Overview of pericarditis and myocarditis associated COVID-19 vaccines (UPDATE 2022)

Introduction

Pericarditis and myocarditis have recently been recognized as adverse drug reactions (ADRs) of the mRNA vaccines against COVID-19, manufactured by Pfizer/BioNTech (Comirnaty) and Moderna (Spikevax). The updated Summaries of Product Characteristics (SmPC) of both vaccines mention that very rare cases of myocarditis and pericarditis have been observed following vaccination [1, 2]. For the vector vaccines of AstraZeneca (Vaxzevria) and Janssen, pericarditis and myocarditis are not labelled as adverse events [3, 4]. In our previous overview, reports of pericarditis and myocarditis have been described with all COVID-19 vaccines [5].

Pericarditis is an inflammatory disorder of the membrane lining that surrounds the heart. It is a common pericardial disease and a relatively common cause of chest pain [6]. The incidence of pericarditis is not exactly known, since the condition is often self-limiting and does not always require diagnostic testing, for it does not influence management of the disease [7,8]. It can be caused by viral infections and non-infectious conditions, such as systemic inflammatory diseases and following myocardial infarction.
Myocarditis is an inflammatory condition of the heart muscle with damage to cardiac cells. Myocarditis can be caused by various infections, auto-immune disorders and exogenous agents. Genetic and environmental factor predispose susceptible people [9].
The incidence of myocarditis is about 10-20 per 100,000 person-years. Young males are at increased risk [6]. In The Netherlands in 2019 pericarditis and myocarditis were registered in various healthcare data systems 19.4 and 2.9 per 100,000 person-years respectively [10]. In figure 2 these Dutch background rates are visualised in more detail [10].

This current update describes the reported cases of pericarditis and myocarditis in The Netherlands following vaccination against Sars-CoV-2 with all available vaccines, including booster vaccination with mRNA vaccines.

Reports

Until January 24th 2022, The Netherlands Pharmacovigilance Centre Lareb received 373 unique individual case safety reports of pericarditis (274 *(73%)*) and myocarditis (99 *(27%)*) following vaccination with COVID-19 vaccines. Characteristics of the reports are summarised in table 1 and figure 1.

a) MYOCARDITIS	**Total**		**Pfizer (Cominaty)**		**Moderna (Spikevax)**		**AstraZeneca (Vaxzevria)**		**Janssen**		**Not specified**
Reports (N, %)	99	*(27%)*	65	(66%)	19	(19%)	6	(6%)	8	(8%)	1
Reporter											
- HCP*	52	(53%)	32	(49%)	10	(53%)	4	(67%)	5	(63%)	1
- Consumer	47	(47%)	33	(51%)	9	(47%)	2	(33%)	3	(37%)	0
Seriousness**											
- Serious	79	(80%)	51	(78%)	14	(74%)	6	(100%)	7	(88%)	1
- - Hospitalisation	69	(70%)	46	(71%)	13	(68%)	5	(83%)	5	(63%)	0
Sex											
- male	73	(74%)	54	(83%)	10	(53%)	2	(33%)	6	(75%)	1
- female	26	(26%)	11	(17%)	9	(47%)	4	(67%)	2	(25%)	
Age (mean, range)											
- male	34.7	(16-90)	34.4	(16-80)	34.7	(24-66)	25.5	(24-27)	31.2	(19-54)	90
- female	45.1	(19-72)	41.5	(19-72)	46.6	(20-67)	55.3	(42-62)	37.5	(24-51)	n.a.
Dose											
- first	46	(46%)	24	(37%)	9	(47%)	4	(67%)	8	(100%)	1
- second	47	(47%)	37	(57%)	8	(42%)	2	(33%)	0		0
- third	6	(6%)	4	(6%)	2	(10%)	0		0		0
Time to onset, mean+range (day)											
- first dose	21.8	(0-167)	19.5	(0-167)	5.9	(0-19)	16.0	(3-50)	48.8	(0-136)	10.0
- second dose	19.5	(0-116)	19.9	(0-116)	18.4	(1-46)	15.0	(15)	n.a.		n.a.

- third dose	6.2	(0-20)	5.8	(0-20)	7.0	(1-13)	n.a.		n.a.		n.a.
Time to onset, median+IQR (day)											
- first dose	5	(1-19)	4	(1-9)	2	(0.5-11.5)	5.5	(3.5-28.5)	33.5	(2-91.5)	n.a.
- second dose	5	(3-22)	5	(3-22)	10	(2-38)	15	(15)	n.a.		n.a.
- third dose	1.5	(1-13)	1.5	(0.5-11)	7	(1-13)	n.a.		n.a.		n.a.
Outcome* **											
- Recovered/ -ing	65	(66%)	46	(71%)	14	(74%)	1	(17%)	4	(50%)	0
- Not rec. / unknown	31	(31%)	18	(28%)	5	(26%)	5	(83%)	2	(25%)	1
- Fatal	3	(3%)	1	(1.5%)	0		0		2	(25%)	0
Medical history											
- COVID 19** **	22	(22%)	14	(22%)	3	(16%)	4	(67%)	1	(13%)	0
- myocarditis	4	(4%)	2	(3%)	2	(11%)	0		0		0
Previous vaccination^											
- 2nd dose	1	(1%)	0		1	(5%)	0		0		0
- symptoms	3		2								

b) *PERICARDITIS*	**Total**		**Pfizer (Cominaty)**		**Moderna (Spikevax)**		**AstraZeneca (Vaxzevria)**		**Janssen**		**Not specified**
Reports (N, %)	274	*(73%)*	193	(70%)	45	(16%)	16	(6%)	18	(7%)	2
Reporter											
- HCP*	53	(19%)	40	(21%)	6	(13%)	4	(25%)	2	(11%)	1
- Consumer	221	(81%)	153	(79%)	39	(87%)	12	(75%)	16	(89%)	1
Seriousness**											
- Serious	111	(41%)	77	(40%)	17	(38%)	11	(69%)	5	(28%)	1
- - Hospitalisation	84	(31%)	58	(30%)	13	(29%)	9	(56%)	3	(17%)	1
Sex											
- male	176	(64%)	119	(62%)	34	(76%)	10	(63%)	12	(67%)	1
- female	98	(36%)	74	(38%)	11	(24%)	6	(37%)	6	(33%)	1
Age (mean, range)											
- male	45.2	(14-86)	44.8	(14-86)	48.1	(22-77)	57.7	(25-68)	29.8	(19-53)	41
- female	46.6	(16-81)	44.5	(16-81)	51.5	(29-68)	61.0	(56-66)	43.7	(21-59)	77
Dose											
- first	112	(41%)	73	(38%)	12	(27%)	8	(50%)	18	(100%)	1
- second	126	(46%)	98	(51%)	20	(44%)	8	(50%)	0		0
- third	36	(13%)	22	(11%)	13	(29%)	0	0	0		1
Time to onset, mean+range (day)											
- first dose	21.3	(0-180)	14.6	(0-159)	14.2	(0-42)	29.4	(2-60)	50.2	(1-180)	1.0
- second dose	26.2	(0-152)	26.2	(0-152)	28.2	(0-122)	21.5	(4-56)	n.a.		n.a.
- third dose	5.4	(0-23)	4.3	(0-16)	7.3	(0-23)	n.a.		n.a.		4.0
Time to onset, median+IQR (day)											
- first dose	9	(3-22.5)	7	(2-17)	4	(9.5-19.5)	29	(12.5-45)	5	(25-80)	n.a.
- second dose	14	(4-39)	3	(14-35)	2.5	(11.5-44.5)	13.5	(5.5-37)	n.a.		n.a.
- third dose	2	(0.8-8)	2	(0.5-7)	2	(0.5-15.5)	n.a.		n.a.		n.a.
Outcome* **											
- Recovered/ -ing	191	(70%)	126	(65%)	37	(82%)	13	(81%)	14	(78%)	1
- Not rec. / unknown	80	(29%)	65	(34%)	8	(18%)	2	(13%)	4	(22%)	1
- Fatal	3	(1%)	2	(1%)	0		1	(6%)	0		0
Medical history											
- COVID 19** **	42	(15%)	32	(17%)	7	(16%)	0		3	(17%)	0
- pericarditis	23	(8%)	15	(8%)	7	(16%)	1	(6%)	0		0
Previous vaccination^											
- 2nd or 3rd dose	9	(3%)	7	(4%)	1	(2%)	1	(6%)	0		0
- 1st + other vaccine	1	(0.4%)	1	(0.5%)							
- symptoms	6	(2%)	6	(3%)	0		0		0		0

Table 1a and b: Report characteristics of myocarditis (a) and pericarditis (b) associated with COVID-19 vaccines in The Netherlands. These are based on MedDRA terminology including the Preferred Terms (PT) Myocarditis (including LLTs perimyocarditis / myopericarditis), Pericarditis, Viral myocarditis, Viral pericarditis, Eosinophilic myocarditis. * HCP= healthcare professional; ** CIOMS criteria seriousness are hospitalization, life-threatening situation, death, disabling, congenital anomaly; *** At time of reporting, the outcome is not always

reported or the patient had not recovered at that moment; **** COVID 19 in medical history any time before suspect vaccination; ^ patients who had pericarditis or myocarditis following the second or third dose and also had diagnosed pericarditis or myocarditis with a previous dose (or other vaccine) or only had typical *symptoms* (chest pain, palpitations) with a previous dose without a clear diagnose.

Pericarditis is reported 2.7 times more often than myocarditis following COVID vaccination, whereas the overall the frequency of pericarditis in general is 6.7 times greater than myocarditis.
Half of the reports of myocarditis is reported by healthcare professionals and 81% of the reports of pericarditis is reported by consumers. Myocarditis is a more serious condition compared to pericarditis, which might explain the relatively high reporting frequency of this condition by healthcare professionals. The CIOMS criteria for seriousness were met in 80% of the cases of myocarditis and in 41% of the cases of pericarditis. Hospitalization was the most reported reason for seriousness, in 70% and 31% of the cases of myocarditis and pericarditis respectively. Other CIOMS criteria are 'life threatening', 'other medically important condition' and 'death'; which were reported 6, and 3 times respectively for myocarditis and 6, 18 and 3 times for pericarditis.

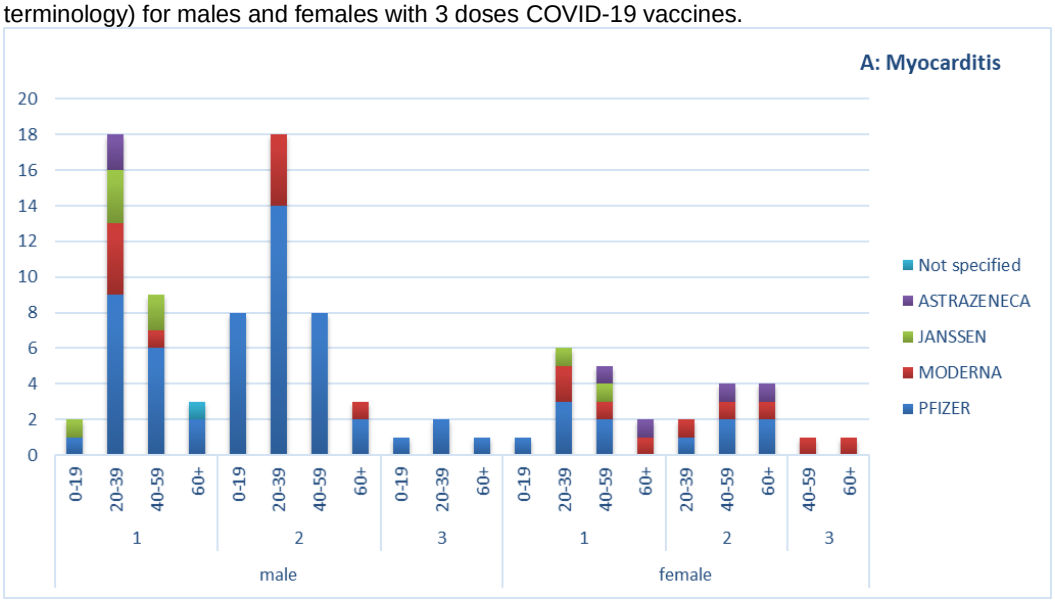
The majority of the cases was reported following an mRNA vaccination, with 86% for pericarditis and 85% for myocarditis respectively, and more following the second dose. Most reports concern young adult males aged < 40 years (see figure 1), for both myocarditis and pericarditis, in 74% and 64% of the cases respectively. The average age for myocarditis is 10 years lower for males (34.7 years) than females (45.1 years), but equal in males and females for pericarditis (45.2-46.6 years). With the AstraZeneca vaccine and myocarditis, the difference in average age for men and women is larger (20 years), and with pericarditis the mean age is higher for both men and women. With Janssen, men who developed pericarditis were younger than women, on average.
The mean times to onset for the first and second dose for both myocarditis and pericarditis are about three weeks, with a wide range. Median times-to-onset show for myocarditis a latency of 5 days and for pericarditis 9-14 days. After the third dose, only a limited time has passed, which explains reports having relatively short times to onset. The spread of all latencies per dose is visualized in appendix A.

