Ad26Cov2.S: 1 and 2 dose trial data and immunogenicity

Peter Smith, Minal Patel, Annelies Wilder-Smith

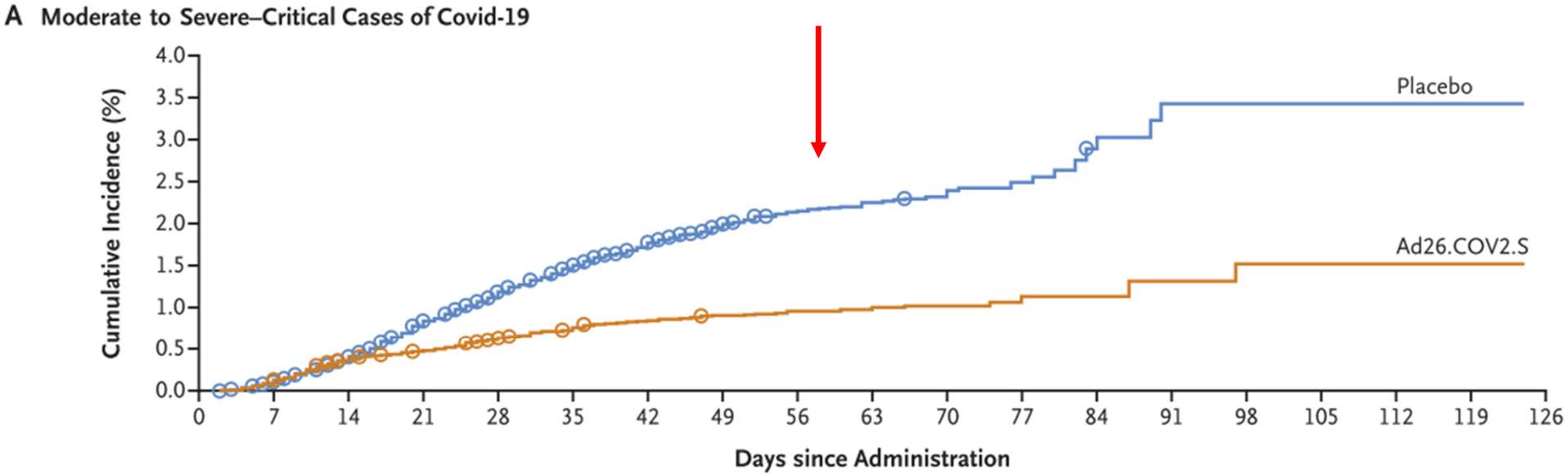
J&J Ad26Cov2.S Phase 3 single dose trial (COV3001)
Headline results (Sep 2020 - Jan 2021)

- 44,000 participants (9.6% seropositive); 1:1 randomisation
- US 44%, Latin America (6 countries) 41%, South Africa 15%
- Efficacy measured from 14 days post vaccination
- 468 symptomatic Covid-19 cases, 464 classified as moderate to severe-critical
- 33% aged 60+ years
- Median follow-up 58 days

Endpoint	Cases in vaccine vs control	Vaccine efficacy (95% CI)
Symptomatic Covid-19	117 vs 351	67% (59,74)
Age 18-59y	*95 vs 260*	*66% (56,73)*
Age 60+y	*22 vs 91*	*74% (58,84)*
Severe-critical Covid-19	14 vs 60	77% (55,89)

Sadoff et al. N Engl J Med 2021;384:2187-201

Median follow up 58 days



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

Sadoff et al. N Engl J Med 2021;384:2187-201

Primary and final efficacy analyses

(events 14+ days post vaccination)

	Primary Analysis (cutoff date January 22, 2021; median follow up 2 months) VE% (95% CI)	Final Analysis (cutoff date July 9, 2021; median follow up 4 months) VE% (95% CI)
Moderate and severe/critical COVID-19	66.9% (59.0, 73.0)	56.3% (51.3, 60.8)
Age 18-59 years	63.7% (53.9, 71.6)	56.6% (51.0, 61.7)
Age ≥60 years	76.3% (61.6, 86.0)	55.0% (42.9, 64.7)
Severe/critical COVID-19	76.7% (54.6, 89.1)	73.3% (63.9, 80.5)
COVID-19 requiring medical intervention	75.0% (-25.3, 97.4)	76.1% (56.9, 87.7)
COVID-19 related deaths	Not calculated	84.5% (47.3, 97.1)

