Supplemental Online Content

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eTable. Eligibility Criteria and Outcome and Covariates Definitions

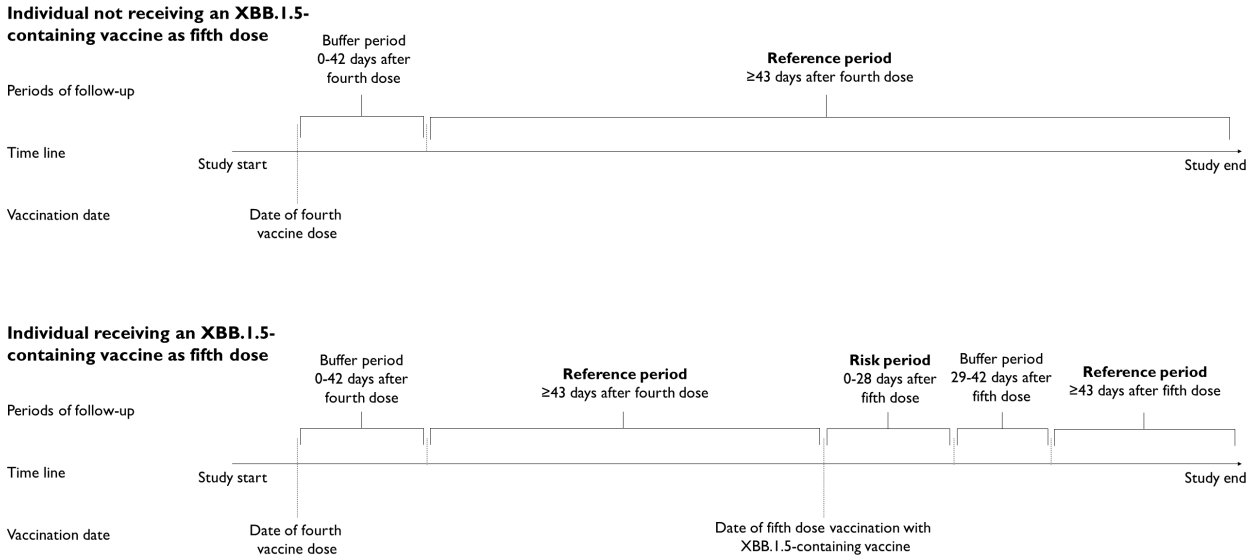
Variable	Details
Eligibility criteria	
Age of ≥65 years	*The Civil Registration System.*[1] The register provides the mandatory unique personal identifier for all permanent residents of Denmark allowing the cross-linkage of all Danish healthcare services and civil registrations systems. The register also holds demographic information such as birthdate, sex, continuously updated information and dates on historical addresses, immigration and emigration status, and death. Age was defined by year of study entry minus birthyear. As such, to be included in our cohort, an individual had to be born in 1958 or earlier (i.e. turning 65 years or older in 2023; age was defined by year of study minus birthyear.
Vaccinated with a primary course and two booster Covid-19 vaccines	*The Danish Vaccination Register.*[2] Defined as registered received three previous Covid-19 vaccines with the BNT162b2 and/or mRNA-1273 as well as and/or AZD1222 vaccine (the latter as part of the primary vaccination course only) and a fourth dose of the bivalent BA.4-5/BA.1-containing mRNA-booster vaccines as per national rollout to the target population. Other vaccine types were rare within our source population and was treated as a censoring event. During the national rollout of the primary vaccination course, vaccination with the AZD1222 vaccine was halted in Denmark in early March 2021.
Third vaccine dose not received earlier than 9 September 2021 and fourth vaccine dose not received earlier than 15 September 2022[a]	*The Danish Vaccination Register.*[2] The dates 9 September 2021 and 15 September 2022 denote the first day of national rollout of the third (i.e., first booster) and fourth (i.e., second booster) vaccine dose to the general Danish population, respectively.
Third or fourth vaccine dose not received within 90 days of the last received dose[b]	*The Danish Vaccination Register.*[2] As vaccination with a third or fourth vaccine dose within 90 days of the last received dose (i.e., second or third dose) do not constitute as a booster dose per se, but rather part of the primary vaccination schedule and/or not recommended for the target population.
Outcomes	The National Patient Register.[3] Both primary and secondary diagnoses recorded during any type of first-time hospital contact using ICD-10 codes.[c]
Ischemic cardiac event	ICD-10: I20-I251
Cerebrovascular event	ICD-10: I60-66, G450-G453
Cerebral infarction (incl. TIA)	ICD-10: I63, I64, G450-453
Arterial thromboembolism	ICD-10: I74
Deep venous thrombosis	ICD-10: I80-82 (not I800, I808C, or I821)
Pulmonary embolism	ICD-10: I26
Myocarditis	ICD-10: I401, I408, I409, I418, I514
Pericarditis	ICD-10: I300, I308, I309, I328
Cerebral venous thrombosis	ICD-10: I636, I676
Thrombocytopenia or coagulative disorders	ICD-10: D65, D683, D686, D688-689, D690, D693-D699 (not D697 or D698A)
Guillain-Barré syndrome	ICD-10: G610
Bell's palsy	ICD-10: G510
Transverse myelitis	ICD-10: G373
Encephalomyelitis or encephalitis	ICD-10: G040, G040A, G048, G049, G058, G361

