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Effectiveness of COVID-19 vaccines to prevent long COVID: data from Norway

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Introduction

The effectiveness of COVID-19 vaccines to prevent long COVID symptoms: staggered cohort study of data from the UK, Spain, and Estonia

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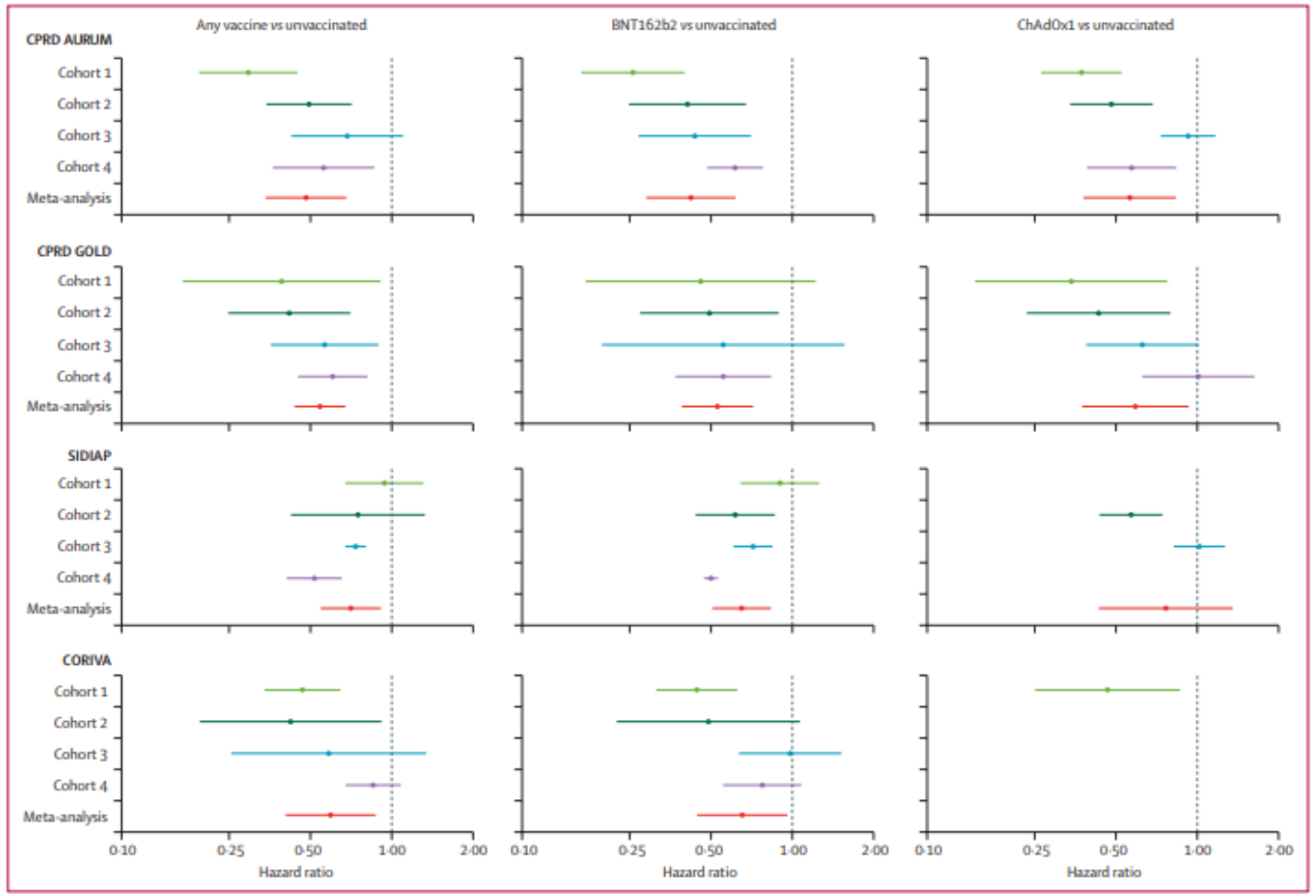
Summary

Background Although vaccines have proved effective to prevent severe COVID-19, their effect on preventing long-term symptoms is not yet fully understood. We aimed to evaluate the overall effect of vaccination to prevent long COVID symptoms and assess comparative effectiveness of the most used vaccines (ChAdOx1 and BNT162b2).

