

# **Blood clots and bleeding events following BNT162b2 and ChAdOx1 nCoV-19 vaccine: an analysis of European data**

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## Keywords for download of SAEs single case reports

For analyses concerning the number of reported SAEs indicating venous thrombosis and bleeding, we used the below-mentioned keywords. If a keywords indicated both venous and arterial thrombosis was taken: 1 “cerebral thrombosis”, 2 “cerebral vascular occlusion”, 3 “cerebral venous sinus thrombosis”, 4 “cerebral venous thrombosis”, 5 “superior sagittal sinus thrombosis”, 6 “transverse sinus thrombosis”, 7 “splenic vein occlusion”, 8 “splenic vein thrombosis”, 9 “mesenteric vein thrombosis”, 10 “mesenteric venous occlusion”, 11 “visceral venous thrombosis”, 12 “hepatic vein thrombosis”, 13 “portal vein occlusion”, 14 “portal vein thrombosis”, 15 “portosplenomesenteric venous thrombosis”, 16 “splenic thrombosis”, 17 “thrombosis mesenteric vessel”, 18 “hepatic vascular thrombosis”, 19 “autoimmune heparin-induced thrombocytopenia”, 20 “heparin-induced thrombocytopenia”, 21 “hypocoagulable state”, 22 “immune thrombocytopenia”, 23 “platelet disorder”, 24 “spontaneous heparin-induced thrombocytopenia syndrome”, 25 “thrombocytopenia”, 26 “severe fever with thrombocytopenia syndrome”, 27 “coagulopathy”, 28 “haemorrhagic diathesis”, 29 “increased tendency to bruise”, 30 “spontaneous haematoma”, 31 “spontaneous haemorrhage”, 32 “thrombocytopenic purpura”, 33 “thrombotic thrombocytopenic purpura”, 34 “mucosal haemorrhage”, 35 “pulmonary haemorrhage”, 36 “haemorrhage subcutaneous”, 37 “haematoma”, 38 “haemorrhage”, 39 “haemorrhagic infarction”, 40 “internal haemorrhage”, 41 “venous haemorrhage”, 42 “diarrhoea haemorrhagic”, 43 “gastric haemorrhage”, 44 “gastrointestinal haemorrhage”, 45 “haematemesis”, 46 “haematochezia”, 47 “haemoperitoneum”, 48 “intestinal haemorrhage”, 49 “intra-abdominal haematoma”, 50 “melaena”, 51 “mesenteric haemorrhage”, 52 “retroperitoneal haemorrhage”, 53 “small intestinal haemorrhage”, 54 “upper gastrointestinal haemorrhage”, 55 “hepatic haemorrhage”, 56 “brain stem haemorrhage”, 57 “cerebellar haematoma”, 58 “cerebellar haemorrhage”, 59 “cerebral haematoma”, 60 “cerebral haemorrhage”, 61 “haemorrhage intracranial”, 62 “haemorrhagic cerebral infarction”, 63 “haemorrhagic stroke”, 64 “haemorrhagic transformation stroke”, 65 “intracranial haematoma”, 66 “intraventricular haemorrhage”, 67 “spinal cord haemorrhage”, 68 “spinal epidural haemorrhage”, 69 “subarachnoid haemorrhage”, 70 “thalamus haemorrhage”, 71 “hypercoagulation”, 72 “thrombotic microangiopathy”, 73 “renal vascular thrombosis”, 74 “renal vein thrombosis”, 75 “axillary vein thrombosis”, 76 “deep vein thrombosis”, 77 “jugular vein thrombosis”, 78 “pelvic venous thrombosis”, 79 “subclavian vein thrombosis”, 80 “thrombosis”, 81 “vascular occlusion”, 82 “vena cava thrombosis”, 83 “venous occlusion”, 84 “venous thrombosis”, 85 “venous thrombosis limb”, 86 “disseminated intravascular coagulation”, 87 “pulmonary artery thrombosis”, 88 “pulmonary embolism”, 89 “pulmonary thrombosis”, 90 “basal ganglia stroke”, 91 “brain stem stroke”, 92 “cerebellar stroke”, 93 “cerebrovascular accident”, 94 “cerebrovascular disorder”, and 95 “lacunar infarction”.

For the analyses reported in Table 1 we used the above-mentioned keywords that were placed in 10 categories linked to thrombocytopenia/bleeding and blood clots. **Cerebral venous thrombosis:** keywords 1 to 6; **splanchnic vein thrombosis:** keywords 7 to 18; **thrombocytopenia:** keywords 19 to 26; **other bleeding events:** keywords 27 to 41; **gastrointestinal bleeding:** keywords 41 to 55; **cerebral bleeding:** keywords 56 to 70; **other venous thrombosis:** keywords 71 to 85; **disseminated intravascular coagulation:** keyword 86; **pulmonary thromboembolism:** keywords 87 to 89; **ischemic stroke:** keywords 90 to 95.

