

Myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS)

and postural orthostatic tachycardia syndrome (POTS)

are frequent post-acute COVID-19 sequelae (PACS)

a network cohort study in six European countries, the US, and Korea



Background: Postural orthostatic tachycardia syndrome (POTS) and myalgic encephalomyelitis / chronic fatigues syndrome (ME/CFS) are debilitating diseases leading to heart racing, fainting, and extreme fatigue and malaise, respectively.

Results: Among 2'521'812 COVID-19 compared to 4'233'145 test negative patients, overall IRRs were 1.24, 1.22, and 1.12 for POTS symptoms, ME/CFS symptoms and diagnoses, respectively (Fig. 1). Increased rates mainly occurred among children and elderly. Autoimmune diseases and diabetes mellitus (DM, control) did not yield increased rates.

Among all 34'549'575 individuals in general database populations, IRs of POTS and ME/CFS diagnoses ranged 17–1'477/100'000 person-years (pys) and 2–473/100'000 pys, respectively (Fig. 2, depending on the database). IRs of MIS ranged lowest with 0.4–16/100'000 pys and those of DM as a benchmark ranged 8–86/100'000 pys. IRs largely depended on the care setting.

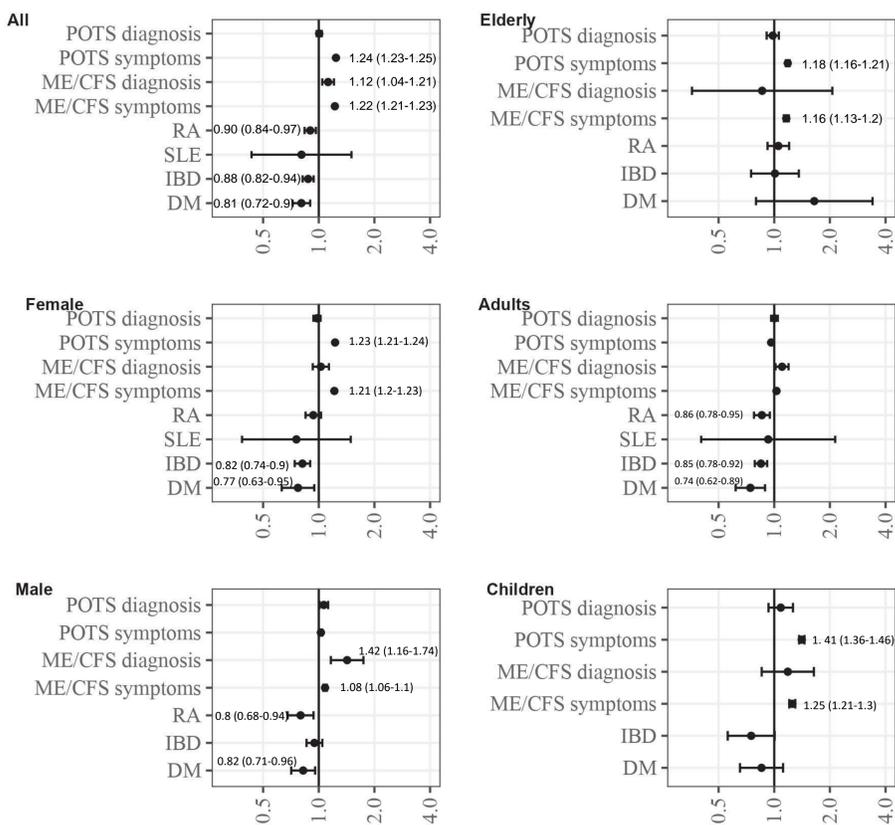


Figure 1. Meta-analysed crude incidence rate ratios with 95% confidence intervals for all outcomes among COVID-19 vs. test negative patients, overall and stratified by age and sex
 Outcomes not depicted because of too few counts: multi-inflammatory syndrome (MIS), juvenile idiopathic arthritis (JIA)
 IBD: inflammatory bowel disease; ME/CFS: myalgic encephalomyelitis / chronic fatigues syndrome; POTS: postural orthostatic tachycardia syndrome; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; DM: diabetes mellitus (control outcome)