Methods We conducted a staggered cohort study using primary care records from the UK (Clinical Practice Research Datalink [CPRD] GOLD and AURUM), Catalonia, Spain (Information System for Research in Primary Care [SIDIAP]), and national health insurance claims from Estonia (CORIVA database). All adults who were registered for at least 180 days as of Jan 4, 2021 (the UK), Feb 20, 2021 (Spain), and Jan 28, 2021 (Estonia) comprised the source population. Vaccination status was used as a time-varying exposure, staggered by vaccine rollout period. Vaccinated people were further classified by vaccine brand according to their first dose received. The primary outcome definition of long COVID was defined as having at least one of 25 WHO-listed symptoms between 90 and 365 days after the date of a PCR-positive test or clinical diagnosis of COVID-19, with no history of that symptom 180 days before SARS-Cov-2 infection. Propensity score overlap weighting was applied separately for each cohort to minimise confounding. Sub-distribution hazard ratios (sHRs) were calculated to estimate vaccine effectiveness against long COVID, and empirically calibrated using negative control outcomes. Random effects meta-analyses across staggered cohorts were conducted to pool overall effect estimates.

Findings A total of 1 618 395 (CPRD GOLD), 5 729 800 (CPRD AURUM), 2 744 821 (SIDIAP), and 77 603 (CORIVA) vaccinated people and 1 640 371 (CPRD GOLD), 5 860 564 (CPRD AURUM), 2 588 518 (SIDIAP), and 302 267 (CORIVA) unvaccinated people were included. Compared with unvaccinated people, overall HRs for long COVID symptoms in people vaccinated with a first dose of any COVID-19 vaccine were 0·54 (95% CI 0·44–0·67) in CPRD GOLD, 0·48 (0·34–0·68) in CPRD AURUM, 0·71 (0·55–0·91) in SIDIAP, and 0·59 (0·40–0·87) in CORIVA. A slightly stronger preventative effect was seen for the first dose of BNT162b2 than for ChAdOx1 (sHR 0·85 [0·60–1·20] in CPRD GOLD and 0·84 [0·74–0·94] in CPRD AURUM).

Interpretation Vaccination against COVID-19 consistently reduced the risk of long COVID symptoms, which highlights the importance of vaccination to prevent persistent COVID-19 symptoms, particularly in adults.



Introduction

The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications

OPEN ACCESS

Original research

The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/heartjnl-2023-323483).

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ABSTRACT

Objective To study the association between COVID-19 vaccination and the risk of post-COVID-19 cardiac and thromboembolic complications.

Methods We conducted a staggered cohort study based on national vaccination campaigns using electronic health records from the UK, Spain and Estonia. Vaccine rollout was grouped into four stages with predefined enrolment periods. Each stage included all individuals eligible for vaccination, with no previous SARS-CoV-2 infection or COVID-19 vaccine at the start date. Vaccination status was used as a time-varying exposure. Outcomes included heart failure (HF), venous thromboembolism (VTE) and arterial thrombosis/thromboembolism (ATE) recorded in four time windows after SARS-CoV-2 infection: 0–30, 31–90, 91–180 and 181–365 days. Propensity score overlap weighting and empirical calibration were used to minimise observed and unobserved confounding, respectively. Fine-Gray models estimated subdistribution hazard ratios (sHR). Random effect meta-analyses were conducted across staggered cohorts and databases.

Results The study included 10.17 million vaccinated and 10.39 million unvaccinated people. Vaccination was associated with reduced risks of acute (30-day) and post-acute COVID-19 VTE, ATE and HF: for example, meta-analytic sHR of 0.22 (95% CI 0.17 to 0.29), 0.53 (0.44 to 0.63) and 0.45 (0.38 to 0.53), respectively, for 0–30 days after SARS-CoV-2 infection, while in the 91–180 days sHR were 0.53 (0.40 to 0.70), 0.72 (0.58 to 0.88) and 0.61 (0.51 to 0.73), respectively.

