University of BRISTOL

PERSPECTIVES ON USING TRUSTED RESEARCH ENVIRONMENTS

Venexia Walker

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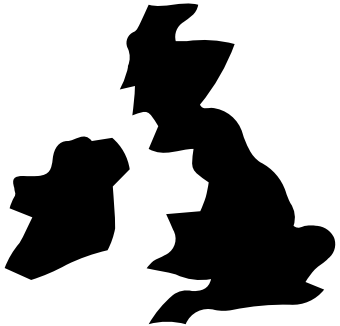
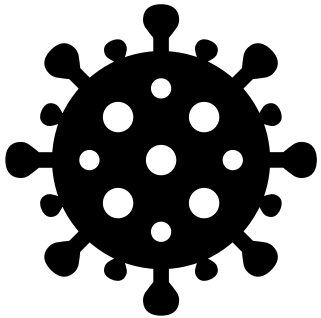
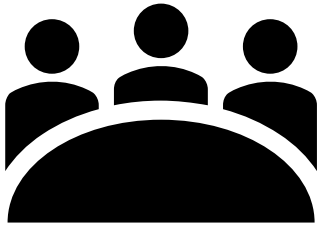
Outline



National linked electronic health records in England



Investigating the consequences of COVID-19



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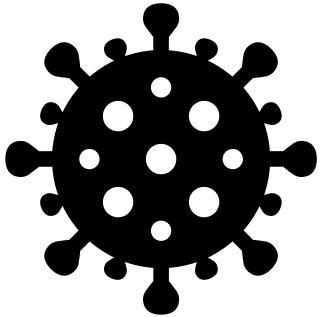

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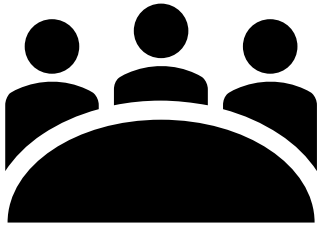


Perspectives on using trusted research environments

From analogue to digital

1984

First electronic medical records introduced in primary care

Early 2000s

Electronic medical records widely adopted in primary care

2019

Only 10% of NHS trusts claimed to have fully digitised hospital records

2024

‘Analogue to digital’ part of the Labour government’s 10-year plan for the NHS

National electronic health record data

Primary Care

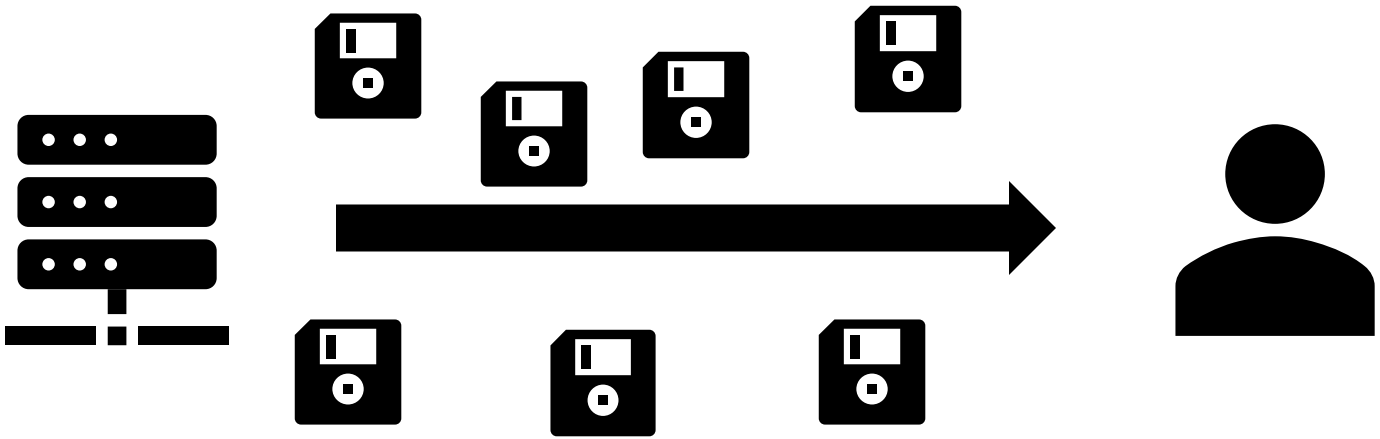
…

- Hospital Episode Statistics
- Index of Multiple Deprivation
- COVID-19 vaccination data
- UK Renal Registry
- …
- Office of National Statistics Death Registry

The rise of the secure data environment

The rise of the secure data environment

Before:



