

BMJ Open Prevalence of long covid symptoms in Tuscany, Italy: a population-representative cross-sectional telephone survey

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ABSTRACT

Objectives Long covid affects over 36 million individuals in the European region, but its clinical profile is still poorly defined, particularly in the general population with less severe acute disease. This study aimed to assess the prevalence of a broad spectrum of symptoms potentially linked to long covid in the general population of Tuscany, Italy.

Methods A cross-sectional study was conducted in January–February 2024 using Computer-Assisted Telephone Interviews in a representative population sample of Tuscany. Based on the WHO questionnaire long covid symptom list, data on 33 symptoms experienced in the past 6 months were collected, along with demographic and clinical characteristics. After excluding patients with COVID-19 within the past 6 months and those failing a screening cognitive test, symptom prevalence and ORs adjusted for sex, time since infection, smoking and concurrent diseases (aOR) were calculated according to COVID-19 history.

Results After excluding 129 failing the cognitive test (6.4%) and 123 recent COVID cases (6.1%), among 1753 participants interviewed, 1013 (57.8%) had a history of COVID-19. The symptoms significantly more prevalent in individuals with previous COVID-19 were fatigue (12.8% vs 8.9%, aOR 1.6 (95% CI 1.2 to 2.2)), concentration impairment (5.5% vs 2.4%, aOR 2.2 (95% CI 1.3 to 3.8)) and skin rashes (4.5% vs 2.4%, aOR 1.9 (95% CI 1.1 to 3.3)). Prevalences and ORs were higher in more recent COVID-19 cases, particularly females and individuals with concurrent diseases.

Conclusions We identified in a population-based study some symptoms significantly more common in individuals with previous COVID-19. This approach complements data collected in clinical settings and in patients selected by greater disease severity. The findings may help future surveillance efforts and targeted public health interventions directed at optimising care pathways and mitigating long-term consequences.

INTRODUCTION

Post-COVID-19 syndrome, or ‘long covid’, is a distinct clinical entity that occurs in individuals with a history of probable or confirmed

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Population-representative telephone survey with estimates of symptom prevalence in the general population, irrespective of care setting.
- ⇒ Presence of a control group of individuals without recent self-reported COVID-19.
- ⇒ Inclusion based on cognitive screening.
- ⇒ Exclusion of individuals with recent COVID-19 (less than 6 months prior to interview).
- ⇒ Potential for recall bias and survey fatigue.

SARS-CoV-2 infection. This condition is characterised by ongoing symptoms beyond the acute phase of infection, usually defined by persistence for more than 3 months from diagnosis.¹ As per the WHO, in the European region, there are over 36 million individuals affected by the disease.² Several studies have examined the clinical characteristics, disease severity, risk and preventive factors.^{3–4} However, its prevalence remains uncertain,^{5–8} particularly in individuals with less severe acute disease, partly due to methodological issues,⁹ to the selected populations and to the different timeframes used to define persistence, which range from a minimum of 4 weeks in the definition of the Centers for Disease Control and Prevention (CDC) and of The National Institute for Clinical Excellence, to 12 weeks as outlined by the WHO.^{10–12} As a result, broader definitions such as the CDC’s threshold might yield higher prevalence estimates, while stricter definitions produce lower, more conservative figures. Furthermore, the wide range of possible symptoms complicates accurate estimates at population level, as distinguishing long covid from other conditions poses significant challenges.^{13,14} This complexity may lead

to variability in diagnostic and care pathways across countries, ultimately impacting timely diagnosis and effective treatment.^{15 16} In Italy, since 2022, national good practice recommendations have been established for managing patients with long covid, and a survey assessed the organisational responses of health services and the characteristics of long covid care centres.^{17 18} As emphasised by the WHO, a clear and updated understanding of long covid is essential for allocating resources to address the clinical, rehabilitative and supportive needs of patients.¹⁹ To achieve this, defining and monitoring the prevalence of long covid in the general population is key for refining its estimates and ensuring an appropriate distribution of healthcare resources.

Aims of the study

To estimate the overall population prevalence of symptoms associated with long covid in the general population of Tuscany, Italy, using a standardised, rapid and reproducible survey methodology, and ensuring that the sample studied is representative of the regional population.

To compare symptom prevalence between individuals with and without a history of COVID-19, in order to identify symptoms commonly associated with long covid that may be overlooked in the clinical setting, leading to missed recognition of the condition.

METHODS

Study design

This study was part of the national project 'Analysis and strategies for responding to the long-term effects of COVID-19 infection (long covid)' funded by the National Centre for Disease Prevention and Control of the Italian Ministry of Health. The present research, jointly conducted by the Agenzia Regionale di Sanità di Tuscany (Italy) and the Department of Health Sciences of the University of Florence (Italy), was designed as a cross-sectional study and carried out in January and February 2024 using the Computer-Assisted Telephone Interview (CATI) methodology.

