scientific reports

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Identifying Long Covid phenotypes and their association with personal characteristics, healthcare use, and daily life burden: population-based study in Belgium

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Long Covid (LC), a multisystem disorder with persistent symptoms > 4 weeks post COVID-19, has impacted healthcare systems substantially. As information is scarce for Belgium, this study aimed to identify LC phenotypes and assess participant characteristics, healthcare use and daily life burden by phenotype. The last survey wave of COVimpact (a longitudinal online cohort study among Belgian adults recruited after SARS-CoV-2 infection) focused on LC with questions on healthcare utilization and perceived daily impact. A latent class analysis (LCA) identified phenotypes, based on symptom type, disease duration, and LC-related disability. Backward multivariable multinomial logistic regression explored predictors of LC class membership. Among 1,840 respondents self-reporting LC, four phenotypes emerged. Class 1 presented mild clinical outcomes, class 2 and 3 presented moderate clinical outcomes, differentiated by symptoms of memory problems and brain fog (class 2), and respiratory problems and muscle/joint pain (class 3), and class 4 included the most severe clinical outcomes. Compared to class 1, being older, female, lower educated, non-European, obese and experiencing moderate to severe acute COVID-19 symptoms predicted higher class severity. Diagnosis, healthcare use and support differed among adults with moderate and severe LC, many reported insufficient healthcare access and major disruption to daily life, including absenteeism from work/school. People with severe LC were the most financially impacted. By distinguishing LC phenotypes, this study enhances understanding of varying healthcare trajectories and daily life impacts. Healthcare planning and support should be more effectively tailored to the specific needs of those affected by LC.

Keywords Long Covid, Cluster analysis, Healthcare utilization, Disease burden, Belgium

Long Covid (LC), a health impairment condition first recognized in May 2020[1], is characterized by persistent symptoms (> 4 weeks) following the acute SARS-CoV-2 infection. LC is a multi-systemic disorder with a large variety of symptoms with most common reported symptoms being fatigue, shortness of breath, breathlessness, cognitive dysfunction, brain fog and muscle pain[2–4]. LC is life-altering for affected individuals and causes substantial disability, reduced quality of life, greater healthcare needs and extended absence from work and social life[1,5–8].

Since the pandemic years, research has been ongoing on identifying different disease subgroups and phenotypes, uncovering corresponding biomarkers, experimental medicine and clinical trials[9,10]. Due to the variability in case definitions for LC, clinical management of LC is inconsistent across time and place and challenges healthcare professionals (HCP)[2,11]. Managing LC can be improved through the identification of LC subtypes as tailored treatment approaches can help HCP, patients and healthcare systems to be better

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prepared and informed[9]. Despite this, as no curative treatment exists, the trajectory of recovery from LC remains uncertain for million individuals[2,12]. Worldwide, there is increased healthcare utilization by LC sufferers leading to additional healthcare and disability spending[1,13]. Barriers to healthcare access and a large diversity in access, quality and equity of care for people with LC have recently been identified[14–16].

In Belgium, efforts were made to support HCP in treating and managing LC patients, with the publication of an evidence-based guideline 'Follow-up and rehabilitation of patients with persistent symptoms after COVID-19 in primary care' (November 2022)[17]. Moreover, through the care trajectory 'post-Covid-19' (since July 2022), diagnosed LC patients can benefit from reimbursement of treatment costs when consulting HCP in primary care for rehabilitation. In this care pathway, general practitioners (GPs) have a key position and are point of referral[18]. Although various studies investigated Belgian LC adults and HCPs' approach[7,19–23], LC's impact on the demand for healthcare, the rising healthcare use and its socioeconomic cost is scarcely investigated in Belgium. This article aims to contribute to this knowledge gap, identified in earlier research[23], through a population-based approach.

This study aims to (1) identify clinical phenotypes among adults in the Belgian general population who self-report Long Covid, and (2) assess associations between these phenotypes and participant characteristics, healthcare utilization and the perceived impact of their health and daily life.

By analyzing self-reported LC experiences and patterns of healthcare use, this study offers insights in symptom persistence and care pathways. Understanding these patterns can inform future healthcare planning and policy development in Belgium.

Methods

Study population and design

COVimpact is a longitudinal online cohort study conducted in Belgium targeting adults (18+) testing positive for SARS-CoV-2[24]. Participants were recruited via national contact tracing[25]. The cohort included a baseline questionnaire (April 2021–Jan 2023) and 3-month follow-ups until April 2023. An additional follow-up survey, specifically on LC, was administered on February 19, 2024. The LC focus was not disclosed in the invitation to avoid bias. Questionnaires were administered in Dutch, French, German, and English.

Of 48,242 baseline participants, 16,427 (35%) completed the LC-specific survey. This analysis includes 2,065 participants (13%) who answered 'yes' to: 'Would you describe yourself as having had Long Covid (i.e. all possible health problems persisting more than 4 weeks after your acute episode of COVID-19 that cannot be explained by anything else)', using a definition consistent with UK ONS Coronavirus Infection Surveys[26] and to capture all LC applied in clinical practice in Belgium (i.e. the CDC definition of > 4 weeks and the NICE definition of > 12 weeks)[27](see Fig. 1).

