Overview of classical thromboembolic events (not VITT) after COVID-19 vaccination (UPDATE)

Introduction

Four COVID-19 vaccines have been authorized and used for immunisation against Covid-19 in The Netherlands: the mRNA vaccines of Comirnaty (Pfizer/BioNTech) [1] and Moderna (SpikeVax®) [2] and the adenovirus vector vaccines Vaxzevria (Oxford/AstraZeneca) [3] and Janssen [4]. These vaccines have been used in the vaccination campaign in different populations and in different numbers. Until 1 December 2021, 24 million vaccines were administered (Pfizer 19 million, Moderna 2 million, AstraZeneca 2.5 million, Janssen 0.8 million), used for approximately 13 million first doses and 11 million second doses [5].

Thromboembolic events
Classical thromboembolism (*without* thrombocytopenia) is a heterogeneous condition with high background incidence rates that vary among type of thrombosis, sex and age [6]. Thrombosis, the formation of blood clots in vessels, and emboli, travelling parts of blood clots through the circulation, may cause obstruction of blood flow and result in tissue anoxia and damage. It is a major cause of morbidity and mortality in a wide range of arterial and venous diseases and patient populations [7]. To note, the rare adverse event of thrombosis with thrombocytopenia, called VITT or TTS, will be discussed separately and is not part of this overview.

VENOUS THROMBOEMBOLISM (VTE)

The most common presentations of venous thrombosis are deep-vein thrombosis (DVT) in limbs and pulmonary embolism, a consequence of embolization to pulmonary arteries, referred to together as venous thromboembolism (VTE). Veins in other sites of the body can also be affected. VTE occurs as a result of stasis in blood flow, injury to vessel walls and a hypercoagulable state. An array of different factors contributes to the risk of VTE. Risk factors can be genetic (e.g. factor V Leiden) or acquired (e.g. active cancer, estrogen use). Independent predictors for occurrence of VTE include a prior event, increasing age, obesity, smoking, combined oral contraceptives, pregnancy, immobilisation and surgery [8]. In The Netherlands, about 50-150 per 100,000 people develop DVT and 20 per 100,000 people develop pulmonary embolism every year [9].

ARTERIAL THROMBOSIS (ATE)

Arterial thrombosis may result from the rupture of atherosclerotic plaques in arteries or from embolisms formed in the heart causing occlusion of arteries. Arterial thrombosis may result in myocardial infarctions (occlusion of coronary arteries), ischaemic stroke and acute ischemia of limbs. Arteries of organs and eyes can also be affected. Various factors increase the risk of developing arterial thrombosis. Classically, the cardiovascular-dependent risk factors implicated in arterial thrombosis have been hypertension, high levels of low-density lipoprotein-cholesterol, atherosclerosis, cardiac arrhythmia and smoking. However, diabetes, obesity, estrogen use, increasing age and the use of certain medications may also contribute to arterial thrombosis [7]. In the Netherlands, every year and per 100,000 people, about 174-293 people have an acute myocardial infarction, 150-200 develop a TIA and 160-240 an ischaemic cerebral infarction [10,11].

CVST

Cerebral venous (sinus) thrombosis (CVST or CVT) is an uncommon cause of stroke and intracerebral haemorrhage [12]. The incidence of CVT is 1.3 per 100,000 people every year, though women aged 30-50 years have an increased risk up to 2.8 per 100,000 [13]. Many risk factors are shared with VTE, and infections of head and neck, anaemia and head trauma are additional risk factors for CVT [14]. Thrombosis of the draining venous system of the brain produces injury by two mechanisms. The first is tissue infarction or brain haemorrhage by obstruction of blood drainage causing oedema and the second is occlusion of sinuses causing less absorption of cerebrospinal fluid (CSF) resulting in increased intracranial pressure which causes severe headache. In many cases, both of these mechanisms occur simultaneously [14].

In October 2021 the EMA decided to list venous thromboembolism (VTE) as a rare side effect of COVID-19 Vaccine Janssen in the product information, A Dear Healthcare Professional Letter (DHPC) was sent to warn about the risk for VTE after the Janssen vaccine; venous thromboembolism has been observed rarely following vaccination with COVID-19 vaccine Janssen. This should be considered for individuals at increased risk for venous thromboembolism. This warning took into account data from clinical studies [15]. In November 2021 the European Medicines Agency (EMA) decided to add cerebrovascular venous and sinus thrombosis (CVST) without thrombocytopenia as a side effect of Vaxzevria. PRAC finalised its assessment of cases reporting CVST without thrombocytopenia after vaccination with Vaxzevria [16]. Thrombosis with thrombocytopenia syndrome (TTS or VITT) was already a known very rare side effect of Vaxzevria and the Janssen vaccine [3, 4]. For the mRNA vaccines, thromboembolic events are not listed.

Since the start of the COVID-19 vaccination campaign, Lareb has been receiving reports of thromboembolic events with all COVID-19 vaccines. The rate of reporting increased with continuing media attention about the potential risks for thromboembolic events with COVID-19 vaccination.

In April 2021 Pharmacovigilance Centre Lareb published a first overview of thromboembolic events with COVID-19 vaccines. The current overview reviews all reports of thromboembolic events reported with the COVID-19 vaccines and is an update of the report published in 2021 [17]. Also, the number of reports on VTE, ATE and CVST are compared to background incidence rates. Reports on VITT/TTS are excluded and will be reviewed separately.

Reports

Until 9 December 2021, Pharmacovigilance Centre Lareb received 2080 unique reports of 2269 reactions of thrombo-embolic events following COVID-19 vaccination. The selected reports contained at least one coded reaction within the broad Standardised MedDRA Query (SMQ) for embolic and thrombotic events. Reports without a clear thrombo-embolic diagnosis, with stent- or graft thrombosis and cases of vaccine induced thrombotic thrombocytopenia (VITT)/ thrombotic thrombocytopenic syndrome (TTS) cases were excluded. An overview of the included reports is shown in table 1. Figures 1 and 2 show the age distribution of the patients, sorted by vaccine and by main group of thromboembolic events. Figure 3 shows the distribution of receive dates of the reports over time.

Table 1: Report characteristics

		Pfizer (Comirnaty)	Moderna (Spikevax)	AstraZeneca (Vaxzevria)	Janssen	Vaccine not specified
All thromboembolic events						
Number of reports (total)		1265	145	567	89	14
Dose	1	710 (56.1%)	70 (48.3%)	423 (74.6%)	89 (100%)	9 (64.3%)
	2	548 (43.3%)	73 (50.3%)	144 (25.4%)	0 (0%)	5 (35.7%)
	3[2)]	7 (0.6%)	2 (1.4%)	0 (0%)	0 (0%)	0 (0%)
Reporter	HCP	492 (38.9%)	61 (42.1%)	247 (43.6%)	29 (32.6%)	9 (64.3%)
	CONS	773 (61.1%)	84 (57.9%)	320 (56.4%)	60 (67.4%)	5 (35.7%)
Serious[1)]		908 (71.8%)	104 (71.7%)	404 (71.3%)	58 (65.2%)	14 (100%)
Fatal outcome		76 (6%)	7 (4.8%)	18 (3.1%)	2 (2.2%)	6 (42.9%)
Venous thromboembolism (VTE)						
Number of reports (tot. VTE)		549	86	299	58	8
Dose	1	299 (54.4%)	42 (48.8%)	219 (73.2%)	58 (100%)	4 (50.0%)
	2	248 (45.2%)	43 (50.0%)	80 (26.8%)	0	4 (50.0%)
	3[2)]	2 (0.4%)	1 (1.2%)	0	0	
Sex	Male	260 (47.4%)	43 (50.0%)	146 (48.8%)	35 (60.3%)	4 (50.0%)
	Female	289 (52.6%)	43 (50.0%)	153 (51.2%)	22 (37.9%)	4 (50.0%)
	Unknown	0	0	0	1 (1.7%)	0
Age (mean, range)	Male	62.9 (20-91)	55.4 (35-74)	62.1 (22-88)	46.5 (21-64)	62.3 (47-74)
	Female	60.0 (18-96)	49.7 (19-91)	57.6 (22-95)	40.5 (18-52)	53.0 (43-74)
Time to onset (mean, range) (days)						
Dose	1	12.7 (1-152)	12.0 (1-61)	16.2 (1-151)	26.9 (1-67)	56.7 (1-164)
	2	19.4 (1-244)	30.6 (1-254)	24.1 (1-147)	n.a.	28.0 (3-91)
	3[2)]	3.0 (1-5)	4.0 (4-4)	n.a.	n.a.	n.a.
Fatal outcome		15 (2.7%)	2 (2.3%)	7 (2.3%)	0	4 (50%)
Reactions	**(top 3)**	Pulmonary embolism (40.0%), DVT (31.5%), Thrombophlebitis (10.1%)				
Arterial thromboembolism (ATE)						

Number of reports (total ATE)		636	52	234	26	6
Dose	1	376 (59.1%)	26 (50.0%)	178 (76.1%)	26 (100%)	4 (66.7%)
	2	256 (40.3%)	25 (48.1%)	56 (23.9%)	0	2 (31.3%)
	3[2)]	4 (0.6%)	1 (1.9%)	0	0	0
Sex	Male	305 (48.0%)	30 (57.7%)	110 (47.0%)	12 (46.1%)	3 (50%)
	Female	331 (52.0%)	22 (42.3%)	124 (53.0%)	13 (50.0%)	3 (50%)
	Unknown	0	0	0	1 (3.8%)	0
Age (mean, range)	Male	68.6 (21-98)	60.1 (43-93)	63.3 (45-92)	48.7 (24-59)	74.7 (52-90)
	Female	72.0 (21-99)	58.4 (29-90)	59.9 (24-91)	51.9 (36-64)	67.3 (50-87)
Time to onset (mean, range) (days)						
Dose	1	10.1 (1-273)	8.5 (1-21)	16.0 (1-150)	22.1 (1-96)	5.0 (1-10)
	2	21.2 (1-259)	17.2 (1-91)	23.3 (1-150)	n.a.	24.0 (14-34)
	3[2)]	3.8 (1-7)	3.0 (3-3)	n.a.	n.a.	n.a.
Fatal outcome		58 (9.1%)	5 (9.6%)	11 (4.7%)	2 (7.7%)	1 (16.7%)
Reactions	**(top 3)**	Ischaemic cerebral infarctions (51.0%), TIA (27.4%), Myocardial infarction (18.1%)				
Cerebral venous sinus thrombosis (CVST)						
Number of reports (total CVST)		10	1	7	0	1
Dose	1	2 (20%)	0	5 (71.4%)	0	1 (100%)
	2	8 (80%)	1 (100%)	2 (28.6%)	0	0
	3[2)]	0	0	0	0	0
Sex	Male	5 (50%)	1 (100%)	5 (71.4%)	n.a.	1 (100%)
	Female	5 (50%)	0	2 (26.8%)	n.a.	0
	Unknown	0	0	0	n.a.	0
Age (mean, range)	Male	50.4 (27-72)	55 (55-55)	64.5 (64-65)	n.a.	63 (63-63)
	Female	49.4 (20-88)	n.a.	44 (25-85)	n.a.	n.a.
Time to onset (mean, range) (days)						
Dose	1	3.0 (1-5)	n.a.	24.6 (8-56)	n.a.	26 (26-26)
	2	11.6 (1-35)	17 (17-17)	91 (30-152)	n.a.	n.a.
	3[2)]	n.a.	n.a.	n.a.	n.a.	n.a.
Fatal outcome		0	0	0	n.a.	0
Other thromboembolism (miscellaneous[3)])						
Number of reports (Total)		84	7	36	7	0
Dose	1	42 (50%)	2 (28.6%)	27 (75%)	7 (100%)	0
	2	41 (48.8%)	5 (71.4%)	9 (25%)	0	0
	3[2)]	1 (1.2%)	0	0	0	0
Sex	Male	35 (41.7%)	3 (42.9%)	18	2 (28.6%)	n.a.
	Female	49 (58.3%)	4 (57.1%)	18	4 (57.1%)	n.a.
	Unknown	0	0	0	1 (14.3%)	n.a.
Age (mean, range)	Male	64.5 (34-93)	59.7 (51-76)	64.7 (61-75)	62.0 (54-70)	n.a.
	Female	61.3 (29-87)	56.8 (35-80)	64.6 (40-96)	43.5 (21-59)	n.a.
Time to onset (days)						
Dose	1	14.3 (1-183)	6.0 (6-6)	21.4 (1-101)	33.2 (1-90)	n.a.
	2	25.8 (1-183)	33.6 (7-112)	19.6 (1-128)	n.a.	n.a.
	3	1.0 (1-1)	n.a.	n.a.	n.a.	n.a.
Fatal outcome		3 (3.6%)	0	1 (2.8%)	0	n.a.
Reactions	**(top 3)**	Ophthalmic thrombosis (73.1%), mesenteric thrombosis (6.2%), TTP (3.9%)				

HCP = healthcare professional, CONS = consumer. [1)] Seriousness according CIOMS criteria: hospitalization, disabling/incapacitating, life threating, death or other medically important condition. [2)] To the date of 9 December 2021 the booster campaign/third doses had not begun yet. N.a. not applicable. [3)] The subgroup of miscellaneous thromboembolic events contains reports in which the venous or arterial origin was not clear.

Most reports were received with the Pfizer vaccine, which was the most frequently used vaccine in the vaccination campaign. The age distribution and number of reports per vaccine relates to the use of vaccine in specific populations, such as AstraZeneca in people aged 60-65 years and Janssen in young adults. At the beginning of December, only a small number of third (booster) vaccinations had been given, which explains the relatively low numbers of reports following the third dose. Due to the nature of the events, the majority is considered as serious because of hospitalisation and/or a life-threatening situation. In total, 106 (5.1%) people died following a thromboembolic event reported after vaccination. The occurrence of an event following vaccination does not mean the event is caused by the vaccine. Background incidence rates for thromboembolic events are high and the times to onset in the reports show a notable variation.

Figure 1: Age distribution of patients in the reports of thromboembolic events with COVID-19 vaccines

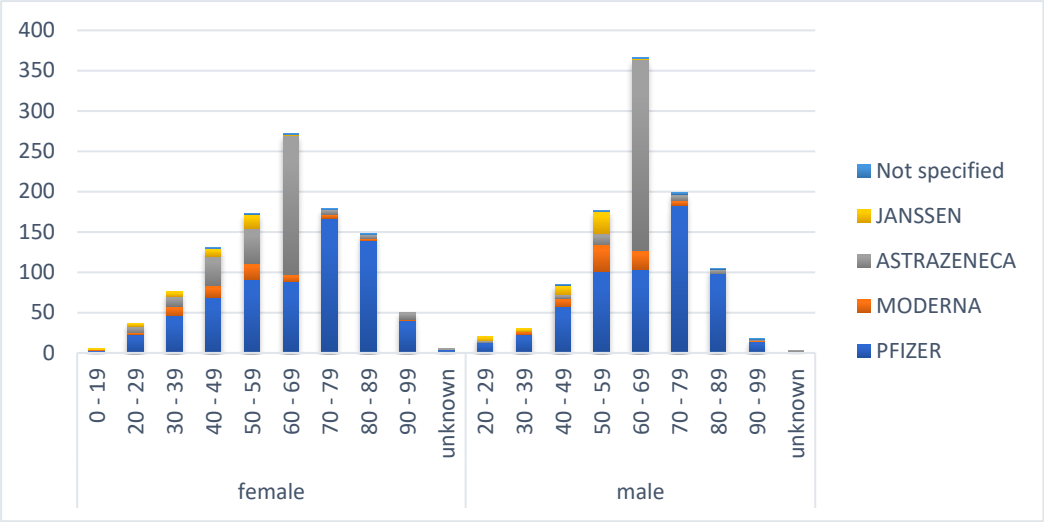


Figure 2: Age distribution of patients in the reports arranged to main groups of thromboembolic events with COVID-19 vaccines

