

## TITLE PAGE

### Manuscript title

Association of COVID-19 vaccines ChAdOx1 and BNT162b2 with major venous, arterial, and thrombocytopenic events: whole population cohort study in 46 million adults in England

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## ABSTRACT

**Importance:** Thromboses after the COVID-19 vaccine ChAdOx1-S have been reported. Better understanding of population-level thrombotic risks after COVID-19 vaccination is needed.

**Objective:** Quantify associations of vaccination with ChAdOx1-S and BNT162b2 with major arterial, venous and thrombocytopenic events.

**Design:** Cohort study based on linked electronic health records, with follow up from December 8<sup>th</sup>, 2020, to March 18<sup>th</sup>, 2021.

**Setting and participants:** Adults registered with an NHS general practice in England and alive on December 8<sup>th</sup>, 2020.

**Exposures:** First dose of vaccination with ChAdOx1-S and BNT162b2.

**Main Outcomes and Measures:** Incidence rates and hazard ratios (HRs) for major arterial, venous and thrombocytopenic outcomes 1-28 and >28 days after first vaccination with ChAdOx1-S or BNT162b2 vaccine. Analyses were performed separately for ages <70 and ≥70 years, and adjusted for age, sex, comorbidities, and social and demographic factors.

**Results:** Of 46,162,942 adults, 21,193,814 (46%) had their first vaccination during follow-up. Adjusted HRs 1-28 days after ChAdOx1-S, compared with pre-vaccination rates, at ages <70 and ≥70 respectively, were 0.97 (95% CI: 0.90-1.05) and 0.58 (0.53–0.63) for venous thromboses, and 0.90 (0.86-0.95) and 0.76 (0.73-0.79) for arterial thromboses. Corresponding HRs for BNT162b2 were 0.81 (0.74–0.88) and 0.57 (0.53–0.62) for venous thromboses, and 0.94 (0.90-0.99) and 0.72 (0.70-0.75) for arterial thromboses. HRs for thrombotic events were higher at younger ages for venous thromboses after ChAdOx1-S, and for arterial thromboses after both vaccines.

Rates of intracranial venous thrombosis (ICVT) and thrombocytopenia in adults aged <70 years were higher 1-28 days after ChAdOx1-S (adjusted HRs 2.27, 95% CI:1.33–3.88 and 1.71, 1.35–2.16 respectively), but not after BNT162b2 (0.59, 0.24–1.45 and 1.00, 0.75–1.34) compared with pre-vaccination. The corresponding absolute excess risks of ICVT 1-28 days after ChAdOx1-S were 0.9–3 per million, varying by age and sex.

### Conclusions and Relevance:

Increases in ICVT and thrombocytopenia after ChAdOx1-S vaccination in adults aged <70 years are small compared with its effect in reducing COVID-19 morbidity and mortality, although more precise estimates for adults <40 years are needed. For people aged ≥70 years, rates of arterial or venous thrombotic, events were generally lower after either vaccine.

## INTRODUCTION

In late February 2021 several groups reported a rare syndrome of thrombosis and thrombocytopenia after vaccination against severe acute respiratory syndrome coronavirus-2 disease 2019 (COVID-19) with ChAdOx1-S (developed by Oxford-AstraZeneca).<sup>1-3</sup> Thromboses were found in unusual sites such as the cerebral venous sinuses, or mesenteric or portal veins. This syndrome, named ‘vaccine-induced immune thrombotic thrombocytopenia’ (VITT), is probably due to an autoimmune response to platelet factor 4 (PF4) in the absence of exposure to heparin.<sup>1</sup> Whether the risk of common thrombotic illnesses is also increased post-vaccination is uncertain, although there have been reports of post-vaccination ischaemic stroke and intracerebral haemorrhage.<sup>1,3,4</sup>

Estimates of vaccine-associated excess risk based on case reports and routine reporting may be biased if diagnostic thresholds vary between vaccinated and unvaccinated individuals or there is less than population-wide coverage. In England, the National Health Service (NHS) provides almost all healthcare; therefore, linked health care records provide comprehensive, population-wide data on outcomes before and after vaccination.<sup>5</sup> Vaccination in England began on December 8<sup>th</sup> 2020: the first groups vaccinated were care home residents, then those aged  $\geq 80$  years and frontline health and social care workers. Those clinically extremely vulnerable were invited alongside people aged  $\geq 70$  years, and those with other co-morbidities aged  $< 65$  alongside people aged  $> 65$  years. Consequently, vaccinated individuals are expected to have higher rates of venous and arterial events.

We conducted a cohort study using routinely collected, linked health data from multiple sources, covering almost the entire English adult population ( $> 46$  million). Associations of ChAdOx1-S and BNT162b2 (developed by Pfizer–BioNTech) with major venous and arterial events and thrombocytopenic haematological outcomes were estimated from the start of the vaccination program to mid-March 2021, before VITT surveillance was widespread.

## **METHODS**

### **Population**

The study population was adults (aged  $\geq 18$  years), alive and registered with an English NHS general practice on December 8th 2020. The data resource<sup>5</sup> includes primary care data (GPES data for Pandemic Planning and Research, GDPDR) from 98% of general practices linked at individual-level to nationwide secondary care data including all NHS hospital admissions (Hospital Episode Statistics (HES) and Secondary Uses Service (SUS) data from 1997 onwards), COVID-19 laboratory testing data, COVID-19 vaccination data (NHS England immunisation management system), national community drug dispensing data (NHS BSA Dispensed Medicines from 2018) and death registrations. We accessed and analysed pseudonymised data within NHS Digital's secure, privacy protecting Trusted Research Environment.<sup>6</sup>

### **Covariates**

Covariates were defined from primary care, hospital admissions, community drug dispensing and COVID-19 laboratory testing data, using phenotyping algorithms verified by specialist physicians (see supplementary data). Phenotypes for comorbidities, risk factors and other covariates used Systematized Nomenclature of Medicine Clinical Terms (SNOMED-CT) concepts for primary care data, and ICD-10 codes for hospital admission data. Sex, age, region, deprivation and smoking status were defined as the latest recorded in primary care records before 8<sup>th</sup> December 2020, and the most recently recorded ethnicity in either primary care or hospital admissions records was used. History of diabetes, depression, obesity, cancer, chronic obstructive pulmonary disease, chronic kidney disease, stroke, MI, DVT or PE, cancer, thrombophilia, liver disease or dementia were defined as any record in primary care and/or hospital admission data before December 8th 2020. The number of unique diseases in SNOMED-CT for the year before December 8<sup>th</sup> 2020 were derived from primary care records and major surgery in the previous year from hospital admission records (using the Office of Population Censuses and Surveys classification of surgical procedures).

A history of coronavirus (SARS-CoV2) infection was defined as either a positive COVID-19 antigen test in national laboratory data covering swab tests performed in the general population and hospitals or a confirmed COVID-19 diagnosis in primary care or hospital admission records. Prior medication was defined using community dispensing data on all prescriptions dispensed by community pharmacists, appliance contractors, and doctors in England. British National Formulary (BNF) codes were used to define the total number of types of medication prescribed and dispensed in the following groups: antiplatelets, antihypertensives, lipid lowering agents, oral anticoagulants, combined oral contraceptives, and hormone replacement therapy.

### **Outcomes**

Outcomes were derived from primary care data, hospital admission data (SUS dataset) and the national death registry (see supplementary material).<sup>7</sup> Specialist clinician-verified SNOMED-CT and ICD-10 rule-based phenotyping algorithms were used to define fatal or non-fatal (i) arterial thrombotic events: myocardial infarction (MI), ischaemic stroke (ischaemic or unclassified stroke, spinal stroke or retinal infarction), other non-stroke non-MI arterial thrombo-embolism; (ii) venous thrombo-embolic events: pulmonary embolism (PE), lower limb deep venous thrombosis (DVT), intracranial venous thrombosis (ICVT), portal vein thrombosis, and venous thrombosis

at other sites; (iii) thrombocytopenic haematological events: any thrombocytopenia (idiopathic, primary, secondary or unspecified), disseminated intravascular coagulation (DIC), and thrombotic thrombocytopenic purpura (TTP); (iv) death from any cause; (v) other vascular outcomes: haemorrhagic stroke (intracerebral or subarachnoid), and mesenteric thrombus for which available codes did not distinguish between arterial or venous causes; and (v) lower limb fracture as a control condition unlikely to be affected by vaccination. The event date was the earliest of: start of hospital episode, death, or recorded date of primary care event or consultation. Events within the death registry were identified based on underlying cause of death and in hospital admission data based on the primary cause of the care episode.

### Statistical analyses

Data were analysed according to a pre-specified plan, published on GitHub on April 27<sup>th</sup> 2021.<sup>8</sup> Follow-up was from December 8<sup>th</sup> 2020 to March 18<sup>th</sup> 2021, the date the European Medicine Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) discussed the first reported complications of vaccination, after which diagnostic effort is expected to be concentrated in people receiving ChAdOx1-S.<sup>9</sup> Any cell numbers <5 and any potentially disclosive numbers <10 are not reported exactly but as <5 and <10 respectively.

Follow up time for each person was split into periods before, and 1-28 and >28 days after, first vaccination. Censoring was at the earliest of the outcome, death, March 18<sup>th</sup> 2021 and, in analyses of specific vaccines, receipt of the other vaccine. Incidence rates per 100,000 people per year were estimated for each outcome, before and 1-28 and >28 days after vaccination.

Cox models with time zero December 8<sup>th</sup> 2020 were fitted, ensuring that all analyses accounted for changes in rates of outcome events with calendar time. Hazard ratios comparing the periods 1-28 and >28 days after vaccination with unvaccinated or pre-vaccination person-time (reference) were estimated. Cox models were fitted separately by age group (<70 and ≥70 years), both overall and separately for males and females. All Cox models were stratified by geographic region. For rare outcomes, sex-specific hazard ratios were estimated from vaccine-sex interaction terms. For computational efficiency, each model included data from all people with, and a 10% random sample of people without, the outcome of interest; analyses incorporated inverse probability weights to account for this sampling. Confidence intervals were derived using robust standard errors.

Region-; age-sex-region-; and fully-adjusted hazard ratios (HR) for associations of ChAdOx1-S and BNT162b2 with outcome events were estimated. The following covariates were included in all fully-adjusted models: (a) sex, age and age<sup>2</sup>, ethnicity, postcode-derived deprivation level; (b) risk factors for venous thromboses (anticoagulant medication, combined oral contraceptive medication, hormone replacement therapy medication, history of PE or DVT, and history of coronavirus infection); (c) risk factors for arterial thromboses (diabetes, hypertension, smoking, antiplatelet medication, blood pressure lowering medication, lipid lowering medication, anticoagulant medication, history of stroke, and history of MI); (d) further covariates selected using a backwards stepwise procedure with p value threshold 0.2, from models using MI as outcome (separately in the four groups defined by age and sex). The covariates had few missing values (apart from ethnicity, for which the 5.9% 'missing' were included as a separate category); hence all analyses used "complete-cases".

Sensitivity analyses examined outcome events recorded as the primary or secondary reason for admission or death in hospital admissions or death records; fatal outcome events (those followed by death from any cause within 28-days); and all venous and all arterial thrombotic outcome events associated with thrombocytopenia. Effect modification by age, sex, ethnicity, medication, diabetes, deprivation and medical history was examined for all venous and all arterial thromboses.

Absolute excess risks of ICVT were estimated by applying estimated hazard ratios to incidence rates of first fatal or non-fatal events in decades of age and sex in 2019, derived from linked hospital and death records.

The study was approved by the Newcastle & North Tyneside 2 Research Ethics Committee (20/NE/0161), the NHS Digital Data Access Request Service (DARS-NIC-381078-Y9C5K) and the British Heart Foundation Data Science Centre CVD-COVID-UK Approvals and Oversight Board.

Data manipulation and analyses used SQL and Python in Databricks and RStudio (Professional) Version 1.3.1093.1 driven by R Version 4.0.3. All code and phenotypes are available at [github.com/BHFDSC/CCU002\\_02](https://github.com/BHFDSC/CCU002_02).

## RESULTS

On December 8<sup>th</sup> 2020, 46,162,942 eligible adults were registered with an English general practice. By March 18<sup>th</sup> 2021, 21,193,814 (46%) had received their first vaccination (8,712,477 BNT162b2; 12,481,337 ChAdOx1-S) (supplementary figure 1). Post-vaccination person years of follow up for ages <40, 40-69 and ≥70 years respectively were, for ChAdOx1-S: 91,206, 417,160 and 401,343 person years; for BNT162b2: 159,856, 427,874, and 583, 890 person years.

The risks per 100,000 from December 8<sup>th</sup> 2020 to March 18<sup>th</sup> 2021 were: any venous thrombosis 45.3, any arterial thrombosis 189; thrombocytopenia 4.2 (Table 1). Risks of venous and arterial thromboses were higher in people with co-morbidities and with increasing age and deprivation, and varied substantially by ethnicity. Absolute and relative increases in risk with increasing age and deprivation were greater for arterial than for venous thromboses. The risk of venous thromboses was higher in people with prior DVT or PE, thrombophilia, or oral anticoagulant medication, while the risk of arterial thromboses was higher in people with prior stroke, MI or antiplatelet medication. The risk of thrombocytopenia increased with age and co-morbidities but varied less markedly with ethnicity and deprivation than the risk of venous or arterial thromboses.

Incidence rates of all events varied substantially pre- and post-vaccination (Table 2). Before vaccination, the incidence rates per 100,000 per year were: all venous thromboses 141 (mostly PE and DVT), ICVT 1.97; portal vein thrombosis 1.15; any arterial thrombosis 549 (with slightly more ischaemic stroke (273) than MI (268)); any thrombocytopenia 13, with very low rates of DIC (0.12) and TTP (0.67). For each vaccine, crude incidence rates of venous and arterial thromboses, haemorrhagic stroke, mesenteric thrombus and thrombocytopenia were higher after than before vaccination in the under 70s, but lower after than before vaccination in the over 70s.

The additional confounding factors selected using backward selection were: for both sexes and age strata, previous diagnosis of cancer, number of unique diseases in the last year, surgery in the last year, obesity, liver disease; additionally for women aged

<70, history of depression and total number of types of medication (by BNF chapters); additionally for men aged <70, history of SARS-CoV2 infection and thrombocytopenia; and additionally for men and women aged  $\geq 70$ , chronic kidney disease and dementia.

Crude hazard ratios were substantially attenuated after adjusting for age, and further attenuated after adjusting for confounding factors. For example, in <70 year-olds the HRs 1-28 days post- versus pre-vaccination were attenuated from 2.81 to 2.27 for ICVT; from 4.85 to 1.71 for thrombocytopenia; and from 3.21 to 0.90 for ischaemic stroke (supplementary table 1).

In people aged <70 years, the fully adjusted HR for any venous thrombosis was 0.97 (95% CI:0.90-1.05) 1–28 days after ChAdOx1-S compared with before vaccination, with similar adjusted HRs for PE and DVT. Compared with before vaccination, the hazard of any venous thrombosis was lower 1-28 days after ChAdOx1-S in people aged  $\geq 70$  (adjusted HR 0.58, 95%CI:0.53–0.63) and 1–28 days after BNT162b2 (<70: HR 0.81, 0.74–0.88;  $\geq 70$  HR: 0.57, 0.53–0.62), with similar adjusted HRs for PE and DVT. (Figure 1, supplementary table 1).

In people aged <70 years, adjusted HRs for ICVT were 2.27 (95%CI: 1.32–3.88) 1-28 days after ChAdOx1-S and 0.59 (0.24–1.45) 1-28 days after BNT162b2. HRs were similar in men and women. In a post-hoc analyses, in people aged <40 years, the HRs 1-28 days after vaccination were 3.73 (1.58–8.83) and 1.07 (0.33–3.48) for ChAdOx1-S and BNT162b2 respectively. The same estimates for people 40-69 years were 1.93 (1.19–2.13) and 0.74 (0.29–1.87). In people aged  $\geq 70$  years, associations of vaccination with ICVT were estimated imprecisely (<10 events for ChAdOx1-S and 8 for BNT162b2 (Figure 1, supplementary table 1).

Adjusted HRs for any arterial thrombosis 1-28 days after ChAdOx1-S were 0.90 (95%CI: 0.86-0.95) and 0.76 (0.73–0.79) in people aged <70 and  $\geq 70$  years respectively. Corresponding HRs 1-28 days after BNT162b2 were 0.94 (0.90-0.99) and 0.72 (0.70–0.75). HRs were similar for MI and ischaemic stroke, and >28 days after vaccination (Figure 2, supplementary table 1).

In people aged <70 years, adjusted HRs for thrombocytopenia were 1.71 (95%CI:1.35–2.16) 1–28 days and 1.69 (1.16–2.46) >28 days after ChAdOx1-S. Corresponding HRs after BNT162b2 were 1.00 (0.75–1.34) and 0.97 (0.66–1.41). For those aged  $\geq 70$  years, adjusted HRs for thrombocytopenia 1-28 days after vaccination were similar for ChAdOx1 (0.79, 95%CI: 0.56–1.10) and BNT162b2 (0.68, 0.51-0.90) (Figure 3, supplementary table 1).

Adjusted HRs for lower limb fracture 1–28 days after ChAdOx1-S were 0.85 (95% CI: 0.77–0.93), and 0.83 (0.78–0.89) in people aged <70 and  $\geq 70$  years respectively. Corresponding HRs after BNT162b2 were 0.93 (0.84–1.02) and 0.69 (0.66–0.73). (Figure 3, supplementary table 1). Adjusted HRs for all-cause mortality 1–28 days after ChAdOx1-S were 0.37 (95%CI: 0.35–0.39), and 0.28 (0.28–0.29) in people aged <70 and  $\geq 70$  years respectively. Corresponding HRs after BNT162b2 were 0.24 (0.22–0.26) and 0.19 (0.19–0.20) (supplementary figure 2, supplementary table 1).

### Subgroup analyses

HRs for all venous and for all arterial thrombotic events 1-28 days after vaccination were lower in older age groups for each vaccine (all interaction p values <0.0001) (supplementary table 2). HRs for venous thromboses were >1 1-28 days after



compared with before vaccination in people aged <50 years for ChAdOx1-S but not BNT162b2. HRs for arterial thromboses were >1 1-28 days after compared with before vaccination in people aged <50 years for both ChAdOx1-S and BNT162b2. A higher proportion of venous thromboses in those aged <40 years compared with those aged ≥40 years were due to ICVT. A higher proportion of arterial thromboses at age <40 was due to stroke than at ages 40–59 and 60–69 years. Less marked trends for lower HRs in older individuals were observed for HRs >28 days after vaccination. Despite modest differences between the magnitude of HRs in subgroups defined by sex, ethnicity, prior COVID, COCP, diabetes, deprivation or history of MI, DVT or PE, anticoagulation or antiplatelet medication, HRs in all of these subgroups were consistent with lower rates of arterial or venous thromboses after vaccination with ChAdOx1-S or BNT162b2.