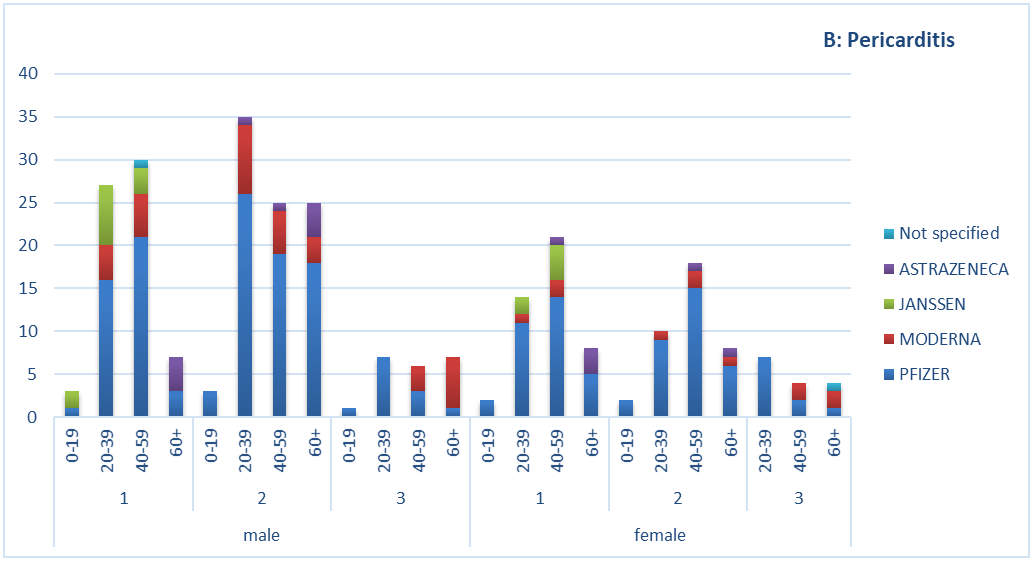
At time of reporting or after having received follow up information, in about one third of the reports the final outcome is unknown. The majority of the patient is recovering. In six reports, a fatal outcome of myocarditis (3) and pericarditis (3) was reported. It concerns four men and two women, aged between 39-74 years; three following Pfizer (one 1st dose, two 2nd dose), two following Janssen (1st dose) and one following the second dose of AstraZeneca. Times to onset varied from 1 to 91 days following vaccination. Other factors that may have contributed to the fatal events were other preexistent cardiac diseases (3) or a viral infection (2).

In 22% of all reports of myocarditis, the patient had had COVID-19 infection at any time before the start of the event of myocarditis following vaccination; for pericarditis this was 15%. Stratified to dose, 13 patients out of 46 (28%) with myocarditis following a first dose and 9 out of 53 (17%) following a second or third dose had had a COVID-19 infection. For pericarditis, 24 patients out of 112 (21%) with pericarditis following a first dose had had a COVID-19 infection and 18 out of 162 (11%) following a second/third dose.

In 4% of the cases of myocarditis, the patient had had myocarditis before; for pericarditis this was 8%. In a minority of the cases myocarditis or pericarditis recurred following the next dose (10 people in total (2.7%)) and few patients had similar symptoms without a clear diagnose following a previous dose (9 people in total (2.4%)). One patient also had had recurrent pericarditis following MMR vaccination and influenza vaccination.

Figure 1. Age distribution of all myocarditis (a) and pericarditis (b) reports (according to MedDRA coding terminology) for males and females with 3 doses COVID-19 vaccines.

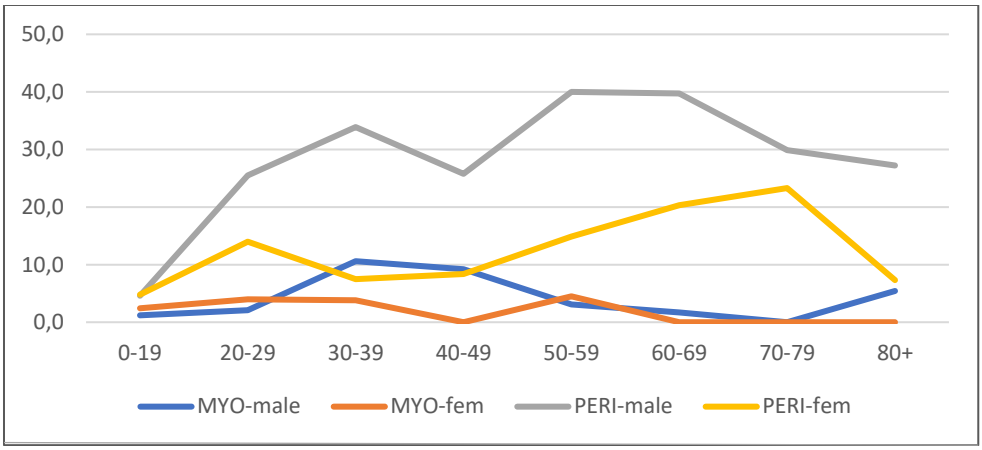




Comparison with background incidence

For calculating observed-over-expected ratios, the SMR (standardized morbidity rate) was used, which uses reported cases as observed (O) and background incidence rates applied to a certain vaccinated population as expected cases (E).
Background incidence rates were determined by PHARMO, based on hospital (ICD10) and general practitioners (ICPC) registration data from 2019. In figure 2 incidence rates of pericarditis and myocarditis from 2019 are shown.

Figure 2: Background incidence rates of myocarditis and pericarditis in The Netherlands, in 2019. Data are based on PHARMO registration data from hospitals and general practitioners in 2019, stratified by age (decade) and sex (male/female) and counted per 100.000 person-years [10].

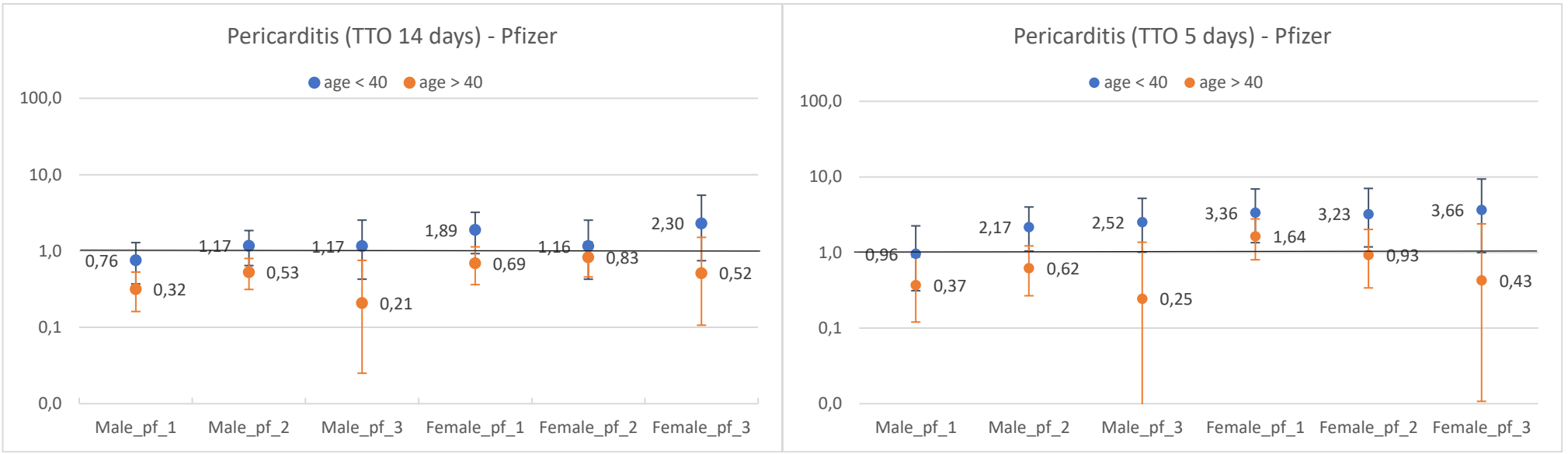


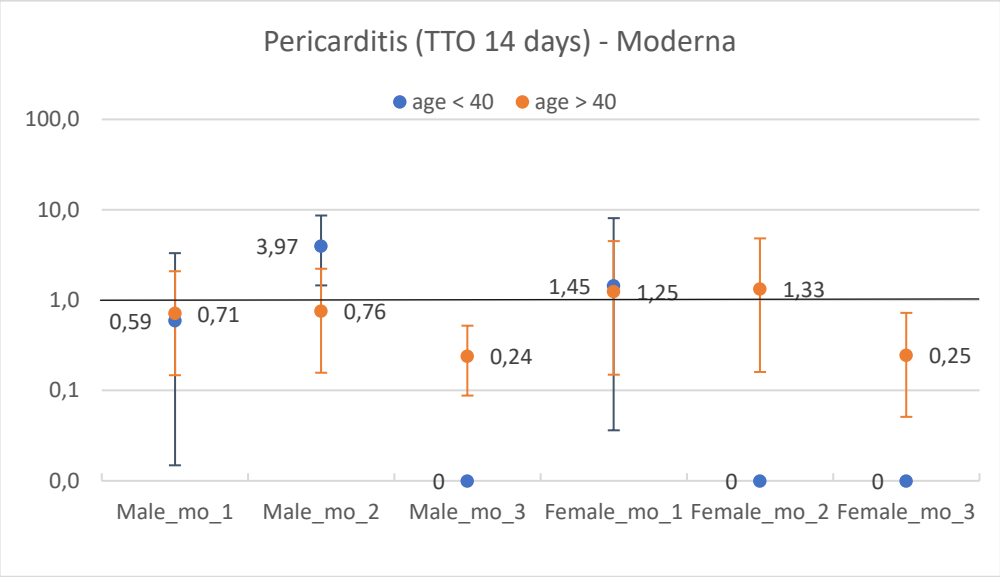
Stratified vaccine exposure data until 10 January 2022 (for risk period of 14 days) and 19 January 2022 (for risk period of 5 days) were obtained from CIMS database of RIVM for men and women per vaccine, dose, by age. By these dates, the booster campaign was in full swing. In the reports, vaccination dates were taken into account accordingly, as well as times to onset of 5 and 14 days respectively. The following formulas were used in calculating SMRs:

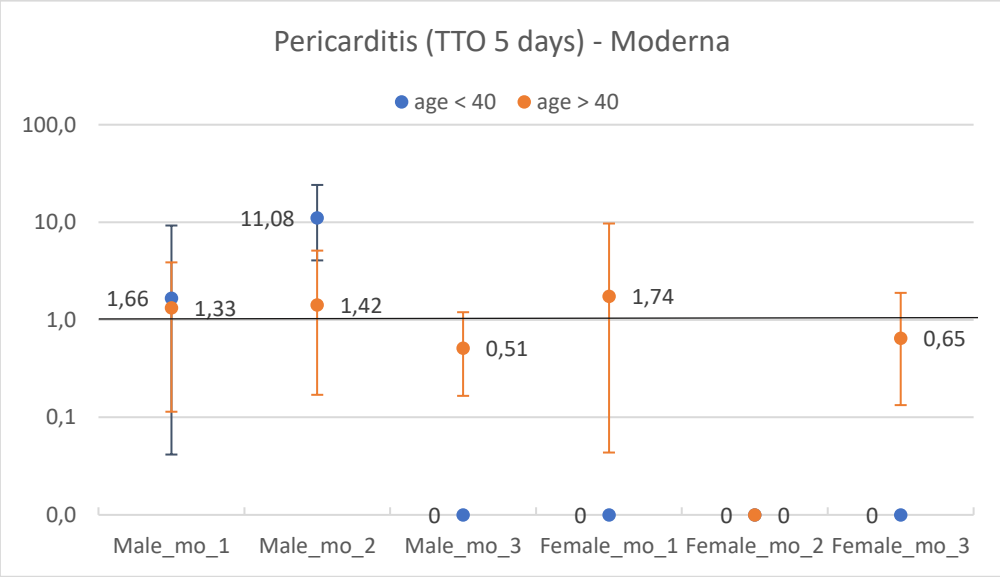
- E = $(N_{\text{events in PHARMO}} / N_{\text{person years in PHARMO}})$*(risk period (days)/365)*$N_{\text{vaccine exposure}}$
- SMR = O / E
- 95% confidence intervals: $\sqrt{((\sum(O -/+1)^2)} / \sum E$; using Poisson distribution tables for low numbers of O (<10) [11]

The results are summarized in figures 3 (mRNA vaccines) and figure 4 (vector vaccines).

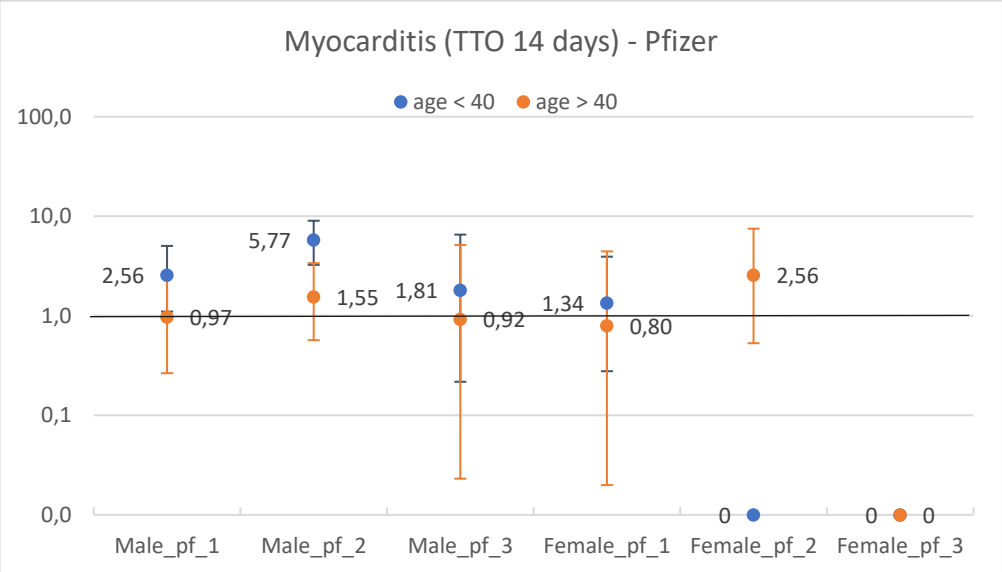
Figure 3: Observed-over-Expected ratios (OE) of myocarditis and pericarditis reports per COVID-19 mRNA vaccine, stratified per dose for men and women and age < 40 and > 40 years. The scale is semi-logarithmic. If there are no cases in a subgroup, OE = 0. If OE ratio > 1, the number of reported cases exceeds the expected number based on background incidence. The error bars show the range of the lower and upper limits of the 95%confidence intervals More details are available in appendix C.

