Johnson & Johnson koronarokottamisen reunaehdot

KRAR

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26.4.2021

Terveyden ja hyvinvoinnin laitos

Johnson & Johnsonin adenovirusvektorirokote

- Ihmisen Ad26 vektorina
- Yhden annoksen sarja, säilyy jääkaapissa 3 kk
- RCT N= 19 630 vacc+ vs. 19 691 placebo = **39 321**
- Tutkittavilla perustauteja 40%:lla
- Tutkimuspaikat: Argentiina, Brasilia, Chile, Kolumbia, Meksiko, Peru, Etelä-Afrikka ja USA
- Päävastemuuttuja = keskivaikea – vaikea/kriittinen lab+ covid-19 tauti 14-28 vrk rokottamisesta
- II annoksen RCT meneillään, valmistuu 8/2021

Johnson & Johnson rokotteen teho ACIP 23.4.2021

Benefits of the Janssen COVID-19 vaccine

- The clinical trial demonstrated efficacy against symptomatic, laboratory-confirmed COVID-19. The overall efficacy was **66.3%** (95% CI: 59.9%, 71.8%)
- Vaccine efficacy against COVID-19 associated hospitalization was **93%** (95% CI: 71%, 98%)
- **Higher** efficacy against **severe** outcomes than for any symptomatic COVID-19
  - VE against **deaths** due to COVID-19**: 100%**

Yht 19 kuolemaa, joista 5 covid-19 related placebo ryhmässä, ei lainkaan rokotusryhmässä

- Efficacy against severe disease† remained high across world regions (**73-82%***), suggesting protection against severe illness with variant strains

†Definition: Respiratory Rate ≥ 30, Heart Rate ≥125, SpO2≤ 93% on room air at sea level or PaO2/FIO2< 300 mm Hg; OR respiratory failure or Acute Respiratory Distress Syndrome (ARDS), defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO; OR evidence of shock (systolic blood pressure <90mmHg, diastolic BP<60mmHg or requiring vasopressors); OR significant acute renal, hepatic or neurologic dysfunction; OR admission to an intensive care unit or death
*Assessed ≥ 14 days post vaccination

33

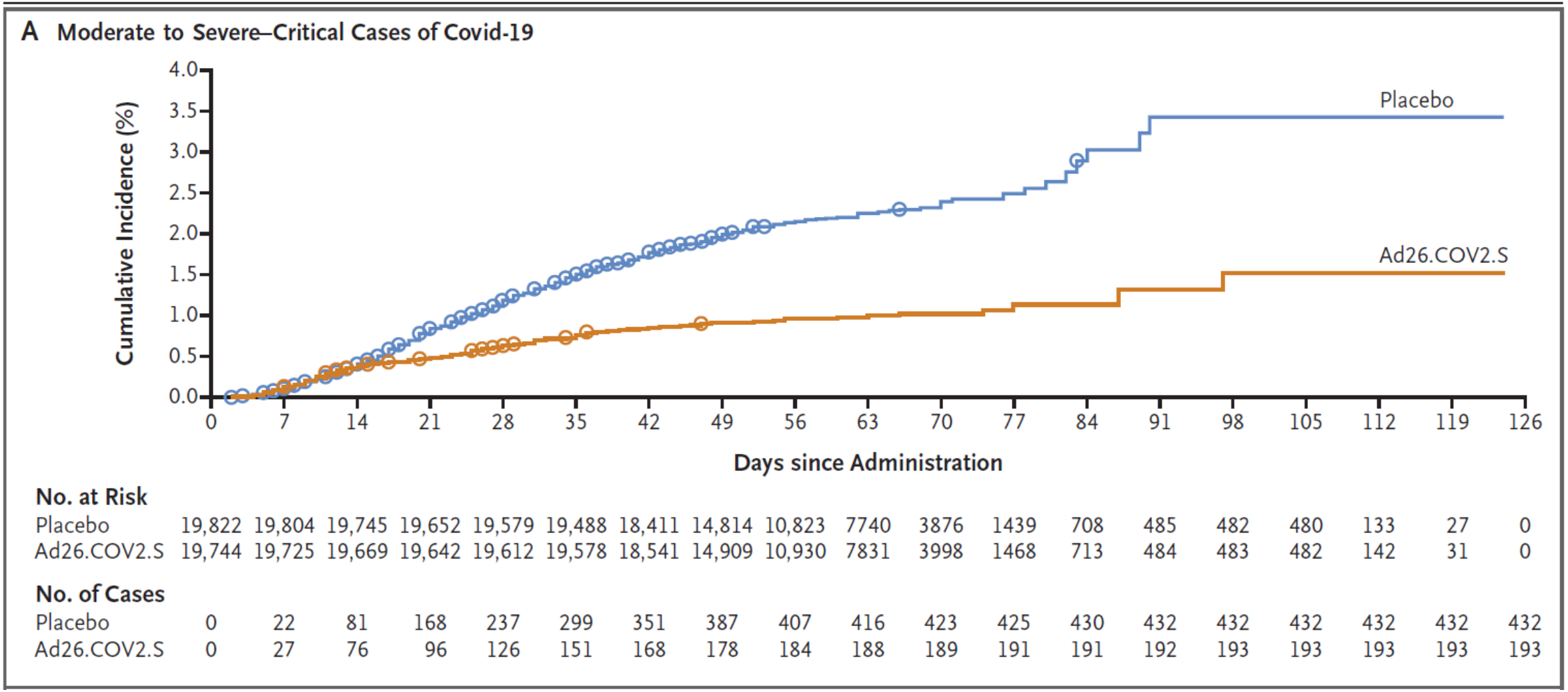
Sadoff ym
NEJM 22.4.2021

Table 2. Vaccine Efficacy against Covid-19 with Onset at Least 14 Days and at Least 28 Days after the Administration of Vaccine or Placebo (Per-Protocol at-Risk Population).*