Janssen analyses of July 9, 2021 data cutoff not verified by FDA

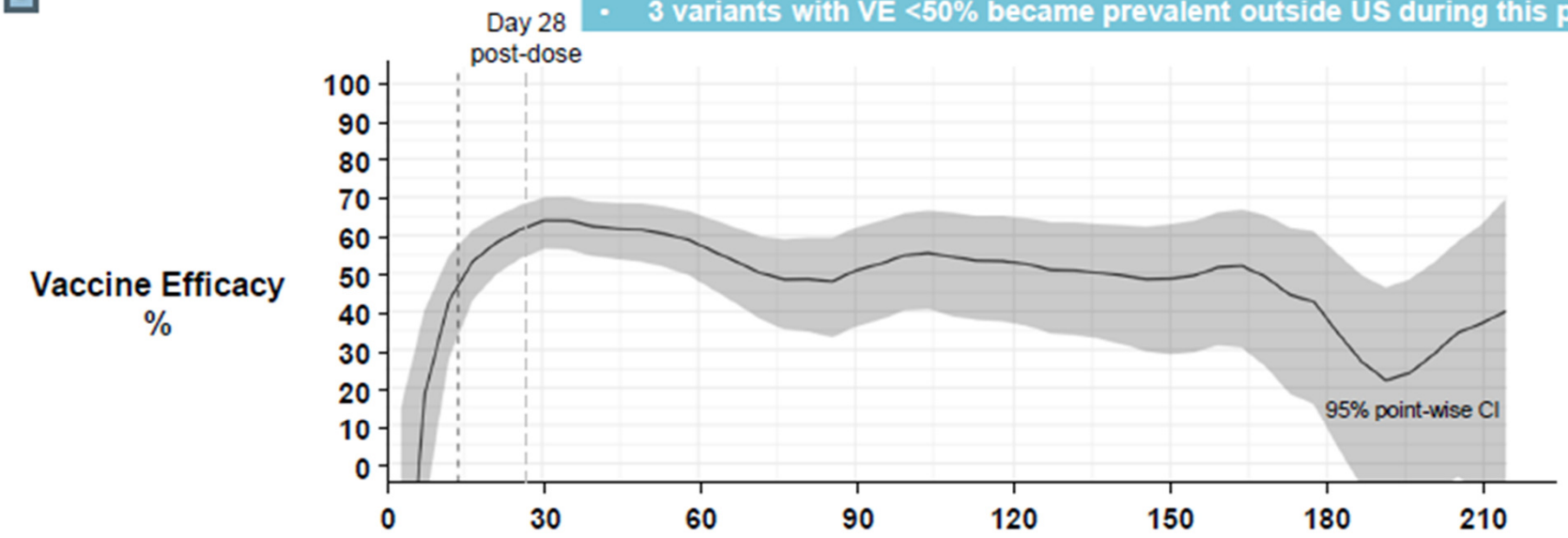
Vaccine efficacy by time since vaccination

	Moderate and severe/critical COVID-19 VE% (95% CI)	Severe/critical COVID-19 VE% (95% CI)
Day 15-28	72.3% (62.1, 80.1)	65.5% (27.3, 85.0)
Day 29-56	61.7% (52.5, 69.2)	85.7% (71.0, 93.7)
Day 57-112	50.8% (40.2, 59.7)	67.8% (44.2, 82.2)
Day 113 to end DB Phase	45.2% (33.0, 55.3)	71.7% (51.4, 84.3)

Efficacy against symptomatic disease by time since vaccination

COV3001: VE for Symptomatic COVID-19

- 53% VE against symptomatic COVID-19 >Day 28
- 3 variants with VE <50% became prevalent outside US during this period



Numbers at risk								
Ad26.COV2.S	19562	19111	17540	15290	10033	5256	3887	1193
Placebo	19589	18902	17052	14622	9328	4745	3531	1098

