

Supplementary to “Venous Thromboembolism following Two Doses of COVID-19 mRNA Vaccines in the US Population, 2020-2022”

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Figure S1: Flow chart of the venous thromboembolism cases showing how data from Vaccine Adverse Event Reporting System were used for Self-controlled Case Series analysis

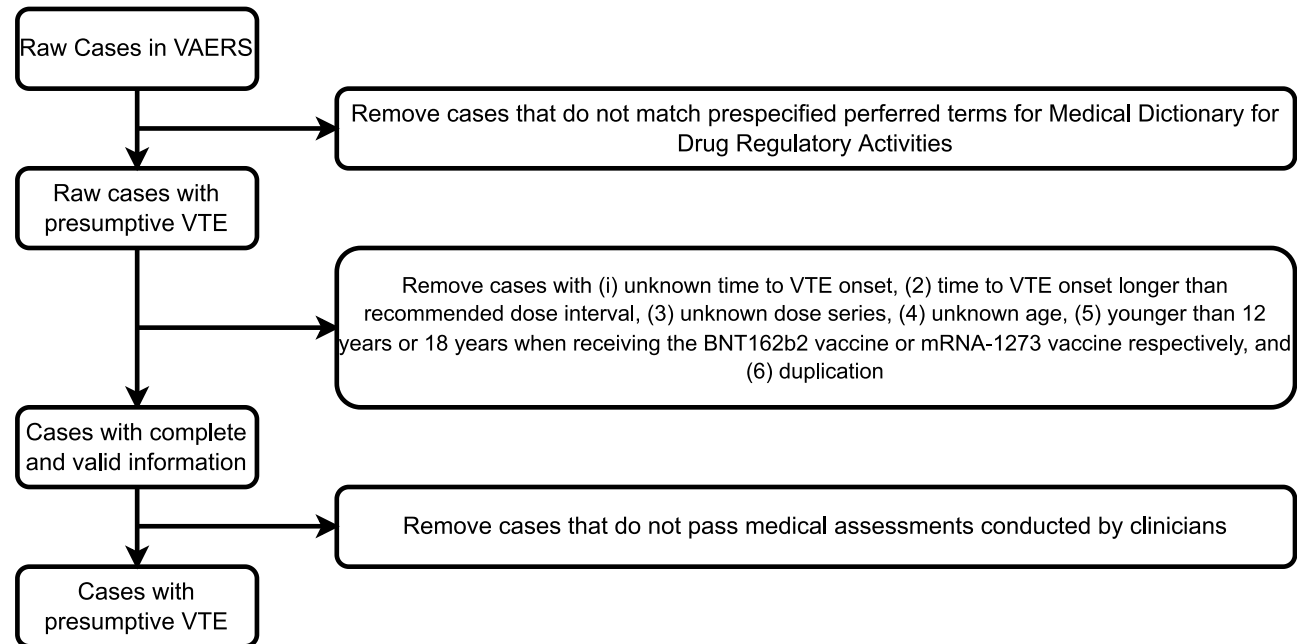


Figure S2: Visualization of the modified SCCS design using BNT162b2 vaccine as an example. Risk periods (0, 1–7, 8–14 days after COVID-19 mRNA vaccination) and the baseline periods (15–21 days after exposure) are shown. The reference period ends at day 21 as the recommended dose interval is 21 days for BNT162b2 vaccine.