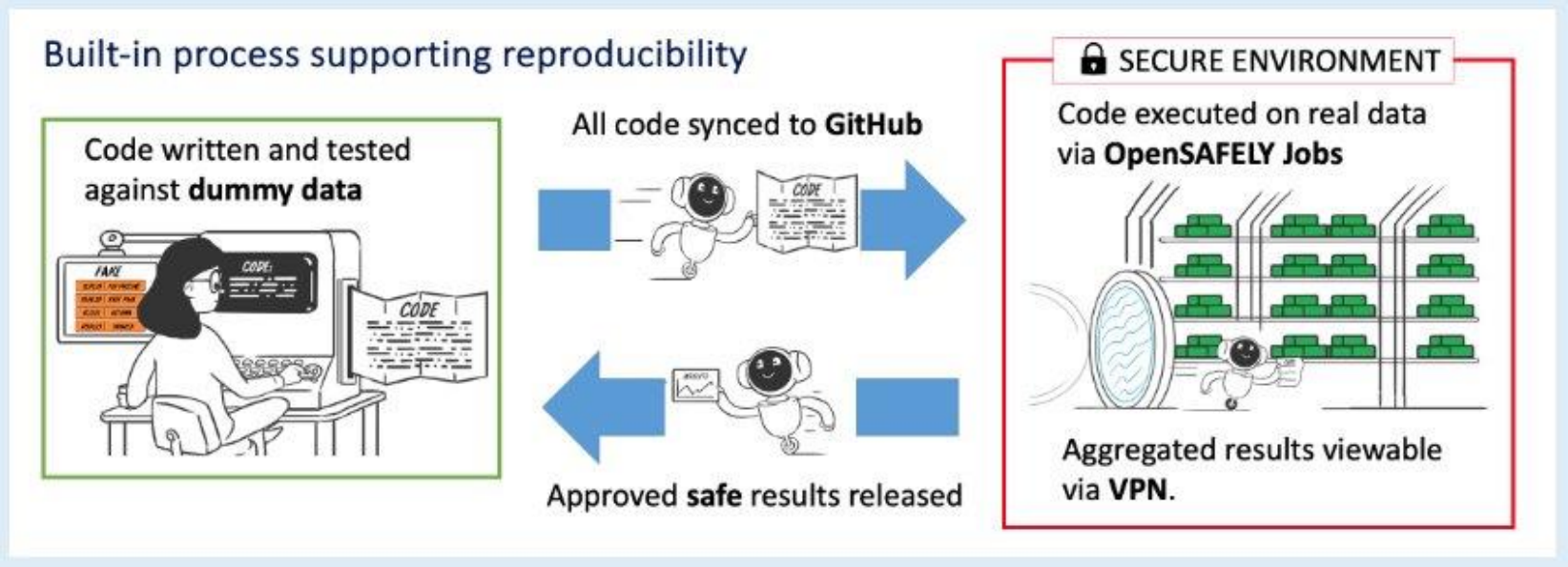
The rise of the secure data environment

In a secure data environment:

How do you access English primary care records for research today?

	COVID-19 research only	
~ 18 million	TPP ~ 24 million EMIS ~ 33 million	~ 55 million
Complete record		Restricted record

OpenSAFELY



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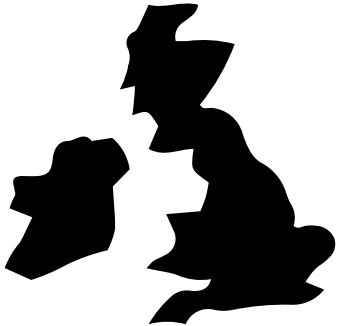

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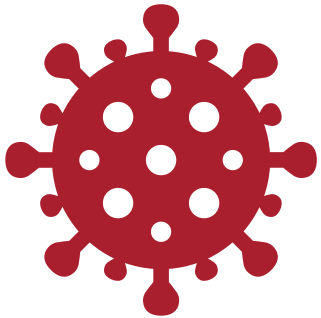
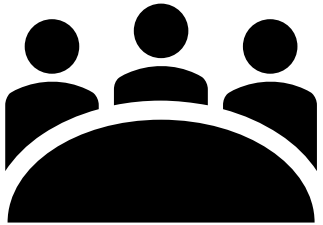


Investigating the consequences of COVID-19



Perspectives on using trusted research environments

Aim

- To examine associations of diagnosed COVID-19 with subsequent clinical events prior to vaccine availability and for unvaccinated and vaccinated people after vaccination became available

- Where possible, to examine associations of diagnosed COVID-19 with subsequent clinical events in subgroups defined by COVID-19 severity, age, sex, ethnicity, prior history of the outcome, and prior COVID-19

Cohorts

Cohort	Sample size	Start date	End date	Variant(s)	Vaccination
Pre-vaccination	~18.6m	01/01/2020	14/12/2021*	Wild type; Alpha	Unlikely though eligible towards end of follow-up
Vaccinated	~14.0m	01/06/2021	14/12/2021	Delta	Received at least two vaccinations
Unvaccinated	~3.2m	01/06/2021	14/12/2021	Delta	Eligible but received no vaccinations