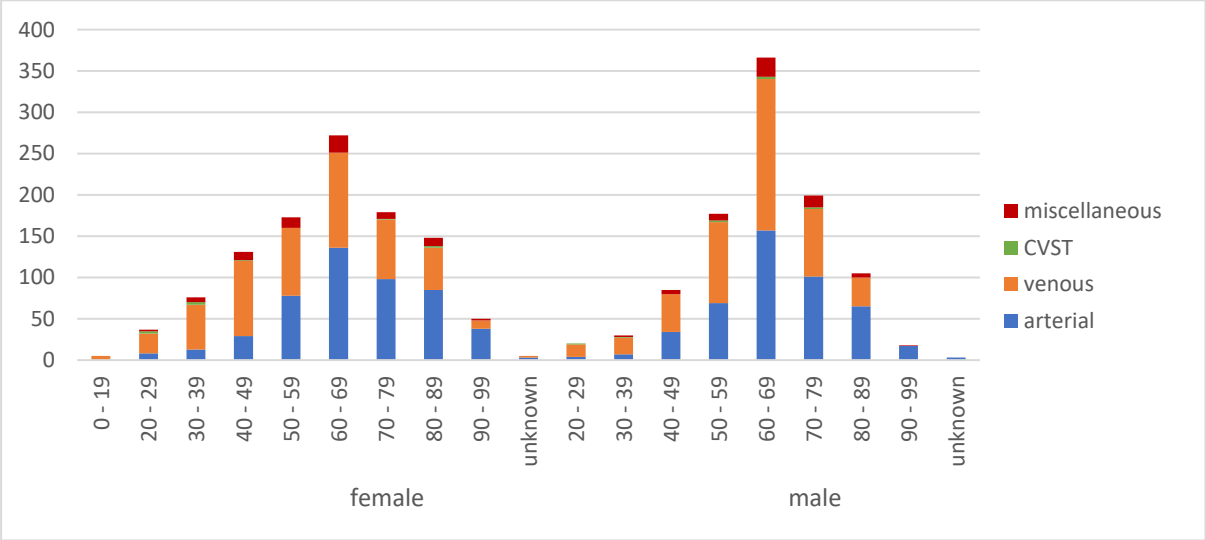
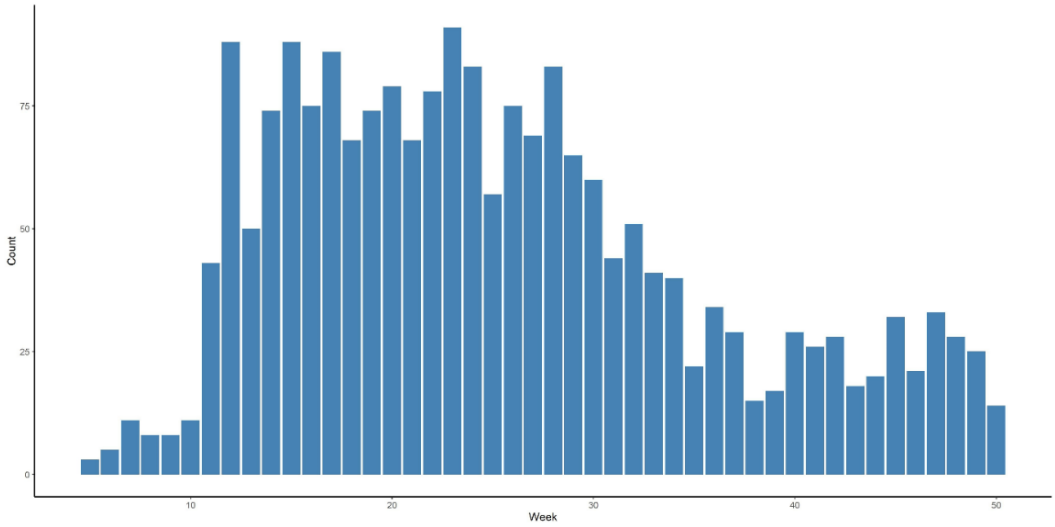


Figure 3: Distribution of receive dates of reports of thromboembolic events with COVID-19 vaccines in 2021.



Comparison with background incidence

To compare the number of reported cases with background incidence rates, standardised morbidity rates (SMR) for CVST and venous and arterial thromboembolic events were calculated with Dutch incidence rates, obtained from PHARMO database from 2019, with risk periods of 14 and 28 days following vaccination.

Background incidence rates

Background incidence rates were determined by PHARMO, based on hospital (ICD10) and general practitioners (ICPC) registration data from 2019. The overall incidence rate for VTE is 249 per 100,000 person years (95% CI 239-260), for ATE 595 per 100,000 person years (95% CI 579-611) and for CVST 2.4 per 100,000 person years (95% 1.5-3.7). Because sex and age are independent risk factors for thromboembolism, stratified data for age and sex were used and summarized in appendix 1.

Vaccination data

Stratified vaccine exposure data until 1 December 2021 were obtained from RIVM, vaccine, dose, sex and age. By this date, most people had two vaccination and the vaccination campaign for booster vaccinations had not begun yet [5].

Calculation method

To compare the number of reported cases with the number of cases that could have been expected in groups of vaccinated people, standardised morbidity rates (SMR) were calculated [18]. The number of reported cases are called ‘Observed’, despite the rate of underreporting is not known. And the number of ‘Expected’ cases were calculated based on stratified and weighted background incidence rates for sex and age in the number of vaccinated people for each vaccine and dose:

$E = (N_{\text{events in PHARMO}} / N_{\text{person years in PHARMO}})*(\text{risk period (days)}/365)*N_{\text{vaccine exposure}}$

$SMR = O / E$

95% confidence intervals: $\sqrt{((\sum(O -/+1)^2)} / \sum E$; using Poisson distribution tables for low numbers of O (<10) [19].

When patients reported more than one thromboembolic event, they were calculated *once* if the events were in the same main group (e.g. pulmonary embolism and deep vein thrombosis). But events from different groups were calculated *separately* (e.g. venous thrombosis and arterial thrombosis).

The total number of reports, regardless of time to onset (TTO), is given in column 'all TTO'; except for those in which TTO is unknown. For risk periods of 14 and 28 days, only those reports with corresponding TTO were taken into account (Observed). Similarly, the number of expected cases in this group of vaccinated people was calculated for the numbers that could occur within 14 or 28 days. If SMR > 1, there are more cases observed that could have been expected. Since the rate of underreporting is unknown, SMR > 1 may not be realistic and SMRs > 0.8 are highlighted as a preliminary cut-off.

Example: 153 women of any age, with the first dose of Pfizer, reported a VTE, of which 114 occurred within 14 days following the first dose of COVID-19 vaccine of Pfizer. In this group of vaccinated women 581 cases of VTE of any cause could have been expected based on background incidence rates. The SMR is 0.20, indicating 20% of the number of cases that could have occurred has been reported.

Results

All results are summarized in tables 3.1 to 3.3 and 4.1 to 4.3 for ages < 60 years. More details and stratified calculations can be found in the appendix (2).

Table 3.1-3.3 Summary of SMR for VTE, ATE and CVST.

Venous thrombo-embolism			ALL TTO	risk period 14 days						risk period 28 days				
Vaccine	Dose	Gender	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
Pfizer	1	Female	all	153	114	581,8	**0,20**	0,16	0,23	139	1163,6	**0,12**	0,10	0,14
Pfizer	1	Male	all	146	107	510,4	**0,21**	0,17	0,25	133	1020,9	**0,13**	0,11	0,15
Pfizer	1	Fem/Male	all	299	221	1092,2	**0,20**	0,18	0,23	272	2184,5	**0,12**	0,11	0,14
Pfizer	2	Female	all	134	87	554,9	**0,16**	0,12	0,19	106	1109,7	**0,10**	0,08	0,11
Pfizer	2	Male	all	114	67	487,6	**0,14**	0,11	0,17	92	975,3	**0,09**	0,08	0,12
Pfizer	2	Fem/Male	all	248	154	1042,5	**0,15**	0,12	0,17	198	2085,0	**0,09**	0,08	0,11
Moderna	1	Female	all	18	8	46,8	**0,17**	0,07	0,34	15	93,5	**0,16**	0,09	0,25
Moderna	1	Male	all	24	17	40,5	**0,42**	0,24	0,65	24	81,0	**0,30**	0,19	0,43
Moderna	1	Fem/Male	all	42	25	87,3	**0,29**	0,18	0,41	39	174,5	**0,22**	0,16	0,30
Moderna	2	Female	all	24	13	43,3	**0,30**	0,16	0,49	18	86,6	**0,21**	0,12	0,32
Moderna	2	Male	all	19	12	37,8	**0,32**	0,16	0,53	14	75,6	**0,19**	0,10	0,30
Moderna	2	Fem/Male	all	43	25	81,1	**0,31**	0,20	0,44	32	162,2	**0,20**	0,13	0,27
AstraZeneca	1	Female	all	121	75	87,6	**0,86**	0,67	1,07	108	175,2	**0,62**	0,50	0,74
AstraZeneca	1	Male	all	98	54	96,0	**0,56**	0,42	0,73	77	192,0	**0,40**	0,31	0,50
AstraZeneca	1	Fem/Male	all	219	129	183,6	**0,70**	0,58	0,83	185	367,2	**0,50**	0,43	0,58
AstraZeneca	2	Female	all	32	20	81,0	**0,25**	0,15	0,37	25	162,1	**0,15**	0,10	0,22
AstraZeneca	2	Male	all	48	27	89,1	**0,30**	0,20	0,43	39	178,2	**0,22**	0,15	0,29
AstraZeneca	2	Fem/Male	all	80	47	170,2	**0,28**	0,20	0,36	64	340,3	**0,19**	0,14	0,24
Janssen	1	Female	all	22	16	25,6	**0,62**	0,35	0,98	18	51,2	**0,35**	0,21	0,54
Janssen	1	Male	all	35	19	27,4	**0,69**	0,41	1,05	22	54,9	**0,40**	0,25	0,59
Janssen	1	Fem/Male	all	58	35	53,1	**0,66**	0,46	0,90	40	106,1	**0,38**	0,27	0,51

Arterial thrombo-embolism				ALL TTO	risk period 14 days					risk period 28 days				
Vaccine	Dose	M/F	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
Pfizer	1	Female	all	204	154	1171,0	**0,13**	0,11	0,15	192	2342,0	**0,08**	0,07	0,09
Pfizer	1	Male	all	172	132	1622,0	**0,08**	0,07	0,10	161	3244,0	**0,05**	0,04	0,06
Pfizer	1	Fem/Male	all	376	286	2793,0	**0,09**	0,09	0,11	353	5586,0	**0,06**	0,06	0,07
Pfizer	2	Female	all	124	72	1136,0	**0,06**	0,05	0,08	98	2272,0	**0,03**	0,03	0,05
Pfizer	2	Male	all	132	92	1566,8	**0,06**	0,05	0,07	108	3133,6	**0,03**	0,03	0,04
Pfizer	2	Fem/Male	all	256	164	2702,8	**0,06**	0,05	0,07	206	5405,6	**0,03**	0,03	0,04
Moderna	1	Female	all	12	9	56,9	**0,16**	0,07	0,30	11	113,7	**0,10**	0,05	0,16
Moderna	1	Male	all	14	11	101,8	**0,11**	0,05	0,18	14	203,6	**0,07**	0,04	0,11
Moderna	1	Fem/Male	all	26	20	158,6	**0,13**	0,08	0,19	25	317,3	**0,08**	0,05	0,11
Moderna	2	Female	all	9	5	52,5	**0,10**	0,04	0,25	8	105,0	**0,08**	0,04	0,16
Moderna	2	Male	all	16	12	95,3	**0,13**	0,06	0,21	13	190,5	**0,07**	0,04	0,11
Moderna	2	Fem/Male	all	25	17	147,8	**0,12**	0,07	0,18	21	295,6	**0,07**	0,04	0,11
AstraZeneca	1	Female	all	99	59	158,5	**0,37**	0,28	0,48	81	317,1	**0,26**	0,20	0,32
AstraZeneca	1	Male	all	79	49	294,1	**0,17**	0,12	0,22	65	588,1	**0,11**	0,08	0,14
AstraZeneca	1	Fem/Male	all	178	108	452,6	**0,24**	0,19	0,29	146	905,2	**0,16**	0,14	0,19
AstraZeneca	2	Female	all	25	12	146,2	**0,08**	0,04	0,14	20	292,4	**0,07**	0,04	0,10
AstraZeneca	2	Male	all	31	15	272,7	**0,06**	0,03	0,09	23	545,4	**0,04**	0,03	0,06
AstraZeneca	2	Fem/Male	all	56	27	418,9	**0,06**	0,04	0,09	43	837,7	**0,05**	0,04	0,07
Janssen	1	Female	all	13	8	22,6	**0,35**	0,15	0,70	9	45,3	**0,20**	0,09	0,38
Janssen	1	Male	all	12	7	60,3	**0,12**	0,06	0,26	11	120,6	**0,09**	0,04	0,15
Janssen	1	Fem/Male	all	26	15	82,9	**0,18**	0,10	0,29	20	165,9	**0,12**	0,07	0,18

CVST				ALL TTO	risk period 14 days					risk period 28 days				
Vaccine	Dose	M/F	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
Pfizer	1	Female	all	1	1	5,3	**0,19**	0,00	1,05	1	10,6	**0,09**	0,00	0,53
Pfizer	1	Male	all	1	1	3,7	**0,27**	0,01	1,50	1	7,4	**0,13**	0,00	0,75
Pfizer	1	Fem/Male	all	2	2	9,0	**0,22**	0,03	0,80	2	18,0	**0,11**	0,01	0,40
Pfizer	2	Female	all	4	2	4,8	**0,41**	0,05	1,49	3	9,7	**0,31**	0,06	0,91
Pfizer	2	Male	all	4	3	3,4	**0,88**	0,18	2,58	4	6,8	**0,59**	0,16	1,51
Pfizer	2	Fem/Male	all	8	5	8,2	**0,61**	0,20	1,42	7	16,5	**0,43**	0,17	0,88
Moderna	1	Female	all	0										
Moderna	1	Male	all	0										
Moderna	1	Fem/Male	all	0										
Moderna	2	Female	all	0										
Moderna	2	Male	all	1	0	0,5	0,00	0,00	7,46	1	1,0	**1,01**	0,03	5,63
Moderna	2	Fem/Male	all	1	0	1,1	0,00	0,00	3,36	1	2,2	**0,46**	0,01	2,54
AstraZeneca	1	Female	all	4	2	0,6	**3,20**	0,38	11,54	2	1,3	**1,60**	0,19	5,77
AstraZeneca	1	Male	all	1	1	0,1	**10,80**	0,27	60,17	1	0,2	**5,40**	0,14	30,09
AstraZeneca	1	Fem/Male	all	5	3	0,7	**4,18**	0,86	12,21	3	1,4	**2,09**	0,43	6,11
AstraZeneca	2	Female	all	1	0	0,6	**0,00**	0,00	6,36	0	1,2	**0,00**	0,00	3,18
AstraZeneca	2	Male	all	1	0	0,1	**0,00**	0,00	42,81	0	0,2	**0,00**	0,00	21,40
AstraZeneca	2	Fem/Male	all	2	0	0,7	**0,00**	0,00	5,54	0	1,3	**0,00**	0,00	2,77
Janssen	1	Female	all	0										
Janssen	1	Male	all	0										
Janssen	1	Fem/Male	all	0										

Table 4.1-4.3 Summary of SMRs for VTE, ATE and CVST in people younger than 60 years. Only subgroups of vaccines and doses are shown in which SMRs differed between people aged < 60 compared to those of all ages.

Arterial thrombo-embolism				ALL TTO	risk period 14 days					risk period 28 days				
Vaccine	Dose	Gender	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
AstraZeneca	1	Female	< 60	27	13	14,3	**0,91**	0,48	1,49	23	28,5	**0,81**	0,51	1,18
AstraZeneca	1	Male	< 60	7	7	12,2	**0,57**	0,23	1,18	7	24,5	**0,29**	0,11	0,59
AstraZeneca	1	Fem/male	< 60	34	20	26,5	**0,76**	0,46	1,13	30	53,0	**0,57**	0,38	0,79

Venous thrombo-embolism				ALL TTO	risk period 14 days					risk period 28 days				
Vaccine	Dose	Gender	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
AstraZeneca	1	Female	< 60	50	32	17,0	**1,88**	1,28	2,61	46	34,0	**1,35**	0,98	1,78
AstraZeneca	1	Male	< 60	8	6	5,5	**1,10**	0,40	2,39	7	10,9	**0,64**	0,26	1,32
AstraZeneca	1	Fem/male	< 60	58	38	22,5	**1,69**	1,19	2,28	53	45,0	**1,18**	0,88	1,53
Janssen	1	Female	< 60	22	16	24,4	**0,66**	0,37	1,02	18	48,8	**0,37**	0,22	0,56
Janssen	1	Male	< 60	34	19	25,9	**0,73**	0,44	1,11	22	51,7	**0,43**	0,26	0,63
Janssen	1	Fem/male	< 60	56	35	50,3	**0,70**	0,48	0,95	40	100,5	**0,40**	0,28	0,53

CVST				ALL TTO	risk period 14 days					risk period 28 days				
Vaccine	Dose	M/F	Age	N reports	N reports (Obs)	N (Exp)	SMR	95% CI		N reports (Obs)	N (Exp)	SMR	95% CI	
Pfizer	1	Female	< 60	1	1	4,3	**0,23**	0,01	1,29	1	8,6	**0,12**	0,00	0,64
Pfizer	1	Male	< 60	1	1	3,1	**0,33**	0,01	1,81	1	6,1	**0,16**	0,00	0,91
Pfizer	1	Fem/male	< 60	2	2	7,4	**0,27**	0,03	0,98	2	14,8	**0,14**	0,02	0,49
Pfizer	2	Female	< 60	2	1	3,9	**0,26**	0,01	1,43	1	7,8	**0,13**	0,00	0,72
Pfizer	2	Male	< 60	2	2	2,8	**0,72**	0,09	2,80	2	5,5	**0,36**	0,04	1,31
Pfizer	2	Fem/male	< 60	4	3	6,6	**0,45**	0,09	1,32	3	13,3	**0,23**	0,05	0,66
AstraZeneca	1	Female	< 60	4	2	0,3	**6,35**	0,76	22,93	2	0,6	**3,18**	0,38	11,46
AstraZeneca	1	Male	< 60	0	0	0,1	**0,00**	0,00	44,82	0	0,2	**0,00**	0,00	22,41
AstraZeneca	1	Fem/male	< 60	4	2	0,4	**5,03**	0,60	18,18	2	0,8	**2,52**	0,30	9,09

VTE

In both 14- and 28-day risk periods for venous thromboembolism, the SMRs of AstraZeneca and Janssen are higher than those of the mRNA vaccines. With AstraZeneca, the SMR of the first dose is higher than the one of the second dose and reaches 1 for women especially, indicating a relatively high number of reported events. Stratified for age < 60 years, the SMR for the first dose of AstraZeneca in men and women exceeds 1, indicating more reports were observed than could have been expected. With a 28 day risk period, the SMR for first the dose of AstraZeneca in women < 60 years also exceeds 1.

