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Static and dynamic scoring systems for post-acute sequelae of SARS-CoV-2 in a Korean Cohort

Gyeongdeok Seo[1,†], Hyejin Joo[2,†], Kyungwoo Song[1,†], Mingyu Kim[1], Eun Ju Jung[3], Eu Suk Kim[4], Jae-Hoon Ko[5], Jin Seo Lee[6], Joon Young Song[7], Jun-Won Seo[8], Jun Yong Choi[9], Ki Tae Kwon[10], Seung Soon Lee[11], Wan Beom Park[12], Won Suk Choi[13], Yae Jee Baek[14], Yong Kyun Kim[15], Hye Won Jeong[16], Jaehun Jung[2], Jacob Lee[17,*]

[1] *Department of Statistics and Data Science, Yonsei University, Seoul, Republic of Korea*
[2] *Department of Preventive Medicine, Korea University College of Medicine, Seoul, Republic of Korea*
[3] *Division of Infectious Diseases, Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Republic of Korea*
[4] *Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea*
[5] *Division of Infectious Diseases, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*
[6] *Division of Infectious Diseases, Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea*
[7] *Division of Infectious Diseases, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea*
[8] *Division of Infectious Diseases, Departments of Internal Medicine, College of Medicine, Chosun University, Gwangju, Republic of Korea*
[9] *Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea*
[10] *Division of Infectious Diseases, Department of Internal Medicine, Kyungpook National University Chilgok Hospital, School of Medicine, Kyungpook National University, Daegu, Republic of Korea*
[11] *Division of Infectious Diseases, Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Republic of Korea*
[12] *Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea*
[13] *Division of Infectious Diseases, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Republic of Korea*
[14] *Division of Infectious Diseases, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, Seoul, Republic of Korea*
[15] *Division of Infectious Diseases, Department of Internal Medicine, Hallym University Sacred Heart Hospital, Anyang, Republic of Korea*
[16] *Department of Internal Medicine, Chungbuk National University College of Medicine, Cheongju, Republic of Korea*
[17] *Division of Infectious Diseases, Department of Internal Medicine, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea*

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ABSTRACT

Objectives: Persistent symptoms after SARS-CoV-2 infection (PASC, long COVID) remain a major public-health concern. We developed a data-driven definition and static and dynamic PASC scoring systems in a multicenter, prospective–retrospective observational cohort across 12 South Korean institutions.
Methods: Adults enrolled December 2022-March 2025 were followed up to 24 months; 8761 were recruited (7208 infected; 1553 controls) and 4668 met analysis criteria (4388 infected; 280 controls). Using participant-reported symptoms, surveys, and laboratory data, we identified nine symptoms robustly associated with PASC, with anosmia/ageusia and fatigue most influential.
Results: A static score integrating indicators observed within 24 months yielded an optimal threshold of 13, classifying 19% of infected participants and 4% of controls as PASC positive. A dynamic score tracking six-month intervals showed symptom burdens peaking at 0-5 months post-infection and declining thereafter; at the same threshold, 33% of infected participants were classified as PASC positive, reflecting temporal fluctuation.

* Corresponding author: Jacob Lee, MD, PhD, Division of Infectious Diseases, Department of Internal Medicine, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, 1 Singil-ro, Yeongdeungpo-gu, Seoul, Republic of Korea.
E-mail addresses: litjacob@gmail.com, litjacob@chol.com, litjacob@hallym.or.kr (J. Lee).
† These authors contributed equally to this work as first authors.

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Conclusion: These data establish a quantitative definition of PASC and introduce a dynamic scoring framework to identify and monitor PASC, supporting future clinical research and practice.

1. Background

The COVID-19 pandemic continues to affect global public health [1]. Beyond the initial illness period, a substantial number of individuals experience persistent, relapsing, or new symptoms, a condition broadly termed post-acute sequelae of SARS-CoV-2 infection (PASC), or long COVID. With symptoms spanning multiple organ systems, this syndrome substantially lowers health-related quality of life and challenges healthcare systems globally [2–4].

PASC has become a significant focus of clinical research globally, with numerous studies investigating its long-term symptom trajectories and diverse clinical presentations to understand the condition better [5]. A landmark effort is the Recovery (RECOVER) Initiative, a large-scale cohort study that developed a data-driven PASC definition using a multi-symptom scoring system and identified 12 key symptoms [6]. A follow-up study a year later refined this definition, increasing symptom specificity by adding indicators like shortness of breath and sleep apnea while removing broader categories such as gastrointestinal symptoms [7]. However, its findings are based on a US population, necessitating robust data from other demographic groups, particularly from Asian populations. Despite growing recognition of PASC, its definition remains heterogeneous, and estimates of its prevalence vary across studies [8,9]. Notably, most existing assessment tools lack a scoring system that reflects the time-dependent importance of symptoms. Furthermore, there has been a lack of research characterizing PASC within the Korean population [10,11]. To address these gaps, our study utilizes a data-driven approach to develop static and dynamic PASC scores from a Korean cohort with frequent, scheduled follow-ups.

We aim to identify core indicators that distinguish infected from uninfected individuals. We then propose two distinct scoring systems: (1) Static PASC score, which provides a cumulative assessment to determine PASC status based on several indicators occurring up to 24 months after infection, and (2) Dynamic PASC score, which tracks the temporal trend of indicators in 6-month intervals, offering insights into the natural history of the condition. By analyzing a comprehensive set of symptoms, surveys, and laboratory data, this research provides a quantitative framework to support clinical diagnosis, guide future research, and ultimately improve patient care.