** Ascertainment of COVID-19 stopped on 18/06/2021 when all adults became eligible for vaccination*

Outcomes

Cardiovascular

Mental health

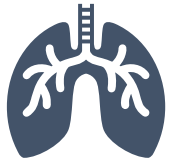
Neurodegenerative

Renal

Diabetes

Autoimmune

Gastrointestinal



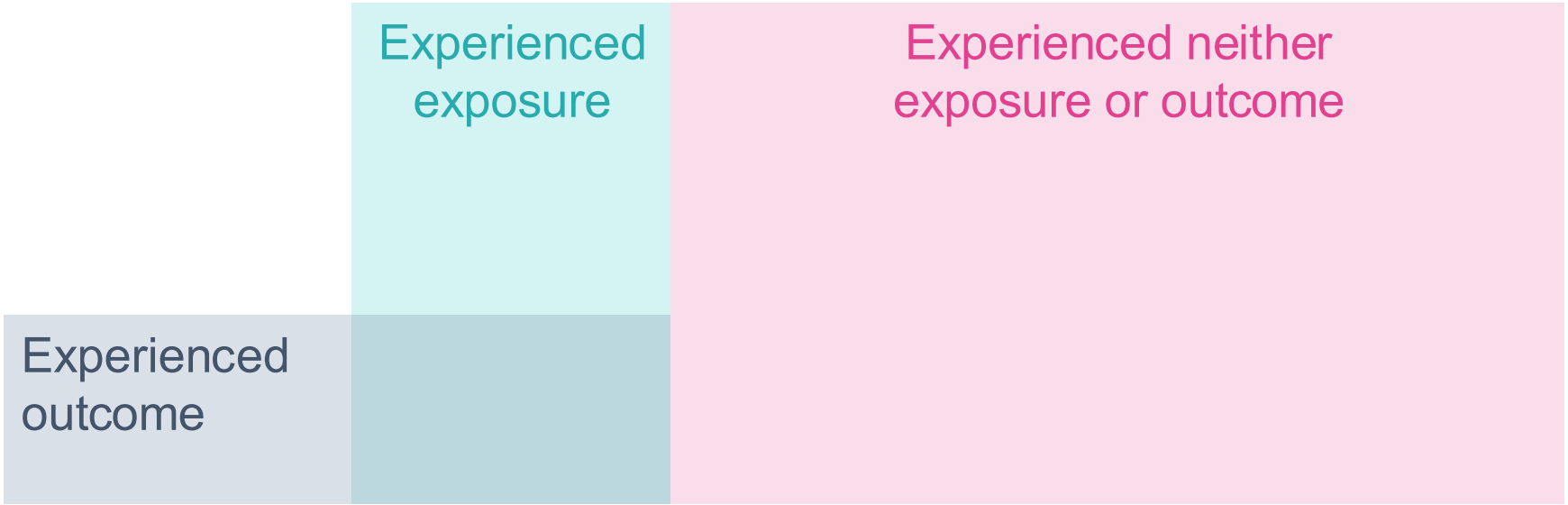
Respiratory

Statistical analyses

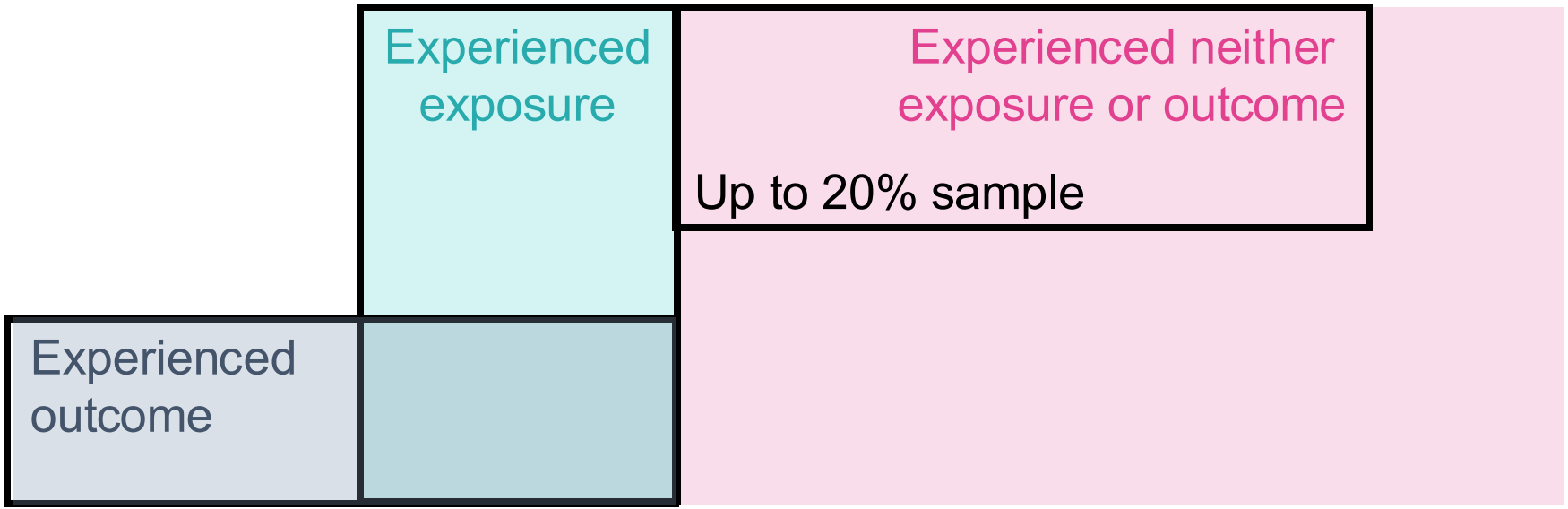
- Time to first event was analysed for each outcome using Cox models fitted with a calendar time scale using the cohort-specific baseline as the origin and stratified by region.