ATE

The SMRs of arterial thromboembolic events are lower than those of venous thromboembolisms and generally below 1. Following the first dose of any vaccine, the SMRs for women are slightly higher than for men. Again, the SMRs for AstraZeneca and Janssen are higher than those of the mRNA vaccines. And in women aged < 60 years with the first dose of AstraZeneca, the number of observed cases reaches the number of expected cases, for both 14 and 28 risk periods.

CVST

The absolute numbers or reports of CVST are small. Note that cases of VITT with CVST are excluded in this overview. Since background incidence of CVST rates are low, even small numbers of observed cases can cause an SMR > 1. This is the case in men (all ages but not < 60 years) that received the second dose of the Pfizer vaccine (risk period 14 days) and the second dose of the Moderna vaccine (risk period 28 days). With the AstraZeneca vaccine, SMRs > 1 for the first dose in both men and women (all ages) in both risk periods of 14 and 28 days. In women aged < 60 years, but not in men, SMR also was > 1. No reports of CVST with the first dose of Moderna and Janssen were received.

Discussion

Literature

A population-based cohort study using nationwide healthcare registers in Denmark and Norway, where the vaccine from *AstraZeneca* was used only, showed an increased incidence of *VTE*. Among recipients of AstraZeneca vaccine, increased rates of venous thromboembolic events, including

cerebral venous thrombosis, were observed. There were no more myocardial infarctions and strokes (ischemic stroke) after vaccination than expected [20].

A case-crossover study in Scotland compared cases of *CVST* recently exposed to vaccination (1-14 days after vaccination) with cases less recently exposed. The incidence of CVT per million doses in the first 14 days after vaccination was 2.2 (95% credible interval 0.9 to 4.1) for the *AstraZeneca* vaccine and 1 (95% credible interval 0.1 to 2.9) for the Pfizer vaccine. The rate ratio for CVST associated with exposure to the AstraZeneca vaccine in the first 14 days compared with exposure 15-84 days after vaccination was 3.2 (95% credible interval 1.1 to 9.5) [21].

A national cohort study in England investigated hospital admissions for a *CVST*, other venous thrombosis or thrombocytopenia between 30th November 2020 and 18th April 2021 through linkage to the national Covid-19 immunization register. The Relative Incidence (RI) for CVST after a first *AstraZeneca* dose in 15-39 and 40-64 year olds was 8.7 (95% confidence interval 5.8-13.0) and 2.2 (1.4-3.2) respectively, p<0.001. The elevated risk period in 15-39 year olds was highest 4-13 days post-vaccination (16.3, 9.9-27.0). The attributable risk (AR) was 16.1 per million doses for 15-39 and 3.2 per million for 40-64 year olds. RIs for other thrombosis admissions were elevated in these age groups with ARs of 36.3 and 16.4 per million respectively as were RIs for thrombocytopenia, with ARs of 11.3 and 10.1 per million respectively. No elevated RIs were found for 65+ year olds or after a second AstraZeneca dose, nor for Pfizer vaccine recipients of any age [22].

The clinical characteristics of 213 post-vaccination CVST cases reported to the European Medicines Agency were studied by a group of experts. Data on adverse drug reactions after SARS-CoV-2 vaccination notified until 8 April 2021 under the Medical Dictionary for Regulatory Activities Term 'Central nervous system vascular disorders' were obtained from the EudraVigilance database. Post-vaccination CVST was compared with 100 European patients with CVST from before the COVID-19 pandemic derived from the International CVST Consortium. In all, 213 CVST cases were identified: 187 after AstraZeneca vaccination and 26 after a mRNA vaccination (25 with Pfizer, and one with Moderna). Thrombocytopenia was reported in 107/187 CVST cases (57%, 95% confidence interval [CI] 50%-64%) in the AstraZeneca group, in none in the mRNA vaccine group (0%, 95% CI 0%-13%) and in 7/100 (7%, 95% CI 3%-14%) in the pre-COVID-19 group [23].

Another study assessed the association between COVID-19 vaccines and risk of thrombocytopenia and thromboembolic events in England among adults. The primary outcomes were hospital admission or death associated with thrombocytopenia, venous thromboembolism, and arterial thromboembolism within 28 days of three exposures: first dose of the AstraZeneca vaccine; first dose of the Pfizer vaccine; and a SARS-CoV-2 positive test. Secondary outcomes were subsets of the primary outcomes: cerebral venous sinus thrombosis (CVST), ischaemic stroke, myocardial infarction, and other rare arterial thrombotic events. The study found increased risk of *venous thromboembolism after AstraZeneca* vaccination (1.10, 1.02 to 1.18 at 8-14 days) and after SARS-CoV-2 infection (13.86, 12.76 to 15.05 at 8-14 days); and an increased risk of *arterial thromboembolism after Pfizer* vaccination (1.06, 1.01 to 1.10 at 15-21 days) and after SARS-CoV-2 infection (2.02, 1.82 to 2.24 at 15-21 days). Secondary analyses found increased risk of *CVST after AstraZeneca* vaccination (4.01, 2.08 to 7.71 at 8-14 days), *after Pfizer vaccination* (3.58, 1.39 to 9.27 at 15-21 days), and after a positive SARS-CoV-2 test; *increased risk of ischemic stroke after Pfizer* (1.12, 1.04 to 1.20 at 15-21 days) and after a positive SARS-CoV-2 test; and increased risk of other *rare arterial thrombotic events after AstraZeneca* vaccination (1.21, 1.02 to 1.43 at 8-14 days) and after a positive SARS-CoV-2 test [24].

In France, *no significant increased risk* of myocardial infarction, ischemic stroke and pulmonary embolism was found *in elderly (75+)* within 14 days following the first and second dose of the *Pfizer* COVID-19 vaccine. This self-controlled case-series with within-person comparisons in a national health data system found relative incidences for myocardial infarction for the first dose of 0.97 (95% CI, 0.88-1.06) and for the second dose 1.04 (95% CI, 0.93-1.16); for ischemic stroke for the first dose, 0.90 (95% CI, 0.84-0.98) and for the second dose 0.92 (95% CI, 0.84-1.02); and for pulmonary embolism for the first dose, 0.85 (95% CI, 0.75-0.96) and for the second dose 1.10 (95% CI, 0.95-1.26) [25].

Background incidence rates

Background incidence rates of thromboembolic conditions vary greatly among different countries, sources of information and between stratified age groups and sources of information [26]. A seminar by Kahn mentioned an annual incidence of acute venous thromboembolism of 1-2 cases per 1000, increasing with age and 4 times higher in high-income countries [27]. Dutch general practitioners' guidelines mention a frequency of 0.5-1.5 per 1000 patients with DVT each year and 0.2 per 1000 for pulmonary embolism [9]. The PHARMO incidence rate for all venous thromboembolisms is 249 per 100,000 person years, which is higher, most likely due to inclusion of all kinds of VTE and hospital records as well.

The most common types of reported arterial thromboses were cerebral infarctions and myocardial infarctions. Incidence rate data from PHARMO are quite similar to those known from Dutch GP guidelines for TIA, ischaemic cerebral infarction and myocardial infarction [10, 11]. The American Heart Association mentioned incidences of acute myocardial infarction of 139 per 100,000 and ischemic stroke of 114 per 100,000 every year [28]. The latter being a little lower compared to Dutch data.

CVST is rare type of venous thrombosis, occurring in brain sinuses. Its annual incidence is about 1.3-2.8 per 100,00 people [13, 29]. Obtained from PHARMO data, its overall incidence in The Netherlands, in 2019, was 2.4 per 100,000, more in women than in men.

Thromboembolism with COVID-19

CVST has been observed as a potential complication of COVID-19 in 2020. In contrast to other of common forms of thrombosis, CVST is known to be caused by infections in about 10% of all observations [14, 29]. Acute COVID-19 disease, however is associated with a broader coagulopathy involving venous and arterial and microcirculatory thromboembolism, predominantly in critically ill hospitalised and ICU admitted patients [30-33]. With the infection beyond upper airways, vascular and endothelial injury is thought to enhance thrombosis in small vessels. Hypercoagulability with increased levels of fibrinogen en fibrin d-dimer caused by inflammatory activity induces thromboembolism in larger vessels as well [33].

Furthermore, post-acute cardiovascular conditions up to 12 months following a Sars CoV 2 infection have been described in a large veterinary healthcare centre in the US [34]. Hazard ratios of cerebrovascular disorders, myocardial infarction and thromboembolic disorders were 1.53 (1.45-1.61), 1.72 (1.56-1.90), 2.39 (2.27-2.52) respectively, when compared to contemporary controls. Hazard ratios and the number of excess burden increased with severity of COVID 19 disease, but were also increased following mild disease [34]. Of note, the data were not corrected for COVID-19 vaccinations.

In the reports Lareb received of thromboembolic events following COVID-19 vaccination, 234 (11.3%) had had corona infection in less than 3 months before vaccination and only five (0.2%) reported to have had COVID-19 shortly before or after developing the thromboembolic event, of which two were hospitalised. The background incidence of COVID-19 with chance of unnoticed infections does not seem to have a major role in the reports.

Mechanism

The mechanism of vaccination related classical thromboembolic events is not elucidated yet. It is hypothesized that the Sars CoV 2 spike glycoprotein (present in both viral vector and mRNA vaccines) has thrombogenic potential causing immune thrombosis, which is known with COVID-19 disease. Possible mechanisms in which this protein is involved, are endothelial dysfunction, platelet function potentiation and dysregulation of complement system [35]. Others mention a possible influence of increasing blood viscosity following vaccination by increasing immunoglobulin concentration, especially for vaccination following COVID 19 infection [36].

Spontaneous reporting

Underreporting is common feature of voluntary reporting systems. Media attention increased the number of thromboembolic events with COVID-19 vaccines, especially in spring and early summer of 2021 (figure 3). To note, the number of reports was highest when vaccination numbers were high and decreased when the vaccination campaign of first two doses came to an end autumn. The number of observed cases in SMR calculations is likely to be underestimated due to underreporting. To estimate the expected number of cases, we were able to use Dutch and stratified background incidence rates, obtained from GP and hospital registrations of 2019. Altered environmental factors due to the COVID-19 pandemic situation, such as influence of COVID-19, reduction of infections in general due to social distancing and less flights and travels due to lockdowns, were not corrected.

Conclusion

Standardised Morbidity Rates as a measure for observed over expected analysis, showed a possible increase of the risk of thromboembolism in some situations. In some subgroups the number of observed reported cases was high compared to the expected numbers. For *AstraZeneca*, CVST is labelled as a rare but known adverse event. In literature, there is convincing evidence for a plausible relationship between this vaccine and CVST. An increased risk for VTE, but not ATE, has also been described [21, 25]. In our reports, a high number of cases was observed compared to the expected numbers of CVST, VTE (the highest in men and women < 60) and ATE (in women < 60) after the first dose of AstraZeneca. This indicates a potential signal of more thrombosis with this vaccine. For *Janssen*, VTE is labelled as an adverse event. In our reports, the SMR of VTE with Janssen did not reach 1 and was 0.62-0.69 for 14 days and 0.35-0.40 for 28 days following vaccination.

For the mRNA vaccines, the number of observed cases of CVST was relatively high compared to the expected numbers, only with the second dose of Pfizer and Moderna. SMRs for VTE were slightly higher than for ATE after vaccination with the Pfizer and Moderna vaccines, but remained below 1.

With our data of spontaneous reporting, a risk of thromboembolic events cannot be confirmed nor excluded. Epidemiological research is needed to detect and quantify the increased risk of thromboembolic events following COVID 19 vaccination.

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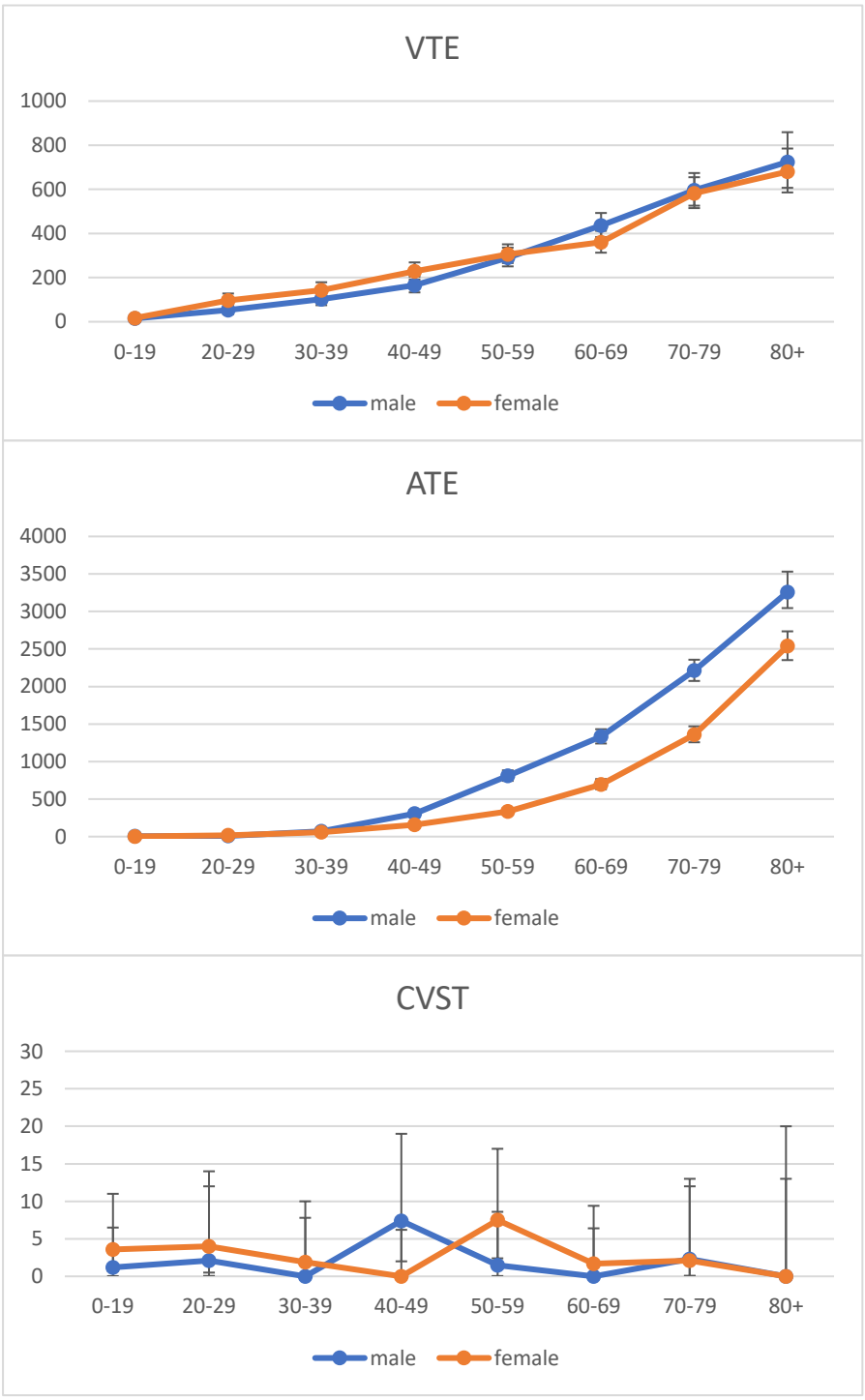
This signal has been raised on April 28, 2022. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl

Supplemental materials

Appendix 1 Stratified background incidence rates (PHARMO, 2019)

Appendix 2 Full tables of SMR calculation for ATE, VTE and CVST

Appendix 1: Stratified background incidence rates (PHARMO, 2019)



Figures 1-3 show incidence rates for VTE, ATE and CVST per 100,000 person years, obtained from PHARMO hospital (ICD10) and general practitioners (ICPC) databases of 2019; as reference for Dutch background incidence rates before COVID-19 pandemic. Included ICPC and ICD10 codes are, for VTE: pulmonary embolism (K93, I26), deep vein thrombosis and thrombophlebitis (K94, I80, I82, O87), other VTE (I81, I82, O008); for CVST: G08, I67.6, O22.5; for ATE: ischemic cerebral infarction (K90, I63), TIA (K89, G45), myocardial infarction (K75, I21, I22), arterial thrombosis (I74).