Variable	≥14 Days after Administration†					≥28 Days after Administration‡				
	Ad26.COV2.S (N = 19,514)		Placebo (N = 19,544)		Vaccine Efficacy (95% CI)	Ad26.COV2.S (N = 19,306)		Placebo (N = 19,178)		Vaccine Efficacy (95% CI)
	no. of cases	*person-yr*	*no. of cases*	*person-yr*	%	*no. of cases*	*person-yr*	*no of cases*	*person-yr*	%
Moderate to severe–critical Covid-19	116	3116.6	348	3096.1	66.9 (59.0–73.4)	66	3102.0	193	3070.7	66.1 (55.0–74.8)
18–59 yr	95	2106.8	260	2095.0	63.7 (53.9–71.6)	52	2097.6	152	2077.0	66.1 (53.3–75.8)
≥60 yr	21	1009.8	88	1001.2	76.3 (61.6–86.0)	14	1004.4	41	993.6	66.2 (36.7–83.0)
Symptomatic Covid-19 of any severity	117	3116.5	351	3095.9	66.9 (59.1–73.4)	66	3102.0	195	3070.5	66.5 (55.5–75.1)
Mild	1	3116.5	3	3095.9	NC§	0	3102.0	2	3070.5	NC§
Moderate	102	3116.6	288	3096.1	64.8 (55.8–72.2)	61	3102.0	159	3070.7	62.0 (48.7–72.2)
Severe–critical	14	3125.1	60	3122.0	76.7 (54.6–89.1)	5	3106.2	34	3082.6	85.4 (54.2–96.9)
Severity-adjusted symptomatic Covid-19¶	117	3116.5	351	3095.9	68.1 (60.3–74.3)	66	3102.0	195	3070.5	69.0 (56.7–77.6)
18–59 yr	95	2106.8	260	2095.0	65.8 (56.2–73.1)	52	2097.6	152	2077.0	69.3 (57.4–77.7)
≥60 yr	22	1009.6	91	1001.0	74.5 (57.9–84.3)	14	1004.4	43	993.5	67.9 (38.2–82.8)
Moderate to severe–critical Covid-19, including noncentrally confirmed cases	173	3113.9	509	3089.1	66.3 (59.9–71.8)	113	3100.3	324	3065.9	65.5 (57.2–72.4)
Covid-19, according to FDA harmonized definition‖	114	3116.6	345	3,096.3	67.2 (59.3–73.7)	65	3102.0	193	3070.6	66.7 (55.6–75.2)
Moderate to severe–critical Covid-19, according to Cox proportional-hazards model**	116	3116.6	348	3,096.1	66.9 (59.1–73.2)	66	3102.0	193	3070.7	66.2 (55.3–74.4)

* All cases of coronavirus disease 2019 (Covid-19) were centrally confirmed unless stated otherwise and occurred in participants who had been seronegative at baseline and negative on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing before 14 or 28 days after the administration of vaccine or placebo, for the respective end points, and were therefore at risk for Covid-19. The follow-up time for each participant was defined as the time from the administration of vaccine or placebo to the onset of Covid-19 or the last available trial measurement (January 22, 2021). Adjusted 95% confidence intervals are shown for moderate and severe–critical Covid-19, severe–critical Covid-19, severity-adjusted Covid-19, and moderate to severe–critical Covid-19, including non–centrally confirmed cases; unadjusted 95% confidence intervals are shown for other end points. The adjusted confidence interval was calculated with implementation of type I error control for multiple testing. Adjusted confidence intervals are presented for the end points that were prespecified for inferential evaluation at the primary analysis and on reaching the associated minimal required number of cases for that end point. Mild cases of Covid-19 were defined as a positive result on RT-PCR testing and the presence of at least one of the following symptoms: fever (body temperature, ≥38.0°C), sore throat, malaise, headache, myalgia, gastrointestinal symptoms,

Keskivaikean-vaikean Covid-19 taudin ilmaantuvuus ajan funktiona tautia vastaan rokotetuilla ja lumeryhmään kuuluvilla