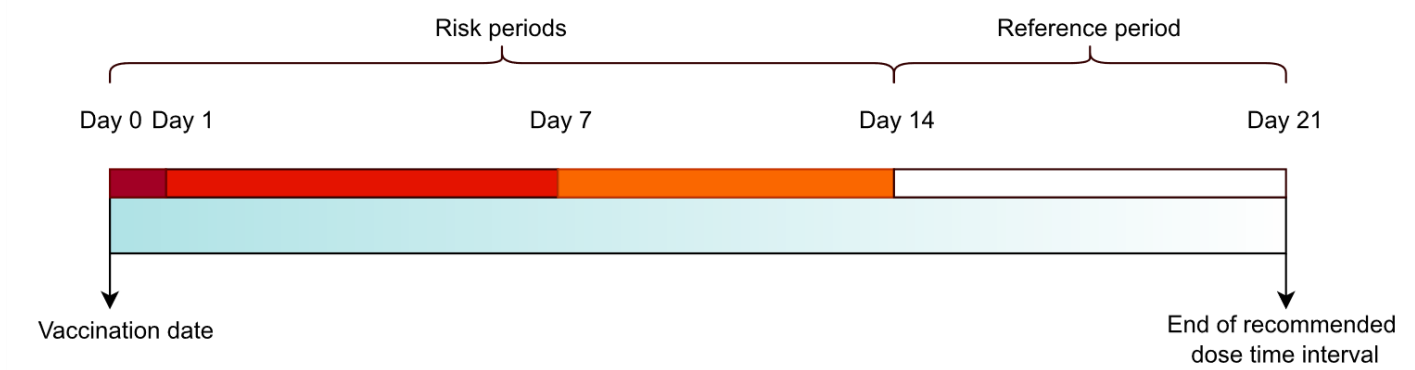


Table S1: Ratio of relative incidences and relative incidences of venous thromboembolism following the first and second dose of COVID-19 mRNA vaccination among females, stratified by age

		No. of Events ^a		RI after dose 1 (95% CI)	RI after dose 2 (95% CI)	Ratio of RIs (95% CI) ^b
		After dose 1	After dose 2			
Female, age>=60						
mRNA-1273						
	No. of days after vaccination, d					
0 ^c	11	13	0.81 (0.24, 2.66)	0.95 (0.29, 3.08)	1.18 (0.46, 3.02)	
1-7	48	51	0.69 (0.28, 1.75)	0.74 (0.3, 1.86)	1.06 (0.57, 1.98)	
8-14	29	24	0.76 (0.38, 1.5)	0.63 (0.31, 1.26)	0.83 (0.4, 1.71)	
15-28	30	28s	1 [Reference]	1 [Reference]	1 [Reference]	
BNT162b2						
	No. of days after vaccination, d					
0 ^c	10	16	0.59 (0.12, 2.85)	0.52 (0.12, 2.28)	0.89 (0.29, 2.68)	
1-7	47	44	0.67 (0.19, 2.35)	0.35 (0.11, 1.13)	0.52 (0.22, 1.25)	
8-14	24	33	0.9 (0.37, 2.3)	0.69 (0.32, 1.52)	0.76 (0.3, 1.95)	
15-21	8	15	1 [Reference]	1 [Reference]	1 [Reference]	
Female, age<60						
mRNA-1273						
	No. of days after vaccination, d					
0 ^c	18	11	1.39 (0.44, 4.47)	1.75 (0.49, 6.22)	1.26 (0.49, 3.25)	
1-7	62	59	0.93 (0.37, 2.36)	1.82 (0.68, 4.95)	1.96 (0.99, 3.87)	
8-14	32	29	0.83 (0.42, 1.64)	1.55 (0.73, 3.39)	1.87 (0.87, 4.02)	
15-28	33	14	1 [Reference]	1 [Reference]	1 [Reference]	

BNT162b2						
		No. of days after vaccination, d				
0 ^c	21	23	0.70 (0.22, 2.22)	1.32 (0.4, 4.41)	1.9 (0.8, 4.52)	
1-7	87	95	0.64 (0.26, 1.61)	1.21 (0.46, 3.24)	1.89 (0.94, 3.81)	
8-14	37	33	0.62 (0.33, 1.19)	0.96 (0.47, 2.04)	1.55 (0.7, 3.41)	
15-21	22	12	1 [Reference]	1 [Reference]	1 [Reference]	

Abbreviations: CI, confidence interval; RI, relative incidence

^a Our analysis excluded (i) reports whose time to symptom onset are unknown or exceed the recommended dose interval to ensure reports were related to a single dose, (ii) reports with unknown dose series, (iii) reports with unknown age, younger than 12 years or 18 years when receiving the BNT162b2 vaccine or mRNA-1273 vaccine respectively, and (iv) duplicated reports.

^b The ratios are estimated by dividing the relative incidences after dose 2 by the relative incidences after dose 1.

