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Poster: Pre-existing conditions associated with Post-acute Sequelae of COVID-19 in Puerto Rico

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Background:

Post-acute sequelae of COVID-19 (PASC) occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection; usually three months from the onset of COVID-19 with symptoms lasting at least two months and cannot be explained by an alternative diagnosis (1). Risk factors, such as SARS-CoV-2 severity, depression/anxiety, allergies, and autoimmune disease, have been associated with PASC (2). Studies stated that the primary risk factors associated with PASC include conditions such as asthma, type 2 diabetes mellitus, obesity, pre-existing clinical depression, hypothyroidism, hypertension, and chronic lung disease (3,4). This is the first population-based assessment in Puerto Rico to evaluate the impact of pre-existing conditions (PECs) on PASC.

Objective:

1. Identify pre-existing conditions associated with post-acute sequelae of SARS-CoV-2 (PASC) among diagnosed cases of COVID-19 in Puerto Rico during two time periods: September 2020 to August 2021 and December 2021 to July 2022.
2. Assess the prevalence of PASC among diagnosed cases of COVID-19 in Puerto Rico during two time periods: September 2020 to August 2021 and December 2021 to July 2022.

Method:

Design: Two phases cross-sectional

Sample: The assessment included a representative random sample of individuals aged ≥21 years (n=720) positive for SARS-CoV-2 in two periods. Phase 1 was from September 2020 to August 2021, and Phase 2 was from December 2021 to July 2022. Participants were identified from the Puerto Rico Department of Health (PRDOH) BioPortal database, which contains information on all COVID-19 cases in Puerto Rico.

In the PRDOH-Bioportal, 827,661 (119, 906 in Phase 1 and 707,755 in Phase 2) confirmed or probable cases of COVID-19 were identified. After applying the inclusion and exclusion criteria, 617,613 (80,428 in Phase 1 and 537,185 in Phase 2) potentially qualified candidates were obtained to participate in the survey. The established inclusion criteria were as follows: individuals aged 21 or older at the time of diagnosis, being a confirmed or probable case of COVID-19, and having a positive test between September 1, 2020, to August 31, 2021, and from December 7, 2021, to July 31, 2022. The exclusion criteria were cases detected by a serological test, individuals younger than 21 years of age at the time of diagnosis, individuals who died from COVID-19, or individuals without a phone number documented. The following diagrams describe the sample selection process for Phase 1(Figure 1), and Phase 2 (Figure 2) and a summary of the process in both phases (Figure 3):