Materials

The questionnaire used in the interviews was developed according to the Italian good practice recommendations on management of persons with long covid and to the questionnaire developed by the Italian National Institute of Health (ISS) for outpatient surveillance of long covid, which is a shorter version of the Post COVID-19 Case Report Form from the WHO Global Clinical Platform for COVID-19.^{17 20} Before administering the questionnaire, a cognitive standardised test was administered with the aim of including only individuals with adequate cognitive and memory capabilities. The test, already used in other national CATI-based cross-sectional surveillance studies (PASSI d'ARGENTO), was designed to assess both short-term memory and medium-term memory.²¹

The first section of the questionnaire collected data on 33 symptoms experienced in the 6 months prior to the interview, regardless of whether the respondent had contracted COVID-19 or not, and without mentioning the disease. The investigated symptoms included: insomnia, fatigue, anxiety, hair loss, weight loss, joint pain/swelling, decreased libido, visual disturbance, persistent muscle pain, hearing impairment, tingling/numbness in arms or legs, low mood/dysphoria, headaches, memory loss, dysmenorrhoea/menstrual disorders, cough, concentration impairment, sexual dysfunction, skin rashes, reduced sense of smell, dyspnoea, sore throat/pharyngeal inflammation, balance disorder, diarrhoea/abdominal pain, loss of appetite, palpitations/tachycardia, reduced sense of taste, chilblains on fingers/toes, mental fog, chest pain, nausea/vomiting, delirium/hallucinations and fever. Of these 33 symptoms, 30 were derived directly from the shortened WHO questionnaire. Among the remaining three symptoms, hair loss was included based on emerging evidence, while decreased libido and sexual dysfunction were taken from the full version of the WHO instrument, which included loss of interest/pleasure and erectile dysfunction.²² To assess symptom frequency and persistence, participants were asked whether they experienced each symptom most of the time or only sporadically over the previous 6 months. Consistent with previous studies, symptoms reported as occurring 'most of the time' were classified as persistent and considered as a proxy indicator of long covid-related manifestations for the purpose of analysis (hereafter referred to as *symptoms potentially associated with long covid*).^{23–25} To minimise heterogeneity and survey fatigue, further information on weekly or monthly symptom rates was not recorded.

Finally, the second section of the questionnaire gathered information on respondents' health status with a focus on COVID-19. General health information included weight, height, smoking habit and the presence of concurrent diseases, as well as a self-reported health status assessed by a Likert scale with scores ranging from 1 (very poor/poor health) to 3 (good/very good health). Additionally, COVID-19-specific data were collected, including vaccination status (number of doses received and date of the last dose), history of COVID-19 infection (including reinfection), date of infection, setting of care during the most recent infection (with details on the length of hospital and intensive care unit stays), as well as any diagnosis of long covid and subsequent follow-up at specialised centres.

Participants

A representative sample of Tuscan (Italy) residents was contacted by a survey and research firm in charge of conducting the telephone interviews. The required sample size was calculated using the formula, $n = (Z^2 * p * (1 - p)) / E^2$, where Z is 1.96 for a 95% confidence level, p is the expected true proportion, and E is the desired precision (half the CI width). Considering a long covid prevalence of 20% (with estimates ranging

from 10% to 30%), a sample size of approximately 1800 was calculated to achieve a precision of $\pm 1.4\%$ to $\pm 2.1\%$.²⁶ The sampling method foresaw a weighted stratification based on age group, sex, area of residence and reference local health authority (Azienda Unità Sanitaria Locale - AUSL) to ensure the sample reflected Tuscany's population demographics (online supplemental material table S0).

Inclusion criteria

Individuals aged 18–85 years, residing in Tuscany as of 1 January 2023, who were eligible for telephone interviews.

Exclusion criteria

- ▶ Individuals under 18 years of age.
- ▶ Individuals over 85 years of age.
- ▶ Non-residents in Tuscany.

Individuals unable to complete the cognitive test were excluded from the interview.

To address the limitations of telephone interviews that gathered symptom data over the previous 6 months without explicitly mentioning COVID-19, individuals who reported having contracted COVID-19 during this period were excluded from the sample. This conservative approach aimed to prevent attributing acute-phase symptoms to long covid, given the questionnaire's inability to determine whether the reported symptoms occurred during the acute stage of the disease.

Statistical analysis

Data were reported descriptively and summarised as proportions for categorical variables and as means with SD for continuous variables.

Individuals with a history of COVID-19 were first categorised, based on the time elapsed since their most recent infection, into two distinct periods: before and after the emergence of the Omicron (B.1.1.529) variant. The references chosen for the timeframe of the onset of Omicron circulation in Italy, December 2021, were the epidemiological bulletins from the ISS.²⁷ Both the pre-Omicron and post-Omicron periods were further divided into four final timeframes: the first pre-Omicron timeframe lasting 16 months and the subsequent three lasting approximately 9 months each. This approach allowed the period of COVID-19 infection to be treated as an ordinal variable in subsequent analyses.

The prevalence of at least one symptom, along with its 95% CI and the mean number of symptoms with its SD, was calculated in both individuals with and without a history of COVID-19. To assess symptom-specific associations and identify determinants of individual symptoms, crude and adjusted ORs (OR and aORs) by sex and age were calculated using binary logistic regression, considering potential confounders such as age and sex. Prevalence and OR analyses were also calculated for subgroups defined by sex, time elapsed since the last COVID-19 infection and the presence of concurrent diseases. Specifically, for the time-based analysis, comparisons were first

made between individuals infected either before or after Omicron onset and those with no history of COVID-19 and then for each of the four time-based subgroups (two pre-Omicron and two post-Omicron) compared with individuals with no history of the disease. Spearman's correlation coefficients were calculated to evaluate the strength of the relationships between each symptom and between the symptoms and self-reported health status. Finally, to confirm symptom-specific associations, multi-variable logistic regression analyses were performed, using age, sex, smoking habits, body mass index (BMI), concurrent diseases, COVID-19 history and vaccination status as explanatory variables, with each symptom as the outcome.