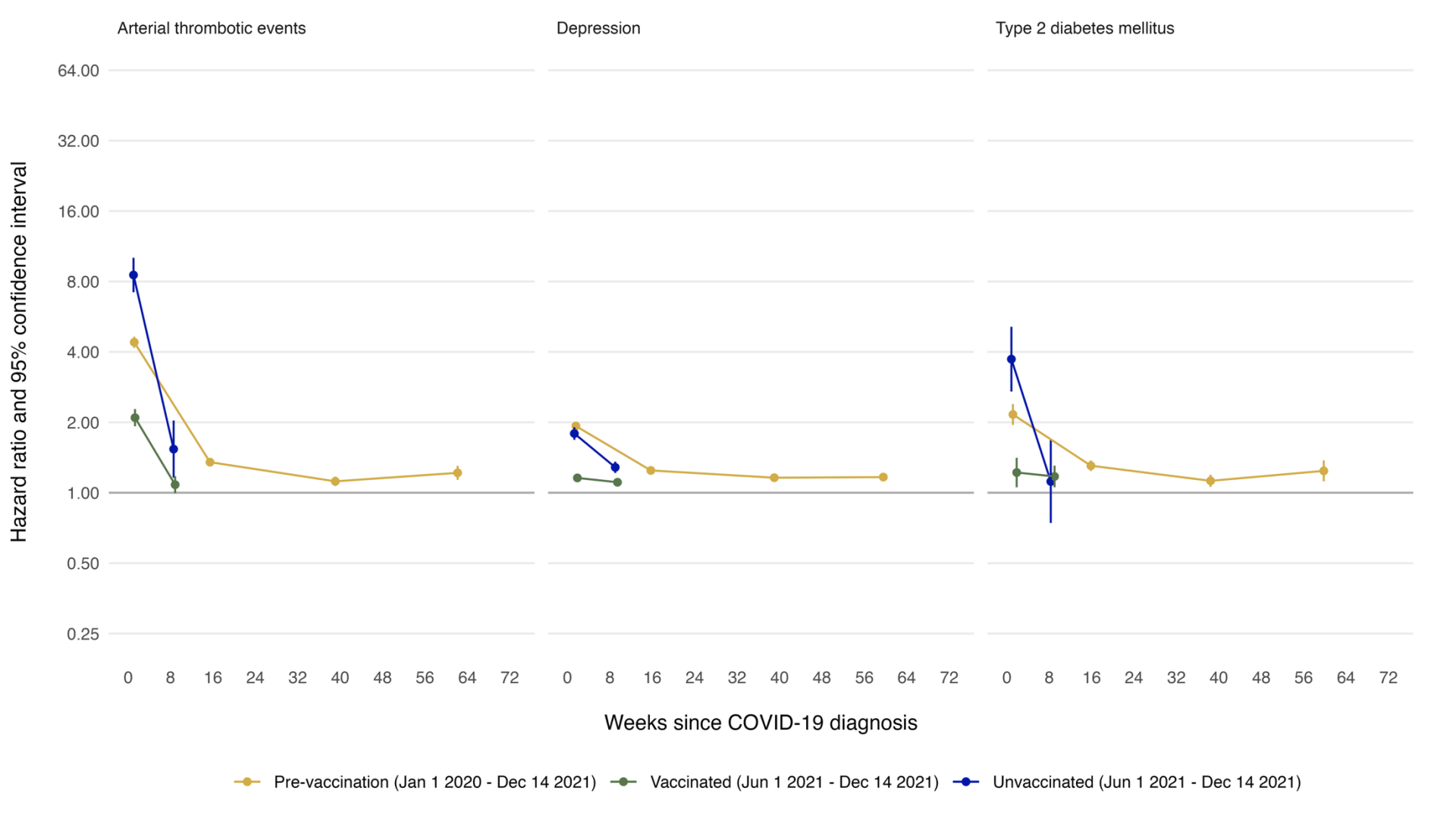
- Adjusted hazard ratios for follow-up after, versus before or without COVID-19, were estimated, splitting follow-up into the day of COVID-19 diagnosis (‘day 0’), the remainder of 1-4 weeks, and 5-28 weeks after COVID-19 for all cohorts and additionally 29-52 and 53-102 weeks after COVID-19 for the pre-vaccine availability cohort.

