bijwerkingen centrumlareb

Overview of thrombo-embolic events with COVID-19 vaccines

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Introduction

Currently, four COVID-19 vaccines have been authorized for immunisation in The Netherlands: the mRNA vaccines of Comirnaty (Pfizer/BioNTech) and Moderna and the adenovirus vector vaccines Vaxzevria (Oxford/AstraZeneca) and Janssen. These vaccines have been used in the vaccination campaign in different populations.

	Startdate	Population	Number of vaccinations up to April 11th (maximal estimated numbers)
Comirnaty (Pfizer/BioNTech)	January 6th, 2021	elderly, healthcare professionals	2,501,835
Moderna	January 25th, 2021	healthcare professionals in primary care and smaller institutions	292,193
Vaxzevria (Oxford/AstraZeneca)	February 12th, 2021	healthcare workers and people from risk groups aged <65 years (from April 8th, only 60-65 years and few > 65 years on demand)	989,187
Janssen	April, 21st, 2021		0

The updated EPAR of AstraZeneca COVID-19 vaccine mentions 'severe and very rare cases of thrombosis in combination with thrombocytopenia (VITT; vaccine-induced immune thrombotic thrombocytopenia) have been reported post-marketing' [1] [2]. On March, 18th EMA stated that the vaccine is not associated with an increase in the overall risk of blood clots (thrombo-embolic events) in those who receive it [3]. With Pfizer and Moderna vaccines, no specific signal for thrombo-embolism has been observed.

Thrombo-embolic complications following vaccination are listed as an AESI (Adverse events with special interest) in routine pharmacovigilance activities for safeguarding the safety profile of vaccines. In Phase III trials with Moderna and AstraZeneca vaccines thrombo-embolic events have occurred in less or similar numbers compared with placebo or reference groups [4-6].

Classical thrombo-embolism (without the combination with low number of platelets) is a heterogeneous condition with high background incidence rates that vary among type of thrombosis, gender and age [7]. Since the start of the COVID-19 vaccination campaign, Lareb has been receiving reports of thrombo-embolic events in general with all COVID-19 vaccines. The rate of reporting increased with continuing media attention about the potential risks for thrombo-embolic events with COVID-19 vaccination.

This is an overview of all reported thrombo-embolic events following COVID-19 vaccinations, up to April, 14th 2021. Also, the number of reports on pulmonary embolism, deep vein thrombosis and ischemic cerebral infarction are compared to currently known background incidence rates.

Reports

The Dutch Pharmacovigilance Centre Lareb received 399 unique reports of thrombo-embolic events with COVID-19 vaccines, until April 14th, 2021.
Reports were selected with at least one reaction coded with the broad SMQ's (Standardised MedDRA Queries) for confirmed venous and/or arterial thrombo-embolic events. Reports only with symptoms (e.g. hemiparesis) without a clear diagnosis were not selected. One report can contain more than one relevant reaction, for instance deep vein thrombosis and pulmonary embolism. An overview of all reports and reported reactions is shown in Tables 1 and 2. Figure 1 shows the age distribution of the patients in the reports with the different vaccines.

Table 1. Summary on demographics of unique reports on thrombo-embolic events with COVID-19 vaccines until April 14th, 2021. HCP = healthcare professional, Cons = consumer. Seriousness is defined with CIOMS criteria: leading to hospitalisation, life-threatening, death, disabling or incapacitating.

Vaccine	Comirnaty (Pfizer)	Vaxzevria (AstraZeneca)	COVID-19 VACCIN Moderna	COVID-19 VACCIN Unspecified
Total number of reports	224	150	21	4
1st vaccination	176 (78.6%)	150 (100%)	15 (71.4%)	3 (75%)
2nd vaccination	48 (21.4%)	0 (0%)	6 (28.6%)	1 (25%)
Reporter HCP	136 (61%)	75 (50%)	14 (67%)	4 (100%)
Reporter Cons	88 (39%)	75 (50%)	7 (33%)	0
Seriousness (%)	200 (89.3%)	136 (90.7%)	21 (100%)	4 (100%)
Outcome fatal (%)	29 (12.9%)	4 (2.7%)	1 (4.8%)	1 (25%)
Male (%)	79 (35.3%)	54 (36%)	14 (66.7%)	3 (75%)
Female (%)	145 (64.7%)	96 (64%)	7 (33.3%)	1 (25%)
Age (median; range)	83 (21 - 99)	61 (22 - 82)	65.5 (45 - 93)	87 (59 - 90)

Table 2. Overview on reported reactions. Note that 437 reactions were reported in 399 unique reports. For Cerebral infarction, Pulmonary embolism, Deep vein thrombosis and Other TE multiple reported preferred terms were summarized. More information on selection and features of the reports is available in Supplementary tables D.