Missing data were handled using complete-case analysis, with participants excluded only from analyses of variables for which data were missing.

Statistical significance was set at $p < 0.05$. All analyses were conducted using Stata V.18 (StataCorp LLC, 1985–2023).

Patient and public involvement

Patients and members of the public were not involved in the development of the research question, study design or selection of outcome measures. During the conduct of the study, participants were contacted by telephone to provide input and feedback. The study results were made available publicly on the Regional Health Agency website in anonymised and aggregated format.

RESULTS

Of the 2005 individuals contacted, 129 (6.4%) were excluded for failing the cognitive test (34 during the short-term memory evaluation and 95 during the medium-term memory evaluation), and 123 (6.1%) were excluded due to a reported COVID-19 infection within the 6 months prior to the interview. This resulted in a final analysed sample of 1753 individuals, of whom 53.1% were female (figure 1).

The health characteristics, COVID-19 history and main outcomes, stratified by sex, are described in table 1.

Overall, participants reported a good health status score, averaging 2.48 out of 3. The mean age was 54.7 years (56.4 years for females). 52.1% of the individuals were non-smokers, with only 22.5% currently smoking (17.5% for females). BMI was within normal range (18.5–24.9) for 52.7% of the individuals, with minor variations across sex. 70.1% of the sample reported no concurrent diseases (66.5% for females). The distribution of concurrent diseases is shown in online supplemental table S1.

Almost all individuals (95.7%) received at least one vaccination shot against COVID-19, with, on average, three vaccine doses received; the latest shot occurred in 2022 for over 50% of the sample. 1013 individuals (57.8%) had a previous COVID-19, with 124 (12.2%) who reported COVID-19 more than once. For 660 individuals (65.2%), the last COVID-19 infection occurred after the circulation

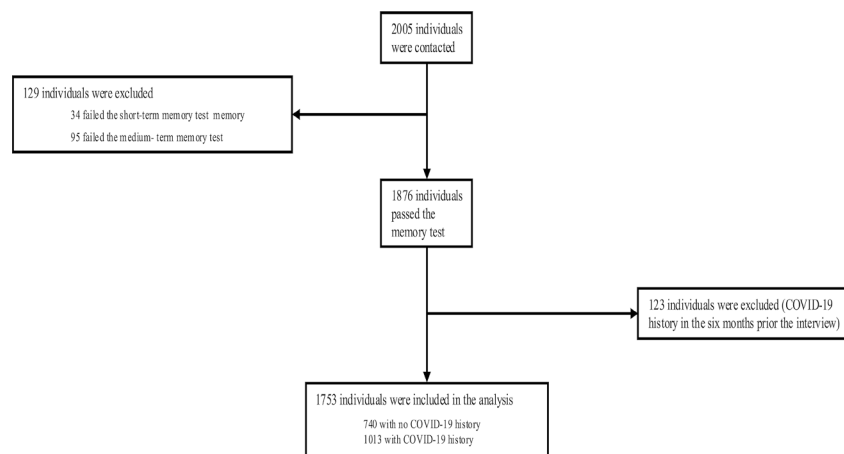


Figure 1 Eligibility determination for the analysed sample.

of the Omicron (B.1.1.529) variant. Regarding the setting of care and treatment received during the acute phase of the disease, 97.2% reported receiving home care without oxygen administration, with only 0.9% requiring home care with oxygen; 1.5% were hospitalised with no admission to intensive care unit (mean length of stay 11.2 days), and only 0.3% had intensive care unit admission (mean length of stay 7.3 days). Finally, only 3.6% of the sample received a diagnosis of long covid, with three individuals reporting follow-up visits in dedicated centres.

In the analysed sample, the prevalence of at least one symptom was 60.2% (95% CI 57.2% to 63.2%) among individuals with a history of COVID-19, and 56.9% (53.5% to 60.5%) for individuals without reported COVID. The mean number of symptoms was 2.8 (SD 2.3) and 2.6 (SD 2.2) in the two groups with and without previous COVID, respectively. Females who had COVID-19 showed the highest prevalence: 64.3% (60.3% to 68.3%) and the highest mean number of symptoms: 3.0 (2.4) (online supplemental material table S2a).

The prevalences and ORs (crude and adjusted by sex and age) for individual symptoms according to history of previous COVID-19 are shown in table 2.

The most prevalent symptom was insomnia, reported by 16.0% (13.7% to 18.2%) of the COVID-19 group, compared with 14.9% (12.3% to 17.4%) in the non-COVID group. Fatigue was the second most prevalent symptom, with prevalences of 12.8% (10.8% to 14.9%) and 8.9% (6.9% to 11.0%), respectively, followed by anxiety (10.9% (9.03% to 12.9%) versus 10.1% (7.96% to 12.3%)) and hair loss (10.4% (8.49% to 12.2%) versus 9.05% (6.99% to 11.1%)), respectively (table 2). Significant differences between groups were observed for concentration impairment: 5.5% (4.1% to 6.9%) versus 2.4% (1.3% to 3.5%) and differences close to significance were observed for skin rashes: 4.5% (3.3% to 5.8%) versus 2.4% (1.3% to 3.5%), and sore throat/pharyngeal inflammation: 2.9% (1.8% to 3.9%) versus 1.5% (0.6% to 2.4%). Calculating age- and sex-adjusted aORs (95% CI) for these symptoms showed that individuals with a previous COVID-19 had an increased probability of presenting with: fatigue (aOR 1.6

(95% CI 1.2 to 2.2)), concentration impairment (aOR 2.2 (95% CI 1.3 to 3.8)), sore throat/pharyngeal inflammation (aOR 2.1 (95% CI 1.0 to 4.2)) and skin rashes (aOR 1.86 (95% CI 1.1 to 3.3)) (table 2 and online supplemental material figure S1).