2. Methods

2.1. Study design

This cohort study included prospective and retrospective components to investigate long-term COVID-19 sequelae in the Korean population and assess symptom trajectories. Adults were enrolled between December 2022 and March 2025 and classified as infected or control participants based on confirmed SARS-CoV-2 infection status.

The infected cohort was stratified by interval from last infection to enrollment: <6 months (predominantly ≤3 months) and ≥6 months (typically 6-24 months). Infection was diagnosed by polymerase chain reaction (PCR) or rapid antigen testing in healthcare facilities. Self-test kit results were not considered confirmed infection for study inclusion.

After enrollment, participants in the <6-month post-infection group were assessed at 1, 3, and 6 months, while those in the ≥6-month post-infection group were evaluated every 6 months. The control group underwent SARS-CoV-2 N-protein antigen testing at their initial visit to exclude asymptomatic cases and confirm a negative status. Control participants were followed at 1-, 3-, and 6-months intervals. Data collection was conducted at 12 institutions (eTable 1); the ≥6-month post-infection group was followed by 10 of them.

A total of 8761 participants were enrolled, comprising 7208 infected individuals and 1553 controls. All participants submitted written informed consent, and the protocol was reviewed by the institutional review boards of each participating center. Comparison of incomplete and final cohorts showed no significant differences in infected group and only minor sex and job variations in controls (eTable 2).

2.2. Participants

We constructed the final cohort using a two-stage exclusion process. The initial stage involved exclusions based on data integrity and adherence to protocol. Key exclusions included control infected during follow-up, individuals who withdrew consent, and those with missing or invalid infection dates. The second stage involved exclusions based on the specific requirement for statistical analysis. Participants were excluded if they lacked sufficient longitudinal data for the dynamic analysis. This two-stage process resulted in a final analysis cohort of 4668 participants, comprising 4388 infected individuals and 280 controls, which were included in both the static and dynamic analyses (Figure 1, eFigure 1).

2.3. Exposures and outcomes

The primary exposure for this analysis was SARS-CoV-2 infection. For the infected participants, who have multiple hospital visits, the index date is defined for each visit as the date of the most recent SARS-CoV-2 infection prior to that visit. For the uninfected participants, the index date was the date of their N-protein antigen test.

Data collection encompassed participant demographics, Charlson Comorbidity Index (CCI) scores [12], 29 self-reported symptoms, 4 standardized questionnaires (e.g., EQ-5D-5L, EQ-VAS, HADS, PHQ-9) [13,14], and 56 laboratory results. We integrated survey scores with symptom reports and binarized all survey and lab variables based on clinical or standard reference ranges (eMethods, eTable 3).

Primary outcomes were self-reported symptoms, questionnaires, and laboratory results (eTable 3), assessed between 1 and 24 months post-index date for the infected group (excluding 0–1-month acute phase) and 0–24 months for the uninfected group. The missing data profiles and procedures for handling them are detailed in eMethods and eTable 4.

2.4. Statistical analysis

We employed Inverse Probability Weighting (IPW) (eMethods), achieving absolute standardized mean differences of less than 0.1 for all covariates (eFigure 2). Inspired by the RECOVER study [6,7],

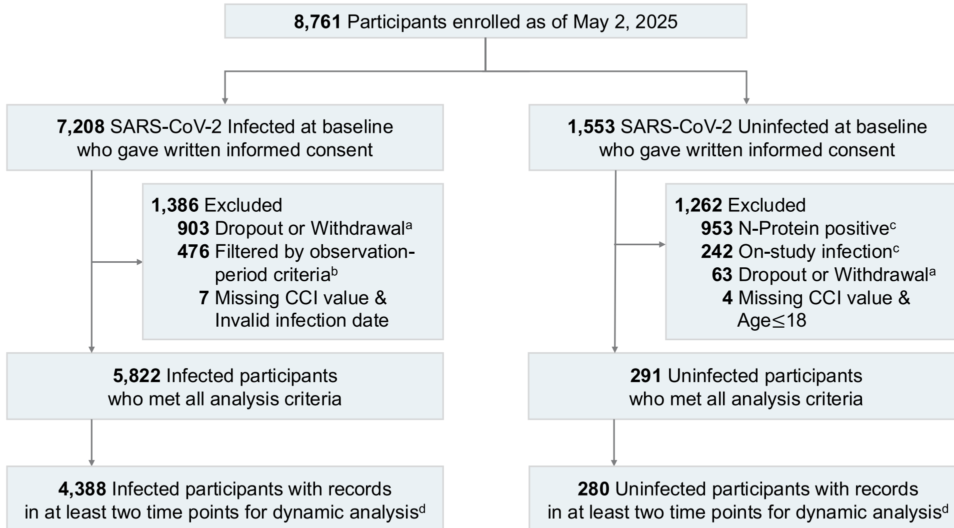

Figure 1. Cohort participants flowchart.

[a]This includes the cases of withdrawal in informed consent by participants or legally acceptable representatives, loss to follow-up, and exclusion based on the investigator's judgment, and other reasons.

