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Long-term, phenome-wide consequences of COVID-19 in England: whole-population linked EHR analysis by vaccination status

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Background

COVID-19 is associated with multi-organ morbidity, but large-scale evaluations of long-term outcomes by vaccination status and disease severity remain limited.

individuals. Findings support continued surveillance and underscore the importance of vaccination in reducing post-acute disease burden.

Objective

Investigate associations between COVID-19 and a wide range of health outcomes, stratified by vaccination status and disease severity. Methods: We analysed linked electronic health records for 49 million adults in England using the NHS Secure Data Environment. We defined three cohorts: pre-vaccination (Jan 2020–Jun 2021; 443 outcomes; $N \approx 49$ million), vaccinated (304 outcomes; Jun–Dec 2021; $N \approx 37$ million), and electively unvaccinated (99 outcomes; Jun–Dec 2021; $N \approx 11$ million). For each cohort, we estimated adjusted hazard ratios (aHRs) comparing incidence after versus before or without COVID-19 diagnosis, overall and by disease severity.

Results

COVID-19 was associated with increased incidence of 90.3%, 86.5%, and 86.9% of outcomes in the pre-vaccination, vaccinated, and unvaccinated cohorts, respectively. Hazards peaked in the first four weeks, then declined but remained elevated for up to two years. aHRs were consistently greater after hospitalised than non-hospitalised COVID-19. Average aHRs were 57% higher in unvaccinated than vaccinated individuals. In the pre-vaccination cohort, the strongest associations were for hepatic failure, empyema and pneumothorax, and pulmonary embolism, whereas the weakest associations were for diseases of the teeth and supporting structures and pregnancy-related outcomes.

Conclusions

COVID-19 is linked to elevated long-term incidence across a broad range of conditions, particularly following hospitalisation. These effects are markedly reduced among vaccinated