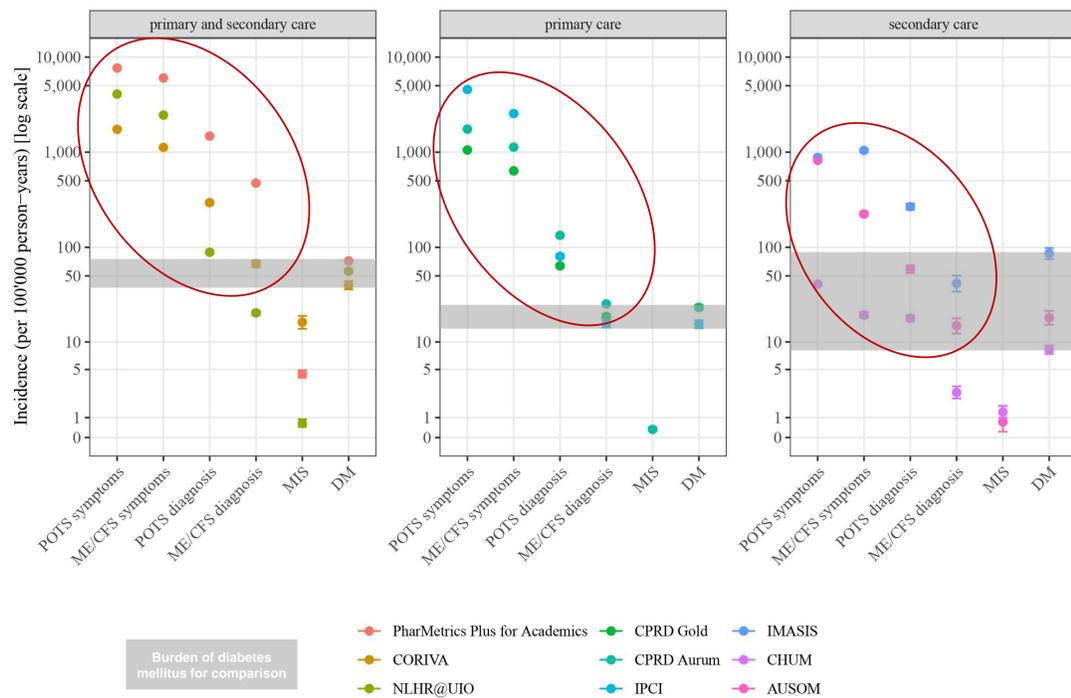


Figure 2. Incidence rates with 95% confidence intervals stratified by care setting

Diseases:

POTS: postural orthostatic tachycardia syndrome; ME/CFS: myalgic encephalomyelitis / chronic fatigues syndrome; MIS: multi-inflammatory syndrome, DM: diabetes mellitus (control outcome)

Databases:

PharMetrics® Plus for Academics; US claims, CORIVA: Healthcare claims from Estonia; NLHR@UiO: Norwegian linked health registry data; CPRD Gold/Aurum: Clinical Practice Research Datalink Gold / Aurum; IPCI: The Integrated Primary Care Information; IMASIS: Hospital records from Parc Salut Mar Barcelona; CHUM: Hospital records from the Montpellier University Hospital; AUSOM: Hospital records from Ajou University Medical Centre;

Methods: Descriptive cohort study in electronic health records and claims from various health care settings in the UK, Netherlands, Norway, Spain, France, Estonia, Korea, and USA (September 2020 until latest available data). Patients had at least 365 days of prior observation (general population), a SARS-Cov-2 negative test (comparator) or a COVID-19 record (exposed patients). We assessed postural orthostatic tachycardia syndrome (POTS), myalgic encephalomyelitis / chronic fatigues syndrome (ME/CFS), multi-inflammatory syndrome (MIS), and several autoimmune diseases. For contextualisation, we assessed any diabetes mellitus (DM). Meta-analysed crude incidence rate ratios (IRR) of outcomes measures after COVID-19 versus negative testing yield the ratios of absolute risks. Incidence rates (IR) of the outcomes in the general population describe the total disease burden.

Limitation: We neither matched groups nor adjusted for confounders, yet we observed sex and age (important confounders) to be mostly balanced. Secondary care data are not representative of the general population.