[b]Participants were excluded if all available visits occurred within 1 month after the index date or the first visit occurred more than 2 years after the index date (eFigure 1). For included participants, corresponding visits were also excluded; participant demographic characteristics were retained.

[c]"N-Protein positive" refers to participants who tested positive on the N-Protein antigen test at their initial visit after selection and were subsequently dropped from the study due to the infection. "On-study infection" refers to cases in the control group who became infected during a study visit.

[d]For the dynamic analysis, participants were required to have symptom and survey data in at least two of the four 6-month follow-up intervals (months 0-5, months 6-11, months 12-17, and months 18-23).

Collectively, participants who were lost to follow-up, lacked data for at least two follow-up intervals as described above, became infected during visits for the control group, or had a missing Charlson Comorbidity Index (CCI) score were defined as incomplete cases. Baseline characteristics for this group are summarized in eTable 2.

we employed a weighted logistic LASSO regression for variable selection. The identified variables are used to calculate static and dynamic PASC scores.

We conducted a subcohort analysis to mitigate potential recall bias and compare post-acute sequelae across pandemic periods. This involved comparing two distinct subcohorts: recent infection subcohort (last infection before initial visit in February or after February 2023, and the entire control group), and past infection subcohort (last infection before initial visit before February 2023, and the entire control group). The selection of February 2023 as the reference point is based on a change in the distribution pattern observed before and after this date (eFigure 3).

2.4.1. Variable selection

Candidate variables were divided into baseline covariates (age, age squared, CCI, and binary indicators for pre-existing symptoms) and post-index health indicators (symptoms present during follow-up, standardized questionnaires, and laboratory tests) (eTable 3). After filtering variables (eTable 4), we fit the weighted logistic LASSO regression model to identify a parsimonious set of indicators with a positive coefficient (eMethods).

2.4.2. Static analysis: PASC score development

The static PASC score provides a cumulative assessment of symptom burden over the entire 24-month post-infection period. A weighted logistic LASSO regression model was employed again to predict infection status using the variables selected in the previous stage. Each symptom's score (static PASC score) was derived by multiplying its final log-odds ratio from the model by 10 and rounding to the nearest integer. A participant's score was calculated by summing the contributions of their reported symptoms. For most symptoms, reported as present (1) or absent (0), the contribution was determined by multiplying this value by the symptom's assigned score. Fatigue was reported on a 0, 0.5, or 1; for this symptom, the resulting product was rounded up.

2.4.3. Dynamic analysis: temporal PASC score trajectories

The dynamic PASC score assesses the longitudinal trajectory of health status across consecutive 6-month intervals (eMethods). The 24-month follow-up was divided into four 6-month intervals: $t = 1$ (0-5 months), $t = 2$ (6-11 months), $t = 3$ (12-17 months), and $t = 4$ (18-23 months). This 6-month discretization harmonizes the follow-up data collected at varying frequencies (1, 3, and 6 months for the <6-month post-infection group vs 6-month intervals for the ≥6-month post-infection group). Since most symptoms occur within the first 6 months but some patients show delayed improvement after 1 year, a 6-month interval provides the granularity to capture both initial recovery and long-term changes.

Acute phase data (0-1 months) were excluded from $t = 1$ for the infected group. Given temporal correlations in symptom trajectories, we employed a functional data analysis approach (eMethods) [15]. Variables with a static score ≥1 were considered in the dynamic analysis. We constructed a Functional Multivariable Logistic Regression (FMLR) model [16,17] that estimates time-varying effects of symptoms on infection. Each symptom score at time t was derived from approximating its impact on the log-odds ratio of COVID-19 infection and scaled by 10 and rounded to the nearest integer (eMethods). A participant's overall score was the sum of symptom values multiplied by scores at each time point, then summed across four points and rounded to the nearest integer.

2.4.4. Infected-only comparative analysis

Given the widespread prevalence of SARS-CoV-2, we focused our analysis specifically on the infected cohort. The outcome was defined as a binary variable indicating whether a patient's static score met or exceeded a specific threshold, signifying the presence of persistent sequelae. This definition was applied analogously to the dynamic score and its corresponding threshold. Predictors included variables used for calculating balancing weights, baseline covariates, post-infection health indicators, vaccination profiles, and viral variants (eTable 5). We utilized Lasso logistic regression to identify and report coefficients with significant magnitudes.

Table 1
Participants' characteristics in the analysis cohort.