No. at Risk

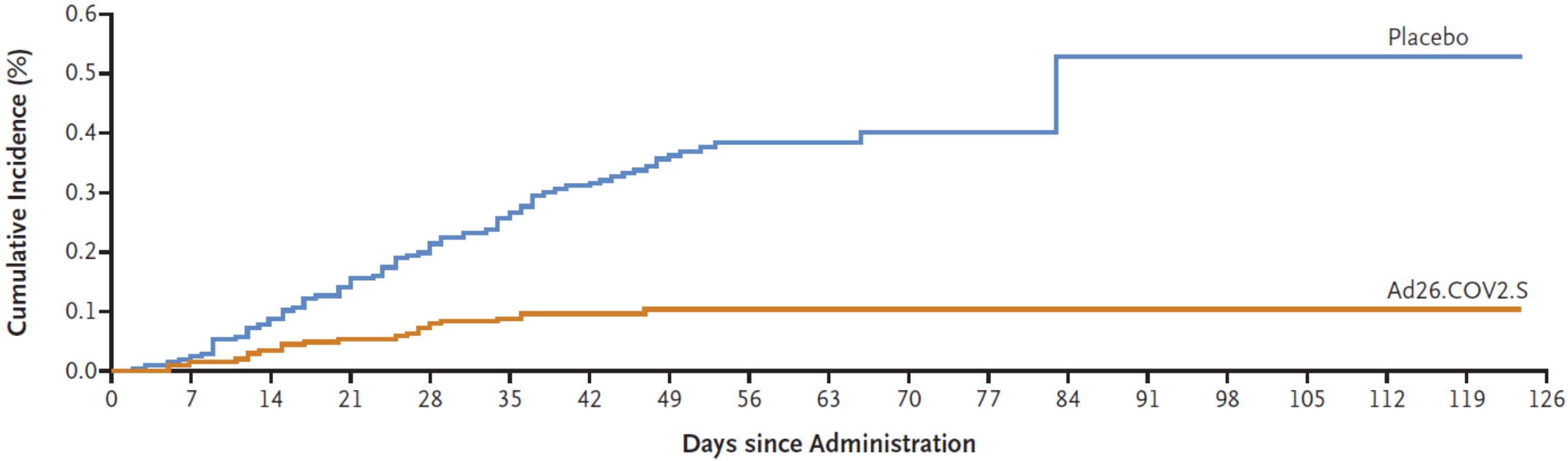
Placebo	19,822	19,804	19,745	19,652	19,579	19,488	18,411	14,814	10,823	7740	3876	1439	708	485	482	480	133	27	0
Ad26.COV2.S	19,744	19,725	19,669	19,642	19,612	19,578	18,541	14,909	10,930	7831	3998	1468	713	484	483	482	142	31	0

No. of Cases

Placebo	0	22	81	168	237	299	351	387	407	416	423	425	430	432	432	432	432	432	432
Ad26.COV2.S	0	27	76	96	126	151	168	178	184	188	189	191	191	192	193	193	193	193	193

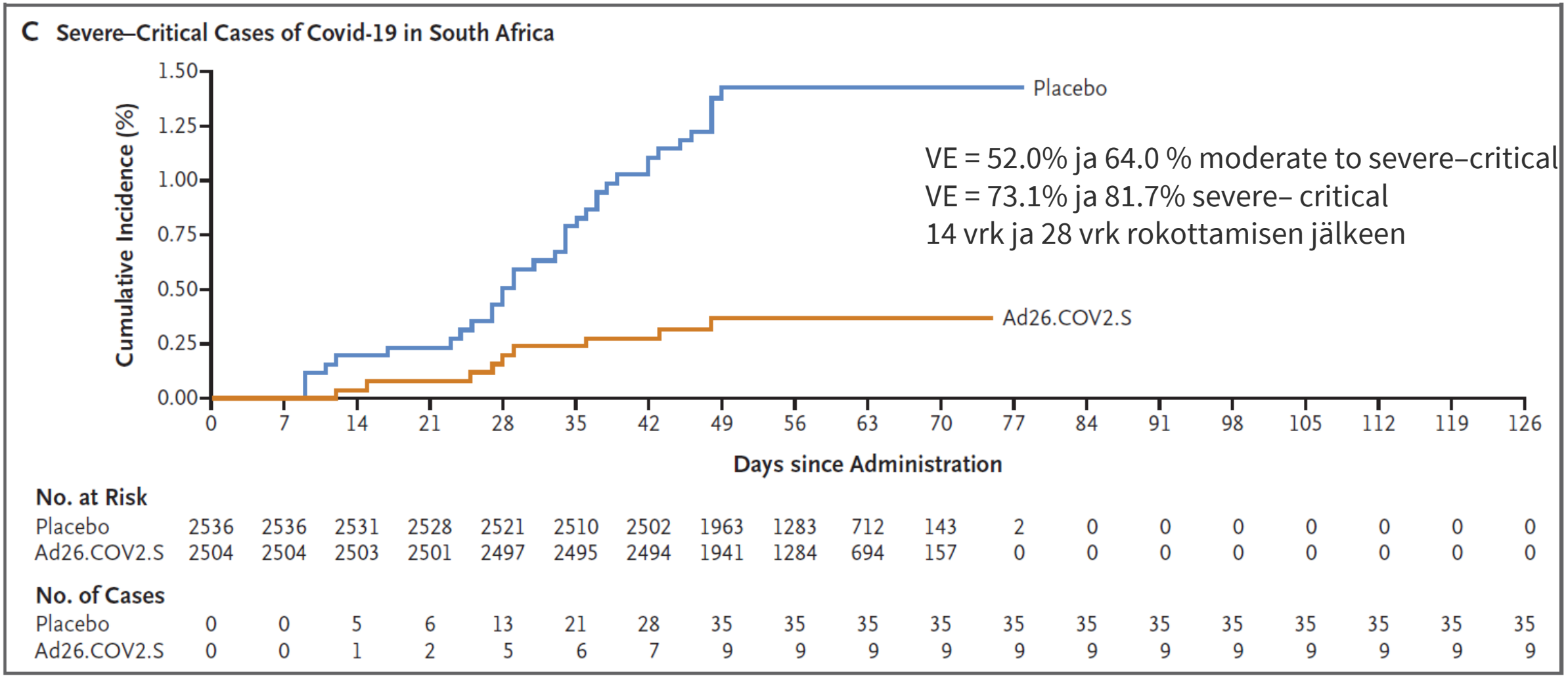
Kriittisen covid-19 taudin ilmaantuvuus ajan funktiona rokotetuilla ja lumeryhmään kuuluvilla