**Table S1.** Gender distribution of vaccines administered doses in Europe

<b>European Countries</b>	<b>Doses administered in female</b>	<b>Doses administered in male</b>	<b>% of doses administered in female</b>	<b>% of doses administered in male</b>	<b>Date of the report</b>	<b>Link to the data source</b>
<b>Belgium</b>	2,108,809	1,323,014	61.45	38.55	25 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>Danmark</b>	1,078,138	723,239	59.85	40.15	25 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>France</b>	11,113,504	8,384,058	57.00	43.00	24 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>Germany</b>	7,273,370	4,091,271	64.00	36.00	24 <sup>th</sup> March 2021	<a href="#">LINK</a>
<b>Italy</b>	10,344,476	7,665,571	57.44	42.56	26 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>Norway</b>	796,434	638,623	55.50	44.50	26 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>Poland</b>	6,150,000	4,185,000	59.51	40.49	26 <sup>th</sup> April 2021	<a href="#">LINK</a>
<b>Spain</b>	4,167,439	1,953,649	68.08	31.92	21 <sup>st</sup> March 2021	<a href="#">LINK</a>
<b>Total of doses administered</b>	43,032,170	28,964,425	59.78	40.22		

**Table S2.** Number of vaccines administered doses in Europe

	<b>BNT162b2</b>							<b>ChAdOx1 nCoV-19</b>						
	<b>Total</b>							<b>Total</b>						
<b>W12 whole Europe<sup>a</sup></b>	52,053,994							13,732,385						
<b>W14 whole Europe<sup>b</sup></b>	68,500,787							19,970,905						
<b>whole Europe<sup>c</sup></b>	71,210,981							20,869,192						
	<b>Total</b>	<b>18-24y</b>	<b>25-49y</b>	<b>50-59y</b>	<b>60-69y</b>	<b>70-79y</b>	<b>80+ y</b>	<b>Total</b>	<b>18-24y</b>	<b>25-49y</b>	<b>50-59y</b>	<b>60-69y</b>	<b>70-79y</b>	<b>80+ y</b>
<b>European countries that provides age groups data (W12)<sup>d</sup> (%)</b>	23,294,890 (44.8%)	550,590	4,847,056	2,790,467	2,283,500	3,713,738	9,109,539	6,221,518 (45.3%)	198,906	2,108,123	1,418,311	1,449,706	711,104	335,368
<b>European countries that provides age groups data (W14)<sup>d</sup> (%)</b>	30541280 (44.6%)	626,808	5,520,384	3,316,348	3,312,870	6,149,992	11,614,878	8,875,503 (44.4%)	253,292	2,551,867	1,672,355	2,317,087	1,632,715	448,187

<sup>a</sup> Data downloaded from European Centre for Disease Prevention and Control (ECDC) European data-bank “Vaccine rollout overview week 12<sup>th</sup>,2021” ([LINK](#))

<sup>b</sup> Data downloaded from European Centre for Disease Prevention and Control (ECDC) European data-bank “Vaccine rollout overview week 14<sup>th</sup>,2021” ([LINK](#))

<sup>c</sup> Data downloaded from European Centre for Disease Prevention and Control (ECDC) European data-bank (COVID-19 Vaccine Tracker tool) on 16<sup>th</sup> of April 2021

<sup>d</sup> Data from the 21 out 30 European Countries that have provided to European Centre for Disease Prevention and Control (ECDC) European data-bank the number of vaccines administered doses in the age groups

**Table S3.** Number of individual patient reports of AE reported in the EudraVigilance database

Reaction groups:	BNT162b2		ChAdOx1 nCoV-19	
	severe AEs	non-severe AEs	severe AEs	non-severe AEs
Blood and lymphatic system disorders	3250	7941	3557	1762
Cardiac disorders	4871	2501	5201	2173
Ear and labyrinth disorders	1993	2190	3495	1516
Eye disorders	2641	1988	5764	2158
Gastrointestinal disorders	12437	20893	35666	20807
General disorders and administration site conditions	28860	74953	77748	63294
Immune system disorders	2805	533	1539	298
Infections and infestations	6981	3179	8208	2423
Injury, poisoning and procedural complications	2918	1032	2849	1492
Investigations	4110	3485	5527	4271
Metabolism and nutrition disorders	1668	896	5457	1520
Musculoskeletal and connective tissue disorders	13947	39767	41336	41186
Nervous system disorders	23413	42332	67785	44088
Psychiatric disorders	3376	2632	7340	2174
Renal and urinary disorders	726	212	1293	452
Reproductive system and breast disorders	570	424	1154	922
Respiratory, thoracic and mediastinal disorders	8860	5094	11841	3983
Skin and subcutaneous tissue disorders	7533	8638	16731	6437
Vascular disorders	4941	3279	6198	2508

**Table S4.** Decisions of EMA and European countries concerning approval of BNT162b2 and ChAdOx1 nCoV-19 vaccines and their administration to people of different ages and different target groups

		Recommendation for vulnerable and fragile <sup>a</sup>	January 2021	February 2021	March 2021	April 2021	May 2021
<b>BNT162b2</b>	people under age of 55 or 65 <sup>b</sup>						
	people over age of 55 or 60 <sup>c</sup>						
<b>ChAdOx1 nCoV-19</b>	people under age of 55 or 65 <sup>c</sup>						
	people over age of 55 or 60 <sup>d</sup>						

<sup>a</sup> European Countries recommendations of specific COVID-19 vaccine products for particular target groups (vulnerable and fragile)

European countries policy, update of 29 March 2021: [LINK](#)

European countries policy, update of 6 May 2021: [LINK](#)

Italian statment, update 9 February 2021: [LINK](#)

Italian statment, update 22 February 2021: [LINK](#)

<sup>b</sup> 21 December 2020: approved by EMA for over 18 people

EMA statment: [LINK](#)

<sup>c</sup> 29 January 2021: approved by EMA for over 18 people, but restricted to 18-54 or 18-64 from European Countries

EMA statment: [LINK](#)

German statment, update 29 January: [LINK](#)

Italian statment, update 9 February 2021: [LINK](#)

Italian statment, update 22 February 2021: [LINK](#)

<sup>d</sup> 15 March and 7 april 2021: confirmed by EMA for over 18 people, but restricted to 18-54 or 18-64 from European Countries