### **Sensitivity analyses**

When using a less restrictive outcome definition (outcomes recorded as primary or secondary reason for admission), estimated HRs were consistent with those from analyses of outcomes in the primary position (supplementary figure 3). Similarly, estimated HRs for fatal outcomes, were similar to HRs for outcomes in the primary position (supplementary figure 4). There were very few people for whom outcomes in the primary position were recorded as well as thrombocytopenia in any position in the same hospital admission or death record (after ChAdOx1-S and BNT162b2 respectively: ICVT 7 and 0; all arterial thromboses 47 and 58; all venous thromboses 37 and 26).

### **Intracranial venous thrombosis**

Characteristics were similar among patients who developed ICVT while unvaccinated, after ChAdOx1 and after BNT162b2. Most were women (66% unvaccinated, 67% ChAdOx1, 79% BNT162b2), of white ethnicity (75% unvaccinated, 92% ChAdOx1, 100% BNT162b2), and had no prior co-morbidities (71% unvaccinated, 50% ChAdOx1, 50% BNT162b2). Patients with post vaccination ICVT were older than those with pre-vaccination ICVT. Post-vaccination, no patients had a recorded history of thrombophilia, and fewer than 5% had a recorded dispensed prescription of oral contraceptive or HRT (supplementary Table 3).

Applying the HR for ICVT 1-28 days after ChAdOx1 to the monthly incidence of ICVT in 2019, the excess risk of ICVT in the month after vaccination with ChAdOx1 among those aged 19–30, 31–39, 40–49, 50–59 and 60–69-years was estimated to be, respectively: 0.9, 1.1, 1.5, 1.5 and 1.6 per million in men and 3.0, 2.7, 2.0, 1.6 and 1.5 per million in women.

## **DISCUSSION**

In this cohort study, which included almost all adults alive in England at the start of the national COVID-19 vaccination programme, vaccination with ChAdOx1-S, but not BNT162b2, was associated with approximately 2-fold higher rates of ICVT and hospitalisations due to thrombocytopenia in people aged under 70 years, after adjusting for a comprehensive range of demographic characteristics and comorbidities. The corresponding absolute increases in the risk of these events were very small. ChAdOx1-S and BNT162b2 were associated with lower hazards of major vascular events after vaccination in those aged ≥70 years. Analyses stratified by age

suggest that in people aged <50 years, rates of venous thromboses were higher 1-28 days after vaccination with ChAdOx1-S, and that rates of arterial thrombotic events were higher 1-28 days after vaccination with ChAdOx1-S or BNT162b2, compared with rates in unvaccinated people.

The large population analysed (including almost 10 times as many vaccinated people as any other published study) adds substantial precision to estimated associations of thromboses with vaccination, which is of particular importance for very rare events and associations in subgroups. The extensive data linkages across different healthcare settings enabled adjustment for a wide range of confounding variables. The analysed population is slightly larger than the mid-year estimate of the 2020 English population aged  $\geq 18$  (44,456,850) that excluded short-term residents and students, and modelled international migrant numbers.<sup>10</sup>

Smaller Danish and Norwegian electronic health record studies reported a small excess of intracranial haemorrhage (2 per 100,000 1–28 days after ChAdOx1-S), cerebral venous thrombosis (3 per 100,000) and other venous thrombosis (2 per 100,000).<sup>11</sup> The randomised trials of ChAdOx1-S, reported no venous thrombotic events among 8597 participants who received the vaccine versus two among 8581 who received placebo.<sup>12</sup> A Scottish study found a risk of 1.13 (0.62–1.63) cases of idiopathic thrombocytopenic purpura per 100,000 after ChAdOx1-S. There was no clear evidence on other outcomes, although the number of post-vaccine events was small.<sup>13</sup> Reporting of ICVT cases to the UK Medicines and Healthcare products Regulatory Agency (MHRA) identified more cases of ICVT with thrombocytopenia after ChAdOx1-S than the present study (44 up to 31<sup>st</sup> March 2021).<sup>14</sup>

Healthcare systems planning to use ChAdOx1-S should balance the very small harms against the known benefits of the vaccine. For older populations, who are most vulnerable to COVID-19, we found no evidence of increased risk of any event with ChAdOx1-S. In younger populations, who have a lower morbidity and mortality due to COVID-19, other available vaccines might be prioritise, especially when the risk of COVID-19 is otherwise low.

Our study has several limitations. First, identification of exposures, covariates and outcomes relies on the accuracy of data collected during routine healthcare. Additional data on results of laboratory and radiology investigations would have improved diagnostic coding, particularly for ascertainment of thrombocytopenia. Second, people who were not registered with an NHS GP (for example the homeless, recent immigrants, those using only private healthcare and those not eligible for NHS care) or who opted out of their data being provided to NHS Digital were excluded. Third, follow up ended on March 18<sup>th</sup> 2021, but a small number of events that occurred before this date may have been excluded because they had yet to be coded or the people affected were still in hospital. Analyses after this date will likely lead to overestimation of associations, because speciality societies recommended further investigations of mild symptoms in vaccinated populations. Fourth, our primary outcome used the primary reason for death or hospital admission, which improves the positive predictive value but may lead to an underestimation of incidence. This is necessary because historical non-incident events are frequently recorded in secondary positions. Analyses of events recorded in any position as fatal within 28 days were consistent with the primary analyses. Fifth, we did not address time-varying confounding, which can occur when factors which vary during follow up, such as admission to hospital, predict both vaccination and outcomes of interest. Sixth, comparison of adjusted and

unadjusted associations suggests that studies that do not adjust for a comprehensive range of potential confounders will overestimate the thrombotic effects of vaccination. However, adjusted associations in this study may still be biased by unmeasured confounding by patient characteristics that predict both vaccination and thromboses and that are difficult to ascertain in electronic health records. Examples include general health at the time of vaccination, and people at higher risk of thromboses (e.g. with end-stage diseases).<sup>15</sup> There were slightly lower post-vaccination rates of the 'negative control' outcome lower limb fracture in those aged  $\geq 70$  years, which implies that this degree of unmeasured confounding may affect results for thrombotic outcomes in that age group.

Associations of vaccination with thromboses varied with age. This may be because in older people small increases in the risk of major thrombotic events after vaccination with ChAdOx1-S were more than offset by reductions in major thrombotic events (particularly PE) subsequent to COVID-19. By contrast, in younger people any increase in risk associated with ChAdOx1-S vaccine is less likely to be offset by a lower risk of COVID-associated thrombosis, because the chance of severe COVID disease is lower in younger than older individuals.

Further analyses assessing the effects of other vaccines and the effects of second doses of these vaccines on thrombotic, neurological and cardiac complications will be important to inform vaccination programs. Access to data from radiology or laboratory systems (which in the UK will rely on regional rather than national data collection systems) will allow more comprehensive case ascertainment and more granular phenotyping. Such efforts are currently underway across the UK.

## DATA SHARING

The de-identified data used in this study is available via the CVD-COVID-UK consortium coordinated by BHF Data Science Centre (<https://www.hdruc.ac.uk/projects/cvd-covid-uk-project/>) for accredited researchers working on approved projects in the NHS Digital trusted research environment. The study protocol, analytic and phenotyping code is available at: [https://github.com/BHFDSC/CCU002\\_02](https://github.com/BHFDSC/CCU002_02)

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### **Conflicts of interest**

None

### **CONTRIBUTIONS**

WW chaired the writing committee. WW, CS, JS and AW conceived the idea, and prepared the protocol and drafted the manuscript. SI, JAC, SK, VW, TB, RD and JS wrote the analytic code. VW, JAC, SK and SI prepared analytic code for open access publication. SI, VW and TB prepared the tables and figures. EO and SH prepared data from NHS Digital. SD, SK and WW prepared phenotype code. AW and JS designed and supervised the statistical analyses. CS is the Director of the BHF Data Science Centre and coordinated approvals for and access to data within the NHS Digital TRE. All authors commented on the protocol, analyses, and manuscript, and approved the final version before submission. All authors had full access to the study data.

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## TABLES

Table 1 Numbers of patients analysed and (in parentheses) risk per 100,000 of venous and arterial events and thrombocytopenia (TCP) during follow up, overall and according to age.

Table 2 Numbers of events and incidence rates pre and post first vaccination. Incidence rate per 100,000 per annum (a) ChAdOx1-S (b) BNT162b2 vaccine

## FIGURE LEGENDS

**Figure 1** Adjusted Hazard ratios for all venous thromboses, intracranial venous thromboses, pulmonary embolism and deep vein thromboses after ChAdOx1-S or BNT162b2 vaccine.

**Figure 2** Adjusted hazard ratios for all arterial thromboses, myocardial infarction, ischaemic stroke and other arterial thromboses after ChAdOx1-S or BNT162b2 vaccine.

**Figure 3** Adjusted hazard ratios for thrombocytopenia haemorrhagic stroke, mesenteric thrombosis, lower limb fracture after ChAdOx1-S or BNT162b2 vaccine

## SUPPLEMENTARY MATERIAL

Protocol

**Supplementary table 1** Unadjusted, age-, sex- and region- adjusted, and fully adjusted hazard ratios for (a) ChAdOx1-S (b) BNT162b2 vaccine

**Supplementary table 2** Stratum specific estimates for (a) venous and (b) arterial events.

**Supplementary table 3.** Characteristics of patient who had an ICVT event before and after vaccination. Only percentage are presented, as disclosure control does not allow numbers <5 to be released

**Supplementary figure 1:** Cumulative frequency of vaccines of different types during follow up

**Supplementary figure 2:** Adjusted hazard ratios for portal vein thrombosis, other venous events, and death after ChAdOx1-S or BNT162b2 vaccine

**Supplementary Figure 3** Hazard ratios for major (A) arterial and (B) venous thrombotic events, and (C) haematological events, other events and lower limb fractures recorded in any position in EHR

**Supplementary Figure 4:** Hazard ratios for major (A) arterial and (B) venous thrombotic events, (C) haematological events, other events and fractures recorded in death record or in hospital record in first position followed by death <28 days



**Table 1. Numbers of patients analysed (in parentheses) risk per 100,000 of venous and arterial events and thrombocytopenia (TCP), overall and according to age.**

		Overall				Age, <70				Age, ≥70			
		All	Venous	Arterial	TCP	All	Venous	Arterial	TCP	All	Venous	Arterial	TCP
N		46162942	20903 (45.3)	87251 (189)	1926 (4.2)	38744171	11835 (30.5)	38283 (98.8)	1167 (3.0)	7418771	9068 (122)	48968 (660)	759 (10.2)
Sex	Male	22765779	10358 (45.5)	51851 (228)	986 (4.3)	19425454	6406 (33.0)	26549 (137)	555 (2.9)	3340325	3952 (118)	25302 (757)	431 (12.9)
	Female	23397163	10545 (45.1)	35400 (151)	940 (4.0)	19318717	5429 (28.1)	11734 (60.7)	612 (3.2)	4078446	5116 (125)	23666 (580)	328 (8.0)
Age	18 - 29	8821973	781 (8.9)	400 (4.5)	143 (1.6)	8821973	781 (8.9)	400 (4.5)	143 (1.6)				
	30 - 49	16131025	3544 (22.0)	6424 (39.8)	338 (2.1)	16131025	3544 (22.0)	6424 (39.8)	338 (2.1)				
	50 - 69	13791173	7510 (54.5)	31459 (228)	686 (5.0)	13791173	7510 (54.5)	31459 (228)	686 (5.0)				
	70 - 79	4674973	4820 (103)	22249 (476)	418 (8.9)					4674973	4820 (103)	22249 (476)	418 (8.9)
	80+	2743798	4248 (155)	26719 (974)	341 (12.4)					2743798	4248 (155)	26719 (974)	341 (12.4)
Ethnicity	Asian or Asian British	3718442	599 (16.1)	5325 (143)	152 (4.1)	3467223	475 (13.7)	3378 (97.4)	125 (3.6)	251219	124 (49.4)	1947 (775)	27 (10.7)
	Black or Black British	1634470	654 (40.0)	2086 (128)	58 (3.5)	1525603	513 (33.6)	1384 (90.7)	45 (2.9)	108867	141 (130)	702 (645)	13 (11.9)
	Mixed	712534	182 (25.5)	642 (90.1)	22 (3.1)	682037	153 (22.4)	426 (62.5)	19 (2.8)	30497	29 (95.1)	216 (708)	3 (9.8)
	Other ethnic groups	1497133	217 (14.5)	1072 (71.6)	39 (2.6)	1427187	162 (11.4)	678 (47.5)	33 (2.3)	69946	55 (78.6)	394 (563)	6 (8.6)
	White	36446855	18995 (52.1)	77118 (212)	1643 (4.5)	29619868	10362 (35.0)	31821 (107)	939 (3.2)	6826987	8633 (126)	45297 (663)	704 (10.3)
	Unknown or missing	2153508	256 (11.9)	1008 (46.8)	12 (0.6)	2022253	170 (8.4)	596 (29.5)	6 (0.3)	131255	86 (65.5)	412 (314)	6 (4.6)
Deprivation <sup>1</sup>	1 - 2	9118746	4565 (50.1)	18830 (206)	365 (4.0)	8069275	3064 (38.0)	10493 (130)	272 (3.4)	1049471	1501 (143)	8337 (794)	93 (8.9)
	3 - 4	9567633	4105 (42.9)	17436 (182)	370 (3.9)	8273028	2454 (29.7)	8370 (101)	234 (2.8)	1294605	1651 (128)	9066 (700)	136 (10.5)
	5 - 6	9355549	4091 (43.7)	17642 (189)	392 (4.2)	7784840	2235 (28.7)	7263 (93.3)	221 (2.8)	1570709	1856 (118)	10379 (661)	171 (10.9)
	7 - 8	9076313	4146 (45.7)	16939 (187)	381 (4.2)	7362375	2128 (28.9)	6334 (86.0)	221 (3.0)	1713938	2018 (118)	10605 (619)	160 (9.3)
	9 - 10	8772902	3926 (44.8)	16024 (183)	406 (4.6)	7000538	1908 (27.3)	5602 (80.0)	210 (3.0)	1772364	2018 (114)	10422 (588)	196 (11.1)
Smoking status	Current	7814045	3079 (39.4)	16115 (206)	260 (3.3)	7287225	2492 (34.2)	11811 (162)	219 (3.0)	526820	587 (111)	4304 (817)	41 (7.8)
	Former	10623072	6930 (65.2)	31768 (299)	581 (5.5)	7826062	3233 (41.3)	11703 (150)	277 (3.5)	2797010	3697 (132)	20065 (717)	304 (10.9)
	Never	25722494	10667 (41.5)	38701 (150)	1053 (4.1)	21674974	5929 (27.4)	14346 (66.2)	643 (3.0)	4047520	4738 (117)	24355 (602)	410 (10.1)
Medical history	Stroke	727218	1020 (140)	21489 (2955)	104 (14.3)	286650	323 (113)	8147 (2842)	40 (14.0)	440568	697 (158)	13342 (3028)	64 (14.5)
	MI	1189182	1436 (121)	24212 (2036)	158 (13.3)	485506	436 (89.8)	10486 (2160)	46 (9.5)	703676	1000 (142)	13726 (1951)	112 (15.9)
	DVT or PE	603351	3263 (541)	4050 (671)	142 (23.5)	341788	1919 (561)	1377 (403)	76 (22.2)	261563	1344 (514)	2673 (1022)	66 (25.2)
	Thrombophilia	44593	146 (327)	202 (453)	23 (51.6)	38136	126 (330)	144 (378)	21 (55.1)	6457	20 (310)	58 (898)	2 (31.0)
	Coronavirus infection <sup>2</sup>	1284984	1131 (88.0)	4167 (324)	101 (7.9)	1124135	576 (51.2)	1642 (146)	63 (5.6)	160849	555 (345)	2525 (1570)	38 (23.6)
	Diabetes	4069412	3654 (89.8)	25595 (629)	423 (10.4)	2460649	1509 (61.3)	9949 (404)	205 (8.3)	1608763	2145 (133)	15646 (973)	218 (13.6)
	Depression	9516020	6272 (65.9)	24146 (254)	500 (5.3)	8040590	4077 (50.7)	12859 (160)	348 (4.3)	1475430	2195 (149)	11287 (765)	152 (10.3)
	Obesity	10918274	8863 (81.2)	31194 (286)	679 (6.2)	8757004	5430 (62.0)	15848 (181)	411 (4.7)	2161270	3433 (159)	15346 (710)	268 (12.4)
	Cancer	6609691	5674 (85.8)	17827 (270)	786 (11.9)	4854822	2583 (53.2)	4462 (91.9)	412 (8.5)	1754869	3091 (176)	13365 (762)	374 (21.3)
	COPD	1582366	2497 (158)	12323 (779)	182 (11.5)	714880	877 (123)	3839 (537)	76 (10.6)	867486	1620 (187)	8484 (978)	106 (12.2)
	Liver disease	230243	284 (123)	1069 (464)	97 (42.1)	173423	208 (120)	547 (315)	75 (43.2)	56820	76 (134)	522 (919)	22 (38.7)
	CKD	2934107	4467 (152)	25816 (880)	526 (17.9)	978886	1179 (120)	5164 (528)	200 (20.4)	1955221	3288 (168)	20652 (1056)	326 (16.7)
	Major surgery <sup>3</sup>	3995870	5407 (135)	24164 (605)	763 (19.1)	2773174	2735 (98.6)	9898 (357)	440 (15.9)	1222696	2672 (219)	14266 (1167)	323 (26.4)
	Dementia	524293	1127 (215)	6073 (1158)	45 (8.6)	48821	81 (166)	415 (850)	10 (20.5)	475472	1046 (220)	5658 (1190)	35 (7.4)
Medications	Antiplatelet	2510382	2814 (112)	36415 (1451)	218 (8.7)	1000010	747 (74.7)	15556 (1556)	65 (6.5)	1510372	2067 (137)	20859 (1381)	153 (10.1)
	BP lowering	8589860	7969 (92.8)	55462 (646)	777 (9.0)	4286561	2779 (64.8)	20579 (480)	305 (7.1)	4303299	5190 (121)	34883 (811)	472 (11.0)
	Lipid lowering	6808408	5796 (85.1)	47859 (703)	564 (8.3)	3212600	1878 (58.5)	19543 (608)	194 (6.0)	3595808	3918 (109)	28316 (787)	370 (10.3)
	Anticoagulant	1338585	2278 (170)	12758 (953)	205 (15.3)	381588	1144 (300)	2773 (727)	57 (14.9)	956997	1134 (118)	9985 (1043)	148 (15.5)
	Oral contraceptive	622529	138 (22.2)	42 (6.7)	8 (1.3)	622529	138 (22.2)	42 (6.7)	8 (1.3)				
	HRT	540722	213 (39.4)	516 (95.4)	16 (3.0)	501957	185 (36.9)	368 (73.3)	14 (2.8)	38765	28 (72.2)	148 (382)	2 (5.2)
Number of diagnoses	0	36455307	12200 (33.5)	38617 (106)	980 (2.7)	31819272	7612 (23.9)	18316 (57.6)	643 (2.0)	4636035	4588 (99.0)	20301 (438)	337 (7.3)
	1 - 5	9573068	8422 (88.0)	46012 (481)	925 (9.7)	6872479	4137 (60.2)	19183 (279)	515 (7.5)	2700589	4285 (159)	26829 (993)	410 (15.2)
	6+	134567	281 (209)	2622 (1948)	21 (15.6)	52420	86 (164)	784 (1496)	9 (17.2)	82147	195 (237)	1838 (2237)	12 (14.6)
Number of medications	0	22970920	3679 (16.0)	9629 (41.9)	321 (1.4)	22122043	3143 (14.2)	7258 (32.8)	290 (1.3)	848877	536 (63.1)	2371 (279)	31 (3.7)
	1 - 5	20875516	12872 (61.7)	56255 (269)	1210 (5.8)	15618756	7203 (46.1)	25416 (163)	713 (4.6)	5256760	5669 (108)	30839 (587)	497 (9.5)
	6+	2316506	4352 (188)	21367 (922)	395 (17.1)	1003372	1489 (148)	5609 (559)	164 (16.3)	1313134	2863 (218)	15758 (1200)	231 (17.6)

<sup>1</sup> Index of Multiple Deprivation deciles where 1 indicates least deprived and 10 indicates most deprived; <sup>2</sup> After 31/12/2019 and prior to 08/12/2020; <sup>3</sup> In the last year.