Conclusions COVID-19 vaccination reduced the risk of post-COVID-19 cardiac and thromboembolic outcomes. These effects were more pronounced for acute COVID-19 outcomes, consistent with known reductions in disease severity following breakthrough versus unvaccinated SARS-CoV-2 infection.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ COVID-19 vaccines proved to be highly effective in reducing the severity of acute SARS-CoV-2 infection.
⇒ While COVID-19 vaccines were associated with increased risk for cardiac and thromboembolic events, such as myocarditis and thrombosis, the risk of complications was substantially higher due to SARS-CoV-2 infection.

WHAT THIS STUDY ADDS

⇒ COVID-19 vaccination reduced the risk of heart failure, venous thromboembolism and arterial thrombosis/thromboembolism in the acute (30 days) and post-acute (31 to 365 days) phase following SARS-CoV-2 infection. This effect was stronger in the acute phase.
⇒ The overall additive effect of vaccination on the risk of post-vaccine and/or post-COVID thromboembolic and cardiac events needs further research.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ COVID-19 vaccines proved to be highly effective in reducing the risk of post-COVID cardiovascular and thromboembolic complications.

Check for updates

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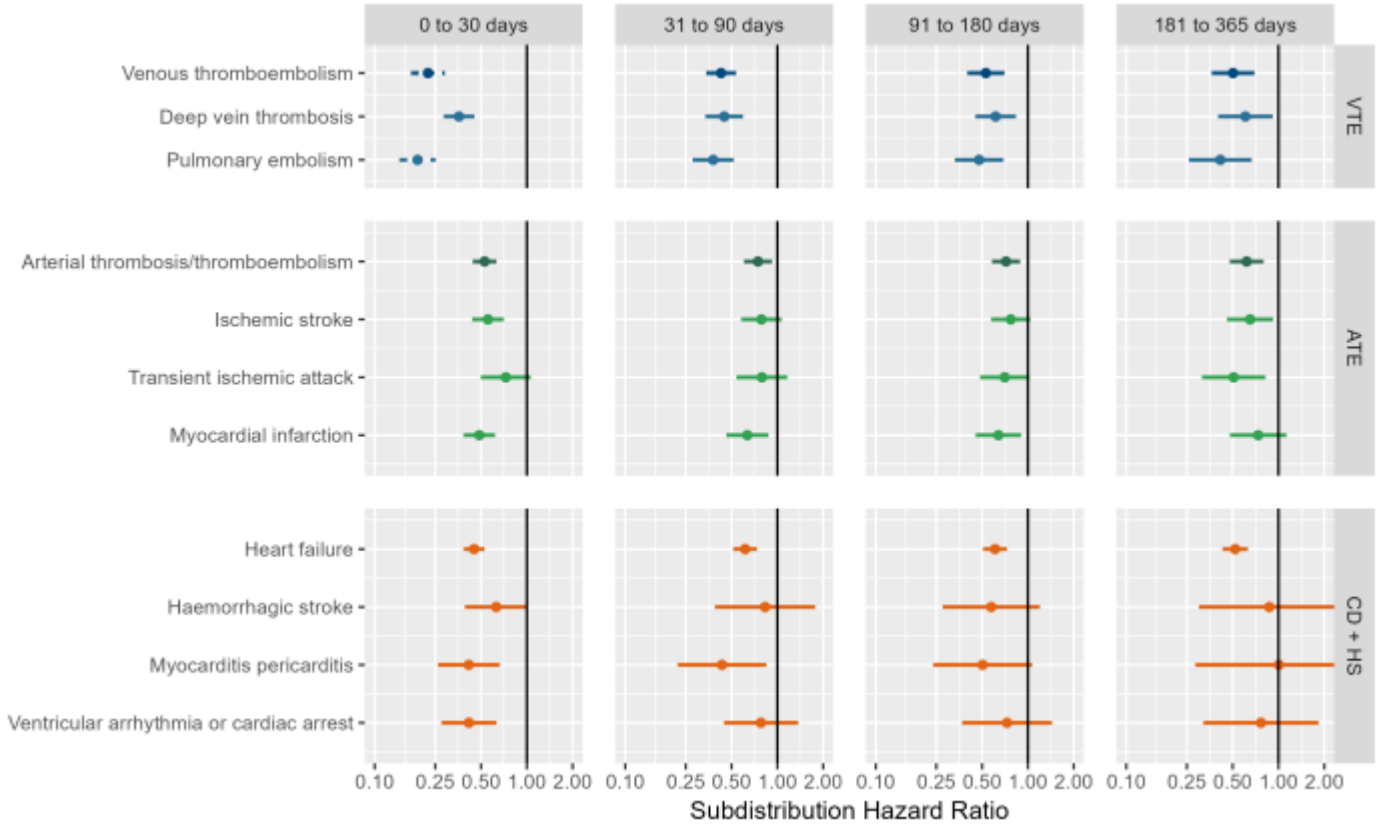
INTRODUCTION