EMA statment, update 15 March 2021: [LINK](#)

EMA statment, update 7 April 2021: [LINK](#)

European countries policy, update of 29 March 2021: [LINK](#)

European countries policy, update of 6 May 2021: [LINK](#)

**Table S5.** Percentage of vaccines doses administered in each age range in Europe

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>European contries that provides age groups data (W12)<sup>a</sup></b>	2.36%	20.81%	11.98%	9.80%	15.94%	39.11%	3.20%	33.88%	22.80%	23.30%	11.43%	5.39%
<b>European contries that provides age groups data (W14)<sup>a</sup></b>	2.05%	18.08%	10.86%	10.85%	20.14%	38.03%	2.85%	28.75%	18.84%	26.11%	18.40%	5.05%

<sup>a</sup> Data from the 21 out 30 European Countries that have provided to European Centre for Disease Prevention and Control (ECDC) European data-bank the number of vaccines administered doses in the age groups

**Table S6.** Number of individual patient reports of severe AE and death related to thrombocytopenia/bleeding and blood clots<sup>a</sup> reported in the EudraVigilance database

	BNT162b2		ChAdOx1 nCoV-19			
	absolute #	BNT162b2 # per 1,000,000 doses	absolute #	ChAdOx1 nCoV-19 # per 1,000,000 doses	severe AE rate of ChAdOx1 nCoV-19 over the severe AE rate of BNT162b2 AEs	fold risk
severe AEs	2528	35.5	3159	151.4	<b>116</b>	<b>4.3</b>
deaths	313	4.4	273	13.1	<b>9</b>	<b>3.0</b>

<sup>a</sup> The terms used to find the individual patient reports related to the specified event are reported in the Material and methods section



**Table S7.** Number of individual patient reports of severe AE related to cerebral venous thrombosis, splanchnic vein thrombosis, thrombocytopenia, and with one or more AEs related to the above events

cerebral venous thrombosis <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	2 <sup>b</sup>	5	3	<b>10</b>	0	3	4	<b>7</b>	1	<b>18</b>
	females	0	11	3	<b>14</b>	8	2	14	<b>24</b>	2	<b>40</b>
	gender not specified	0	0	0	<b>0</b>	0	0	0	<b>0</b>	0	<b>0</b>
	total severe AEs	2	16	6	<b>24</b>	8	5	18	<b>31</b>	3	<b>58</b>
<b>ChAdOx1 nCoV-19</b>	males	7	19	14	<b>40</b>	6	5	0	<b>11</b>	5	<b>56</b>
	females	10	78	34	<b>122</b>	17	4	2	<b>23</b>	6	<b>151</b>
	gender not specified	0	0	0	<b>0</b>	0	0	0	<b>0</b>	2	<b>2</b>
	total severe AEs	17	97	48	<b>162</b>	23	9	2	<b>34</b>	13	<b>209</b>
splanchnic vein thrombosis <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	0	1	2	<b>3</b>	3	1	1	<b>5</b>	0	<b>8</b>
	females	0	1	1	<b>2</b>	2	1	2	<b>5</b>	0	<b>7</b>
	gender not specified	0	0	0	<b>0</b>	0	0	0	<b>0</b>	0	<b>0</b>
	total severe AEs	0	2	3	<b>5</b>	5	2	3	<b>10</b>	0	<b>15</b>
<b>ChAdOx1 nCoV-19</b>	males	0	9	5	<b>14</b>	8	2	0	<b>10</b>	1	<b>25</b>
	females	2	21	5	<b>28</b>	4	2	0	<b>6</b>	2	<b>36</b>
	gender not specified	0	0	0	<b>0</b>	0	0	0	<b>0</b>	0	<b>0</b>
	total severe AEs	2	30	10	<b>42</b>	12	4	0	<b>16</b>	3	<b>61</b>

thrombocytopenia <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	5	14	15	34	7	25	28	60	4	98
	females	4	41	16	61	10	13	30	53	4	118
	gender not specified	0	0	0	0	0	1	1	2	1	3
	total severe AEs	9	55	31	95	17	39	59	115	9	219
<b>ChAdOx1 nCoV-19</b>	males	9	53	36	98	30	16	5	51	15	164
	females	12	120	73	205	54	24	13	91	19	315
	gender not specified	0	0	0	0	0	1	0	1	6	7
	total severe AEs	21	173	109	303	84	41	18	143	40	486
cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	7 <sup>b</sup>	20	17	44	10	28	33	71	5	120
	females	4	53	20	77	20	16	43	79	6	162
	gender not specified	0	0	0	0	0	1	1	2	1	3
	total severe AEs	11	73	37	121	30	45	77	152	12	285
<b>ChAdOx1 nCoV-19</b>	males	12	64	50	126	37	23	5	65	19	210
	females	18	165	91	274	66	28	15	109	25	408
	gender not specified	0	0	0	0	0	1	0	1	8	9
	total severe AEs	30	229	141	400	103	52	20	175	52	627

<sup>a</sup> The terms used to find the individual patient reports related to the specified event are reported in the Material and methods section

<sup>b</sup> One case happened in a 16 years old boy but is considered in the 18-24 age range