	Comirnaty (Pfizer)	Vaxzevria (AstraZeneca)	COVID-19 VACCIN Moderna	COVID-19 VACCIN Unspecified	Total
Cerebral infarction	**77**	**42**	**4**	**4**	**127**
Pulmonary embolism	**37**	**38**	**7**		**82**
Deep vein thrombosis	**34**	**24**	**4**		**62**
Other thrombo-embolism (TE)	**91**	**63**	**6**	**1**	**161**
Transient ischaemic attack	48	17	3		68
Myocardial infarction	19	10	2	1	32
Thrombophlebitis	8	15			23
Eye thrombo-embolism	7	6	1		14
Thrombosis (not specified)	7	4			11
Cerebral Venous Sinus Thrombosis	2	3			5
Renal vein thrombosis		1			1
Disseminated intravascular coagulation		1			1
Mesenteric vein thrombosis		1			1
Portal vein thrombosis		1			1
Embolism		1			1
Embolism arterial		1			1
Splenic vein thrombosis		1			1
Cardiac ventricular thrombosis	1				1
Subclavian vein thrombosis		1			1
Aortic embolus		1			1
Thrombosis mesenteric vessel	1				1
Peripheral artery thrombosis		1			1
Peripheral embolism		1			1
Total	**241**	**170**	**21**	**5**	**437**

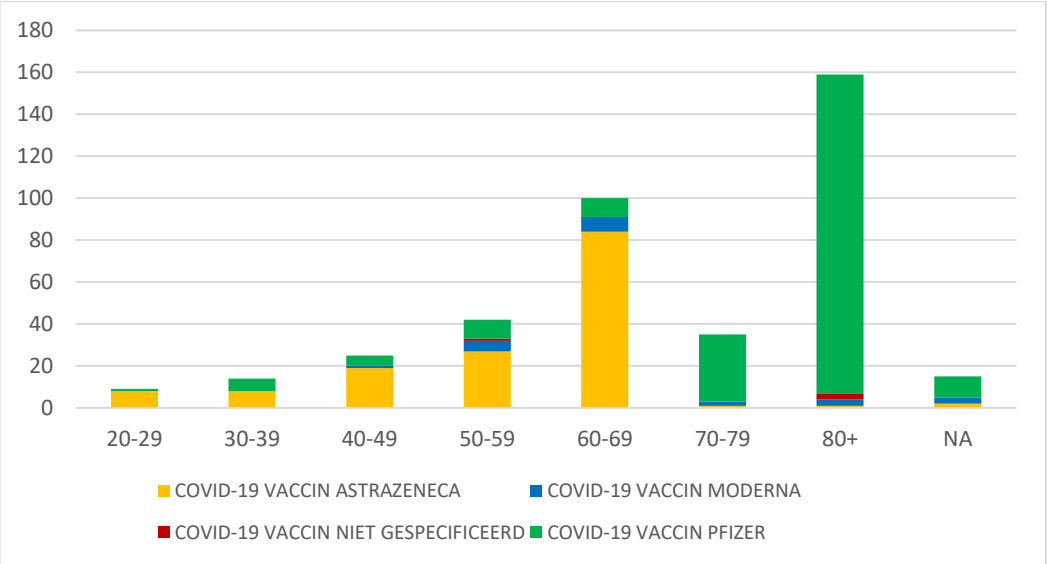

Figure 1. Age differentiation of reported thrombo-embolic events with COVID-19 vaccines, based on unique reports.

With all vaccines, reporting of thrombo-embolic events in general increased after first media attention of cases of the rare and specific combination thrombosis and thrombocytopenia (VITT) following AstraZeneca vaccination. In figure 2, time-lines for vaccination data, event data as well as receive dates from reported cases are shown.