^c Zero refers to the day of vaccination.

0 ^c	21	23	0.70 (0.22, 2.22)	1.32 (0.4, 4.41)	1.9 (0.8, 4.52)
1-7	87	95	0.64 (0.26, 1.61)	1.21 (0.46, 3.24)	1.89 (0.94, 3.81)
8-14	37	33	0.62 (0.33, 1.19)	0.96 (0.47, 2.04)	1.55 (0.7, 3.41)
15-21	22	12	1 [Reference]	1 [Reference]	1 [Reference]

21

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22

12

1 [Reference]

1 [Reference]

1 [Reference]

^a Our analysis excluded (i) reports whose time to symptom onset are unknown or exceed the recommended dose interval to ensure reports were related to a single dose, (ii) reports with unknown dose series, (iii) reports with unknown age, younger than 12 years or 18 years when receiving the BNT162b2 vaccine or mRNA-1273 vaccine respectively, and (iv) duplicated reports.

^cZero refers to the day of vaccination.

Table S2: Ratio of relative incidences and relative incidences of venous thromboembolism following the first and second dose of COVID-19 mRNA vaccination among males, stratified by age

		No. of Events ^a		RI after dose 1 (95% CI)	RI after dose 2 (95% CI)	Ratio of RIs (95% CI) ^b
		After dose 1	After dose 2			
Male, age>=60						
mRNA-1273						
No. of days after vaccination, d						
0 ^c	7	4	0.6 (0.15, 2.39)	0.20 (0.04, 0.84)	0.33 (0.08, 1.31)	
1-7	55	74	1.04 (0.37, 3.00)	0.81 (0.30, 2.17)	0.78 (0.38, 1.60)	
8-14	33	21	1.41 (0.65, 3.16)	0.52 (0.24, 1.11)	0.37 (0.16, 0.85)	
15-28	15	26	1 [Reference]	1 [Reference]	1 [Reference]	
BNT162b2						
No. of days after vaccination, d						
0 ^c	10	12	0.63 (0.14, 2.81)	0.28 (0.06, 1.17)	0.44 (0.14, 1.37)	
1-7	62	53	0.70 (0.21, 2.34)	0.42 (0.14, 1.28)	0.60 (0.26, 1.41)	
8-14	36	16	0.57 (0.23, 1.49)	0.68 (0.32, 1.45)	1.18 (0.45, 3.11)	
15-21	16	9	1 [Reference]	1 [Reference]	1 [Reference]	
Male, age<60						
mRNA-1273						
No. of days after vaccination, d						
0 ^c	14	3	1.36 (0.38, 4.84)	0.51 (0.09, 2.48)	0.38 (0.09, 1.51)	
1-7	45	47	0.83 (0.31, 2.30)	1.53 (0.54, 4.47)	1.84 (0.90, 3.79)	
8-14	32	22	1.00 (0.49, 2.07)	1.22 (0.54, 2.79)	1.21 (0.54, 2.71)	
15-28	27	17	1 [Reference]	1 [Reference]	1 [Reference]	
BNT162b2						

No. of days after vaccination, d					
0 ^c	4	8	0.18 (0.03, 0.84)	0.42 (0.1, 1.76)	2.35 (0.60, 9.20)
1-7	61	63	0.60 (0.21, 1.75)	0.73 (0.25, 2.16)	1.22 (0.58, 2.54)
8-14	30	24	0.67 (0.32, 1.40)	0.63 (0.29, 1.38)	0.94 (0.41, 2.18)
15-21	17	17	1 [Reference]	1 [Reference]	1 [Reference]
Abbreviations: CI, confidence interval; RI, relative incidence					
^a Our analysis excluded (i) reports whose time to symptom onset are unknown or exceed the recommended dose interval to ensure reports were related to a single dose, (ii) reports with unknown dose series, (iii) reports with unknown age, younger than 12 years or 18 years when receiving the BNT162b2 vaccine or mRNA-1273 vaccine respectively, and (iv) duplicated reports.					
^b The ratios are estimated by dividing the relative incidences after dose 2 by the relative incidences after dose 1.					
^c Zero refers to the day of vaccination.					