B Severe–Critical Cases of Covid-19



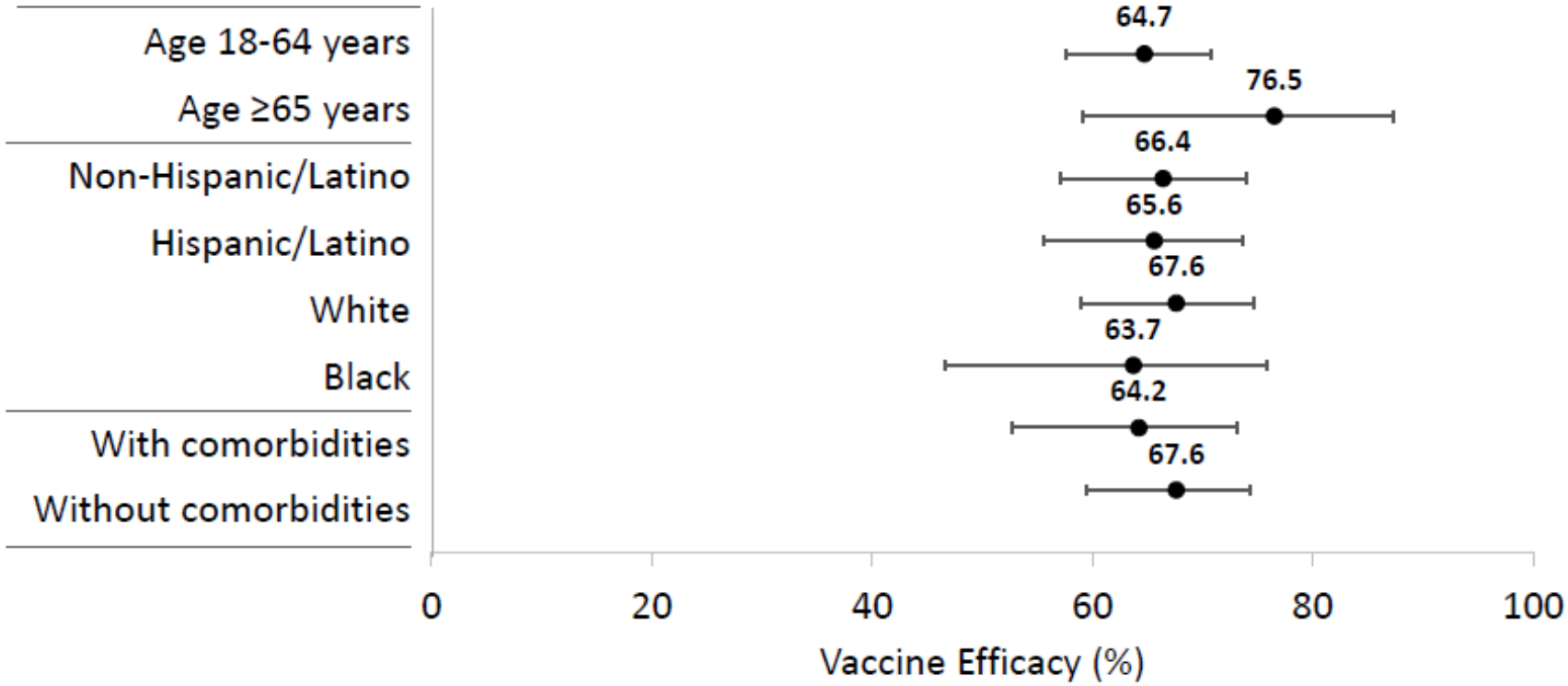
No. at Risk																		
Placebo	19,822	19,817	19,799	19,779	19,760	19,725	18,682	15,088	11,069	7939	3995	1485	732	500	497	495	137	29	0
Ad26.COV2.S	19,744	19,741	19,734	19,725	19,718	19,705	18,685	15,043	11,046	7919	4039	1481	720	490	490	489	146	31	0
No. of Cases																			
Placebo	0	5	18	32	44	55	65	73	76	76	77	77	78	78	78	78	78	78	78
Ad26.COV2.S	0	3	7	11	16	18	20	21	21	21	21	21	21	21	21	21	21	21	21

Vakavan - kriittisen covid-19 taudin ilmaantuvuus ajan funktiona rokotetuilla ja lumeryhmään kuuluvilla Etelä-Afrikassa kun vallitsevana viruksen oli ns. Etelä-Afrikan variantti B.1.351



Benefits of the Janssen COVID-19 vaccine

- **Similar** efficacy for across age, sex, race, and ethnicity categories, and those with underlying medical conditions at ≥14 days post-vaccination



Tehotutkimustuloksia eri COVID-19 rokotteilla*, oireiset ja oireettomat

Rokote	Infektio**	Metodi	Rokotetut	Lumeryhmä	Rokotteen teho** (95% LV)
BioNTech Pfizer*	**Covid-19 oireinen**	PCR	14 (0.1%)	38 (0.3%)	**95%** (90.3; 97.6)
Moderna	Oireeton	Nielunäyte 2. annoksen antohetkellä	14 (0.1%)	38 (0.3%)	**66 %** (ei LV)
	Covid-19 oireinen	PCR	11	185	**94.1 %** (89.3; 96.8)
Astra Zeneca	Oireeton	Viikottain otettu nielunäyte PCR	11	13	**16%** (-88%, 62%)
	Covid-19 oireinen & Oireeton	PCR	28	84	**67%** (49%, 78%)
Janssen	Oireeton	Serokonversio (0-päivään 71)	18	50	**65.5** (39.9; 81.1)
	Covid-19 oireinen	PCR	116	348	**66.9 %** (59.0; 73.4)