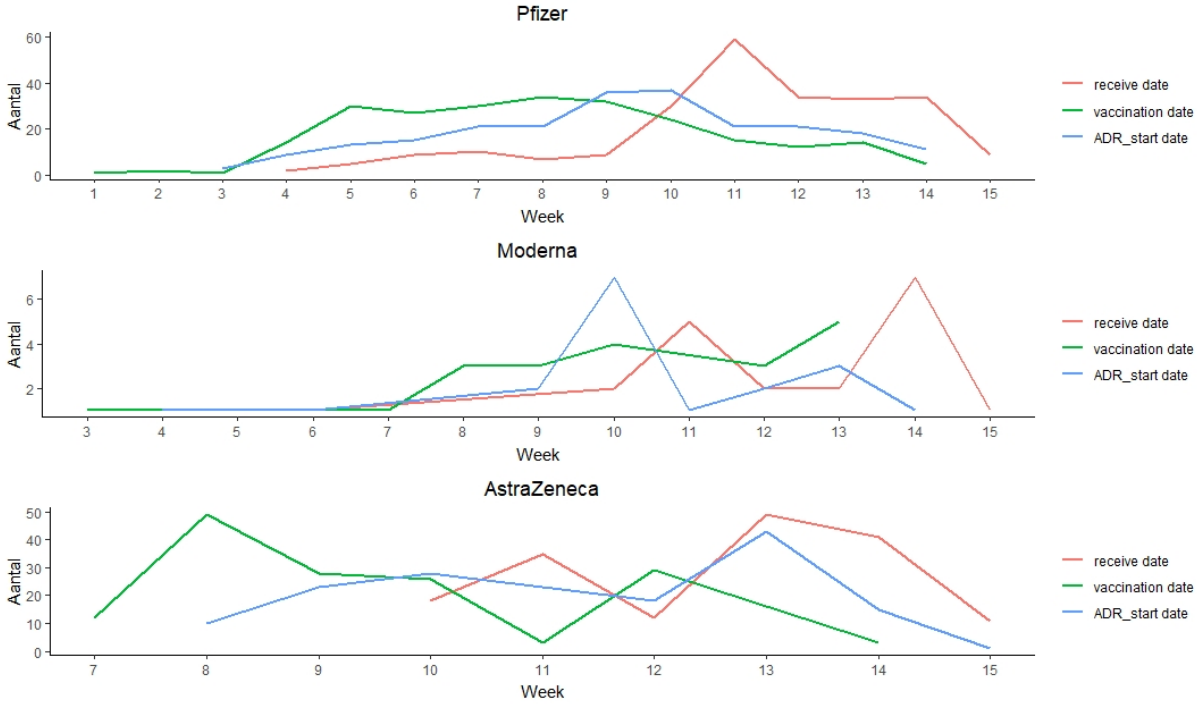

Figure 2. Numbers of reports outlined by vaccination date (green line), start date reaction (blue line) and reporting date (red line), reported from January 6th until April 14th. Note the change in intervals on x- and y-axis.

The three main groups of reported reactions (cerebral infarction, pulmonary embolism and deep vein thrombosis) are described in more detail below.

Deep vein thrombosis

Deep vein thrombosis was reported 62 times (34 Pfizer, 24 AstraZeneca, 4 Moderna). Median time

to onset was 4 days for Pfizer, 11.5 days for AstraZeneca and 7.5 days for Moderna. Time-to-onset was < 16 days in 49 cases (80%). In eleven cases time-to-onset was longer than 32 days. At time of reporting, 30 out of 62 persons (48%) had recovered or were recovering; however none had a fatal outcome.
Of note, median age of DVT with Pfizer was 82 (20 reports aged 80+ years) and with AstraZeneca 56 (10 reports aged 60-69 years).
Other details on the reports are shown in Supplementary table 1.

Pulmonary embolism

Pulmonary embolism (PE) was reported 81 times (37 Pfizer, 38 AstraZeneca, 7 Moderna). Median time to onset was 12.5 days for Pfizer, 11.1 days for AstraZeneca and 8 days for Moderna. Time-to-onset was < 16 days in 60 cases (74%). In one case time-to-onset was longer than 32 days. At time of reporting, 42 persons out of 82 (51%) had recovered or were recovering; however 5 reports had a fatal outcome.
Of note, median age of PE with Pfizer was 81 (20 reports aged 80+ years) and with AstraZeneca 59 (18 reports aged 60-69 years).
Other details on the reports are shown in Supplementary table 2.