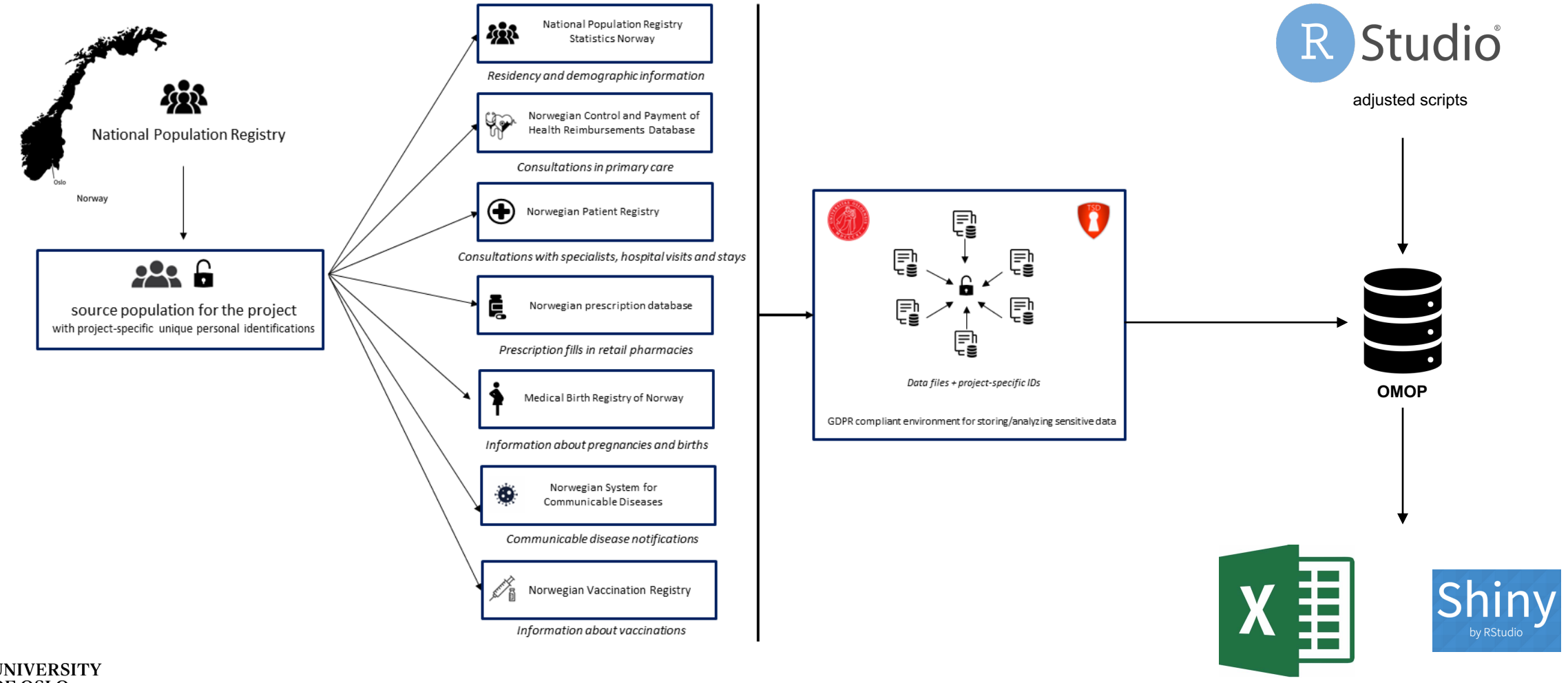
COVID-19 vaccines were approved under emergency authorisation in December 2020 and showed high effectiveness against SARS-CoV-2 infection, COVID-19-related hospitalisation and death.[1 2] However, concerns were raised after spontaneous reports of unusual thromboembolic events following adenovirus-based COVID-19 vaccines, an association that was further assessed in observational studies.[3 4] More recently, mRNA-based vaccines were found to be associated with a risk of rare myocarditis events.[5 6]