Appendix 2: Full tables of SMR calculation for ATE, VTE and CVST

Arterial thrombosis									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* (# O > E=0)**	**95% CI SMR** *(* O<10 with poisson table)*		
PFIZER									
Female_0-19_D1	0	501841	2	83117	0,46	0,00	0,00	7,97	*
Female_20-29_D1	1	600233	8	49833	3,70	0,27	0,01	1,51	*
Female_30-39_D1	2	660918	31	53150	14,79	0,14	0,02	0,49	*
Female_40-49_D1	2	663068	93	59364	39,84	0,05	0,01	0,18	*
Female_50-59_D1	18	778345	223	66960	99,43	0,18	0,11	0,28	
Female_60-69_D1	22	504442	411	59025	134,73	0,16	0,10	0,24	
Female_70-79_D1	50	787778	638	46906	410,99	0,12	0,09	0,16	
Female_80+_D1	59	479768	688	27107	467,06	0,13	0,10	0,16	
Female_total_D1	154	4976393	2094	445462	1170,99	***0,13***	***0,11***	***0,15***	
Male_0-19_D1	0	518024	4	86035	0,92	0,00	0,00	3,99	*
Male_20-29_D1	0	596893	4	47106	1,94	0,00	0,00	1,90	*
Male_30-39_D1	4	683277	34	47191	18,88	0,21	0,06	0,54	*
Male_40-49_D1	10	666747	166	54226	78,29	0,13	0,06	0,23	*
Male_50-59_D1	17	801888	525	64749	249,39	0,07	0,04	0,11	
Male_60-69_D1	24	450484	768	57595	230,40	0,10	0,07	0,15	
Male_70-79_D1	39	737681	953	43077	625,97	0,06	0,04	0,08	
Male_80+_D1	38	333119	592	18174	416,20	0,09	0,06	0,12	
Male_total_D1	132	4788113	3046	418153	1622,00	***0,08***	***0,07***	***0,10***	
Total D1	286	9764506	5140	863615	2792,99	***0,10***	***0,09***	***0,11***	
Female <60_D1	23	3204405	357	312424	158,21	***0,15***	***0,09***	***0,21***	
Male < 60_D1	31	3266829	733	299307	349,43	***0,09***	***0,06***	***0,12***	
Total <60_D1	54	6471234	1090	611731	507,64	***0,11***	***0,08***	***0,14***	
Female_0-19_D2	0	422191	2	83117	0,39	0,00	0,00	9,47	*
Female_20-29_D2	1	517303	8	49833	3,19	0,31	0,01	1,75	*
Female_30-39_D2	2	588725	31	53150	13,17	0,15	0,02	0,55	*
Female_40-49_D2	6	603966	93	59364	36,29	0,17	0,06	0,36	*
Female_50-59_D2	8	726853	223	66960	92,85	0,09	0,04	0,17	*
Female_60-69_D2	11	495644	411	59025	132,38	0,08	0,04	0,14	
Female_70-79_D2	18	769492	638	46906	401,45	0,04	0,03	0,07	
Female_80+_D2	26	468718	688	27107	456,30	0,06	0,04	0,08	
Female_total_D2	72	4592892	2094	445462	1136,02	***0,06***	***0,05***	***0,08***	
Male_0-19_D2	0	437062	4	86035	0,78	0,00	0,00	4,73	*
Male_20-29_D2	2	501576	4	47106	1,63	1,22	0,15	4,42	*
Male_30-39_D2	1	611401	34	47191	16,90	0,06	0,00	0,33	*
Male_40-49_D2	5	607992	166	54226	71,39	0,07	0,02	0,16	*
Male_50-59_D2	12	743727	525	64749	231,30	0,05	0,03	0,09	
Male_60-69_D2	21	441441	768	57595	225,78	0,09	0,06	0,14	
Male_70-79_D2	33	720283	953	43077	611,20	0,05	0,04	0,07	
Male_80+_D2	18	326394	592	18174	407,80	0,04	0,03	0,07	
Male_total_D2	92	4389876	3046	418153	1566,78	***0,06***	***0,05***	***0,07***	
Total D2	164	8982768	5140	863615	2702,80	***0,06***	***0,05***	***0,07***	

Arterial thrombosis									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	2	83117	0,01	0,00	0,00	311,96	*
Female_20-29_D1	0	81652	8	49833	0,50	0,00	0,00	7,34	*
Female_30-39_D1	1	87177	31	53150	1,95	0,51	0,01	2,86	*
Female_40-49_D1	0	129966	93	59364	7,81	0,00	0,00	0,47	*
Female_50-59_D1	4	146072	223	66960	18,66	0,21	0,06	0,55	*
Female_60-69_D1	2	26439	411	59025	7,06	0,28	0,03	1,02	*
Female_70-79_D1	1	13522	638	46906	7,05	0,14	0,00	0,79	*
Female_80+_D1	1	14187	688	27107	13,81	0,07	0,00	0,40	*
Female_total_D1	9	511831	2094	445462	56,86	***0,16***	***0,07***	***0,30***	*
Male_0-19_D1	0	12633	4	86035	0,02	0,00	0,00	163,79	*
Male_20-29_D1	0	74564	4	47106	0,24	0,00	0,00	15,19	*
Male_30-39_D1	0	79918	34	47191	2,21	0,00	0,00	1,67	*
Male_40-49_D1	1	127191	166	54226	14,93	0,07	0,00	0,37	*
Male_50-59_D1	4	157958	525	64749	49,13	0,08	0,02	0,21	*
Male_60-69_D1	4	29694	768	57595	15,19	0,26	0,07	0,67	*
Male_70-79_D1	2	15801	953	43077	13,41	0,15	0,02	0,54	*
Male_80+_D1	0	5330	592	18174	6,66	0,00	0,00	0,55	*
Male_total_D1	11	503089	3046	418153	101,79	***0,11***	***0,05***	***0,18***	
Total D1	20	1014920	5140	863615	158,65	***0,13***	***0,08***	***0,19***	
Female <60_D1	7	457683	357	312424	28,93	***0,24***	***0,10***	***0,50***	*
Male < 60_D1	5	452264	733	299307	66,53	***0,08***	***0,02***	***0,18***	*
Total <60_D1	12	909947	1090	611731	95,47	***0,13***	***0,06***	***0,21***	
Female_0-19_D2	0	11005	2	83117	0,01	0,00	0,00	363,30	*
Female_20-29_D2	1	73517	8	49833	0,45	2,21	0,06	12,30	*
Female_30-39_D2	0	80225	31	53150	1,79	0,00	0,00	2,06	*
Female_40-49_D2	1	120520	93	59364	7,24	0,14	0,00	0,77	*
Female_50-59_D2	1	136781	223	66960	17,47	0,06	0,00	0,32	*
Female_60-69_D2	0	24672	411	59025	6,59	0,00	0,00	0,56	*
Female_70-79_D2	1	12681	638	46906	6,62	0,15	0,00	0,84	*
Female_80+_D2	1	12682	688	27107	12,35	0,08	0,00	0,45	*
Female_total_D2	5	472083	2094	445462	52,52	***0,10***	***0,04***	***0,25***	*
Male_0-19_D2	0	10636	4	86035	0,02	0,00	0,00	194,55	*
Male_20-29_D2	0	65513	4	47106	0,21	0,00	0,00	17,29	*
Male_30-39_D2	0	73704	34	47191	2,04	0,00	0,00	1,81	*
Male_40-49_D2	3	118921	166	54226	13,96	0,21	0,04	0,63	*
Male_50-59_D2	4	148142	525	64749	46,07	0,09	0,02	0,22	*
Male_60-69_D2	2	27849	768	57595	14,24	0,14	0,02	0,51	*
Male_70-79_D2	2	14996	953	43077	12,73	0,16	0,02	0,57	*
Male_80+_D2	1	4786	592	18174	5,98	0,17	0,00	0,93	*
Male_total_D2	12	464547	3046	418153	95,25	***0,13***	***0,06***	***0,21***	
Total_D2	17	936630	5140	863615	147,78	***0,12***	***0,07***	***0,18***	

Arterial thrombosis									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* (# O > E=0)**	**95% CI SMR *(* O<10 with poisson table)***		
ASTRAZENECA									
Female_0-19_D1	0	3382	2	83117	0,00	0,00	0,00	1182,16	*
Female_20-29_D1	2	35017	8	49833	0,22	9,28	1,11	33,48	*
Female_30-39_D1	2	35502	31	53150	0,79	2,52	0,30	9,09	*
Female_40-49_D1	4	48915	93	59364	2,94	1,36	0,37	3,48	*
Female_50-59_D1	5	80677	223	66960	10,31	0,49	0,16	1,13	*
Female_60-69_D1	40	466347	411	59025	124,55	0,32	0,23	0,43	
Female_70-79_D1	2	10661	638	46906	5,56	0,36	0,04	1,30	*
Female_80+_D1	4	14545	688	27107	14,16	0,28	0,08	0,72	*
Female_total_D1	59	695046	2094	445462	158,53	***0,37***	***0,28***	***0,48***	
Male_0-19_D1	0	1328	4	86035	0,00	0,00	0,00	1558,15	*
Male_20-29_D1	0	12748	4	47106	0,04	0,00	0,00	88,87	*
Male_30-39_D1	0	14552	34	47191	0,40	0,00	0,00	9,18	*
Male_40-49_D1	2	18824	166	54226	2,21	0,90	0,11	3,27	*
Male_50-59_D1	5	30787	525	64749	9,57	0,52	0,17	1,22	*
Male_60-69_D1	38	513107	768	57595	262,43	0,14	0,10	0,20	
Male_70-79_D1	1	11619	953	43077	9,86	0,10	0,00	0,56	*
Male_80+_D1	3	7637	592	18174	9,54	0,31	0,06	0,92	*
Male_total_D1	49	610602	3046	418153	294,07	***0,17***	***0,12***	***0,22***	
Total D1	108	1305648	5140	863615	452,60	***0,24***	***0,19***	***0,29***	
Female <60_D1	13	203493	357	312424	14,26	***0,91***	***0,48***	***1,49***	
Male < 60_D1	7	78239	733	299307	12,23	***0,57***	***0,23***	***1,18***	*
Total <60_D1	20	281732	1090	611731	26,49	***0,76***	***0,46***	***1,13***	
Female_0-19_D2	0	3148	2	83117	0,00	0,00	0,00	1270,04	*
Female_20-29_D2	0	32418	8	49833	0,20	0,00	0,00	18,49	*
Female_30-39_D2	0	32572	31	53150	0,73	0,00	0,00	5,06	*
Female_40-49_D2	0	45128	93	59364	2,71	0,00	0,00	1,36	*
Female_50-59_D2	3	74869	223	66960	9,56	0,31	0,06	0,92	*
Female_60-69_D2	9	433279	411	59025	115,72	0,08	0,04	0,15	*
Female_70-79_D2	0	9751	638	46906	5,09	0,00	0,00	0,73	*
Female_80+_D2	0	12505	688	27107	12,17	0,00	0,00	0,30	*
Female_total_D2	12	643670	2094	445462	146,19	***0,08***	***0,04***	***0,14***	
Male_0-19_D2	0	1205	4	86035	0,00	0,00	0,00	1717,19	*
Male_20-29_D2	0	11742	4	47106	0,04	0,00	0,00	96,49	*
Male_30-39_D2	0	13569	34	47191	0,37	0,00	0,00	9,84	*
Male_40-49_D2	0	17600	166	54226	2,07	0,00	0,00	1,79	*
Male_50-59_D2	0	28784	525	64749	8,95	0,00	0,00	0,41	*
Male_60-69_D2	14	477217	768	57595	244,08	0,06	0,03	0,09	
Male_70-79_D2	0	10649	953	43077	9,04	0,00	0,00	0,41	*
Male_80+_D2	1	6507	592	18174	8,13	0,12	0,00	0,69	*
Male_total_D2	15	567273	3046	418153	272,68	***0,06***	***0,03***	***0,09***	
Total D2	27	1210943	5140	863615	418,87	***0,06***	***0,04***	***0,09***	

Arterial thrombosis									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN									
Female_0-19_D1	0	16783	2	83117	0,02	0,00	0,00	238,22	*
Female_20-29_D1	0	86405	8	49833	0,53	0,00	0,00	6,94	*
Female_30-39_D1	1	43185	31	53150	0,97	1,04	0,03	5,77	*
Female_40-49_D1	0	55045	93	59364	3,31	0,00	0,00	1,12	*
Female_50-59_D1	6	118748	223	66960	15,17	0,40	0,15	0,86	*
Female_60-69_D1	1	5799	411	59025	1,55	0,65	0,02	3,60	*
Female_70-79_D1	0	1282	638	46906	0,67	0,00	0,00	5,52	*
Female_80+_D1	0	438	688	27107	0,43	0,00	0,00	8,65	*
Female tot D1	8	327685	2094	445462	22,63	***0,35***	***0,15***	***0,70***	*
Male_0-19_D1	0	26060	4	86035	0,05	0,00	0,00	79,40	*
Male_20-29_D1	1	145455	4	47106	0,47	2,11	0,05	11,76	*
Male_30-39_D1	0	60585	34	47191	1,67	0,00	0,00	2,20	*
Male_40-49_D1	3	65513	166	54226	7,69	0,39	0,08	1,14	*
Male_50-59_D1	3	145152	525	64749	45,14	0,07	0,01	0,19	*
Male_60-69_D1	0	6388	768	57595	3,27	0,00	0,00	1,13	*
Male_70-79_D1	0	1729	953	43077	1,47	0,00	0,00	2,52	*
Male_80+_D1	0	442	592	18174	0,55	0,00	0,00	6,68	*
Male_total_D1	7	451324	3046	418153	60,32	***0,12***	***0,06***	***0,26***	*
Total D1	15	779009	5140	863615	82,95	***0,18***	***0,10***	***0,29***	
Female <60_D1	7	320166	357	312424	19,99	***0,35***	***0,14***	***0,72***	*
Male < 60_D1	7	442765	733	299307	55,03	***0,13***	***0,05***	***0,26***	*
Total <60_D1	14	762931	1090	611731	75,02	***0,19***	***0,10***	***0,30***	

Arterial thrombosis									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN									
Female_0-19_D1	0	16783	2	83117	0,03	0,00	0,00	119,11	*
Female_20-29_D1	0	86405	8	49833	1,06	0,00	0,00	3,47	*
Female_30-39_D1	1	43185	31	53150	1,93	0,52	0,01	2,88	*
Female_40-49_D1	0	55045	93	59364	6,62	0,00	0,00	0,56	*
Female_50-59_D1	7	118748	223	66960	30,34	0,23	0,09	0,48	*
Female_60-69_D1	1	5799	411	59025	3,10	0,32	0,01	1,80	*
Female_70-79_D1	0	1282	638	46906	1,34	0,00	0,00	2,76	*
Female_80+_D1	0	438	688	27107	0,85	0,00	0,00	4,33	*
Female tot D1	9	327685	2094	445462	45,27	***0,20***	***0,09***	***0,38***	*
Male_0-19_D1	0	26060	4	86035	0,09	0,00	0,00	39,70	*
Male_20-29_D1	1	145455	4	47106	0,95	1,06	0,03	5,88	*
Male_30-39_D1	0	60585	34	47191	3,35	0,00	0,00	1,10	*
Male_40-49_D1	4	65513	166	54226	15,38	0,26	0,07	0,67	*
Male_50-59_D1	6	145152	525	64749	90,28	0,07	0,02	0,14	*
Male_60-69_D1	0	6388	768	57595	6,53	0,00	0,00	0,56	*
Male_70-79_D1	0	1729	953	43077	2,93	0,00	0,00	1,26	*
Male_80+_D1	0	442	592	18174	1,10	0,00	0,00	3,34	*
Male_total_D1	11	451324	3046	418153	120,63	***0,09***	***0,04***	***0,15***	
Total_D1	20	779009	5140	863615	165,90	***0,12***	***0,07***	***0,18***	
Female <60_D1	8	320166	357	312424	39,98	***0,20***	***0,09***	***0,39***	*
Male < 60_D1	11	442765	733	299307	110,06	***0,10***	***0,05***	***0,17***	
Total <60_D1	19	762931	1090	611731	150,04	***0,13***	***0,08***	***0,19***	