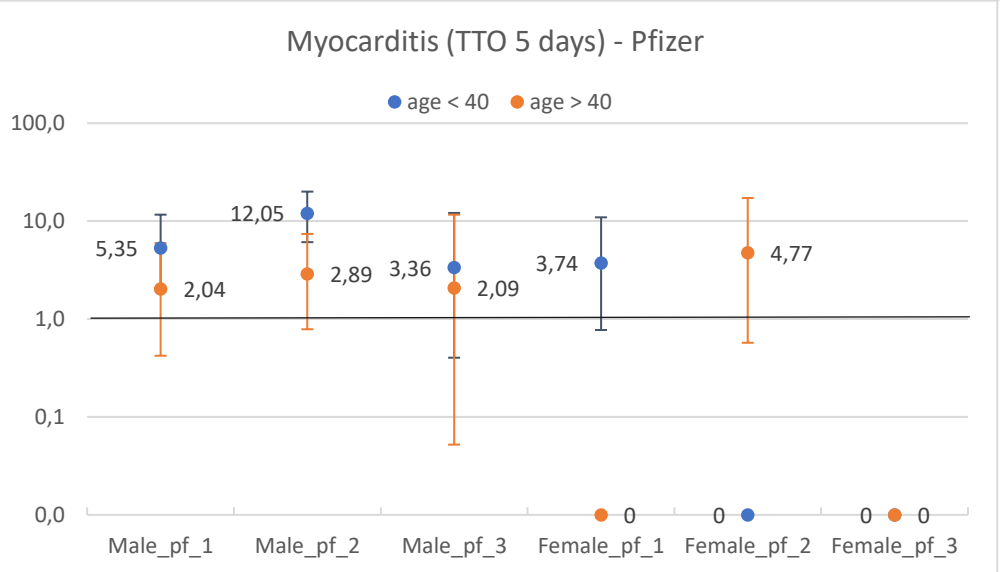


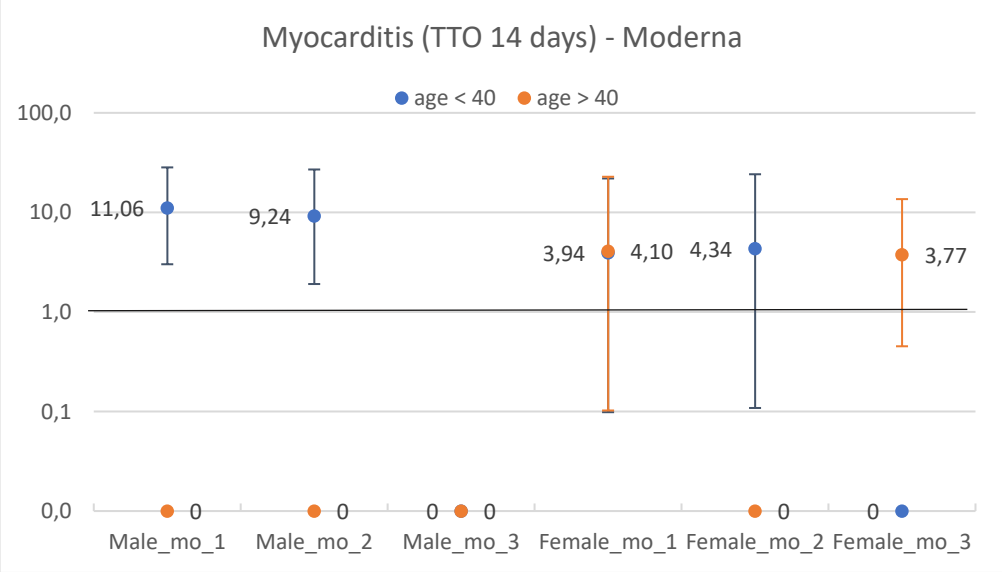

Pericarditis (TTO 14 days) - Moderna
age < 40
age > 40
100,0
10,0
1,0
0,1
0,0
0,59
0,71
3,97
0,76
0
0,24
1,45
1,25
0
1,33
0
0,25
Male_mo_1
Male_mo_2
Male_mo_3
Female_mo_1
Female_mo_2
Female_mo_3


Pericarditis (TTO 5 days) - Moderna
age < 40
age > 40
100,0
10,0
1,0
0,1
0,0
1,66
1,33
11,08
1,42
0
0,51
0
1,74
0
0
0
0,65
Male_mo_1
Male_mo_2
Male_mo_3
Female_mo_1
Female_mo_2
Female_mo_3

bijwerkingen centrumlareb







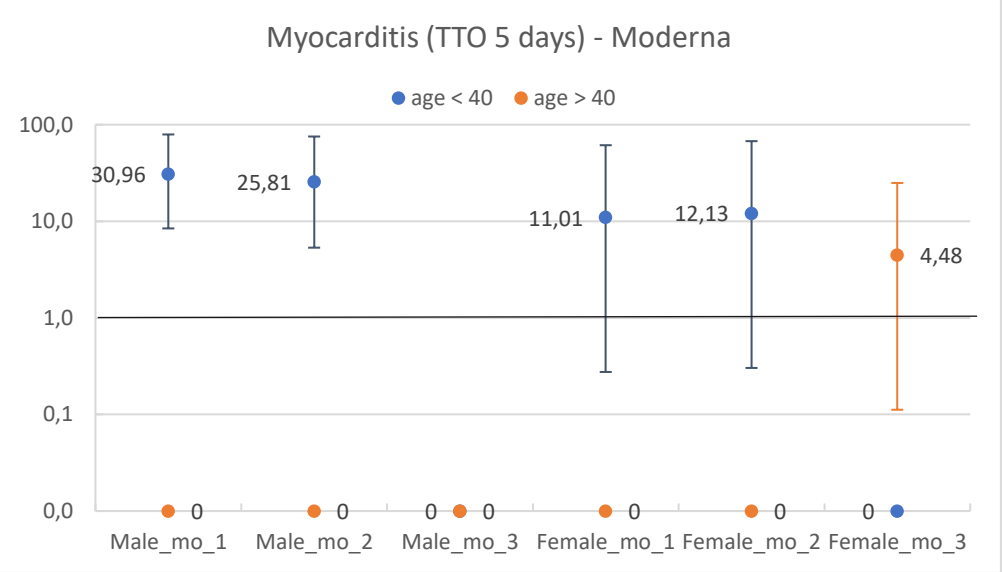
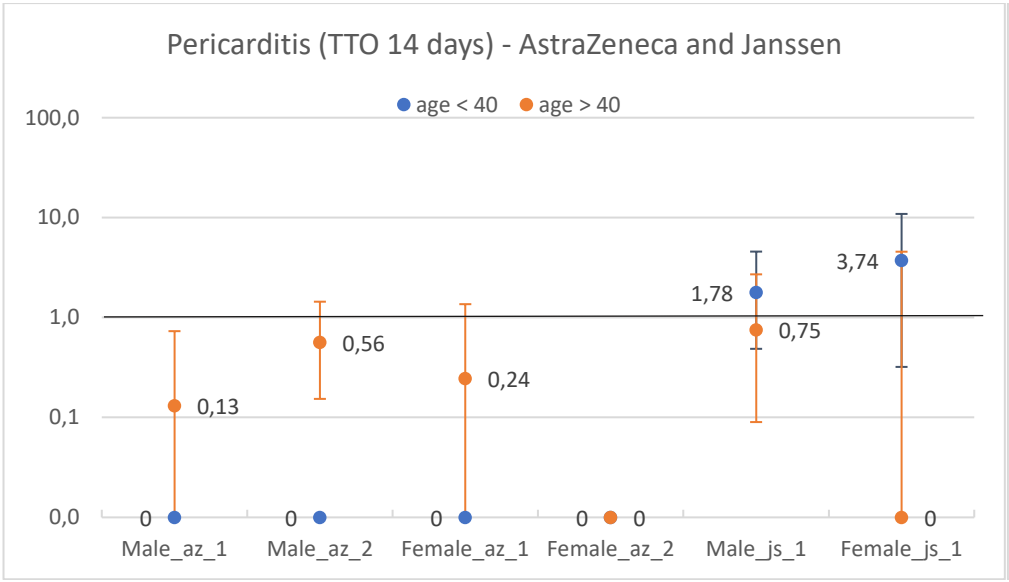
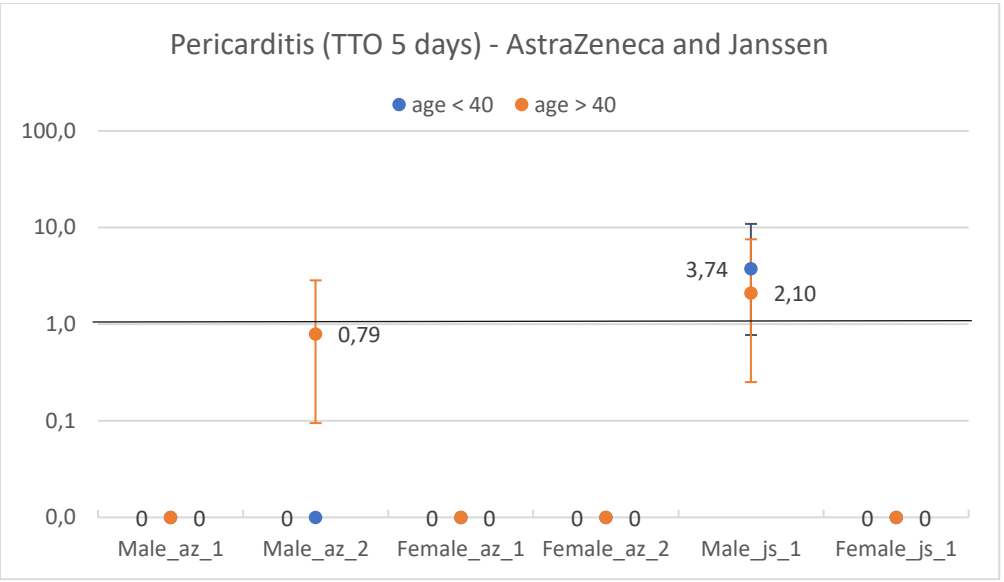
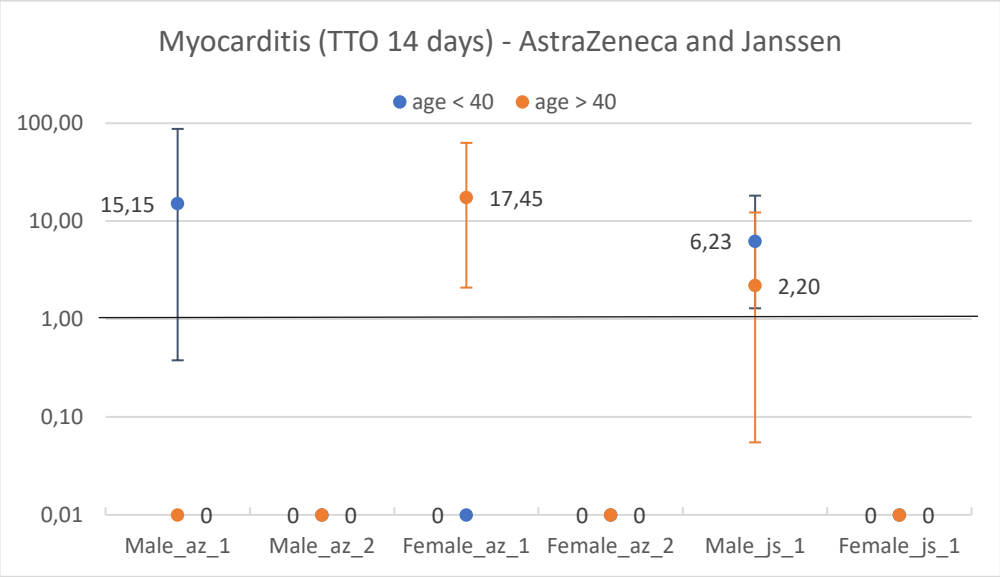
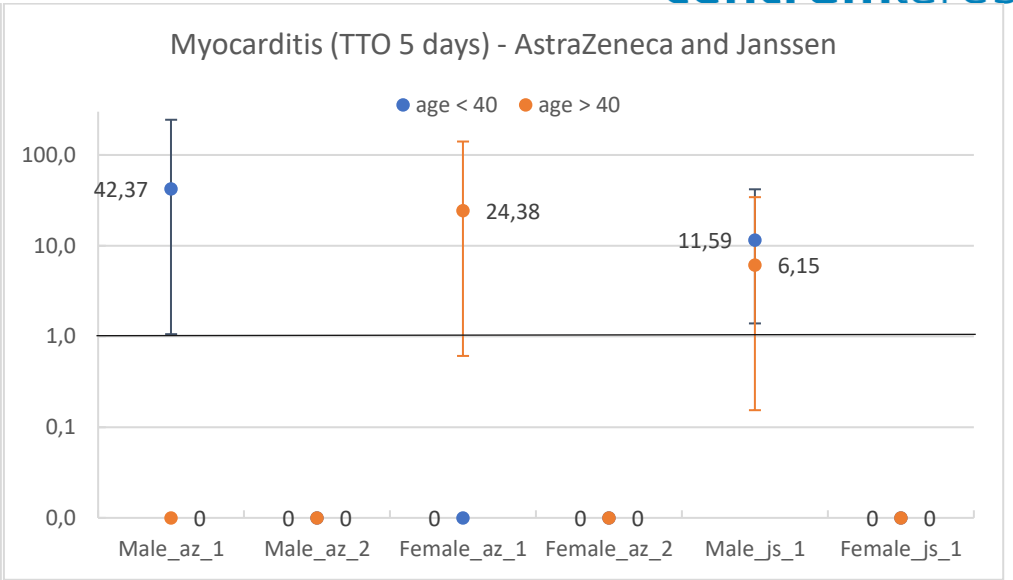


Figure 4: Observed-over-Expected ratios (OE) of myocarditis and pericarditis reports for COVID-19 vector vaccines, stratified per dose for men and women and age < 40 and > 40 years. The scale is semi-logarithmic. If there are no cases in a subgroup, OE = 0. If OE ratio > 1, the number of reported cases exceeds the expected number based on background incidence. The error bars show the range of the lower and upper limits of the 95%confidence intervals More details are available in appendix C.