Table S3: Ratio of relative incidences and relative incidences of venous thromboembolism following the first and second dose of COVID-19 mRNA vaccination, assuming 80% of reports can meet the Brighton Collaboration Criteria ultimately^a

		No. of Events		RI following dose 1 (95% CI)	RI following dose 2 (95% CI)	Ratio of RIs (95% CI)
		After dose 1	After dose 2			
mRNA-1273						
	No. of days after vaccination, d					
	0 ^c	45	27	1.31 (0.67, 2.58)	1.08 (0.52, 2.23)	0.82 (0.47, 1.45)
	1-7	163	188	0.91 (0.54, 1.55)	1.44 (0.84, 2.49)	1.59 (1.10, 2.29)
	8-14	108	79	1.02 (0.70, 1.50)	1.03 (0.68, 1.57)	1.01 (0.66, 1.53)
	15-28	89	66	1 [Reference]	1 [Reference]	1 [Reference]
BNT162b2						
	No. of days after vaccination, d					
	0 ^c	36	48	0.62 (0.29, 1.34)	0.81 (0.38, 1.72)	1.31 (0.74, 2.32)
	1-7	198	225	0.75 (0.41, 1.35)	0.83 (0.46, 1.51)	1.12 (0.73, 1.70)
	8-14	82	102	0.68 (0.44, 1.04)	0.83 (0.55, 1.26)	1.22 (0.76, 1.96)
	15-21	49	46	1 [Reference]	1 [Reference]	1 [Reference]
Abbreviations: CI, confidence interval; RI, relative incidence						
^a Our analysis excluded (i) reports whose time to symptom onset are unknown or exceed the recommended dose interval to ensure reports were related to a single dose, (ii) reports with unknown dose series, (iii) reports with unknown age, younger than 12 years or 18 years when receiving the BNT162b2 vaccine or mRNA-1273 vaccine, respectively, and (iv) duplicated reports.						
^b The ratios are estimated by dividing the relative incidences following dose 2 by the relative incidences following dose 1.						
^c Zero refers to the day of vaccination.						

Table S4: Ratio of relative incidences and relative incidences of venous thromboembolism following the first and second dose of COVID-19 mRNA vaccination, after excluding all deceased patients^a

		No. of Events		RI following dose 1 (95% CI)	RI following dose 2 (95% CI)	Ratio of RIs (95% CI)
		After dose 1	After dose 2			
mRNA-1273						
	No. of days after vaccination, d					
	0 ^c	45	27	1.31 (0.67, 2.58)	1.08 (0.52, 2.23)	0.82 (0.47, 1.45)
	1-7	163	188	0.91 (0.54, 1.55)	1.44 (0.84, 2.49)	1.59 (1.10, 2.29)
	8-14	108	79	1.02 (0.70, 1.50)	1.03 (0.68, 1.57)	1.01 (0.66, 1.53)
	15-28	89	66	1 [Reference]	1 [Reference]	1 [Reference]
BNT162b2						
	No. of days after vaccination, d					
	0 ^c	36	48	0.62 (0.29, 1.34)	0.81 (0.38, 1.72)	1.31 (0.74, 2.32)
	1-7	198	225	0.75 (0.41, 1.35)	0.83 (0.46, 1.51)	1.12 (0.73, 1.70)
	8-14	82	102	0.68 (0.44, 1.04)	0.83 (0.55, 1.26)	1.22 (0.76, 1.96)
	15-21	49	46	1 [Reference]	1 [Reference]	1 [Reference]
Abbreviations: CI, confidence interval; RI, relative incidence						
^a Our analysis excluded (i) reports whose time to symptom onset are unknown or exceed the recommended dose interval to ensure reports were related to a single dose, (ii) reports with unknown dose series, (iii) reports with unknown age, younger than 12 years or 18 years when receiving the BNT162b2 vaccine or mRNA-1273 vaccine, respectively, and (iv) duplicated reports.						
^b The ratios are estimated by dividing the relative incidences following dose 2 by the relative incidences following dose 1.						
^c Zero refers to the day of vaccination.						