Characteristic[a]	No. (%)		
	Infected ($N = 4388$)	Uninfected ($N = 280$)	Uninfected, weighted ($N = 4656$)
Age (years)			
Median [IQR]	44.0 [34.0-56.0]	45.0 [35.0-54.0]	43.0 [35.0-54.0]
Sex			
Female	3191 (73)	180 (64)	3415 (73)
Male	1197 (27)	100 (36)	1241 (27)
COVID-19 vaccination[b]			
Unvaccinated	132 (3)	7 (2)	100 (2)
1 dose	42 (1)	3 (1)	56 (1)
2 doses	710 (16)	39 (14)	574 (12)
3 doses	2651 (61)	164 (59)	2800 (60)
4 doses	252 (6)	16 (6)	267 (6)
5 doses	557 (12)	44 (16)	760 (16)
6 or more doses	44 (1)	7 (2)	98 (2)
Marital status			
Married	3043 (69)	176 (63)	3196 (69)
Unmarried	1345 (31)	104 (37)	1460 (31)
Insurance type			
National health insurance	4321 (98)	277 (99)	4566 (98)
Medical aid	67 (2)	3 (1)	90 (2)
Alcohol consumption			
Yes	2004 (46)	140 (50)	2144 (46)
No	2384 (54)	140 (50)	2512 (54)
Smoking status			
Current	349 (8)	51 (18)	411 (9)
Never	4039 (92)	229 (82)	4245 (91)
Job status (pre-infection)			
Employed	3190 (73)	205 (73)	3406 (73)
Unemployed	1198 (27)	75 (27)	1250 (27)
Household members			
1	760 (18)	63 (23)	816 (18)
2	933 (21)	56 (20)	988 (21)
3	1030 (23)	71 (25)	1185 (25)
4	1328 (30)	74 (26)	1372 (29)
≥5	337 (8)	16 (6)	295 (6)
Region			
Metropolitan area	3838 (87)	228 (81)	3993 (86)
Non-metropolitan area	550 (13)	52 (19)	663 (14)
Education status			
Elementary school	75 (2)	4 (1)	103 (2)
Middle school	157 (3)	11 (4)	120 (3)
High school	817 (19)	47 (17)	819 (18)
College	2836 (65)	181 (65)	3037 (65)
Graduate school or higher	503 (11)	37 (13)	576 (12)

[a] Characteristics for the excluded participants are described in eTable 2. Additionally, the characteristics of those in the subcohort are described in eTable 6 and eTable 7.
[b] Vaccination information was included in the analysis to characterize the participants, though it was not directly factored into the Inverse Probability Weighting (IPW) process.

3. Results

3.1. Participant characteristics

The distribution of COVID-19 vaccination status was similar across both groups, with approximately 60% of participants in each group having received three doses (Table 1). Current smoking was more prevalent in the uninfected group (18%) compared to the infected group (8%). Household composition, region, and education were generally balanced. These distributions were further confirmed in the weighted uninfected group, which was adjusted to match the infected group on key covariates. We also visualized the characteristics of participants for the subcohort (eTables 6 and 7).

3.2. Symptom frequency

Across all participants in the analysis cohort, those with a history of infection showed markedly higher odds of experiencing a broad spectrum of post-acute symptoms compared to the uninfected group (eFigure 4). Respiratory symptoms, including cough (aOR 2.64, 95% CI 2.35-2.97) and sputum (aOR 2.13, 95% CI 1.92-2.37), were elevated among infected individuals. Neurologic symptoms such as headache (aOR 2.97, 95% CI 2.61-3.39), dizziness (aOR 2.82, 95% CI 2.47-3.23), and anosmia/ageusia (aOR 9.31, 95% CI 7.02-12.35) showed strong associations, alongside fatigue (aOR 3.62, 95% CI 3.23-4.06). Infected participants consistently reported more symptoms across multiple organ systems, highlighting the infection's broad impact. A similar tendency is also noted in the subcohort (eTable 8, eFigures 5 and 6).

3.3. PASC-defining symptoms and static score

The initial variable selection process identified a total of 10 features, including sleep disturbance. Subsequently, to calculate a static score for the analysis cohort, the LASSO regression model was applied again. The nine features ultimately reported were those that received a score of 1 or higher from this final static model: fatigue, anosmia/ageusia, palpitations, difficulty concentrating, rash, muscle weakness, chest pain, menstrual cycle changes,

Table 2
Static PASC score and dynamic PASC score.

Symptoms	Static score[a]		Dynamic score[a]			
	Coefficients	Static score	Score at $t = 1$[b]	Score at $t = 2$[b]	Score at $t = 3$[b]	Score at $t = 4$[b]
Fatigue[c]	0.925	9	5	5	5	5
Anosmia/ageusia	0.517	5	10	7	5	4
Palpitations	0.452	5	2	2	1	1
Difficulty concentrating	0.349	3	1	1	1	1
Rash	0.298	3	3	2	2	1
Muscle weakness	0.25	2	1	1	1	1
Chest pain	0.221	2	4	3	2	1
Menstrual cycle changes	0.186	2	2	1	1	1
Cough	0.089	1	2	2	2	1

Abbreviation: PASC, post-acute sequelae of SARS-CoV-2 infection.
[a] Both Static and Dynamic PASC scores were calculated by multiplying the log-odds ratio coefficient from the final model for each symptom by 10 and rounding to the nearest integer. For the dynamic PASC score, the log-odds ratio at each time point was derived through approximations (eMethods). Data from the acute phase of infection (months 0-1) were excluded for the infected group. Static PASC score aggregated symptoms over the entire period, whereas the dynamic score aggregated them by specific intervals.
[b] For the dynamic analysis, the 24-month follow-up period was divided into four 6-month intervals: $t = 1$ (0-5 months), $t = 2$ (6-11 months), $t = 3$ (12-17 months), and $t = 4$ (18-23 months).
[c] Fatigue was assessed using the Fatigue Assessment Scale (FAS), a validated self-reported instrument designed to measure the severity of fatigue.

and cough (Table 2). Fatigue and anosmia/ageusia received high static PASC scores (9 and 5, respectively). Symptoms such as dizziness, cognitive difficulties, and myalgia were correlated with the selected symptoms (eTable 9). Participants' scores were calculated, and the optimal threshold for the PASC score was determined using the uninfected cohort, such that no more than 5% were classified as PASC-positive. Based on this criterion, the optimal threshold for the PASC score was set at 13 (Figure 2). At this threshold, 19% among infected participants are classified into PASC positive (eTable 10). The distribution of PASC scores also differed between the post-infection and control groups with over 70% of control group having a score of zero (eTable 11). The process of calculating the threshold utilized all 10 of the initially selected variables, and the average AUROC based on 5-fold cross-validation is reported as 0.705.