Myocarditis (TTO 14 days) - AstraZeneca and Janssen
age < 40
age > 40
100,00
10,00
1,00
0,10
0,01
15,15
17,45
6,23
2,20
0
0 0
0
0 0
0 0
Male_az_1
Male_az_2
Female_az_1
Female_az_2
Male_js_1
Female_js_1


Myocarditis (TTO 5 days) - AstraZeneca and Janssen
age < 40
age > 40
100,0
10,0
1,0
0,1
0,0
42,37
24,38
11,59
6,15
0
0 0
0
0 0
0 0
Male_az_1
Male_az_2
Female_az_1
Female_az_2
Male_js_1
Female_js_1

As is shown in figure 3, the number of reports of ***myocarditis*** with ***mRNA vaccines*** is higher than expected for men < 40 with all doses of Pfizer and the 1st and 2nd dose of Moderna; for Pfizer this is also the case for men aged > 40 (in both 5 and 14 days). For women younger than 40 years, myocarditis has been reported more often than expected with the 1st dose of Pfizer and 1st and 2nd dose of Moderna. For women > 40 the SMRs are > 1 with the second dose of Pfizer and the first and third dose of Moderna; with the first Moderna dose only in a risk period of 14 days.

For ***pericarditis*** with ***mRNA vaccines***, the number of reports is higher than expected for men and women aged < 40 years who received the Pfizer vaccine and any dose, if the risk period is as short as 5 days. And for women > 40 years who received the first dose of Pfizer, the SMR exceeded 1; with the second dose SMR reached 1. For Moderna pericarditis was reported more often than expected within 5 days after the first and second dose in men (< 40 and > 40 years) and in women > 40 years with the first dose. In a 14-day risk period, the number of reports was also more than expected in women > 40 years receiving the second dose.

The numbers of reports of ***myocarditis and pericarditis*** with ***vector vaccines*** are lower than those of the mRNA vaccines (table 1). Comparison of the reported numbers with background incidence rates also show smaller absolute numbers in the selected subgroups. But even small numbers can result in SMR > 1, when the expected number in a certain vaccinated group is also small (figure 4). This is the case for myocarditis in men < 40 years and women > 40 years with the 1st doses of AstraZeneca and Janssen. For pericarditis, the number of reports was higher than expected for men < 40 and women < 40 years with Janssen, in a 14-day risk period; in a 5-day risk period only for men (both age groups) the SMRs exceeded 1.

Other sources of information

Literature

In the past year, a lot of articles on myocarditis and pericarditis following the use of COVID-19 mRNA vaccines have been published. Recently, reviews and systematic analyses have been published as well [12-16]. Generally, most cases of myocarditis (and pericarditis) have been observed in young males following the second dose of an mRNA vaccine, usually within the first 5 days following vaccination and the course is often mild. If myocarditis occurred after the first dose, a prior COVID-19 infection was associated [14]. The pooled incidence from studies following an mRNA COVID-19 vaccination is 0.001-0.0004% for myocarditis and pericarditis respectively [15]. A population study in Israel found an excess risk myocarditis of 3, and of pericarditis of 1 per 100,000 vaccinated persons [16, 17]. An overall risk of myocarditis and pericarditis following COVID-19 disease is much higher, with risk ratios of 18.3 and 5.4 respectively [16].

Literature on myocarditis and pericarditis with other types of COVID-19 vaccines is scarce. A case-control study conducted in Hong Kong found 7 and 20 cases of myocarditis following the inactivated CoronaVac and mRNA vaccine Pfizer/BioNTech, respectively. However, an increased risk was only found with the Pfizer vaccine, predominantly with the second dose and in younger males [18]. A self-controlled case series in England found increased risks of myocarditis associated in the first week with the first dose of AstraZeneca and Pfizer and with the first and second doses of Moderna in 1-28 days after vaccination, as well as after a positive Sars CoV 2 test [19]. A database study in the VAERS database in the US analyzed reported events of myocarditis and pericarditis following mRNA vaccines and the adenovector vaccine of Janssen and did not find a strong signal for myo- and pericarditis with Janssen, based on a ROR (reporting odds ratio) of 1.39 (95% CI 0.99-1.97) compared to a ROR of 5.37 (95% CI 4.10-7.04) with Pfizer and 2.91 (95% CI 2.21 -3.83) with Moderna [20]. However, RORs can only be used to generate potential signals and cannot be used to confirm or quantify a signal.
And few case reports with vector vaccines were found: 1) a fifty year old Belgian man with myocarditis, 5 days after the 2nd dose of AstraZeneca [21], 2) an Iranian 29-year old man with myocarditis in 48 hours following the second dose of the Sputnik V vaccine [22], 3) a 33-year old male from the US who developed myocarditis in 2 days following a single dose of Janssen [23] and 4) a 67-year old women from Germany with reactivation of cytomegalovirus accompanied by a viral pericarditis in 2 week following the first dose of the AstraZeneca vaccine [24].
During a phase III clinical trial with the novel recombinant nanoparticle spike protein (Novavax) vaccine, 1 case in 7020 participants of myocarditis occurred, 3 days after the second dose (21 days after the first dose). A viral origin for the condition was suspected, but an association with the vaccine cannot be excluded [25, 26].

Sars-CoV-2 (COVID-19) infection is also associated with myocarditis and pericarditis [27]. An Israeli study showed an 18 times increased risk for myocarditis after Sars-CoV-2 infection compared to healthy controls, whereas following vaccination the risk was 3 times increased [17].

Mechanism
The mechanism by which myocarditis and pericarditis is not fully elucidated yet. There are several hypothesis of mechanism that could be involved. First, an inappropriate inflammatory response is suggested, similar to myocardial and pericardial involvement in SARS-CoV-2 infection (COVID-19). In younger people, mRNA vaccines tend to have a more potent immunogenicity and reactogenicity, resulting in an exaggerated immune response in predisposed individuals. Second, the timing of less than 5 days following a second dose or exposure could fit a delayed hypersensitivity reaction. Third, molecular mimicry between the SARS-CoV-2 spike protein and an (unknown) myocardial protein could explain the more pronounced condition with COVID-19 compared to vaccination [28]. However, these proposed mechanisms do not explain the differences in the association between mRNA and adenovector vaccines and the predominance in younger males. It is also not clear whether lipid nanoparticles, present in mRNA vaccines and also in the recombinant protein vaccine Novavax, play a role in myocardial damage [25].

Discussion

Report characteristics
In our reports, myocarditis and pericarditis were reported with any dose of mRNA and to a lesser extent also with vector based COVID-19 vaccines, more in men than in women but among all age groups. The majority of the patients had recovered or was recovering at time of reporting. In six reports (1.6%) a fatal outcome was reported. Although pericarditis and myocarditis are now known ADRs with mRNA vaccines, it is impossible to exclude any other cause in every single report.
Although the majority of our reports of myocarditis and pericarditis had a time to onset within one week, there is a large range in times to onset in our reports. In literature a common time to onset is 5 days following vaccination. It cannot be ruled out that extensive media attention has triggered reporting of the conditions by any cause and not necessarily associated with the vaccination. With adenovector vaccine reports, the ‘typical pattern’ of young men within a few days following a second dose, is even less present: mainly first dose and longer and varying latencies and older ages in women are present, although that might be explained by the targeted age group of 60-65 year old people for AstraZeneca.

In our reports, 15-22% of the patients had COVID-19 in their medical history, which is similar to all reports with COVID-19 vaccines in general (about 18%). However, undiagnosed COVID-19 cannot be excluded. Only two people had a confirmed Sars-CoV-2 infection shortly before the reported pericarditis. Similarly to the literature, the percentage of people with a history of COVID-19 is higher in reports of myocarditis/pericarditis following the first dose than the second dose [28]. With the booster dose, this percentage increases again, probably due to the pandemic wave with the delta variant.

Recurrence of myocarditis and pericarditis following subsequent vaccinations was reported once with myocarditis and nine times with pericarditis. Another nine patients had symptoms of chest pain or palpitations with a previous dose, which was not further diagnosed. One patient had pericarditis in the past following other vaccinations. There is no information available in the reports of ‘negative rechallenges’; having no adverse event with a second or third dose after having had myocarditis or pericarditis with a previous dose is not likely to be reported.

The frequency of myocarditis and pericarditis following COVID-19 vaccination cannot be determined based on spontaneous reporting, since not all true adverse drug reactions will be reported due to underreporting and not all reported events will be causally related to the vaccination.
In the Netherlands, the average reporting rate for pericarditis is 9.2 per million vaccinations, and for myocarditis from 3.3 per million vaccinations. For details, see appendix B.

Considerations with the Observed over Expected method
An observed-over-expected ratio (OE) can correct for background incidence and vaccine exposure. Since the mechanism of myocarditis and pericarditis following vaccination is unknown, there is no standardized risk window. In literature, the majority of cases occurred within 5 days up to two weeks following vaccination. In some studies, 4 weeks or one month were taken into account and with smallpox vaccination, the risk window for myocarditis was set on 30 days [29]. Therefore, the at-risk-periods were set on 5 and 14 days following each vaccine dose. Events with a short latency are more likely to be considered vaccine related by the reporter, although reports with latencies up to 6 months were received as well. SMR calculations with an at-risk-period of 28 days showed a similar pattern of those with 14 days with smaller outcomes; these data are not shown in this overview.

Underreporting is a common feature of voluntary reporting systems. Since the extent of underreporting is unknown, the number of observed cases can be underestimated. Media attention however may have increased awareness and diagnosing of pericarditis and myocarditis, as well as willingness to report these conditions following vaccination with COVID-19 vaccines. Before the COVID-19 vaccination campaign, symptoms of pericarditis and myocarditis were not always diagnosed and registered as it was seen a self-limiting condition. This difference may have caused an overestimation of the current observed-over-expected analysis. COVID-19 as an infection is associated with myocarditis and pericarditis as well, which background incidence rates from 2019 are likely to be lower than in 2020 or 2021.

In the vaccination campaign, the preferred booster vaccination for people > 45 years was the Moderna vaccine (half a dose) and for people 18-45 years the Pfizer vaccine [32]. This choice might have reduced the number of cases (and reports) of myocarditis and pericarditis with the booster dose of Moderna. At the vaccination cut-off dates of this analysis, the booster campaign had not finished yet which influenced the number of exposed people and the time to report adverse events following the third (booster) administration. This explains the relatively low number of reports and the low average time to onset of pericarditis and myocarditis following these third doses (table 1).

In general, more cases of myocarditis and pericarditis have been reported than expected following COVID-19 vaccination. Our reports, in part, differ from the well known pattern of 'young males with second dose of mRNA vaccines'. First, with mRNA vaccines in a 5- and 14-day risk period with the *1st and 2nd doses* an excess of cases of myocarditis was seen in *both men and women*, *aged < 40 and in all ages*. For pericarditis, the incidence rates also exceeded 1 with Pfizer in people < 40 and for some groups with Moderna as well.
Although the absolute numbers of reports of myocarditis and pericarditis with vector vaccines are lower than for mRNA vaccines, SMRs with the *first doses* of AstraZeneca and Janssen exceeded 1. This indicates that more cases have been reported than could have been expected based on background incidence rates. So far, myocarditis and pericarditis are not confirmed as adverse events following these vector vaccines [3, 4]. An artificial increase of diagnosis and reporting of myocarditis and pericarditis compared to 2019 practices is also possible. However, in literature an increase of cases of myocarditis with the first dose of AstraZeneca has been described before [19].

Conclusion

Compared to the previous overview of reports of myocarditis and pericarditis with COVID-19 vaccines in The Netherlands, this update adds a more complete review of all reported events of myocarditis and pericarditis in the first year of the vaccination campaign, including the start of the booster vaccinations.
The total number of reports of myocarditis and pericarditis increased from 194 (October 2021) to 373 (January 2022). The current comparison with background incidence rates with larger age groups provides a more robust outcome. The results show that myocarditis and pericarditis has been reported more frequently than expected in several subgroups of patients with *all* available vaccines. Increased awareness and diagnosis of these conditions may have contributed to the overall high SMR outcomes. However, based on the reports with vector vaccines and comparison with background incidence rates, an association with myocarditis and pericarditis cannot be confirmed nor ruled out, although absolute numbers are small.
It is not possible to quantify the exact risk of myocarditis and pericarditis following COVID-19 vaccination for the Dutch population based on the number of spontaneously reported cases. Additional research is needed to quantify this risk and to specify people at risk with mRNA vaccines. This also counts for a potential association with the viral vector vaccines.