Arterial thrombosis									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
PFIZER									
Female_0-19_D1	0	501841	2	83117	0,93	0,00	0,00	3,98	*
Female_20-29_D1	2	600233	8	49833	7,39	0,27	0,03	0,98	*
Female_30-39_D1	2	660918	31	53150	29,57	0,07	0,01	0,24	*
Female_40-49_D1	7	663068	93	59364	79,69	0,09	0,04	0,18	*
Female_50-59_D1	21	778345	223	66960	198,85	0,11	0,06	0,16	
Female_60-69_D1	29	504442	411	59025	269,45	0,11	0,07	0,15	
Female_70-79_D1	62	787778	638	46906	821,98	0,08	0,06	0,10	
Female_80+_D1	69	479768	688	27107	934,12	0,07	0,06	0,09	
Female_total_D1	192	4976393	2094	445462	2341,98	***0,08***	***0,07***	***0,09***	
Male_0-19_D1	0	518024	4	86035	1,85	0,00	0,00	2,00	*
Male_20-29_D1	0	596893	4	47106	3,89	0,00	0,00	0,95	*
Male_30-39_D1	5	683277	34	47191	37,76	0,13	0,04	0,31	*
Male_40-49_D1	11	666747	166	54226	156,58	0,07	0,03	0,12	
Male_50-59_D1	23	801888	525	64749	498,78	0,05	0,03	0,07	
Male_60-69_D1	29	450484	768	57595	460,81	0,06	0,04	0,09	
Male_70-79_D1	50	737681	953	43077	1251,93	0,04	0,03	0,05	
Male_80+_D1	43	333119	592	18174	832,41	0,05	0,04	0,07	
Male_total_D1	161	4788113	3046	418153	3244,00	***0,05***	***0,04***	***0,06***	
Total D1	353	9764506	5140	863615	5585,98	***0,06***	***0,06***	***0,07***	
Female <60_D1	32	3204405	357	312424	316,43	***0,10***	***0,07***	***0,14***	
Male < 60_D1	39	3266829	733	299307	698,85	***0,06***	***0,04***	***0,08***	
Total <60_D1	71	6471234	1090	611731	1015,28	***0,07***	***0,05***	***0,09***	
Female_0-19_D2	0	422191	2	83117	0,78	0,00	0,00	4,73	*
Female_20-29_D2	1	517303	8	49833	6,37	0,16	0,00	0,87	*
Female_30-39_D2	3	588725	31	53150	26,34	0,11	0,02	0,33	*
Female_40-49_D2	9	603966	93	59364	72,58	0,12	0,06	0,24	*
Female_50-59_D2	12	726853	223	66960	185,70	0,06	0,03	0,11	
Female_60-69_D2	15	495644	411	59025	264,75	0,06	0,03	0,09	
Female_70-79_D2	22	769492	638	46906	802,90	0,03	0,02	0,04	
Female_80+_D2	36	468718	688	27107	912,61	0,04	0,03	0,05	
Female_total_D2	98	4592892	2094	445462	2272,03	***0,04***	***0,03***	***0,05***	
Male_0-19_D2	0	437062	4	86035	1,56	0,00	0,00	2,37	*
Male_20-29_D2	2	501576	4	47106	3,27	0,61	0,07	2,21	*
Male_30-39_D2	1	611401	34	47191	33,79	0,03	0,00	0,16	*
Male_40-49_D2	9	607992	166	54226	142,78	0,06	0,03	0,12	*
Male_50-59_D2	12	743727	525	64749	462,60	0,03	0,01	0,04	
Male_60-69_D2	24	441441	768	57595	451,56	0,05	0,03	0,08	
Male_70-79_D2	39	720283	953	43077	1222,41	0,03	0,02	0,04	
Male_80+_D2	21	326394	592	18174	815,60	0,03	0,02	0,04	
Male_total_D2	108	4389876	3046	418153	3133,56	***0,03***	***0,03***	***0,04***	
Total D2	206	8982768	5140	863615	5405,59	***0,04***	***0,03***	***0,04***	

Arterial thrombosis									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	2	83117	0,02	0,00	0,00	155,98	*
Female_20-29_D1	0	81652	8	49833	1,01	0,00	0,00	3,67	*
Female_30-39_D1	1	87177	31	53150	3,90	0,26	0,01	1,43	*
Female_40-49_D1	0	129966	93	59364	15,62	0,00	0,00	0,24	*
Female_50-59_D1	5	146072	223	66960	37,32	0,13	0,04	0,31	*
Female_60-69_D1	2	26439	411	59025	14,12	0,14	0,02	0,51	*
Female_70-79_D1	2	13522	638	46906	14,11	0,14	0,02	0,51	*
Female_80+_D1	1	14187	688	27107	27,62	0,04	0,00	0,20	*
Female_total_D1	11	511831	2094	445462	113,72	***0,10***	***0,05***	***0,16***	
Male_0-19_D1	0	12633	4	86035	0,05	0,00	0,00	81,90	*
Male_20-29_D1	0	74564	4	47106	0,49	0,00	0,00	7,60	*
Male_30-39_D1	0	79918	34	47191	4,42	0,00	0,00	0,84	*
Male_40-49_D1	2	127191	166	54226	29,87	0,07	0,01	0,24	*
Male_50-59_D1	5	157958	525	64749	98,25	0,05	0,02	0,12	*
Male_60-69_D1	5	29694	768	57595	30,37	0,16	0,05	0,38	*
Male_70-79_D1	2	15801	953	43077	26,82	0,07	0,01	0,27	*
Male_80+_D1	0	5330	592	18174	13,32	0,00	0,00	0,28	*
Male_total_D1	14	503089	3046	418153	203,58	***0,07***	***0,04***	***0,11***	
Total D1	25	1014920	5140	863615	317,30	***0,08***	***0,05***	***0,11***	
Female <60	6	457683	357	312424	57,87	***0,10***	***0,04***	***0,23***	*
Male < 60	7	452264	733	299307	133,07	***0,05***	***0,02***	***0,11***	*
Totaal <60	13	909947	1090	611731	190,93	***0,07***	***0,04***	***0,11***	
Female_0-19_D2	0	11005	2	83117	0,02	0,00	0,00	181,65	*
Female_20-29_D2	1	73517	8	49833	0,91	1,10	0,03	6,15	*
Female_30-39_D2	0	80225	31	53150	3,59	0,00	0,00	1,03	*
Female_40-49_D2	2	120520	93	59364	14,48	0,14	0,02	0,50	*
Female_50-59_D2	3	136781	223	66960	34,94	0,09	0,02	0,25	*
Female_60-69_D2	0	24672	411	59025	13,18	0,00	0,00	0,28	*
Female_70-79_D2	1	12681	638	46906	13,23	0,08	0,00	0,42	*
Female_80+_D2	1	12682	688	27107	24,69	0,04	0,00	0,23	*
Female_total_D2	8	472083	2094	445462	105,05	***0,08***	***0,04***	***0,16***	*
Male_0-19_D2	0	10636	4	86035	0,04	0,00	0,00	97,27	*
Male_20-29_D2	0	65513	4	47106	0,43	0,00	0,00	8,65	*
Male_30-39_D2	0	73704	34	47191	4,07	0,00	0,00	0,91	*
Male_40-49_D2	3	118921	166	54226	27,93	0,11	0,02	0,31	*
Male_50-59_D2	4	148142	525	64749	92,14	0,04	0,01	0,11	*
Male_60-69_D2	3	27849	768	57595	28,49	0,11	0,02	0,31	*
Male_70-79_D2	2	14996	953	43077	25,45	0,08	0,01	0,28	*
Male_80+_D2	1	4786	592	18174	11,96	0,08	0,00	0,47	*
Male_total_D2	13	464547	3046	418153	190,51	***0,07***	***0,04***	***0,11***	
Total D2	21	936630	5140	863615	295,55	***0,07***	***0,04***	***0,11***	

Arterial thrombosis									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
ASTRAZENECA									
Female_0-19_D1	0	3382	2	83117	0,01	0,00	0,00	591,08	*
Female_20-29_D1	2	35017	8	49833	0,43	4,64	0,56	16,74	*
Female_30-39_D1	2	35502	31	53150	1,59	1,26	0,15	4,55	*
Female_40-49_D1	6	48915	93	59364	5,88	1,02	0,37	2,22	*
Female_50-59_D1	13	80677	223	66960	20,61	0,63	0,33	1,03	
Female_60-69_D1	52	466347	411	59025	249,10	0,21	0,15	0,27	
Female_70-79_D1	2	10661	638	46906	11,12	0,18	0,02	0,65	*
Female_80+_D1	4	14545	688	27107	28,32	0,14	0,04	0,36	*
Female_total_D1	81	695046	2094	445462	317,06	***0,26***	***0,20***	***0,32***	
Male_0-19_D1	0	1328	4	86035	0,00	0,00	0,00	779,07	*
Male_20-29_D1	0	12748	4	47106	0,08	0,00	0,00	44,44	*
Male_30-39_D1	0	14552	34	47191	0,80	0,00	0,00	4,59	*
Male_40-49_D1	2	18824	166	54226	4,42	0,45	0,05	1,63	*
Male_50-59_D1	5	30787	525	64749	19,15	0,26	0,08	0,61	*
Male_60-69_D1	54	513107	768	57595	524,87	0,10	0,08	0,13	
Male_70-79_D1	1	11619	953	43077	19,72	0,05	0,00	0,28	*
Male_80+_D1	3	7637	592	18174	19,08	0,16	0,03	0,46	*
Male_total_D1	65	610602	3046	418153	588,13	***0,11***	***0,08***	***0,14***	
Total D1	146	1305648	5140	863615	905,19	***0,16***	***0,14***	***0,19***	
Female <60_D1	23	203493	357	312424	28,52	***0,81***	***0,51***	***1,18***	
Male < 60_D1	7	78239	733	299307	24,46	***0,29***	***0,11***	***0,59***	*
Totaal <60_D1	30	281732	1090	611731	52,98	***0,57***	***0,38***	***0,79***	
Female_0-19_D2	0	3148	2	83117	0,01	0,00	0,00	635,02	*
Female_20-29_D2	0	32418	8	49833	0,40	0,00	0,00	9,24	*
Female_30-39_D2	1	32572	31	53150	1,46	0,69	0,02	3,82	*
Female_40-49_D2	2	45128	93	59364	5,42	0,37	0,04	1,33	*
Female_50-59_D2	3	74869	223	66960	19,13	0,16	0,03	0,46	*
Female_60-69_D2	14	433279	411	59025	231,44	0,06	0,03	0,10	
Female_70-79_D2	0	9751	638	46906	10,17	0,00	0,00	0,36	*
Female_80+_D2	0	12505	688	27107	24,35	0,00	0,00	0,15	*
Female_total_D2	20	643670	2094	445462	292,38	***0,07***	***0,04***	***0,10***	
Male_0-19_D2	0	1205	4	86035	0,00	0,00	0,00	858,60	*
Male_20-29_D2	0	11742	4	47106	0,08	0,00	0,00	48,24	*
Male_30-39_D2	0	13569	34	47191	0,75	0,00	0,00	4,92	*
Male_40-49_D2	1	17600	166	54226	4,13	0,24	0,01	1,35	*
Male_50-59_D2	0	28784	525	64749	17,90	0,00	0,00	0,21	*
Male_60-69_D2	19	477217	768	57595	488,15	0,04	0,02	0,06	
Male_70-79_D2	1	10649	953	43077	18,07	0,06	0,00	0,31	*
Male_80+_D2	2	6507	592	18174	16,26	0,12	0,01	0,44	*
Male_total_D2	23	567273	3046	418153	545,35	***0,04***	***0,03***	***0,06***	
Total D2	43	1210943	5140	863615	837,73	***0,05***	***0,04***	***0,07***	

Venous thrombosis (excl CVST)									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
PFIZER									
Female_0-19_D1	0	501841	14	83112	3,24	0,00	0,00	1,14	*
Female_20-29_D1	8	600233	48	49817	22,18	0,36	0,16	0,71	*
Female_30-39_D1	9	660918	76	53128	36,26	0,25	0,11	0,47	*
Female_40-49_D1	21	663068	135	59336	57,86	0,36	0,22	0,54	
Female_50-59_D1	15	778345	205	66958	91,40	0,16	0,09	0,26	
Female_60-69_D1	14	504442	213	59134	69,69	0,20	0,11	0,32	
Female_70-79_D1	32	787778	274	47058	175,94	0,18	0,12	0,25	
Female_80+_D1	15	479768	186	27338	125,20	0,12	0,07	0,19	
Female tot D1	114	4976393	1151	445881	581,79	***0,20***	***0,16***	***0,23***	
Male_0-19_D1	0	518024	13	86029	3,00	0,00	0,00	1,23	*
Male_20-29_D1	5	596893	25	47098	12,15	0,41	0,13	0,96	*
Male_30-39_D1	4	683277	48	47182	26,66	0,15	0,04	0,38	*
Male_40-49_D1	9	666747	90	54258	42,42	0,21	0,10	0,40	*
Male_50-59_D1	16	801888	189	64912	89,55	0,18	0,10	0,28	
Male_60-69_D1	20	450484	252	57831	75,29	0,27	0,16	0,40	
Male_70-79_D1	36	737681	259	43415	168,80	0,21	0,15	0,29	
Male_80+_D1	17	333119	133	18358	92,57	0,18	0,11	0,28	
Male_total_D1	107	4788113	1009	419083	510,45	***0,21***	***0,17***	***0,25***	
Total D1	221	9764506	2160	864964	1092,24	***0,20***	***0,18***	***0,23***	
Female <60_D1	53	3204405	478	312351	210,96	***0,25***	***0,19***	***0,32***	
Male < 60_D1	34	3266829	365	299479	173,79	***0,20***	***0,13***	***0,27***	
Totaal <60_D1	87	6471234	843	611830	384,75	***0,23***	***0,18***	***0,28***	
Female_0-19_D2	1	422191	14	83112	2,73	0,37	0,01	2,04	*
Female_20-29_D2	4	517303	48	49817	19,12	0,21	0,06	0,54	*
Female_30-39_D2	11	588725	76	53128	32,30	0,34	0,17	0,58	
Female_40-49_D2	10	603966	135	59336	52,71	0,19	0,09	0,35	*
Female_50-59_D2	16	726853	205	66958	85,36	0,19	0,11	0,29	
Female_60-69_D2	7	495644	213	59134	68,48	0,10	0,04	0,21	*
Female_70-79_D2	22	769492	274	47058	171,85	0,13	0,08	0,19	
Female_80+_D2	16	468718	186	27338	122,32	0,13	0,07	0,20	
Female_total_D2	87	4592892	1151	445881	554,86	***0,16***	***0,12***	***0,19***	
Male_0-19_D2	0	437062	13	86029	2,53	0,00	0,00	1,46	*
Male_20-29_D2	1	501576	25	47098	10,21	0,10	0,00	0,55	*
Male_30-39_D2	3	611401	48	47182	23,86	0,13	0,03	0,37	*
Male_40-49_D2	7	607992	90	54258	38,68	0,18	0,07	0,37	*
Male_50-59_D2	18	743727	189	64912	83,06	0,22	0,13	0,33	
Male_60-69_D2	11	441441	252	57831	73,78	0,15	0,07	0,25	
Male_70-79_D2	19	720283	259	43415	164,82	0,12	0,07	0,17	
Male_80+_D2	8	326394	133	18358	90,70	0,09	0,04	0,17	*
Male_total_D2	67	4389876	1009	419083	487,64	***0,14***	***0,11***	***0,17***	
Total D2	154	8982768	2160	864964	1042,50	***0,15***	***0,12***	***0,17***	