AstraZenecan ja Johnson&Johnsonin adenovirusvektori rokotteiden yhtäläisyyksiä ja eroja

	AZ*	J&J***
vektori	Simpanssin adenovirus	Ihmisen adenovirus A26
Viruspartikkelien määrä	5 x10^{10} n 2,5 × 10^{8} infektoivaa yksikköä (Inf.U)	vähintään 8,92 log10 infektoivaa yksikköä (Inf.U).
Piikkiproteiini	Prefuusio	Prefuusio
Teho 1. annoksen jälkeen covid-19+	70,4% (95% CI 54,8–80,6)	66,3 % (95% CI 59,9 – 71,8)
Teho 1. annoksen jälkeen vaikea covid-19	94%** (95% CI 73 – 99)	76.7% (95% CI, 54.6 to 89.1] ≥14 days 85.4% (95% CI, 54.2 to 96.9] ≥28 days
Teho 2. annoksen jälkeen	62·1% (95% CI 41·0–75·7)	?

*Voysey et al Lancet Dec2020; ** Vasileiou et al. Lancet Feb2021; ***Sadoff et al, NEJM April2021

J&J rokotteen jälkeen ilmaantunut TTS riski

Potential Harms of the Janssen COVID-19 vaccine

- 7.98 million vaccine doses administered* and 15 confirmed TTS cases as of April 21, 2021
  - Additional potential TTS cases under review, including potential male cases

	Females			Males		
Age group	**Cases**	**Doses admin**	**Reporting rate†**	**Cases***	**Doses admin**	**Reporting rate†**
18-49 years old	13	1,866,294	**7.0** per million	0	1,977,330	**0** per million
50+ years old	2	2,125,239	**0.9** per million	0	2,010,144	**0** per million

* Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; Some age- and sex-specific doses administered data were imputed

† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

* One TTS case occurred in the Phase 3 trial in a male aged 18-49 years.

Acronyms: Thrombosis with Thrombocytopenia Syndrome (TTS)

Kuinka suuri osuus haitoista yleisesti löytyy VAERS järjestelmästä?

- Passiivinen järjestelmä, joka luottaa terveydenhuoltohenkilöstön/ rokotettujen raportointiin
- Lievissä haitoissa aliraportointia - osaltaan tarkoituksenmukaista
- Vakavissa haitoissa pyritään mahdollisimman korkeaan raportoitujen osuuteen:

  Suolentuppeumista löytyi rotavirusrokotusten jälkeen **47%** tapauksista (Verstraeten 2001)

  Paralyyttisistä polioista löytyi poliorokotteen jällkeen **68%**

  (Rosenthal ja Chen 1995)

Verstraeten, T ym. Enhancing vaccine safety surveillance: a capture-recapture analysis of intussusception after rotavirus vaccination. Am J Epidemiol 2001;154:1006-101

Rosenthal ja Chen. The reporting sensitivities of two passive surveillance systems for vaccine adverse events. Am J Public Health 1995;85:1706-170

VEARSiin raportoutujen Guillain-Barré tapausten osuus

Table 2
VAERS reporting sensitivity for Guillain-Barré Syndrome (GBS) after three vaccines.

Vaccine	Rate in VSD within 42 days of vaccination	Rate in Vaccine Adverse Event Reporting System (VAERS)	VAERS Reporting Sensitivity
2009 H1N1inactivated pandemic vaccine	6.08 per million doses administered during the 2009–2010 season [17]	1.33 per million doses estimated to have been given Oct. 2009-Jan. 2010 [16][1]	22%
		3.35 per million doses administered in military population for ages 17–44 years with report date of Aug. 2009-Dec. 2010 [19][2]	55%
		0.93 per million doses estimated to have been given in non-military population for ages 17–44 years with report date of Aug. 2009-Dec. 2010 [19][3]	15%
Human papillomavirus vaccine, quadrivalent (4vHPV)	0.36 cases per million doses administered 2006–2015 [21]	0.23 cases per million doses distributed 2009–2015 [15][4]	64%
2012–2013 influenza season inactivated influenza vaccine (IIV)	4.94 cases per million doses administered during the 2012–2013 season [22]	0.59 cases per million doses distributed [23] [5]	12%

Miller ER ym. The reporting sensitivity of the Vaccine Adverse Event Reporting System (VAERS) for anaphylaxis and for Guillain-Barré syndrome. Vaccine 2020;38(47):7458-6.3

VEARSiin raportoitujen anafylaksioiden osuus

Table 1
VAERS reporting sensitivity for anaphylaxis after seven vaccines.

