SCIENCE BRIEFS

Risk of Vaccine-Induced Thrombotic Thrombocytopenia (VITT) following the AstraZeneca/ COVISHIELD Adenovirus Vector COVID-19 Vaccines

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About Us: The Ontario COVID-19 Science Advisory Table is a group of scientific experts and health system leaders who evaluate and report on emerging evidence relevant to the COVID-19 pandemic, to inform Ontario's response. Our mandate is to provide weekly summaries of relevant scientific evidence for the COVID-19 Health Coordination Table of the Province of Ontario, integrating information from existing scientific tables, Ontario's universities and agencies, and the best global evidence. The Science Table summarizes its findings for the Health Coordination Table and the public in Science Briefs.

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The views and findings expressed in this Science Brief are those of the authors and do not necessarily reflect the views of all of the members of the Ontario COVID-19 Science

Key Message

Published estimates of the risk of vaccine-induced thrombotic thrombocytopenia (VITT) from countries with moderate to high data quality range from 1 case per 26,500 to 1 case per 127,300 first doses of AstraZeneca/COVISHIELD administered (Table 1).

The risk of VITT in Canada as of April 28, 2021 has been estimated to be approximately 1 per 100,000 doses, but several presumptive cases are still under investigation.

Country	Cases	Estimated Persons Receiving 1st Dose of Vaccine	Incidence	Data Quality	Peer Reviewed	Case Ascertainment and Estimation of Denominator Population
Norway[1]	5	132,472	1:26,500	High	Yes	Centralized electronic health record system used to ascertain cases. Vaccination paused after cases discovered allowing accurate estimation of the denominator population at risk of VITT.
Netherlands[2]	8	400,000	1:50,000	Uncertain	No	Unclear.
Denmark[3]	2	148,792	1:74,400	High	No	Centralized electronic health record system used to ascertain cases. Vaccination paused after cases discovered allowing accurate estimation of the denominator population at risk of VITT.
UK[4]	242	22,600,000	1:93,400	Moderate	No	Ambispective pharmacovigilance for thrombotic events after vaccination, frequency of cases may therefore be underestimated initially. Vaccination ongoing, size of the denominator population therefore overestimated.
Canada[5]	-	-	1:100,000	Uncertain	No	Retrospective ascertainment of cases since April 2021, frequency of cases may therefore be underestimated. Vaccination ongoing, size of the denominator population therefore overestimated.
Germany[6]	21	2,270,000	1:108,100	Uncertain	No	Unclear.

Advisory Table, its Working Groups, and its partners.

Germany[6]	21	2,270,000	1:108,100	Uncertain	No	Unclear.
France[7]	23	2,725,089	1:118,500	Moderate	No	Ambispective pharmacovigilance for thrombotic events after vaccination, frequency of cases may therefore be underestimated initially. Vaccination ongoing and no distinction made between first and second doses, size of the denominator population therefore overestimated.
Australia[8]	11	1,400,000	1:127,300	Moderate	No	Ambispective pharmacovigilance for thrombotic events after vaccination, frequency of cases may therefore be underestimated initially. Vaccination ongoing and no distinction made between first and second doses, size of the denominator population therefore overestimated.
Italy[9]	11	1,630,000	1:148,200	Uncertain	No	Unclear.
Spain[10]	12	2,575,716	1:214,600	Uncertain	No	Unclear.

Table 1. Estimated Risk of VITT Following First Doses of AstraZeneca/COVISHIELD COVID-19 Vaccine, by Country
Estimated risks of VITT after first doses of AstraZeneca/COVISHIELD vaccines by countries, with countries ordered by risk of VITT, from highest to lowest risk of VITT. See methods section for a description of methodology. VITT, vaccine-induced thrombotic thrombocytopenia.

Background

The AstraZeneca/COVISHIELD COVID-19 vaccine is associated with immune thrombosis that is similar to heparin-induced thrombocytopenia (HIT).[11] Affected individuals have antibodies targeted against platelet factor 4 (PF4) that presumably induce massive platelet activation, reducing the platelet count and causing thrombosis. It has been referred to as VITT. To date, reported cases of VITT occurred between 4 and 28 days after administration of the AstraZeneca/COVISHIELD COVID-19 vaccine.[11]

Questions

What is the reported risk of VITT following the first dose of the AstraZeneca/COVISHIELD COVID-19 vaccine in different countries?

Findings

Published estimates of the risk of VITT from countries with moderate to high data quality range from 1 case per 26,500[1] to 1 case per 127,300[8] first doses of AstraZeneca/COVISHIELD administered (Table 1). Countries with higher data quality tend to show higher estimates of the risk of VITT.

The quality of the data varies among countries and depends on the accuracy of case ascertainment (the number of reported VITT cases used as numerator) and the reliability of the estimated size of the vaccinated population (denominator population who received the first dose of the vaccine and was at risk of VITT). The numerator in this ratio is more difficult to ascertain with certainty due to underdiagnosis.