References

1. EMA. SmPC Comirnaty. Via: https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf (accessed at 1-10-2021)
2. EMA. SmPC Spikevax. Via: https://www.ema.europa.eu/en/documents/overview/spikevax-previously-covid-19-vaccine-moderna-epar-medicine-overview_en.pdf (accessed at 1-10-2021)
3. EMA. SmPC Vaxzevria. https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf (accessed at 30-3-2022)
4. EMA. SmPC Janssen. https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-janssen-epar-product-information_en.pdf (accessed at 30-3-2022)
5. Lareb. Overview of pericarditis and myocarditis associated with COVID vaccines. Nov 2022. https://www.lareb.nl/media/zsdapxpk/signals_2021_overview-of-pericarditis-and-myocarditis-associated-with-covid-vaccines.pdf
6. Spangler, S. MedScape: Acute Pericarditis (Apr 02, 2019). Via: https://emedicine.medscape.com/article/156951-overview (accessed at 1-10-2021)

7. Lane, S, Shakir, S. Reports of myocarditis and pericarditis following mRNA COVID-19 vaccines: A review of spontaneously reported data from the UK, Europe, and the US. medRxiv 2021.09.09.21263342; doi: https://doi.org/10.1101/2021.09.09.21263342. Via: https://www.medrxiv.org/content/10.1101/2021.09.09.21263342v1
8. Imazio M. Noninfectious pericarditis: management challenges for cardiologists. Kardiol Pol. 2020 May 25;78(5):396-403. doi: 10.33963/KP.15353. Epub 2020 May 11. PMID: 32394692. https://pubmed.ncbi.nlm.nih.gov/32394692/
9. Tang, WHW. MedScape: Myocarditis (Jul 06, 2021). Via: https://emedicine.medscape.com/article/156330-overview#a6 (accessed at 1-10-2021)
10. PHARMO. Data request pericarditis and myocarditis (2019), 21-10-2021.
11. Lazaros G, Klein AL, Hatziantoniou S, Tsioufis C, Tsakris A, Anastassopoulou C. The Novel Platform of mRNA COVID-19 Vaccines and Myocarditis: Clues into the Potential Underlying Mechanism. Vaccine. 2021 Aug 16;39(35):4925-4927. doi: 10.1016/j.vaccine.2021.07.016. Epub 2021 Jul 13. PMID: 34312010; PMCID: PMC8275472.
12. Matta A, Kunadharaju R, Osman M, Jesme C, McMiller Z, Johnson EM, Matta D, Kallamadi R, Bande D. Clinical Presentation and Outcomes of Myocarditis Post mRNA Vaccination: A Meta-Analysis and Systematic Review. Cureus. 2021 Nov 3;13(11):e19240. doi: 10.7759/cureus.19240. PMID: 34877217; PMCID: PMC8641964.
13. Goyal M, Ray I, Mascarenhas D, Kunal S, Sachdeva RA, Ish P. Myocarditis post SARS-CoV-2 vaccination: a systematic review. QJM. 2022 Mar 3:hcac064. doi: 10.1093/qjmed/hcac064. Epub ahead of print. PMID: 35238384; PMCID: PMC8903459.
14. Bellos I, Karageorgiou V, Viskin D. Myocarditis following mRNA Covid-19 vaccination: A pooled analysis. Vaccine. 2022 Mar 15;40(12):1768-1774. doi: 10.1016/j.vaccine.2022.02.017. Epub 2022 Feb 7. PMID: 35153093; PMCID: PMC8818354.
15. Fatima M, Ahmad Cheema H, Ahmed Khan MH, Shahid H, Saad Ali M, Hassan U, Wahaj Murad M, Aemaz Ur Rehman M, Farooq H. Development of myocarditis and pericarditis after COVID-19 vaccination in adult population: A systematic review. Ann Med Surg (Lond). 2022 Apr;76:103486. doi: 10.1016/j.amsu.2022.103486. Epub 2022 Mar 11. PMID: 35291413; PMCID: PMC8912977.
16. Gnanenthiran SR, Limaye S. COVID-19 mRNA vaccines and myopericarditis. Intern Med J. 2022 Mar 15. doi: 10.1111/imj.15748. Epub ahead of print. PMID: 35289493.
17. Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, Hernán MA, Lipsitch M, Kohane I, Netzer D, Reis BY, Balicer RD. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. N Engl J Med. 2021 Sep 16;385(12):1078-1090. doi: 10.1056/NEJMoa2110475. Epub 2021 Aug 25. PMID: 34432976; PMCID: PMC8427535.
18. Lai FTT, Li X, Peng K, Huang L, Ip P, Tong X, Chui CSL, Wan EYF, Wong CKH, Chan EWY, Siu DCW, Wong ICK. Carditis After COVID-19 Vaccination With a Messenger RNA Vaccine and an Inactivated Virus Vaccine : A Case-Control Study. Ann Intern Med. 2022 Mar;175(3):362-370. doi: 10.7326/M21-3700. Epub 2022 Jan 25. PMID: 35073155; PMCID: PMC8814917.
19. Patone M, Mei XW, Handunnetthi L, Dixon S, Zaccardi F, Shankar-Hari M, Watkinson P, Khunti K, Harnden A, Coupland CAC, Channon KM, Mills NL, Sheikh A, Hippisley-Cox J. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med. 2022 Feb;28(2):410-422. doi: 10.1038/s41591-021-01630-0. Epub 2021 Dec 14. PMID: 34907393; PMCID: PMC8863574.
20. Li M, Yuan J, Lv G, Brown J, Jiang X, Lu ZK. Myocarditis and Pericarditis following COVID-19 Vaccination: Inequalities in Age and Vaccine Types. J Pers Med. 2021 Oct 28;11(11):1106. doi: 10.3390/jpm11111106. PMID: 34834458; PMCID: PMC8624452.
21. Van Kerkhove O, Renders F, Leys M. A case of myocarditis following ChAdOx1 nCov-19 vaccination. Acta Cardiol. 2022 Feb 21:1-3. doi: 10.1080/00015385.2022.2040825. Epub ahead of print. PMID: 35189775.
22. Naghashzadeh F, Shafaghi S, Dorudinia A, Naji SA, Marjani M, Amin A, Mohamadifar A, Noorali S, Kashani BS. Myocarditis following rAd26 and rAd5 vector-based COVID-19 vaccine: case report. ESC Heart Fail. 2022 Apr;9(2):1483-1486. doi: 10.1002/ehf2.13821. Epub 2022 Feb 1. PMID: 35106967; PMCID: PMC8934948.
23. Sulemankhil, I., Abdelrahman, M., & Negi, S. I. (2021). Temporal association between the COVID-19 Ad26.COV2.S vaccine and acute myocarditis: A case report and literature review. Cardiovascular revascularization medicine : including molecular interventions, S1553-8389(21)00578-9. Advance online publication. https://doi.org/10.1016/j.carrev.2021.08.012
24. Plüß, M., Mese, K., Kowallick, J. T., Schuster, A., Tampe, D., & Tampe, B. (2022). Case Report: Cytomegalovirus Reactivation and Pericarditis Following ChAdOx1 nCoV-19 Vaccination Against SARS-CoV-2. Frontiers in immunology, 12, 784145. https://doi.org/10.3389/fimmu.2021.784145
25. Tsilingiris D, Vallianou NG, Karampela I, Liu J, Dalamaga M. Potential implications of lipid nanoparticles in the pathogenesis of myocarditis associated with the use of mRNA vaccines against SARS-CoV-2. Metabol Open. 2022 Mar;13:100159. doi: 10.1016/j.metop.2021.100159. Epub 2021 Dec 17. PMID: 34938983; PMCID: PMC86774
26. 26.P.T. Heath, E.P. Galiza, D.N. Baxter, M. Boffito, D. Browne, F. Burns, et al. Safety and efficacy of NVX-CoV2373 covid-19 vaccine; 385 (2021), pp. 1172-1183, 10.1056/NEJMoa2107659
27. Nassar M, Nso N, Gonzalez C, Lakhdar S, Alshamam M, Elshafey M, Abdalazeem Y, Nyein A, Punzalan B, Durrance RJ, Alfishawy M, Bakshi S, Rizzo V. COVID-19 vaccine-induced myocarditis: Case report with literature review. Diabetes Metab Syndr. 2021 Sep-Oct;15(5):102205. doi: 10.1016/j.dsx.2021.102205. Epub 2021 Jul 10. Erratum in: Diabetes Metab Syndr. 2021 Sep-Oct;15(5):102277. PMID: 34293552; PMCID: PMC8270733.
28. Hajra A, Gupta M, Ghosh B, Ashish K, Patel N, Manek G, Rai D, Sreenivasan J, Goel A, Lavie CJ, Bandyopadhyay D. Proposed Pathogenesis, Characteristics, and Management of COVID-19 mRNA Vaccine-Related Myopericarditis. Am J Cardiovasc Drugs. 2022 Jan;22(1):9-26. doi: 10.1007/s40256-021-00511-8. Epub 2021 Nov 24. Erratum in: Am J Cardiovasc Drugs. 2021 Dec 21;: PMID: 34817850; PMCID: PMC8612108.
29. Imazio, M. Myopericarditis. In: Up to Date. Version date: Jul 20, 2021. Accessed at 8-11-2021
30. Spangler, S. Acute Pericarditis. MedScape, via: https://emedicine.medscape.com/article/156951-overview#a7 (Version date April 2019)
31. Tavora, FR. Myocarditis Pathology. MedScape, via: https://emedicine.medscape.com/article/1612533-overview#a2 (Version date November 2021)
32. Rijksinstituut voor Volksgezondheid en Milieu. COVID-19-vaccinatie Uitvoeringsrichtlijn. Via: https://lci.rivm.nl/richtlijnen/covid-19-vaccinatie (Version date 25 maart 2022 (version 2.7))

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

Supplements

Appendix A: Spread of latencies (summarized per week) for myocarditis and pericarditis with all COVID-19 vaccines. With the first dose, 42% of pericarditis and 59% of myocarditis started within one week following vaccination.

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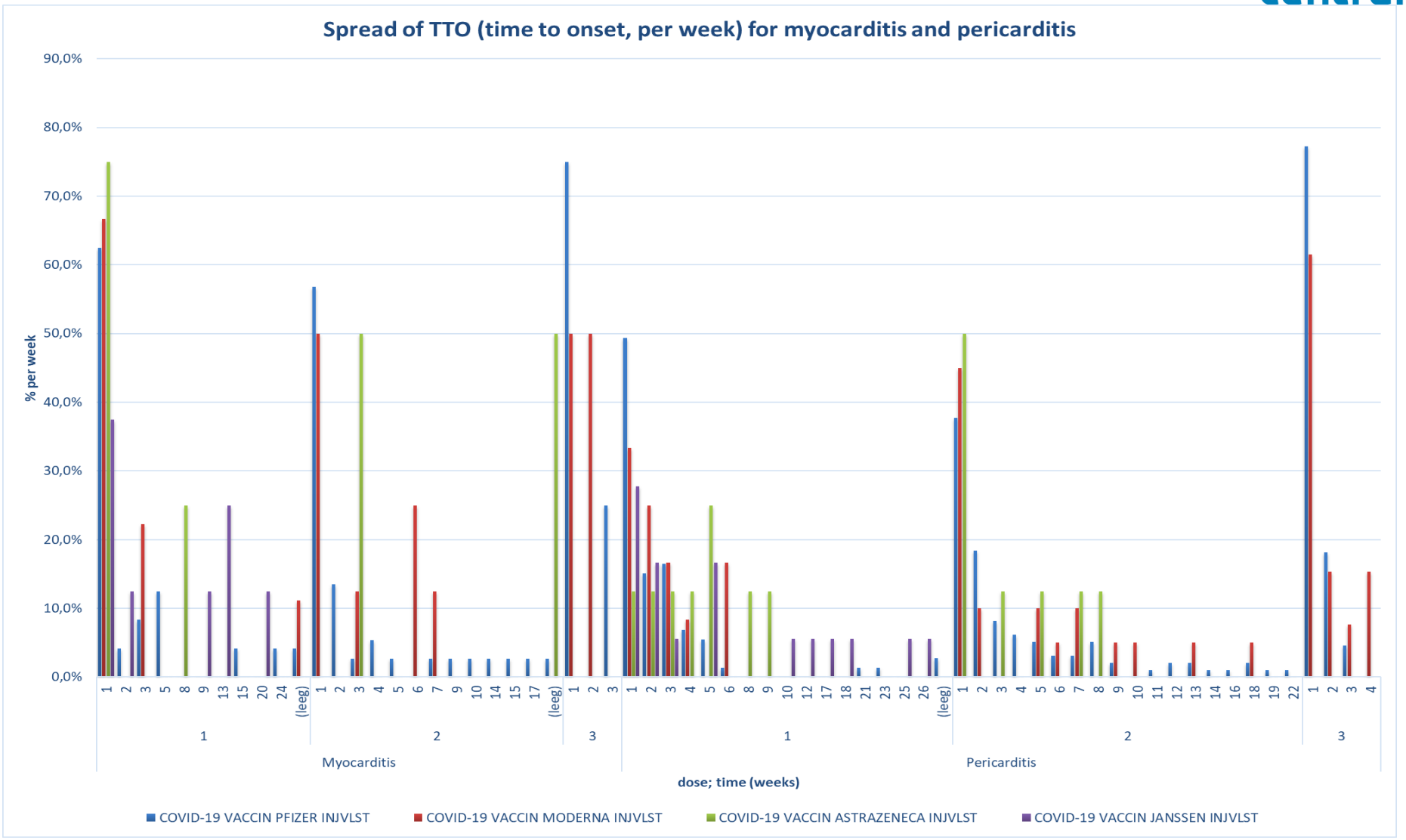

Appendix B: Reporting rates of myocarditis and pericarditis with COVID-19 vaccines. Vaccine numbers are obtained from RIVM (CIMS numbers, until 10-1-2022); reporting rates in *n* reports per million vaccinations.