Venous thrombosis (excl CVST)									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	14	83112	0,08	0,00	0,00	44,56	*
Female_20-29_D1	0	81652	48	49817	3,02	0,00	0,00	1,22	*
Female_30-39_D1	2	87177	76	53128	4,78	0,42	0,05	1,51	*
Female_40-49_D1	0	129966	135	59336	11,34	0,00	0,00	0,33	*
Female_50-59_D1	3	146072	205	66958	17,15	0,17	0,04	0,51	*
Female_60-69_D1	1	26439	213	59134	3,65	0,27	0,01	1,52	*
Female_70-79_D1	2	13522	274	47058	3,02	0,66	0,08	2,39	*
Female_80+_D1	0	14187	186	27338	3,70	0,00	0,00	1,00	*
Female tot D1	8	511831	1151	445881	46,75	***0,17***	***0,07***	***0,34***	*
Male_0-19_D1	0	12633	13	86029	0,07	0,00	0,00	50,39	*
Male_20-29_D1	0	74564	25	47098	1,52	0,00	0,00	2,43	*
Male_30-39_D1	2	79918	48	47182	3,12	0,64	0,08	2,32	*
Male_40-49_D1	1	127191	90	54258	8,09	0,12	0,00	0,69	*
Male_50-59_D1	8	157958	189	64912	17,64	0,45	0,20	0,89	*
Male_60-69_D1	6	29694	252	57831	4,96	1,21	0,44	2,63	*
Male_70-79_D1	0	15801	259	43415	3,62	0,00	0,00	1,02	*
Male_80+_D1	0	5330	133	18358	1,48	0,00	0,00	2,49	*
Male_total_D1	17	503089	1009	419083	40,50	***0,42***	***0,24***	***0,65***	
Total D1	25	1014920	2160	864964	87,26	***0,29***	***0,18***	***0,41***	
Female <60 D1	5	457683	478	312351	36,38	***0,14***	***0,04***	***0,32***	*
Male < 60 D1	11	452264	365	299479	30,44	***0,36***	***0,18***	***0,61***	
Totaal <60 D1	16	909947	843	611830	66,82	***0,24***	***0,13***	***0,37***	
Female_0-19_D2	0	11005	14	83112	0,07	0,00	0,00	51,90	*
Female_20-29_D2	0	73517	48	49817	2,72	0,00	0,00	1,36	*
Female_30-39_D2	2	80225	76	53128	4,40	0,45	0,05	1,64	*
Female_40-49_D2	4	120520	135	59336	10,52	0,38	0,10	0,97	*
Female_50-59_D2	4	136781	205	66958	16,06	0,25	0,07	0,64	*
Female_60-69_D2	3	24672	213	59134	3,41	0,88	0,18	2,57	*
Female_70-79_D2	0	12681	274	47058	2,83	0,00	0,00	1,30	*
Female_80+_D2	0	12682	186	27338	3,31	0,00	0,00	1,11	*
Female_total_D2	13	472083	1151	445881	43,32	***0,30***	***0,16***	***0,49***	
Male_0-19_D2	0	10636	13	86029	0,06	0,00	0,00	59,86	*
Male_20-29_D2	0	65513	25	47098	1,33	0,00	0,00	2,77	*
Male_30-39_D2	1	73704	48	47182	2,88	0,35	0,01	1,94	*
Male_40-49_D2	3	118921	90	54258	7,57	0,40	0,08	1,16	*
Male_50-59_D2	6	148142	189	64912	16,54	0,36	0,13	0,79	*
Male_60-69_D2	2	27849	252	57831	4,65	0,43	0,05	1,55	*
Male_70-79_D2	0	14996	259	43415	3,43	0,00	0,00	1,08	*
Male_80+_D2	0	4786	133	18358	1,33	0,00	0,00	2,77	*
Male_total_D2	12	464547	1009	419083	37,80	***0,32***	***0,16***	***0,53***	
Total D2	25	936630	2160	864964	81,12	***0,31***	***0,20***	***0,44***	

Venous thrombosis (excl CVST)									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* (# O > E=0)**	**95% CI SMR** *(* O<10 with poisson table)*		
ASTRAZENECA									
Female_0-19_D1	0	3382	14	83112	0,02	0,00	0,00	168,87	*
Female_20-29_D1	1	35017	48	49817	1,29	0,77	0,02	4,30	*
Female_30-39_D1	3	35502	76	53128	1,95	1,54	0,32	4,50	*
Female_40-49_D1	18	48915	135	59336	4,27	4,22	2,46	6,44	
Female_50-59_D1	10	80677	205	66958	9,47	1,06	0,51	1,94	*
Female_60-69_D1	39	466347	213	59134	64,43	0,61	0,43	0,81	
Female_70-79_D1	2	10661	274	47058	2,38	0,84	0,10	3,03	*
Female_80+_D1	2	14545	186	27338	3,80	0,53	0,06	1,90	*
Female tot D1	75	695046	1151	445881	87,61	***0,86***	***0,67***	***1,07***	
Male_0-19_D1	0	1328	13	86029	0,01	0,00	0,00	479,40	*
Male_20-29_D1	2	12748	25	47098	0,26	7,71	0,92	27,82	*
Male_30-39_D1	0	14552	48	47182	0,57	0,00	0,00	6,50	*
Male_40-49_D1	0	18824	90	54258	1,20	0,00	0,00	3,08	*
Male_50-59_D1	4	30787	189	64912	3,44	1,16	0,32	2,98	*
Male_60-69_D1	47	513107	252	57831	85,76	0,55	0,40	0,72	
Male_70-79_D1	0	11619	259	43415	2,66	0,00	0,00	1,39	*
Male_80+_D1	1	7637	133	18358	2,12	0,47	0,01	2,62	*
Male_total_D1	54	610602	1009	419083	96,01	***0,56***	***0,42***	***0,73***	
Total D1	129	1305648	2160	864964	183,62	***0,70***	***0,58***	***0,83***	
Female <60_D1	32	203493	478	312351	17,01	***1,88***	***1,28***	***2,61***	
Male < 60_D1	6	78239	365	299479	5,47	***1,10***	***0,40***	***2,39***	*
Totaal <60_D1	38	281732	843	611830	22,48	***1,69***	***1,19***	***2,28***	
Female_0-19_D2	0	3148	14	83112	0,02	0,00	0,00	181,42	*
Female_20-29_D2	0	32418	48	49817	1,20	0,00	0,00	3,08	*
Female_30-39_D2	1	32572	76	53128	1,79	0,56	0,01	3,12	*
Female_40-49_D2	4	45128	135	59336	3,94	1,02	0,28	2,60	*
Female_50-59_D2	2	74869	205	66958	8,79	0,23	0,03	0,82	*
Female_60-69_D2	12	433279	213	59134	59,86	0,20	0,10	0,33	
Female_70-79_D2	1	9751	274	47058	2,18	0,46	0,01	2,56	*
Female_80+_D2	0	12505	186	27338	3,26	0,00	0,00	1,13	*
Female_total_D2	20	643670	1151	445881	81,04	***0,25***	***0,15***	***0,37***	
Male_0-19_D2	0	1205	13	86029	0,01	0,00	0,00	528,33	*
Male_20-29_D2	0	11742	25	47098	0,24	0,00	0,00	15,44	*
Male_30-39_D2	0	13569	48	47182	0,53	0,00	0,00	6,97	*
Male_40-49_D2	0	17600	90	54258	1,12	0,00	0,00	3,30	*
Male_50-59_D2	3	28784	189	64912	3,21	0,93	0,19	2,73	*
Male_60-69_D2	23	477217	252	57831	79,76	0,29	0,18	0,42	
Male_70-79_D2	1	10649	259	43415	2,44	0,41	0,01	2,29	*
Male_80+_D2	0	6507	133	18358	1,81	0,00	0,00	2,04	*
Male_total_D2	27	567273	1009	419083	89,12	***0,30***	***0,20***	***0,43***	
Total D2	47	1210943	2160	864964	170,15	***0,28***	***0,20***	***0,36***	

Venous thrombosis (excl CVST)									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
JANSSEN									
Female_0-19_D1	1	16783	14	83112	0,11	9,22	0,23	51,37	*
Female_20-29_D1	1	86405	48	49817	3,19	0,31	0,01	1,74	*
Female_30-39_D1	3	43185	76	53128	2,37	1,27	0,26	3,70	*
Female_40-49_D1	7	55045	135	59336	4,80	1,46	0,58	3,00	*
Female_50-59_D1	4	118748	205	66958	13,94	0,29	0,08	0,73	*
Female_60-69_D1	0	5799	213	59134	0,80	0,00	0,00	4,61	*
Female_70-79_D1	0	1282	274	47058	0,29	0,00	0,00	12,89	*
Female_80+_D1	0	438	186	27338	0,11	0,00	0,00	32,28	*
Female tot D1	16	327685	1151	445881	25,62	***0,62***	***0,35***	***0,98***	
Male_0-19_D1	0	26060	13	86029	0,15	0,00	0,00	24,43	*
Male_20-29_D1	2	145455	25	47098	2,96	0,68	0,08	2,44	*
Male_30-39_D1	3	60585	48	47182	2,36	1,27	0,26	3,71	*
Male_40-49_D1	5	65513	90	54258	4,17	1,20	0,39	2,80	*
Male_50-59_D1	9	145152	189	64912	16,21	0,56	0,25	1,05	*
Male_60-69_D1	0	6388	252	57831	1,07	0,00	0,00	3,46	*
Male_70-79_D1	0	1729	259	43415	0,40	0,00	0,00	9,33	*
Male_80+_D1	0	442	133	18358	0,12	0,00	0,00	30,04	*
Male_total_D1	19	451324	1009	419083	27,44	***0,69***	***0,41***	***1,05***	
Total_D1	35	779009	2160	864964	53,06	***0,66***	***0,46***	***0,90***	
Female <60_D1	16	320166	478	312351	24,42	***0,66***	***0,37***	***1,02***	
Male < 60_D1	19	442765	365	299479	25,86	***0,73***	***0,44***	***1,11***	
Total <60_D1	35	762931	843	611830	50,27	***0,70***	***0,48***	***0,95***	

Venous thrombosis (excl CVST)									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
JANSSEN									
Female_0-19_D1	1	16783	14	83112	0,22	4,61	0,12	25,68	*
Female_20-29_D1	2	86405	48	49817	6,39	0,31	0,04	1,13	*
Female_30-39_D1	3	43185	76	53128	4,74	0,63	0,13	1,85	*
Female_40-49_D1	7	55045	135	59336	9,61	0,73	0,29	1,50	*
Female_50-59_D1	5	118748	205	66958	27,89	0,18	0,06	0,42	*
Female_60-69_D1	0	5799	213	59134	1,60	0,00	0,00	2,30	*
Female_70-79_D1	0	1282	274	47058	0,57	0,00	0,00	6,44	*
Female_80+_D1	0	438	186	27338	0,23	0,00	0,00	16,14	*
Female tot D1	18	327685	1151	445881	51,24	***0,35***	***0,21***	***0,54***	
Male_0-19_D1	0	26060	13	86029	0,30	0,00	0,00	12,21	*
Male_20-29_D1	2	145455	25	47098	5,92	0,34	0,04	1,22	*
Male_30-39_D1	3	60585	48	47182	4,73	0,63	0,13	1,85	*
Male_40-49_D1	6	65513	90	54258	8,34	0,72	0,26	1,57	*
Male_50-59_D1	11	145152	189	64912	32,42	0,34	0,17	0,57	
Male_60-69_D1	0	6388	252	57831	2,14	0,00	0,00	1,73	*
Male_70-79_D1	0	1729	259	43415	0,79	0,00	0,00	4,66	*
Male_80+_D1	0	442	133	18358	0,25	0,00	0,00	15,02	*
Male_total_D1	22	451324	1009	419083	54,88	***0,40***	***0,25***	***0,59***	
Total_D1	40	779009	2160	864964	106,13	***0,38***	***0,27***	***0,51***	
Female <60_D1	18	320166	478	312351	48,84	***0,37***	***0,22***	***0,56***	
Male < 60_D1	22	442765	365	299479	51,71	***0,43***	***0,26***	***0,63***	
Totaal <60_D1	40	762931	843	611830	100,55	***0,40***	***0,28***	***0,53***	

Venous thrombosis (excl CVST)									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
PFIZER									
Female_0-19_D1	0	501841	14	83112	6,48	0,00	0,00	0,57	*
Female_20-29_D1	9	600233	48	49817	44,37	0,20	0,09	0,38	*
Female_30-39_D1	14	660918	76	53128	72,53	0,19	0,10	0,31	
Female_40-49_D1	24	663068	135	59336	115,73	0,21	0,13	0,30	
Female_50-59_D1	21	778345	205	66958	182,81	0,11	0,07	0,17	
Female_60-69_D1	15	504442	213	59134	139,39	0,11	0,06	0,17	
Female_70-79_D1	36	787778	274	47058	351,87	0,10	0,07	0,14	
Female_80+_D1	20	479768	186	27338	250,40	0,08	0,05	0,12	
Female tot D1	139	4976393	1151	445881	1163,58	***0,12***	***0,10***	***0,14***	
Male_0-19_D1	0	518024	13	86029	6,01	0,00	0,00	0,61	*
Male_20-29_D1	5	596893	25	47098	24,31	0,21	0,07	0,48	*
Male_30-39_D1	6	683277	48	47182	53,32	0,11	0,04	0,24	*
Male_40-49_D1	13	666747	90	54258	84,84	0,15	0,08	0,25	
Male_50-59_D1	23	801888	189	64912	179,11	0,13	0,08	0,19	
Male_60-69_D1	22	450484	252	57831	150,59	0,15	0,09	0,22	
Male_70-79_D1	45	737681	259	43415	337,59	0,13	0,10	0,18	
Male_80+_D1	19	333119	133	18358	185,14	0,10	0,06	0,16	
Male_total_D1	133	4788113	1009	419083	1020,90	***0,13***	***0,11***	***0,15***	
Total D1	272	9764506	2160	864964	2184,47	***0,12***	***0,11***	***0,14***	
Female <60	68	3204405	478	312351	421,91	***0,16***	***0,12***	***0,20***	
Male < 60	47	3266829	365	299479	347,58	***0,14***	***0,10***	***0,18***	
Totaal <60	115	6471234	843	611830	769,50	***0,15***	***0,12***	***0,18***	
Female_0-19_D2	2	422191	14	83112	5,46	0,37	0,04	1,32	*
Female_20-29_D2	4	517303	48	49817	38,24	0,10	0,03	0,27	*
Female_30-39_D2	14	588725	76	53128	64,61	0,22	0,12	0,35	
Female_40-49_D2	11	603966	135	59336	105,41	0,10	0,05	0,18	
Female_50-59_D2	19	726853	205	66958	170,71	0,11	0,07	0,17	
Female_60-69_D2	10	495644	213	59134	136,95	0,07	0,03	0,13	
Female_70-79_D2	23	769492	274	47058	343,71	0,07	0,04	0,10	
Female_80+_D2	23	468718	186	27338	244,64	0,09	0,06	0,14	
Female_total_D2	106	4592892	1151	445881	1109,72	***0,10***	***0,08***	***0,11***	
Male_0-19_D2	0	437062	13	86029	5,07	0,00	0,00	0,73	*
Male_20-29_D2	4	501576	25	47098	20,42	0,20	0,05	0,50	*
Male_30-39_D2	5	611401	48	47182	47,72	0,10	0,03	0,24	*
Male_40-49_D2	12	607992	90	54258	77,36	0,16	0,08	0,26	
Male_50-59_D2	21	743727	189	64912	166,12	0,13	0,08	0,19	
Male_60-69_D2	13	441441	252	57831	147,56	0,09	0,05	0,14	
Male_70-79_D2	27	720283	259	43415	329,63	0,08	0,05	0,12	
Male_80+_D2	10	326394	133	18358	181,40	0,06	0,03	0,10	*
Male_total_D2	92	4389876	1009	419083	975,28	***0,09***	***0,08***	***0,12***	
Total D2	198	8982768	2160	864964	2085,00	***0,09***	***0,08***	***0,11***	