If considered separately (online supplemental material table S3), females showed higher prevalences than males for symptoms described above. In females, fatigue's prevalence was 17.1% (14.0% to 20.2%) for the COVID-19 group versus 10.9% (7.75% to 14.0%) for the non-COVID-19 group, with an aOR of 1.86 (95% CI 1.24 to 2.77), while in males it just accounted for 7.64% (5.21% to 10.1%) versus 6.87% (4.27% to 9.47%), respectively, with an aOR of 1.21 (95% CI 0.71 to 2.09). For concentration impairment, prevalence in females was significantly higher in the COVID-19 group: 7.21% (5.06% to 9.36%) versus 1.60% (0.33% to 2.86%) with an aOR of 4.88 (95% CI 2.04 to 11.72), while in males prevalences were comparable between the two groups: 3.49 (1.81 to 5.18) versus 3.30 (1.46 to 5.13), respectively, with an aOR of 0.94 (95% CI 0.43 to 2.02). Females with a history of COVID-19 also had a significantly higher risk of reporting a reduced sense of taste compared with those without such a history, with a prevalence of 2.88% (1.49% to 4.27%) compared with 1.06% (0.03% to 2.10%), for an aOR of 3.37 (95% CI 1.10 to 10.27). Full breakdown is shown in online supplemental material table S3.

The distribution of symptom prevalence and aORs based on the timing of the latest COVID-19 infection, categorised as either pre-Omicron or post-Omicron variant emergence, is presented in online supplemental material table S4.

Although some associations approached statistical significance, no significant difference in symptom prevalence was observed between individuals who had COVID-19 prior to the Omicron wave and those who had never been infected. However, adjusting for sex and age, the analyses showed that individuals infected pre-Omicron compared with those never infected had an increased risk (aOR) of fatigue (aOR 1.66 (95% CI 1.09 to 2.53)), concentration impairment (aOR 2.01 (95% CI 1.02 to 3.98)) and headaches (aOR 1.71 (95% CI 1.00 to 2.92)) (figure 2).

Table 1 Summary of health characteristics, COVID-19 history and outcomes, categorised by sex

	Total (n=1753)	Female (n=931)	Male (n=822)
Mean self-reported health status score (SD)	2.5 (0.6)	2.4 (0.6)	2.5 (0.6)
Mean age (SD)	54.7 (17.9)	56.4 (17.8)	52.8 (17.7)
Smoking (n, %)			
Current smoker	394 (22.5)	163 (17.5)	231 (28.1)
Former smoker	445 (25.4)	184 (19.8)	261 (31.7)
Non-smoker	914 (52.1)	584 (62.7)	330 (40.2)
BMI category (n, %)			
<18.5	53 (3.02)	46 (4.94)	7 (0.9)
18.5–24.9	924 (52.7)	527 (56.6)	397 (48.3)
25–29.9	586 (33.4)	251 (27.0)	335 (40.7)
30–39.9	181 (10.3)	103 (11.1)	78 (9.49)
>40	9 (0.5)	4 (0.4)	5 (0.6)
Number of concurrent diseases* (n, %)			
0	1229 (70.1)	619 (66.5)	610 (74.2)
1	315 (18.0)	192 (20.6)	123 (15.0)
2	142 (8.1)	79 (8.5)	63 (7.7)
≥3	67 (3.8)	41 (4.4)	26 (3.2)
SARS-CoV-2 vaccination (n, %)			
Unvaccinated	75 (4.3)	39 (4.2)	36 (4.4)
One or two doses	323 (18.4)	164 (17.6)	159 (19.3)
Three or more doses	1355 (77.3)	728 (78.2)	627 (76.3)
COVID-19 disease (n, %)			
No	740 (42.2)	376 (40.4)	364 (44.3)
Yes	1013 (57.8)	555 (59.6)	458 (55.7)
Reinfection (n, %)	124 (12.2)	67 (12.1)	74 (16.1)
Period of infection† (n, %)			
Pre-Omicron (B.1.1.529)	353 (34.8)	179 (32.3)	174 (38.0)
Post-Omicron (B.1.1.529)	660 (65.2)	376 (67.7)	284 (62.0)
Setting of care during acute infection † (n, %)			
At home, no oxygen needed	985 (97.3)	539 (97.1)	446 (97.4)
At home, oxygen needed	10 (0.9)	6 (1.1)	4 (0.9)
At hospital, no admission to intensive care unit (mean length of stay (days) (SD))	15 (1.5) (11.2 (7.2))	9 (1.6) (12.7 (8.2))	6 (1.3) (8.6 (4.7))
At hospital, in intensive care unit (mean length of stay (days) (SD))	3 (0.3) (7.3 (6.6))	1 (0.2) (15 (0))	2 (0.4) (3.5 (0.7))
Long covid (n, %)			
Diagnosis received	37 (3.6)	16 (2.9)	21 (4.6)
Follow-up at specialised centres	3 (0.3)	–	3 (0.6)

*Number of concurrent diseases includes cardiac disease, malignancy, liver disease, renal disease, cerebrovascular disease, endocrine disease, neurological disease and rheumatic disease. Details in online supplemental material table S1.

