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Declarations

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Conflicts of Interest None. SdeL has received funding through his University for vaccine related research from AstraZeneca, GSK, Sanofi, Seqirus, MSD and Takeda. He has been a member of advisory boards for AstraZeneca, Sanofi and Seqirus.

Ethics Approval EMIS Health's COVID-19 Symptom Surveillance tool covered the underpinning research infrastructure and governance, including approval and consent procedures for voluntary participation as articulated in EMIS Health's privacy policy. Processing of personal and sensitive data is conducted by EMIS Health under the legal basis of medical research or public interest. The data used for this study underwent previous full anonymisation by EMIS Health. The research team had access to a dataset stripped of all personal identifiers. As a result, the study was not subject to ethics review or General Data Protection Regulation (GDPR) requirements.

Consent to Participate EMIS Health obtained explicit consent from each survey participant (or their guardian, if aged 16–18 years) and provided de-identified data to the research team.

Consent for Publication (from patients/participants) Medical research to answer legitimate research questions in the public interest is justified under schedule 1, sections 2–4 of the Data Protection Act 2018 and in the presence of appropriate data subject safeguards. The legal basis for EMIS's processing of data is consent or approval for exemption under Section 251 of the NHS Act 2006.

Availability of Data and Material The data that support the findings of this study are available from EMIS Health in collaboration with the University of Oxford and the UK Royal College of General Practitioner but restrictions apply: the data were used under license agreement for the current study, and so are not publicly available. Anonymised data are however available from the authors upon reasonable request and with permission of EMIS Health, the University of Oxford and the UK Royal College of General Practitioner.

Code Availability Codes are available from the authors upon request.

Authors' Contributions Conceptualisation, CA, CN, SdeL. and SP; methodology, CA, CN, SP; formal analysis, CA and IT; writing—original draft preparation, C.A. and I.T.; writing—review and editing, CA, CN, IT, SdeL, SP; funding acquisition, SP and SdeL. All authors have read, reviewed, and agreed to the published version of the manuscript.

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