	Vaccine	Myocarditis (N)	/1 million	Pericarditis (N)	/1 million
ASTRAZENECA					
1	1299173	4	3.1	8	6.2
2	1207086	2	1.7	8	6.6
total	*2506259*	*6*	*2.4*	*16*	*6.4*
JANSSEN					
1	738878	8	10.8	18	24.4
total	*738878*	*8*	*10.8*	*18*	*24.4*
MODERNA					
1	981297	9	9.2	12	12.2
2	906742	8	8.8	20	22.1
3	3833824	2	0.5	13	3.4
total	*5721863*	*19*	*3.3*	*45*	*7.9*
PFIZER					
1	9396394	24	2.6	73	7.8
2	8738302	37	4.2	98	11.2
3	2759334	4	1.4	22	8.0
total	*20894030*	*65*	*3.1*	*193*	*9.2*
NOT SPECIFIED					
1		1		1	
3				1	
total		*1*		*2*	
ALL					
1	**12415742**	**46**	**3.7**	**112**	**9.0**
2	**10852130**	**47**	**4.3**	**126**	**11.6**
3	**6593158**	**6**	**0.9**	**36**	**5.5**
total	***29861030***	***99***	***3.3***	***274***	***9.2***

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Appendix C: Detailed observed-over-expected (SMR) calculations for myocarditis and pericarditis, per COVID-19 vaccine and risk period (5 and 14 days).

Myocarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)* **:moet nog!**		
PFIZER - dose 1										
Male 0-19	1	509863	1	86036	0,08	12,32				
Male 20-39	5	1194366	6	94328	1,04	4,80				
Male 40-59	2	1404275	7	119311	1,13	1,77				
Male > 60	1	1496898	2	119904	0,34	2,92				
Male_all age	**9**	**4605402**	**16**	**419579**	**2,59**		**3,47**	**1,59**	**6,59**	*
Male_< 40	**6**	**1704229**	**7**	**180364**	**1,12**		**5,35**	**1,96**	**11,64**	*
Male_> 40	**3**	**2901173**	**9**	**239215**	**1,47**		**2,04**	**0,42**	**5,96**	*
Female 0-19	1	494868	2	83117	0,16	6,13				
Female 20-39	2	1201284	4	103023	0,64	3,13				
Female 40-59	0	1383693	3	126492	0,45	0,00				
Female > 60	0	1740728	0	133851	0,00	n.a.				
Female_all age	**3**	**4820573**	**9**	**446483**	**1,25**		**2,40**	**0,50**	**7,01**	*
Female_< 40	**3**	**1696152**	**6**	**186140**	**0,80**		**3,74**	**0,77**	**10,93**	*
Female_> 40	**0**	**3124421**	**3**	**260343**	**0,45**		**0,00**	**0,00**	**8,21**	*
Total_all age	**12**	**9425975**	**25**	**866062**	**3,84**		**3,12**	**1,58**	**5,18**	
PFIZER - dose 2										
Male 0-19	4	439788	1	86036	0,07	57,12				
Male 20-39	8	1062432	6	94328	0,93	8,64				
Male 40-59	3	1306239	7	119311	1,05	2,86				
Male > 60	1	1468738	2	119904	0,34	2,98				
Male_all age	**16**	**4277197**	**16**	**419579**	**2,38**		**6,72**	**3,78**	**10,50**	
Male_< 40	**12**	**1502220**	**7**	**180364**	**1,00**		**12,05**	**6,10**	**20,01**	
Male_> 40	**4**	**2774977**	**9**	**239215**	**1,385423**		**2,89**	**0,79**	**7,39**	*
Female 0-19	0	426627	2	83117	0,14	0,00				
Female 20-39	0	1075907	4	103023	0,57	0,00				
Female 40-59	2	1290937	3	126492	0,42	4,77				
Female > 60	0	1708172	0	133851	0,00					
Female_all age	**2**	**4501643**	**9**	**446483**	**1,13**		**1,77**	**0,21**	**6,38**	*
Female_< 40	**0**	**1502534**	**6**	**186140**	**0,71**		**0,00**	**0,00**	**5,18**	*
Female_> 40	**2**	**2999109**	**3**	**260343**	**0,419412**		**4,77**	**0,57**	**17,21**	*
Total_all age	**18**	**8778840**	**25**	**866062**	**3,51**		**5,12**	**2,99**	**7,82**	
PFIZER - dose 3 (booster)										
Male 0-19	0	51395	1	86036	0,01	0,00				
Male 20-39	2	674270	6	94328	0,59	3,40				
Male 40-59	0	483724	7	119311	0,39	0,00				
Male > 60	1	395378	2	119904	0,09	11,07				
Male_all age	**3**	**1604767**	**16**	**419579**	**1,07**		**2,79**	**0,58**	**8,16**	*
Male_< 40	**2**	**725665**	**7**	**180364**	**0,60**		**3,36**	**0,40**	**12,12**	*
Male_> 40	**1**	**879102**	**9**	**239215**	**0,48**		**2,09**	**0,05**	**11,63**	*
Female 0-19	0	58543	2	83117	0,02	0,00				
Female 20-39	0	720501	4	103023	0,38	0,00				
Female 40-59	0	608934	3	126492	0,20	0,00				
Female > 60	0	522902	0	133851	0,00	n.a.				
Female_all age	**0**	**1910880**	**9**	**446483**	**0,60**		**0,00**	**0,00**	**6,15**	*
Female_< 40	**0**	**779044**	**6**	**186140**	**0,40**		**0,00**	**0,00**	**9,17**	*
Female_> 40	**0**	**1131836**	**3**	**260343**	**0,20**		**0,00**	**0,00**	**18,65**	*
Total_all age	**3**	**3515647**	**25**	**866062**	**1,68**		**1,79**	**0,37**	**5,24**	*

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Myocarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
MODERNA - dose 1										
Male 0-19	0	11931	1	86036	0,00	0,00				
Male 20-39	4	146092	6	94328	0,13	31,42				
Male 40-59	0	275732	7	119311	0,22	0,00				
Male > 60	0	50432	2	119904	0,01	0,00				
Male_all age	**4**	**484187**	**16**	**419579**	**0,36**		**11,04**	**3,01**	**28,26**	*
Male_< 40	**4**	**158023**	**7**	**180364**	**0,13**		**30,96**	**8,44**	**79,26**	*
Male_> 40	**0**	**326164**	**9**	**239215**	**0,23**		**0,00**	**0,00**	**15,83**	*
Female 0-19	0	12180	2	83117	0,00	0,00				
Female 20-39	1	163151	4	103023	0,09	11,52				
Female 40-59	0	268645	3	126492	0,09	0,00				
Female > 60	0	53792	0	133851	0,00	#				
Female_all age	**1**	**497768**	**9**	**446483**	**0,18**		**5,62**	**0,14**	**31,28**	*
Female_< 40	**1**	**175331**	**6**	**186140**	**0,09**		**11,01**	**0,28**	**61,35**	*
Female_> 40	**0**	**322437**	**3**	**260343**	**0,09**		**0,00**	**0,00**	**42,28**	*
Total_all age	**5**	**981955**	**25**	**866062**	**0,54**		**9,25**	**3,00**	**21,60**	*
MODERNA - dose 2										
Male 0-19	0	10072	1	86036	0,00	0,00				
Male 20-39	3	131542	6	94328	0,11	26,17				
Male 40-59	0	258684	7	119311	0,21	0,00				
Male > 60	0	47523	2	119904	0,01	0,00				
Male_all age	**3**	**447821**	**16**	**419579**	**0,33**		**8,96**	**1,85**	**26,18**	*
Male_< 40	**3**	**141614**	**7**	**180364**	**0,12**		**25,81**	**5,33**	**75,46**	*
Male_> 40	**0**	**306207**	**9**	**239215**	**0,218763**		**0,00**	**0,00**	**16,87**	*
Female 0-19	0	10526	2	83117	0,00	0,00				
Female 20-39	1	148465	4	103023	0,08	12,66				
Female 40-59	0	251082	3	126492	0,08	0,00				
Female > 60	0	50029	0	133851	0,00	n.a.				
Female_all age	**1**	**460102**	**9**	**446483**	**0,16**		**6,10**	**0,15**	**33,96**	*
Female_< 40	**1**	**158991**	**6**	**186140**	**0,08**		**12,13**	**0,30**	**67,57**	*
Female_> 40	**0**	**301111**	**3**	**260343**	**0,081574**		**0,00**	**0,00**	**45,24**	*
Total_all age	**4**	**907923**	**25**	**866062**	**0,50**		**8,02**	**2,18**	**20,52**	*
MODERNA - dose 3 (booster)										
Male 0-19	0	111	1	86036	0,00	0,00				
Male 20-39	0	1638	6	94328	0,00	0,00				
Male 40-59	0	773249	7	119311	0,62	0,00				
Male > 60	0	1324838	2	119904	0,30	0,00				
Male_all age	**0**	**2099836**	**16**	**419579**	**0,93**		**0,00**	**0,00**	**3,99**	*
Male_< 40	**0**	**1749**	**7**	**180364**	**0,00**		**0,00**	**0,00**	**2553,76**	*
Male_> 40	**0**	**2098087**	**9**	**239215**	**0,924178**		**0,00**	**0,00**	**3,99**	*
Female 0-19	0	134	2	83117	0,00	0,00				
Female 20-39	0	1594	4	103023	0,00	0,00				
Female 40-59	1	687254	3	126492	0,22	4,48				
Female > 60	0	1378989	0	133851	0,00	n.a.				
Female_all age	**1**	**2067971**	**9**	**446483**	**0,22**		**4,46**	**0,11**	**24,85**	*
Female_< 40	**0**	**1728**	**6**	**186140**	**0,00**		0,00	**0,00**	**4136,93**	*
Female_> 40	**1**	**2066243**	**3**	**260343**	**0,223281**		**4,48**	**0,11**	**24,95**	*
Total_all age	**1**	**4167807**	**25**	**866062**	**1,15**		**0,87**	**0,02**	**4,84**	*

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Myocarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN- dose 1										
Male 0-19	1	24994	1	86036	0,00	251,29				
Male 20-39	1	193474	6	94328	0,17	5,93				
Male 40-59	1	200009	7	119311	0,16	6,22				
Male > 60	0	7656	2	119904	0,00	0,00				
Male_all age	**3**	**426133**	**16**	**419579**	**0,34**		**8,95**	**1,85**	**26,17**	*
Male_< 40	**2**	**218468**	**7**	**180364**	**0,17**		**11,59**	**1,39**	**41,84**	*
Male_> 40	**1**	**207665**	**9**	**239215**	**0,16**		**6,15**	**0,15**	**34,28**	*
Female 0-19	0	16224	2	83117	0,01	0,00				
Female 20-39	0	123803	4	103023	0,07	0,00				
Female 40-59	0	167404	3	126492	0,05	0,00				
Female > 60	0	6808	0	133851	0,00	n.a.				
Female_all age	**0**	**314239**	**9**	**446483**	**0,13**		**0,00**	**0,00**	**29,38**	*
Female_< 40	**0**	**140027**	**6**	**186140**	**0,07**		**0,00**	**0,00**	**51,83**	*
Female_> 40	**0**	**174212**	**3**	**260343**	**0,05**		**0,00**	**0,00**	**67,85**	*
Total_all age	**3**	**740372**	**25**	**866062**	**0,46**		**6,51**	**1,35**	**19,04**	*

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Myocarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
AstraZeneca- dose 1										
Male 0-19	0	1286	1	86036	0,00	0,00				
Male 20-39	1	26853	6	94328	0,02	42,74				
Male 40-59	0	49254	7	119311	0,04	0,00				
Male > 60	0	533206	2	119904	0,12	0,00				
Male_all age	**1**	**610599**	**16**	**419579**	**0,19**		**5,40**	**0,14**	**31,19**	*
Male_< 40	**1**	**28139**	**7**	**180364**	**0,02**		**42,37**	**1,06**	**244,46**	*
Male_> 40	**0**	**582460**	**9**	**239215**	**0,16**		**0,00**	**0,00**	**22,86**	*
Female 0-19	0	3263	2	83117	0,00	0,00				
Female 20-39	0	68293	4	103023	0,04	0,00				
Female 40-59	1	126252	3	126492	0,04	24,38				
Female > 60	0	491513	0	133851	0,00	n.a.				
Female_all age	**1**	**689321**	**9**	**446483**	**0,08**		**12,75**	**0,32**	**73,58**	*
Female_< 40	**0**	**71556**	**6**	**186140**	**0,04**		**0,00**	**0,00**	**98,67**	*
Female_> 40	**1**	**617765**	**3**	**260343**	**0,04**		**24,38**	**0,61**	**140,67**	*
Total_all age	**2**	**1299920**	**25**	**866062**	**0,26**		**7,59**	**0,91**	**27,41**	*
AstraZeneca- dose 2										
Male 0-19	0	1154	1	86036	0,00	0,00				
Male 20-39	0	24569	6	94328	0,02	0,00				
Male 40-59	0	45812	7	119311	0,04	0,00				
Male > 60	0	497001	2	119904	0,11	0,00				
Male_all age	**0**	**568536**	**16**	**419579**	**0,17**		**0,00**	**0,00**	**21,46**	*
Male_< 40	**0**	**25723**	**7**	**180364**	**0,02**		**0,00**	**0,00**	**170,90**	*
Male_> 40	**0**	**542813**	**9**	**239215**	**0,15**		**0,00**	**0,00**	**24,54**	*
Female 0-19	0	3022	2	83117	0,00	0,00				
Female 20-39	0	62516	4	103023	0,03	0,00				
Female 40-59	0	116578	3	126492	0,04	0,00				
Female > 60	0	457037	0	133851	0,00	0,00				
Female_all age	**0**	**639153**	**9**	**446483**	**0,07**		**0,00**	**0,00**	**51,16**	*
Female_< 40	**0**	**65538**	**6**	**186140**	**0,03**		**0,00**	**0,00**	**107,75**	*
Female_> 40	**0**	**573615**	**3**	**260343**	**0,04**		**0,00**	**0,00**	**97,43**	*
Total_all age	**0**	**1207689**	**25**	**866062**	**0,24**		**0,00**	**0,00**	**15,12**	