Venous thrombosis (excl CVST)									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	14	83112	0,17	0,00	0,00	22,28	*
Female_20-29_D1	0	81652	48	49817	6,04	0,00	0,00	0,61	*
Female_30-39_D1	2	87177	76	53128	9,57	0,21	0,03	0,75	*
Female_40-49_D1	4	129966	135	59336	22,68	0,18	0,05	0,45	*
Female_50-59_D1	6	146072	205	66958	34,31	0,17	0,06	0,38	*
Female_60-69_D1	1	26439	213	59134	7,31	0,14	0,00	0,76	*
Female_70-79_D1	2	13522	274	47058	6,04	0,33	0,04	1,20	*
Female_80+_D1	0	14187	186	27338	7,40	0,00	0,00	0,50	*
Female tot D1	15	511831	1151	445881	93,51	***0,16***	***0,09***	***0,25***	
Male_0-19_D1	0	12633	13	86029	0,15	0,00	0,00	25,20	*
Male_20-29_D1	0	74564	25	47098	3,04	0,00	0,00	1,22	*
Male_30-39_D1	2	79918	48	47182	6,24	0,32	0,04	1,16	*
Male_40-49_D1	1	127191	90	54258	16,18	0,06	0,00	0,34	*
Male_50-59_D1	11	157958	189	64912	35,28	0,31	0,15	0,53	
Male_60-69_D1	9	29694	252	57831	9,93	0,91	0,42	1,72	*
Male_70-79_D1	1	15801	259	43415	7,23	0,14	0,00	0,77	*
Male_80+_D1	0	5330	133	18358	2,96	0,00	0,00	1,25	*
Male_total_D1	24	503089	1009	419083	81,00	***0,30***	***0,19***	***0,43***	
Total D1	39	1014920	2160	864964	174,51	***0,22***	***0,16***	***0,30***	
Female <60_D1	12	457683	478	312351	72,76	***0,16***	***0,08***	***0,27***	
Male < 60_D1	14	452264	365	299479	60,89	***0,23***	***0,12***	***0,37***	
Totaal <60_D1	26	909947	843	611830	133,64	***0,19***	***0,13***	***0,28***	
Female_0-19_D2	1	11005	14	83112	0,14	7,03	0,18	39,17	*
Female_20-29_D2	0	73517	48	49817	5,43	0,00	0,00	0,68	*
Female_30-39_D2	3	80225	76	53128	8,80	0,34	0,07	1,00	*
Female_40-49_D2	6	120520	135	59336	21,03	0,29	0,10	0,62	*
Female_50-59_D2	5	136781	205	66958	32,12	0,16	0,05	0,36	*
Female_60-69_D2	3	24672	213	59134	6,82	0,44	0,09	1,29	*
Female_70-79_D2	0	12681	274	47058	5,66	0,00	0,00	0,65	*
Female_80+_D2	0	12682	186	27338	6,62	0,00	0,00	0,56	*
Female_total_D2	18	472083	1151	445881	86,64	***0,21***	***0,12***	***0,32***	
Male_0-19_D2	0	10636	13	86029	0,12	0,00	0,00	29,93	*
Male_20-29_D2	0	65513	25	47098	2,67	0,00	0,00	1,38	*
Male_30-39_D2	1	73704	48	47182	5,75	0,17	0,00	0,97	*
Male_40-49_D2	3	118921	90	54258	15,13	0,20	0,04	0,58	*
Male_50-59_D2	7	148142	189	64912	33,09	0,21	0,08	0,44	*
Male_60-69_D2	3	27849	252	57831	9,31	0,32	0,07	0,94	*
Male_70-79_D2	0	14996	259	43415	6,86	0,00	0,00	0,54	*
Male_80+_D2	0	4786	133	18358	2,66	0,00	0,00	1,39	*
Male_total_D2	14	464547	1009	419083	75,60	***0,19***	***0,10***	***0,30***	
Total D2	32	936630	2160	864964	162,24	***0,20***	***0,13***	***0,27***	

Venous thrombosis (excl CVST)									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
ASTRAZENECA									
Female_0-19_D1	0	3382	14	83112	0,04	0,00	0,00	84,44	*
Female_20-29_D1	3	35017	48	49817	2,59	1,16	0,24	3,39	*
Female_30-39_D1	4	35502	76	53128	3,90	1,03	0,28	2,63	*
Female_40-49_D1	22	48915	135	59336	8,54	2,58	1,60	3,79	
Female_50-59_D1	17	80677	205	66958	18,95	0,90	0,51	1,39	
Female_60-69_D1	55	466347	213	59134	128,86	0,43	0,32	0,55	
Female_70-79_D1	3	10661	274	47058	4,76	0,63	0,13	1,84	*
Female_80+_D1	4	14545	186	27338	7,59	0,53	0,14	1,35	*
Female tot D1	108	695046	1151	445881	175,23	***0,62***	***0,50***	***0,74***	
Male_0-19_D1	0	1328	13	86029	0,02	0,00	0,00	239,70	*
Male_20-29_D1	2	12748	25	47098	0,52	3,85	0,46	13,91	*
Male_30-39_D1	0	14552	48	47182	1,14	0,00	0,00	3,25	*
Male_40-49_D1	0	18824	90	54258	2,40	0,00	0,00	1,54	*
Male_50-59_D1	5	30787	189	64912	6,88	0,73	0,24	1,70	*
Male_60-69_D1	68	513107	252	57831	171,52	0,40	0,31	0,50	
Male_70-79_D1	0	11619	259	43415	5,32	0,00	0,00	0,69	*
Male_80+_D1	2	7637	133	18358	4,24	0,47	0,06	1,70	*
Male_total_D1	77	610602	1009	419083	192,02	***0,40***	***0,31***	***0,50***	
Total D1	185	1305648	2160	864964	367,25	***0,50***	***0,43***	***0,58***	
Female <60_D1	46	203493	478	312351	34,01	***1,35***	***0,98***	***1,78***	
Male < 60_D1	7	78239	365	299479	10,94	***0,64***	***0,26***	***1,32***	*
Totaal <60_D1	53	281732	843	611830	44,96	***1,18***	***0,88***	***1,53***	
Female_0-19_D2	0	3148	14	83112	0,04	0,00	0,00	90,71	*
Female_20-29_D2	0	32418	48	49817	2,40	0,00	0,00	1,54	*
Female_30-39_D2	1	32572	76	53128	3,57	0,28	0,01	1,56	*
Female_40-49_D2	5	45128	135	59336	7,88	0,63	0,21	1,48	*
Female_50-59_D2	2	74869	205	66958	17,58	0,11	0,01	0,41	*
Female_60-69_D2	16	433279	213	59134	119,72	0,13	0,08	0,21	
Female_70-79_D2	1	9751	274	47058	4,36	0,23	0,01	1,28	*
Female_80+_D2	0	12505	186	27338	6,53	0,00	0,00	0,57	*
Female_total_D2	25	643670	1151	445881	162,08	***0,15***	***0,10***	***0,22***	
Male_0-19_D2	0	1205	13	86029	0,01	0,00	0,00	264,17	*
Male_20-29_D2	0	11742	25	47098	0,48	0,00	0,00	7,72	*
Male_30-39_D2	0	13569	48	47182	1,06	0,00	0,00	3,48	*
Male_40-49_D2	0	17600	90	54258	2,24	0,00	0,00	1,65	*
Male_50-59_D2	4	28784	189	64912	6,43	0,62	0,17	1,59	*
Male_60-69_D2	34	477217	252	57831	159,52	0,21	0,15	0,29	
Male_70-79_D2	1	10649	259	43415	4,87	0,21	0,01	1,14	*
Male_80+_D2	0	6507	133	18358	3,62	0,00	0,00	1,02	*
Male_total_D2	39	567273	1009	419083	178,23	***0,22***	***0,15***	***0,29***	
Total D2	64	1210943	2160	864964	340,31	***0,19***	***0,14***	***0,24***	

CVST									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
PFIZER									
Female_0-19_D1	0	501841	3	83117	0,69	0,00	0,00	5,31	*
Female_20-29_D1	1	600233	2	49835	0,92	1,08	0,03	6,03	*
Female_30-39_D1	0	660918	1	53163	0,48	0,00	0,00	7,74	*
Female_40-49_D1	0	663068	0	59406	0,00				
Female_50-59_D1	0	778345	5	67062	2,23	0,00	0,00	1,66	*
Female_60-69_D1	0	504442	1	59228	0,33	0,00	0,00	11,30	*
Female_70-79_D1	0	787778	1	47181	0,64	0,00	0,00	5,76	*
Female_80+_D1	0	479768	0	27419	0,00				
Female tot D1	1	4976393	13	446411	5,29	***0,19***	***0,00***	***1,05***	*
Male_0-19_D1	0	518024	1	86036	0,23	0,00	0,00	15,98	*
Male_20-29_D1	0	596893	1	47107	0,49	0,00	0,00	7,59	*
Male_30-39_D1	0	683277	0	47204	0,00				
Male_40-49_D1	0	666747	4	54297	1,88	0,00	0,00	1,96	*
Male_50-59_D1	1	801888	1	65000	0,47	2,11	0,05	11,77	*
Male_60-69_D1	0	450484	0	57935	0,00				
Male_70-79_D1	0	737681	1	43532	0,65	0,00	0,00	5,68	*
Male_80+_D1	0	333119	0	18417	0,00				
Male_total_D1	1	4788113	8	419528	3,72	***0,27***	***0,01***	***1,50***	*
Total D1	2	9764506	21	865939	9,01	***0,22***	***0,03***	***0,80***	*
Female <60_D1	1	3204405	11	312583	4,32	***0,23***	***0,01***	***1,29***	*
Male < 60_D1	1	3266829	7	299644	3,07	***0,33***	***0,01***	***1,81***	*
Totaal <60_D1	2	6471234	18	612227	7,40	***0,27***	***0,03***	***0,98***	*
Female_0-19_D2	0	422191	3	83117	0,58	0,00	0,00	6,31	*
Female_20-29_D2	1	517303	2	49835	0,80	1,26	0,03	6,99	*
Female_30-39_D2	0	588725	1	53163	0,42	0,00	0,00	8,69	*
Female_40-49_D2	0	603966	0	59406	0,00				
Female_50-59_D2	0	726853	5	67062	2,08	0,00	0,00	1,78	*
Female_60-69_D2	0	495644	1	59228	0,32	0,00	0,00	11,50	*
Female_70-79_D2	0	769492	1	47181	0,63	0,00	0,00	5,90	*
Female_80+_D2	1	468718	0	27419	0,00	#			
Female_total_D2	2	4592892	13	446411	4,83	***0,41***	***0,05***	***1,49***	*
Male_0-19_D2	0	437062	1	86036	0,19	0,00	0,00	18,94	*
Male_20-29_D2	1	501576	1	47107	0,41	2,45	0,06	13,64	*
Male_30-39_D2	1	611401	0	47204	0,00	#			
Male_40-49_D2	0	607992	4	54297	1,72	0,00	0,00	2,15	*
Male_50-59_D2	0	743727	1	65000	0,44	0,00	0,00	8,41	*
Male_60-69_D2	0	441441	0	57935	0,00				
Male_70-79_D2	1	720283	1	43532	0,63	1,58	0,04	8,78	*
Male_80+_D2	0	326394	0	18417	0,00				
Male_total_D2	3	4389876	8	419528	3,39	***0,88***	***0,18***	***2,58***	*
Total D2	5	8982768	21	865939	8,23	***0,61***	***0,20***	***1,42***	*
Female <60_D2	1	2859038	11	312583	3,88	***0,26***	*0,01*	*1,43*	*
Male < 60_D2	2	2901758	7	299644	2,76	***0,72***	*0,09*	*2,80*	*
Totaal <60_D2	3	5760796	18	612227	6,64	***0,45***	***0,09***	***1,32***	*

CVST									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	3	83117	0,02	0,00	0,00	207,97	*
Female_20-29_D1	0	81652	2	49835	0,13	0,00	0,00	29,36	*
Female_30-39_D1	0	87177	1	53163	0,06	0,00	0,00	58,67	*
Female_40-49_D1	0	129966	0	59406	0,00				
Female_50-59_D1	0	146072	5	67062	0,42	0,00	0,00	8,83	*
Female_60-69_D1	0	26439	1	59228	0,02	0,00	0,00	215,51	*
Female_70-79_D1	0	13522	1	47181	0,01	0,00	0,00	335,67	*
Female_80+_D1	0	14187	0	27419	0,00				
Female tot D1	0	511831	13	446411	0,65	***0,00***	***0,00***	***28,20***	*
Male_0-19_D1	0	12633	1	86036	0,01	0,00	0,00	655,19	*
Male_20-29_D1	0	74564	1	47107	0,06	0,00	0,00	60,78	*
Male_30-39_D1	0	79918	0	47204	0,00				
Male_40-49_D1	0	127191	4	54297	0,36	0,00	0,00	10,27	*
Male_50-59_D1	0	157958	1	65000	0,09	0,00	0,00	39,59	*
Male_60-69_D1	0	29694	0	57935	0,00				
Male_70-79_D1	0	15801	1	43532	0,01	0,00	0,00	265,04	*
Male_80+_D1	0	5330	0	18417	0,00				
Male_total_D1	0	503089	8	419528	0,53	***0,00***	***0,00***	***6,92***	*
Total D1	0	1014920	21	865939	1,19	***0,00***	***0,00***	***3,11***	*
Female <60 D1	0	457683	11	312583	0,62	***0,00***	***0,00***	***5,91***	*
Male < 60 D1	0	452264	7	299644	0,52	***0,00***	***0,00***	***7,11***	*
Totaal <60 D1	0	909947	18	612227	1,14	***0,00***	***0,00***	***3,23***	*
Female_0-19_D2	0	11005	3	83117	0,02	0,00	0,00	242,20	*
Female_20-29_D2	0	73517	2	49835	0,11	0,00	0,00	32,61	*
Female_30-39_D2	0	80225	1	53163	0,06	0,00	0,00	63,75	*
Female_40-49_D2	0	120520	0	59406	0,00				
Female_50-59_D2	0	136781	5	67062	0,39	0,00	0,00	9,43	*
Female_60-69_D2	0	24672	1	59228	0,02	0,00	0,00	230,95	*
Female_70-79_D2	0	12681	1	47181	0,01	0,00	0,00	357,94	*
Female_80+_D2	0	12682	0	27419	0,00				
Female_total_D2	0	472083	13	446411	0,60	***0,00***	***0,00***	***6,11***	*
Male_0-19_D2	0	10636	1	86036	0,00	0,00	0,00	778,20	*
Male_20-29_D2	0	65513	1	47107	0,05	0,00	0,00	69,17	*
Male_30-39_D2	0	73704	0	47204	0,00				
Male_40-49_D2	0	118921	4	54297	0,34	0,00	0,00	10,98	*
Male_50-59_D2	0	148142	1	65000	0,09	0,00	0,00	42,21	*
Male_60-69_D2	0	27849	0	57935	0,00				
Male_70-79_D2	0	14996	1	43532	0,01	0,00	0,00	279,27	*
Male_80+_D2	0	4786	0	18417	0,00				
Male_total_D2	0	464547	8	419528	0,49	***0,00***	***0,00***	***7,46***	*
Total D2	0	936630	21	865939	1,10	***0,00***	***0,00***	***3,36***	*

CVST									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
ASTRAZENECA									
Female_0-19_D1	0	3382	3	83117	0,00	0,00	0,00	788,11	*
Female_20-29_D1	1	35017	2	49835	0,05	18,55	0,46	103,33	*
Female_30-39_D1	1	35502	1	53163	0,03	39,04	0,98	217,46	*
Female_40-49_D1	0	48915	0	59406	0,00				
Female_50-59_D1	0	80677	5	67062	0,23	0,00	0,00	15,99	*
Female_60-69_D1	0	466347	1	59228	0,30	0,00	0,00	12,22	*
Female_70-79_D1	0	10661	1	47181	0,01	0,00	0,00	425,76	*
Female_80+_D1	0	14545	0	27419	0,00				
Female tot D1	2	695046	13	446411	0,63	***3,20***	***0,38***	***11,54***	*
Male_0-19_D1	0	1328	1	86036	0,00	0,00	0,00	6232,66	*
Male_20-29_D1	0	12748	1	47107	0,01	0,00	0,00	355,50	*
Male_30-39_D1	0	14552	0	47204	0,00				
Male_40-49_D1	0	18824	4	54297	0,05	0,00	0,00	69,37	*
Male_50-59_D1	0	30787	1	65000	0,02	0,00	0,00	203,11	*
Male_60-69_D1	1	513107	0	57935	0,00	#			
Male_70-79_D1	0	11619	1	43532	0,01	0,00	0,00	360,44	*
Male_80+_D1	0	7637	0	18417	0,00				
Male_total_D1	1	610602	8	419528	0,09	***10,80***	***0,27***	***60,17***	*
Total D1	3	1305648	21	865939	0,72	***4,18***	***0,86***	***12,21***	*
Female <60_D1	2	203493	11	312583	0,31	***6,35***	***0,76***	***22,93***	*
Male < 60_D1	0	78239	7	299644	0,08	***0,00***	***0,00***	***44,82***	*
Totaal <60_D1	2	281732	18	612227	0,40	***5,03***	***0,60***	***18,18***	*
Female_0-19_D2	0	3148	3	83117	0,00	0,00	0,0	846,69	*
Female_20-29_D2	0	32418	2	49835	0,05	0,00	0,0	73,95	*
Female_30-39_D2	0	32572	1	53163	0,02	0,00	0,0	157,02	*
Female_40-49_D2	0	45128	0	59406	0,00				
Female_50-59_D2	0	74869	5	67062	0,21	0,00	0,0	17,23	*
Female_60-69_D2	0	433279	1	59228	0,28	0,00	0,0	13,15	*
Female_70-79_D2	0	9751	1	47181	0,01	0,00	0,0	465,49	*
Female_80+_D2	0	12505	0	27419	0,00				
Female_total_D2	0	643670	13	446411	0,58	***0,00***	***0,00***	***6,36***	*
Male_0-19_D2	0	1205	1	86036	0,00	0,00	0,00	6868,86	*
Male_20-29_D2	0	11742	1	47107	0,01	0,00	0,00	385,95	*
Male_30-39_D2	0	13569	0	47204	0,00				
Male_40-49_D2	0	17600	4	54297	0,05	0,00	0,00	74,20	*
Male_50-59_D2	0	28784	1	65000	0,02	0,00	0,00	217,25	*
Male_60-69_D2	0	477217	0	57935	0,00				
Male_70-79_D2	0	10649	1	43532	0,01	0,00	0,00	393,27	*
Male_80+_D2	0	6507	0	18417	0,00				
Male_total_D2	0	567273	8	419528	0,09	***0,00***	***0,00***	***42,81***	*
Total D2	0	1210943	21	865939	0,67	***0,00***	***0,00***	***5,54***	*