Statistical analyses

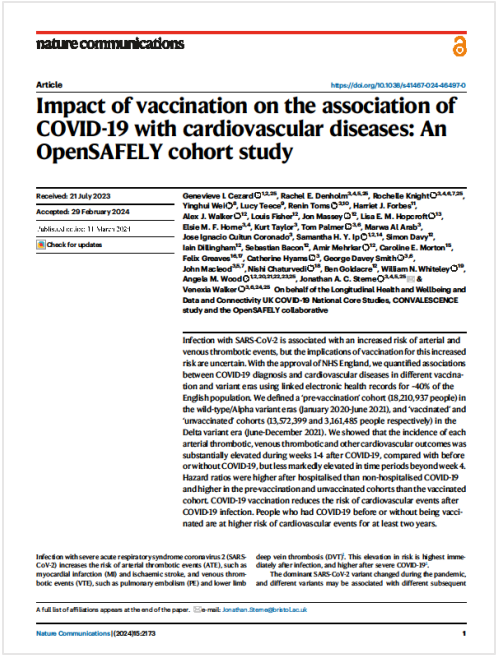


Statistical analyses




Arterial thrombotic events
Depression
Type 2 diabetes mellitus
Hazard ratio and 95% confidence interval
64.00
32.00
16.00
8.00
4.00
2.00
1.00
0.50
0.25
0
8
16
24
32
40
48
56
64
72
Weeks since COVID-19 diagnosis
Pre-vaccination (Jan 1 2020 - Dec 14 2021)
Vaccinated (Jun 1 2021 - Dec 14 2021)
Unvaccinated (Jun 1 2021 - Dec 14 2021)

Read more...



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Article

https://doi.org/10.1038/s41467-024-46497-0

Impact of vaccination on the association of COVID-19 with cardiovascular diseases: An OpenSAFELY cohort study

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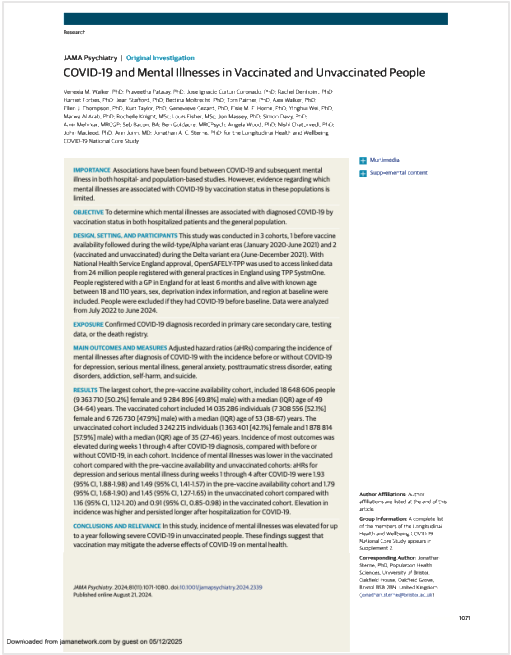
Check for updates

Genevieve I. Cezard[1,2,39], Rachel E. Denholm[3,4,5,39], Rochelle Knight[3,4,6,7,39], Yinghui Wei[8], Lucy Teece[9], Renin Toms[10,39], Harriet J. Forbes[11], Alex J. Walker[12], Louis Fisher[13], Jon Massey[14], Lisa E. M. Hopcroft[13], Elsie M. F. Horne[3,4], Kurt Taylor[15], Tom Palmer[16,17], Marwa Al Arab[3], Jose Ignacio Quiton Coronado[3], Samantha H. Y. Ip[18,19], Simon Davy[20], Iain Dillingham[21], Sebastian Bacon[22], Amir Mehrkar[23], Caroline E. Morton[24], Felix Greaves[25,26], Catherine Hyams[27], George Davey Smith[28,29], John Macleod[28,7], Nishi Chaturvedi[30], Ben Goldacre[31], William N. Whiteley[32], Angela M. Wood[33,34,35,36,37], Jonathan A. C. Sterne[38,4,6,39] & Venexia Walker[28,4,6,34,39] On behalf of the Longitudinal Health and Wellbeing and Data and Connectivity UK COVID-19 National Core Studies, CONVALESCENCE study and the OpenSAFELY collaborative

Infection with SARS-CoV-2 is associated with an increased risk of arterial and venous thrombotic events, but the implications of vaccination for this increased risk are uncertain. With the approval of NHS England, we quantified associations between COVID-19 diagnosis and cardiovascular diseases in different vaccination and variant eras using linked electronic health records for ~40% of the English population. We defined a 'pre-vaccination' cohort (18,210,937 people) in the wild-type/Alpha variant era (January 2020-June 2021), and 'vaccinated' and 'unvaccinated' cohorts (13,572,399 and 3,361,485 people respectively) in the Delta variant era (June-December 2021). We showed that the incidence of each arterial thrombotic, venous thrombotic and other cardiovascular outcomes was substantially elevated during weeks 1-4 after COVID-19, compared with before or without COVID-19, but less markedly elevated in time periods beyond week 4. Hazard ratios were higher after hospitalised than non-hospitalised COVID-19 and higher in the pre-vaccination and unvaccinated cohorts than the vaccinated cohort. COVID-19 vaccination reduces the risk of cardiovascular events after COVID-19 infection. People who had COVID-19 before or without being vaccinated are at higher risk of cardiovascular events for at least two years.