Cerebral infarction

Ischaemic cerebral infarctions (excl. CVST and TIA) were reported 127 times (77 Pfizer, 42 AstraZeneca, 4 Moderna, 4 unspecified vaccines). Median time to onset was 4 days for Pfizer, 9 days for AstraZeneca and 4 days for Moderna. Time-to-onset was < 16 days in 102 cases (80%). Four cases had a time-to-onset longer than 32 days. At time of reporting, 65 out of 132 (51%) had recovered or were recovering; however 20 reports had a fatal outcome.
Of note, median age of cerebral infarction with Pfizer was 85 (58 reports aged 80+ years) and with AstraZeneca 63 (25 reports aged 60-69 years).
The number of cerebral venous sinus thrombosis (CVST) was 2 following Pfizer and 3 following AstraZeneca vaccination respectively. With AstraZeneca only one also had a low platelet count, suspected for VITT.
Other details on the reports are shown in Supplementary table 3.

Comparison with background incidence

For two major categories of thrombo-embolic events: DVT and/or PE and cerebral infarction, the observed number of reported cases was compared to the expected number based on background incidences.

Observed
All reported cases, specified above, were included as observed cases, although rate of underreporting is not known. If one person had DVT/PE and a cerebral infarction, he is counted in both subgroups.

Expected
To define the numerator for the expected cases, weekly cumulative vaccine exposure data were obtained from RIVM. These data entail an estimation of maximum vaccination numbers, based on estimated vaccinations by all parties involved in the vaccination campaign [8]. Unfortunately, these data are not stratified by age and gender.

Background incidences on deep vein thrombosis, pulmonary embolism and cerebral infarction were obtained from various sources.

- For PE and DVT recently published data on background incidences rates from Denmark in 2010-2018 [7] were used, because no recent Dutch data on background incidence rates were available yet. Note that all cases of DVT and PE are added up, in accordance with the original article. Since AstraZeneca vaccine has been given mostly to people < 65 year, the numbers of reports (people ages <65) were compared with specified background incidences both total population and for < 65 year as well, in accordance with the original article.

- For ischaemic cerebral infarction, incidence rate was obtained from the Hartstichting (2020), based on number from CBS (Central Bureau for Statistics), Dutch Hospital Data and NIVEL on 2019 [9].

Observed over expected ratio (O/E)

Two scenarios were used to calculate the observed over expected ratios for reports of deep vein thrombosis, pulmonary embolism and cerebral infarction, both corrected for time being at risk and reported times-to-onset (TTO):

- In the first scenario, a 16-day at-risk-period was chosen, based on estimated time-at-risk for other thrombotic events following immunisation [2]. The cut-off date for receiving reports was April, 14th. To allow all patients to complete the risk-period, a cut-off date for both vaccination dates and vaccine exposure dates was set on March, 28th. Only reports with a time-to-onset (TTO) of < 16 days were included.
- In the second scenario, the risk-period was doubled to 32 days. The cut-off date for receiving reports was April, 14th. To allow all patients to complete the risk-period, a cut-off date for both vaccination dates and vaccine exposure dates was set on March, 14th. All reports with a time-to-onset (TTO) of < 32 days were included.

For both scenarios, O/E ratio was calculated using maximum vaccine exposure data in the calculations using the formula below [10]. Results of all calculations are summarized in Table 3.1 for DVT/PE and in table 3.2 for cerebral infarction.

- $N_{Expected}$ = ($N_{Vaccine\_exposure}$ * (At risk period / 365) * 1/100,000) * Incidence rate
- O/E ratio = $N_{Observed}/N_{Expected}$

An O/E ratio of > 1 means that more cases were observed (reported) than were expected based on background incidence in a given period/ with corresponding given time-to-onset.

Table 3.1: Observed over expected calculations for the total of DVT and PE cases compared to Danish background incidence, analogous to Ostergaard [7]: incidence rate of DVT/PE in total population of 18-99 year old was 170 (168-171) per 100,000-person years and for people < 65 years old 91 (89-92) per 100,000 person-years; calculated for both 16 day and 32 day risk-periods. *Vaccine exposure was not adjusted in AstraZeneca age groups, because this vaccine was intended for people < 65 years. #Because of given data sources with confidence intervals could not be calculated. The results should be interpreted as estimations.