Vaccine	Incidence Rate in Vaccine Safety Datalink (VSD)[1,2]	Reporting Rate in Vaccine Adverse Event Reporting System (VAERS)	VAERS Reporting Sensitivity
Measles, Mumps & Rubella (MMR)	5.14 per million doses administered 2009–2011 [7]	1.31 per million doses distributed 2006–2016 [10][3]	25%
Pneumococcal Polysaccharide 23 valent (PPSV23)	2.86 per million doses administered 2009–2011 [7]	0.38 per million doses distributed 2006–2016 [10] [3] 0.77 per million doses distributed 2004–2013 [13] [4]	13% 27%
Varicella	5.77 per million doses administered 2009–2011 [7]	1.2 per million doses distributed 2006–2016 [10] [3]	21%
Zoster live (ZVL)	6.58 per million doses administered 2009–2011 [7]	1.6 per million doses distributed 2006–2015 [14] [4]	24%
Human papillomavirus vaccine, quadrivalent (4vHPV)	2.58 per million doses administered 2009–2011 [7]	0.63 per million doses distributed 2009–2015 [15] [4]	24%
2009 H1N1 inactivated pandemic influenza A	2.11 per million doses administered 2009–2011 [7]	1.6 per million doses estimated to have been given from Oct. 2009 to Jan. 2010 [16] [5]	76%
Influenza (all types)	1.53 per million doses administered 2009–2011 [7]	0.2 per million doses administered 2010–2016 [10] [3]	13%

Miller ER ym. The reporting sensitivity of the Vaccine Adverse Event Reporting System (VAERS) for anaphylaxis and for Guillain-Barré syndrome. Vaccine 2020;38(47):7458-63.

Summary of population-level risks and benefits by recommendation, all scenarios

Recommendation for all persons aged 18+

- **Risks:** Expect **26–45 TTS** cases, depending on uptake
- **Benefits:** Depend on uptake, amount of transmission
  - **800–3,500 fewer ICU** admissions
  - **600–1,400 fewer deaths**

Recommendation for all persons aged 50+

Risks: Expect **2–3 TTS** cases, depending on uptake

Benefits: Depend on uptake, amount of transmission

300–1000 fewer ICU admissions

40–250 fewer deaths

Note: Benefits of vaccination apply to the whole population over a 6-month period, and result from direct and indirect effects.

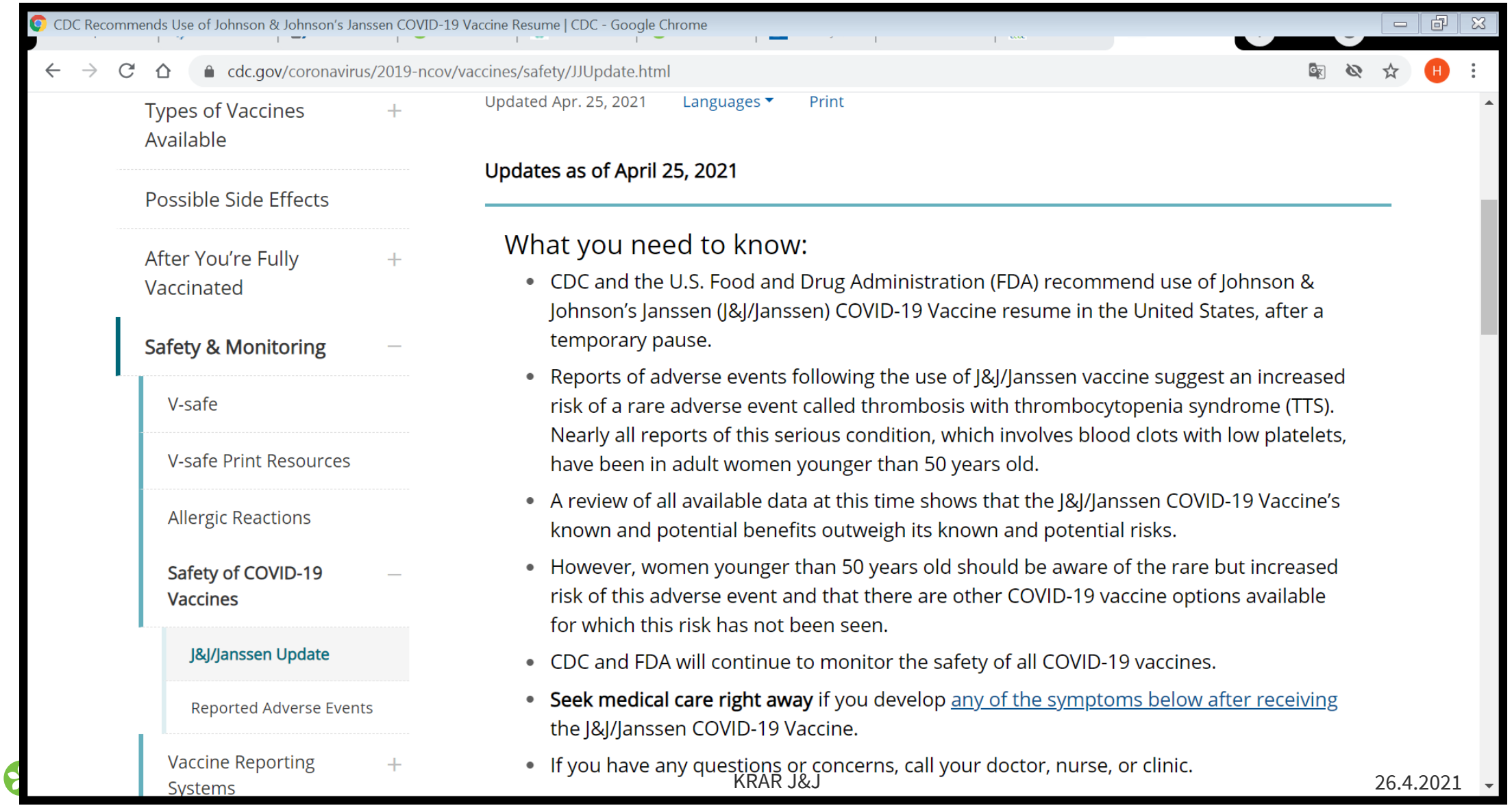
Acronyms: Thrombosis with Thrombocytopenia Syndrome (TTS)