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Myocarditis										
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
PFIZER - dose 1										
Male 0-19	1	506056	1	86036	0,23	4,43				
Male 20-39	7	1190742	6	94328	2,91	2,41				
Male 40-59	3	1402066	7	119311	3,16	0,95				
Male > 60	1	1493444	2	119904	0,96	1,05				
Male_all age	**12**	**4592308**	**16**	**419579**	**7,24**		**1,66**	**0,84**	**2,75**	
Male_< 40	**8**	**1696798**	**7**	**180364**	**3,13**		**2,56**	**1,10**	**5,03**	*
Male_> 40	**4**	**2895510**	**9**	**239215**	**4,11**		**0,97**	**0,27**	**2,49**	*
Female 0-19	1	491198	2	83117	0,45	2,21				
Female 20-39	2	1196209	4	103023	1,78	1,12				
Female 40-59	1	1380642	3	126492	1,26	0,80				
Female > 60	0	1735729	0	133851	0,00	n.a.				
Female_all age	**4**	**4803778**	**9**	**446483**	**3,49**		**1,15**	**0,31**	**2,93**	*
Female_< 40	**3**	**1687407**	**6**	**186140**	**2,23**		**1,34**	**0,28**	**3,92**	*
Female_> 40	**1**	**3116371**	**3**	**260343**	**1,26**		**0,80**	**0,02**	**4,43**	*
Total_all age	**16**	**9396086**	**25**	**866062**	**10,73**		**1,49**	**0,84**	**2,33**	
PFIZER - dose 2										
Male 0-19	4	435726	1	86036	0,19	20,59				
Male 20-39	12	1056431	6	94328	2,58	4,66				
Male 40-59	5	1302149	7	119311	2,93	1,71				
Male > 60	1	1464982	2	119904	0,94	1,07				
Male_all age	**22**	**4259288**	**16**	**419579**	**6,64**		**3,31**	**2,05**	**4,88**	
Male_< 40	**16**	**1492157**	**7**	**180364**	**2,77**		**5,77**	**3,25**	**9,02**	
Male_> 40	**6**	**2767131**	**9**	**239215**	**3,87**		**1,55**	**0,57**	**3,38**	*
Female 0-19	0	422510	2	83117	0,39	0,00				
Female 20-39	0	1067896	4	103023	1,59	0,00				
Female 40-59	2	1285879	3	126492	1,17	1,71				
Female > 60	1	1702596	0	133851	0,00	#				
Female_all age	**3**	**4478881**	**9**	**446483**	**3,15**		**0,95**	**0,20**	**2,78**	*
Female_< 40	**0**	**1490406**	**6**	**186140**	**1,98**		**0,00**	**0,00**	**1,86**	*
Female_> 40	**3**	**2988475**	**3**	**260343**	**1,17**		**2,56**	**0,53**	**7,50**	*
Total_all age	**25**	**8738169**	**25**	**866062**	**9,79**		**2,55**	**1,63**	**3,68**	
PFIZER - dose 3 (booster)										
Male 0-19	0	27097	1	86036	0,01	0,00				
Male 20-39	2	447742	6	94328	1,09	1,83				
Male 40-59	0	378828	7	119311	0,85	0,00				
Male > 60	1	358678	2	119904	0,23	4,36				
Male_all age	**3**	**1212345**	**16**	**419579**	**2,19**		**1,37**	**0,28**	**4,01**	*
Male_< 40	**2**	**474839**	**7**	**180364**	**1,10**		**1,81**	**0,22**	**6,54**	*
Male_> 40	**1**	**737506**	**9**	**239215**	**1,08**		**0,92**	**0,02**	**5,15**	*
Female 0-19	0	33817	2	83117	0,03	0,00				
Female 20-39	0	514671	4	103023	0,77	0,00				
Female 40-59	0	513254	3	126492	0,47	0,00				
Female > 60	0	485229	0	133851	0,00	n.a.				
Female_all age	**0**	**1546971**	**9**	**446483**	**1,26**		**0,00**	**0,00**	**2,92**	*
Female_< 40	**0**	**548488**	**6**	**186140**	**0,80**		**0,00**	**0,00**	**4,63**	*
Female_> 40	**0**	**998483**	**3**	**260343**	**0,47**		**0,00**	**0,00**	**7,90**	*
Total_all age	**3**	**2759316**	**25**	**866062**	**3,45**		**0,87**	**0,18**	**2,54**	*

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Myocarditis										
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
MODERNA - dose 1										
Male 0-19	0	11920	1	86036	0,01	0,00				
Male 20-39	4	146011	6	94328	0,36	11,23				
Male 40-59	0	275544	7	119311	0,62	0,00				
Male > 60	0	50409	2	119904	0,03	0,00				
Male_all age	**4**	**483884**	**16**	**419579**	**1,01**		**3,95**	**1,08**	**10,10**	*
Male_< 40	**4**	**157931**	**7**	**180364**	**0,36**		**11,06**	**3,01**	**28,32**	*
Male_> 40	**0**	**325953**	**9**	**239215**	**0,65**		**0,00**	**0,00**	**5,66**	*
Female 0-19	0	12170	2	83117	0,01	0,00				
Female 20-39	1	163025	4	103023	0,24	4,12				
Female 40-59	0	268440	3	126492	0,24	0,00				
Female > 60	1	53759	0	133851	0,00	#				
Female_all age	**2**	**497394**	**9**	**446483**	**0,50**		**4,01**	**0,48**	**14,49**	*
Female_< 40	**1**	**175195**	**6**	**186140**	**0,25**		**3,94**	**0,10**	**21,93**	*
Female_> 40	**1**	**322199**	**3**	**260343**	**0,24**		**4,10**	**0,10**	**22,81**	*
Total_all age	**6**	**981278**	**25**	**866062**	**1,51**		**3,97**	**1,45**	**8,99**	*
MODERNA - dose 2										
Male 0-19	0	10044	1	86036	0,00	0,00				
Male 20-39	3	131311	6	94328	0,32	9,36				
Male 40-59	0	258383	7	119311	0,58	0,00				
Male > 60	0	47491	2	119904	0,03	0,00				
Male_all age	**3**	**447229**	**16**	**419579**	**0,94**		**3,20**	**0,66**	**9,36**	*
Male_< 40	**3**	**141355**	**7**	**180364**	**0,32**		**9,24**	**1,91**	**27,00**	*
Male_> 40	**0**	**305874**	**9**	**239215**	**0,61**		**0,00**	**0,00**	**6,03**	*
Female 0-19	0	10504	2	83117	0,01	0,00				
Female 20-39	1	148243	4	103023	0,22	4,53				
Female 40-59	0	250783	3	126492	0,23	0,00				
Female > 60	0	49968	0	133851	0,00	n.a.				
Female_all age	**1**	**459498**	**9**	**446483**	**0,46**		**2,18**	**0,05**	**12,15**	*
Female_< 40	**1**	**158747**	**6**	**186140**	**0,23**		**4,34**	**0,11**	**24,17**	*
Female_> 40	**0**	**300751**	**3**	**260343**	**0,23**		**0,00**	**0,00**	**16,17**	*
Total_all age	**4**	**906727**	**25**	**866062**	**1,40**		**2,87**	**0,78**	**7,34**	*
MODERNA - dose 3 (booster)										
Male 0-19	0	102	1	86036	0,00	0,00				
Male 20-39	0	1437	6	94328	0,00	0,00				
Male 40-59	0	655454	7	119311	1,48	0,00				
Male > 60	0	1267709	2	119904	0,81	0,00				
Male_all age	**0**	**1924702**	**16**	**419579**	**2,29**		**0,00**	**0,00**	**0,44**	*
Male_< 40	**0**	**1539**	**7**	**180364**	**0,00**		**0,00**	**0,00**	**1039,03**	*
Male_> 40	**0**	**1923163**	**9**	**239215**	**2,29**		**0,00**	**0,00**	**1,61**	*
Female 0-19	0	123	2	83117	0,00	0,00				
Female 20-39	0	1388	4	103023	0,00	0,00				
Female 40-59	1	583484	3	126492	0,53	1,88				
Female > 60	1	1324123	0	133851	0,00	#				
Female_all age	**2**	**1909118**	**9**	**446483**	**0,53**		**3,75**	**0,45**	**13,55**	*
Female_< 40	**0**	**1511**	**6**	**186140**	**0,00**		**0,00**	**0,00**	**1692,22**	*
Female_> 40	**2**	**1907607**	**3**	**260343**	**0,53**		**3,77**	**0,45**	**13,60**	*
Total_all age	**2**	**3833820**	**25**	**866062**	**2,82**		**0,71**	**0,09**	**2,56**	*

Myocarditis										
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN - dose 1										
Male 0-19	1	24911	1	86036	0,01	90,04				
Male 20-39	2	192917	6	94328	0,47	4,25				
Male 40-59	1	199774	7	119311	0,45	2,22				
Male > 60	0	7628	2	119904	0,00	0,00				
Male_all age	**4**	**425230**	**16**	**419579**	**0,94**		**4,27**	**1,16**	**10,94**	*
Male_< 40	**3**	**217828**	**7**	**180364**	**0,48**		**6,23**	**1,29**	**18,20**	*
Male_> 40	**1**	**207402**	**9**	**239215**	**0,45**		**2,20**	**0,06**	**12,26**	*
Female 0-19	0	16164	2	83117	0,01	0,00				
Female 20-39	0	123453	4	103023	0,18	0,00				
Female 40-59	0	167211	3	126492	0,15	0,00				
Female > 60	0	6786	0	133851	0,00	n.a.				
Female_all age	**0**	**313614**	**9**	**446483**	**0,35**		**0,00**	**0,00**	**10,52**	*
Female_< 40	**0**	**139617**	**6**	**186140**	**0,20**		**0,00**	**0,00**	**18,56**	*
Female_> 40	**0**	**173997**	**3**	**260343**	**0,15**		**0,00**	**0,00**	**24,26**	*
Total_all age	**4**	**738844**	**25**	**866062**	**1,29**		**3,11**	**0,85**	**7,96**	*

Myocarditis										
Risk period / TTO 14 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
AstraZeneca - dose 1										
Male 0-19	0	1283	1	86036	0,00	0,00				
Male 20-39	1	26812	6	94328	0,07	15,29				
Male 40-59	0	49226	7	119311	0,11	0,00				
Male > 60	0	533153	2	119904	0,34	0,00				
Male_all age	**1**	**610474**	**16**	**419579**	**0,52**		**1,93**	**0,05**	**11,14**	*
Male_< 40	**1**	**28095**	**7**	**180364**	**0,07**		**15,15**	**0,38**	**87,44**	*
Male_> 40	**0**	**582379**	**9**	**239215**	**0,45**		**0,00**	**0,00**	**8,17**	*
Female 0-19	0	3251	2	83117	0,00	0,00				
Female 20-39	0	68111	4	103023	0,10	0,00				
Female 40-59	1	125989	3	126492	0,11	8,73				
Female > 60	1	491336	0	133851	0,00	#				
Female_all age	**2**	**688687**	**9**	**446483**	**0,22**		**9,13**	**1,10**	**32,96**	*
Female_< 40	**0**	**71362**	**6**	**186140**	**0,10**		**0,00**	**0,00**	**35,33**	*
Female_> 40	**2**	**617325**	**3**	**260343**	**0,11**		**17,45**	**2,09**	**63,00**	*
Total_all age	**3**	**1299161**	**25**	**866062**	**0,74**		**4,07**	**0,84**	**11,90**	*
AstraZeneca- dose 2										
Male 0-19	0	1153	1	86036	0,00	0,00				
Male 20-39	0	24535	6	94328	0,06	0,00				
Male 40-59	0	45764	7	119311	0,10	0,00				
Male > 60	0	497004	2	119904	0,32	0,00				
Male_all age	**0**	**568456**	**16**	**419579**	**0,48**		**0,00**	**0,00**	**7,67**	*
Male_< 40	**0**	**25688**	**7**	**180364**	**0,06**		**0,00**	**0,00**	**61,12**	*
Male_> 40	**0**	**542768**	**9**	**239215**	**0,42**		**0,00**	**0,00**	**8,77**	*
Female 0-19	0	3012	2	83117	0,00	0,00				
Female 20-39	0	62344	4	103023	0,09	0,00				
Female 40-59	0	116327	3	126492	0,11	0,00				
Female > 60	0	456939	0	133851	0,00	n.a.				
Female_all age	**0**	**638622**	**9**	**446483**	**0,20**		**0,00**	**0,00**	**18,32**	*
Female_< 40	**0**	**65356**	**6**	**186140**	**0,10**		**0,00**	**0,00**	**38,59**	*
Female_> 40	**0**	**573266**	**3**	**260343**	**0,11**		**0,00**	**0,00**	**34,87**	*
Total_all age	**0**	**1207078**	**25**	**866062**	**0,68**		**0,00**	**0,00**	**5,40**	*