**Table 2(a) Numbers and incidence rates pre-, post-first ChAdOx1-S. Incidence rate per 100,000 per annum. Disclosure control prevents presentation of n>5**

		Pre vaccination or unvaccinated		Post vaccination ≤28 days		Post vaccination >28 days	
Outcome	Age	N (events)	Incidence rate (95% CI)	N (events)	Incidence rate (95% CI)	N (events)	Incidence rate (95% CI)
All venous	All	14769	140.7 (138.5–143.0)	2006	309.0 (295.8–322.9)	995	382.6 (359.6–407.2)
	<70	9892	104.3 (102.2–106.3)	902	219.5 (205.7–234.3)	234	240.6 (211.7–273.5)
	≥70	4877	484.5 (471.1–498.3)	1104	463.4 (436.9–491.6)	761	467.5 (435.4–501.9)
Intracranial venous thrombosis	All	207	1.97 (1.72–2.26)	27	4.16 (2.85–6.06)	9	3.46 (1.80–6.65)
	<70	188	1.98 (1.72–2.29)	22	5.35 (3.52–8.13)	<10	5.14 (2.14–12.35)
	≥70	19	1.89 (1.20–2.96)	5	2.10 (0.87–5.04)	<5	2.45 (0.92–6.54)
Portal vein thrombosis	All	121	1.15 (0.96–1.38)	14	2.16 (1.28–3.64)	9	3.46 (1.80–6.65)
	<70	98	1.03 (0.85–1.26)	9	2.19 (1.14–4.21)	<5	2.06 (0.51–8.22)
	≥70	23	2.28 (1.52–3.44)	5	2.10 (0.87–5.04)	<10	4.30 (2.05–9.01)
Pulmonary embolism	All	8473	80.7 (79.0–82.5)	1203	185.3 (175.1–196.1)	587	225.7 (208.1–244.7)
	<70	5399	56.9 (55.4–58.4)	515	125.3 (114.9–136.6)	134	137.8 (116.3–163.2)
	≥70	3074	305.3 (294.7–316.3)	688	288.7 (267.9–311.1)	453	278.2 (253.7–305.0)
Deep vein thrombosis	All	5664	54.0 (52.6–55.4)	739	113.8 (105.9–122.3)	374	143.8 (129.9–159.1)
	<70	3971	41.9 (40.6–43.2)	345	83.9 (75.5–93.3)	90	92.5 (75.3–113.8)
	≥70	1693	168.1 (160.3–176.3)	394	165.3 (149.8–182.5)	284	174.4 (155.2–195.9)
Other	All	459	4.37 (3.99–4.79)	51	7.85 (5.97–10.33)	30	11.5 (8.1–16.5)
	<70	359	3.78 (3.41–4.20)	34	8.27 (5.91–11.58)	9	9.25 (4.81–17.78)
	≥70	100	9.93 (8.16–12.08)	17	7.13 (4.43–11.47)	21	12.9 (8.4–19.8)
All arterial	All	57602	549.1 (544.7–553.6)	8256	1274.4 (1247.2–1302.1)	4634	1787.0 (1736.3–1839.2)
	<70	31396	331.0 (327.4–334.7)	2993	729.4 (703.8–756.0)	755	777.4 (723.9–834.9)
	≥70	26206	2607.7 (2576.3–2639.5)	5263	2215.7 (2156.7–2276.4)	3879	2391.5 (2317.4–2467.9)
Myocardial infarction	All	28134	268.1 (265.0–271.3)	3814	587.9 (569.6–606.9)	2050	788.9 (755.5–823.8)
	<70	17341	182.8 (180.1–185.5)	1628	396.4 (377.6–416.2)	363	373.4 (336.9–413.9)
	≥70	10793	1072.7 (1052.6–1093.1)	2186	918.3 (880.6–957.6)	1687	1037.3 (988.9–1088.0)
Ischaemic stroke (ischaemic, unknown, retinal and spinal)	All	28639	272.9 (269.8–276.1)	4334	668.2 (648.6–688.4)	2539	977.6 (940.3–1016.4)
	<70	13505	142.4 (140.0–144.8)	1309	318.7 (301.9–336.4)	377	387.8 (350.6–429.0)
	≥70	15134	1504.7 (1480.9–1528.9)	3025	1271.6 (1227.1–1317.7)	2162	1330.4 (1275.5–1387.7)
Other arterial	All	1308	12.5 (11.8–13.2)	189	29.1 (25.2–33.6)	98	37.7 (30.9–45.9)
	<70	775	8.17 (7.61–8.76)	82	19.9 (16.1–24.8)	22	22.6 (14.9–34.3)
	≥70	533	52.9 (48.6–57.6)	107	44.9 (37.1–54.2)	76	46.6 (37.3–58.4)
<b>Other</b>							
Disseminated intravascular coagulation	All	13	0.12 (0.07–0.21)	<5	0.46 (0.15–1.43)	<5	-
	<70	5	0.05 (0.02–0.13)	<5	0.49 (0.12–1.95)	<5	-
	≥70	8	0.79 (0.40–1.59)	<5	0.42 (0.06–2.98)	<5	-
Thrombotic thrombocytopenic purpura	All	70	0.67 (0.53–0.84)	<5	0.62 (0.23–1.64)	<5	0.77 (0.19–3.07)
	<70	64	0.67 (0.53–0.86)	<5	0.73 (0.24–2.26)	<5	2.06 (0.51–8.22)
	≥70	6	0.60 (0.27–1.33)	<5	0.42 (0.06–2.98)	<5	-
Any thrombocytopenia	All	1357	12.9 (12.3–13.6)	200	30.8 (26.8–35.4)	89	34.2 (27.8–42.1)
	<70	915	9.64 (9.04–10.29)	124	30.2 (25.3–36.0)	41	42.1 (31.0–57.2)
	≥70	442	43.9 (40.0–48.2)	76	31.9 (25.5–39.9)	48	29.5 (22.2–39.1)
Haemorrhagic stroke (intra-cerebral or subarachnoid)	All	3747	35.7 (34.6–36.9)	487	75.0 (68.6–82.0)	289	111.1 (99.0–124.6)
	<70	2028	21.4 (20.5–22.3)	157	38.2 (32.7–44.7)	45	46.3 (34.5–62.0)
	≥70	1719	170.7 (162.8–179.0)	330	138.4 (124.3–154.2)	244	149.8 (132.1–169.8)
Mesenteric thrombosis	All	1170	11.1 (10.5–11.8)	171	26.3 (22.7–30.6)	109	41.9 (34.7–50.5)
	<70	531	5.60 (5.14–6.09)	56	13.6 (10.5–17.7)	20	20.6 (13.3–31.9)
	≥70	639	63.5 (58.7–68.6)	115	48.2 (40.2–57.9)	89	54.6 (44.4–67.2)
Lower limb fracture	All	18347	174.9 (172.3–177.4)	2657	409.4 (394.2–425.3)	1632	628.0 (598.3–659.2)
	<70	8732	92.0 (90.1–94.0)	539	131.2 (120.5–142.7)	155	159.4 (136.2–186.5)
	≥70	9615	955.8 (936.9–975.1)	2118	890.0 (852.9–928.7)	1477	908.3 (863.2–955.9)
Death	All	123580	1177.5 (1170.9–1184.1)	16192	2493.1 (2455.0–2531.8)	11738	4510.6 (4429.7–4592.9)
	<70	68803	714.1 (710.5–717.7)	10110	1471.0 (1451.4–1490.4)	6887	2820.6 (2762.6–2878.6)
	≥70	93778	9312.7 (9253.3–9372.5)	14252	5978.2 (5880.8–6077.1)	10841	6653.3 (6529.2–6779.7)

**Table 2(b) Numbers and incidence rates pre-, post-first BNT162b2. Incidence rate per 100,000 per annum. Disclosure control prevents presentation of n>5**

Outcome	Age	Pre vaccination or unvaccinated		Post vaccination ≤28 days		Post vaccination >28 days	
		N (events)	Incidence rate (95%)	N (events)	Incidence rate (95%)	N (events)	Incidence rate (95%)
All venous	All	14769	140.7 (138.5–143.0)	1546	250.1 (237.9–262.9)	1587	287.0 (273.2–301.5)
	<70	9892	104.3 (102.2–106.3)	548	154.9 (142.4–168.4)	259	110.8 (98.1–125.2)
	≥70	4877	484.5 (471.1–498.3)	998	377.7 (355.0–401.9)	1328	415.9 (394.1–438.9)
Intracranial venous thrombosis	All	207	1.97 (1.72–2.26)	13	2.10 (1.22–3.62)	6	1.08 (0.49–2.41)
	<70	188	1.98 (1.72–2.29)	5	1.41 (0.59–3.39)	<5	1.28 (0.41–3.98)
	≥70	19	1.89 (1.20–2.96)	8	3.03 (1.51–6.05)	<5	0.94 (0.30–2.91)
Portal vein thrombosis	All	121	1.15 (0.96–1.38)	5	0.81 (0.34–1.94)	12	2.17 (1.23–3.82)
	<70	98	1.03 (0.85–1.26)	<5	0.56 (0.14–2.26)	6	2.57 (1.15–5.71)
	≥70	23	2.28 (1.52–3.44)	<5	1.13 (0.37–3.52)	6	1.88 (0.84–4.18)
Pulmonary embolism	All	8473	80.7 (79.0–82.5)	928	150.1 (140.8–160.1)	955	172.7 (162.1–184.0)
	<70	5399	56.9 (55.4–58.4)	306	86.5 (77.3–96.7)	141	60.3 (51.2–71.2)
	≥70	3074	305.3 (294.7–316.3)	622	235.3 (217.6–254.6)	814	254.8 (237.9–273.0)
Deep vein thrombosis	All	5664	54.0 (52.6–55.4)	555	89.8 (82.6–97.6)	590	106.7 (98.4–115.6)
	<70	3971	41.9 (40.6–43.2)	213	60.2 (52.6–68.8)	103	44.1 (36.3–53.5)
	≥70	1693	168.1 (160.3–176.3)	342	129.4 (116.4–143.9)	487	152.4 (139.5–166.6)
Other	All	459	4.37 (3.99–4.79)	55	8.89 (6.83–11.59)	39	7.05 (5.15–9.65)
	<70	359	3.78 (3.41–4.20)	28	7.91 (5.46–11.46)	13	5.56 (3.23–9.58)
	≥70	100	9.93 (8.16–12.08)	27	10.2 (7.0–14.9)	26	8.14 (5.54–11.95)
All arterial	All	57602	549.1 (544.7–553.6)	7960	1289.8 (1261.7–1318.4)	8799	1594.8 (1561.8–1628.5)
	<70	31396	331.0 (327.4–334.7)	2263	640.2 (614.4–667.2)	876	375.1 (351.1–400.8)
	≥70	26206	2607.7 (2576.3–2639.5)	5697	2160.4 (2105.0–2217.2)	7923	2490.0 (2435.7–2545.4)
Myocardial infarction	All	28134	268.1 (265.0–271.3)	3722	602.5 (583.4–622.2)	4023	728.0 (705.9–750.9)
	<70	17341	182.8 (180.1–185.5)	1285	363.3 (344.0–383.7)	489	209.3 (191.6–228.7)
	≥70	10793	1072.7 (1052.6–1093.1)	2437	922.9 (886.9–960.2)	3534	1107.9 (1072.0–1145.1)
Ischaemic stroke (ischaemic, unknown, retinal and spinal)	All	28639	272.9 (269.8–276.1)	4143	670.6 (650.5–691.4)	4702	851.2 (827.2–875.9)
	<70	13505	142.4 (140.0–144.8)	949	268.2 (251.7–285.9)	369	157.9 (142.6–174.9)
	≥70	15134	1504.7 (1480.9–1528.9)	3194	1209.9 (1168.6–1252.6)	4333	1359.3 (1319.4–1400.4)
Other arterial	All	1308	12.5 (11.8–13.2)	156	25.2 (21.6–29.5)	167	30.2 (25.9–35.1)
	<70	775	8.17 (7.61–8.76)	46	13.0 (9.7–17.3)	26	11.1 (7.6–16.3)
	≥70	533	52.9 (48.6–57.6)	110	41.6 (34.5–50.2)	141	44.1 (37.4–52.0)
<b>Other</b>							
Disseminated intravascular coagulation	All	13	0.12 (0.07–0.21)	<5	0.32 (0.08–1.29)	<5	0.36 (0.09–1.45)
	<70	5	0.05 (0.02–0.13)	<5	0.28 (0.04–2.01)	<5	-
	≥70	8	0.79 (0.40–1.59)	<5	0.38 (0.05–2.69)	<5	0.63 (0.16–2.50)
Thrombotic thrombocytopenic purpura	All	70	0.67 (0.53–0.84)	<5	0.65 (0.24–1.72)	<5	0.36 (0.09–1.45)
	<70	64	0.67 (0.53–0.86)	<5	0.85 (0.27–2.63)	<5	0.86 (0.21–3.42)
	≥70	6	0.60 (0.27–1.33)	<5	0.38 (0.05–2.69)	<5	-
Any thrombocytopenia	All	1357	12.9 (12.3–13.6)	136	22.0 (18.6–26.0)	144	26.0 (22.1–30.6)
	<70	915	9.64 (9.04–10.29)	55	15.5 (11.9–20.2)	32	13.7 (9.7–19.4)
	≥70	442	43.9 (40.0–48.2)	81	30.6 (24.6–38.1)	112	35.1 (29.1–42.2)
Haemorrhagic stroke (intra-cerebral or subarachnoid)	All	3747	35.7 (34.6–36.9)	440	71.2 (64.8–78.1)	579	104.7 (96.5–113.5)
	<70	2028	21.4 (20.5–22.3)	93	26.3 (21.4–32.2)	55	23.5 (18.1–30.7)
	≥70	1719	170.7 (162.8–179.0)	347	131.3 (118.2–145.8)	524	164.0 (150.6–178.7)
Mesenteric thrombosis	All	1170	11.1 (10.5–11.8)	161	26.0 (22.3–30.4)	217	39.2 (34.3–44.8)
	<70	531	5.60 (5.14–6.09)	18	7.91 (5.46–11.46)	18	7.70 (4.85–12.22)
	≥70	639	63.5 (58.7–68.6)	133	50.3 (42.4–59.6)	199	62.3 (54.2–71.6)
Lower limb fracture	All	18347	174.9 (172.3–177.4)	2573	416.2 (400.5–432.6)	3176	574.6 (554.9–594.9)
	<70	8732	92.0 (90.1–94.0)	443	125.2 (114.0–137.4)	228	97.6 (85.7–111.1)
	≥70	9615	955.8 (936.9–975.1)	2130	806.2 (772.7–841.2)	2948	923.9 (891.2–957.9)
Death	All	123580	1177.5 (1170.9–1184.1)	9117	1474.4 (1444.4–1504.9)	13935	2518.7 (2477.3–2560.9)
	<70	29802	314.1 (310.5–317.7)	775	218.9 (204.0–234.9)	531	227.2 (208.7–247.4)
	≥70	93778	9312.7 (9253.3–9372.5)	8342	3155.6 (3088.6–3224.1)	13404	4194.8 (4124.4–4266.4)

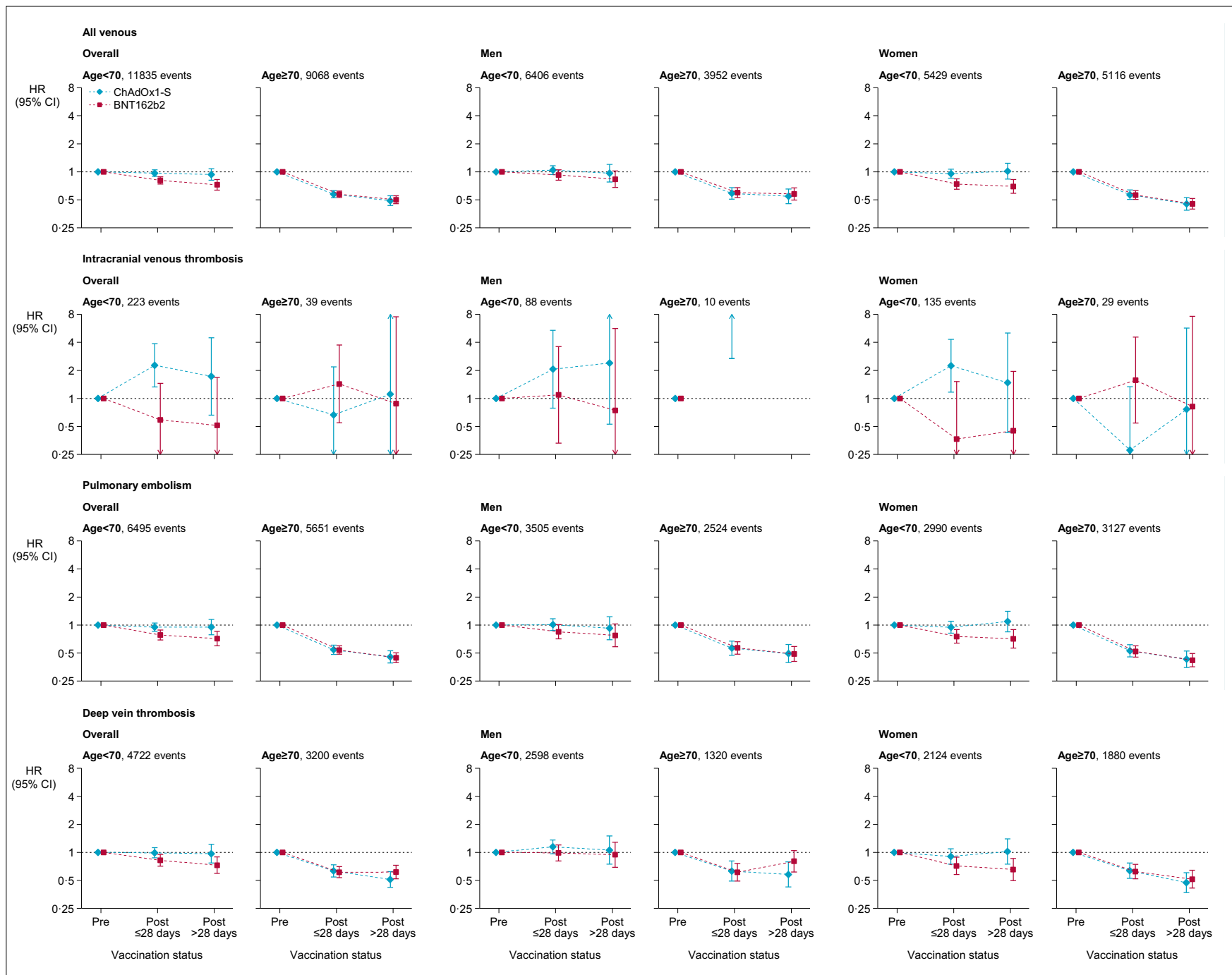


Figure 1 Adjusted Hazard ratios for all venous thromboses, intracranial venous thromboses, pulmonary embolism and deep vein thromboses after ChAdOx1-S or BNT162b2 vaccine