DVT/PE	At-risk-period / TTO (days)	Number of reports (O)	*Vaccine exposure (number of vaccinations)*	*Incidence rate (per 100,000 person-years) (95%))*	Expected (E)	O/E#
Pfizer	16	44	1875475	170 (168-171)	140	**0.32**
	32	52	1518223	170 (168-171)	226	**0.23**
AstraZeneca	16	37	553734	[18-99 year] 170 (168-171)	41	**0.90**
	32	38	434698	[18-99 year] 170 (168-171)	65	**0.59**
	16	35	*553734	[<65 year] 91 (89-92)	22	**1.59**
	32	37	*434698	[<65 year] 91 (89-92)	34	**1.07**
Moderna	16	5	206744	170 (168-171)	15	**0.33**
	32	4	126717	170 (168-171)	19	**0.21**

For ischaemic cerebral infarction observed cases were compared with background incidence estimates from the Hartstichting [9].

Table 3.2: Observed over expected calculations for Ischaemic cerebral infarction cases compared to Hartstichting data from 2019 background incidences; calculated for both 16 day and 32 day risk-periods. Reports of TIA and CVST were not included. Background incidence rate total population for 'all stroke' (not TIA): 226 per 100,000; 80% is ischaemic: 181 per 100,000 person-years [9, 11] #Because of given data sources with confidence intervals could not be calculated. The results should be interpreted as estimations.

Ischemic cerebral infarction	At-risk-period / TTO	Number of reports (O)	*Vaccine exposure (Number of vaccinations)*	*Incidence rate (per 100,000 person-years) (95%))*	Expected (E)	O/E ratio#
Pfizer	16	63	1875475	181	149	**0.42**
	32	58	1518223	181	241	**0.24**
AstraZeneca	16	25	553734	181	44	**0.52**
	32	30	434698	181	69	**0.44**
Moderna	16	4	206744	181	16	**0.24**
	32	4	126717	181	20	**0.20**

Cases of (suspected) VITT

Among all reported thrombo-embolic events are 9 that were suspected or confirmed cases for VITT with AstraZeneca vaccine (until April, 14th 2021). In short, these consider 8 women (aged 23 to 63) and 1 male (aged 56) who developed thrombosis in combination with thrombocytopenia. Types of thrombotic events were: arterial limb thrombosis (2), deep vein thrombosis (2), pulmonary embolism (3), cerebral venous sinus thrombosis with renal thrombosis, diffuse intravasal coagulation, thrombosis of portal, splenic and mesenteric veins. In 3 cases specific testing confirmed the diagnosis, in others HIT tests were negative (2), unknown (2) or not performed (2). The reporting rate of these cases with AstraZeneca vaccine was 0,91 per 100.000, based on 9 cases (until April, 14th 2021) with 989187 vaccinations (maximum estimate until April, 11th 2021).

Risk factors for thrombo-embolic events

All included reports were checked on known risk factors for thrombo-embolism in general, such as previous thrombo-embolism, use of hormonal therapy, cardiovascular risk factors, malignancy, coagulopathies or myeloproliferative conditions, pregnancy, concomitant medication with prothrombotic features, smoking, obesity, recent immobilisation or surgery, history of or current Sars-CoV-2 infection or dose adjustment of anticoagulant therapy because of the vaccination procedure.
In 74% of the reports at least one classical risk factor for thrombo-embolism was mentioned. In half of all cases one or more cardiovascular conditions were present. In reports about deep vein thrombosis obesity and a previous thrombo-embolic event were mentioned in 29% and 26% of the cases respectively. Obesity and the use of hormonal therapy were mentioned in reports of pulmonary embolism following AstraZeneca vaccination, in 36 and 22%. In reports of cerebral infarction, a previous thrombo-embolic event (including TIA) and cardiovascular risk factors were mentioned, in 18% and 59% of the cases respectively.

Discussion

Information from literature
Vaccination with COVID-19 adenovector vaccines, such as Vaxzevria (AstraZeneca), can result in development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4 as a rare adverse effect, now known as VITT (vaccine-induced immune thrombotic thrombocytopenia) [2].
For thrombo-embolic events in general, a markedly low platelet count is not a common clinical feature and the formation of antibodies against PF4 is an extremely rare mechanism leading to thrombosis. Classical venous thromboembolism is a multicausal disease, and its incidence is increased in inflammatory states such as infections, sepsis, and inflammatory bowel disease. Carli et al. wrote the first case-report of classical deep vein thrombosis following the second COVID-19 vaccination with the Pfizer mRNA vaccine. They suggested that the intense immunological response could have triggered the thrombotic event, but differently from VITT [12]. A

similar mechanism has been hypothesized in the Janssen COVID-19 vaccine's Risk Management Plan [13-18]. However, thus far these concepts have not been proven with other vaccines, such as the inactivated influenza vaccination which was not associated with venous thromboembolism in adults older than 50 years [19].

