The Epidemiology of Post COVID-19 Conditions (long COVID)

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Some Challenges

• Variability and inconsistency in clinical disease definition

• Who is at high risk? Screening biases: Who seeks care and who gets diagnosed? Disparities and health inequities in long COVID.

• Do vaccines/boosters help?

• What is an ideal study design, data and analysis?


Chen Chen,1,5 Spencer R. Haupert,1,6 Lauren Zimmermann,1,2,6 Xu Shi,1 Lars G. Fritsche,1,5,8 and Bhramar Mukherjee1,2,3,4,8

Studies | Prevalence (95% CI)
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Fernández-de-Las-Peñas et al Spain | 0.81 [0.79; 0.84]
Huang et al China | 0.76 [0.74; 0.78]
Wong-Chew et al Mexico | 0.76 [0.74; 0.78]
Ghosn et al France | 0.68 [0.65; 0.71]
Areekal et al India | 0.66 [0.61; 0.71]
Lemhofer et al Germany | 0.62 [0.57; 0.67]
Mumnblt et al Russia | 0.58 [0.56; 0.60]
Maestre-Muñiz et al Spain | 0.57 [0.53; 0.61]
Shang et al China | 0.55 [0.52; 0.59]
Desgranges et al Switzerland | 0.53 [0.48; 0.58]
Hirschcluck et al USA | 0.52 [0.48; 0.57]
Venturelli et al Italy | 0.51 [0.48; 0.55]
Morin et al France | 0.51 [0.46; 0.56]
Xiong et al China | 0.50 [0.45; 0.54]
Yomogida et al USA | 0.48 [0.43; 0.53]
Zhang et al China | 0.45 [0.43; 0.47]
Budhiraj et al India | 0.40 [0.37; 0.43]
Peghin et al Europe | 0.40 [0.36; 0.44]
Righi et al Europe | 0.39 [0.35; 0.44]
Taquet et al USA+others | 0.37 [0.36; 0.37]
Cirulli et al USA | 0.36 [0.31; 0.41]
Chopra et al USA | 0.33 [0.28; 0.37]
Augustin et al Europe | 0.28 [0.24; 0.32]
Spotnitz et al USA | 0.28 [0.27; 0.28]
Huang et al California | 0.27 [0.25; 0.30]
Menges et al Switzerland | 0.26 [0.22; 0.30]
Evans et al UK | 0.22 [0.20; 0.25]
Nai et al India | 0.22 [0.20; 0.24]
Sudre et al UK/SE/US | 0.13 [0.12; 0.14]
Perl et al USA | 0.09 [0.08; 0.10]
Lamp et al Germany | 0.09 [0.06; 0.12]
Total | 0.43 [0.39; 0.46]

Heterogeneity: $\chi^2_{30} = 13875.94 (P < .001)$, $I^2 = 100$

Figure 2. Forest plot for worldwide post-coronavirus disease 2019 condition prevalence. Prevalence estimates and 95% confidence intervals (CIs) are provided for each study with a relevant measure and for the meta-analysis of all such studies. For individual studies, the horizontal line represents the estimate, whiskers represent the CI, the size of the box represents the weight assigned to the study, and the color shading reflects the hospitalization status of the study population, as noted in the legend. For the pooled estimate, the width of the diamond represents the CI, meta-analyzed prevalence and 95% CIs are calculated using random-effects model(s) with inverse variance weighting as described under Methods. Measures of heterogeneity of prevalence estimates are provided.
Risk factors for long COVID

• Biological Sex (in 40-50y, women twice more likely than men)

• Age (Office of National Statistics study in UK says highest prevalence in mid-life 35-69y)

• Pre-existing conditions (asthma, poor mental health), obesity

• Symptom burden during acute phase of COVID (> 5 symptoms, Multisystem Inflammatory Syndrome), changes to gut microbiome

• Viral load, autoantibodies, previous Epstein-Barr virus infection

https://www.gavi.org/vaccineswork/nine-factors-could-boost-your-risk-long-covid
https://www.nature.com/articles/s41467-022-30836-0
https://www.nature.com/articles/s41591-021-01292-y
Do vaccines help?

- Two doses/primary series vaccination
  - Vaccination **after** SARS-CoV-2 infection (~9% reduction in odds)
  - Vaccination **before** SARS-CoV-2 infection (Reduction in risk, but wide range of estimates 10%-40% reduction with two doses)

- Booster/Bivalent booster compared to primary series vaccination
  - No clear evidence, need longer follow-up time

https://www.bmj.com/content/377/bmj-2021-069676
https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00354-6/fulltext
https://www.nature.com/articles/s41591-022-01840-0
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Evidence gathering: Data Sources

- Prospective studies that observe people over time
- Clinical surveillance to collect information from select public health sources on cases of post-COVID conditions
- Medical chart review to collect data on the health and medical care of patients with post-COVID conditions
- Analyses of electronic healthcare data and large patient databases, medical claims
- State and national health surveys using harmonized instruments
- Evaluation of models of care, particularly in underrepresented and marginalized communities

https://studies.recovercovid.org/
https://www.opensafely.org/
Analysis and data needs

• Careful about causal conclusions from observational data

• Sensitivity analysis: Selection Bias, Control Selection

• Prediction of sub-types as opposed to treating it as a single syndrome

• Genetics of COVID-19 and long COVID

• Role of repeated infections

• Need global data on diverse populations

https://www.covid19hg.org/
https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00299-6/fulltext
How data are collected matters to get at your questions!

### Biased Data Collection, Measurements, Exclusionary Cohorts

### The Vicious Cycle

#### Blindly Trained Algorithms and Models

#### Incorrect Conclusions

#### Misguided Policies

#### Exacerbating Inequity & Disparity
Questions?