Figure 1. The sampling selection process for Phase 1

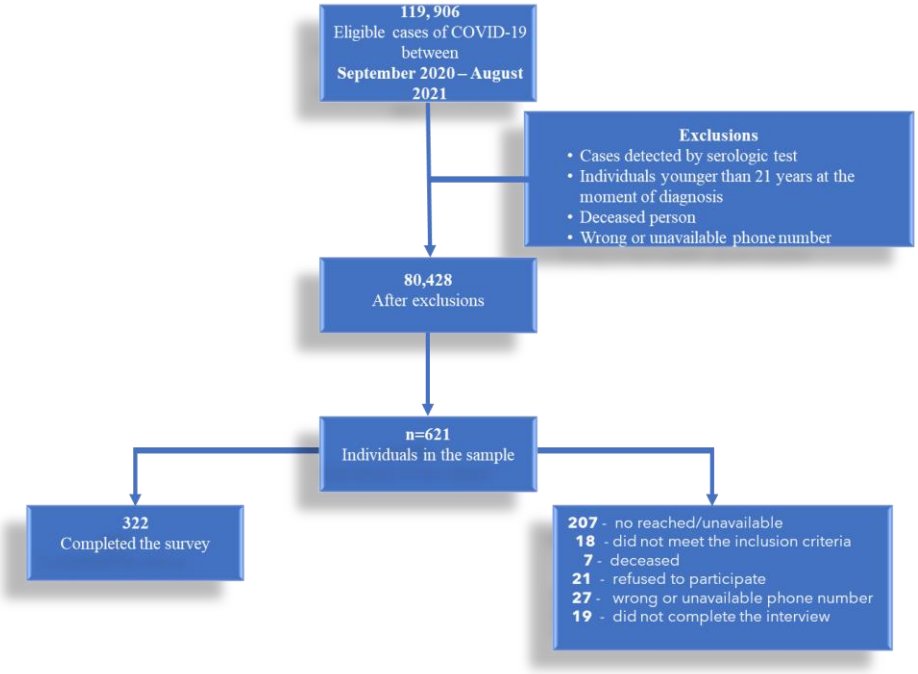


Figure 2. The sampling selection process for Phase 2

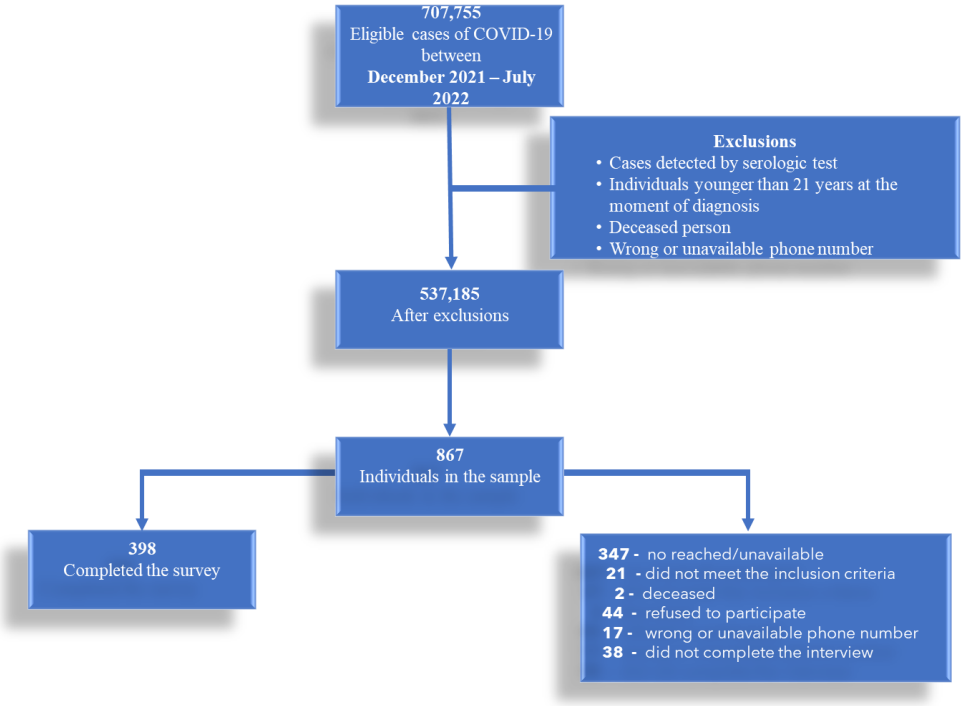
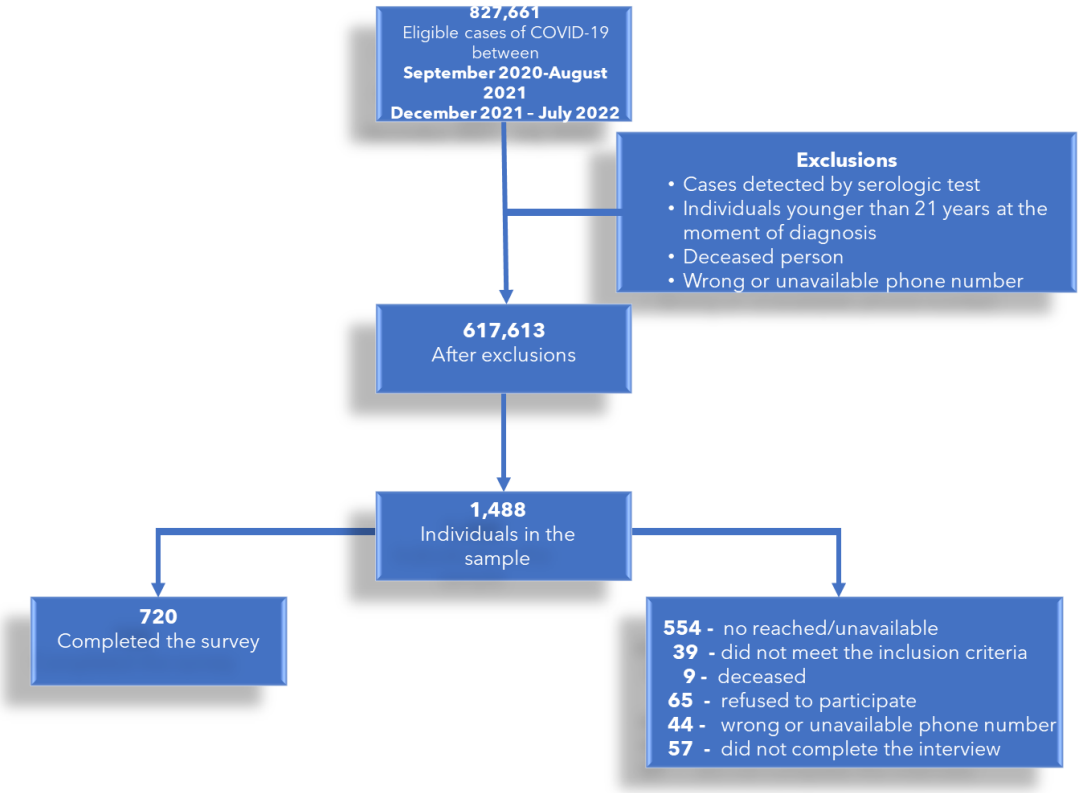