3.4. Temporal trend of PASC: dynamic analysis

The dynamic analysis shows how the significance of PASC symptoms changes over the 24-month follow-up period. Dynamic PASC scores assigned to most symptoms were highest during the first period and subsequently declined (Table 2). Fatigue remains consistent across all time points, indicating its persistent significance; consequently, individuals experiencing fatigue throughout the follow-up period are highly likely to be classified as PASC positive. Anosmia/ageusia exhibits high scores at $t = 1$, followed by a notable decrease by $t = 4$. Despite this reduction, their scores remain significant, highlighting it as a key, albeit diminishing, long-term symptom.

The optimal threshold, based on participants' overall scores, has been identified as 13 points (Figure 2), with an average AUROC of 0.661. This threshold determines the PASC-positive group, which is characterized by a high prevalence of symptoms in the early post-infection period. At this threshold, 33% of infected participants are classified as PASC positive (eTable 12). Furthermore, the proportion of infected participants exceeding this threshold at each time point showed a monotonic decrease, based on participants' scores calculated and rounded individually for each period: 10.4% at $t = 1$, 5% at $t = 2$, 2.1% at $t = 3$, and 0.4% at $t = 4$. The PASC positive group reveals a multi-systemic disorder characterized by fatigue, muscle weakness, and difficulty concentrating, most of which gradually decline over time (Figure 3, eTable 13).

3.5. Subcohort analysis

Subcohort analysis involved two groups: the recent infection subcohort ($n = 2117$) and the past infection subcohort ($n = 2831$). In static analysis, the recent infection subcohort reported eleven significant symptoms, which newly included sleep disturbance and K, which is an abnormal Potassiu level. The past infection subcohort reported ten symptoms; CRP, an abnormal C-reactive protein level, emerged as an indicator. The PASC positivity for the threshold showed a similar tendency in both subcohort cases (eFigure 7).

A key difference was chest pain, which scored highly in the past infection subcohort but scored 1 in the recent infection subcohort (eTables 14 and 15). This finding goes along with previous research, which shows that chest pain was more prevalent during the pre-Omicron wave, as the past infection subcohort consists of patients infected during the early Omicron and pre-Omicron periods [18]. The symptom reporting rate at $t = 1$ was higher in the recent infection subcohort (eTables 16 and 17). This is likely attributable to the shorter interval between infection and the initial study visit, which increases the probability of symptom reporting at that time point.

3.6. Infected group comparison

The comparative analysis, restricted to the infected cohort, reveals that fatigue and anosmia/ageusia are the key determinants for both static and dynamic PASC outcomes. In terms of static coefficients, fatigue, anosmia/ageusia, and palpitations were identified as major contributors. Additionally, rash and difficulty concentrating showed notable associations. Regarding dynamic coefficients, fatigue and anosmia/ageusia remained dominant, while rash and chest pain were observed as moderate contributors.

4. Discussion

This study utilizes data from Korea's first large-scale post-COVID-19 study to provide scientific evidence for policy development. As the first primary PASC cohort in the country, it offers insights into an East Asian population. The multicenter, longitudinal follow-up with standardized protocols ensured the collection of high-quality, systematic data. We identified nine symptoms that distinguish individuals with a history of SARS-CoV-2 infection