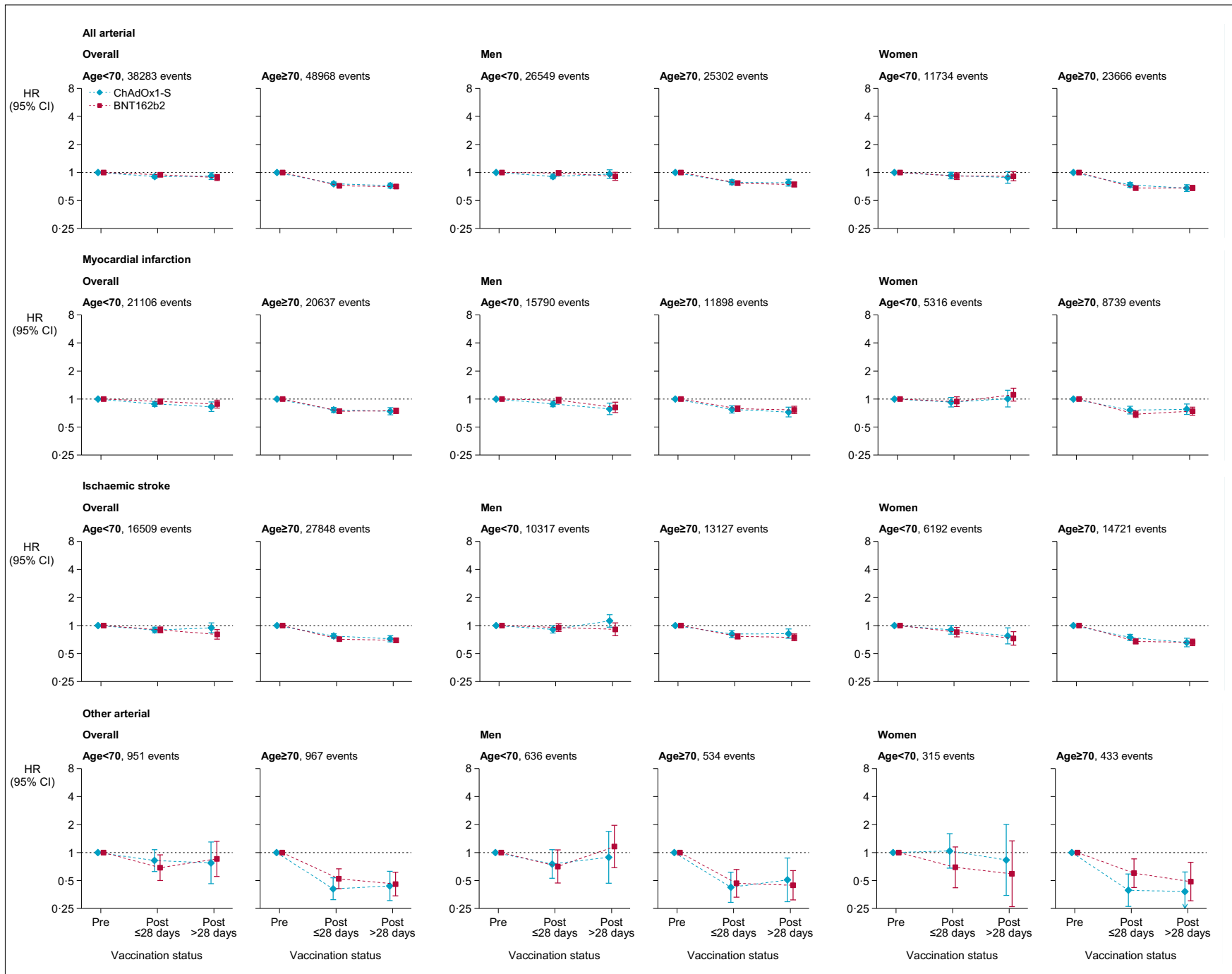


Figure 2 Adjusted hazard ratios for all arterial thromboses, myocardial infarction, ischemic stroke and other arterial thromboses after ChAdOx1-S or BNT162b2 vaccine

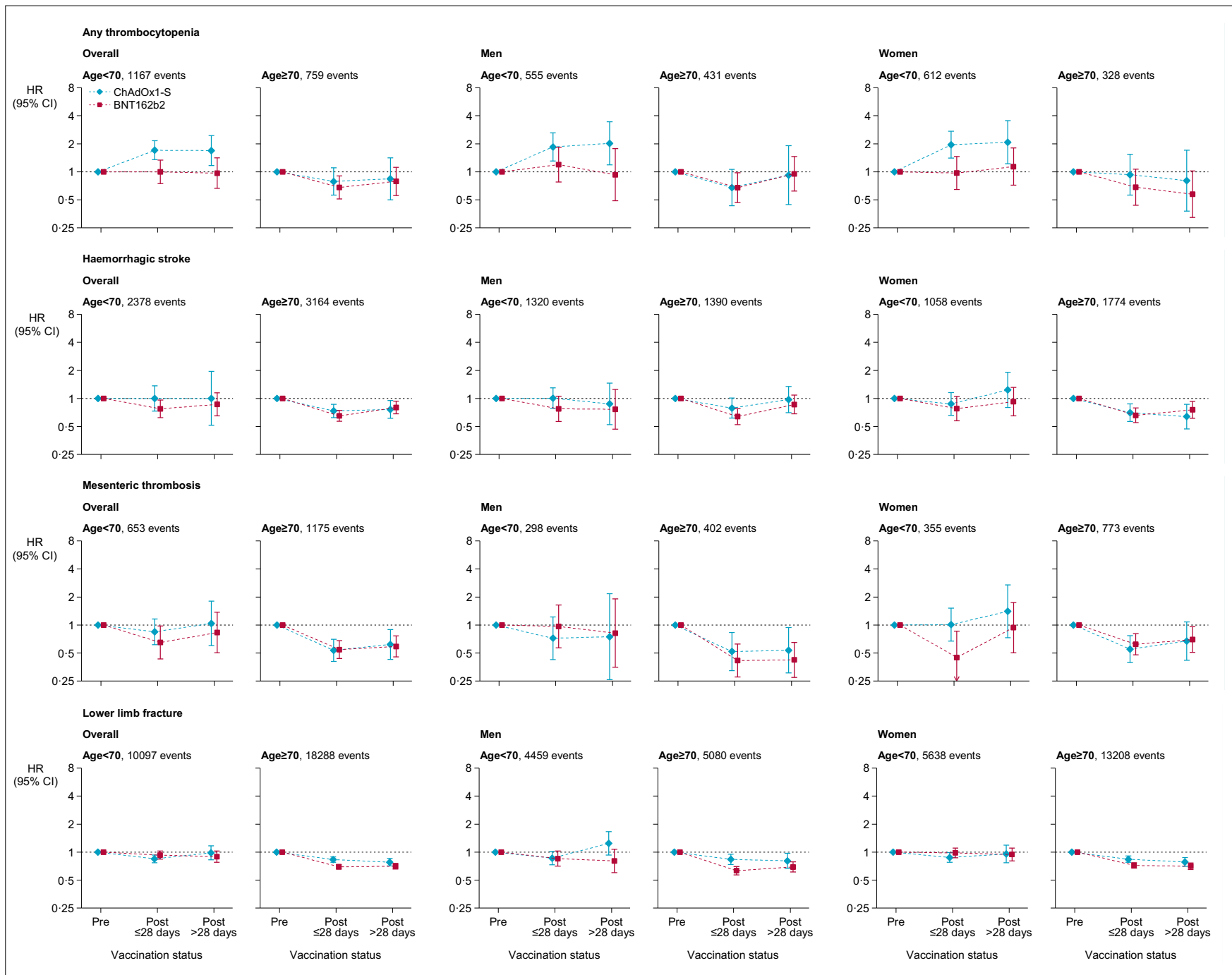


Figure 3 Adjusted hazard ratios for thrombocytopenia, haemorrhagic stroke, mesenteric thrombosis, lower limb fracture after ChAdOx1-S or BNT162b2 vaccine

## SUPPLEMENTARY TABLES AND FIGURES

**Supplementary Table 1:** Hazard ratios (95% CIs) for thrombotic and other outcomes 1-28 and >28 days post-vaccination, compared with pre-vaccination rates. All analyses were stratified on geographical region (A) ChAdOx1-S vaccine (B) BNT162b2 vaccine

Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
<b>(A) ChAdOx1-S vaccine</b> <b>All venous events</b>	<70	Overall	2.33 (2.16–2.51)	1.32 (1.22–1.43)	0.97 (0.90–1.05)	2.74 (2.39–3.14)	1.60 (1.38–1.84)	0.94 (0.81–1.08)
		Men	2.68 (2.41–2.97)	1.33 (1.19–1.49)	1.04 (0.93–1.16)	3.13 (2.54–3.84)	1.52 (1.23–1.89)	0.97 (0.78–1.20)
		Women	2.08 (1.87–2.31)	1.31 (1.17–1.47)	0.96 (0.85–1.07)	2.56 (2.13–3.07)	1.67 (1.38–2.02)	1.02 (0.84–1.23)
	≥70	Overall	0.65 (0.59–0.72)	0.64 (0.59–0.70)	0.58 (0.53–0.63)	0.67 (0.59–0.76)	0.58 (0.52–0.65)	0.49 (0.44–0.55)
		Men	0.65 (0.56–0.76)	0.65 (0.56–0.74)	0.59 (0.51–0.68)	0.70 (0.58–0.84)	0.63 (0.53–0.75)	0.55 (0.46–0.65)
		Women	0.65 (0.58–0.74)	0.64 (0.56–0.71)	0.57 (0.50–0.64)	0.64 (0.54–0.76)	0.54 (0.47–0.64)	0.45 (0.39–0.53)
Intracranial venous thrombosis	<70	Overall	2.81 (1.70–4.64)	2.99 (1.75–5.09)	2.27 (1.33–3.88)	2.37 (0.91–6.12)	2.47 (0.95–6.42)	1.72 (0.66–4.49)
		Men	2.72 (1.15–6.39)	2.58 (0.99–6.74)	2.06 (0.79–5.37)	3.43 (0.74–15.87)	3.37 (0.71–15.90)	2.40 (0.53–10.86)
		Women	2.69 (1.45–5.00)	3.27 (1.74–6.17)	2.24 (1.17–4.31)	1.75 (0.52–5.93)	2.14 (0.63–7.22)	1.47 (0.43–5.04)
	≥70	Overall	0.62 (0.17–2.23)	0.65 (0.19–2.21)	0.67 (0.20–2.18)	1.35 (0.13–13.46)	1.13 (0.14–9.20)	1.11 (0.14–9.02)
		Men	10.8 (3.3–35.8)	8.99 (2.75–29.42)	10.1 (2.7–38.5)	-	-	-
		Women	0.27 (0.05–1.42)	0.29 (0.06–1.43)	0.28 (0.06–1.34)	0.87 (0.10–7.32)	0.82 (0.11–6.24)	0.76 (0.10–5.70)
Portal vein thrombosis	<70	Overall	2.49 (1.20–5.14)	1.56 (0.72–3.40)	1.00 (0.24–4.15)	2.76 (0.73–10.51)	1.99 (0.53–7.52)	1.00 (0.06–18.18)
		Men	3.38 (1.40–8.17)	1.95 (0.76–5.02)	1.22 (0.48–3.08)	3.55 (0.52–24.13)	2.16 (0.32–14.52)	0.98 (0.14–6.75)
		Women	1.74 (0.48–6.26)	1.06 (0.28–4.07)	0.72 (0.18–2.86)	2.39 (0.37–15.53)	1.57 (0.24–10.12)	0.86 (0.12–6.28)
	≥70	Overall	0.66 (0.11–4.06)	0.67 (0.10–4.24)	0.61 (0.10–3.71)	2.72 (0.49–15.02)	3.00 (0.48–18.99)	2.61 (0.41–16.52)
		Men	0.43 (0.09–2.09)	0.42 (0.08–2.15)	0.37 (0.07–1.90)	8.60 (2.33–31.70)	7.99 (1.93–33.03)	7.99 (2.03–31.38)
		Women	0.92 (0.06–13.23)	0.92 (0.06–13.99)	0.82 (0.06–11.05)	0.87 (0.12–6.02)	0.95 (0.12–7.39)	0.86 (0.11–6.92)
Pulmonary embolism	<70	Overall	2.54 (2.30–2.80)	1.28 (1.15–1.43)	0.95 (0.85–1.05)	3.12 (2.61–3.73)	1.63 (1.34–1.96)	0.95 (0.79–1.15)
		Men	2.83 (2.46–3.24)	1.27 (1.09–1.48)	1.01 (0.87–1.17)	3.32 (2.52–4.38)	1.43 (1.07–1.91)	0.92 (0.69–1.23)
		Women	2.35 (2.04–2.70)	1.30 (1.12–1.52)	0.95 (0.82–1.10)	3.09 (2.44–3.92)	1.81 (1.41–2.32)	1.09 (0.85–1.41)
	≥70	Overall	0.62 (0.55–0.70)	0.60 (0.54–0.68)	0.54 (0.48–0.61)	0.61 (0.52–0.72)	0.54 (0.46–0.62)	0.45 (0.39–0.53)
		Men	0.63 (0.52–0.75)	0.62 (0.52–0.74)	0.57 (0.47–0.67)	0.63 (0.50–0.79)	0.57 (0.46–0.70)	0.49 (0.40–0.62)
		Women	0.61 (0.52–0.72)	0.59 (0.51–0.69)	0.53 (0.45–0.61)	0.60 (0.48–0.75)	0.51 (0.42–0.63)	0.43 (0.35–0.53)
Deep vein thrombosis	<70	Overall	2.08 (1.85–2.34)	1.34 (1.18–1.52)	0.99 (0.87–1.12)	2.37 (1.90–2.96)	1.58 (1.25–1.99)	0.97 (0.77–1.22)
		Men	2.61 (2.22–3.07)	1.48 (1.25–1.76)	1.15 (0.97–1.36)	2.85 (2.04–3.98)	1.62 (1.14–2.29)	1.06 (0.75–1.50)
		Women	1.67 (1.40–2.00)	1.21 (1.00–1.46)	0.90 (0.75–1.09)	2.12 (1.57–2.86)	1.57 (1.15–2.13)	1.02 (0.75–1.40)
	≥70	Overall	0.73 (0.62–0.86)	0.71 (0.61–0.83)	0.63 (0.54–0.74)	0.71 (0.57–0.88)	0.62 (0.51–0.75)	0.51 (0.42–0.62)
		Men	0.72 (0.56–0.94)	0.71 (0.55–0.91)	0.63 (0.49–0.81)	0.77 (0.56–1.06)	0.70 (0.51–0.95)	0.58 (0.42–0.79)
		Women	0.73 (0.59–0.90)	0.72 (0.59–0.87)	0.64 (0.53–0.77)	0.67 (0.51–0.88)	0.57 (0.45–0.73)	0.47 (0.37–0.60)
Other	<70	Overall	2.48 (1.70–3.62)	1.60 (1.06–2.40)	1.02 (0.69–1.52)	3.04 (1.54–6.00)	2.04 (1.01–4.09)	0.94 (0.47–1.91)
		Men	2.61 (1.51–4.53)	1.45 (0.79–2.64)	1.02 (0.57–1.83)	3.17 (1.13–8.90)	1.74 (0.60–5.05)	0.89 (0.31–2.58)
		Women	2.38 (1.42–4.00)	1.74 (1.01–2.98)	1.12 (0.65–1.91)	3.15 (1.29–7.73)	2.40 (0.97–5.96)	1.26 (0.50–3.17)
	≥70	Overall	0.46 (0.21–1.01)	0.46 (0.21–0.99)	0.43 (0.20–0.92)	1.13 (0.50–2.54)	1.03 (0.48–2.21)	0.93 (0.42–2.03)
		Men	0.38 (0.11–1.30)	0.39 (0.12–1.31)	0.33 (0.10–1.08)	1.10 (0.36–3.39)	1.02 (0.34–3.04)	0.79 (0.26–2.36)
		Women	0.52 (0.19–1.44)	0.51 (0.20–1.36)	0.50 (0.19–1.32)	1.16 (0.37–3.63)	1.03 (0.36–2.98)	0.98 (0.33–2.94)

Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
All arterial events	<70	Overall	3.02 (2.90–3.14)	1.25 (1.20–1.31)	0.90 (0.86–0.95)	3.55 (3.29–3.83)	1.57 (1.45–1.70)	0.91 (0.84–1.00)
		Men	3.42 (3.26–3.60)	1.26 (1.20–1.34)	0.91 (0.86–0.96)	4.70 (4.27–5.17)	1.66 (1.50–1.84)	0.96 (0.86–1.07)
		Women	2.96 (2.76–3.18)	1.24 (1.14–1.34)	0.93 (0.86–1.00)	3.30 (2.90–3.75)	1.43 (1.25–1.64)	0.88 (0.77–1.02)
	≥70	Overall	0.89 (0.85–0.93)	0.84 (0.80–0.87)	0.76 (0.73–0.79)	1.03 (0.97–1.10)	0.83 (0.78–0.87)	0.72 (0.68–0.77)
		Men	0.90 (0.85–0.96)	0.87 (0.82–0.92)	0.78 (0.74–0.83)	1.06 (0.97–1.16)	0.89 (0.82–0.96)	0.78 (0.71–0.85)
		Women	0.88 (0.82–0.94)	0.80 (0.76–0.85)	0.73 (0.69–0.78)	1.02 (0.93–1.12)	0.77 (0.71–0.83)	0.68 (0.62–0.74)
Myocardial infarction	<70	Overall	2.85 (2.70–3.01)	1.24 (1.17–1.32)	0.88 (0.83–0.94)	2.93 (2.63–3.26)	1.40 (1.24–1.56)	0.83 (0.73–0.93)
		Men	3.23 (3.02–3.44)	1.25 (1.17–1.35)	0.89 (0.83–0.95)	3.52 (3.08–4.03)	1.33 (1.15–1.53)	0.78 (0.68–0.90)
		Women	2.93 (2.63–3.26)	1.22 (1.09–1.38)	0.92 (0.82–1.04)	3.56 (2.95–4.29)	1.58 (1.29–1.92)	1.01 (0.82–1.24)
	≥70	Overall	0.86 (0.80–0.92)	0.83 (0.78–0.88)	0.76 (0.71–0.81)	0.97 (0.89–1.07)	0.83 (0.76–0.90)	0.74 (0.68–0.81)
		Men	0.88 (0.80–0.96)	0.85 (0.78–0.93)	0.77 (0.71–0.84)	0.96 (0.84–1.09)	0.84 (0.74–0.94)	0.73 (0.64–0.82)
		Women	0.85 (0.76–0.94)	0.80 (0.72–0.88)	0.76 (0.69–0.84)	1.03 (0.90–1.19)	0.82 (0.72–0.93)	0.78 (0.68–0.88)
Ischaemic stroke <sup>4</sup>	<70	Overall	3.21 (3.02–3.41)	1.25 (1.17–1.34)	0.90 (0.84–0.96)	4.36 (3.91–4.86)	1.76 (1.56–1.98)	0.94 (0.84–1.07)
		Men	3.73 (3.44–4.05)	1.28 (1.17–1.40)	0.91 (0.83–0.99)	6.58 (5.73–7.57)	2.14 (1.84–2.49)	1.12 (0.96–1.31)
		Women	2.91 (2.64–3.20)	1.21 (1.09–1.35)	0.90 (0.81–1.00)	3.10 (2.59–3.71)	1.32 (1.09–1.59)	0.77 (0.63–0.94)
	≥70	Overall	0.92 (0.87–0.98)	0.85 (0.81–0.90)	0.77 (0.73–0.82)	1.08 (0.99–1.18)	0.83 (0.77–0.90)	0.72 (0.67–0.78)
		Men	0.94 (0.85–1.03)	0.89 (0.82–0.96)	0.81 (0.74–0.88)	1.14 (1.01–1.30)	0.93 (0.83–1.04)	0.82 (0.73–0.92)
		Women	0.92 (0.84–1.00)	0.82 (0.77–0.89)	0.75 (0.69–0.80)	1.04 (0.92–1.17)	0.76 (0.68–0.84)	0.66 (0.59–0.73)
Other arterial	<70	Overall	3.18 (2.48–4.07)	1.24 (0.93–1.64)	0.82 (0.63–1.07)	4.20 (2.62–6.73)	1.68 (0.99–2.86)	0.77 (0.46–1.30)
		Men	3.17 (2.29–4.40)	1.05 (0.73–1.51)	0.75 (0.53–1.07)	5.56 (3.07–10.06)	1.66 (0.86–3.20)	0.89 (0.47–1.69)
		Women	3.67 (2.51–5.37)	1.59 (1.03–2.46)	1.04 (0.68–1.59)	3.60 (1.64–7.91)	1.74 (0.73–4.18)	0.83 (0.35–2.01)
	≥70	Overall	0.44 (0.33–0.59)	0.45 (0.34–0.59)	0.41 (0.31–0.53)	0.55 (0.38–0.79)	0.49 (0.35–0.70)	0.44 (0.31–0.63)
		Men	0.46 (0.31–0.67)	0.45 (0.31–0.66)	0.42 (0.29–0.61)	0.61 (0.35–1.05)	0.56 (0.33–0.95)	0.51 (0.30–0.87)
		Women	0.43 (0.28–0.66)	0.44 (0.30–0.67)	0.39 (0.26–0.59)	0.51 (0.30–0.86)	0.44 (0.27–0.71)	0.38 (0.23–0.62)
<b>Haematological events</b>								
Any thrombocytopenia	<70	Overall	4.85 (3.87–6.07)	3.00 (2.34–3.85)	1.71 (1.35–2.16)	7.48 (5.31–10.53)	4.68 (3.24–6.77)	1.69 (1.16–2.46)
		Men	6.47 (4.62–9.06)	3.52 (2.42–5.13)	1.85 (1.30–2.63)	13.2 (8.1–21.4)	6.84 (3.99–11.73)	2.02 (1.18–3.44)
		Women	3.81 (2.80–5.17)	2.65 (1.89–3.71)	1.95 (1.40–2.72)	4.59 (2.78–7.58)	3.34 (1.98–5.64)	2.08 (1.22–3.54)
	≥70	Overall	0.92 (0.65–1.29)	0.87 (0.63–1.22)	0.79 (0.56–1.10)	1.14 (0.66–1.95)	0.99 (0.59–1.65)	0.84 (0.50–1.41)
		Men	0.84 (0.53–1.32)	0.79 (0.50–1.22)	0.68 (0.43–1.06)	1.37 (0.64–2.91)	1.17 (0.57–2.38)	0.92 (0.45–1.90)
		Women	1.04 (0.62–1.75)	0.99 (0.61–1.63)	0.93 (0.56–1.54)	1.02 (0.46–2.24)	0.88 (0.42–1.85)	0.80 (0.38–1.70)
<b>Other events</b>								
Haemorrhagic stroke <sup>5</sup>	<70	Overall	2.25 (1.88–2.69)	1.05 (0.86–1.27)	1.00 (0.73–1.37)	2.87 (2.10–3.92)	1.39 (1.00–1.93)	1.00 (0.51–1.95)
		Men	2.68 (2.11–3.41)	1.15 (0.89–1.49)	1.01 (0.78–1.30)	2.86 (1.74–4.71)	1.21 (0.72–2.04)	0.87 (0.52–1.46)
		Women	1.93 (1.48–2.52)	0.93 (0.70–1.24)	0.87 (0.66–1.16)	2.94 (1.95–4.42)	1.47 (0.95–2.27)	1.23 (0.80–1.91)
	≥70	Overall	0.83 (0.69–1.00)	0.78 (0.66–0.92)	0.73 (0.62–0.87)	1.09 (0.84–1.40)	0.84 (0.67–1.04)	0.76 (0.61–0.95)
		Men	0.86 (0.65–1.14)	0.82 (0.64–1.05)	0.79 (0.62–1.01)	1.34 (0.93–1.94)	1.03 (0.75–1.43)	0.97 (0.70–1.34)
		Women	0.81 (0.63–1.03)	0.75 (0.60–0.94)	0.70 (0.56–0.87)	0.92 (0.65–1.30)	0.71 (0.52–0.96)	0.64 (0.47–0.86)



Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
Mesenteric thrombosis	<70	Overall	3.25 (2.42–4.37)	1.24 (0.89–1.73)	0.84 (0.61–1.16)	5.47 (3.33–8.99)	2.16 (1.24–3.77)	1.04 (0.60–1.80)
		Men	2.87 (1.72–4.77)	0.98 (0.57–1.71)	0.72 (0.43–1.22)	4.34 (1.59–11.83)	1.42 (0.48–4.25)	0.75 (0.26–2.17)
		Women	3.39 (2.36–4.87)	1.43 (0.94–2.17)	1.01 (0.67–1.52)	5.66 (3.21–9.99)	2.59 (1.36–4.94)	1.40 (0.73–2.69)
	≥70	Overall	0.66 (0.49–0.89)	0.60 (0.46–0.79)	0.53 (0.41–0.70)	0.95 (0.64–1.43)	0.74 (0.52–1.05)	0.62 (0.43–0.89)
		Men	0.65 (0.39–1.09)	0.61 (0.38–0.98)	0.52 (0.32–0.83)	0.81 (0.44–1.49)	0.69 (0.40–1.18)	0.54 (0.31–0.94)
		Women	0.66 (0.46–0.95)	0.60 (0.44–0.84)	0.55 (0.40–0.77)	1.00 (0.60–1.68)	0.76 (0.48–1.20)	0.67 (0.42–1.08)
Lower limb fracture	<70	Overall	1.71 (1.55–1.87)	1.01 (0.91–1.11)	0.85 (0.77–0.93)	2.26 (1.91–2.67)	1.35 (1.13–1.60)	0.98 (0.83–1.17)
		Men	1.35 (1.15–1.58)	0.98 (0.83–1.16)	0.86 (0.73–1.02)	2.22 (1.67–2.93)	1.60 (1.20–2.14)	1.24 (0.93–1.66)
		Women	1.91 (1.70–2.15)	1.03 (0.91–1.16)	0.88 (0.78–0.99)	2.21 (1.80–2.72)	1.25 (1.01–1.55)	0.95 (0.77–1.18)
	≥70	Overall	1.11 (1.02–1.21)	0.94 (0.88–1.01)	0.83 (0.78–0.89)	1.56 (1.39–1.76)	0.95 (0.87–1.04)	0.78 (0.71–0.85)
		Men	1.06 (0.90–1.24)	0.94 (0.83–1.08)	0.84 (0.73–0.95)	1.50 (1.19–1.89)	0.97 (0.81–1.17)	0.81 (0.67–0.97)
		Women	1.11 (1.01–1.22)	0.95 (0.88–1.03)	0.84 (0.77–0.91)	1.51 (1.32–1.73)	0.95 (0.85–1.06)	0.78 (0.70–0.87)
Death	<70	Overall	1.96 (1.87–2.06)	0.60 (0.57–0.63)	0.37 (0.35–0.39)	4.51 (4.20–4.85)	1.41 (1.30–1.53)	0.51 (0.47–0.56)
		Men	2.35 (2.20–2.51)	0.63 (0.58–0.67)	0.44 (0.41–0.47)	6.47 (5.87–7.13)	1.57 (1.40–1.75)	0.75 (0.67–0.85)
		Women	1.69 (1.56–1.82)	0.56 (0.52–0.61)	0.36 (0.33–0.39)	3.48 (3.13–3.89)	1.21 (1.07–1.37)	0.50 (0.44–0.57)
	≥70	Overall	0.35 (0.34–0.36)	0.34 (0.33–0.35)	0.28 (0.28–0.29)	0.49 (0.47–0.51)	0.38 (0.37–0.39)	0.27 (0.26–0.28)
		Men	0.31 (0.30–0.32)	0.32 (0.31–0.33)	0.26 (0.25–0.27)	0.44 (0.42–0.47)	0.37 (0.35–0.38)	0.26 (0.24–0.27)
		Women	0.39 (0.37–0.40)	0.36 (0.35–0.37)	0.30 (0.29–0.31)	0.54 (0.51–0.56)	0.39 (0.38–0.41)	0.29 (0.27–0.30)

Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
<b>(B) BNT162b2 vaccine All venous events</b>	<70	Overall	1.47 (1.35–1.61)	1.01 (0.93–1.11)	0.81 (0.74–0.88)	1.14 (1.01–1.29)	0.88 (0.77–1.00)	0.73 (0.64–0.83)
		Men	1.98 (1.75–2.23)	1.15 (1.01–1.30)	0.92 (0.81–1.05)	1.56 (1.28–1.89)	1.02 (0.83–1.25)	0.83 (0.68–1.02)
		Women	1.20 (1.06–1.37)	0.91 (0.80–1.03)	0.74 (0.65–0.84)	1.01 (0.86–1.20)	0.81 (0.69–0.96)	0.70 (0.59–0.83)
	≥70	Overall	0.65 (0.60–0.71)	0.56 (0.52–0.61)	0.57 (0.53–0.62)	0.68 (0.62–0.75)	0.50 (0.46–0.55)	0.50 (0.45–0.55)
		Men	0.67 (0.59–0.76)	0.59 (0.52–0.66)	0.60 (0.53–0.67)	0.75 (0.65–0.87)	0.59 (0.51–0.68)	0.58 (0.50–0.67)
		Women	0.64 (0.58–0.72)	0.54 (0.49–0.60)	0.56 (0.50–0.63)	0.63 (0.56–0.72)	0.45 (0.40–0.51)	0.45 (0.40–0.52)
Intracranial venous thrombosis	<70	Overall	0.76 (0.31–1.85)	0.72 (0.29–1.78)	0.59 (0.24–1.45)	0.65 (0.20–2.13)	0.59 (0.18–1.93)	0.51 (0.16–1.68)
		Men	1.60 (0.50–5.16)	1.39 (0.43–4.49)	1.09 (0.33–3.61)	1.04 (0.14–7.77)	0.92 (0.12–7.05)	0.74 (0.10–5.62)
		Women	0.39 (0.10–1.60)	0.44 (0.11–1.78)	0.37 (0.09–1.52)	0.48 (0.11–2.07)	0.51 (0.12–2.20)	0.45 (0.10–1.95)
	≥70	Overall	1.65 (0.64–4.29)	1.25 (0.48–3.26)	1.43 (0.55–3.75)	1.13 (0.13–9.75)	0.71 (0.08–6.56)	0.88 (0.10–7.52)
		Men	-	-	-	-	-	-
		Women	2.01 (0.69–5.88)	1.45 (0.49–4.26)	1.57 (0.54–4.54)	1.26 (0.13–11.94)	0.73 (0.07–7.29)	0.82 (0.09–7.61)
Portal vein thrombosis	<70	Overall	0.58 (0.15–2.30)	0.44 (0.11–1.72)	0.29 (0.07–1.17)	3.06 (1.29–7.24)	2.84 (1.19–6.74)	2.19 (0.89–5.37)
		Men	1.28 (0.33–4.95)	0.81 (0.21–3.09)	0.51 (0.13–2.04)	-	-	-
		Women	-	-	-	5.30 (1.98–14.22)	4.28 (1.55–11.78)	3.95 (1.39–11.20)
	≥70	Overall	0.49 (0.10–2.28)	0.43 (0.10–1.87)	0.42 (0.09–1.91)	0.67 (0.23–1.97)	0.54 (0.19–1.56)	0.48 (0.17–1.38)
		Men	0.85 (0.17–4.38)	0.55 (0.11–2.66)	0.49 (0.10–2.46)	1.26 (0.36–4.41)	0.70 (0.23–2.17)	0.48 (0.17–1.38)
		Women	0.22 (0.01–3.38)	0.24 (0.01–3.80)	0.26 (0.02–4.47)	0.37 (0.09–1.52)	0.44 (0.10–2.01)	0.46 (0.11–2.04)
Pulmonary embolism	<70	Overall	1.52 (1.36–1.71)	0.99 (0.87–1.11)	0.78 (0.69–0.88)	1.20 (1.02–1.43)	0.89 (0.75–1.06)	0.71 (0.60–0.85)
		Men	1.93 (1.63–2.28)	1.05 (0.88–1.25)	0.85 (0.71–1.01)	1.56 (1.19–2.05)	0.97 (0.74–1.29)	0.77 (0.58–1.03)
		Women	1.32 (1.13–1.56)	0.94 (0.79–1.10)	0.75 (0.64–0.89)	1.10 (0.88–1.37)	0.84 (0.67–1.05)	0.71 (0.57–0.89)
	≥70	Overall	0.61 (0.55–0.68)	0.53 (0.48–0.59)	0.54 (0.49–0.60)	0.61 (0.54–0.69)	0.45 (0.40–0.51)	0.45 (0.39–0.50)
		Men	0.64 (0.55–0.75)	0.56 (0.48–0.65)	0.57 (0.49–0.66)	0.65 (0.54–0.77)	0.50 (0.42–0.59)	0.49 (0.41–0.59)
		Women	0.59 (0.52–0.68)	0.51 (0.44–0.58)	0.52 (0.45–0.60)	0.58 (0.49–0.68)	0.42 (0.36–0.49)	0.42 (0.36–0.49)
Deep vein thrombosis	<70	Overall	1.38 (1.21–1.59)	1.03 (0.89–1.18)	0.82 (0.71–0.95)	1.05 (0.86–1.28)	0.85 (0.69–1.04)	0.73 (0.59–0.89)
		Men	1.93 (1.60–2.33)	1.23 (1.01–1.49)	0.99 (0.81–1.20)	1.55 (1.15–2.10)	1.10 (0.81–1.48)	0.94 (0.69–1.28)
		Women	1.08 (0.88–1.33)	0.87 (0.71–1.08)	0.72 (0.58–0.89)	0.88 (0.67–1.15)	0.74 (0.56–0.97)	0.65 (0.50–0.86)
	≥70	Overall	0.69 (0.60–0.79)	0.58 (0.51–0.67)	0.61 (0.53–0.70)	0.81 (0.69–0.96)	0.59 (0.50–0.70)	0.61 (0.52–0.73)
		Men	0.66 (0.53–0.82)	0.59 (0.48–0.73)	0.61 (0.49–0.76)	0.95 (0.74–1.23)	0.78 (0.60–1.01)	0.80 (0.61–1.05)
		Women	0.71 (0.59–0.85)	0.59 (0.49–0.70)	0.62 (0.52–0.74)	0.72 (0.58–0.90)	0.49 (0.40–0.61)	0.52 (0.41–0.64)
Other	<70	Overall	2.16 (1.47–3.19)	1.60 (1.07–2.37)	1.18 (0.79–1.77)	1.64 (0.93–2.90)	1.34 (0.75–2.40)	1.03 (0.57–1.87)
		Men	3.25 (1.93–5.50)	2.03 (1.16–3.54)	1.46 (0.83–2.57)	2.14 (0.86–5.34)	1.51 (0.59–3.86)	1.03 (0.39–2.70)
		Women	1.48 (0.82–2.65)	1.20 (0.67–2.16)	0.98 (0.54–1.77)	1.55 (0.75–3.21)	1.31 (0.63–2.74)	1.21 (0.57–2.55)
	≥70	Overall	1.13 (0.66–1.94)	0.97 (0.58–1.64)	1.01 (0.60–1.72)	0.86 (0.39–1.88)	0.66 (0.31–1.41)	0.67 (0.30–1.47)
		Men	1.50 (0.77–2.95)	1.25 (0.65–2.42)	1.27 (0.64–2.49)	1.51 (0.50–4.51)	1.09 (0.36–3.34)	1.07 (0.33–3.44)
		Women	0.79 (0.31–2.04)	0.72 (0.30–1.75)	0.75 (0.30–1.85)	0.42 (0.17–1.06)	0.36 (0.15–0.88)	0.36 (0.14–0.91)
All arterial events	<70	Overall	2.21 (2.12–2.31)	1.31 (1.25–1.37)	0.94 (0.90–0.99)	1.45 (1.35–1.55)	1.08 (1.01–1.16)	0.88 (0.82–0.95)
		Men	3.06 (2.90–3.22)	1.44 (1.36–1.52)	0.99 (0.93–1.05)	2.17 (1.99–2.38)	1.19 (1.08–1.31)	0.91 (0.82–1.00)
		Women	1.85 (1.71–1.99)	1.11 (1.02–1.20)	0.92 (0.84–0.99)	1.44 (1.30–1.60)	0.96 (0.86–1.07)	0.91 (0.81–1.02)
	≥70	Overall	0.90 (0.87–0.93)	0.69 (0.66–0.71)	0.72 (0.70–0.75)	1.15 (1.10–1.20)	0.69 (0.66–0.72)	0.71 (0.68–0.74)
		Men	0.96 (0.91–1.00)	0.75 (0.71–0.78)	0.77 (0.73–0.81)	1.17 (1.11–1.25)	0.74 (0.70–0.79)	0.74 (0.70–0.79)
		Women	0.84 (0.80–0.89)	0.63 (0.60–0.66)	0.68 (0.65–0.71)	1.13 (1.06–1.20)	0.64 (0.61–0.68)	0.68 (0.64–0.73)

Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
Myocardial infarction	<70	Overall	2.24 (2.12–2.37)	1.39 (1.30–1.47)	0.94 (0.88–1.00)	1.42 (1.29–1.55)	1.14 (1.04–1.26)	0.88 (0.80–0.97)
		Men	3.07 (2.87–3.28)	1.51 (1.40–1.62)	0.97 (0.90–1.05)	1.98 (1.76–2.23)	1.13 (1.00–1.28)	0.81 (0.71–0.93)
		Women	1.94 (1.74–2.17)	1.15 (1.03–1.30)	0.94 (0.83–1.06)	1.78 (1.54–2.05)	1.18 (1.02–1.37)	1.11 (0.95–1.30)
	≥70	Overall	0.93 (0.88–0.98)	0.74 (0.71–0.78)	0.74 (0.70–0.78)	1.19 (1.12–1.27)	0.78 (0.73–0.83)	0.75 (0.70–0.80)
		Men	0.99 (0.92–1.06)	0.81 (0.76–0.86)	0.79 (0.73–0.84)	1.20 (1.10–1.31)	0.82 (0.76–0.89)	0.76 (0.70–0.83)
		Women	0.85 (0.78–0.92)	0.66 (0.61–0.72)	0.69 (0.63–0.74)	1.20 (1.08–1.33)	0.74 (0.67–0.81)	0.74 (0.67–0.82)
Ischaemic stroke <sup>4</sup>	<70	Overall	2.18 (2.05–2.33)	1.23 (1.14–1.31)	0.90 (0.83–0.97)	1.46 (1.32–1.62)	1.00 (0.89–1.11)	0.80 (0.72–0.90)
		Men	3.05 (2.80–3.32)	1.38 (1.26–1.51)	0.95 (0.86–1.05)	2.40 (2.08–2.77)	1.26 (1.09–1.46)	0.91 (0.78–1.07)
		Women	1.76 (1.59–1.96)	1.05 (0.94–1.17)	0.85 (0.76–0.95)	1.18 (1.01–1.38)	0.77 (0.66–0.90)	0.73 (0.61–0.86)
	≥70	Overall	0.88 (0.84–0.93)	0.65 (0.63–0.68)	0.71 (0.68–0.75)	1.13 (1.06–1.19)	0.64 (0.60–0.67)	0.69 (0.66–0.73)
		Men	0.94 (0.88–1.00)	0.71 (0.66–0.75)	0.77 (0.72–0.82)	1.17 (1.07–1.27)	0.69 (0.64–0.75)	0.75 (0.69–0.81)
		Women	0.84 (0.78–0.89)	0.61 (0.58–0.65)	0.68 (0.63–0.72)	1.09 (1.01–1.19)	0.60 (0.56–0.65)	0.66 (0.61–0.71)
Other arterial	<70	Overall	1.72 (1.28–2.31)	0.95 (0.70–1.30)	0.69 (0.50–0.94)	1.63 (1.10–2.43)	1.13 (0.74–1.72)	0.85 (0.55–1.32)
		Men	2.31 (1.58–3.37)	0.99 (0.66–1.49)	0.71 (0.47–1.07)	3.22 (2.02–5.13)	1.56 (0.95–2.58)	1.16 (0.69–1.96)
		Women	1.46 (0.90–2.37)	0.88 (0.54–1.45)	0.69 (0.42–1.15)	0.93 (0.43–1.99)	0.65 (0.30–1.43)	0.59 (0.26–1.33)
	≥70	Overall	0.59 (0.46–0.76)	0.51 (0.40–0.65)	0.52 (0.41–0.67)	0.64 (0.47–0.85)	0.47 (0.35–0.62)	0.46 (0.34–0.62)
		Men	0.49 (0.35–0.69)	0.46 (0.32–0.65)	0.47 (0.33–0.66)	0.52 (0.37–0.74)	0.46 (0.32–0.66)	0.44 (0.31–0.64)
		Women	0.74 (0.51–1.08)	0.59 (0.41–0.84)	0.60 (0.42–0.85)	0.83 (0.50–1.37)	0.50 (0.31–0.79)	0.49 (0.30–0.78)
<b>Haematological events</b>								
Any thrombocytopenia	<70	Overall	2.10 (1.60–2.77)	1.48 (1.11–1.97)	1.00 (0.75–1.34)	2.03 (1.42–2.92)	1.54 (1.07–2.23)	0.97 (0.66–1.41)
		Men	3.31 (2.23–4.91)	2.07 (1.35–3.16)	1.19 (0.78–1.83)	2.95 (1.61–5.42)	2.02 (1.08–3.79)	0.93 (0.49–1.78)
		Women	1.50 (1.01–2.22)	1.17 (0.78–1.74)	0.97 (0.65–1.46)	1.58 (1.00–2.50)	1.32 (0.83–2.08)	1.14 (0.72–1.80)
	≥70	Overall	0.85 (0.64–1.13)	0.72 (0.54–0.95)	0.68 (0.51–0.90)	1.22 (0.87–1.71)	0.90 (0.64–1.25)	0.79 (0.56–1.12)
		Men	0.87 (0.61–1.26)	0.73 (0.51–1.05)	0.68 (0.47–0.97)	1.55 (1.03–2.32)	1.12 (0.75–1.67)	0.95 (0.62–1.46)
		Women	0.82 (0.53–1.29)	0.71 (0.46–1.09)	0.68 (0.44–1.07)	0.84 (0.48–1.48)	0.63 (0.36–1.09)	0.57 (0.32–1.02)
<b>Other events</b>								
Haemorrhagic stroke <sup>5</sup>	<70	Overall	1.39 (1.13–1.71)	0.83 (0.67–1.03)	0.77 (0.62–0.96)	1.31 (1.00–1.73)	0.90 (0.68–1.19)	0.86 (0.65–1.15)
		Men	1.65 (1.22–2.23)	0.86 (0.63–1.18)	0.77 (0.57–1.05)	1.43 (0.89–2.29)	0.86 (0.53–1.40)	0.77 (0.47–1.25)
		Women	1.28 (0.95–1.72)	0.80 (0.59–1.08)	0.78 (0.58–1.05)	1.34 (0.95–1.88)	0.89 (0.62–1.26)	0.92 (0.65–1.31)
	≥70	Overall	0.80 (0.69–0.91)	0.59 (0.52–0.68)	0.65 (0.57–0.74)	1.28 (1.09–1.50)	0.72 (0.62–0.84)	0.80 (0.68–0.94)
		Men	0.82 (0.67–1.01)	0.59 (0.48–0.71)	0.64 (0.52–0.78)	1.45 (1.14–1.83)	0.78 (0.62–0.98)	0.86 (0.68–1.09)
		Women	0.78 (0.65–0.94)	0.60 (0.50–0.72)	0.66 (0.55–0.79)	1.16 (0.93–1.44)	0.68 (0.56–0.84)	0.76 (0.61–0.93)
Mesenteric thrombosis	<70	Overall	1.61 (1.10–2.36)	0.84 (0.56–1.26)	0.65 (0.43–0.97)	1.77 (1.11–2.84)	1.08 (0.66–1.75)	0.83 (0.50–1.37)
		Men	2.91 (1.78–4.75)	1.29 (0.77–2.17)	0.97 (0.57–1.64)	2.21 (0.99–4.94)	1.15 (0.50–2.62)	0.82 (0.35–1.91)
		Women	0.91 (0.49–1.67)	0.55 (0.29–1.03)	0.45 (0.23–0.86)	1.61 (0.90–2.88)	1.09 (0.60–1.98)	0.94 (0.50–1.75)
	≥70	Overall	0.72 (0.57–0.90)	0.54 (0.43–0.67)	0.54 (0.44–0.68)	1.06 (0.81–1.37)	0.61 (0.48–0.78)	0.59 (0.45–0.76)
		Men	0.57 (0.37–0.86)	0.41 (0.27–0.61)	0.42 (0.28–0.62)	0.82 (0.53–1.29)	0.44 (0.29–0.66)	0.42 (0.27–0.65)
		Women	0.80 (0.61–1.04)	0.61 (0.47–0.80)	0.62 (0.48–0.81)	1.18 (0.86–1.63)	0.72 (0.53–0.98)	0.70 (0.51–0.96)
Lower limb fracture	<70	Overall	1.44 (1.31–1.59)	1.03 (0.93–1.14)	0.93 (0.84–1.02)	1.24 (1.08–1.42)	0.95 (0.83–1.09)	0.89 (0.78–1.03)
		Men	1.19 (0.99–1.42)	0.94 (0.78–1.12)	0.85 (0.71–1.02)	0.99 (0.74–1.31)	0.83 (0.62–1.11)	0.80 (0.60–1.07)
		Women	1.49 (1.33–1.67)	1.08 (0.96–1.21)	0.98 (0.87–1.10)	1.27 (1.09–1.48)	1.00 (0.85–1.17)	0.94 (0.80–1.11)
	≥70	Overall	0.99 (0.93–1.05)	0.65 (0.62–0.69)	0.69 (0.66–0.73)	1.48 (1.38–1.59)	0.67 (0.63–0.72)	0.71 (0.66–0.76)
		Men	0.95 (0.85–1.06)	0.58 (0.52–0.64)	0.63 (0.57–0.70)	1.60 (1.40–1.83)	0.65 (0.57–0.73)	0.69 (0.61–0.79)
		Women	1.00 (0.93–1.07)	0.68 (0.64–0.73)	0.72 (0.67–0.77)	1.42 (1.30–1.55)	0.68 (0.63–0.73)	0.71 (0.65–0.77)

Outcome	Age	Sex	1-28 days post-vaccination			>28 days post vaccination s		
			Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>	Unadjusted <sup>1</sup>	Age and sex adjusted <sup>2</sup>	Fully adjusted <sup>3</sup>
Death	<70	Overall	0.74 (0.69–0.79)	0.35 (0.32–0.37)	0.24 (0.22–0.26)	0.91 (0.84–1.00)	0.52 (0.48–0.57)	0.33 (0.30–0.37)
		Men	1.06 (0.97–1.17)	0.39 (0.36–0.43)	0.28 (0.25–0.31)	1.62 (1.44–1.82)	0.69 (0.61–0.79)	0.44 (0.39–0.51)
		Women	0.56 (0.50–0.63)	0.29 (0.26–0.33)	0.22 (0.19–0.25)	0.66 (0.58–0.75)	0.38 (0.34–0.44)	0.28 (0.25–0.33)
	≥70	Overall	0.22 (0.22–0.23)	0.16 (0.16–0.16)	0.19 (0.19–0.20)	0.30 (0.29–0.31)	0.16 (0.16–0.16)	0.19 (0.18–0.19)
		Men	0.23 (0.22–0.24)	0.16 (0.15–0.16)	0.19 (0.18–0.20)	0.33 (0.32–0.34)	0.16 (0.15–0.17)	0.19 (0.18–0.19)
		Women	0.21 (0.20–0.22)	0.16 (0.16–0.17)	0.20 (0.19–0.20)	0.27 (0.26–0.28)	0.16 (0.15–0.17)	0.19 (0.18–0.19)

<sup>1</sup>Stratified by region

<sup>2</sup>Adjusted for age, age<sup>2</sup>, sex and stratified by region

<sup>3</sup>Adjusted for age, age<sup>2</sup>, sex, ethnicity, deprivation, smoking and co-morbidities, and stratified by region

<sup>4</sup>Ischaemic stroke: including ischaemic stroke, stroke of uncertain cause, and spinal stroke

<sup>5</sup>Hemorrhagic stroke: including intracranial hemorrhage and subarachnoid hemorrhage

**Supplementary table 2 (a) Fully adjusted hazard ratios (HRs) for the association of ChAdOx1-S and BNT162b2 with venous events 1-28 and >28 days after vaccination, within pre-specified subgroups. P values for between subgroup differences were derived using Wald tests. OCP: oral contraceptive. HRT: hormone replacement therapy**

		ChAdOx1-S vaccine				BNT162b2 vaccine					
		N (Events)	Post vaccination ≤28 days		Post vaccination >28 days		N (Events)	Post vaccination ≤28 days		Post vaccination >28 days	
Subgroup		3001	HR (95% CI) <sup>1</sup>	P value	HR (95% CI) <sup>1</sup>	P value	3133	HR (95% CI) <sup>1</sup>	P value	HR (95% CI) <sup>1</sup>	P value
Age groups	18-29	40	2.30 (1.63–3.25)	<0.0001	1.29 (0.58–2.90)	0.003	29	0.99 (0.60–1.62)	0.005	0.99 (0.57–1.71)	0.839
	30-39	63	1.33 (1.01–1.75)		0.85 (0.46–1.59)		60	0.90 (0.65–1.25)		0.71 (0.47–1.07)	
	40-49	145	1.32 (1.09–1.61)		1.52 (1.09–2.13)		122	0.96 (0.77–1.21)		0.75 (0.56–1.01)	
	50-59	270	0.93 (0.81–1.07)		1.00 (0.77–1.30)		237	0.78 (0.66–0.92)		0.69 (0.55–0.86)	
	60-69	618	0.87 (0.79–0.96)		0.89 (0.73–1.07)		359	0.78 (0.69–0.89)		0.67 (0.55–0.83)	
	70-79	1124	0.75 (0.69–0.82)		0.79 (0.71–0.88)		823	0.69 (0.62–0.77)		0.73 (0.65–0.82)	
	80-89	546	0.79 (0.69–0.89)		0.73 (0.63–0.84)		1255	0.63 (0.56–0.70)		0.67 (0.61–0.74)	
	>90	195	0.76 (0.62–0.94)		0.75 (0.59–0.95)		248	0.80 (0.65–0.99)		0.67 (0.55–0.81)	
Sex	Male	1338	0.81 (0.75–0.87)	0.029	0.74 (0.66–0.82)	0.005	1423	0.70 (0.64–0.76)	0.150	0.66 (0.60–0.72)	0.024
	Female	1663	0.90 (0.84–0.97)		0.89 (0.81–0.98)		1710	0.75 (0.70–0.81)		0.74 (0.69–0.81)	
Ethnicity	White	2856	0.86 (0.82–0.91)	0.018	0.82 (0.76–0.89)	0.429	2977	0.72 (0.68–0.77)	0.002	0.71 (0.66–0.76)	0.691
	Asian or Asian British	38	0.51 (0.34–0.77)		0.66 (0.38–1.14)		56	0.69 (0.48–0.98)		0.57 (0.38–0.86)	
	Black or Black British	53	0.91 (0.66–1.25)		0.62 (0.35–1.10)		42	0.62 (0.41–0.94)		0.61 (0.39–0.97)	
	Mixed	10	0.47 (0.21–1.06)		0.76 (0.28–2.06)		12	0.74 (0.36–1.51)		0.43 (0.16–1.17)	
	Other Ethnic Groups	17	0.73 (0.37–1.43)		1.63 (0.80–3.32)		23	1.30 (0.75–2.24)		0.94 (0.48–1.84)	
	Unknown	21	1.11 (0.65–1.89)		1.14 (0.50–2.58)		15	0.74 (0.36–1.51)		0.68 (0.32–1.47)	
Missing	6	2.59 (1.05–6.42)	1.29 (0.18–9.32)	8	3.85 (1.67–8.87)	1.33 (0.33–5.43)					
Deprivation	1-2 (least)	564	0.76 (0.68–0.85)	0.138	0.76 (0.65–0.89)	0.43	489	0.65 (0.57–0.74)	0.095	0.54 (0.47–0.62)	<0.0001
	3-4	560	0.86 (0.77–0.96)		0.80 (0.68–0.93)		576	0.76 (0.67–0.85)		0.70 (0.62–0.80)	
	5-6	625	0.90 (0.81–1.00)		0.82 (0.71–0.96)		606	0.70 (0.62–0.79)		0.67 (0.59–0.76)	
	7-8	632	0.87 (0.78–0.97)		0.80 (0.69–0.93)		687	0.73 (0.65–0.82)		0.71 (0.63–0.80)	
	9-10 (most)	609	0.91 (0.81–1.01)		0.92 (0.79–1.06)		770	0.81 (0.72–0.91)		0.88 (0.79–0.98)	
Prior thrombocytopenia	No	3001	0.86 (0.82–0.91)	0.030	0.82 (0.76–0.89)	0.127	3132	0.73 (0.69–0.78)	0.014	0.71 (0.66–0.75)	0.372
	Yes	0	0.54 (0.35–0.82)		0.54 (0.31–0.93)		<5	0.37 (0.21–0.63)		0.58 (0.38–0.89)	
Prior thrombophilia	No	2986	0.86 (0.81–0.91)	0.093	0.82 (0.76–0.89)	0.130	3116	0.73 (0.69–0.77)	0.254	0.70 (0.66–0.75)	0.924
	Yes	15	0.50 (0.27–0.94)		0.38 (0.14–1.03)		17	0.48 (0.23–0.99)		0.68 (0.34–1.37)	
Prior venous event	No	3001	0.95 (0.90–1.01)	<0.0001	0.96 (0.88–1.05)	<0.0001	3133	0.80 (0.76–0.86)	<0.0001	0.78 (0.73–0.84)	<0.0001
	Yes	0	0.54 (0.48–0.61)		0.42 (0.35–0.50)		0	0.44 (0.38–0.51)		0.44 (0.38–0.51)	
Prior COVID infection	No	2839	0.88 (0.83–0.93)	<0.001	0.85 (0.79–0.93)	<0.0001	3012	0.74 (0.70–0.79)	0.001	0.72 (0.68–0.77)	<0.001
	Yes	162	0.60 (0.49–0.74)		0.49 (0.37–0.64)		121	0.47 (0.36–0.61)		0.45 (0.34–0.58)	
OCP	No	2996	1.15 (0.99–1.35)	0.382	1.03 (0.77–1.39)	0.786	3129	0.84 (0.70–1.00)	0.195	0.77 (0.61–0.97)	0.270
	Yes	5	0.69 (0.22–2.17)		1.26 (0.31–5.09)		<5	0.33 (0.08–1.34)		0.34 (0.08–1.41)	
HRT	No	2972	0.78 (0.73–0.83)	0.514	0.75 (0.69–0.82)	0.532	3112	0.69 (0.65–0.73)	0.554	0.66 (0.62–0.71)	0.949
	Yes	29	0.92 (0.56–1.50)		0.96 (0.45–2.05)		21	0.57 (0.30–1.08)		0.65 (0.34–1.23)	
Anticoagulant	No	2759	0.98 (0.92–1.03)	<0.0001	0.98 (0.90–1.07)	<0.0001	2875	0.84 (0.79–0.89)	<0.0001	0.83 (0.77–0.89)	<0.0001
	Yes	242	0.34 (0.29–0.40)		0.28 (0.22–0.35)		258	0.25 (0.21–0.31)		0.27 (0.22–0.32)	
Antiplatelet	No	2503	0.89 (0.84–0.95)	<0.001	0.84 (0.77–0.92)	0.081	2513	0.75 (0.71–0.80)	0.011	0.72 (0.67–0.77)	0.220
	Yes	498	0.69 (0.61–0.78)		0.73 (0.62–0.85)		620	0.62 (0.55–0.71)		0.66 (0.58–0.75)	
Prior MI or stroke	No	2603	0.88 (0.83–0.93)	0.004	0.87 (0.80–0.95)	<0.0001	2680	0.74 (0.70–0.79)	0.021	0.72 (0.67–0.77)	0.086
	Yes	398	0.71 (0.62–0.82)		0.58 (0.48–0.69)		453	0.62 (0.53–0.72)		0.63 (0.55–0.73)	
Prior diabetes	No	2363	0.88 (0.83–0.93)	0.053	0.85 (0.78–0.93)	0.034	2456	0.74 (0.70–0.79)	0.149	0.71 (0.66–0.76)	0.639
	Yes	638	0.78 (0.70–0.87)		0.72 (0.62–0.83)		677	0.67 (0.60–0.76)		0.69 (0.61–0.78)	