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Pericarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
PFIZER - dose 1										
Male 0-19	0	509863	4	86035	0,32	0,00				
Male 20-39	5	1194366	28	94317	4,86	1,03				
Male 40-59	4	1404275	40	119294	6,45	0,62				
Male > 60	1	1496898	41	119887	7,01	0,14				
Male_all age	**10**	**4605402**	**113**	**419533**	**18,64**		**0,54**	**0,26**	**0,99**	*
Male_< 40	**5**	**1704229**	**32**	**180352**	**5,18**		**0,96**	**0,31**	**2,25**	*
Male_> 40	**5**	**2901173**	**81**	**239181**	**13,46**		**0,37**	**0,12**	**0,87**	*
Female 0-19	1	494868	4	83116	0,33	3,07				
Female 20-39	6	1201284	11	103022	1,76	3,41				
Female 40-59	9	1383693	15	126485	2,25	4,00				
Female > 60	2	1740728	25	133840	4,45	0,45				
Female_all age	**18**	**4820573**	**55**	**446463**	**8,79**		**2,05**	**1,20**	**3,13**	
Female_< 40	**7**	**1696152**	**15**	**186138**	**2,08**		**3,36**	**1,35**	**6,92**	*
Female_> 40	**11**	**3124421**	**40**	**260325**	**6,70**		**1,64**	**0,80**	**2,78**	
Total_all age	**28**	**9425975**	**168**	**865996**	**27,43**		**1,02**	**0,67**	**1,44**	
PFIZER - dose 2										
Male 0-19	1	439788	4	86035	0,28	3,57				
Male 20-39	9	1062432	28	94317	4,32	2,08				
Male 40-59	4	1306239	40	119294	6,00	0,67				
Male > 60	4	1468738	41	119887	6,88	0,58				
Male_all age	**18**	**4277197**	**113**	**419533**	**17,48**		**1,03**	**0,60**	**1,57**	
Male_< 40	**10**	**1502220**	**32**	**180352**	**4,60**		**2,17**	**1,04**	**4,00**	*
Male_> 40	**8**	**2774977**	**81**	**239181**	**12,88**		**0,62**	**0,27**	**1,22**	*
Female 0-19	1	426627	4	83116	0,28	3,56				
Female 20-39	5	1075907	11	103022	1,57	3,18				
Female 40-59	5	1290937	15	126485	2,10	2,38				
Female > 60	1	1708172	25	133840	4,37	0,23				
Female_all age	**12**	**4501643**	**55**	**446463**	**8,32**		**1,44**	**0,73**	**2,39**	
Female_< 40	**6**	**1502534**	**15**	**186138**	**1,85**		**3,23**	**1,19**	**7,04**	*
Female_> 40	**6**	**2999109**	**40**	**260325**	**6,47**		**0,93**	**0,34**	**2,02**	*
Total_all age	**30**	**8778840**	**168**	**865996**	**25,80**		**1,16**	**0,78**	**1,63**	
PFIZER - dose 3 (booster)										
Male 0-19	1	51395	4	86035	0,03	30,55				
Male 20-39	6	674270	28	94317	2,74	2,19				
Male 40-59	1	483724	40	119294	2,22	0,45				
Male > 60	0	395378	41	119887	1,85	0,00				
Male_all age	**8**	**1604767**	**113**	**419533**	**6,85**		**1,17**	**0,50**	**2,30**	*
Male_< 40	**7**	**725665**	**32**	**180352**	**2,77**		**2,52**	**1,01**	**5,20**	*
Male_> 40	**1**	**879102**	**81**	**239181**	**4,07**		**0,25**	**0,01**	**1,37**	*
Female 0-19	0	58543	4	83116	0,04	0,00				
Female 20-39	4	720501	11	103022	1,05	3,80				
Female 40-59	1	608934	15	126485	0,99	1,01				
Female > 60	0	522902	25	133840	1,34	0,00				
Female_all age	**5**	**1910880**	**55**	**446463**	**3,42**		**1,46**	**0,47**	**3,41**	*
Female_< 40	**4**	**779044**	**15**	**186138**	**1,09**		**3,66**	**1,00**	**9,37**	*
Female_> 40	**1**	**1131836**	**40**	**260325**	**2,33**		**0,43**	**0,01**	**2,39**	*
Total_all age	**13**	**3515647**	**168**	**865996**	**10,27**		**1,27**	**0,34**	**1,53**	

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Pericarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	***Obs/Exp (# O > E=0)***	**SMR**	***95% CI SMR (* O<10 with poisson table)***		
MODERNA - dose 1										
Male 0-19	0	11931	4	86035	0,01	0,00				
Male 20-39	1	146092	28	94317	0,59	1,68				
Male 40-59	2	275732	40	119294	1,27	1,58				
Male > 60	0	50432	41	119887	0,24	0,00				
Male_all age	**3**	**484187**	**113**	**419533**	**2,10**		**1,43**	**0,29**	**4,17**	*
Male_< 40	**1**	**158023**	**32**	**180352**	**0,60**		**1,66**	**0,04**	**9,26**	*
Male_> 40	**2**	**326164**	**81**	**239181**	**1,50**		**1,33**	**0,11**	**3,88**	*
Female 0-19	0	12180	4	83116	0,01	0,00				
Female 20-39	0	163151	11	103022	0,24	0,00				
Female 40-59	1	268645	15	126485	0,44	2,29				
Female > 60	0	53792	25	133840	0,14	0,00				
Female_all age	**1**	**497768**	**55**	**446463**	**0,82**		**1,22**	**0,03**	**6,79**	*
Female_< 40	**0**	**175331**	**15**	**186138**	**0,25**		**0,00**	**0,00**	**14,96**	*
Female_> 40	**1**	**322437**	**40**	**260325**	**0,57**		**1,74**	**0,04**	**9,70**	*
Total_all age	**4**	**981955**	**168**	**865996**	**2,93**		**1,37**	**0,37**	**3,50**	*
MODERNA - dose 2										
Male 0-19	0	10072	4	86035	0,01	0,00				
Male 20-39	6	131542	28	94317	0,53	11,22				
Male 40-59	1	258684	40	119294	1,19	0,84				
Male > 60	1	47523	41	119887	0,22	4,49				
Male_all age	**8**	**447821**	**113**	**419533**	**1,95**		**4,10**	**1,77**	**8,07**	*
Male_< 40	**6**	**141614**	**32**	**180352**	**0,54**		**11,08**	**4,06**	**24,12**	*
Male_> 40	**2**	**306207**	**81**	**239181**	**1,41**		**1,42**	**0,17**	**5,12**	*
Female 0-19	0	10526	4	83116	0,04	0,00				
Female 20-39	0	148465	11	103022	1,22	0,00				
Female 40-59	0	251082	15	126485	2,28	0,00				
Female > 60	0	50029	25	133840	0,72	0,00				
Female_all age	**0**	**460102**	**55**	**446463**	**4,26**		**0,00**	**0,00**	**0,87**	*
Female_< 40	**0**	**158991**	**15**	**186138**	**1,25**		**0,00**	**0,00**	**2,94**	*
Female_> 40	**0**	**301111**	**40**	**260325**	**3,00**		**0,00**	**0,00**	**1,23**	*
Total_all age	**8**	**907923**	**168**	**865996**	**6,21**		**1,29**	**0,56**	**2,54**	*
MODERNA - dose 3 (booster)										
Male 0-19	0	111	4	86035	0,00	0,00				
Male 20-39	0	1638	28	94317	0,01	0,00				
Male 40-59	3	773249	40	119294	3,55	0,84				
Male > 60	2	1324838	41	119887	6,21	0,32				
Male_all age	**5**	**2099836**	**113**	**419533**	**9,77**		**0,51**	**0,17**	**1,20**	*
Male_< 40	**0**	**1749**	**32**	**180352**	**0,01**		**0,00**	**0,00**	**548,13**	*
Male_> 40	**5**	**2098087**	**81**	**239181**	**9,76**		**0,51**	**0,17**	**1,20**	*
Female 0-19	0	134	4	83116	0,00	0,00				
Female 20-39	0	1594	11	103022	0,00	0,00				
Female 40-59	2	687254	15	126485	1,12	1,79				
Female > 60	1	1378989	25	133840	3,53	0,28				
Female_all age	**3**	**2067971**	**55**	**446463**	**4,65**		**0,65**	**0,13**	**1,89**	*
Female_< 40	**0**	**1728**	**15**	**186138**	**0,00**		**0,00**	**0,00**	**1524,92**	*
Female_> 40	**3**	**2066243**	**40**	**260325**	**4,64**		**0,65**	**0,13**	**1,89**	*
Total_all age	**8**	**4167807**	**168**	**865996**	**14,41**		**0,56**	**0,24**	**1,09**	*

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Pericarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
JANSSEN - dose 1										
Male 0-19	0	24994	4	86035	0,02	0,00				
Male 20-39	3	193474	28	94317	0,79	3,81				
Male 40-59	2	200009	40	119294	0,92	2,18				
Male > 60	0	7656	41	119887	0,04	0,00				
Male_all age	**5**	**426133**	**113**	**419533**	**1,76**		**2,85**	**0,92**	**6,64**	*
Male_< 40	**3**	**218468**	**32**	**180352**	**0,80**		**3,74**	**0,77**	**10,93**	*
Male_> 40	**2**	**207665**	**81**	**239181**	**0,95**		**2,10**	**0,25**	**7,56**	*
Female 0-19	0	16224	4	83116	0,01	0,00				
Female 20-39	0	123803	11	103022	0,18	0,00				
Female 40-59	0	167404	15	126485	0,27	0,00				
Female > 60	0	6808	25	133840	0,02	0,00				
Female_all age	**0**	**314239**	**55**	**446463**	**0,48**		**0,00**	**0,00**	**7,67**	*
Female_< 40	**0**	**140027**	**15**	**186138**	**0,19**		**0,00**	**0,00**	**19,24**	*
Female_> 40	**0**	**174212**	**40**	**260325**	**0,29**		**0,00**	**0,00**	**12,75**	*
Total_all age	**5**	**740372**	**168**	**865996**	**2,24**		**2,23**	**0,72**	**5,21**	*

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Pericarditis										
Risk period / TTO 5 days	**N reports Observed**	**N persons vaccine exposed**	**N Events - 1 yr PHARMO**	**N pyrs PHARMO**	**Expected**	**Obs/Exp** *(# O > E=0)*	**SMR**	**95% CI SMR** *(* O<10 with poisson table)*		
AstraZeneca - dose 1										
Male 0-19	0	1286	4	86035	0,00	0,00				
Male 20-39	0	26853	28	94317	0,11	0,00				
Male 40-59	0	49254	40	119294	0,23	0,00				
Male > 60	0	533206	41	119887	2,50	0,00				
Male_all age	**0**	**610599**	**113**	**419533**	**2,83**		**0,00**	**0,00**	**1,30**	*
Male_< 40	**0**	**28139**	**32**	**180352**	**0,11**		**0,00**	**0,00**	**33,54**	*
Male_> 40	**0**	**582460**	**81**	**239181**	**2,72**		**0,00**	**0,00**	**1,35**	*
Female 0-19	0	3263	4	83116	0,00	0,00				
Female 20-39	0	68293	11	103022	0,10	0,00				
Female 40-59	0	126252	15	126485	0,21	0,00				
Female > 60	1	491513	25	133840	1,26	0,80				
Female_all age	**1**	**689321**	**55**	**446463**	**1,56**		**0,64**	**0,02**	**3,56**	*
Female_< 40	**0**	**71556**	**15**	**186138**	**0,10**		**0,00**	**0,00**	**36,16**	*
Female_> 40	**1**	**617765**	**40**	**260325**	**1,46**		**0,68**	**0,02**	**3,81**	*
Total_all age	**1**	**1299920**	**168**	**865996**	**4,40**		**0,23**	**0,01**	**1,27**	*
AstraZeneca- dose 2										
Male 0-19	0	1154	4	86035	0,00	0,00				
Male 20-39	0	24569	28	94317	0,10	0,00				
Male 40-59	0	45812	40	119294	0,21	0,00				
Male > 60	2	497001	41	119887	2,33	0,86				
Male_all age	**2**	**568536**	**113**	**419533**	**2,64**		**0,76**	**0,09**	**2,74**	*
Male_< 40	**0**	**25723**	**32**	**180352**	**0,10**		**0,00**	**0,00**	**36,66**	*
Male_> 40	**2**	**542813**	**81**	**239181**	**2,54**		**0,79**	**0,09**	**2,84**	*
Female 0-19	0	3022	4	83116	0,00	0,00				
Female 20-39	0	62516	11	103022	0,09	0,00				
Female 40-59	0	116578	15	126485	0,19	0,00				
Female > 60	0	457037	25	133840	1,17	0,00				
Female_all age	**0**	**639153**	**55**	**446463**	**1,45**		**0,00**	**0,00**	**2,54**	*
Female_< 40	**0**	**65538**	**15**	**186138**	**0,09**		**0,00**	**0,00**	**39,49**	*
Female_> 40	**0**	**573615**	**40**	**260325**	**1,36**		**0,00**	**0,00**	**2,72**	*
Total_all age	**2**	**1207689**	**168**	**865996**	**4,09**		**0,49**	**0,06**	**1,76**	*