On the other hand, SARS-CoV-2 infection can trigger cardiac and thromboembolic complications.[7 8] Previous studies showed that, while slowly decreasing over time, the risk for serious complications remain high for up to a year after infection.[9 10] Although acute and post-acute cardiac and thromboembolic complications following COVID-19 are rare, they present a substantial burden to the



Replication using Norwegian Linked Health Registries

Description of data source and study pipeline



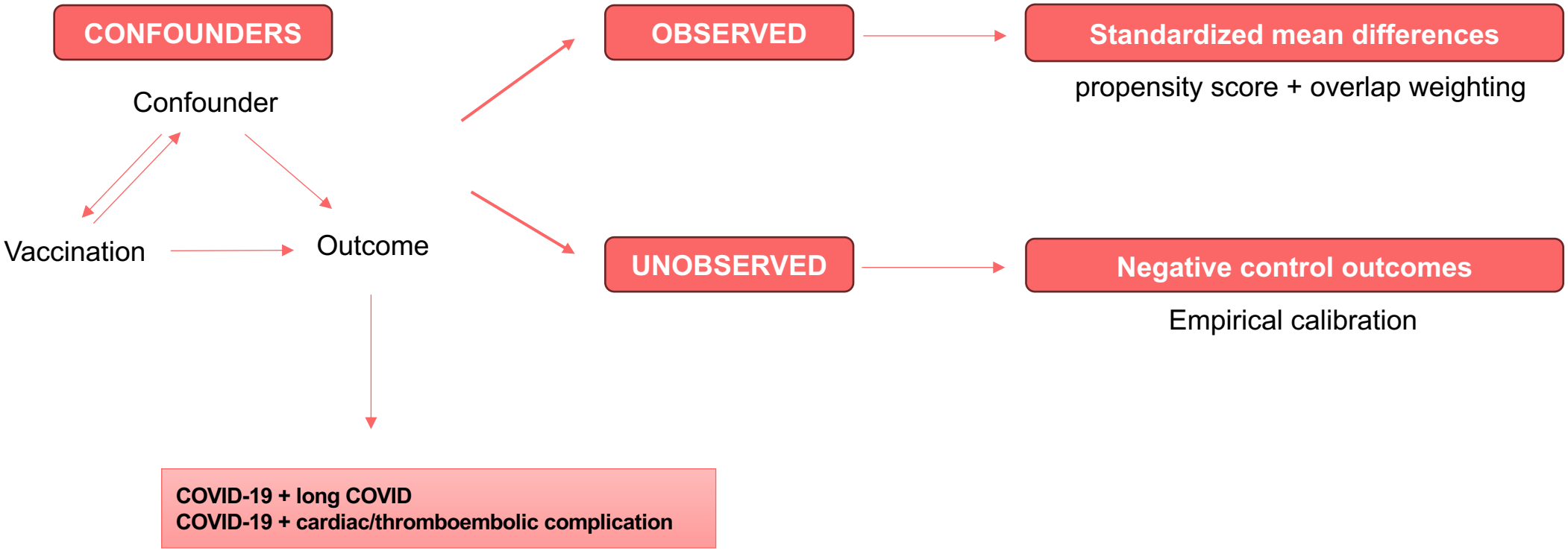
Norwegian vaccination campaign rollout

Replication using Norwegian Linked Health Registries

	NORWAY		
	Priority group	**Operationalized**	**Enrolment windows***
	1) Nursing homes		excluded as probably vaccinated before 09/01/2021 [Nursing home residents vaccinated by week 2] Misclassification for HC workers likely
	2) Healthcare workers		
Study 1	3) Age ≥ 85years	Age ≥ 75 years	09/01/2021 - 12/03/2021 [Week 2 - Week 11]
	4) Age 75-84 years		
Study 2	5) Age: 65-75 years, and 18-64 years with high risk	Age ≥ 65 years and ≥ 18 years with high risk	13/03/2021 - 16/04/2021 [Week 12 - Week 16]
Study 3	6) Age: 55-64 years with underlying conditions	Age ≥ 18 years with underlying conditions	17/04/2021 - 07/05/2021 [Week 16 - Week 19]
	7) Age: 45-54 years with underlying conditions		
	8) Age: 18-44 years with underlying conditions		
Study 4	9) 55-64 years	Age ≥ 18 years	08/05/2021 - 06/08/2021 [Week 19 - Week 32]
	10) 45-54 years		
	11) 18-44 years		

Method

By Núria Mercadé Besora



https://github.com/oxford-pharmacoepi/LongcovidVaccineEffectiveness
https://github.com/oxford-pharmacoepi/vaccineEffectOnPostCovidCardiacThromboembolicEvents