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) increases the risk of arterial thrombotic events (ATE), such as myocardial infarction (MI) and ischaemic stroke, and venous thrombotic events (VTE), such as pulmonary embolism (PE) and lower limb deep vein thrombosis (DVT). This elevation in risk is highest immediately after infection, and higher after severe COVID-19[1–3]. The dominant SARS-CoV-2 variant changed during the pandemic, and different variants may be associated with different subsequent

A full list of affiliations appears at the end of the paper. e-mail: Jonathan.Sterne@bristol.ac.uk



Research

JAMA Psychiatry | Original Investigation

COVID-19 and Mental Illnesses in Vaccinated and Unvaccinated People

Venexia M. Walker, PhD; Praveetha Patalay, PhD; Jose Ignacio Quiton Coronado, PhD; Rachel Denholm, PhD; Harriet Forbes, PhD; Jean Stafford, PhD; Martina Modesto Inc, PhD; Tom Palmer, PhD; Kate Walker, PhD; Peter J. Thompson, PhD; Kurt Taylor, PhD; Genevieve Cezard, PhD; Elsie M. F. Horne, PhD; Yinghui Wei, PhD; Marwa Al Arab, PhD; Rochelle Knight, MSc; Louis Fisher, MSc; Jon Massey, PhD; Simon Davy, PhD; Kate Mehrkar, MRCGP; Sebastian Bacon, BA; Ben Goldacre, MRCPsych; Angela Wood, PhD; Nishi Chaturvedi, PhD; John Macleod, PhD; Ann John, MD; Jonathan A. C. Sterne, PhD; for the Longitudinal Health and Wellbeing COVID-19 National Core Study

IMPORTANCE Associations have been found between COVID-19 and subsequent mental illness in both hospital- and population-based studies. However, evidence regarding which mental illnesses are associated with COVID-19 by vaccination status in these populations is limited.

OBJECTIVE To determine which mental illnesses are associated with diagnosed COVID-19 by vaccination status in both hospitalized patients and the general population.

DESIGN, SETTING, AND PARTICIPANTS This study was conducted in 3 cohorts, 1 before vaccine availability followed during the wild-type/Alpha variant eras (January 2020-June 2021) and 2 (vaccinated and unvaccinated) during the Delta variant era (June-December 2021). With National Health Service England approval, OpenSAFELY-TPP was used to access linked data from 24 million people registered with general practices in England using TPP SystmOne. People registered with a GP in England for at least 6 months and alive with known age between 18 and 110 years, sex, deprivation index information, and region at baseline were included. People were excluded if they had COVID-19 before baseline. Data were analyzed from July 2022 to June 2024.

EXPOSURE Confirmed COVID-19 diagnosis recorded in primary care secondary care, testing data, or the death registry.

MAIN OUTCOMES AND MEASURES Adjusted hazard ratios (aHRs) comparing the incidence of mental illnesses after diagnosis of COVID-19 with the incidence before or without COVID-19 for depression, serious mental illness, general anxiety, posttraumatic stress disorder, eating disorders, addiction, self-harm, and suicide.

RESULTS The largest cohort, the pre-vaccine availability cohort, included 18 648 606 people (9 363 710 [50.2%] female and 9 284 896 [49.8%] male) with a median (IQR) age of 49 (34-64) years. The vaccinated cohort included 14 035 286 individuals (7 308 556 [52.1%] female and 6 726 730 [47.9%] male) with a median (IQR) age of 53 (38-67) years. The unvaccinated cohort included 3 242 215 individuals (1 363 401 [42.1%] female and 1 878 814 [57.9%] male) with a median (IQR) age of 35 (27-46) years. Incidence of most outcomes was elevated during weeks 1 through 4 after COVID-19 diagnosis, compared with before or without COVID-19, in each cohort. Incidence of mental illnesses was lower in the vaccinated cohort compared with the pre-vaccine availability and unvaccinated cohorts; aHRs for depression and serious mental illness during weeks 1 through 4 after COVID-19 were 1.93 (95% CI, 1.88-1.98) and 1.49 (95% CI, 1.41-1.57) in the pre-vaccine availability cohort and 1.79 (95% CI, 1.68-1.90) and 1.45 (95% CI, 1.27-1.65) in the unvaccinated cohort compared with 1.36 (95% CI, 1.12-1.20) and 0.91 (95% CI, 0.85-0.98) in the vaccinated cohort. Elevation in incidence was higher and persisted longer after hospitalization for COVID-19.

CONCLUSIONS AND RELEVANCE In this study, incidence of mental illnesses was elevated for up to a year following severe COVID-19 in unvaccinated people. These findings suggest that vaccination may mitigate the adverse effects of COVID-19 on mental health.

Multimedia

Supplemental content

Author Affiliations Author affiliations are listed at the end of this article.

Group Information A complete list of the members of the Longitudinal Health and Wellbeing COVID-19 National Core Study appears in Supplement 2.

Corresponding Author: Jonathan Sterne, PhD, Population Health Sciences, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, United Kingdom (Jonathan.sterne@bristol.ac.uk).