**Table S8.** Number of individual patient reports of death related to cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia

cerebral venous thrombosis <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	0	0	0	0	0	1	0	1	0	1
	females	0	0	1	1	0	0	3	3	0	4
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	0	0	1	1	0	1	3	4	0	5
<b>ChAdOx1 nCoV-19</b>	males	2	10	0	12	2	1	0	3	1	16
	females	2	18	7	27	7	2	0	9	1	37
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	4	28	7	39	9	3	0	12	2	53
splanchnic vein thrombosis <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	0	0	0	0	0	0	1	1	0	1
	females	0	0	1	1	0	0	1	1	0	2
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	0	0	1	1	0	0	2	2	0	3
<b>ChAdOx1 nCoV-19</b>	males	0	1	1	2	1	0	0	1	0	3
	females	0	4	2	6	0	0	0	0	0	6
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	0	5	3	8	1	0	0	1	0	9

thrombocytopenia <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	0	0	3	3	0	7	3	10	1	14
	females	0	1	1	2	1	0	3	4	0	6
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	0	1	4	5	1	7	6	14	1	20
<b>ChAdOx1 nCoV-19</b>	males	1	13	3	17	2	1	0	3	2	22
	females	2	23	14	39	12	4	1	17	2	58
	gender not specified	0	0	0	0	0	0	0	0	1	1
	total severe AEs	3	36	17	56	14	5	1	20	5	81
cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia <sup>a</sup>											
		18-24	25-49	50-59	severe AEs in 18-59	60-69	70-79	80+	severe AEs in 60+	age not specified	total severe AEs
<b>BNT162b2</b>	males	0	0	3	3	0	7	4	11	1	15
	females	0	1	3	4	1	0	7	8	0	12
	gender not specified	0	0	0	0	0	0	0	0	0	0
	total severe AEs	0	1	6	7	1	7	11	19	1	27
<b>ChAdOx1 nCoV-19</b>	males	3	16	4	23	3	2	0	5	3	31
	females	2	27	16	45	14	5	1	20	3	68
	gender not specified	0	0	0	0	0	0	0	0	1	1
	total severe AEs	5	43	20	68	17	7	1	25	7	100

<sup>a</sup> The terms used to find the individual patient reports related to the specified event are reported in the Material and methods section

**Table S9.** Number of individual patient reports of severe AE per million doses related to cerebral venous thrombosis

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	1.37	1.32	0.78	1.17	0.35	0.70	30.23	17.17	12.97	4.59	2.60	1.90
<b>simulation 1<sup>b</sup></b>	1.65	1.69	0.92	1.39	0.27	0.67	20.48	17.91	13.00	5.31	2.18	1.97
<b>simulation 2<sup>b</sup></b>	1.41	1.26	0.72	1.29	0.57	0.59	40.91	15.96	11.89	8.21	1.73	2.29
<b>simulation 3<sup>b</sup></b>	1.66	1.30	0.80	1.68	0.29	0.70	21.02	21.11	18.41	3.48	2.50	1.70
<b>simulation 4<sup>b</sup></b>	1.73	1.35	0.70	1.22	0.34	0.70	24.19	21.80	17.23	3.13	2.85	2.14
<b>simulation 5<sup>b</sup></b>	1.44	1.27	0.76	1.28	0.51	0.60	39.75	16.20	10.78	8.16	1.82	2.56

<sup>a</sup> Severe AEs per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of severe AE reports concerning subjects within each range age (Table S7) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Severe AEs per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S10.** Number of individual patient reports of death per million doses related to cerebral venous thrombosis

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	0.00	0.00	0.13	0.00	0.07	0.11	3.36	5.33	1.78	1.65	0.78	0.00
<b>simulation 1<sup>b</sup></b>	0.00	0.00	0.15	0.00	0.05	0.11	2.28	5.56	1.78	1.91	0.65	0.00
<b>simulation 2<sup>b</sup></b>	0.00	0.00	0.12	0.00	0.11	0.09	4.55	4.96	1.63	2.96	0.52	0.00
<b>simulation 3<sup>b</sup></b>	0.00	0.00	0.13	0.00	0.06	0.11	2.34	6.56	2.53	1.25	0.75	0.00
<b>simulation 4<sup>b</sup></b>	0.00	0.00	0.12	0.00	0.07	0.11	2.69	6.77	2.36	1.13	0.85	0.00
<b>simulation 5<sup>b</sup></b>	0.00	0.00	0.13	0.00	0.10	0.09	4.42	5.03	1.48	2.94	0.55	0.00

<sup>a</sup> Deaths per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of death reports concerning subjects within each range age (Table S8) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Deaths per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S11.** Number of individual patient reports of severe AE per million doses related to splanchnic vein thrombosis

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	0.00	0.16	0.39	0.65	0.14	0.11	3.36	5.33	2.67	2.29	1.04	0.00
<b>simulation 1<sup>b</sup></b>	0.00	0.20	0.46	0.77	0.11	0.11	2.28	5.56	2.68	2.65	0.87	0.00
<b>simulation 2<sup>b</sup></b>	0.00	0.15	0.36	0.72	0.23	0.09	4.55	4.96	2.45	4.10	0.69	0.00
<b>simulation 3<sup>b</sup></b>	0.00	0.15	0.40	0.93	0.12	0.11	2.34	6.56	3.79	1.74	1.00	0.00
<b>simulation 4<sup>b</sup></b>	0.00	0.16	0.35	0.68	0.14	0.11	2.69	6.77	3.55	1.56	1.14	0.00
<b>simulation 5<sup>b</sup></b>	0.00	0.15	0.38	0.71	0.21	0.09	4.42	5.03	2.22	4.08	0.73	0.00

<sup>a</sup> Severe AEs per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of severe AE reports concerning subjects within each range age (Table S7) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Severe AEs per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S12.** Number of individual patient reports of severe AE per million doses related to thrombocytopenia