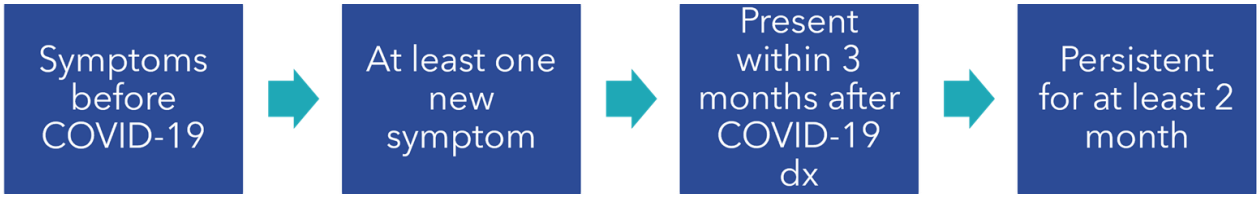
Figure 3. A summary of the sampling selection process for Phase 1 and Phase 2



Definition: PASC occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19, with symptoms lasting at least two months and cannot be explained by an alternative diagnosis. Symptoms may be new onset, following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time (1).

Data collection: The information analyzed in the survey was obtained from the PRDOH-BioPortal and the participants' self-reported information through telephone interviews. The personal information obtained from the PRDOH-BioPortal was validated during the interview with the participants. An algorithm was used to detect participants who had any pre-COVID-19 symptoms and who developed any new symptoms that lasted for two months after acute infection (Figure 4).

Figure 4. Algorithm for detecting participants who had pre-COVID-19 symptoms but developed new symptoms within the first three months after acute infection



Data analysis:

The statistical analysis for this assessment was done using R (version 4.2.2; R Foundation). Descriptive data for baseline characteristics of the participants with and without PASC were calculated using frequencies and percentages for categorical variables and with means and standard deviations for continuous variables. A crude odd ratio (OR) was calculated to estimate the magnitude of the association between PASC and PECs. The strength of the association between PECs and PASC was estimated with a logistic regression model adjusting for period, age, and sex across the two analyzed periods simultaneously. The prevalence of PASC for the two time periods was estimated with 95% confidence intervals. Adjusted prevalence ratio (PR) for age and sex were also calculated through unconditional logistic regression. After applying the exclusion criteria to the total number of positive cases of COVID-19 in each phase, the number of people with PASC in Puerto Rico was estimated.

Results:

A total of 720 individuals were successfully interviewed. Most participants were females (57.6%), were in the age group of 21-49 years (60.7%), their average age was 45.4 years, had more than a high school diploma (63.0%), were smokers (19.4%), were confirmed cases of COVID-19 (54.0%), were hospitalized due to COVID-19 (4.7%), reported PASC (42.9%), reported PECs (63.3%), had the first dose of COVID-19 vaccine (96.5%) and had the second dose of COVID-19 vaccine (94.3%) (Table 1).

In Phase 1, most participants were females (56.8%), were in the age group of 21-49 years (61.8%), had more than a high school diploma (61.1%), were smokers (20.1%), were confirmed cases of COVID-19 (76.7%), were hospitalized due to COVID-19 (8.1%), reported PASC (46.3%), reported PECs (51.9%), had the first dose of COVID-19 vaccine (95.0%) and had the second dose of COVID-19 vaccine (91.3%).