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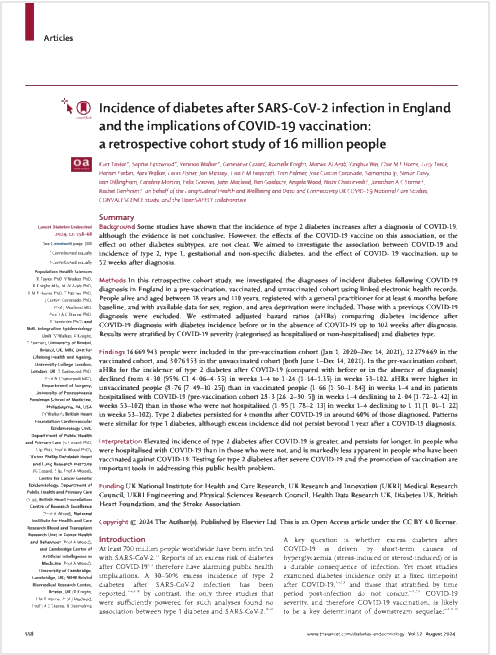

Articles

Incidence of diabetes after SARS-CoV-2 infection in England and the implications of COVID-19 vaccination: a retrospective cohort study of 16 million people

oa

Kurt Taylor*, Sophie Eastwood*, Venexia Walker*, Genevieve Cezard, Rochelle Knight, Marwa Al Arab, Yinghui Wei, Elsie M F Horne, Lucy Teece, Harriet Forbes, Kate Walker, Louis Fisher, Jon Massey, Lisa E M Hopcroft, Tom Palmer, Jose Quiton Coronado, Samantha Ip, Simon Davy, Iain Dillingham, Caroline Morton, Felix Greaves, John Macleod, Ben Goldacre, Angela Wood, Nishi Chaturvedi†, Jonathan A C Sterne†, Rachel Denholm† on behalf of the Longitudinal Health and Wellbeing and Data and Connectivity UK COVID-19 National Core Studies, CONVALESCENCE study and the OpenSAFELY collaborative

Lancet Diabetes Endocrinol 2024; 12: 158–68

Summary

Background Some studies have shown that the incidence of type 2 diabetes increases after a diagnosis of COVID-19, although the evidence is not conclusive. However, the effects of the COVID-19 vaccine on this association, or the effect on other diabetes subtypes, are not clear. We aimed to investigate the association between COVID-19 and incidence of type 2, type 1, gestational and non-specific diabetes, and the effect of COVID-19 vaccination, up to 52 weeks after diagnosis.

Methods In this retrospective cohort study, we investigated the diagnoses of incident diabetes following COVID-19 diagnosis in England in a pre-vaccination, vaccinated, and unvaccinated cohort using linked electronic health records. People alive and aged between 18 years and 110 years, registered with a general practitioner for at least 6 months before baseline, and with available data for sex, region, and area deprivation were included. Those with a previous COVID-19 diagnosis were excluded. We estimated adjusted hazard ratios (aHRs) comparing diabetes incidence after COVID-19 diagnosis with diabetes incidence before or in the absence of COVID-19 up to 104 weeks after diagnosis. Results were stratified by COVID-19 severity (categorised as hospitalised or non-hospitalised) and diabetes type.

Findings 16 669 943 people were included in the pre-vaccination cohort (Jan 1, 2020–Dec 14, 2021), 12 279 669 in the vaccinated cohort, and 3 076 751 in the unvaccinated cohort (both June 1–Dec 14, 2021). In the pre-vaccination cohort, aHRs for the incidence of type 2 diabetes after COVID-19 (compared with before or in the absence of diagnosis) declined from 4·38 [95% CI 4·06–4·51] in weeks 1–4 to 1·24 (1·14–1·35) in weeks 53–102. aHRs were higher in unvaccinated people (8·76 [7·49–10·25]) than in vaccinated people (1·66 [1·50–1·84]) in weeks 1–4 and in patients hospitalised with COVID-19 (pre-vaccination cohort 23·3 [22·2–30·3]) in weeks 1–4 declining to 2·84 (1·72–2·42) in weeks 53–102) than in those who were not hospitalised (1·95 [1·78–2·13] in weeks 1–4 declining to 1·11 [1·01–1·22] in weeks 53–102). Type 2 diabetes persisted for 4 months after COVID-19 in around 60% of those diagnosed. Patterns were similar for type 1 diabetes, although excess incidence did not persist beyond 1 year after a COVID-19 diagnosis.

Interpretation Elevated incidence of type 2 diabetes after COVID-19 is greater, and persists for longer, in people who were hospitalised with COVID-19 than in those who were not, and is markedly less apparent in people who have been vaccinated against COVID-19. Testing for type 2 diabetes after severe COVID-19 and the promotion of vaccination are important tools in addressing this public health problem.