†Referred to the latest COVID-19 infection if two or more infections were experienced.

BMI, body mass index.

Conversely, individuals in the Omicron phase group showed significantly higher prevalence rates than those with no COVID-19 history for concentration impairment, and differences approaching statistical significance for

fatigue, skin rashes and sore throat (online supplemental material table S4), that translated in the age- and sex-adjusted analyses in an increased risk of fatigue (aOR 1.25 (95% CI 1.05 to 1.48)), concentration impairment

Table 2 Prevalences and ORs of symptoms potentially associated with long covid reported in the 6 months prior to the interview according to history of previous COVID-19

Symptom	History of COVID-19		OR* (95% CI)	P value	aOR*† (95% CI)	P value
	No	Yes				
	N; % (95% CI)	N; % (95% CI)				
Fever	1; 0.14 (0.00 to 0.40)	2; 0.20 (0.00 to 0.47)	1.46 (0.13 to 16.15)	0.76	1.83 (0.16 to 20.98)	0.63
Fatigue	66; 8.92 (6.87 to 10.97)	130; 12.83 (10.77 to 14.89)	1.5 (1.10 to 2.06)	0.01	1.6 (1.16 to 2.21)	<0.001
Cough	39; 5.27 (3.66 to 6.88)	58; 5.73 (4.29 to 7.16)	1.09 (0.72 to 1.66)	0.68	1.04 (0.68 to 1.59)	0.84
Dyspnoea	30; 4.05 (2.63 to 5.48)	41; 4.05 (2.83 to 5.26)	1 (0.62 to 1.61)	0.99	1.1 (0.67 to 1.79)	0.71
Headaches	31; 4.19 (2.75 to 5.63)	67; 6.61 (5.08 to 8.14)	1.62 (1.05 to 2.51)	0.03	1.39 (0.89 to 2.16)	0.15
Anxiety	75; 10.14 (7.96 to 12.31)	111; 10.96 (9.03 to 12.88)	1.09 (0.80 to 1.49)	0.58	1.06 (0.77 to 1.46)	0.71
Delirium/hallucinations	1; 0.14 (0.00 to 0.40)	2; 0.2 (0.00 to 0.47)	1.46 (0.13 to 16.15)	0.76	1.71 (0.15 to 19.07)	0.66
Low mood/dysphoria	44; 5.95 (4.24 to 7.65)	69; 6.81 (5.26 to 8.36)	1.16 (0.78 to 1.71)	0.47	1.21 (0.81 to 1.79)	0.36
Mental fog	6; 0.81 (0.16 to 1.46)	16; 1.58 (0.81 to 2.35)	1.96 (0.76 to 5.04)	0.16	1.99 (0.77 to 5.15)	0.16
Insomnia	110; 14.86 (12.30 to 17.43)	162; 15.99 (13.73 to 18.25)	1.09 (0.84 to 1.42)	0.52	1.13 (0.87 to 1.48)	0.36
Concentration impairment	18; 2.43 (1.32 to 3.54)	56; 5.53 (4.12 to 6.94)	2.35 (1.37 to 4.03)	<0.001	2.21 (1.28 to 3.82)	<0.001
Memory loss	37; 5.00 (3.43 to 6.57)	61; 6.02 (4.56 to 7.49)	1.22 (0.80 to 1.85)	0.36	1.39 (0.90 to 2.13)	0.13
Tingling/numbness in arms or legs	45; 6.08 (4.36 to 7.80)	69; 6.81 (5.26 to 8.36)	1.13 (0.77 to 1.66)	0.54	1.3 (0.88 to 1.94)	0.19
Balance disorder	21; 2.84 (1.64 to 4.03)	26; 2.57 (1.59 to 3.54)	0.9 (0.50 to 1.62)	0.73	1.07 (0.59 to 1.94)	0.81
Hearing impairment	53; 7.16 (5.30 to 9.02)	71; 7.01 (5.44 to 8.58)	0.98 (0.68 to 1.41)	0.9	1.27 (0.87 to 1.86)	0.22
Visual disturbance	58; 7.84 (5.90 to 9.77)	74; 7.31 (5.70 to 8.91)	0.93 (0.65 to 1.33)	0.68	1.08 (0.75 to 1.56)	0.66
Reduced sense of smell	26; 3.51 (2.19 to 4.84)	44; 4.34 (3.09 to 5.60)	1.25 (0.76 to 2.04)	0.38	1.44 (0.87 to 2.38)	0.15
Reduced sense of taste	13; 1.76 (0.81 to 2.70)	23; 2.27 (1.35 to 3.19)	1.3 (0.65 to 2.58)	0.46	1.53 (0.76 to 3.06)	0.23
Sore throat/pharyngeal inflammation	11; 1.49 (0.61 to 2.36)	29; 2.86 (1.84 to 3.89)	1.95 (0.97 to 3.94)	0.06	2.08 (1.02 to 4.23)	0.04
Nausea/vomiting	6; 0.81 (0.16 to 1.46)	9; 0.89 (0.31 to 1.47)	1.1 (0.39 to 3.09)	0.86	1.13 (0.40 to 3.23)	0.82
Diarrhoea/abdominal pain	20; 2.70 (1.53 to 3.87)	25; 2.47 (1.51 to 3.42)	0.91 (0.50 to 1.65)	0.76	0.95 (0.52 to 1.74)	0.87