CVST									
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN									
Female_0-19_D1	0	16783	3	83117	0,02	0,00	0,00	158,81	*
Female_20-29_D1	0	86405	2	49835	0,13	0,00	0,00	27,74	*
Female_30-39_D1	0	43185	1	53163	0,03	0,00	0,00	118,43	*
Female_40-49_D1	0	55045	0	59406	0,00				
Female_50-59_D1	0	118748	5	67062	0,34	0,00	0,00	10,87	*
Female_60-69_D1	0	5799	1	59228	0,00	0,00	0,00	982,57	*
Female_70-79_D1	0	1282	1	47181	0,00	0,00	0,00	3540,55	*
Female_80+_D1	0	438	0	27419	0,00				
Female tot D1	0	327685	13	446411	0,53	***0,00***	***0,00***	***6,94***	
Male_0-19_D1	0	26060	1	86036	0,01	0,00	0,00	317,61	*
Male_20-29_D1	0	145455	1	47107	0,12	0,00	0,00	31,16	*
Male_30-39_D1	0	60585	0	47204	0,00				
Male_40-49_D1	0	65513	4	54297	0,19	0,00	0,00	19,93	*
Male_50-59_D1	0	145152	1	65000	0,09	0,00	0,00	43,08	*
Male_60-69_D1	0	6388	0	57935	0,00				*
Male_70-79_D1	0	1729	1	43532	0,00	0,00	0,00	2422,17	*
Male_80+_D1	0	442	0	18417	0,00				
Male_total_D1	0	451324	8	419528	0,40	***0,00***	***0,00***	***9,17***	*
Total_D1	0	779009	21	865939	0,93	***0,00***	***0,00***	***3,95***	*
Female <60_D1	0	320166	11	312583	0,53	***0,00***	***0,00***	***7,00***	*
Male < 60_D1	0	442765	7	299644	0,40	***0,00***	***0,00***	***9,21***	*
Total <60_D1	0	762931	18	612227	0,93	***0,00***	***0,00***	***3,98***	*

CVST									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)*** *(# O > E=0)*	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN									
Female_0-19_D1	0	16783	3	83117	0,05	0,00	0,00	79,41	*
Female_20-29_D1	0	86405	2	49835	0,27	0,00	0,00	13,87	*
Female_30-39_D1	0	43185	1	53163	0,06	0,00	0,00	59,22	*
Female_40-49_D1	0	55045	0	59406	0,00				
Female_50-59_D1	0	118748	5	67062	0,68	0,00	0,00	5,43	*
Female_60-69_D1	0	5799	1	59228	0,01	0,00	0,00	491,29	*
Female_70-79_D1	0	1282	1	47181	0,00	0,00	0,00	1770,27	*
Female_80+_D1	0	438	0	27419	0,00				
Female tot D1	0	327685	13	446411	1,06	***0,00***	***0,00***	***3,47***	
Male_0-19_D1	0	26060	1	86036	0,02	0,00	0,00	158,81	*
Male_20-29_D1	0	145455	1	47107	0,24	0,00	0,00	15,58	*
Male_30-39_D1	0	60585	0	47204	0,00				
Male_40-49_D1	0	65513	4	54297	0,37	0,00	0,00	9,97	*
Male_50-59_D1	0	145152	1	65000	0,17	0,00	0,00	21,54	*
Male_60-69_D1	0	6388	0	57935	0,00				*
Male_70-79_D1	0	1729	1	43532	0,00	0,00	0,00	1211,09	*
Male_80+_D1	0	442	0	18417	0,00				
Male_total_D1	0	451324	8	419528	0,80	***0,00***	***0,00***	***4,59***	*
Total_D1	0	779009	21	865939	1,87	***0,00***	***0,00***	***1,98***	*
Female <60_D1	0	320166	11	312583	1,05	***0,00***	***0,00***	***3,50***	*
Male < 60_D1	0	442765	7	299644	0,80	***0,00***	***0,00***	***4,60***	*
Total <60_D1	0	762931	18	612227	1,86	***0,00***	***0,00***	***1,99***	*

CVST									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
PFIZER									
Female_0-19_D1	0	501841	3	83117	1,39	0,00	0,00	2,66	*
Female_20-29_D1	1	600233	2	49835	1,85	0,54	0,01	3,01	*
Female_30-39_D1	0	660918	1	53163	0,95	0,00	0,00	3,87	*
Female_40-49_D1	0	663068	0	59406	0,00				
Female_50-59_D1	0	778345	5	67062	4,45	0,00	0,00	0,83	*
Female_60-69_D1	0	504442	1	59228	0,65	0,00	0,00	5,65	*
Female_70-79_D1	0	787778	1	47181	1,28	0,00	0,00	2,88	*
Female_80+_D1	0	479768	0	27419	0,00				
Female tot D1	1	4976393	13	446411	10,58	***0,09***	***0,00***	***0,53***	*
Male_0-19_D1	0	518024	1	86036	0,46	0,00	0,00	7,99	*
Male_20-29_D1	0	596893	1	47107	0,97	0,00	0,00	3,80	*
Male_30-39_D1	0	683277	0	47204	0,00				
Male_40-49_D1	0	666747	4	54297	3,77	0,00	0,00	0,98	*
Male_50-59_D1	1	801888	1	65000	0,95	1,06	0,03	5,89	*
Male_60-69_D1	0	450484	0	57935	0,00				
Male_70-79_D1	0	737681	1	43532	1,30	0,00	0,00	2,84	*
Male_80+_D1	0	333119	0	18417	0,00				
Male_total_D1	1	4788113	8	419528	7,45	***0,13***	***0,00***	***0,75***	*
Total D1	2	9764506	21	865939	18,03	***0,11***	***0,01***	***0,40***	*
Female <60_D1	1	3204405	11	312583	8,64	***0,12***	***0,00***	***0,64***	*
Male < 60_D1	1	3266829	7	299644	6,15	***0,16***	***0,00***	***0,91***	*
Totaal <60_D1	2	6471234	18	612227	14,79	***0,14***	***0,02***	***0,49***	*
Female_0-19_D2	0	422191	3	83117	1,17	0,00	0,00	3,16	*
Female_20-29_D2	1	517303	2	49835	1,59	0,63	0,02	3,50	*
Female_30-39_D2	0	588725	1	53163	0,85	0,00	0,00	4,34	*
Female_40-49_D2	0	603966	0	59406	0,00				
Female_50-59_D2	0	726853	5	67062	4,16	0,00	0,00	0,89	*
Female_60-69_D2	0	495644	1	59228	0,64	0,00	0,00	5,75	*
Female_70-79_D2	1	769492	1	47181	1,25	0,80	0,00	2,95	*
Female_80+_D2	1	468718	0	27419	0,00	#			
Female_total_D2	3	4592892	13	446411	9,66	***0,31***	***0,06***	***0,91***	*
Male_0-19_D2	0	437062	1	86036	0,39	0,00	0,00	9,47	*
Male_20-29_D2	1	501576	1	47107	0,82	1,22	0,03	6,82	*
Male_30-39_D2	1	611401	0	47204	0,00	#			
Male_40-49_D2	0	607992	4	54297	3,44	0,00	0,00	1,07	*
Male_50-59_D2	0	743727	1	65000	0,88	0,00	0,00	4,20	*
Male_60-69_D2	0	441441	0	57935	0,00				
Male_70-79_D2	2	720283	1	43532	1,27	1,58	0,19	5,69	*
Male_80+_D2	0	326394	0	18417	0,00				
Male_total_D2	4	4389876	8	419528	6,79	***0,59***	***0,16***	***1,51***	*
Total D2	7	8982768	21	865939	16,45	***0,43***	***0,17***	***0,88***	*
Female <60_D1	1	2859038	11	312583	7,77	***0,13***	***0,00***	***0,72***	*
Male < 60_D1	2	2901758	7	299644	5,52	***0,36***	***0,04***	***1,31***	*
Totaal <60_D1	3	5760796	18	612227	13,29	***0,23***	***0,05***	***0,66***	*

CVST									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
MODERNA									
Female_0-19_D1	0	12816	3	83117	0,04	0,00	0,00	103,99	*
Female_20-29_D1	0	81652	2	49835	0,25	0,00	0,00	14,68	*
Female_30-39_D1	0	87177	1	53163	0,13	0,00	0,00	29,33	*
Female_40-49_D1	0	129966	0	59406	0,00				
Female_50-59_D1	0	146072	5	67062	0,84	0,00	0,00	4,42	*
Female_60-69_D1	0	26439	1	59228	0,03	0,00	0,00	107,76	*
Female_70-79_D1	0	13522	1	47181	0,02	0,00	0,00	167,84	*
Female_80+_D1	0	14187	0	27419	0,00				
Female tot D1	0	511831	13	446411	1,30	***0,00***	***0,00***	***2,83***	*
Male_0-19_D1	0	12633	1	86036	0,01	0,00	0,00	327,59	*
Male_20-29_D1	0	74564	1	47107	0,12	0,00	0,00	30,39	*
Male_30-39_D1	0	79918	0	47204	0,00				
Male_40-49_D1	0	127191	4	54297	0,72	0,00	0,00	5,13	*
Male_50-59_D1	0	157958	1	65000	0,19	0,00	0,00	19,79	*
Male_60-69_D1	0	29694	0	57935	0,00				
Male_70-79_D1	0	15801	1	43532	0,03	0,00	0,00	132,52	*
Male_80+_D1	0	5330	0	18417	0,00				
Male_total_D1	0	503089	8	419528	1,07	***0,00***	***0,00***	***3,46***	*
Total D1	0	1014920	21	865939	2,37	***0,00***	***0,00***	***1,56***	*
Female <60 D1	0	457683	11	312583	1,25	***0,00***	***0,00***	***2,96***	*
Male < 60 D1	0	452264	7	299644	1,04	***0,00***	***0,00***	***3,56***	*
Totaal <60 D1	0	909947	18	612227	2,29	***0,00***	***0,00***	***1,61***	*
Female_0-19_D2	0	11005	3	83117	0,03	0,00	0,00	121,10	*
Female_20-29_D2	0	73517	2	49835	0,23	0,00	0,00	16,30	*
Female_30-39_D2	0	80225	1	53163	0,12	0,00	0,00	31,88	*
Female_40-49_D2	0	120520	0	59406	0,00				
Female_50-59_D2	0	136781	5	67062	0,78	0,00	0,00	4,72	*
Female_60-69_D2	0	24672	1	59228	0,03	0,00	0,00	115,47	*
Female_70-79_D2	0	12681	1	47181	0,02	0,00	0,00	178,97	*
Female_80+_D2	0	12682	0	27419	0,00				
Female_total_D2	0	472083	13	446411	1,21	***0,00***	***0,00***	***3,06***	*
Male_0-19_D2	0	10636	1	86036	0,01	0,00	0,00	389,10	*
Male_20-29_D2	0	65513	1	47107	0,11	0,00	0,00	34,59	*
Male_30-39_D2	0	73704	0	47204	0,00				
Male_40-49_D2	0	118921	4	54297	0,67	0,00	0,00	5,49	*
Male_50-59_D2	1	148142	1	65000	0,17	5,72	0,14	31,86	*
Male_60-69_D2	0	27849	0	57935	0,00				
Male_70-79_D2	0	14996	1	43532	0,03	0,00	0,00	139,64	*
Male_80+_D2	0	4786	0	18417	0,00				
Male_total_D2	1	464547	8	419528	0,99	***1,01***	***0,03***	***5,63***	*
Total D2	1	936630	21	865939	2,20	***0,46***	***0,01***	***2,54***	*

CVST									
Risk period / TTO 28 days	**N reports Observed**	**N persons vaccine exposed**	**N Events 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp *(SMR)* *(# O > E=0)***	**95% CI SMR *(* O<10 with poisson table)***		
ASTRAZENECA									
Female_0-19_D1	0	3382	3	83117	0,01	0,00	0,00	394,05	*
Female_20-29_D1	1	35017	2	49835	0,11	9,28	0,23	51,67	*
Female_30-39_D1	1	35502	1	53163	0,05	19,52	0,49	108,73	*
Female_40-49_D1	0	48915	0	59406	0,00				
Female_50-59_D1	0	80677	5	67062	0,46	0,00	0,00	8,00	*
Female_60-69_D1	0	466347	1	59228	0,60	0,00	0,00	6,11	*
Female_70-79_D1	0	10661	1	47181	0,02	0,00	0,00	212,88	*
Female_80+_D1	0	14545	0	27419	0,00				
Female tot D1	2	695046	13	446411	1,25	***1,60***	***0,19***	***5,77***	*
Male_0-19_D1	0	1328	1	86036	0,00	0,00	0,00	3116,33	*
Male_20-29_D1	0	12748	1	47107	0,02	0,00	0,00	177,75	*
Male_30-39_D1	0	14552	0	47204	0,00				
Male_40-49_D1	0	18824	4	54297	0,11	0,00	0,00	34,69	*
Male_50-59_D1	0	30787	1	65000	0,04	0,00	0,00	101,56	*
Male_60-69_D1	1	513107	0	57935	0,00	#			
Male_70-79_D1	0	11619	1	43532	0,02	0,00	0,00	180,22	*
Male_80+_D1	0	7637	0	18417	0,00				
Male_total_D1	1	610602	8	419528	0,19	***5,40***	***0,14***	***30,09***	*
Total D1	3	1305648	21	865939	1,44	***2,09***	***0,43***	***6,11***	*
Female <60_D1	2	203493	11	312583	0,63	***3,18***	***0,38***	***11,46***	*
Male < 60_D1	0	78239	7	299644	0,16	***0,00***	***0,00***	***22,41***	*
Totaal <60_D1	2	281732	18	612227	0,79	***2,52***	***0,30***	***9,09***	*
Female_0-19_D2	0	3148	3	83117	0,01	0,00	0,0	423,35	*
Female_20-29_D2	0	32418	2	49835	0,10	0,00	0,0	36,97	*
Female_30-39_D2	0	32572	1	53163	0,05	0,00	0,0	78,51	*
Female_40-49_D2	0	45128	0	59406	0,00				
Female_50-59_D2	0	74869	5	67062	0,43	0,00	0,0	8,62	*
Female_60-69_D2	0	433279	1	59228	0,56	0,00	0,0	6,58	*
Female_70-79_D2	0	9751	1	47181	0,02	0,00	0,0	232,74	*
Female_80+_D2	0	12505	0	27419	0,00				
Female_total_D2	0	643670	13	446411	1,16	***0,00***	***0,00***	***3,18***	*
Male_0-19_D2	0	1205	1	86036	0,00	0,00	0,00	3434,43	*
Male_20-29_D2	0	11742	1	47107	0,02	0,00	0,00	192,98	*
Male_30-39_D2	0	13569	0	47204	0,00				
Male_40-49_D2	0	17600	4	54297	0,10	0,00	0,00	37,10	*
Male_50-59_D2	0	28784	1	65000	0,03	0,00	0,00	108,62	*
Male_60-69_D2	0	477217	0	57935	0,00				
Male_70-79_D2	0	10649	1	43532	0,02	0,00	0,00	196,64	*
Male_80+_D2	0	6507	0	18417	0,00				
Male_total_D2	0	567273	8	419528	0,17	***0,00***	***0,00***	***21,40***	*
Total D2	0	1210943	21	865939	1,33	***0,00***	***0,00***	***2,77***	*