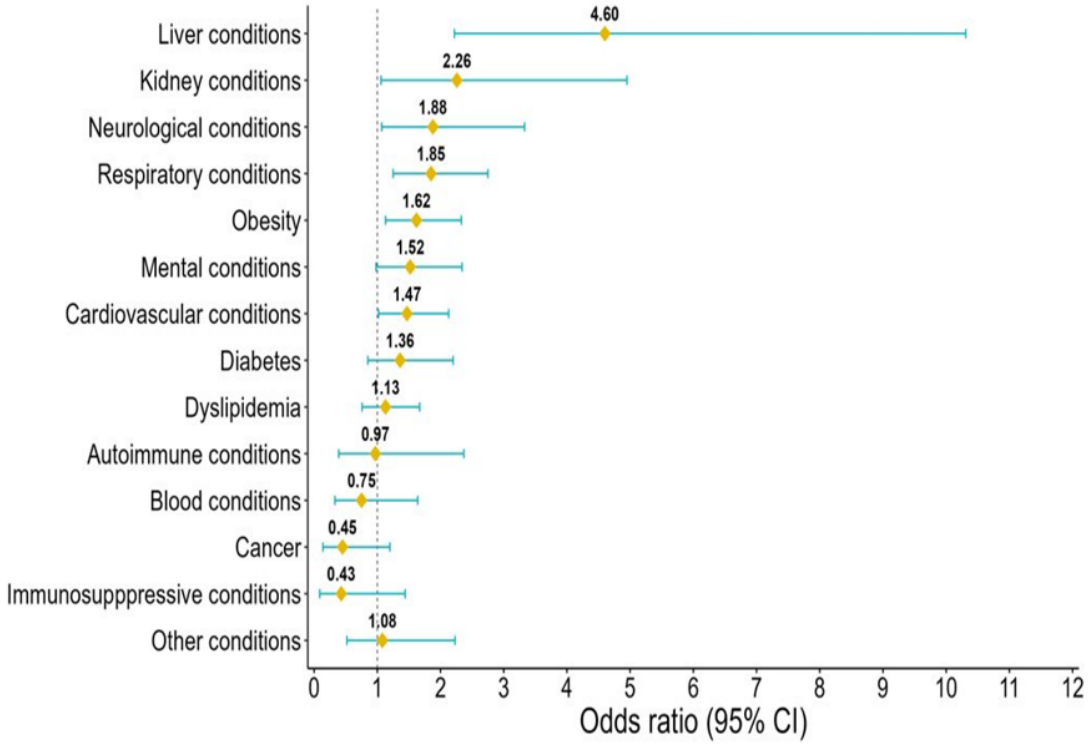
In phase 2, most participants were females (58.3%), were in the age group of 21-49 years (59.8%), had more than a high school diploma (64.6%), were smokers (18.9%), were probable cases of COVID-19 (64.3%), were hospitalized due to COVID-19 (2.5%), reported PASC (40.2%), reported PECs (76.5%), had the first dose of COVID-19 vaccine (97.7%) and had the second dose of COVID-19 vaccine (96.7%).

Table 1. Descriptive of the sample

Characteristics	Total n (%)	Phase 1 n (%)	Phase 2 n (%)
Total	720 (100.0)	322 (44.7)	398 (55.3)
Sex			
Male	305 (42.4)	139 (43.2)	166 (41.7)
Female	415 (57.6)	183 (56.8)	232 (58.3)
Age			
21-49	437 (60.7)	199 (61.8)	238 (59.8)
50-64	189 (26.2)	90 (28.0)	99 (24.9)
65+	94 (13.1)	33 (10.2)	61 (15.3)
Education (n=703)			
Less than a High School Diploma	50 (7.1)	25 (8.2)	25 (6.3)
High School Diploma	210 (29.9)	94 (30.8)	116 (29.1)
More than a High School Diploma	443 (63.0)	186 (61.1)	257 (64.6)
Smoker (n=716)	139 (19.4)	64 (20.1)	75 (18.9)
Case Type			
Confirmed	389 (54.0)	247 (76.7)	142 (35.7)
Probable	331 (46.0)	75 (23.3)	256 (64.3)
Hospitalized (n=656)	31 (4.7)	21 (8.1)	10 (2.5)
PASC	309 (42.9)	149 (46.3)	160 (40.2)
PEC (n=700)	456 (63.3)	167 (51.9)	289 (76.5)
Vaccine 1	695 (96.5)	306 (95.0)	389 (97.7)
Vaccine 2	679 (94.3)	294 (91.3)	385 (96.7)
Booster (n=595)	433 (72.8)	154 (70.3)	279 (74.2)