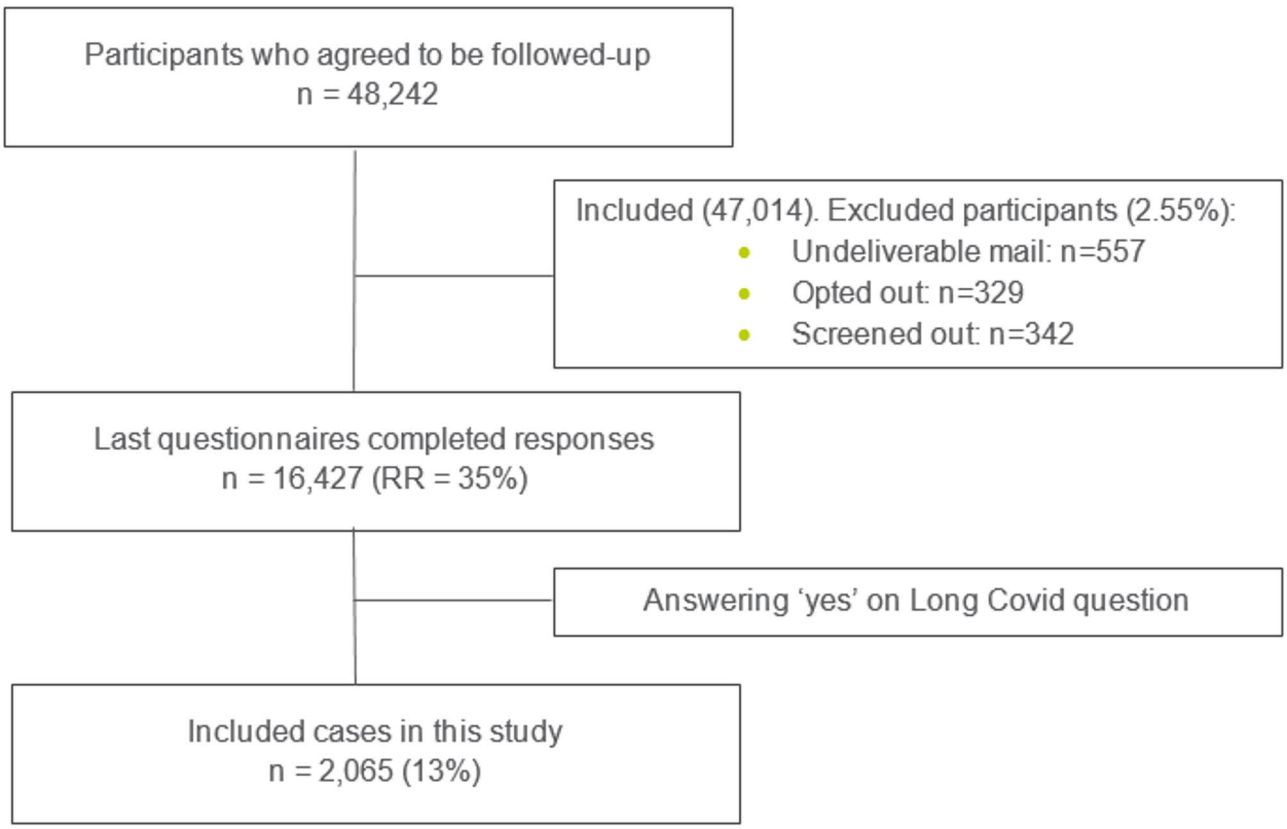

Fig. 1. Flow diagram.

Measures

The primary outcome was the Long Covid (LC) phenotype, identified through latent class analysis (LCA) based on symptom type (14 items), duration (5 categories), and impact on daily activities (3 categories).

Collected covariates included sociodemographic variables (age, sex, education, ethnicity) and self-reported risk factors in line with existing literature on COVID-19 and LC[5–7,11,15,28]: urban residency, healthcare worker status, smoking, BMI, chronic disease, COVID-19 vaccination status, COVID-19 hospitalization, and severity of the acute infection(s).

Healthcare utilization was measured through LC-related consultations, diagnosis, treatment/advice received, and self-perceived access to care. When answering 'yes' on the question 'Did you visit a healthcare provider(s) for your long-term (Long Covid) complaints?', respondents were asked to specify from a list of 27 conventional HCP which healthcare providers they had consulted. For the analyses, five dichotomous variables were created to determine whether respondents had consulted a GP, specialist, physiotherapist, mental health professional (including psychiatrist, psychologist, psychotherapist and neuropsychologist) and other HCP (including occupational therapist, dietician, speech therapist, nurse at home, social worker, emergency department and other (specify)). Respondents could indicate various reasons for not consulting HCP when answering 'no' on this question. When answering 'yes' on the question 'Did you receive treatment or advice from healthcare provider(s) for your long-term (Long Covid) complaints?', respondents could check each treatment or advice they had received from a list of 14 answer options. For the analyses, five dichotomous variables were created to determine the type of received treatment or advice: (1) medication (including prescription medicine, medicine without prescription and oxygen at home), (2) self-management advice (including self-management advice, energy management and advice on healthy diet and lifestyle), (3) exercise programs (including physical exercise programme, breathing exercises, interventions aimed at voice, cough, chewing and swallowing problems and treatment of odor and taste disorders), (4) psychological-cognitive support (including psychological interventions and cognitive treatment) and (5) alternative or other treatment. Access to care was assessed with the question: 'How was access to care for your long-term (Long Covid) complaints?' with the following response options: quick access to necessary care, moderate access, no sufficient access and don't know.

LC's perceived impact included self-reported work/school absence and financial hardship. Perceived financial hardship due to LC was assessed with the question 'Have you suffered financial loss as a result of your long-term (Long Covid) complaints?', with the following response options: no, yes but without bringing me in big trouble, yes and this loss caused me (major) problems and not applicable. All variables were self-reported.

Data management

Data were collected through LimeSurvey and securely stored on servers managed by Sciensano. All data processing adhered to relevant privacy regulations and data protection standards. All methods were performed in accordance with relevant guidelines and regulations (Declaration of Helsinki). Informed consent was obtained from all participants at baseline, each follow-up and the final survey. Participants could indicate whether they wished to be contacted for future follow-ups.

Statistical analysis

In LCA, classes were added until the model best fits the data. A complete case analysis ($N = 1{,}840$, among all self-reported LC sufferers: $N = 2{,}065$) was applied, excluding 225 individuals with missing values on key variables (representing < 11% of the total sample; missingness was found to be at random (Supplementary Table S1)). The Bayesian Information Criterion (BIC) was used to determine the optimal number of classes (i.e. lowest BIC value). The four-class solution (BIC value of 34710.78) provided the best fit, compared to the model with two, three or five latent classes (goodness-of-fit indicators for 2- to 5-class LCA models are available in Supplementary Table S2). Moreover, the interpretation of the four-class solution was clinically relevant and aligned with distinct LC subgroups identified in previous research[12,23,29,30]. A sensitivity analysis excluding participants with symptom duration < 3 months ($N = 286$) was performed to assess potential changes in the latent class structure. The results showed that restricting to WHO's clinical case definition (≥ 3 months) did not affect the phenotype composition (Supplementary Table S3, Figure S1, Figure S2).