Reports
A high number of reports concerning thrombo-embolism was received by spontaneous reporting by healthcare professionals and consumers in equally divided numbers. The majority of cases were considered serious, due to the potentially life-threatening characteristics of the conditions. Out of 399 reports, in 35 outcome was fatal (8.8% fatality rate). The majority of fatal cases concern elderly people (80+) with cerebral infarction after being vaccinated with Pfizer vaccine.
Most of the cases reported had time-to-onset of 16 days or less (Supplementary table D.). This is a plausible time frame of being alert to unexpected events, as well as for immunological or inflammatory responses following immunisation as well [14].
It has to be noted that the distribution of reports among certain age groups greatly reflects vaccination patterns, as Pfizer is mainly used in elderly people and AstraZeneca in people younger than 65 year in this period.
Well known risk factors for thrombo-embolism in general were present in the majority of reported cases. These are reflective for the vaccinated population with cardiovascular risk factors in people with increasing age, hormonal contraceptive use in younger vaccinated women and obesity in risk groups that specifically were invited for vaccination.

Limitations O/E method
Underreporting is a common feature of voluntary reporting systems. Media attention has increased the number of reports of thrombo-embolic events after vaccination with COVID-19 vaccines. This has led to a reduction in underreporting in a given time-at-risk window. With all vaccines, reporting of all thrombo-embolic events increased after media attention of cases of the rare and specific combination thrombosis and thrombocytopenia (VITT) following AstraZeneca vaccination. Figure 2 shows the delay in reporting after occurrence of the events. Media attention started in week 8 and increased in week 11 and 13. Based on these figures, there is no large difference in reporting rate increases between all three vaccines.

In our O/E method, the reported cases are considered as observed cases. However, the extent of underreporting is unknown. This may lead to an underestimation of the observed number of cases.
The exact cohort size (numerator) is unknown as well, as we had to calculate with an unstratified estimate of vaccine exposure.
Thrombo-embolism has a high background incidence. The overall risk on thrombo-embolic events increases with age and may differ between men and women for some specific conditions.
Comparing events in a specific vaccinated population with total-population-background incidence rates, may cause inaccurate results. Patients at-risk-for-COVID-19 may share some risk factors for thrombo-embolic events in general, such as older age and obesity. If the vaccinated population has a high baseline risk for thrombo-embolic events, E should be higher (e.g. use of Pfizer in predominantly in elderly). If the vaccinated population has a low baseline risk for thrombo-embolic events, E should be lower (e.g. AstraZeneca predominantly used in younger people).
Since AstraZeneca has been used mostly for people < 65 years, we also compared the observed reports with the background rate for this age-specific population, showing a larger observed over expected ratio.
The accuracy of calculations also depends on quality of data used for background incidence. We observed large differences between reported background incidence rates in literature and in incidence rate databases of different countries [7, 20]. The recent study of Østergaard in Denmark calculated an incidence of 170 per 100,000 person-years for both DVT and PE (added up) in total population. We chose to use the Danish background incidence rates because of the actually and thoroughly conducted study. Danish population also resembles Dutch population in terms of age distribution.

Conclusion

We examined a possible increase in the overall risk of blood clots (thrombo-embolism) in people who received one of the COVID vaccines. A relatively high number of reports of 'normal' thrombo-

embolic events with all COVID-19 vaccines was received. Although taken with various limitations, the number of reported cases has reached thresholds for expected cases in certain scenarios.

Compared to Danish background incidence rates for total population, the number of reported cases of DVT and pulmonary embolism in The Netherlands with AstraZeneca vaccine in a 16-day at-risk-period, almost reaches the number that could have been expected by coincidence. Compared to the background incidence rates for people below 65 years, the number of reported cases of DVT and lung embolism in The Netherlands with AstraZeneca is higher than expected by coincidence. For the other vaccines, the number of reported cases is about one-third of what could have been expected from background incidence.

Based on the current analysis, a causal relation between vaccination and the observed events cannot be concluded nor rejected, given the plausible time window and the high background rates or thrombo-embolism in general. For reassurance, more detailed epidemiological research is needed.