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	6.16	4.43	4.14	2.33	2.86	2.29	38.62	31.33	30.26	16.70	11.72	18.98
<b>simulation 1<sup>b</sup></b>	7.43	5.68	4.93	2.77	2.19	2.19	26.17	32.69	30.33	19.31	9.80	19.71
<b>simulation 2<sup>b</sup></b>	6.33	4.23	3.82	2.59	4.70	1.92	52.28	29.13	27.75	29.88	7.80	22.95
<b>simulation 3<sup>b</sup></b>	7.46	4.35	4.27	3.35	2.41	2.29	26.86	38.52	42.95	12.67	11.25	16.99
<b>simulation 4<sup>b</sup></b>	7.77	4.53	3.74	2.45	2.82	2.30	30.91	39.78	40.20	11.39	12.80	21.44
<b>simulation 5<sup>b</sup></b>	6.47	4.25	4.04	2.55	4.21	1.96	50.79	29.56	25.15	29.69	8.21	25.64

<sup>a</sup> Severe AEs per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of severe AE reports concerning subjects within each range age (Table S7) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Severe AEs per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information



**Table S13.** Number of individual patient reports of death per million doses related to splanchnic vein thrombosis

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	0.00	0.00	0.13	0.00	0.00	0.07	0.00	0.83	0.76	0.18	0.00	0.00
<b>simulation 1<sup>b</sup></b>	0.00	0.00	0.15	0.00	0.00	0.07	0.00	0.87	0.76	0.21	0.00	0.00
<b>simulation 2<sup>b</sup></b>	0.00	0.00	0.12	0.00	0.00	0.06	0.00	0.77	0.70	0.33	0.00	0.00
<b>simulation 3<sup>b</sup></b>	0.00	0.00	0.13	0.00	0.00	0.07	0.00	1.02	1.08	0.14	0.00	0.00
<b>simulation 4<sup>b</sup></b>	0.00	0.00	0.12	0.00	0.00	0.07	0.00	1.06	1.01	0.13	0.00	0.00
<b>simulation 5<sup>b</sup></b>	0.00	0.00	0.13	0.00	0.00	0.06	0.00	0.79	0.63	0.33	0.00	0.00

<sup>a</sup> Deaths per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of death reports concerning subjects within each range age (Table S8) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Deaths per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S14.** Number of individual patient reports of death per million doses related to thrombocytopenia

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	0.00	0.08	0.52	0.13	0.56	0.22	5.04	6.50	4.58	2.75	1.30	0.95
<b>simulation 1<sup>b</sup></b>	0.00	0.10	0.62	0.15	0.43	0.21	3.41	6.78	4.59	3.18	1.09	0.99
<b>simulation 2<sup>b</sup></b>	0.00	0.07	0.48	0.14	0.92	0.19	6.82	6.04	4.20	4.93	0.87	1.15
<b>simulation 3<sup>b</sup></b>	0.00	0.08	0.53	0.19	0.47	0.22	3.50	7.99	6.50	2.09	1.25	0.85
<b>simulation 4<sup>b</sup></b>	0.00	0.08	0.47	0.14	0.55	0.22	4.03	8.25	6.08	1.88	1.42	1.07
<b>simulation 5<sup>b</sup></b>	0.00	0.07	0.50	0.14	0.82	0.19	6.62	6.13	3.80	4.89	0.91	1.28

<sup>a</sup> Deaths per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of death reports concerning subjects within each range age (Table S8) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Deaths per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S15.** Number of individual patient reports of severe AE per million doses related to cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	8.21	5.90	5.04	4.01	3.28	2.95	53.74	41.67	39.16	20.56	14.85	20.88
<b>simulation 1<sup>b</sup></b>	9.91	7.57	6.01	4.78	2.51	2.83	36.42	43.47	39.26	23.77	12.42	21.68
<b>simulation 2<sup>b</sup></b>	8.44	5.64	4.65	4.46	5.39	2.48	72.73	38.74	35.91	36.78	9.88	25.24
<b>simulation 3<sup>b</sup></b>	9.95	5.80	5.20	5.77	2.76	2.96	37.37	51.23	55.58	15.59	14.25	18.69
<b>simulation 4<sup>b</sup></b>	10.36	6.04	4.55	4.22	3.23	2.96	43.01	52.90	52.03	14.01	16.22	23.59
<b>simulation 5<sup>b</sup></b>	8.63	5.66	4.92	4.39	4.82	2.53	70.66	39.31	32.55	36.54	10.40	28.20

<sup>a</sup> Severe AEs per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of severe AE reports concerning subjects within each range age (Table S7) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Severe AEs per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S16.** Number of individual patient reports of death per million doses related to cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia

	BNT162b2						ChAdOx1 nCoV-19					
	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>europaean mean<sup>a</sup></b>	0.00	0.08	0.78	0.13	0.49	0.44	8.40	7.83	5.47	3.40	1.82	0.95
<b>simulation 1<sup>b</sup></b>	0.00	0.10	0.92	0.15	0.37	0.42	5.69	8.17	5.48	3.93	1.53	0.99
<b>simulation 2<sup>b</sup></b>	0.00	0.07	0.72	0.14	0.80	0.37	11.36	7.28	5.01	6.07	1.21	1.15
<b>simulation 3<sup>b</sup></b>	0.00	0.08	0.80	0.19	0.41	0.44	5.84	9.63	7.76	2.58	1.75	0.85
<b>simulation 4<sup>b</sup></b>	0.00	0.08	0.70	0.14	0.48	0.44	6.72	9.95	7.26	2.31	1.99	1.07
<b>simulation 5<sup>b</sup></b>	0.00	0.07	0.76	0.14	0.72	0.38	11.04	7.39	4.54	6.04	1.28	1.28