Descriptive statistics summarized the distribution of key variables across LC phenotypes. Class differences in sociodemographic and clinical characteristics, healthcare use, and perceived impact were assessed using Chi-square tests ($p < .05$). No missing data were found for the primary outcome; missingness in covariates was < 3% and randomly distributed across LC phenotypes (Supplementary Table S4).

Finally, the association between participant's sociodemographic characteristics, risk factors and medical characteristics, healthcare utilization and perceived impact of LC and the four phenotypes was assessed through a multivariable multinomial logistic regression model. Pairwise correlation coefficients indicated very weak or weak (< 0.4) relationship between all independent variables, except for the variables 'visit HCP for LC complaints (yes/no)' (0.91) and 'received treatment or advice from HCP (yes/no)' (0.74) leading to exclusion of these two variables. Sensitivity analyses showed that the effect of missing values was minimal, and the following analyses were performed using a complete case approach (N complete = 1526). Backward elimination is generally preferred over the forward selection approach due to its ability to consider all candidate predictors simultaneously, leading to more parsimonious and robust models[31]. A backward multivariable multinomial logistic regression model, removing terms with ≥ 0.2, was conducted. The categorical dependent variable consisted of four classes, with class 1 (people with mild LC) as the reference group. Odds ratios (OR) and 95% confidence intervals (95% CI) were reported. A p-value of < 0.05 was considered statistically significant.

The LCA was performed in R software using the 'poLCA' package. Data management and analysis were performed in StataSE 17.

Results

Identifying classes among self-reported adults with Long Covid

Four clinical phenotypes were identified through LCA. All participants were grouped into 'class 1' ($N = 512$, 28%), 'class 2' ($N = 588$, 32%), 'class 3' ($N = 337$, 18%) and 'class 4' ($N = 403$, 22%). Latent class probabilities conditional to class membership are presented in Table 1. Figure 2 shows symptom clusters from the four-class solution of the latent class analysis.

Class 1 had participants with mild clinical outcomes on all LCA variables, i.e. lowest probability on various LC symptoms and highest probability on limited symptom duration (< 9 months, 47%) and limited daily disability of LC condition (50% answering 'not at all severe'). We therefore labelled class 1 as 'mild LC'. Class 2 was the largest and had participants with a high probability on concentration and/or memory problems (71%) and brain fog (37%) with medium symptom duration (9 months to 2.5 years, 56%) and high probability of moderate daily impact (69% answering 'yes, a little severe'). We labelled this second class as 'moderate LC with neurocognitive symptoms'. Participants of class 3 had also moderate clinical outcomes, i.e. medium symptom duration (9 months to 2.5 years, 49%) and high probability of moderate self-perceived impact on everyday functioning (72% answering 'yes, a little severe') but had a high probability of breathing problems (74%) and muscle or joint pain (83%). We labelled this third class as 'moderate LC with respiratory–musculoskeletal symptoms'. Fatigue was highly prevalent among members of class 2 (92%) and class 3 (97%). Class 4 included participants with the most severe clinical outcomes. Members of class 4 had the highest probability on LC symptoms as (general) fatigue (99%), breathing problems (77%), headache (65%), concentration and/or memory problems (90%), brain fog (61%), sleep problems (79%), depression (56%), anxiety (51%), gastrointestinal complaints (56%) and hair loss (30%) (see Fig. 2). Class 4 members also had the highest probability on symptom duration (1.5 years up to over 2.5 years, 71%) and severe perceived LC impact on daily living (60%). We therefore labelled this fourth class as 'severe LC'.

		Latent class analysis (LCA)			
		$N = 1840$			
	Whole sample	Class 1	Class 2	Class 3	Class 4
N	1840	512	588	337	403
%	100%	27.83%	31.96%	18.32%	21.90%
		Mild LC	Moderate LC with neurocognitive symptoms	Moderate LC with respiratory–musculoskeletal symptoms	Severe LC
	%	Probabilities			
Type of LC symptoms					
(general) fatigue	84.8	55%	92%	97%	99%
breathing problems	59.6	45%	52%	74%	77%
headache	36.2	7%	24%	64%	65%
concentration and/or memory problems	53.4	6%	71%	49%	90%
brain fog	28.6	3%	37%	13%	61%
muscle or joint pain	47.5	15%	29%	83%	83%
loss or change of sense/smell/taste	30.1	28%	21%	40%	37%
sleep problems/sleep disorder	35.3	6%	24%	45%	79%
depression/depressive feelings	21.9	3%	20%	13%	56%
anxiety/anxiety attacks	17.8	1%	14%	11%	51%
gastrointestinal complaints	22.6	5%	10%	32%	56%
hair loss	11.1	2%	8%	8%	30%
persistent fever	5.2	2%	1%	13%	8%
other symptoms	17.1	30%	11%	6%	20%
Duration of LC symptoms					
< 3 months	15.5	27%	13%	19%	2%
3–9 months	16	20%	17%	17%	8%
9 months - 1.5 years	20.8	19%	23%	21%	19%
1.5–2.5 years	32.3	23%	33%	28%	47%
more than 2.5 years	15.3	11%	13%	15%	24%
Daily disability of LC condition					
No, not at all severe	20.8	50%	14%	13%	3%
Yes, a little severe	56	44%	69%	72%	37%
Yes, a lot severe	23.2	6%	17%	15%	60%

Table 1. Descriptive statistics and latent class analysis of Long Covid (LC) symptoms, symptom duration and daily disability of Long Covid ($N = 1840$).