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1.1. Supplementary materials (in public version)

Table 1: Overview on reported thrombo-embolic reactions with COVID-19 vaccins, until April 14th, 2021.

1.1 Deep vein thrombosis.
Included Meddra Preferred Terms (PT) from this selection: Deep vein thrombosis, Venous thrombosis limb
Excluded: Thrombophlebitis, Thrombophlebitis superficial

Vaccine	COVID-19 VACCIN PFIZER	COVID-19 VACCIN ASTRAZENECA	COVID-19 VACCIN MODERNA
Reports			
Total number of reports	34	23	4
1st vaccination	25 (73.5%)	23 (100%)	2 (50%)
2nd vaccination	9 (26.5%)	0 (0%)	2 (50%)
Seriousness (%)	28 (82.4%)	20 (87%)	4 (100%)
Outcome fatal (%)	0 (0%)	0 (0%)	0 (0%)
Male (%)	10 (29.4%)	11 (47.8%)	2 (50%)
Female (%)	24 (70.6%)	12 (52.2%)	2 (50%)
Age (median; range)	82 (50 - 89)	56 (22 - 64)	56 (45 - 65)
age 0-19	0	0	0
age 20-29	0	2	0
age 30-39	0	1	0
age 40-49	0	2	1
age 50-59	5	7	1
age 60-69	1	10	2
age 70-79	6	0	0
age 80+	20	0	0
age unk	2	1	0
Reactions*			
Total number of reactions	34	24	4
TTO (mean; range)	8.5 (0 - 49)	11.5 (1 - 29)	11 (1 - 28)
TTO (median; IQR)	4 (2.25 - 11)	10 (3.75 - 16.75)	7.5 (3.25 - 15.25)
TTO < 16 days	29	17	3
TTO < 32 days	32	24	4
Outcome recovered (%)	19 (55.9%)	9 (37.5%)	2 (50%)

* The number of reactions can be more than the number of individual reports.

Table 1.2 Pulmonary embolism

Included Meddra Preferred Terms (PT) from this selection: Pulmonary embolism

Vaccine	COVID-19 VACCIN PFIZER	COVID-19 VACCIN ASTRAZENECA	COVID-19 VACCIN MODERNA
Reports			
Total number of reports	36	38	7
1st vaccination	25 (69.4%)	38 (100%)	5 (71.4%)
2nd vaccination	11 (30.6%)	0 (0%)	2 (28.6%)
Seriousness (%)	36 (100%)	38 (100%)	7 (100%)
Outcome fatal (5)	3 (8.3%)	2 (5.3%)	0 (0%)
Male (%)	18 (50%)	12 (31.6%)	5 (71.4%)
Female (%)	18 (50%)	26 (68.4%)	2 (28.6%)
Age (median; range)	81 (36 - 95)	59 (23 - 82)	56 (52 - 67)
age 0-19	0	0	0
age 20-29	0	3	0
age 30-39	4	4	0
age 40-49	0	7	0
age 50-59	2	5	3
age 60-69	2	18	1
age 70-79	7	0	0
age 80+	20	1	0
age unk	1	0	3
Reactions*			
Total number of reactions	37	38	7
TTO (mean; range)	12.4 (1 - 34)	11.1 (0 - 30)	8 (1 - 19)
TTO (median; IQR)	12.5 (5 - 17.25)	10.5 (5.5 - 16.75)	8 (5.5 - 8.5)
TTO < 16 days	26	26	6
TTO < 32 days	35	38	7
Outcome recovered (%)	21 (56.8%)	18 (47.4%)	3 (42.9%)

* The number of reactions can be more than the number of individual reports.

Table 1.3 Cerebral infarction (ischaemic)

Included Meddra Preferred Terms (PT) from this selection: Basilar artery thrombosis (3), Brain stem infarction (2), Carotid artery occlusion (2), Carotid artery thrombosis (2), Cerebellar infarction (3), Cerebral artery thrombosis (1), Cerebral infarction (39), Cerebral ischaemia (1), Cerebral thrombosis (2), Cerebrovascular accident (26), Ischaemic cerebral infarction (43), Lacunar infarction (1), Thalamic infarction (1), Arterial thrombosis (1 report = cerebral)
Not included: TIA (68), CVST (5)

