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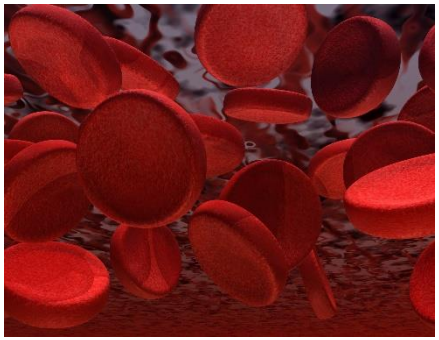
THROMBOEMBOLIC- AND THROMBOCYTOPENIC SAFETY OF SARS-COV-2 VACCINATION IN THE NORDIC COUNTRIES: THREE OBSERVATIONAL APPROACHES



EMA TTS Workshop

June 27, 2022

Prof. Anders Hviid, Statens Serum Institut

A TRILOGY OF STUDIES

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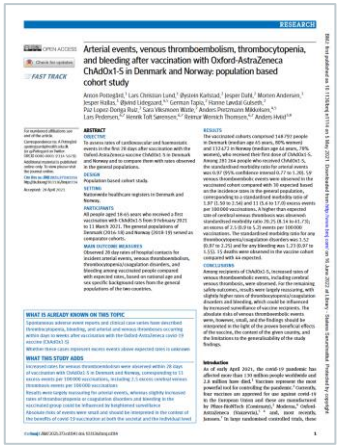

Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study

BMJ, May 5 2021

DK, NO

Observed vs expected

AZD1222

Feb 9 – Mar 11, 2021

281 264 participants

Association of AZD1222 and BNT162b2 COVID-19 Vaccination With Thromboembolic and Thrombocytopenic Events in Frontline Personnel

A Retrospective Cohort Study

Annals, Feb 1 2022

DK

Frontline personel cohort

AZD1222, BNT162b2

Dec 27, 2020 – Apr 13, 2021

355 209 participants

Analysis of Thromboembolic and Thrombocytopenic Events After the AZD1222, BNT162b2, and MRNA-1273 COVID-19 Vaccines in 3 Nordic Countries

JAMA Netw, Jun 15 2022

DK, NO, FI

Self-controlled design

AZD1222, BNT162b2, mRNA-1273

Jan 1, 2020 – May 16, 2021

265 339 hospital contacts

WHY 3 DIFFERENT APPROACHES?

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	Main advantage	Main disadvantage
Observed vs Expected	Can evaluate rare event associations especially early in vaccination roll-out.	No confounder control except age and sex, and compares separate calendar periods (historical comparator).
Contemporary cohort analysis	Nationwide cohort with limited concern about selection- and recall bias. Concurrent comparator. Adjustment.	Relies on availability of confounder information.
Self-controlled case series	No time-invariant confounding by design.	Assumption that having the outcome has no significant influence on future probability of exposure.

AZD1222 RESULTS – CVT AND TP

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AZD1222	Obs vs exp	Frontline per.	Self-controlled
Relative risks			
CVT	20.3 (8.1 to 41.7)	NA	12.0 (5.4 to 27.0)
TP	3.0 (1.8 to 4.8)	NA	4.3 (3.0 to 6.2)
Excess events per 100,000 vac.			
CVT	2.5 (0.9 to 5.2)	1.7 (-0.6 to 4.0)	1.6 (0.6 to 2.6)
TP	4.2 (1.6 to 8.0)	2.4 (-1.1 to 5.9)	4.9 (2.9 to 6.9)

BNT162B2 RESULTS – CVT AND TP

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BNT162b2	Obs vs exp	Frontline per.	Self-controlled
Relative risks			
CVT	NA	NA	1.8 (1.0 to 3.3)
TP	NA	NA	1.0 (0.9 to 1.2)
Excess events per 100,000 vac.			
CVT	NA	NE (0 unvac.)	0.1 (-0.1 to 0.3)
TP	NA	NE (0 vac.)	0.2 (-0.3 to 0.7)

MRNA-1273 RESULTS – CVT AND TP

mRNA-1273	Obs vs exp	Frontline per.	Self-controlled
Relative risks			
CVT	NA	NA	NE
TP	NA	NA	0.9 (0.5 to 1.6)
Excess events per 100,000 vac.			
CVT	NA	NA	NE
TP	NA	NA	-0.5 (-1.7 to 0.7)

CONCLUSIONS

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- AZD1222 increases the risk of CVT and TP within 28-days of vaccination
- Both CVT and TP are rare after AZD1222; 1.6 to 2.5 cases per 100,000 vaccinations for CVT and 2.4 to 4.9 cases per 100,000 vaccinations for TP
- A similar pattern was not observed for either mRNA vaccine
- The BNT162b2 and CVT association in the SCCS study (RR 1.8, 1.0-3.3) was not consistent in sensitivity analyses or across countries
- The associated excess risk was very low, 1 per 1,000,000 vaccinations

REFERENCES

- Pottegård A, Lund LC, Karlstad Ø, et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. *BMJ*. 2021;373:n1114. doi:10.1136/bmj.n1114

- Hviid A, Hansen JV, Thiesson EM, Wohlfahrt J. Association of AZD1222 and BNT162b2 COVID-19 Vaccination With Thromboembolic and Thrombocytopenic Events in Frontline Personnel. *Ann Intern Med*. 2022;175(4):541-546. doi:10.7326/m21-2452

- Berild J, Larsen V, Thiesson E, et al. Analysis of Thromboembolic and Thrombocytopenic Events After the AZD1222, BNT162b2, and MRNA-1273 COVID-19 Vaccines in 3 Nordic Countries. *JAMA Netw Open*. 2022;5(6). (in press)