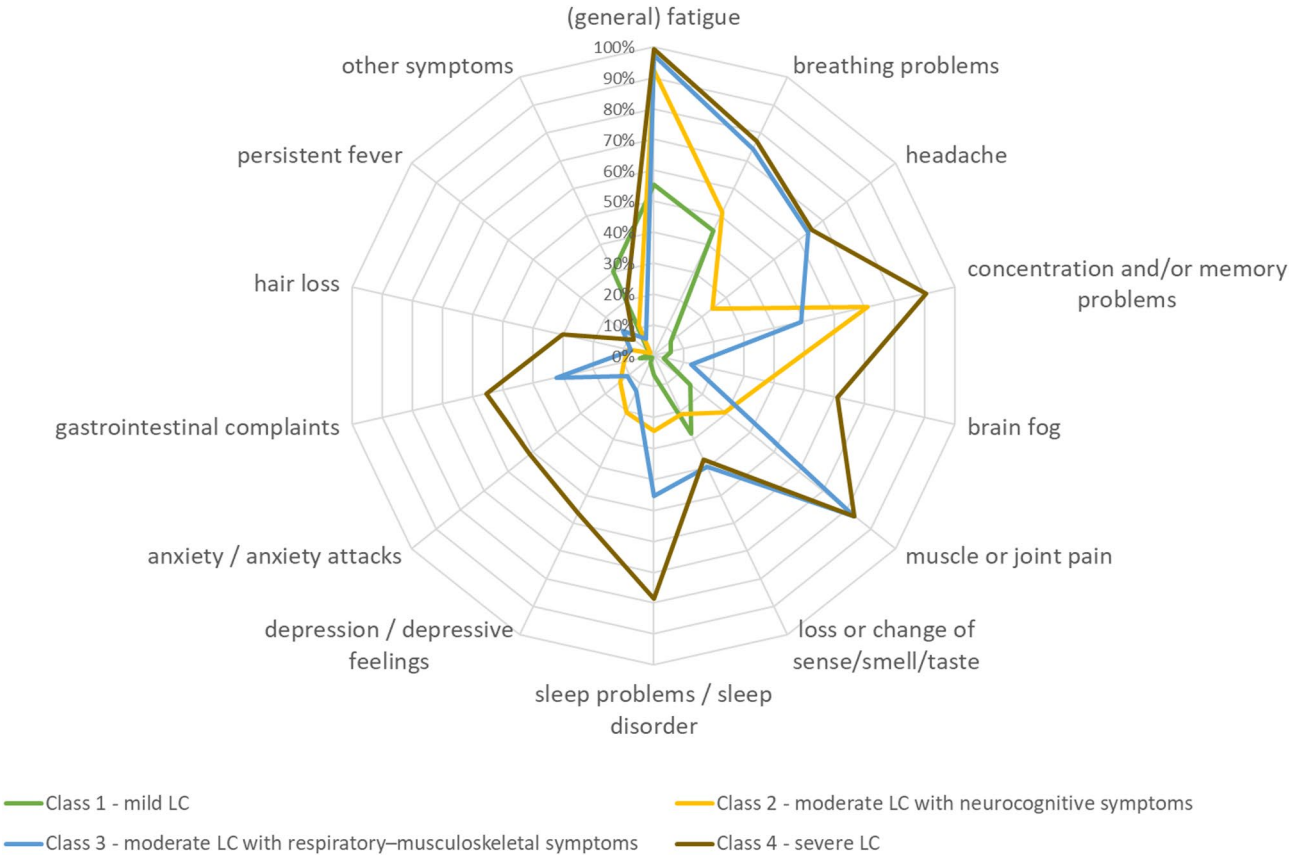

Fig. 2. Four-class solution of the latent class analysis of self-reported adults with Long Covid (LC) symptoms ($N = 1840$).

Exploring personal characteristics, healthcare use and daily life burden between Long Covid phenotypes

Table 2 describes the characteristics of all adults with self-reported LC ($N = 1,840$). Most respondents were female (68%) and median age was 49 (IQR = 17) years. One in three (35%) had a high educational level (master education or higher) and 83% had a Belgian origin. The majority (69%) who lived in an urban area, was not a healthcare worker (81%) and was a non-smoker (88%). Of all respondents, 23% were obese and half (49%) had a chronic condition. The vast majority (93%) was fully vaccinated against COVID-19. Of all respondents, 5% were hospitalized during the acute COVID-19 infection. Over half of the respondents (56%) identified the severity of their acute SARS-CoV-2 infection(s) as moderate and 33% as having severe symptoms. About two out of three respondents (62%) sought healthcare for their LC complaints, with GPs being the most frequently consulted providers. Of all respondents, one in four (25%) was diagnosed with LC by HCP. About one in three (31%) received treatment or advice from HCP for LC complaints: this was mainly medication, exercise programs or self-management advice. Healthcare access for LC complaints was easy for 28%, while 14% mentioned no sufficient access. Two fifths of respondents (39%) reported absenteeism from school or work due to LC symptoms and 29% had experienced financial impact.

Reasons for not seeking HCP for LC complaints are presented in Supplementary Table S5. The main reasons mentioned were 'I expected little help from a HCP for these complaints' (49%), 'symptoms disappeared on their own after some time' (37%) and 'lack of time due to work, no childcare or other' (20%). Significant differences between phenotypes demonstrate that 'disappearance of symptoms' was mainly mentioned by adults with mild LC (56%), while individuals with moderate and severe LC more frequently reported 'expecting little help from a HCP for LC complaints' (class 2 = 55%, class 3 = 50%, class 4 = 51%) and 'lack of time' (class 2 = 22%, class 3 = 24%, class 4 = 33%). In addition, one out of three people with severe LC (33%) also mentioned 'lack of information'.

Significant differences between LC phenotypes were visible for almost all independent variables (see p-value in Table 2). Table 3 presents the association between the four phenotypes and participant characteristics, healthcare utilization and the perceived impact of their daily living.