Having any PECs was statistically associated with PASC (OR: 1.86; 95% CI= 1.31- 2.64). After adjustment for age, sex, and phase following preexisting conditions were statistically significant ($p<0.05$) associated with the development of PASC: liver disease (Liver failure, Cirrhosis, Fatty liver, Hepatitis A, Hepatitis B, Hepatitis C, Autoimmune hepatitis): ORadj: 4.60 (95% CI: 2.22–10.31), kidney disease (Acute kidney failure, Kidney stone, Diabetic nephropathy, Glomerulonephritis, Kidney cysts): ORadj: 2.26 (95% CI: 1.06-4.95), neurological conditions (Dementia, Alzheimer's, Migraine, Epilepsy, Parkinson's, Stroke, Ataxia, Vertigo): ORadj: 1.88 (95% CI=1.07-3.33), respiratory conditions (Asthma, COPD, Fibrosis, Pulmonary hypertension, Pulmonary embolism, Dysplasia, Bronchiectasis): ORadj: 1.85, (95% CI=1.25-2.75), Obesity: ORadj: 1.62 (95% CI= 1.13 - 2.33) and cardiovascular disease (High blood pressure, Angina, Heart attack, Heart failure, Arrhythmia, Endocarditis, Valve disease): ORadj: 1.47 (95% CI=1.02-2.13) (Graph 1).

Graph 1. Association between pre-existence conditions and PASC



The overall prevalence was 42.9 (IC 95%: 39.3%- 46.5%). The estimated prevalence of PASC in Phase 1 was 46.3% (95% CI: 40.7% - 51.9%), while in Phase 2 was 40.2% (95% CI: 35.3% - 45.2%) (Table 2). Based on these prevalence estimations, the estimated number of individuals experiencing PASC in Puerto Rico during Phase 1 was 37,238 people (95% CI: 31,734 - 41,742), and in Phase 2 was 216,485 (95% CI: 189,626 - 242,807). The estimated prevalence of PASC in Phase 2 is 23% lower than the estimated prevalence of PASC in Phase 1, adjusting for age, sex, and region (PRadj: 0.77, 95% CI: 0.57, 1.04) (p>0.05).

Table 2. Prevalence estimations by Phases and prevalence rate

Phase	PASC			PR_{crude} 95% CI	$PR^*_{adjusted}$ 95% CI
	No	Yes	Total		
1	173 **53.7%**	149 **46.3%**	322 **100%**	Reference	Reference
2	238 **59.8%**	160 **40.2%**	398 **100%**	0.78 (0.58,1.05)	0.77 (0.57, 1.04)

Conclusion:

Results suggest that having any PECs may heighten the likelihood of PASC, particularly liver, kidney, or cardiovascular diseases, neurological or respiratory conditions, and obesity. Other studies found respiratory conditions such as asthma as risk factors for PASC (5). The prevalence of PASC in Puerto Rico is similar to the estimated global prevalence (43.0%, 95% CI; 39.0%-46.0%) (5). There is no statistically significant difference in the prevalence of PASC across different phases (46.3% estimated prevalence for Phase 1 and 40.2% estimated prevalence for Phase 2, respectively). Nevertheless, the crude number of individuals experiencing PASC in Phase 2 is greater than in Phase 1. It is noteworthy that Phase 2 coincided with the predominance of the Omicron variant in Puerto Rico and marked the highest incidence of COVID-19. The debate continues regarding whether a milder clinical presentation in individuals with recent SARS-CoV-2 infection leads to a reduced risk of developing PASC. After conducting a study involving nearly 56,000 adults in the United Kingdom who were diagnosed with COVID-19 between December 2021 and March 2022, the researcher determined that patients infected with the SARS-CoV-2 Omicron variant consistently exhibited a lower risk of developing PASC compared to those infected with the SARS-CoV-2 Delta variant (6). Infection with pre-Omicron SARS-CoV-2 variants and pre-existing medical conditions are among the most important clinical predictors (7). However, further analysis is needed to inform clinical and public health recommendations.

Limitations

Some of the limitations of the survey include: (1) Data related to pre-existing symptoms and medical conditions were self-reported by the participants and lacked verification through a medical assessment. (2) Patient self-reporting could have led to underestimation or overestimation of associations and prevalence estimates. (3) The characteristics of people who agreed to participate in the survey may differ from those who declined to participate. (4) Another limitation is the possibility of memory bias due to the time elapsed between the diagnosis of COVID-19 and the time of the interview. (5) There is a possibility of interviewer bias. (6) A standardized questionnaire was used to collect information, but it was not validated, and limitations in the comprehension of some questions were identified during the interview period.

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