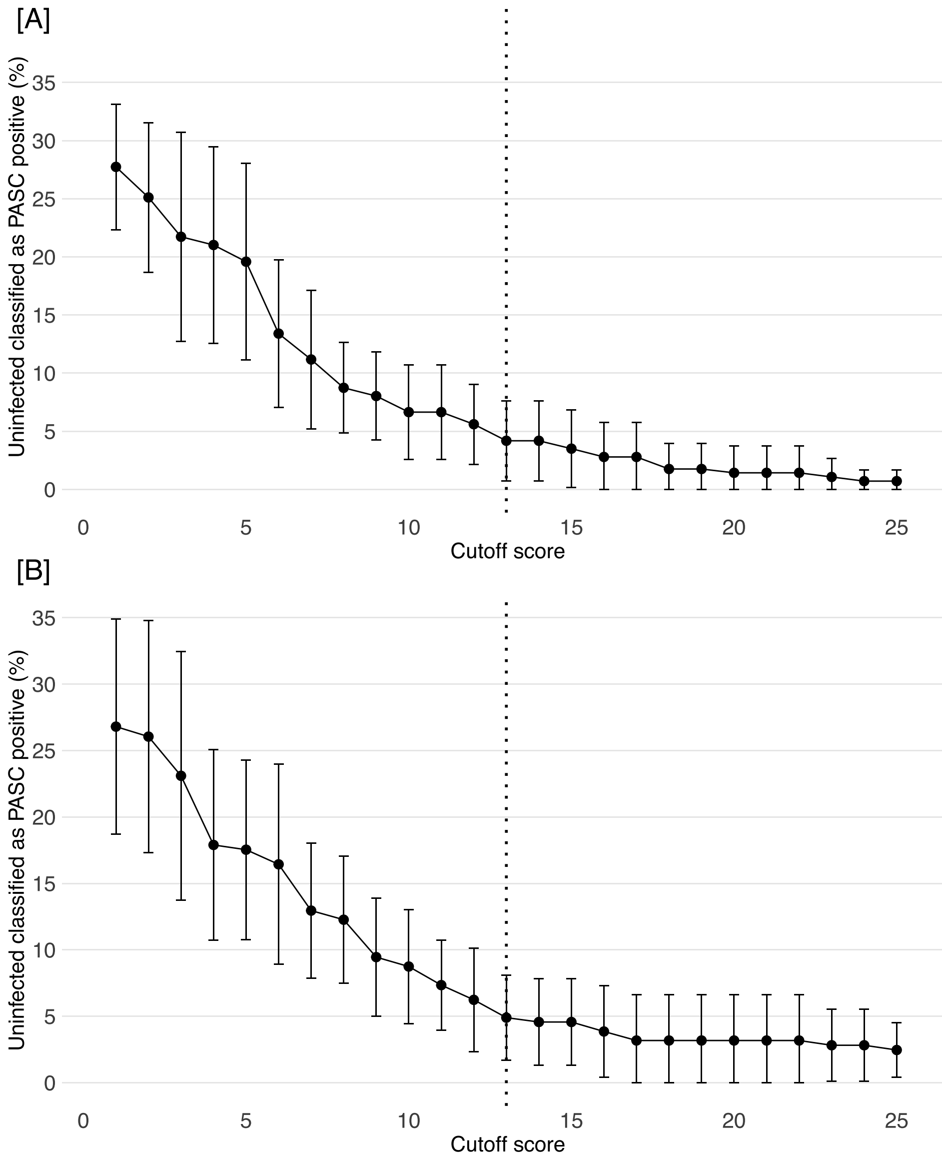

Figure 2. PASC positivity in uninfected for optimal PASC threshold. [A] Static PASC Threshold, [B] Dynamic PASC Threshold. Each threshold was chosen as ≤5% positivity among the uninfected. We used our threshold at 5%, a value comparable to that used in the study [6]. The interval denotes the standard deviation of the rate across 5-fold cross-validation.

from the uninfected group. The outcomes are consistent with prior investigations, highlighting fatigue, anosmia/ageusia, palpitations, and chest pain as key PASC symptoms [3,19,20]. However, our study of a Korean cohort also identified menstrual cycle changes and rash as contributors, which may reflect different characteristics of our study population [21,22].

The dynamic analysis revealed that symptoms did not exhibit uniform trajectories throughout the 24-month follow-up period. For instance, fatigue stands out as a persistent symptom, whereas anosmia/ageusia peaks in the early post-acute phase (t = 1-t = 2) and then declines. In addition, for the dynamic PASC-positive group from the recent infection subcohort, the reporting of mental health questionnaires showed a slower decline over time, suggesting the need for long-term attention to psychiatric sequelae [23–25].

Static and dynamic analyses yield different scopes of the PASC burden. While a static score identifies a smaller subgroup with symptoms, our dynamic score captures the varying impact of symptoms over time, placing a larger group experiencing a burden at some point. This demonstrates that single-time-point assessments risk underestimating the actual disease burden and may overlook patients' persistent suffering [26,27]. Our dynamic score provides a quantitative framework for measuring PASC as a chronic condition. These scoring systems may serve practical tools for clinicians and policymakers. The static score helps identify patients at risk for persistent symptoms, while the dynamic score captures temporal changes to inform prognosis and follow-up. Despite showing modest AUROC, these tools offer a standardized framework indispensable for patient stratification. They are particularly valuable in large-scale public health surveillance for efficiently targeting high-risk groups and optimizing policy decisions.

A comparison between two subcohorts revealed distinct PASC profiles, with the past infection subcohort exhibiting a higher score for chest pain. The difference likely reflects the influence of factors from later stages of the pandemic, such as the predominance of the XBB variant and evolving population immunity, given that the recent infection subcohort was primarily infected during this wave (eFigure 3) [28,29].