Compared to individuals with mild LC (class 1), people with moderate LC with neurocognitive symptoms (class 2) and severe LC (class 4) were more likely to be older (OR class 2 31–50 years = 1.60, $p<.05$; OR class 4 51–65 years = 1.98, $p<.05$). Adults with moderate LC with respiratory–musculoskeletal symptoms (class 3) and severe LC (class 4) were more likely to be women (OR class 3 = 1.67, $p<.01$; OR class 4 = 2.18, $p<.001$) and were lower educated (OR class 3-bachelor education = 0.53, $p<.01$, OR class 3-master education or higher = 0.41,

		Whole sample		Mild Long Covid		Moderate Long Covid with neurocognitivesymptoms		Moderate Long Covid with respiratory–musculoskeletal symptoms		Severe Long Covid		p-value for differences between classes
		N=1840		Class 1		Class 2		Class 3		Class 4		
		N=1840		N=512		N=588		N=337		N=403		
		N	%	N	%	N	%	N	%	N	%	
Sociodemographic characteristics												
Age												0.000*
	18-30	121	6.77	48	9.72	38	6.61	22	6.77	13	3.32	
	31-50	799	44.74	192	38.87	278	48.35	137	42.15	192	48.98	
	51-65	708	39.64	191	38.66	217	37.74	129	39.69	171	43.62	
	66+	158	8.85	63	12.75	42	7.30	37	11.38	16	4.08	
Sex												0.000*
	Men	581	31.59	204	39.84	201	34.18	96	28.49	80	19.90	
	Women	1258	68.41	308	60.16	387	65.82	241	71.51	322	80.10	
Educational status												0.000*
	Secondary school or lower	499	27.86	110	22.00	140	24.43	130	39.51	119	30.59	
	Bachelor education	664	37.07	189	37.80	212	37.00	123	37.39	140	35.99	
	Master education or higher	628	35.06	201	40.20	221	38.57	76	23.10	130	33.42	
Ethnicity												0.101
	Belgian	1529	83.46	427	83.89	483	82.71	294	87.50	325	80.65	
	European	145	7.91	44	8.64	43	7.36	24	7.14	34	8.44	
	Non-European	158	8.62	38	7.47	58	9.93	18	5.36	44	10.92	
Risk factors and medical characteristics												
Urban residency												0.000*
	No	565	31.15	140	27.72	153	26.38	135	40.54	137	34.60	
	Yes	1249	68.85	365	72.28	427	73.62	198	59.46	259	65.40	
Healthcare worker												0.745
	No	1461	80.99	411	81.71	468	81.39	261	78.85	321	81.27	
	Yes	343	19.01	92	18.29	107	18.61	70	78.85	74	18.73	
Smoking habits												0.009*
	No	1608	88.16	460	90.73	515	87.73	283	84.73	350	88.38	
	Yes, occasionally	95	5.21	16	3.16	39	6.64	16	4.79	24	6.06	
	Yes, everyday	121	6.63	31	6.11	33	5.62	35	10.48	22	5.56	
Body mass index (BMI)												0.002*
	Normal (18.5–24.9)	692	38.59	221	44.02	231	40.03	110	33.54	130	33.68	
	Overweight (25–29.9)	688	38.37	193	38.45	204	35.36	138	42.07	153	39.64	
	Obesity (≥30.0)	413	23.03	88	17.53	142	24.61	80	24.39	103	26.68	
Chronic disease												0.005*
	No	939	51.28	286	56.08	310	52.99	164	48.66	179	44.86	
	Yes	892	48.72	224	43.92	275	47.01	173	51.34	220	55.14	
COVID-19 vaccination status												0.038*
	None	87	4.88	16	3.28	31	5.33	10	3.07	30	7.77	
	Yes, partial (one dose)	30	1.68	7	1.43	9	1.55	5	1.53	9	2.33	
	Yes, complete (2+ doses)	1665	93.43	465	95.29	542	93.13	311	95.40	347	89.90	
Hospitalization following COVID-19												0.020*
	No	1740	95.03	493	96.86	558	95.71	311	92.56	378	93.80	
	Yes	91	4.97	16	3.14	25	4.29	25	7.44	25	6.20	
Severity of acute COVID-19 infection(s)												0.000*
	With limited symptoms	201	11.03	94	18.69	64	11.00	20	5.95	23	5.72	
	With moderate symptoms	1024	56.17	314	62.43	341	58.59	184	54.76	185	46.02	
	With severe symptoms	598	32.80	95	18.89	177	30.41	132	39.29	194	48.26	
Long Covid and healthcare utilization												
Visit HCP for Long Covid complaints												0.000*

Continued

		Whole sample		Mild Long Covid		Moderate Long Covid with neurocognitivesymptoms		Moderate Long Covid with respiratory–musculoskeletal symptoms		Severe Long Covid		p-value for differences between classes
		N=1840		N=512		N=588		N=337		N=403		
		N	%	N	%	N	%	N	%	N	%	
	No	700	38.04	231	45.12	260	44.22	119	35.31	90	22.33	
	Yes	1140	61.96	281	54.88	328	55.78	218	64.69	313	77.67	
If yes on visit HCP, which HCP did you consult (multichoice)												
	GP	1061	93.07	246	87.54	302	92.07	211	96.79	302	96.49	0.000*
	Specialist	511	44.82	110	39.15	133	40.55	84	38.53	184	58.79	0.000*
	Physiotherapist	291	25.53	27	9.61	71	21.65	46	21.10	147	46.96	0.000*
	Mental health professional[§]	224	19.65	11	3.91	56	17.07	14	6.42	143	45.69	0.000*
	Other HCP[§§]	235	20.61	38	13.52	58	17.68	32	14.68	107	34.19	0.000*
Diagnosed with Long Covid by HCP												0.000*
	No	1371	74.51	438	85.55	447	76.02	255	75.67	231	57.32	
	Yes	469	25.49	74	14.45	141	23.98	82	24.33	172	42.68	
Received treatment or advice from HCP												0.000*
	No	1261	68.53	359	70.12	446	75.85	222	65.88	234	58.06	
	Yes	579	31.47	153	29.88	142	24.15	115	34.12	169	41.94	
If yes on treatment, which type of treatment or advice for Long Covid complaints? (multichoice)												
	Medication	386	66.67	107	69.93	72	50.70	83	72.17	124	73.37	0.000*
	Self-management advice	253	43.70	36	23.53	61	42.96	47	40.87	109	64.50	0.000*
	Exercise programs	266	45.94	50	32.68	64	45.07	52	45.22	100	59.17	0.000*
	Psychological-cognitive support	119	20.55	2	1.31	27	19.01	10	8.70	80	47.34	0.000*
	Alternative or other treatment	131	22.63	24	15.69	29	20.42	19	16.52	59	34.91	0.000*
Access to care for Long Covid complaints												0.000*
	Quick access	507	27.55	183	35.74	145	24.66	105	31.16	74	18.36	
	Moderate access	245	13.32	42	8.20	66	11.22	46	13.65	91	22.58	
	No sufficient access	252	13.70	27	5.27	68	11.56	39	11.57	118	29.28	
	Don't know	344	18.70	93	18.16	128	21.77	66	19.58	57	14.14	
	Not applicable	492	26.74	167	32.62	181	30.78	81	24.04	63	15.63	
Perceived impact of Long Covid												
Absent (from school or work) due to Long Covid symptoms												0.000*
	No	1130	61.41	410	80.08	379	64.46	189	56.08	152	37.72	
Continued												
	Yes	710	38.59	102	19.92	209	35.54	148	43.92	251	62.28	