Funding UK National Institute for Health and Care Research, UK Research and Innovation (UKRI) Medical Research Council, UKRI Engineering and Physical Sciences Research Council, Health Data Research UK, Diabetes UK, British Heart Foundation, and the Stroke Association

Introduction

At least 700 million people worldwide have been infected with SARS-CoV-2.[1] Reports of an excess risk of diabetes after COVID-19[2–5] therefore have alarming public health implications. A 30–50% excess incidence of type 2 diabetes after SARS-CoV-2 infection has been reported.[2–5] By contrast, the only three studies that were sufficiently powered for such analyses found no association between type 1 diabetes and SARS-CoV-2.[2–4] A key question is whether excess diabetes after COVID-19 is driven by short-term causes of hyperglycaemia (stress-induced or steroid-induced) or is a durable consequence of infection. Yet most studies examined diabetes incidence only at a fixed timepoint after COVID-19,[2–4] and those that stratified by time period post-infection do not consider[2–4] COVID-19 severity, and therefore COVID-19 vaccination, is likely to be a key determinant of downstream sequelae.[2–4]

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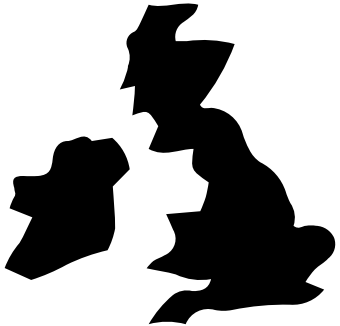

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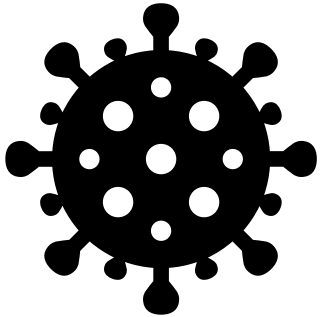
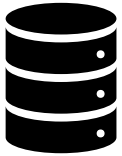


Investigating the consequences of COVID-19

Perspectives on using trusted research environments

What's changed?



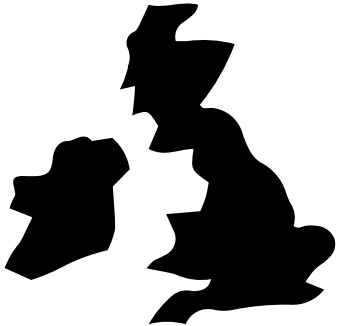
Bigger data

Bigger teams

More open science

More impact

Summary



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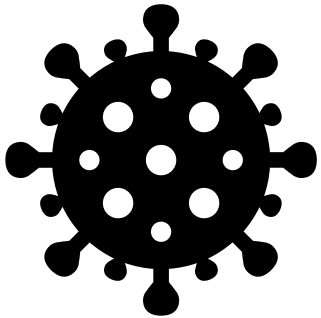

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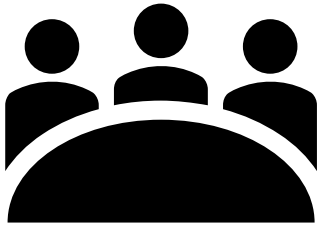


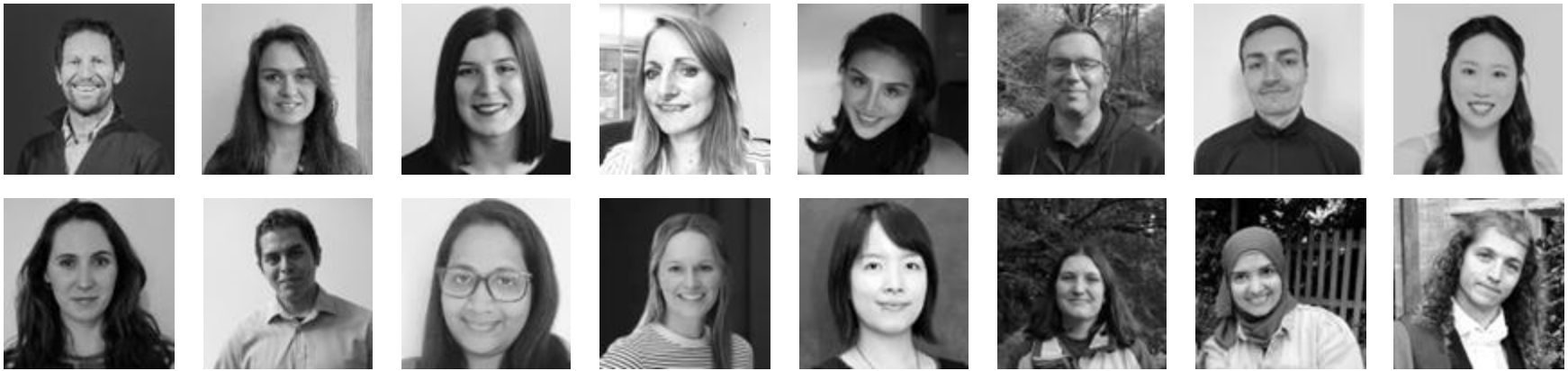
Perspectives on using trusted research environments

This work was supported by:

MRC Integrative Epidemiology Unit

COVID-19 LONGITUDINAL HEALTH & WELLBEING NATIONAL CORE STUDY

COVID-19 National Core Study
CONVALESCENCE STUDY
Coronovirus post-acute long-term effects: constructing an evidence base



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