The risk of VITT in Canada as of April 28, 2021 has been estimated to be approximately 1 per 100,000 first doses.[5]

Interpretation

Published estimates of the risk of VITT currently range from 1 case per 26,500 to 1 case per 127,300 first doses of AstraZeneca/COVISHIELD administered. The risk of VITT in Canada has been estimated to be approximately 1 per 100,000 doses, but several possible cases are still under investigation. Early data from the United Kingdom suggests that the risk of VITT after second doses of AstraZeneca/ COVISHIELD vaccines is likely lower than after first doses.[4]

Methods Used in This Science Brief

We examined data up until May 7, 2021 from countries which have publicly reported VITT cases and had estimates of numbers of prior vaccinations with AstraZeneca/ COVISHIELD COVID-19 vaccines. We excluded countries which had not yet approved the vaccine, elected to not use it, had not publicly reported data within the study period, or had reported some cases but no reported vaccination counts.

We examined information from regulatory authorities, press releases, scientific journals, and media reports. We included only reports of VITT cases with thrombosis associated with thrombocytopenia after vaccination. Cases with only clotting (i.e., arterial or venous thrombosis) and no documented thrombocytopenia were excluded. To estimate the risk of VITT, we matched the announcement date of cases to the number of vaccinations given approximately two weeks prior to the date.

Data were considered to be of high quality (1) if there was reliable case ascertainment, typically enabled by a universal electronic health record system, and (2) if the denominator population at risk of developing VITT 4 to 28 days after vaccination could be reliably estimated, for example if countries had paused vaccination after reports of thrombotic events. Data were considered to be of moderate quality if (1) there was dedicated pharmacovigilance undertaken to identify cases, which was prospective or ambispective (including both a retrospective and prospective element), and (2) the denominator population at risk of developing VITT 4 to 28 days after vaccination could not be reliably estimated. Data were considered to be of uncertain quality if case ascertainment was unclear or only performed retrospectively.

Author Contributions

PJ, AO and MP conceived the Science Brief. PJ, AO and NMS wrote the first draft of the Science Brief. PJ and AO performed the analyses. All authors revised the Science Brief critically for important intellectual content and approved the final version.

References

1. Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021 Apr 9;7.
2. Lareb. Side effect thrombosis with low platelet count reported eight times [Internet]. Bijwerkinjen Centrum Lareb. 2021. Available from: https://www.lareb.nl/nl/news/bijwerking-trombose-met-laag-aantal-bloedplaatjes-acht-keer-gemeld
3. Danish Medicines Agency. Status on reviewed reports of suspected side effects of the COVID-19 Vaccine AstraZeneca after vaccination of more than 140,000 Danes [Internet]. Laegemiddelstyrelsen. 2021. Available from: https://

laegemiddelstyrelsen.dk/en/news/2021/status-on-reviewed-reports-of-suspected-side-effects-of-the-covid-19-vaccine-astrazeneca-after-vaccination-of-more-than-140,000-danes/

4. Medicines and Healthcare products Regulatory Agency. Coronavirus vaccine - weekly summary of Yellow Card reporting - – Data included: 09/12/2020 to 05/04/2021 [Internet]. GOV.UK. 2021. Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting
5. National Advisory Committee on Immunization (NACI). An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI) [Internet]. 2021 May 3. Available from: https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/recommendations-use-covid-19-vaccines-en.pdf
6. AP. Coronavirus vaccine: Germany reports more AstraZeneca clot cases. Business Standard [Internet]. 2021 Mar 29. Available from: https://www.business-standard.com/article/current-affairs/coronavirus-vaccine-germany-reports-more-astrazeneca-clot-cases-121032900737_1.html
7. ANSM. Update on COVID-19 vaccine surveillance - Period from 04/02/2021 to 04/08/2021 [Internet]. L'Agence nationale de sécurité du médicament et des produits de santé. 2021. Available from: https://ansm.sante.fr/uploads/2021/04/16/rapport-n9-covid-19-vaccine-astrazeneca-15-04-21-vfa.pdf
8. Therapeutic Goods Administration. COVID-19 vaccine weekly safety report - 06-05-2021 [Internet]. 2021 May 6. Available from: https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-06-05-2021
9. Amante A. Italy Reported Four Clot Deaths After AstraZeneca Shots, Data Shows. US News [Internet]. 2021 Apr 15. Available from: https://www.usnews.com/news/world/articles/2021-04-15/italy-reported-four-clot-deaths-after-astrazeneca-shots-data-shows
10. Mendez I. Health studies twelve cases of thrombi in people vaccinated with AstraZeneca. SUR [Internet]. 2021 Apr 13. Available from: https://www.diariosur.es/nacional/trombos-vacuna-astrazeneca-20210412215543-nt.html
11. Pai M, Stall NM, Grill A, et al. Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) following adenovirus vector COVID-19 vaccination. Science Briefs of the Ontario COVID-19 Science Advisory Table. 2021;2(17). https://doi.org/10.47326/ocsat.2021.02.17.2.0