<sup>a</sup> Deaths per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of death reports concerning subjects within each range age (Table S8) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Deaths per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S17:** Single patient reports of severe AE per 1 million doses related to the specified AE categories determined by thrombocytopenia/bleeding and blood clots events

		Severe AEs/1,000,000 doses																								
		BNT162b2												ChAdOx1 nCoV-19												
		18-64y						65+ y						18-64y						65+ y						
		europaean mean <sup>a</sup>	sim 1 <sup>b</sup>	sim 2 <sup>b</sup>	sim 3 <sup>b</sup>	sim 4 <sup>b</sup>	sim 5 <sup>b</sup>	europaean mean <sup>a</sup>	sim 1 <sup>b</sup>	sim 2 <sup>b</sup>	sim 3 <sup>b</sup>	sim 4 <sup>b</sup>	sim 5 <sup>b</sup>	europaean mean <sup>a</sup>	sim 1 <sup>b</sup>	sim 2 <sup>b</sup>	sim 3 <sup>b</sup>	sim 4 <sup>b</sup>	sim 5 <sup>b</sup>	europaean mean <sup>a</sup>	sim 1 <sup>b</sup>	sim 2 <sup>b</sup>	sim 3 <sup>b</sup>	sim 4 <sup>b</sup>	sim 5 <sup>b</sup>	
Severe AEs more frequent in younger	cerebral venous thrombosis	1.1	1.3	1.0	1.1	1.1	1.1	0.6	0.5	0.6	0.6	0.6	0.6	13.5	13.6	13.9	14.5	14.2	13.5	2.6	2.5	2.4	2.3	2.4	2.6	
	splanchnic vein thrombosis	0.3	0.4	0.3	0.3	0.3	0.3	0.2	0.1	0.2	0.1	0.2	0.2	3.8	3.9	3.9	4.1	4.0	3.8	1.0	1.0	1.0	0.9	0.9	1.0	
	thrombocytopenia	4.0	5.1	4.0	4.3	4.1	4.0	2.3	2.1	2.3	2.2	2.3	2.3	27.1	27.4	27.9	29.3	28.5	27.1	11.8	11.6	11.3	10.5	10.9	11.8	
	other bleeding events	7.3	9.2	7.2	7.9	7.4	7.3	3.0	2.6	3.0	2.8	2.9	3.0	18.8	19.1	19.4	20.3	19.8	18.8	8.3	8.2	8.0	7.4	7.7	8.3	
Severe AEs with similar rate in younger and older	gastrointestinal bleeding	3.1	3.9	3.0	3.3	3.1	3.1	2.1	1.9	2.2	2.1	2.1	2.1	7.4	7.5	7.6	8.0	7.8	7.4	4.9	4.8	4.7	4.3	4.5	4.9	
	cerebral bleeding	1.8	2.2	1.8	1.9	1.8	1.8	3.0	2.7	3.0	2.9	3.0	3.0	10.8	10.9	11.1	11.7	11.3	10.8	8.2	8.0	7.8	7.3	7.6	8.2	
	other venous thrombosis	8.6	10.7	8.4	9.2	8.7	8.6	7.6	6.8	7.7	7.3	7.6	7.6	51.4	52.1	52.9	55.5	54.1	51.4	47.5	46.5	45.3	42.2	43.8	47.5	
	disseminated intravascular coagulation	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.5	1.5	1.5	1.6	1.5	1.5	1.5	1.5	1.5	1.5	1.4	1.4	1.5
	pulmonary thromboembolism	6.2	7.7	6.1	6.6	6.2	6.2	8.7	7.8	8.8	8.4	8.7	8.7	29.6	30.0	30.5	32.0	31.1	29.6	35.2	34.4	33.6	31.2	32.5	35.2	
Severe AEs more frequent in older	ischemic stroke	4.4	5.5	4.3	4.7	4.4	4.4	8.5	7.6	8.6	8.2	8.4	8.5	15.1	15.3	15.6	16.4	15.9	15.1	28.6	28.0	27.3	25.4	26.4	28.6	

<sup>a</sup> Severe AEs per million doses were calculated as follows: 1) the number of doses of a specific vaccine given to the European population was multiplied by the fraction of the subjects within an age range calculated considering the data from the European Countries giving these pieces of information; 2) the number of severe AE reports concerning subjects within each range age (Table S7) was divided by the number obtained with the above-described procedure and multiplied by 1,000,000

<sup>b</sup> Severe AEs per million doses were calculated as reported above but the fraction of the subjects within an age range was calculated considering the data from only five European Countries randomly chosen among the ones giving the appropriate information

**Table S18.** Frequency of thrombohemorrhagic events in vaccine-untreated and BNT162b2-treated population

	events/1 million persons per year			
	general incidence 18-65y <sup>a</sup>		BNT162b2 18-64y	
	Denmark	Norway	observation period	
			1 month	0.5 month
<b>venous thromboembolic events</b>	1580	1260	407	814
<b>cerebral venous thrombosis</b>	20	10	13	26
<b>splanchnic vein thrombosis</b>	40	60	3.6	7.2
<b>thrombocytopenia</b>	150	380	49	97
<b>gastric/gastrointestinal bleeding<sup>b</sup></b>	180	n.a.	37	74
<b>cerebral bleeding</b>	200	140	22	43
<b>disseminated intravascular coagulation</b>	10	20	1.0	1.9
<b>pulmonary thromboembolism</b>	570	570	70	148
<b>stroke<sup>c</sup></b>	400	60	53	105

<sup>a</sup> data from Pottegård and colleagues that excluded from the analysis patients with a history of a given outcome during a one year fixed washout period