Continued

Table 2 Continued

Symptom	History of COVID-19		OR* (95% CI)	P value	aOR*† (95% CI)	P value
	No	Yes				
	N; % (95% CI)	N; % (95% CI)				
Loss of appetite	19; 2.57 (1.43 to 3.71)	20; 1.97 (1.12 to 2.83)	0.76 (0.40 to 1.44)	0.41	0.83 (0.44 to 1.59)	0.58
Chest pain	6; 0.81 (0.16 to 1.46)	11; 1.09 (0.45 to 1.72)	1.34 (0.49 to 3.65)	0.56	1.48 (0.54 to 4.08)	0.44
Joint pain/swelling	59; 7.97 (6.02 to 9.92)	80; 7.90 (6.24 to 9.56)	0.99 (0.70 to 1.41)	0.95	1.14 (0.80 to 1.63)	0.48
Persistent muscle pain	49; 6.62 (4.83 to 8.41)	73; 7.21 (5.61 to 8.80)	1.1 (0.75 to 1.59)	0.63	1.22 (0.83 to 1.79)	0.31
Chilblains on fingers/toes	12; 1.62 (0.71 to 2.53)	17; 1.68 (0.89 to 2.47)	1.04 (0.49 to 2.18)	0.93	1.01 (0.47 to 2.15)	0.98
Palpitations/tachycardia	19; 2.57 (1.43 to 3.71)	23; 2.27 (1.35 to 3.19)	0.88 (0.48 to 1.63)	0.69	0.99 (0.53 to 1.84)	0.96
Skin rashes	18; 2.43 (1.32 to 3.54)	46; 4.54 (3.26 to 5.82)	1.91 (1.10 to 3.32)	0.02	1.86 (1.06 to 3.26)	0.03
Hair loss	67; 9.05 (6.99 to 11.12)	105; 10.37 (8.49 to 12.24)	1.16 (0.84 to 1.60)	0.36	1.21 (0.87 to 1.68)	0.25
Dysmenorrhoea/menstrual disorders	11; 2.93 (1.22 to 4.63)	33; 5.95 (3.98 to 7.91)	2.1 (1.05 to 4.20)	0.04	1.71 (0.85 to 3.47)	0.13
Decreased libido	39; 7.94 (5.55 to 10.33)	47; 6.54 (4.73 to 8.34)	0.81 (0.52 to 1.26)	0.35	0.97 (0.61 to 1.52)	0.88
Sexual dysfunction	25; 5.09 (3.15 to 7.04)	31; 4.31 (2.83 to 5.80)	0.84 (0.49 to 1.44)	0.53	1.04 (0.60 to 1.81)	0.89
Weight loss	61; 8.24 (6.26 to 10.22)	59; 5.82 (4.38 to 7.27)	0.69 (0.47 to 1.00)	0.05	0.77 (0.53 to 1.13)	0.18

The bold in the first line of the table represents the variables / indicators while the bold across the remaining part of the table indicated statistical significance.
 *Yes versus no.
 †aOR=OR adjusted by sex and age.

(aOR 1.52 (95% CI 1.14 to 2.03)), sore throat/pharyngeal inflammation (aOR 1.61 (95% CI 1.12 to 2.31)) and skin rashes (aOR 1.43 (95% CI 1.07 to 1.93)), with mental fog, approaching statistical significance (aOR 1.61 (95% CI 0.99 to 2.62)) (figure 2).

In analyses adjusted by age that addressed risk of symptoms by sex and phase of infection, males infected in the pre-Omicron period, compared with males without COVID-19, had significantly higher odds of experiencing headaches (aOR 2.83 (95% CI 1.08 to 7.40), $p=0.03$). Females infected in the pre-Omicron phase compared with females without COVID-19 showed significantly higher odds of a reduced sense of taste (aOR 5.82 (95% CI 1.67 to 20.27)), fatigue (aOR 2.22 (95% CI 1.34 to 3.69)) and concentration impairment (aOR 4.77 (95% CI 1.74 to 13.08)). Fatigue (aOR 1.28 (95% CI 1.03 to 1.59)), concentration impairment (aOR 2.20 (95% CI 1.40 to 3.45)) and sore throat (aOR 1.76 (95% CI 1.10

to 2.82)) were also more likely in women infected in the Omicron phase compared with those without COVID-19. Full breakdown is available in online supplemental material table 5.

When accounting for the time elapsed since the acute phase of infection, individuals who experienced COVID-19 during the most recent Omicron phase (within the last 14 months from interview) exhibited significantly higher prevalences of fatigue (aOR 17.72 (95% CI 13.02 to 22.41)), and concentration impairment (aOR 6.69 (95% CI 3.62 to 9.77)), compared with other subgroups. Correspondingly, their aORs for these symptoms were the highest among all COVID-19 groups (aOR 2.11 (95% CI 1.40 to 3.20) and aOR 2.92 (95% CI 1.46 to 5.80), respectively) (online supplemental material table S6b and figure S2).