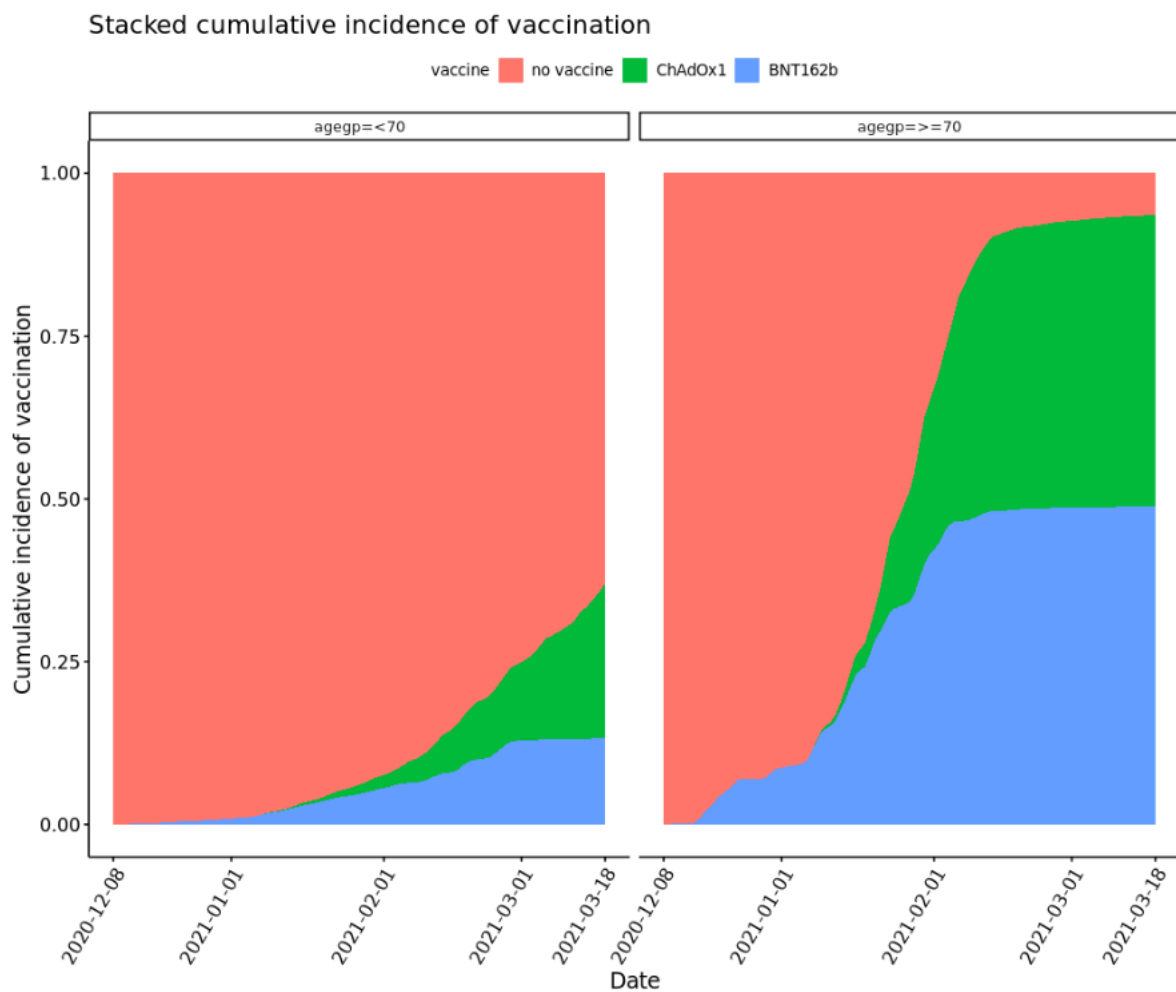
specified subgroups. P values for between subgroup differences were derived using Wald tests. OCP: oral contraceptive. HRT: hormone replacement therapy

Subgroup	All arterial	ChAdOx1-S vaccine				BNT162b2 vaccine					
		N (Events)	Post vaccination ≤28 days		Post vaccination >28 days		N (Events)	Post vaccination ≤28 days		Post vaccination >28 days	
		12890	HR (95% CI) <sup>1</sup>	P value	HR (95% CI) <sup>1</sup>	P value	16759	HR (95% CI) <sup>1</sup>	P value	HR (95% CI) <sup>1</sup>	P value
Age groups	18-29	12	1.72 (0.89–3.33)	<0.0001	1.84 (0.59–5.73)	0.031	21	2.01 (1.13–3.57)	<0.0001	1.85 (0.96–3.59)	<0.0001
	30-39	54	1.51 (1.11–2.06)		1.54 (0.87–2.72)		67	1.36 (1.00–1.86)		1.09 (0.74–1.61)	
	40-49	277	1.37 (1.20–1.57)		1.29 (0.99–1.69)		284	1.17 (1.01–1.36)		0.86 (0.70–1.05)	
	50-59	963	0.98 (0.91–1.05)		0.89 (0.76–1.04)		1062	1.06 (0.98–1.14)		0.81 (0.72–0.91)	
	60-69	2442	0.85 (0.81–0.90)		0.90 (0.82–0.99)		1705	0.89 (0.84–0.95)		0.83 (0.76–0.92)	
	70-79	5030	0.90 (0.86–0.94)		0.93 (0.88–0.99)		3993	0.85 (0.81–0.89)		0.91 (0.86–0.96)	
	80-89	2826	0.86 (0.81–0.91)		0.88 (0.82–0.94)		7733	0.74 (0.71–0.78)		0.79 (0.76–0.82)	
	>90	1286	0.85 (0.78–0.93)		0.86 (0.78–0.94)		1894	0.72 (0.66–0.79)		0.78 (0.73–0.84)	
Sex	Male	7116	0.78 (0.75–0.80)	<0.0001	0.75 (0.71–0.79)	<0.0001	9292	0.77 (0.74–0.79)	<0.0001	0.71 (0.68–0.73)	<0.0001
	Female	5774	0.89 (0.86–0.93)		0.87 (0.83–0.92)		7467	0.85 (0.82–0.88)		0.89 (0.85–0.92)	
Ethnicity	White	11729	0.82 (0.79–0.84)	<0.0001	0.80 (0.77–0.84)	0.180	15492	0.80 (0.78–0.82)	<0.0001	0.79 (0.76–0.81)	<0.0001
	Asian or Asian British	647	0.84 (0.76–0.93)		0.74 (0.64–0.86)		728	0.75 (0.67–0.84)		0.63 (0.56–0.71)	
	Black or Black British	217	0.90 (0.75–1.07)		0.89 (0.70–1.15)		190	0.77 (0.62–0.94)		0.79 (0.64–0.99)	
	Mixed	72	1.19 (0.90–1.57)		0.56 (0.32–0.98)		85	1.10 (0.82–1.49)		0.81 (0.57–1.17)	
	Other Ethnic Groups	113	0.93 (0.73–1.18)		0.90 (0.64–1.28)		121	0.89 (0.69–1.15)		0.76 (0.57–1.01)	
	Unknown	80	0.88 (0.67–1.16)		0.75 (0.49–1.16)		103	0.87 (0.64–1.18)		1.09 (0.83–1.44)	
	Missing	32	3.01 (1.98–4.57)		1.91 (0.89–4.08)		40	2.87 (1.81–4.56)		2.87 (1.80–4.58)	
Deprivation	1-2 (least)	2498	0.76 (0.71–0.80)	<0.001	0.71 (0.66–0.77)	<0.0001	2788	0.75 (0.71–0.79)	<0.0001	0.69 (0.65–0.73)	<0.0001
	3-4	2514	0.81 (0.76–0.85)		0.76 (0.71–0.82)		2980	0.76 (0.72–0.81)		0.74 (0.69–0.78)	
	5-6	2683	0.85 (0.81–0.90)		0.79 (0.74–0.85)		3489	0.78 (0.74–0.83)		0.79 (0.75–0.84)	
	7-8	2616	0.83 (0.78–0.87)		0.86 (0.80–0.92)		3693	0.82 (0.78–0.87)		0.83 (0.79–0.88)	
	9-10 (most)	2541	0.89 (0.85–0.95)		0.88 (0.82–0.95)		3772	0.90 (0.85–0.95)		0.85 (0.80–0.89)	
Prior thrombocytopenia	No	12889	0.82 (0.80–0.85)	0.334	0.80 (0.77–0.84)	0.499	16758	0.80 (0.78–0.82)	0.920	0.78 (0.76–0.81)	0.136
	Yes	<5	0.75 (0.61–0.91)		0.73 (0.57–0.95)		<5	0.81 (0.66–1.00)		0.67 (0.54–0.82)	
Prior thrombophilia	No	12864	0.82 (0.80–0.85)	0.059	0.80 (0.77–0.83)	0.620	16735	0.80 (0.78–0.82)	0.499	0.78 (0.76–0.81)	0.098
	Yes	26	0.48 (0.28–0.84)		0.66 (0.32–1.39)		24	0.66 (0.38–1.15)		0.43 (0.21–0.88)	
Prior venous event	No	12874	0.83 (0.81–0.85)	0.029	0.80 (0.77–0.84)	0.504	16751	0.81 (0.78–0.83)	0.022	0.79 (0.76–0.81)	0.002
	Yes	16	0.73 (0.66–0.82)		0.77 (0.67–0.88)		8	0.70 (0.63–0.79)		0.66 (0.59–0.74)	
Prior COVID infection	No	12227	0.84 (0.81–0.86)	<0.0001	0.83 (0.79–0.86)	<0.0001	16234	0.81 (0.79–0.84)	<0.0001	0.80 (0.77–0.82)	<0.0001
	Yes	663	0.63 (0.57–0.70)		0.51 (0.45–0.59)		525	0.57 (0.50–0.65)		0.51 (0.45–0.59)	
OCP	No	12889	0.91 (0.79–1.05)	0.983	0.89 (0.67–1.18)	<0.0001	16759	0.91 (0.79–1.06)	<0.0001	0.94 (0.75–1.16)	<0.0001
	Yes	<5	0.89 (0.12–6.51)		0.00 (0.00–0.00)		0	0.00 (0.00–0.00)		0.00 (0.00–0.00)	
HRT	No	12832	0.85 (0.82–0.87)	0.293	0.84 (0.80–0.88)	0.820	16671	0.81 (0.78–0.83)	0.061	0.79 (0.76–0.81)	0.070
	Yes	58	1.01 (0.73–1.40)		0.79 (0.45–1.37)		88	1.10 (0.79–1.51)		1.08 (0.77–1.52)	
Anticoagulant	No	10726	0.84 (0.82–0.87)	<0.001	0.82 (0.78–0.85)	0.015	13715	0.83 (0.81–0.86)	<0.0001	0.80 (0.77–0.83)	<0.001
	Yes	2164	0.74 (0.69–0.79)		0.74 (0.68–0.80)		3044	0.66 (0.62–0.70)		0.71 (0.67–0.76)	
Antiplatelet	No	7636	0.99 (0.96–1.03)	<0.0001	1.06 (1.01–1.11)	<0.0001	9770	0.96 (0.93–0.99)	<0.0001	1.05 (1.01–1.09)	<0.0001
	Yes	5254	0.65 (0.63–0.68)		0.59 (0.55–0.62)		6989	0.65 (0.63–0.67)		0.55 (0.53–0.57)	
Prior MI or stroke	No	6931	1.09 (1.05–1.13)	<0.0001	1.18 (1.12–1.24)	<0.0001	9428	1.08 (1.04–1.12)	<0.0001	1.22 (1.17–1.26)	<0.0001
	Yes	5959	0.64 (0.61–0.66)		0.60 (0.57–0.63)		7331	0.60 (0.57–0.62)		0.51 (0.49–0.53)	
Prior diabetes	No	8742	0.85 (0.83–0.88)	<0.0001	0.84 (0.80–0.88)	<0.001	11689	0.84 (0.82–0.87)	<0.0001	0.82 (0.79–0.85)	<0.0001
	Yes	4148	0.77 (0.73–0.80)		0.73 (0.69–0.78)		5070	0.72 (0.69–0.76)		0.70 (0.67–0.74)	

**Supplementary table 3. Characteristics of patient who had an ICVT event before and after vaccination. Only percentage are presented, as disclosure control does not allow numbers <5 to be released**

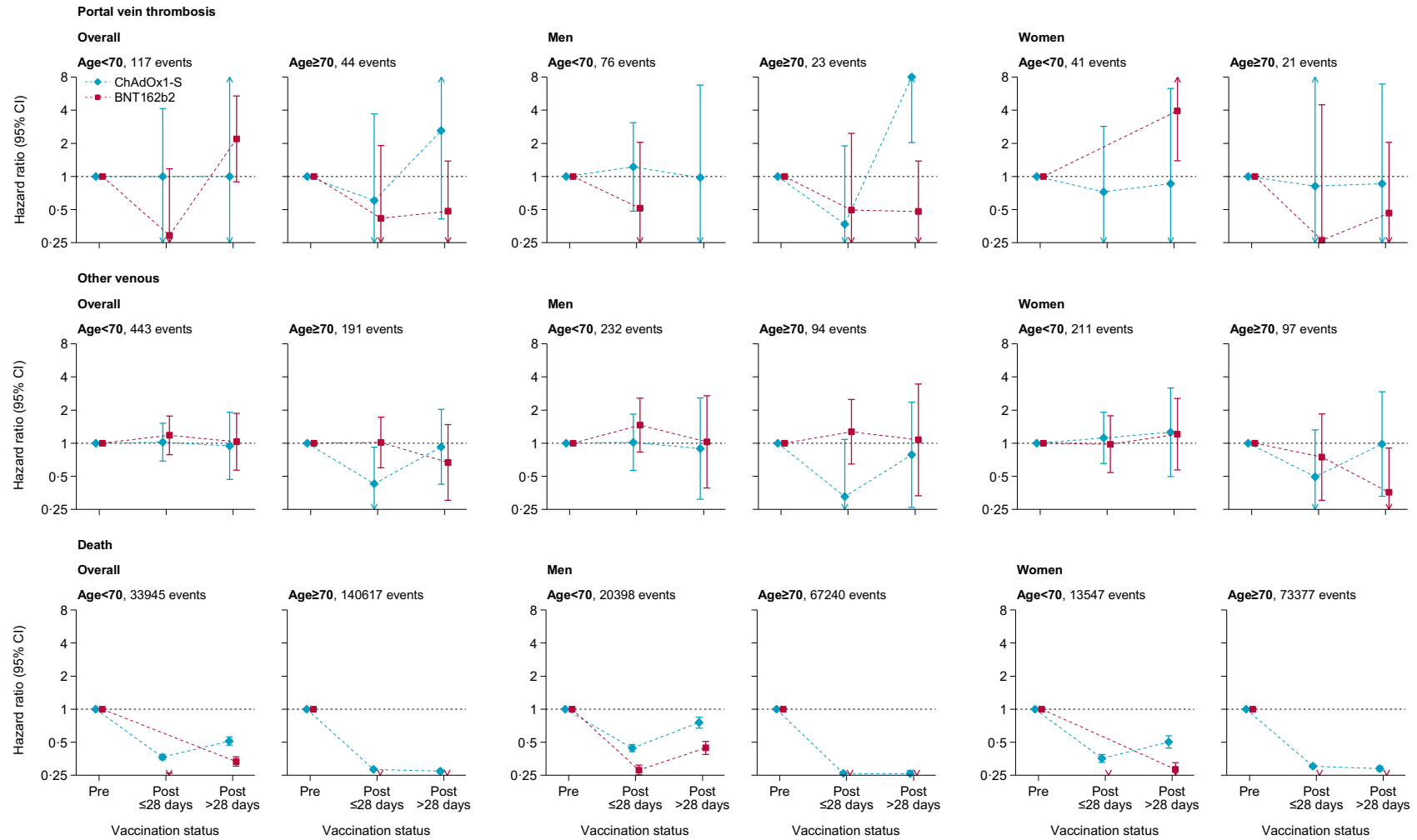
		ICVT before vaccination %	ICVT after ChAdOx1, %	ICVT after BNT162b, %	p-value <sup>1</sup>
N		<210	<40	<20	<0.0001
Sex	Male	40	33	21	0.24
	Female	60	67	79	
Age	18 - 29	19	17	0	<0.0001
	30 - 49	42	22	26	
	50 - 69	30	36	16	
	70 - 79	6	11	21	
	80+	3	14	37	
Ethnicity	Asian or Asian British	15	6	0	0.38
	Black or Black British	5	3	0	
	Mixed	2	0	0	
	Other ethnic groups	1	0	0	
	White	75	92	100	
	Unknown or missing	1	0	0	
Deprivation <sup>2</sup>	1 - 2	29	17	11	0.19
	3 - 4	20	14	26	
	5 - 6	25	25	21	
	7 - 8	13	25	16	
	9 - 10	13	19	26	
Smoking status	Current	19	28	11	0.5
	Former	21	17	32	
	Never	57	56	58	
Medical history	Stroke	5	6	11	<0.0001
	MI	3	6	0	0.01
	DVT or PE	8	6	5	<0.0001
	Thrombophilia	1	0	0	0.05
	Coronavirus infection <sup>3</sup>	6	6	0	<0.0001
	Diabetes	10	17	37	<0.0001
	Depression	26	36	16	<0.0001
	Obesity	37	31	42	<0.0001
	Cancer	17	28	37	<0.0001
	COPD	2	11	16	0.78
	Liver disease	<1	3	0	0.61
	CKD	5	11	32	0.25
	Major surgery <sup>4</sup>	18	8	11	<0.0001
Dementia	2	3	0	0.03	
Medications	Antiplatelet	5	6	16	0.01
	BP lowering	15	28	42	<0.0001
	Lipid lowering	12	22	26	<0.0001
	Anticoagulant	10	11	11	<0.0001
	Oral contraceptive	4	0	0	<0.0001
	HRT	1	0	0	0.05
Number of diagnoses <sup>5</sup>	0	71	50	58	0.04
	1 - 5	29	50	42	
Number of medications	0	31	11	2	0.02
	1 - 5	62	83	5	
	6+	7	6	2	

<sup>1</sup> Approximation if Chi squared test included one or more zero counts; <sup>2</sup> Index of Multiple Deprivation deciles where 1 indicates least deprived and 10 indicates most deprived; <sup>3</sup> After 31/12/2019 and prior to 08/12/2020; <sup>4</sup> In the last year; <sup>5</sup> The category '6+' contained no individuals and so was excluded.