<sup>b</sup> data regarding general incidence refers to "intestinal bleeding" and data regarding SAE due to BNT162b2 refers to "gastrointestinal bleeding"

<sup>c</sup> data of general incidence refers to "stroke, unspecified" and data regarding SAE due to BNT162b2 refers to "ischemic stroke"

**Table S19.** Number of individual patient reports of AE per million doses administered, calculated considering the number of doses administered in Europe at W12

	<b>BNT162b2</b>	<b>ChAdOx1 nCoV-19</b>
overall number of individual patient reports of AE per million doses administered	2,778	12,335
number of individual patient reports of severe AE caused by the thrombocytopenia/bleeding and blood clots events per million doses administered	48.6	230.0
number of individual patient reports of severe AE caused by CVT events <sup>a</sup> per million doses administered	1.1	15.2
number of individual patient reports of severe AE caused by splanchnic vein thrombosis events <sup>a</sup> per million doses administered	0.3	4.4
number of individual patient reports of severe AE caused by thrombocytopenia events <sup>a</sup> per million doses administered	4.2	35.4
number of individual patient reports of severe AE caused by the three merged categories events <sup>a</sup> per million doses administered	5.5	45.7

<sup>a</sup> The terms used to find the individual patient reports related to the specified event are reported in the Material and methods section

**Table S20.** Percentage of deaths over the number of individual patient reports of severe AE related to cerebral venous thrombosis, splanchnic vein thrombosis, thrombocytopenia, and with one or more AEs related to the above events

	BNT162b2							ChAdOx1 nCoV-19						
	Overall <sup>a</sup>	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y	Overall <sup>a</sup>	18-24y	25-49y	50-59y	60-69y	70-79y	80+ y
<b>cerebral venous thrombosis<sup>b</sup></b>	8.6%	0.0%	0.0%	16.7%	0.0%	20.0%	16.7%	25.4%	23.5%	28.9%	14.6%	39.1%	33.3%	0.0%
<b>splanchnic vein thrombosis<sup>b</sup></b>	20.0%	<sup>c</sup>	0.0%	33.3%	0.0%	0.0%	66.7%	14.8%	0.0%	16.7%	30.0%	8.3%	0.0%	<sup>c</sup>
<b>thrombocytopenia<sup>b</sup></b>	9.1%	0.0%	1.8%	12.9%	5.9%	17.9%	10.2%	16.7%	14.3%	20.8%	15.6%	16.7%	12.2%	5.6%
<b>cerebral venous thrombosis and/or splanchnic vein thrombosis and/or thrombocytopenia<sup>b</sup></b>	9.5%	0.0%	1.4%	16.2%	3.3%	15.6%	14.3%	15.9%	16.7%	18.8%	14.2%	16.5%	13.5%	5.0%

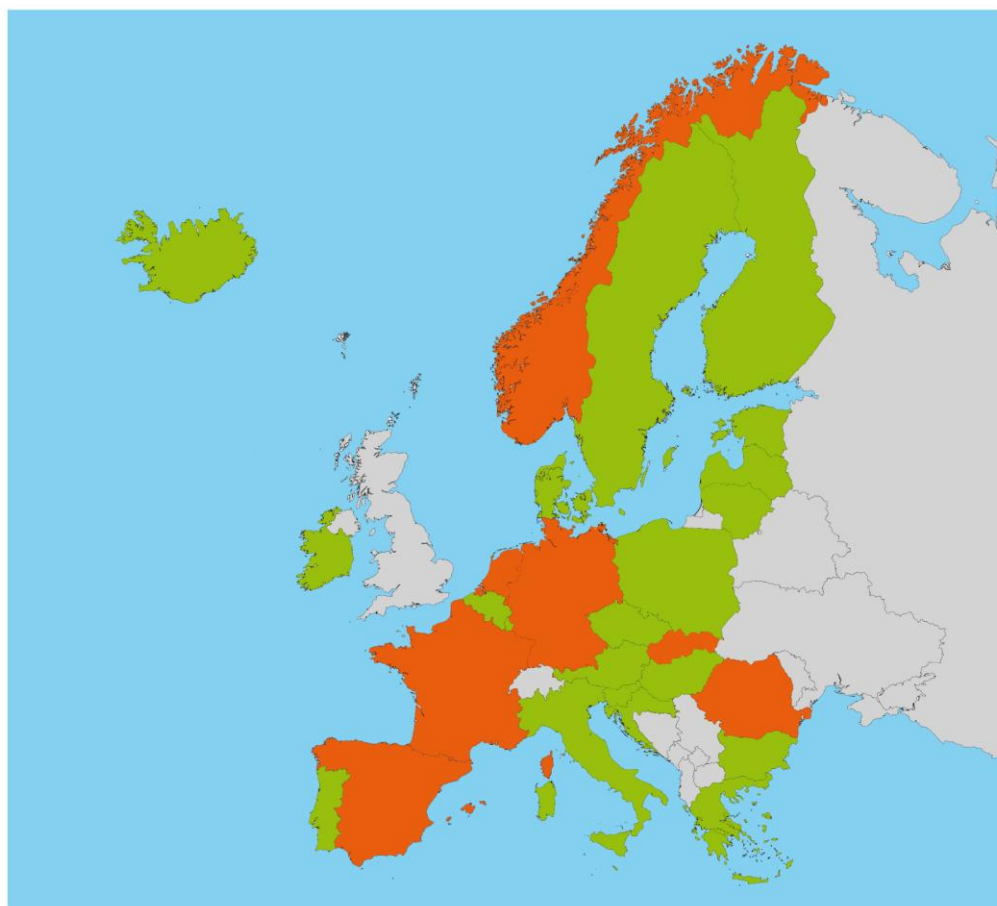
<sup>a</sup> The overall percentage of deaths over the number of individual patient reports of severe AE also consider the reports in which the age was not specified