Evaluating differences by concurrent diseases (online supplemental material table S7) showed that individuals

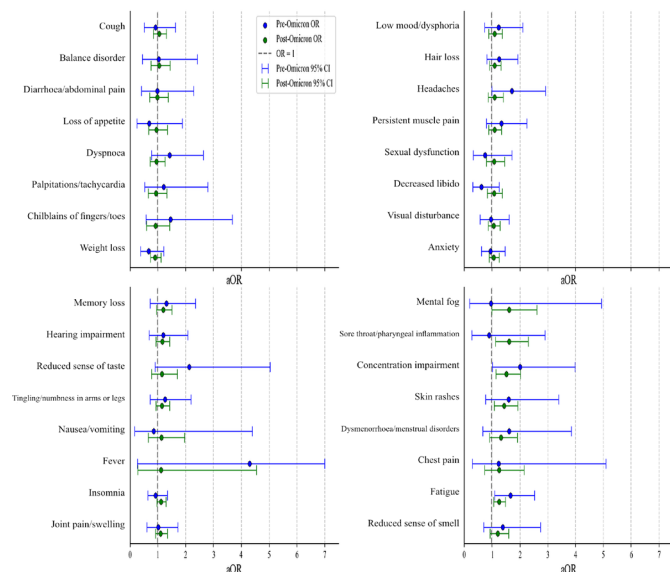


Figure 2 aORs of symptoms potentially associated with long covid reported in the 6 months prior to the interview, categorised by period (pre-Omicron or post-Omicron variant circulation). Individuals with no COVID-19 history were used as a comparison. aOR, adjusted OR.

with one or more concurrent diseases and a history of COVID-19 had significantly higher prevalence than non-COVID-19 counterparts to report concentration impairment, 8.50% (5.37% to 11.62%) versus 2.75% (0.58% to 4.92%). This subgroup with comorbidities presented a significantly increased probability (aOR) of presenting with fatigue (aOR 1.55 (95% CI 0.99 to 2.43)), concentration impairment (aOR 2.93 (95% CI 1.17 to 7.35)), sore throat/pharyngeal inflammation (aOR 4.23 (95% CI 1.19 to 15.01)) and memory loss (aOR 2.05 (95% CI 1.03 to 4.08)) (online supplemental material table S7).

Accounting for self-reported health status, a mild negative correlation was found with symptoms like fatigue, dyspnoea, joint pain and muscle pain, regardless of COVID-19 history. When accounting for the Omicron variant and comorbidities, fatigue remained mildly negatively correlated, losing strength only in those without concurrent diseases (online supplemental material figure S3, S4, S6). Additionally, a strong positive correlation emerged between reduced taste and smell in individuals with a pre-Omicron COVID-19 history (online supplemental material figure S5).

Finally, the multivariable analysis showed that a positive history of COVID-19 was significantly associated with fatigue (aOR 1.66 (95% CI 1.19 to 2.33)), concentration impairment (aOR 2.26 (95% CI 1.29 to 3.94)), skin rashes (aOR 1.96 (95% CI 1.11 to 3.45)) and sore throat (aOR 2.06 (95% CI 1.00 to 4.24)) (figure 3, online supplemental material table S8).

DISCUSSION

This study aimed to assess the prevalence of long covid-associated symptoms in the general population of

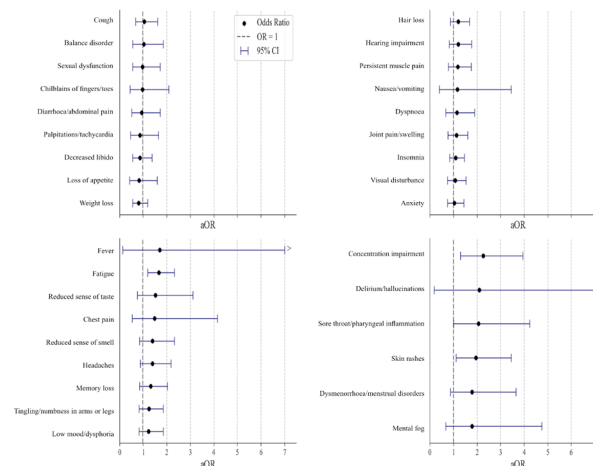


Figure 3 Associations between COVID-19 history and symptom odds. Multivariable analysis used each symptom as an outcome and age (older individuals (≥ 65 years) or younger individuals (0–64 years)), body mass index, smoking habits, concurrent disease and vaccination history as explanatory variables. Individuals with a COVID-19 history and the aOR for each symptom are arranged from lowest to highest. The detailed results of the multivariable analysis are presented in the online supplemental material table S8. aOR, adjusted OR

Tuscany, Italy, comparing individuals with and without a previous history of COVID-19. The results showed that symptoms potentially associated with long covid were consistently frequent across all groups with a history of COVID-19, especially in females, with fatigue and concentration impairment emerging as particularly prevalent. We observed a slightly higher prevalence of at least one symptom potentially associated with long covid compared with existing studies.^{28 29} As noted, these discrepancies may be caused by methodological or population differences.⁹ Additionally, the definition of the disease is rapidly evolving, with a symptom-based definition recently proposed.³ Regardless of the definition used, the magnitude of the problem appears to be larger than the current level of attention suggests in Europe,⁸ particularly when focusing on the burden of specific symptoms, which revealed consistent trends across groups. Insomnia was the most prevalent symptom overall but showed no significant differences between individuals with and without a history of COVID-19, whereas fatigue and concentration impairment were consistently more common in those with a history of COVID-19. Although the observed prevalences of these two symptoms were lower than expected (21–29% for fatigue and 13–32% for concentration impairment), possibly because recent infections were excluded and the population studied had usually very mild acute SARS-CoV-2 disease, their impact should not be overlooked.^{28 30–33} Reinforcing this point, those symptoms, along with brain fog, memory disturbances—more frequent in individuals with concurrent diseases—and headaches—more frequent in males during pre-Omicron circulation—were described to be part of the symptom cluster defined as ‘chronic