Vaccine	COVID-19 VACCIN PFIZER	COVID-19 VACCIN ASTRAZENECA	COVID-19 VACCIN MODERNA	COVID-19 VACCIN UNSPECIFIED
Reports				
Total number of reports	77	42	4	4
1st vaccination	61 (79.2%)	42 (100%)	2 (50%)	3 (75%)
2nd vaccination	16 (20.8%)	0 (0%)	2 (50%)	1 (25%)
Seriousness (%)	76 (98.7%)	42 (100%)	4 (100%)	4 (100%)
Outcome fatal (%)	18 (23.4%)	2 (4.8%)	0 (0%)	2 50%)
Male (%)	28 (36.4%)	15 (35.7%)	4 (100%)	2 (50%)
Female (%)	49 (63.6%)	27 (64.3%)	0 (0%)	2 (50%)
Age (median; range)	*85 (21 - 99)*	*62 (24 - 82)*	*68 (63 - 93)*	*85 (59 - 87)*
age 0-19	0	0	0	0
age 20-29	0	1	0	0
age 30-39	0	0	0	0
age 40-49	1	1	0	0
age 50-59	2	13	0	1
age 60-69	3	25	3	0
age 70-79	7		0	0
age 80+	59	1	1	3
age unk	5	1	0	0
Reactions*				
Total number of reactions	77	42	4	4
TTO (mean; range)	6.6 (0 - 33)	12.5 (1 - 39)	4.5 (4 - 6)	2.5 (1 - 4)
TTO (median; IQR)	4 (1 - 8)	9 (3 - 18)	4 (4 - 4.5)	2.5 (1 - 4)
TTO < 16 days	67	27	4	4
TTO < 32 days	73	38	4	4
Outcome recovered (%)	35 (45.5%)	25 (59.5%)	3 (75%)	2 (50%)

* The number of reactions can be more than the number of individual reports.

Table 1.4 Other thrombo-embolic events

Included Meddra Preferred Terms (PT) from this selection:
Cardiac: Acute myocardial infarction (7), Cardiac ventricular thrombosis (1), Myocardial infarction (25)
Eye: Amaurosis fugax (2), Eye infarction (1), Optic nerve infarction (1), Retinal artery occlusion (5), Retinal vein occlusion (5)
General: Aortic embolus (1), Disseminated intravascular coagulation (1), Embolism (1 unspecified), Thrombosis (11 unspecified)
Gastric: Mesenteric vein thrombosis (1), Thrombosis mesenteric vessel (1), Splenic vein thrombosis (1)
Organs: Portal vein thrombosis (1), Renal vein thrombosis (1),
Arterial: Peripheral artery thrombosis (1), Embolism arterial (leg) (1), Peripheral embolism (leg) (1)

Vaccine	COVID-19 VACCIN PFIZER	COVID-19 VACCIN ASTRAZENECA	COVID-19 VACCIN MODERNA	COVID-19 VACCIN UNSPECIFIED
Reports				
Total number of reports	27	35	1	3
1st vaccination	27 (100%)	29 (82.9%)	1 (100%)	3 (100%)
2nd vaccination	0 (0%)	6 (17.1%)	0 (0%)	0 (0%)
Seriousness (%)	26 (96.3%)	32 (91.4%)	1 (100%)	3 (100%)
Outcome fatal (5)	1 (3.7%)	11 (31.4%)	0 (0%)	1 (33.3%)
Male (%)	11 (40.7%)	13 (37.1%)	1 (100%)	1 (33.3%)
Female (%)	16 (59.3%)	22 (62.9%)	0 (0%)	2 (66.7%)
Age (median; range)	61 (27 - 71)	85 (37 - 96)	90 (90 - 90)	80 (51 - 90)
age 0-19	0	0	0	0
age 20-29	0	0	0	0
age 30-39	6	3	0	0
age 40-49	3	2	0	0
age 50-59	0	0	0	1
age 60-69	16	1	0	0
age 70-79	1	5	0	0
age 80+	0	26	1	2
age unk	0	0	0	0
Reactions*				
Total number of reactions	31	35	1	3
TTO (mean; range)	7.6 (0 - 28)	6.1 (0.1 - 27)	10 (10 - 10)	8 (5 - 13)
TTO (median; IQR)	7 (2 - 10)	4 (2 - 8)	10 (10 - 10)	6 (5.5 - 9.5)
TTO < 16 days	28	32	1	3
TTO < 32 days	31	34	1	3
Outcome recovered (%)	14 (45.2%)	12 (34.3%)	0 (0%)	1 (33.3%)

* The number of reactions can be more than the number of individual reports.