Narcolepsy	ICD-10: G474
Appendicitis	ICD-10: K35-K37
Aseptic arthritis	ICD-10: M10, M119, M130, M131, M139
Type 1 diabetes mellitus	ICD-10: E10
Subacute thyroiditis	ICD-10: E061
Heart failure	ICD-10: I110, I420, I426-I429, I50, J81,
Arrythmia	ICD-10: I44-I49
Acute liver failure	ICD-10: K71, K72
Acute kidney failure	ICD-10: D593, I12, I13, N00-N02, N04-N05, N08, N10, N141, N142, N144, N17, N19, R34
Acute pancreatitis	ICD-10: K850, K853, K858, K859
Erythema multiforme	ICD-10: L51
Seizure	ICD-10: G40, G41
Arterial aneurysm	ICD-10: I71, I72
Uveitis	ICD-10: H20, H30
Covariates	
Sex	*The Civil Registration System.*[1] Defined by registered sex.
Age	*The Civil Registration System.*[1] Age was defined by year of study (i.e., year 2022 or 2023) minus birthyear and categorized by ≥/< 65 years.
Calendar time	*The Civil Registration System.*[1] Treated as a time-varying covariates in 3-month bins.
Region of residency	*The Civil Registration System.*[1] Defined by the last registered address and categorized according: Northern Denmark Region, Central Denmark Region, Region of Southern Denmark, Capital Region of Denmark, and Region Zealand.
Vaccination priority groups	*The Danish Vaccination Register.*[2] The register holds information on all (mandatorily) recorded administered vaccines in Denmark including information on vaccination date, -type, -dose, and -product batch. In addition, during the Covid-19 pandemic, the register was allocated information on governmentally prioritized Covid-19 vaccine groups assigned according to whether an individual was considered as being at high risk of severe Covid-19 (categorized binarily).
Comorbidities	*The National Patient Register.*[3] The register holds information on all hospital contacts (secondary healthcare facilities) in Denmark including information on the contact duration and treating physician-assigned diagnoses (registered according to the ICD 10-codes). We defined comorbidity status as any registered primary or secondary diagnosis regardless of the hospital contact type between 1 January 2018 and baseline (15 September 2022) and indexed by the number of comorbidities as a sum (0, 1, or ≥2 comorbidities).
Asthma	ICD-10: J45, J46
Chronic respiratory disorder	ICD-10: E84, J41-J44, J47, J84
Chronic cardiac disorder	ICD-10: I05-I08, I20-I28, I34-I37, I42-I51
Renal disorder	ICD-10: N03, N05, N07, N18, N19, N25-N27
Diabetes	ICD-10: E10-E14
Autoimmune disorder	ICD-10: D510, D590, D591, D690, D693, D86, E035, E039, E050, E055, E059, E063, E065, E271, E272, E310, G04, G131, G35, G36, G61, G700, H20, I00, I02, K50, K51, K732, K743, K900, L10, L12, L130, L40, L63, L80, M05, M06, M08,

	M30, M311, M313, M315, M316, M317, M32-M34, M350-M353, M358, M359, M45, M60
Epilepsy	ICD-10 codes: G40, G41
Malignancy	ICD-10 codes: C00-C96 (not C44), D70-D72, D730, D81-D84
Psychiatric disorder	ICD-10 codes: F00-F99

ICD-10 denotes International Classification of Diseases System, version 10, TIA transient cerebral ischemic attack, and NA not applicable. [a]Similarly, we censored individuals vaccinated with a fifth dose prior to 1 October 2023 (first day of national rollout of the fifth vaccine dose to the general population). [b]Similarly, we censored individuals receiving a fifth dose within 90 days of the fourth dose. We also excluded individuals with history of the respective outcome under studied prior to the follow-up period. [c] Only incident outcome events were studied by excluding those individuals with a history of the respective studied outcome during a washout period from 1 January 2018 to day 28 after the fourth dose from that specific outcome analysis.

eFigure. Schematic Figure of the Study Design



The risk period was from day 0 to day 28 following a fifth dose of Covid-19 vaccination with an XBB.1.5-containing vaccine. The reference period consisted of both a) ≥43 days following a fourth dose (up until the day before a fifth dose vaccination) and b) ≥43 days following a fifth dose (up until study end). Individuals could contribute with person-time during both the 28-day risk period and the two reference periods. The day 0-42 period after a fourth dose and day 29-42 period after a fifth dose was considered a buffer period and not included in the risk period or in the reference period follow-up. Among the 1,076,531 included individuals, 902,803 received a fifth dose with an XBB.1.5-containing vaccine (i.e., contributed with both risk and reference period person-time), and 172,756 did not receive a fifth dose (i.e., contributed with reference period person-time only) during follow-up; the distribution of person-time allocated to the potential risk and reference period for the two potential follow-ups are presented in the bottom and top panel examples, respectively. Outcome rates during the risk and reference period were compared by incidence rate ratios using adjusted Poisson regression.

eReferences

1. Schmidt, M., Pedersen, L. & Sørensen, H. T. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol* **29**, 541–549 (2014).
2. Krause, T. G., Jakobsen, S., Haarh, M. & Mølbak, K. The Danish vaccination register. *Euro Surveill* **17**, 20155 (2012).
3. Schmidt, M. *et al.* The Danish National Patient Registry: a review of content, data quality, and research potential. *Clinical Epidemiology* 449 (2015) doi:10.2147/CLEP.S91125.