Miten Yhdysvalloissa J&J rokotetta pitäisi käyttää? ACIP kokouksessa esitetyt vaihtoehdot

Policy Options for Janssen Policy Recommendations

- Recommend **against** use for all persons
- Reaffirm recommendations for **all** age and sex
  - FDA to include warning statement with EUA
- Recommend vaccination only for adults **≥50 years of age**
- Reaffirm recommendations for use; women aged <50 years should **be aware** of the increased risk of TTS, and **may choose** another COVID-19 vaccine (i.e. mRNA vaccines)

CDC:n ja FDA:n suositus J&J rokotteen käytöstä = kaikille > 18 v, mutta



Miten eri pohjoismaat suhtautuvat J&J rokotteeseen ?

Maa	Indikaatio	Kommentti
Islanti	≥ 18 v	https://www.landlaeknir.is/koronaveira/bolusetning/
Norja	Ei vielä päätöstä Kokous 29.4	
Ruotsi	≥ 65 v	https://www.folkhalsomyndigheten.se/nyheter-och-press/nyhetsarkiv/2021/april/beslut-om-att-avvakta-anvandning-av-janssens-vaccin-i-sverige/ Ruotsin epidemiologinen tilanne huono, x10 vrt
Suomi	Ei vielä päätöstä	
Tanska	Ei vielä päätöstä	

COVID-19 Janssen Vaccine, status in Europe (26.4.2021)

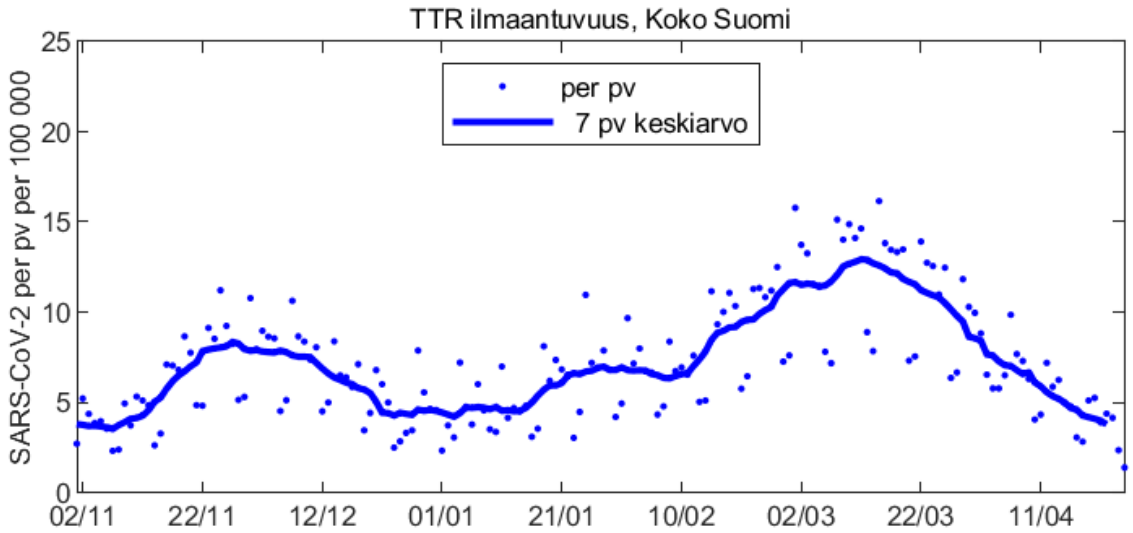
1	Bulgaria	Decision pending
2	Czech Republic	Decision pending **– Vaccinations started**
3	Denmark	Decision pending
4	Estonia	Decision pending
5	Finland	Decision pending
6	Ireland	Decision pending
7	Malta	Decision pending
8	Norway	Decision pending
9	United Kingdom	Decision pending
10	Austria	No restrictions
11	Croatia	No restrictions
12	Cyprus	No restrictions
13	Hungary	No restrictions
14	Luxembourg	No restrictions **– Vaccinations started**
15	Poland	No restrictions **– Vaccinations started**
16	Romania	No restrictions
17	Slovakia	No restrictions
18	Slovenia	No restrictions
19	Latvia	No restrictions **– Vaccinations started**
20	Lithuania	No restrictions **– Vaccinations started**
21	Greece	No restrictions
22	Luxemburg	No restrictions
23	Belgium	No restrictions **– Vaccinations started**
24	Germany	No restrictions
25	Netherlands	No restrictions **– Vaccinations started**
26	Iceland	No restrictions **– Vaccinations started**
27	Portugal	No restrictions
28	France	No formal restrictions * **- Vaccinations started**
29	Italy	No formal restrictions ** **- Vaccinations started**
30	Spain	No formal restrictions *** **- Vaccinations started**
31	Sweden	Restricted to ≥65 years