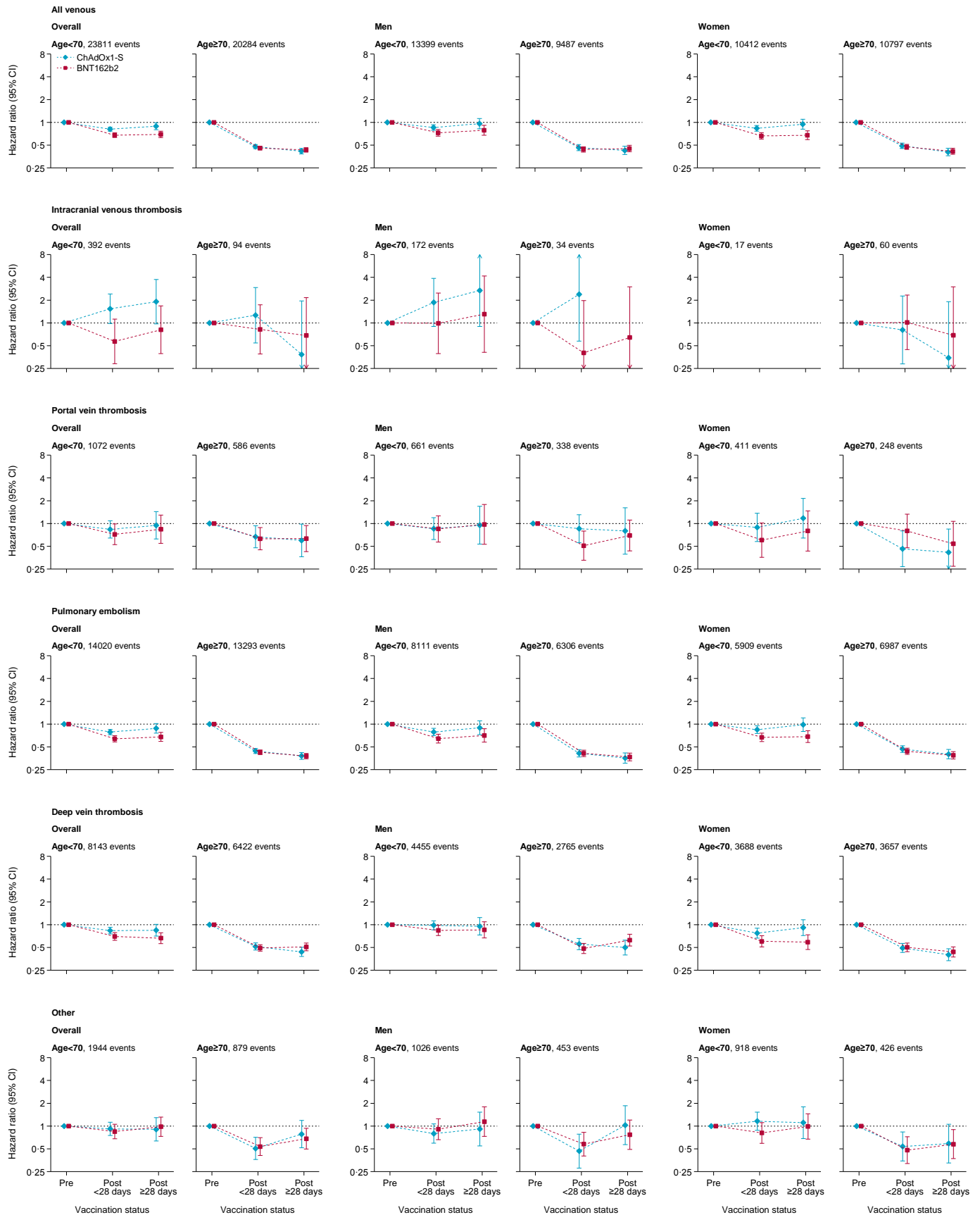
Supplementary figure 1: Cumulative incidence of vaccines of different types during follow up



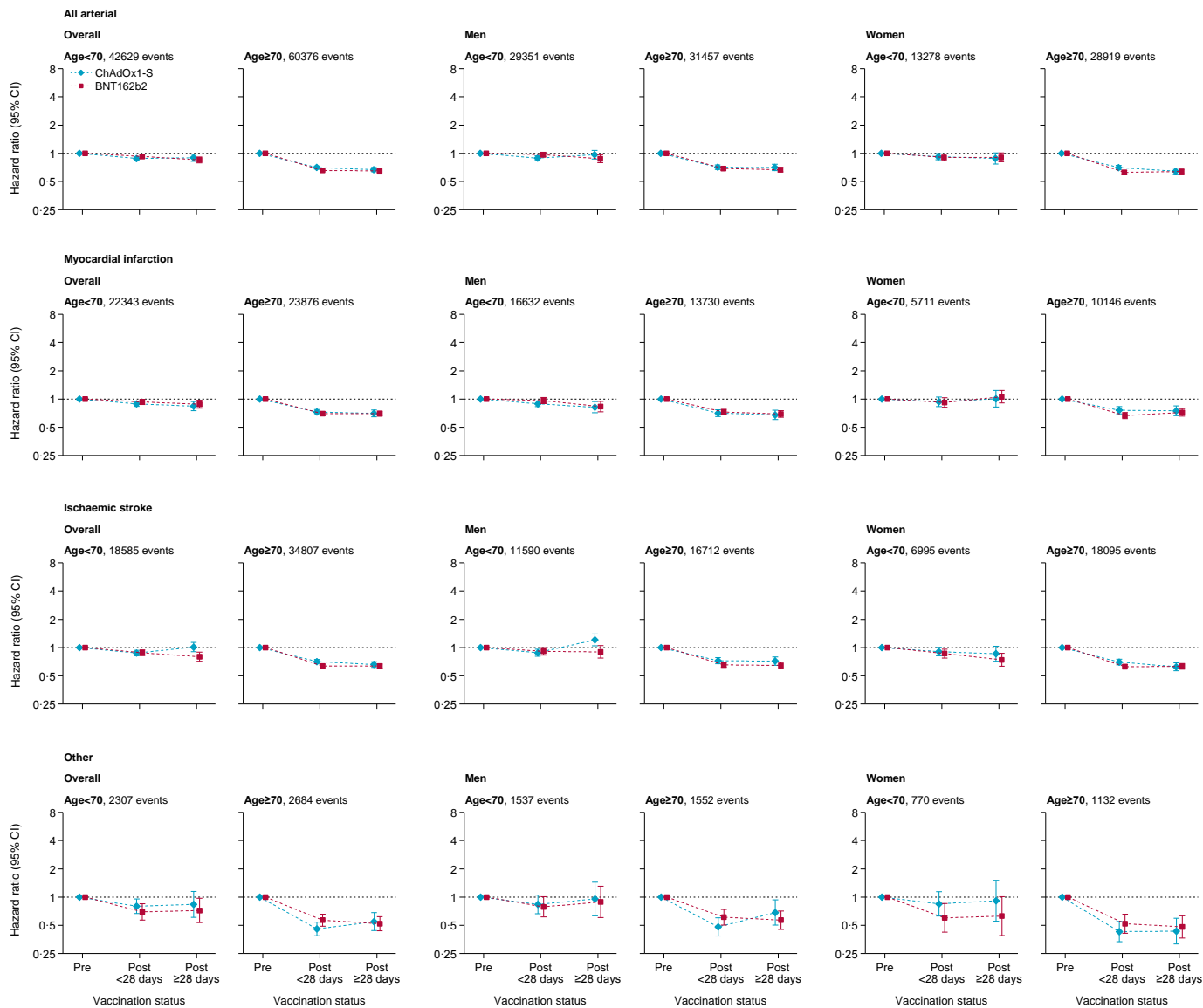


**Supplementary figure 2: Adjusted hazard ratios for portal vein thrombosis, other venous events, and death after ChAdOx1-S or BNT162b2 vaccine**

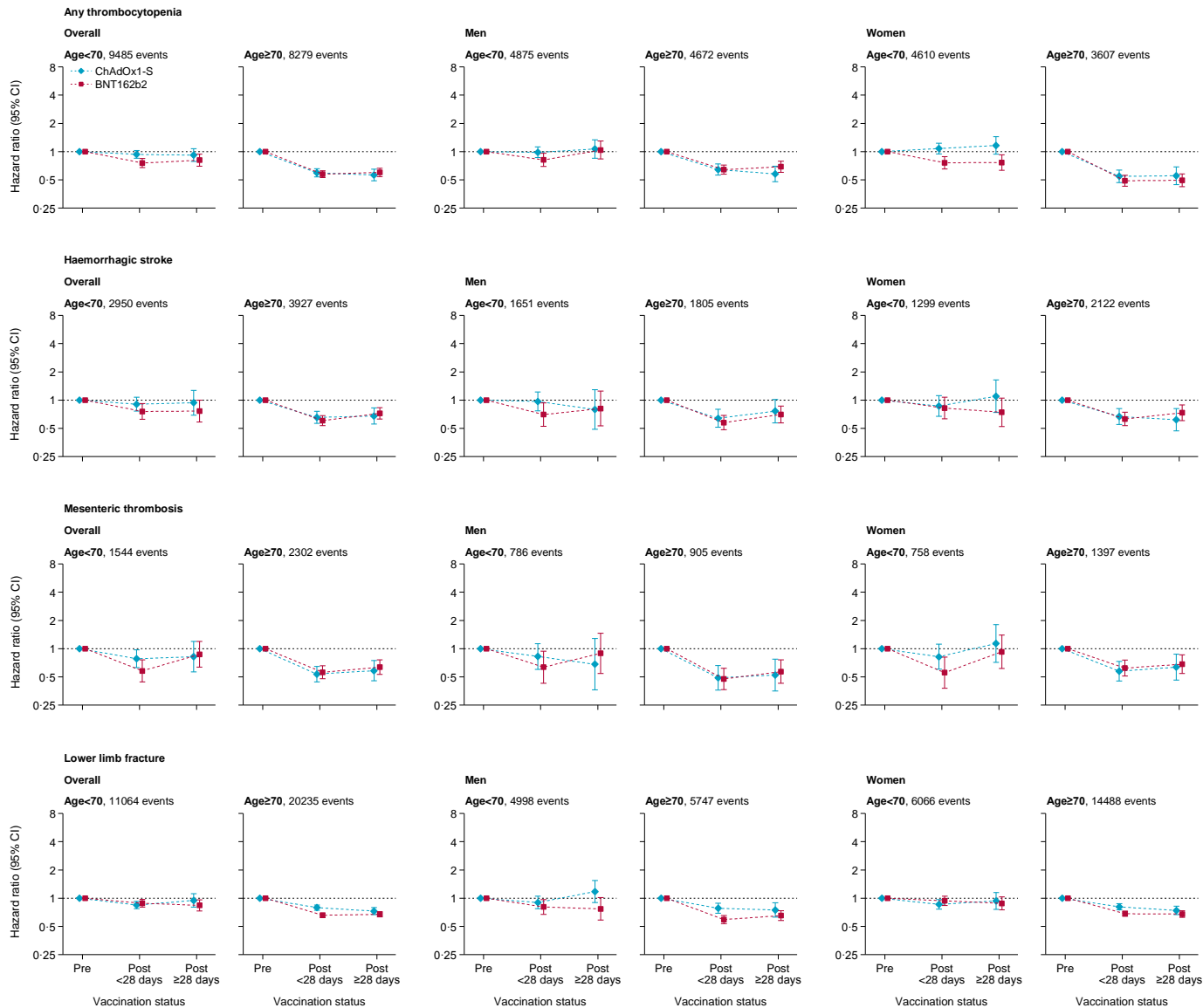
### A Venous



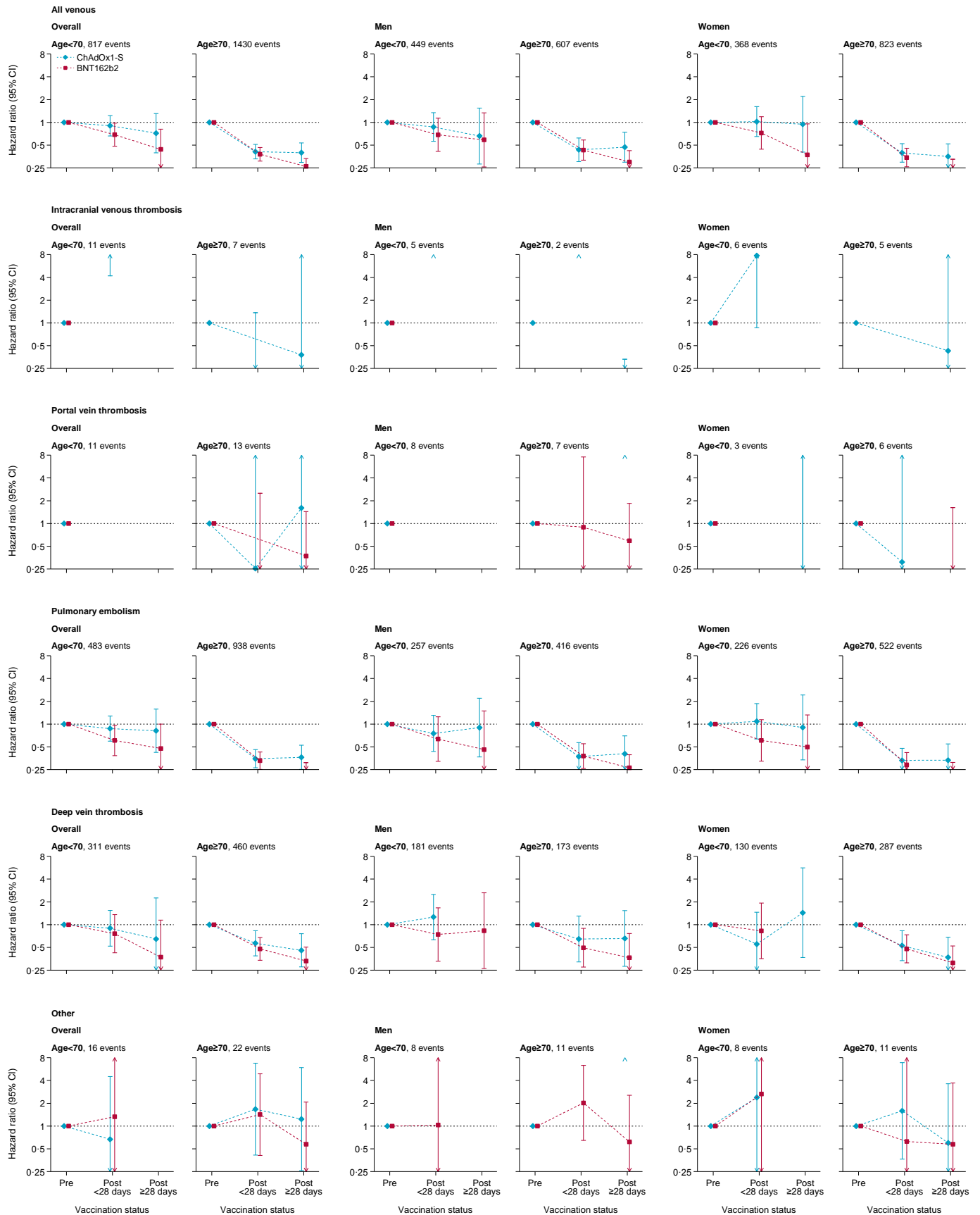
## B Arterial



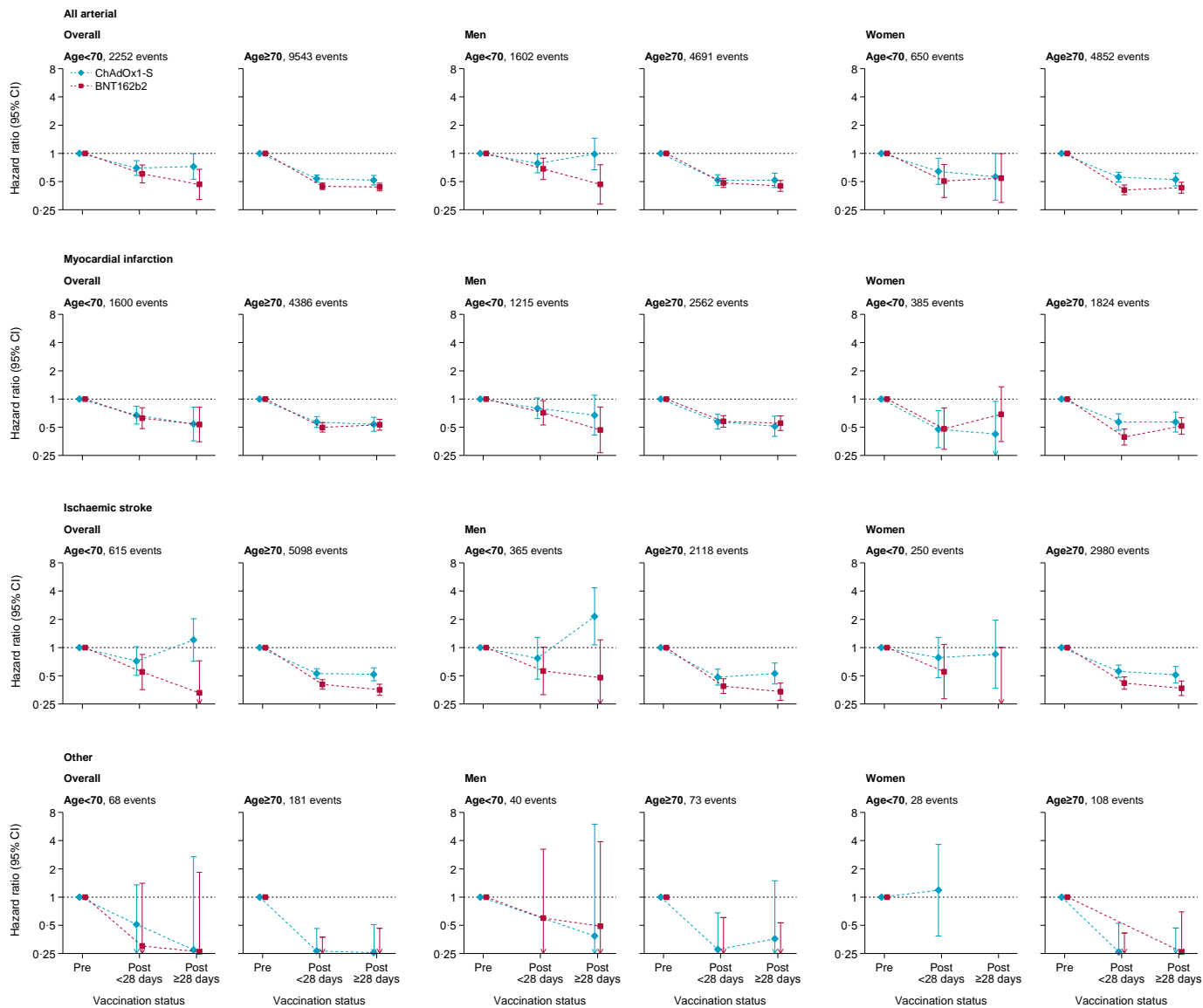
**C Other**



### A Venous



## B Arterial



**C Other**