		Whole sample		Mild Long Covid		Moderate Long Covid with neurocognitivesymptoms		Moderate Long Covid with respiratory–musculoskeletal symptoms		Severe Long Covid		p-value for differences between classes
		N=1840		N=512		N=588		N=337		N=403		
		N	%	N	%	N	%	N	%	N	%	
Financial loss as a result of Long Covid complaints												0.000*
	No	1175	65.97	431	85.35	391	68.48	215	66.98	138	35.94	
	Yes, but no major impact	419	23.53	53	10.50	132	23.12	74	23.05	160	41.67	
	Yes, with major impact	97	5.45	3	0.59	20	3.50	8	2.49	66	17.19	
	Not applicable	90	5.05	18	3.56	28	4.90	24	7.48	20	5.21	

Table 2. Descriptive statistics and latent class analysis of Long Covid (LC) symptoms, symptom duration and daily disability of Long Covid ($N = 1840$). Missing data: age group = 54 (3%); sex = 1 (0%); educational status = 49 (3%); ethnicity = 8 (0%); urban residency = 26 (1%); healthcare worker = 36 (2%); smoking habits = 16 (1%); BMI = 47 (3%); chronic disease = 9 (0%); COVID-19 vaccination status = 58 (3%); hospitalization following COVID-19 = 9 (0%); severity of acute COVID-19 infection(s) = 17 (1%); financial loss = 59 (3%). *p<0.05 (Chi-squared test). §mental health professional: including psychiatrist, psychologist, psychotherapist and neuropsychologist. §§other HCP: including occupational therapist, dietician, speech therapist, nurse at home, social worker, emergency department and other.

$p<.001$; OR class 4-bachelor education = 0.56, $p<.05$). Members of class 2 and class 4 had higher odds of being non-European (OR class 2 = 1.70, $p<.05$; OR class 4 = 2.60, $p<.01$) compared to class 1 members.

Related to respondents' risk factors and medical characteristics, people with moderate LC with respiratory–musculoskeletal symptoms (class 3) were less likely to live in urban areas (OR = 0.69, $p<.05$). Adults from all classes were more likely to be obese (OR class 2 = 1.72, $p<.01$; OR class 3 = 1.90, $p<.01$; OR class 4 = 2.34, $p<.001$) compared to adults with mild LC, and class 3 and class 4 members were also more overweighted (OR class 3 = 1.51, $p<.05$; OR class 4 = 1.65; $p<.05$). Severe LC adults (class 4) were less likely to be fully vaccinated against COVID-19, compared to individuals with mild LC (OR = 0.26, $p<.001$). Respondents from all phenotypes had higher odds of moderate (OR class 2 = 1.62, $p<.05$; OR class 3 = 2.29, $p<.01$; OR class 4 = 2.65, $p<.01$) and severe symptoms (OR class 2 = 2.64, $p<.001$; OR class 3 = 4.35, $p<.001$; OR class 4 = 5.80, $p<.001$) of the acute SARS-CoV-2infection(s).

Respondents' healthcare use, care delivery and healthcare seeking behavior were significantly different on all investigated aspects between people with moderate LC with neurocognitive symptoms (class 2) and severe LC (class 4) compared to mild LC adults (class 1), while differences were less visible for people with moderate LC with respiratory–musculoskeletal symptoms (class 3). Adults with severe LC (class 4) had higher odds of visiting physiotherapists for their LC complaints (OR = 2.64, $p<.01$), and people with moderate LC with neurocognitive symptoms (class 2) and severe LC (class 4) consulted mental health professionals more (OR class 2 = 2.23, $p<.05$; OR class 4 = 5.90, $p<.001$). Members of class 2 and class 4 were more likely to be diagnosed with LC by HCP (OR class 2 = 1.90, $p<.01$; OR class 4 = 2.58, $p<.001$), were less likely to receive medication as LC treatment (OR class 2 = 0.37, $p<.001$; OR class 4 = 0.58, $p<.05$) but had a higher probability of receiving psychological-cognitive support from their HCP (OR class 2 = 6.27, $p<.05$; OR class 4 = 8.50, $p<.01$). Respondents from all classes had higher odds of having no sufficient access to care for LC complaints (OR class 2 = 2.75, $p<.001$; OR class 3 = 2.71, $p<.01$; OR class 4 = 9.60, $p<.001$) and people with severe LC (class 4) were also more likely to have moderate access to care (OR = 2.50, $p<.01$) compared to adults with mild LC.

Investigating LC daily life burden among the clinical phenotypes revealed that respondents from all moderate and severe classes were more likely to be absent from work or school due to LC symptoms (OR class 2 = 1.62, $p<.01$; OR class 3 = 2.14, $p<.001$; OR class 4 = 2.51, $p<.001$). Members of class 2 and class 4 reported more financial loss with limited impact due to LC (OR class 2 = 1.97, $p<.01$; OR class 4 = 3.94, $p<.001$). People with severe LC (class 4) had higher odds of perceiving financial hardship with major impact (OR = 9.75, $p<.01$) compared to people with mild LC.