Results

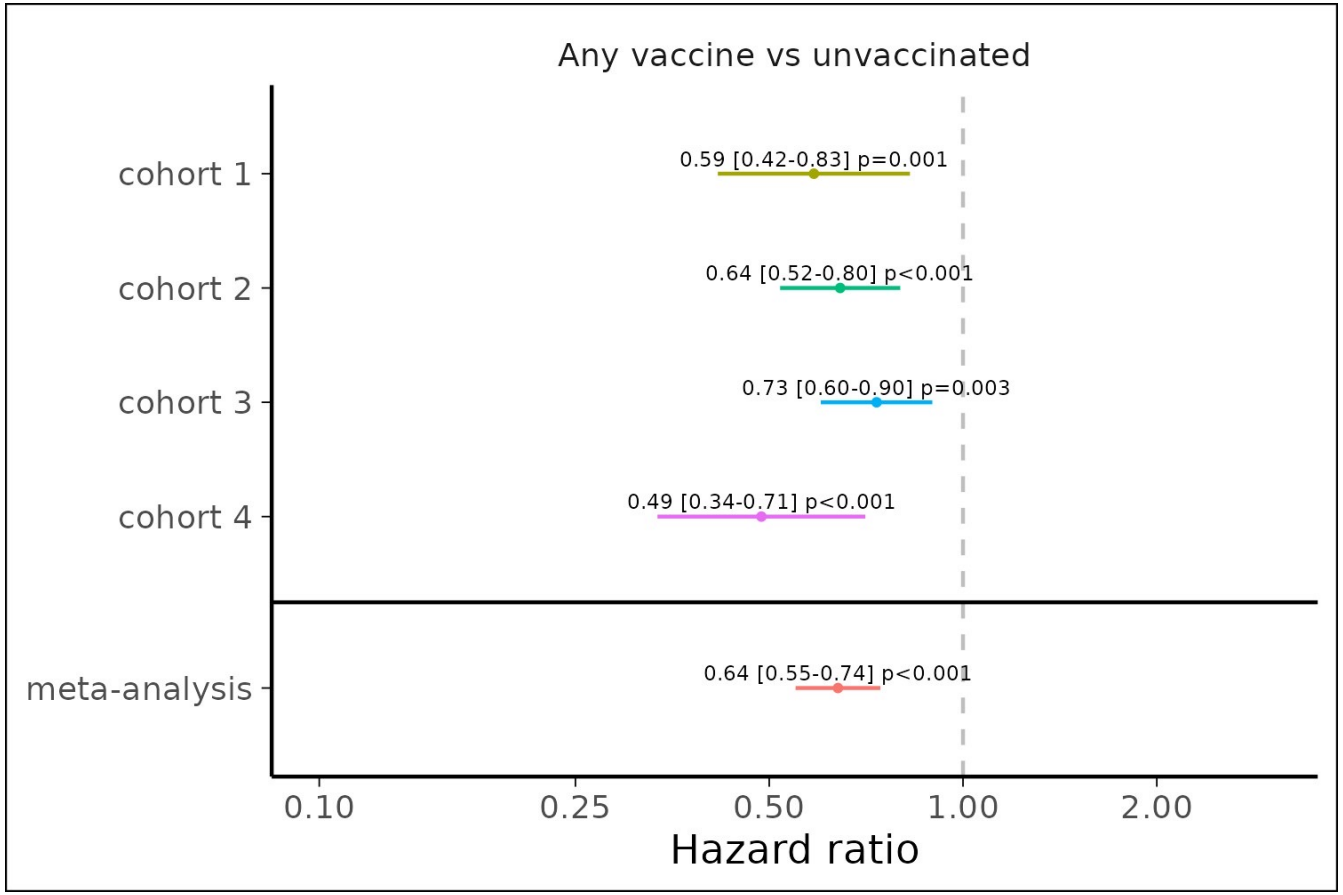
Record counts

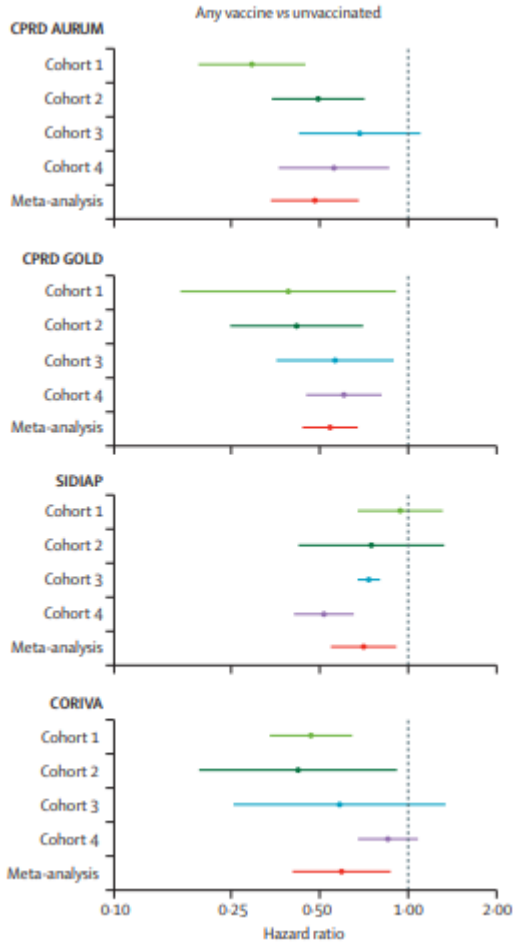
Database name	Staggered cohort	Vaccinated			Unvaccinated		
		Individuals (N)	COVID-19 (N)	LongCOVID-19 (N (%))	Individuals (N)	COVID-19 (N)	LongCOVID-19 (N (%))
NLHR@UiO							
	Cohort 1*	197,174	782	168 (21.48%)	224,223	4,113	751 (18.26%)
	Cohort 2	434,723	3,266	520 (15.92%)	321,977	7,000	643 (9.19%)
	Cohort 3	263,057	2,814	370 (13.15%)	438,151	18,544	1,267 (6.83%)
	Cohort 4	1,469,697	39,210	518 (1.32%)	548,584	41,971	261 (0.62%)

*Cohort 1-2-3-4 include individuals with age ≥ 75 years, age ≥ 65 years and ≥ 18 years with high risk for severe SARS-CoV-2 infection, age ≥ 18 years with underlying conditions and age ≥ 18 years without history of SARS-CoV-2 infection or COVID-19 vaccination, respectively