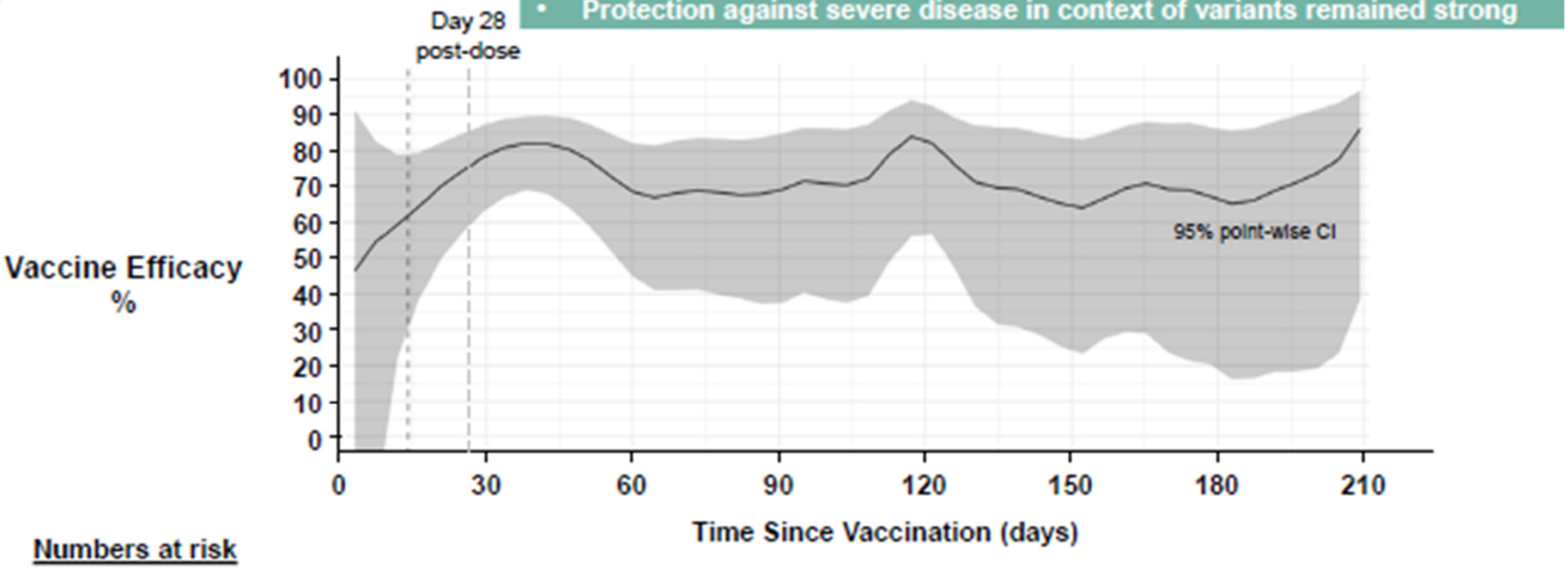
3001

Vaccines and Related Biological Products Advisory Committee October 14-15, 2021 Meeting

Efficacy against severe disease by time since vaccination

COV3001: Persistent VE Against Severe COVID-19

- 75% VE against severe/critical COVID-19 >Day 28
- Protection against severe disease in context of variants remained strong



Numbers at risk								
Ad26.COV2.S	19562	19230	17764	15591	10284	5432	4045	1307
Placebo	19589	19134	17521	15202	9815	5046	3796	1260

3001

Vaccines and Related Biological Products Advisory Committee October 14-15, 2021 Meeting

Efficacy against variants

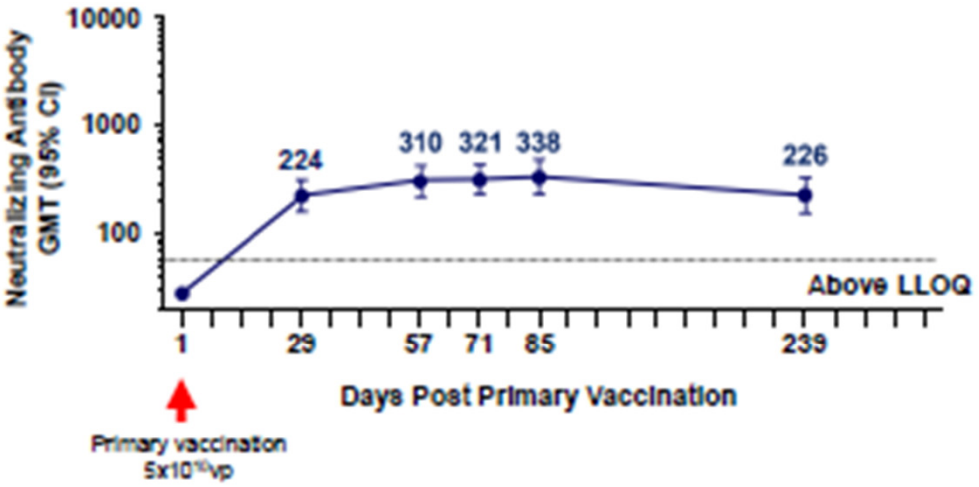
(Final efficacy analysis 14+ days post vaccination)

	Ad26.COV2.S N=19400 Cases	Placebo N=19398 Cases	VE% (95% CI)
Reference strain	32	108	71.5% (57.3, 81.4)
B.1.1.7 (Alpha)	9	29	70.1% (35.1, 87.6)
B.1.351 (Beta)	36	56	38.1% (4.2, 60.4)
B.1.617.2/AY.1/AY.2 (Delta)	11	10	-6.0% (-178.3, 59.2)
B.1.427/429 (Epsilon)	8	17	54.7% (-10.8, 83.1)
P.1 (Gamma)	74	112	36.4% (13.9, 53.2)
C.37 (Lambda)	43	46	10.0% (-39.5, 42.0)
P.2 (Zeta)	34	93	64.9% (47.3, 77.0)
B.1.621 (Mu)	38	57	35.8% (1.5, 58.6)