Discussion

Key findings

This population-based study among Belgian adults who self-report LC identified four clinical phenotypes, forming a clear gradient in symptom burden, duration, and daily impact. Class 1 represented mild LC. Classes 2 and 3, both moderate, were differentiated by predominant neurocognitive (e.g. brain fog, memory issues) versus respiratory–musculoskeletal symptoms (e.g. breathing, joint pain). Class 4 included the most severe profile, with the highest probability of 10 LC symptoms, long duration (≥ 1.5 years), and severe impact on daily life. These phenotypes align with earlier findings[12,23,29,30,32,33].

	Moderate LC with neurocognitive symptoms			Moderate LC with respiratory–musculoskeletal symptoms			Severe LC		
	Class 2			Class 3			Class 4		
Independent variables	**OR**	**[95% CI]**	***p*-value**	**OR**	**[95% CI]**	***p*-value**	**OR**	**[95% CI]**	***p*-value**
Socio-demographic characteristics									
Age (ref=18-30y)									
31–50	1.60	[1.06; 2.41]	*	0.94	[0.59; 1.50]		1.82	[0.96; 3.47]	
51–65	1.29	[0.85; 1.96]		0.77	[0.48; 1.24]		1.98	[1.04; 3.76]	*
Sex (ref=men)									
Women	1.23	[0.91; 1.65]		1.67	[1.18; 2.38]	**	2.18	[1.44; 3.32]	***
Educational status (ref=secondary school or lower)									
Bachelor education	0.83	[0.58; 1.21]		0.53	[0.36; 0.80]	**	0.56	[0.35; 0.89]	*
Master education or higher	0.84	[0.57; 1.22]		0.41	[0.27; 0.64]	***	0.63	[0.39; 1.02]	
Ethnicity (ref=Belgian)									
Non-European	1.70	[1.01; 2.87]	*	1.35	[0.69; 2.66]		2.60	[1.35; 5.00]	**
Risk factors and medical characteristics									
Urban residency (ref=no)									
Yes	1.05	[0.77; 1.45]		0.69	[0.48; 0.97]	*	0.79	[0.52; 1.18]	
Smoking habits (ref=no)									
Yes, everyday	0.85	[0.46; 1.57]		1.66	[0.89; 3.11]		0.76	[0.34; 1.69]	
Body mass index (BMI) (ref=normal)									
Overweight (25–29.9)	1.16	[0.84; 1.61]		1.51	[1.03; 2.20]	*	1.65	[1.07; 2.55]	*
Obesity (≥30.0)	1.72	[1.18; 2.53]	**	1.90	[1.22; 2.96]	**	2.34	[1.43; 3.83]	***
COVID-19 vaccination status (ref=none)									
Yes, complete (2+ doses)	0.53	[0.28; 1.01]		0.63	[0.29; 1.35]		0.26	[0.12; 0.55]	***
Hospitalization following COVID-19 (ref=no)									
Yes	0.85	[0.38; 1.91]		1.50	[0.68; 3.32]		0.57	[0.22; 1.45]	
Severity of acute COVID-19 infection(s) (ref=with limited symptoms)									
With moderate symptoms	1.62	[1.08; 2.44]	*	2.29	[1.31; 4.00]	**	2.65	[1.34; 5.24]	**
With severe symptoms	2.64	[1.63; 4.26]	***	4.35	[2.35; 8.06]	***	5.80	[2.80; 12.04]	***
Long Covid and healthcare utilization									
Visit of … for Long Covid complaints (ref=no)									
Physiotherapist	1.68	[0.94; 2.99]		1.74	[0.95; 3.22]		2.64	[1.42; 4.89]	**
Mental health professional	2.23	[1.03; 4.84]	*	1.15	[0.45; 2.99]		5.90	[2.65; 13.15]	***
Diagnosed with Long Covid by HCP (ref=no)									
Yes	1.90	[1.28; 2.80]	**	1.50	[0.97; 2.33]		2.58	[1.62; 4.10]	***
Received treatment or advice from HCP (ref=no)									
Medication	0.37	[0.24; 0.56]	***	0.74	[0.49; 1.13]		0.58	[0.36; 0.94]	*
Psychological-cognitive support	6.27	[1.37; 28.71]	*	3.40	[0.64; 18.15]		8.50	[1.82; 39.70]	**
Access to care for Long Covid complaints (ref=quick access)									
Moderate access	1.53	[0.89; 2.64]		1.39	[0.77; 2.51]		2.50	[1.32; 4.71]	**
No sufficient access	2.75	[1.52; 4.98]	***	2.71	[1.41; 5.18]	**	9.60	[4.94; 18.65]	***
Don't know	2.02	[1.33; 3.07]	***	1.46	[0.90; 2.37]		2.72	[1.51; 4.89]	***
Not applicable	1.46	[1.00; 2.12]	*	1.08	[0.70; 1.69]		1.71	[0.98; 2.98]	
Perceived impact of Long Covid									
Absent (from school or work) due to Long Covid symptoms (ref=no)									
Yes	1.62	[1.14; 2.30]	**	2.14	[1.45; 3.16]	***	2.51	[1.62; 3.88]	***
Financial loss as a result of Long Covid complaints (ref=no)									
Yes, but no major impact	1.97	[1.30; 3.00]	**	1.56	[0.98; 2.49]		3.94	[2.45; 6.34]	***
Yes, with major impact	3.40	[0.73; 15.87]		1.19	[0.22; 6.47]		9.75	[2.10; 45.20]	**

Table 3. Backward multivariable multinomial logistic regression results for predictors of Long Covid (LC) class membership ($N = 1526$). The categorical dependent variable consisted of four groups: class 1 - mild Long Covid (reference), class 2, class 3 and class 4. *** $p<.001$, ** $p<.01$, * $p<.05$.

GPs were the most consulted HCP, consistent with other studies[6,8,9,34]. A higher proportion of respondents reported expecting limited help from HCPs for their LC complaints in Belgium compared to the study by Kosowan[6]. This may reflect low perceived treatment effectiveness and limited confidence in available care options, and highlights the need for improved provider training and public awareness, an issue also acknowledged by Belgian GPs[22]. In our study, only one in four was diagnosed with LC by HCP, and about one in three (31%) received treatment or advice from HCP for LC complaints, which is in line with other research[33,34]. About one in seven reported insufficient access to necessary LC care, primarily associated with subjective barriers, such as dissatisfaction or perceived lack of treatment effectiveness, rather than objective constraints (e.g. financial difficulties or logistical barriers to service availability), consistent with findings from prior studies[14]. Absence from school or work because of LC was mentioned by 39% of our respondents, demonstrating its impact on daily living, in Belgium and other settings[6,8,9].