fatigue-like syndrome', the most common among the four recently described for long covid and proposed as a marker of disease severity.³ The impact of other symptoms should also not be underestimated: symptoms such as sore throat, reduced sense of taste and skin-related issues presented a non-negligible correlation, with prevalence estimates largely consistent with other studies.^{28 30–34} From a public health perspective, healthcare systems should adapt to evolving epidemiological signals by incorporating flexible, tailored approaches. In this regard, our study further demonstrates the role of sex differences—where males consistently exhibited lower prevalence and odds of persistent symptoms—and of comorbidities, both of which represent established factors influencing symptom persistence.^{3 35 36} Our results also confirm existing literature indicating that pre-Omicron infections are associated with more persistent symptoms,³ with symptoms such as fatigue and concentration impairment presenting significant associations with previous COVID-19 history. Given that individuals with a history of COVID-19 showed a 50% to 75% increase in the aOR of nearly all the symptoms discussed, these findings, given the size of the population infected, suggest a disease burden greater than initially anticipated and underscore the need for continuous monitoring and comprehensive intervention strategies. To our knowledge, there are no active surveillance systems for long covid in Europe, with available data mostly relying on cohort studies or non-representative samples, often lacking the regional or population-wide focus needed to accurately assess the prevalence of this condition.^{37–41}

Studies like the one presented can contribute to a better understanding of this condition, especially given the rapidly changing epidemiological landscape. In this context, a primary strength of our study is the comparison between respondents with and without a history of COVID-19 in a non-clinical setting. This approach allowed us to determine the underlying prevalence of symptoms not directly attributable to COVID-19, enabling the identification of risk coefficients associated with a reported infection. Another strength is the utilisation of a population-based telephone survey, which minimises selection bias and helps to provide a more representative estimation of symptom prevalence across the general population. This is particularly relevant, as most published studies have focused on patients who were previously hospitalised or referred to specialised centres, thereby concentrating on more severe cases, while the general population remains under-represented in the scientific literature. We strongly believe that this approach can complement clinical data while offering a useful perspective that could contribute to future efforts aimed at monitoring long covid symptoms at the population level. Moreover, despite the high prevalence of symptoms, it is noteworthy that only a few clinical long covid diagnoses were made in our sample, and very few

cases were followed up in specialised centres. This may open to several hypotheses, including a low severity of long covid symptoms within this population, diagnostic challenges, insufficient attention from primary care providers or limited access to specialised centres. All these factors highlight areas for future research and improvements in healthcare provision for post-COVID-19 conditions, aiming to ensure efficient and equitable care.

This study shows some limitations. First, due to the methodology used, no laboratory confirmation of COVID-19 was available, and no clinical assessment of participants by healthcare personnel could be performed during remote interviews.

Second, the exclusion of individuals who failed the memory test and of those who had contracted COVID-19 in the 6 months prior to the interview may have introduced a selection bias. Excluding individuals based on the memory test improved data reliability by minimising recall bias and enhancing the overall quality of the information collected, but may also have affected prevalence estimates. According to the literature, this test likely led to the exclusion of a small number of participants with symptoms potentially associated with long covid, especially those in the 66–85 age group (about 5–10% among over 65 and less than 5% among those under 65), thus contributing to underestimating the prevalence of symptoms such as memory loss and brain fog.⁴² Based on the design of the questionnaire—which focused on symptoms potentially associated with long covid experienced over the past 6 months—this exclusion was crucial for the analysis, considering the high circulation of SARS-CoV-2 and other influenza-like viruses during the study period. The exclusion of symptoms attributable to the acute phase of the illness allowed a more accurate attribution of symptoms to cases of long covid, ultimately increasing specificity at the expense of sensitivity, possibly leading to an underestimation of the prevalence of respiratory symptoms such as dyspnoea.³⁰ Notably, these two potential sources of underestimation suggest that the actual prevalence of symptoms—and thus the overall magnitude of the problem—may be even greater than reported.

Third, the effects of vaccination and prior COVID-19 hospitalisation could not be fully assessed, since over 90% of participants were vaccinated and very few had been hospitalised. This limited the assessment of the impact of severe acute disease, intensive care and respiratory support, which are known to affect symptom persistence.

Fourth, although the interviewed sample was representative of the region, some minorities, such as migrants or disadvantaged groups, were not adequately reached, as the CATI approach precluded access to those without stable phone contact. As a result, the prevalence of symptoms may be further underestimated by the exclusion of these particularly

at-risk groups, who are often less effectively reached by healthcare systems.⁴³

Finally, other limitations include risk of false positive findings due to multiple testing across symptoms, cross-sectional design of the study, survey fatigue from the lengthy questionnaire and the difficulty of attributing common symptoms such as insomnia and fatigue solely to long covid, given the definition used in the study. While the multivariate analysis accounted for the number of comorbidities, unmeasured conditions may still have influenced the results.

CONCLUSION

This study highlights the prevalence in the general population of symptoms potentially associated with long covid, particularly fatigue and concentration impairment, identifying higher risk in specific subgroups. By documenting population-level symptom prevalences in a defined region—where most prior studies relied on a single-centre or hospital-based sample not representative of the general population—this work contributes to the global understanding of long covid and may support public health planning, resource allocation and clinical management in similar populations. This is particularly relevant as targeted public health interventions—whether symptom-specific or focused on vulnerable subgroups—may help optimise care pathways and mitigate long-term consequences.

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

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