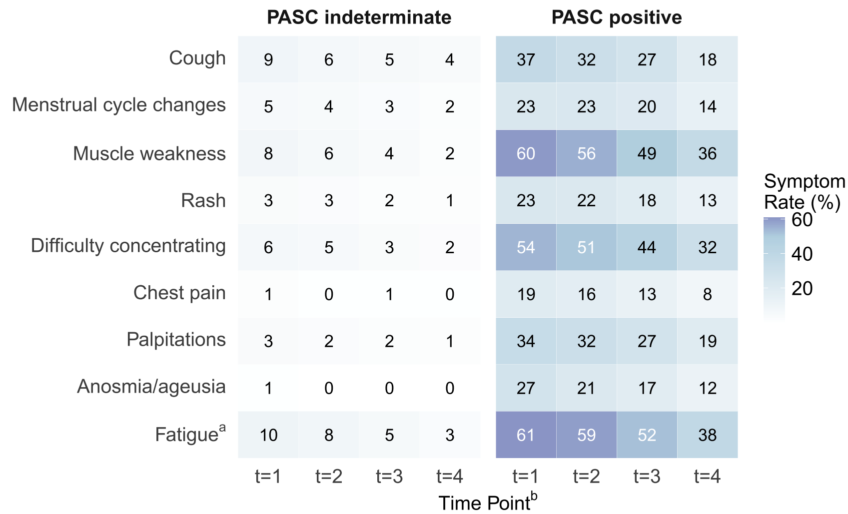

Figure 3. Heatmap of symptom frequency by PASC status. Illustration of the prevalence of symptoms with the dynamic score of 1 or higher, stratified by PASC status. PASC status was defined as PASC-positive if a participant's score was greater than or equal to the dynamic threshold, and PASC-indeterminate otherwise. For all symptom frequencies for PASC-positive, see eTable 13 in the Supplement. Data from the acute phase of infection (months 0-1) were excluded for the infected group.
[a]Fatigue was measured on a scale of 0, 0.5, and 1, with the value itself used to calculate the rate.
[b]Time point implies four 6-month intervals: $t = 1$ (0-5 months), $t = 2$ (6-11 months), $t = 3$ (12-17 months), and $t = 4$ (18-23 months).

Our study differs from the RECOVERY initiative study in its data, population, and analytical approach [6]. We used data from a Korean cohort with regular follow-ups, and our variable selection included questionnaires and lab results. It enables the identification of potentially distinct PASC phenotypes, such as the prominence of menstrual cycle changes and rash, as observed in our findings. Analytically, our dynamic model is designed to capture the longitudinal trajectory of the condition.

4.1. Strengths

This study has several notable strengths. It is based on a large, multicenter, retrospective–prospective cohort established at a national level for PASC research in Korea, with follow-up of up to 24 months, enabling high-quality data collection and sufficient power to examine temporal trends. The dynamic scoring system represents a methodological advancement by incorporating time-varying symptom weights to capture the evolving clinical presentation of PASC. The multi-institutional design across 12 centers enhances representativeness within the Korean healthcare context, while integrating self-reported symptoms, validated psychometric instruments, and laboratory results provides a multidimensional view of PASC.

4.2. Limitations

However, this study also has several limitations that should be considered when interpreting the results. First, despite employing inverse probability weighting to balance the cohorts, unmeasured confounding remains a possibility. A large number of participants in the uninfected control group were censored after becoming infected during the follow-up. While the analysis revealed that there were no statistically significant baseline differences in those lost to attrition (eTable 2), attrition bias cannot be excluded.

Second, this study relies primarily on self-reported symptoms, which can be subject to recall bias. However, it is crucial to recognize that patient-reported outcomes (PROs) are increasingly valued as critical endpoints in clinical research [30].

Third, there is the absence of an objective biomarker or gold standard for diagnosis. Consequently, it was impossible to calculate traditional diagnostic accuracy metrics for the symptom-based PASC definition used in this study. While the threshold may seem arbitrary, it provides a standardized reference for comparison and replication. At the current stage of PASC research, this method represents a feasible approach for operationally defining cases in large-scale cohort studies.

Fourth, COVID-19 exhibits seasonality and cyclical epidemic patterns, and specific seasons or transmission waves may lead to increased reporting of non-specific symptoms. We acknowledge this as an inherent limitation of studies relying on self-reported data.

Finally, the follow-up period of this study coincided with a time of active COVID-19 vaccination campaigns and the emergence of new viral variants. There were limitations in ideally incorporating detailed data, such as the timing of vaccination, type of vaccine, and number of doses, as time-varying covariates in the model. Moreover, the proposed scoring systems require iterative refinement and external validation in independent cohorts, particularly in other Asian populations. This study provides a data-driven framework for defining and monitoring PASC in a large Korean cohort.

5. Conclusions

The static and dynamic scoring systems offer valuable tools for both clinical practice and research, with the dynamic score providing novel insights into the fluctuating, chronic nature of the condition. Furthermore, it can be applied to more advanced causal inference methods for better estimating the impact of SARS-CoV-2 infection on long-term health outcomes.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data sharing statement

The data used for this study are not publicly available at present in accordance with KDCA policies. However, the data may become available in the future, subject to the authority of the KDCA.

Declaration of AI and AI-assisted technologies in the writing process

Generative AI tools used to correct grammar and spelling errors. After using this tool, the authors carefully reviewed and edited the content as needed and take full responsibility for the final version of the publication.

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Ethical approval

All participants submitted written informed consent, and the protocol was reviewed by the institutional review boards of each participating center.

Author contributions

Dr Lee had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Jung, Lee, Song, Joo. Acquisition, analysis, or interpretation of data: Lee, Jung, Kim, Ko, Lee, Song, Seo, Choi, Kwon, Lee, Park, Choi, Baek, Kim, Jeong. Drafting of the manuscript: Seo, Joo, Song, Jung. Critical review of the manuscript for important intellectual content: All authors. Statistical analysis: Seo, Song, Kim. Obtained funding: Lee. Administrative, technical, or material support: Jung, Joo. Supervision: Lee, Jung.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108378.