Differences by phenotype

Clear variation emerged across LC phenotypes in terms of personal characteristics, healthcare use, and daily burden. Respondents with more severe LC were more likely to be older, female, and lower educated, confirming known risk patterns[9,29]. Classes 2 and 4 also included more non-Europeans, consistent with disparities noted by Chilunga[15]. Obesity was more prevalent in moderate/severe classes, confirming other studies[5,23,29]. Vaccination was lower among those with severe LC, suggesting an association between vaccination status and the risk of severe LC[35]. More severe acute infections were reported in moderate and severe classes, echoing prior studies[29].

Healthcare use by phenotype

Care needs and service use varied substantially across phenotypes. Compared to mild LC, noticeable differences in diagnosis, healthcare use and treatment were found especially in classes 2 and 4. This reflects heterogeneity in how LC is recognized and managed[1,16]. Class 2 (neurocognitive symptoms) showed higher rates of LC diagnosis, mental health consultations, and use of psychological-cognitive support, but less medication. Access to care was often perceived as inadequate. These findings align with research on the intersection of neurological and mental health effects of LC[36]. Class 3 (respiratory–musculoskeletal symptoms) also reported insufficient access, but less variation in treatment patterns compared to class 1. This may reflect better recognition of respiratory and musculoskeletal symptoms by HCP[37]. Class 4 (severe LC) involved more diagnoses, greater use of physiotherapy and mental health services, more psychological support, and more reported care barriers. These patterns are consistent with increased care needs among those with long disease duration and severe symptoms[9,14,33,38].

Impact on daily life

Adults with moderate and severe LC experienced significant life disruptions, particularly absence from work or school - a finding echoed in other settings[6,8,9]. Additionally, financial hardship was concentrated in class 2 and especially class 4. Our findings confirm the potential of LC to cause economic strain, particularly for lower-educated individuals who are already economically vulnerable. These results align with Datta et al.[39], who found LC-related financial stress across income and education levels, with lost work hours as a major driver.

Strengths and limitations

Strengths of this study include the population-based approach for identifying clinical phenotypes of Long Covid. As the entry point of the COVimpact study were all Belgian adults recently being tested positive for SARS-CoV-2 and monitored over time through baseline and follow-up questionnaires, numerous people responded to the final LC survey. This led to a large sample size of people with self-reported LC in Belgium ($N > 2{,}000$) to be used for phenotypes identification, compared to other settings (for example Ireland ($N = 233$), Sweden ($N = 506$), Spain ($N = 905$)[29,30,32]. Moreover, participants were initially recruited after SARS-CoV-2 infection and followed over time, resulting in rich data on symptoms, risk factors, healthcare use, access to care, and daily impact. The inclusion of individuals beyond those in formal care settings allowed the capture of self-reported outcomes often missing in medical records[40].

This study has several limitations. Despite being termed 'population-based', the cohort suffered from selection biases that may limit generalizability. Participation was voluntary and online, which led to overrepresentation of certain groups compared to the eligible population (as shown by the published study protocol[24] which reported a higher proportion of people aged 46–65 years, women, and individuals reporting at least one acute COVID-19 symptom among study participants). There was substantial attrition by the final survey (35% response rate of original cohort), and loss to follow-up introduced further bias (particularly among older aged adults) in the composition of respondents (Supplementary Table S6). This may have affected the prevalence of subgroups and the estimated associations. Thus, the final sample may not be representative of all Belgian COVID survivors, especially those who recovered quickly or did not self-identify as having LC. Moreover, LC status was self-reported based on symptoms > 4 weeks after infection, a broader definition than the WHO's clinical case definition (≥ 3 months), which may have included people with shorter symptom duration. Additionally, data on healthcare utilization, access to care, and daily impact were self-reported, and may therefore be subject to reporting bias among study participants.

Conclusion

The classification performed in this study gives valuable insight into different healthcare use trajectories of people with Long Covid. Healthcare utilization and financial impact of LC were greater among individuals with moderate or severe LC. Deeper understanding of care needs and healthcare accessibility help people with LC navigate through specific care pathways. A multidisciplinary care approach is favorable in this context, given the heterogeneous symptoms, diversity in disease duration and daily life burden. HCP must be supported with

more tailored and updated knowledge, development of diagnostic tools, validated treatments and medical support regarding care and follow-up of LC subgroups. By avoiding delayed and forgone medical care, daily life functioning and economic wellbeing of people with LC can be improved. As LC poses substantial burden to healthcare systems, future healthcare planning and policy development in Belgium should be tailored to the specific needs of those affected by Long Covid.

Data availability

The data are not publicly available because they contain information that could compromise the privacy of the study participants. Reasonable inquiries about access may be sent to the corresponding author.

Received: 24 October 2025; Accepted: 30 March 2026
Published online: 03 April 2026

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Acknowledgements

This research has benefited from the statistical consult (Lieven Desmet) with Statistical Methodology and Computing Service, technological platform at UCLouvain – SMCS/LIDAM, UCLouvain.The authors would like to thank everyone who participated in the COVIMPACT study.

Author contributions

SM, PS and RC designed the study. SM and PS collected the data. SM, PS and NS performed the analysis and interpretation of the data. SM drafted the manuscript and SM, PS, RC, DC, DVC and NS critically revised the manuscript. All authors approved the final version of the manuscript.

Funding

Sciensano (national Institute of Public Health) internal funding.

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval and consent to participate

Informed consent was obtained at baseline, each follow-up and the final survey. Participants could indicate whether they wished to be contacted for future follow-ups. The study has been approved by the ethics committee of Ghent university hospital, B.U.N.: B6702021000287. A favorable advice for the extension of the study with the final LC-specific survey was given by the forementioned ethics committee on January 12, 2024.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-026-47228-9.

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