<sup>b</sup> The terms used to find the individual patient reports related to the specified event are reported in the Material and methods section

<sup>c</sup> In this age group are not reported severe AEs related to the specified event

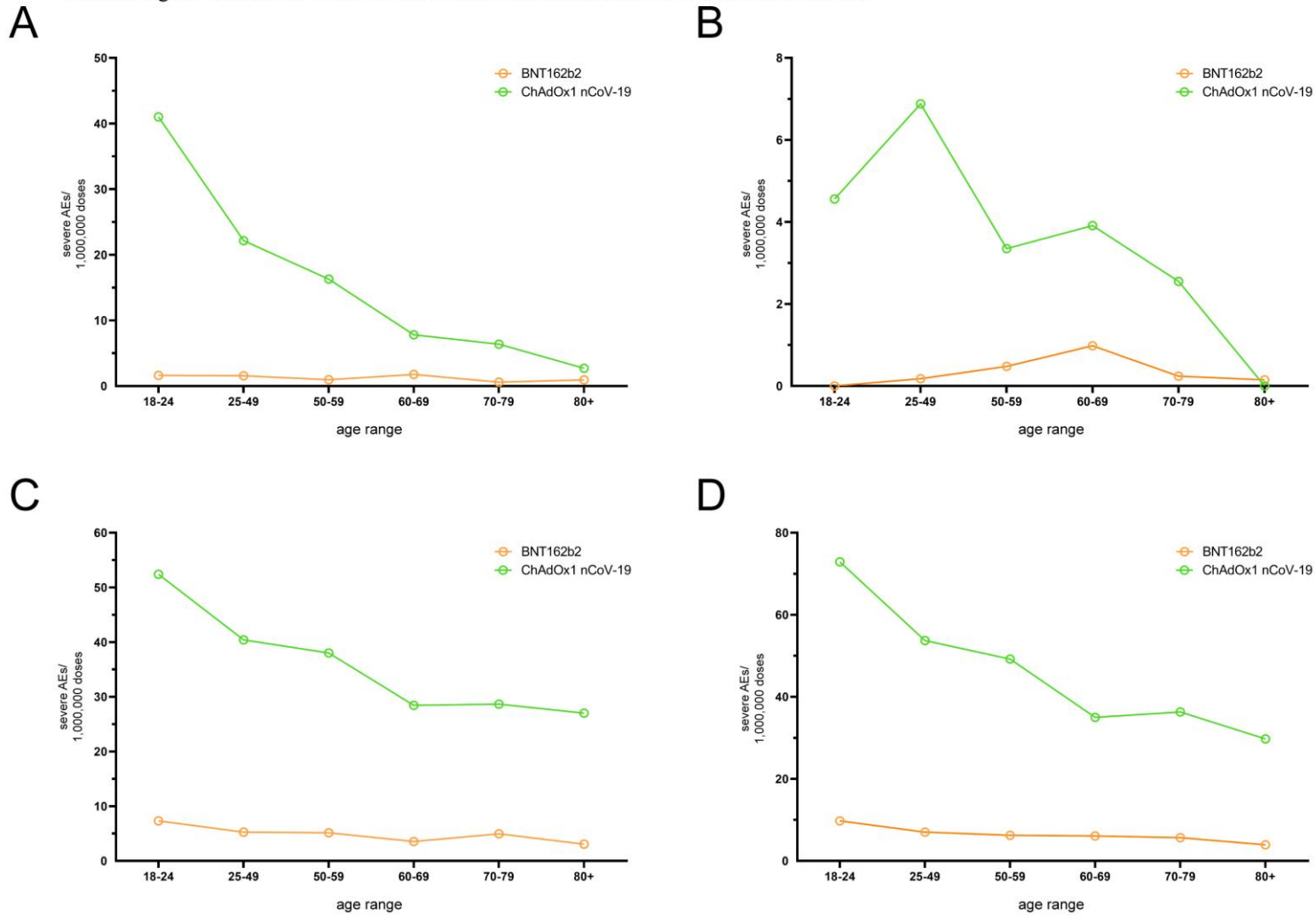


**Figure S1.** European countries providing information about administration of a specific vaccine in each age group.



-  Countries that provide data of a specific vaccine administration in each age range
-  Countries that do not provide data of a specific vaccine administration in each age range

**Figure S2.** Frequency of individual cases with specific AEs among BNT162b2 and ChAdOx1 nCoV-19 recipients divided into age groups and calculated considering the number of vaccines administered 2 weeks before the last observed AEs.



The frequency of individual cases with specific AEs divided into age ranges was obtained by normalization of the number of individual cases (Table S7) with the doses supposedly administered to each age range in Europe at week-12 (Table S2). We needed to evaluate the doses supposedly administered to each age range in Europe. Hence, we considered the doses administered by the European countries providing data regarding administration of each vaccine to age ranges (Figure S1) and set up a method to evaluate the dose variance (see the Material and methods section for details). The frequency (Mean±SD) of individual cases with SAEs consisting of cerebral venous thrombosis (A), splanchnic venous thrombosis (B), thrombocytopenia (C), and cerebral venous thrombosis and/or splanchnic venous thrombosis and/or thrombocytopenia (D) are reported. The frequency of AEs reported in panel D is lower than the sum of the frequency of AEs reported in panels A, B, and C because one individual case may suffer from 2 or 3 AEs simultaneously.