References

[1] World Health Organization. WHO coronavirus (COVID-19) dashboard. https://covid19.who.int/. [accessed 28 February 2025].
[2] Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, et al. Symptoms, complications and management of long COVID: a review. *J R Soc Med* 2021;**114**(9):428–42.
[3] Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol* 2023;**21**(3):133–46.
[4] Ladds E, Rushforth A, Wieringa S, Taylor S, Rayner C, Husain L, et al. Persistent symptoms after Covid-19: qualitative study of 114 "long Covid" patients and draft quality principles for services. *BMC Health Serv Res* 2020;**20**(1):1144.
[5] Kitsios GD, Blacka S, Jacobs JJ, Mirza T, Naqvi A, Gentry H, et al. Subphenotypes of self-reported symptoms and outcomes in long COVID: a prospective cohort study with latent class analysis. *BMJ Open* 2024;**14**(3):e077869.
[6] Thaweethai T, Jolley SE, Karlson EW, Levitan EB, Levy B, McComsey GA, et al. Development of a definition of postacute sequelae of SARS-CoV-2 infection. *JAMA* 2023;**329**(22):1934–46.
[7] Geng LN, Erlandson KM, Hornig M, Letts R, Selvaggi C, Ashktorab H, et al. 2024 update of the RECOVER-adult long COVID research index. *JAMA* 2025;**333**(8):694–700.
[8] Bowe B, Xie Y, Al-Aly Z. Postacute sequelae of COVID-19 at 2 years. *Nat Med* 2023;**29**(9):2347–57.
[9] Chen C, Haupert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review. *J Infect Dis* 2022;**226**(9):1593–607.
[10] Son H-E, Hong Y-S, Lee S, Son H. Prevalence, risk factors, and impact of long COVID among adults in South Korea. *Healthcare* 2024;**12**(20):2062.
[11] Kim Y, Bae S, Chang H-H, Kim S-W. Characteristics of long COVID and the impact of COVID-19 vaccination on long COVID 2 years following COVID-19 infection: prospective cohort study. *Sci Rep* 2024;**14**(1):854.
[12] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**(5):373–83.
[13] Zigmond AS, Snaith RP. The hospital Anxiety and Depression scale. *Acta Psychiatr Scand* 2007;**67**(6):361–70.
[14] Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *J Gen Intern Med* 2001;**16**(9):606–13.
[15] Ramsay J, Silverman BW. *Functional data analysis*. New York: Springer; 2013.
[16] Guo S, Zhang J, Wu Y, McLain AC, Hardin JW, Olatosi B, et al. Functional multivariable logistic regression with an application to HIV viral suppression prediction. *Biom J* 2024;**66**(5):e202300081.
[17] Yao F, Müller H-G, Wang J-L. Functional data analysis for sparse longitudinal data. *J Am Stat Assoc* 2005;**100**(470):577–90.
[18] Valdivieso-Martinez B, Lopez-Sanchez V, Sauri I, Diaz J, Calderon JM, Gas-Lopez ME, et al. Impact of long SARS-CoV-2 Omicron infection on the health care burden: comparative case-control study between omicron and pre-omicron waves. *JMIR Public Health Surveill* 2024;**10**:e53580.
[19] Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A, et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep* 2021;**11**(1):16144.
[20] Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022;**28**(3):583–90.
[21] Pollack B, von Saltza E, McCorkell L, Santos L, Hultman A, Cohen AK, et al. Female reproductive health impacts of long COVID and associated illnesses including ME/CFS, POTS, and connective tissue disorders: a literature review. *Front Rehabil Sci* 2023;**4**:1122673.
[22] Cayón Figueroa B, Mendoza Rojas W, Tiburcio Jiménez D. Dermatological complications due to post–COVID–19 syndrome: a systematic review. *Med Int* 2024;**5**(1):9.
[23] Zhang Y, Chinchilli VM, Ssentongo P, Ba DM. Association of long COVID with mental health disorders: a retrospective cohort study using real-world data from the USA. *BMJ Open* 2024;**14**(2):e079267.
[24] Spudich S, Nath A. Nervous system consequences of COVID-19. *Science* 2022;**375**(6578):267–9.
[25] Ahmad I, Edin A, Granvik C, Kumm Persson L, Tevell S, Månsson E, et al. High prevalence of persistent symptoms and reduced health-related quality of life 6 months after COVID-19. *Front Public Health* 2023;**11**:1104267.
[26] Fernández-de-las-Peñas C, Cancela-Cilleruelo I, Rodríguez-Jiménez J, Fuensalida-Novo S, Martín-Guerrero JD, Pellicer-Valero OJ, et al. Trajectory of post–COVID self-reported fatigue and dyspnoea in individuals who had been hospitalized by COVID-19: the LONG-COVID-EXP multicenter study. *Biomedicines* 2023;**11**(7):1863.
[27] Ballouz T, Menges D, Anagnostopoulos A, Domenghino A, Aschmann HE, Frei A, et al. Recovery and symptom trajectories up to two years after SARS-CoV-2 infection: population based, longitudinal cohort study. *BMJ* 2023;**381**:e074425.
[28] Hernández-Aceituno A, García-Hernández A, Larumbe-Zabala E. COVID-19 long-term sequelae: omicron versus Alpha and Delta variants. *Infect Dis Now* 2023;**53**(5):104688.
[29] Antonelli M, Pujol JC, Spector TD, Ourselin S, Steves CJ. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2. *Lancet* 2022;**399**(10343):2263–4.
[30] Peipert JD, Zhao F, Lee J-W, Shen S-E, Ip E, O'Connell N, et al. Patient-reported adverse events and early treatment discontinuation among patients with multiple Myeloma. *JAMA Net Open* 2024;**7**(3):e243854.