Results

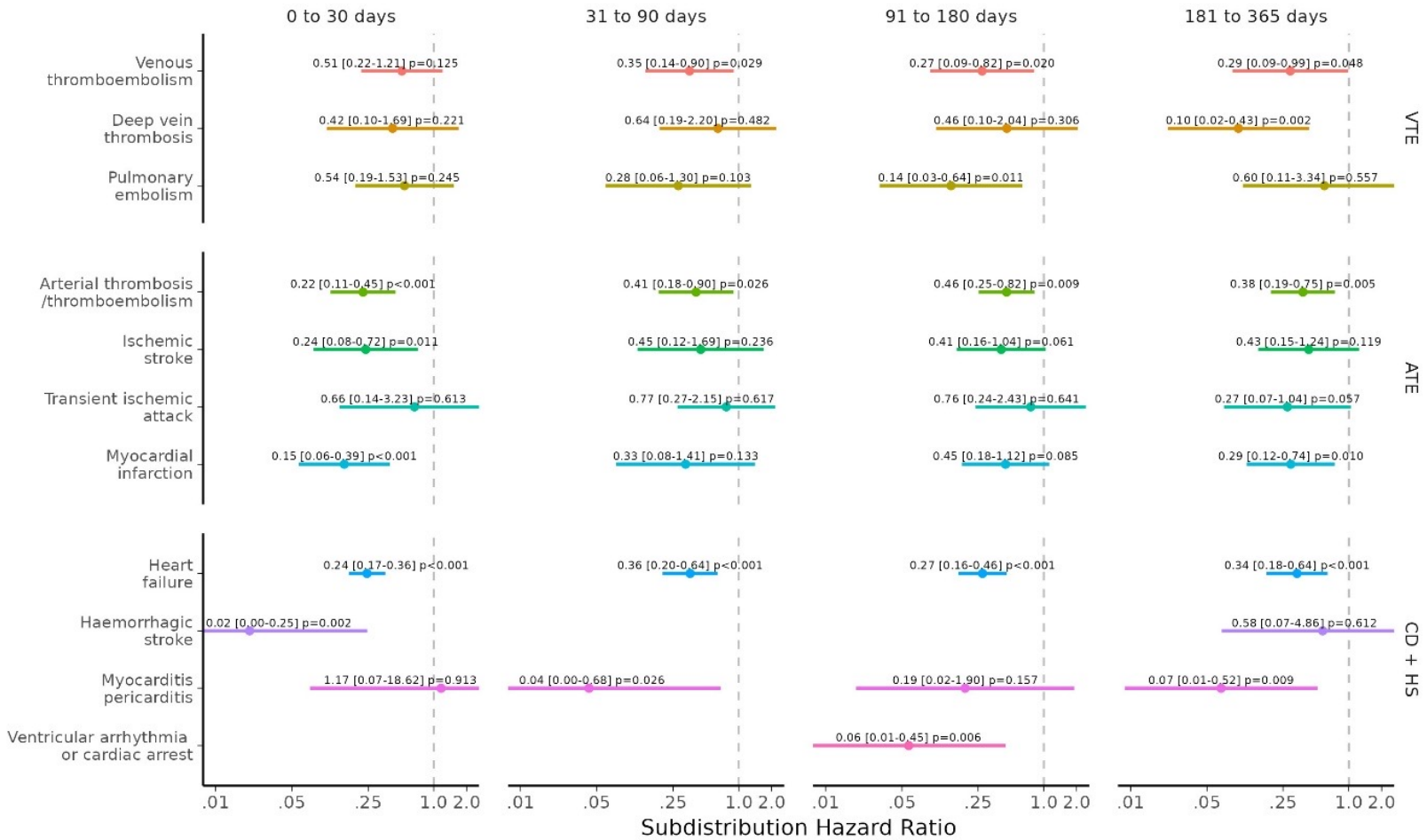
Effectiveness against long COVID





Results

Effectiveness against post COVID thromboembolic and cardiovascular complications



Conclusion

- vaccination with any COVID-19 vaccine reduced the risk of developing long COVID symptoms across all study cohorts: meta-analytic sHR=0.64 [95%CI: 0.55-0.74]
- vaccination was associated with reduced risk of various post COVID thromboembolic and cardiovascular complications during both acute (0-30 days) and post-acute (31-90 days and 91-180 days) phases

consistent with previous findings from other countries

usefulness of federated analytics pipeline with data in OMOP CDM

Study team

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