** MoH operational recommendation to vaccinate 55+ year-olds. NITAG decision pending*

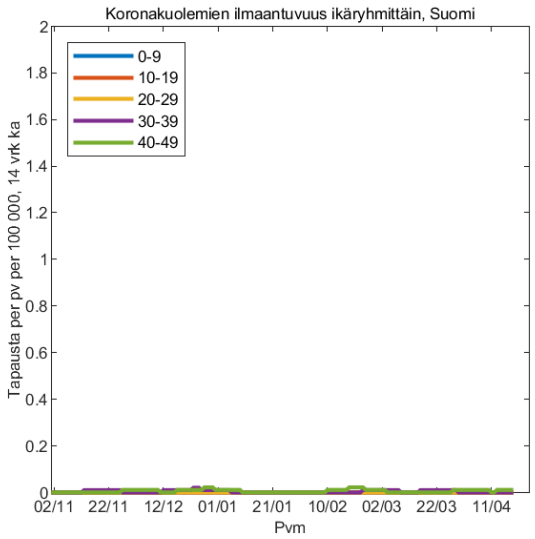
*** Indication to prioritise 60+ year-olds as part of current recommendation with regards to vaccine deployment strategy, rather than a formal restriction*

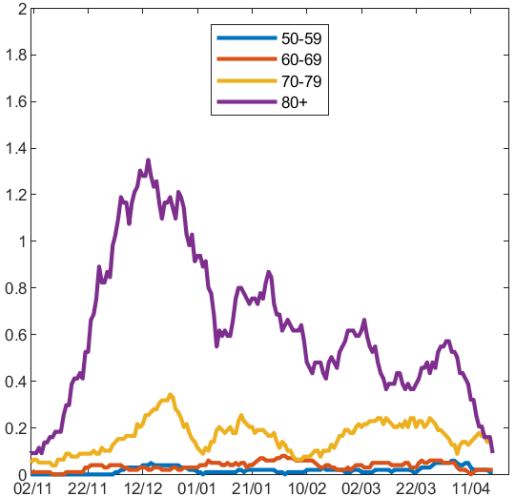
**** Indication to vaccinate 70-79 year-olds as part of current prioritisation of unvaccinated older adults*

Suomen epidemiatilanne

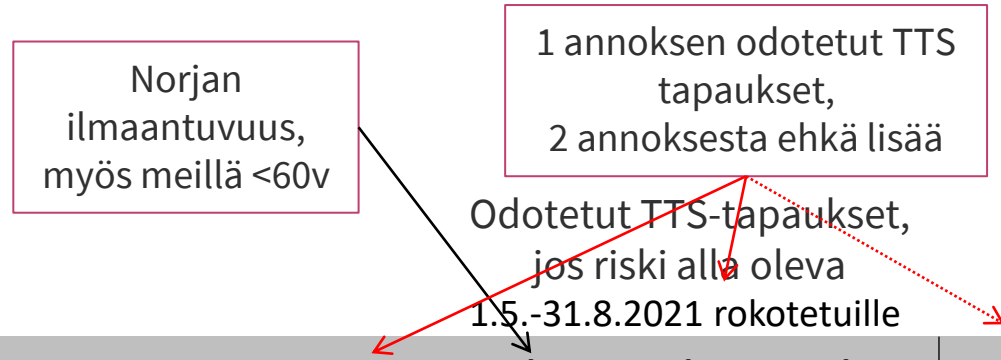


Kuolemat ikäryhmittäin





Vertailu TTS riskiin



90% rokotuskattavuus

Skenaario		Tapaukset	ESH	Teho	Kuolemat*	LY*	Uusia ADV-rokotettuja	3/100 000	2/100 000	1/100 000	2. annokset
Nykytaso jatkuu	ADV lopetetaan	6138	250	35	11	186	0	0	0	0	0
	ADV 65+	6080	248	35	11	184	0	0	0	0	151910
	ADV 60+	6043	246	35	11	181	5157	0.2	0.1	0.1	199762
	ADV 55+	5995	243	34	11	179	104090	3.1	2.1	1.0	326475
	ADV 50+	5957	242	34	11	178	201337	6.0	4.0	2.0	442050
	ADV 30+	5913	241	34	11	177	621879	18.7	12.4	6.2	885311
Korkeampi epidemia	ADV lopetetaan	17550	601	80	34	555	0	0	0	0	0
	ADV 65+	16757	577	77	32	531	0	0	0	0	151910
	ADV 60+	16429	564	75	31	517	5157	0.2	0.1	0.1	199762
	ADV 55+	16002	549	73	31	501	104090	3.1	2.1	1.0	326475
	ADV 50+	15642	537	71	30	490	201337	6.0	4.0	2.0	442050
	ADV 30+	15114	524	70	29	478	621879	18.7	12.4	6.2	885311

*) Ajalta 1.5.-31.8.2021 saaduista tartunnoista johtuvat koronakuolemat

Vaihtoehtoja J&J –rokotteen käytölle

Vaihtoehto	Viivästys rokotusohjelmalle	Kommentti
Ei oteta käyttöön	Aiemman KRAR-kokouksen mukainen arvio viivästykselle ja sen mukaiset vaikutukset	
65+ ikäraja kuten AZ		
Alhaisempi ikäraja – mikä?		Vrt. USA <50, naiset erityiskohtelu
Käyttöön kaikille	Ei viivästystä	

Arvioitu saapumismäärä 40 000 per vko

Ehdotuksemme KRAR:lle

- Tunnelmat epävarmat
- Jos TTS biologinen mekanismi on adenovirusvektoriin liittyvä, oletusarvo on, että J&J TTS riski on todennäköisesti samaa luokkaa kuin AZ:n
- Käyttösuositus linjassa AZ rokotteen käyttösuosituksen kanssa: ikäraja 65v