Janssen analysis not verified by FDA

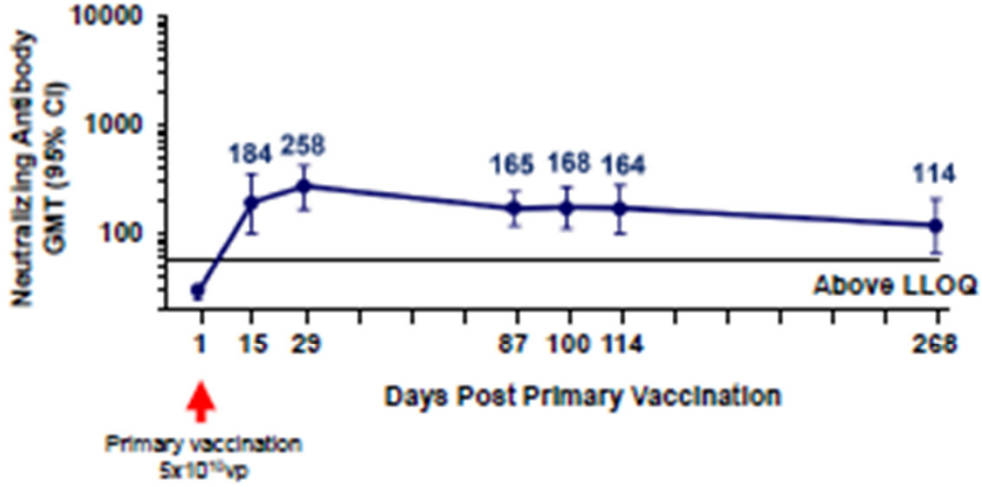
Janssen COV1001: Humoral Immune Responses Persist Over Time, Following a Single Dose (18-55 and ≥ 65 years)

18-55 Years, N=25



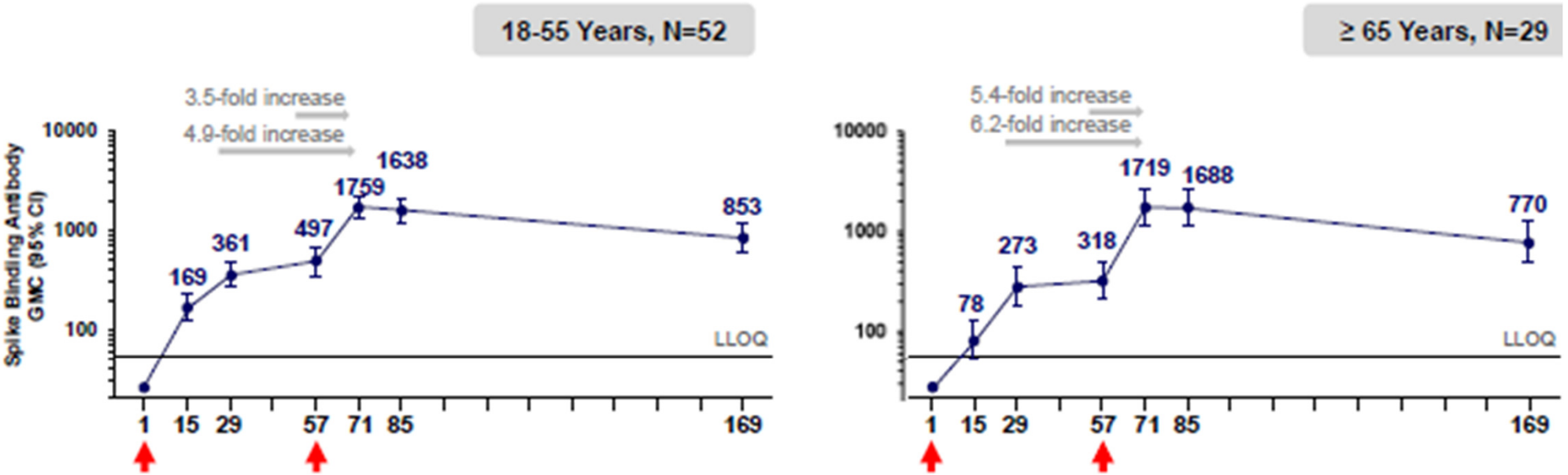
N	25	24	25	24	24	22	
% Responders	96						
% Detectable antibodies			100	100	100	95	

≥ 65 Years, N=24



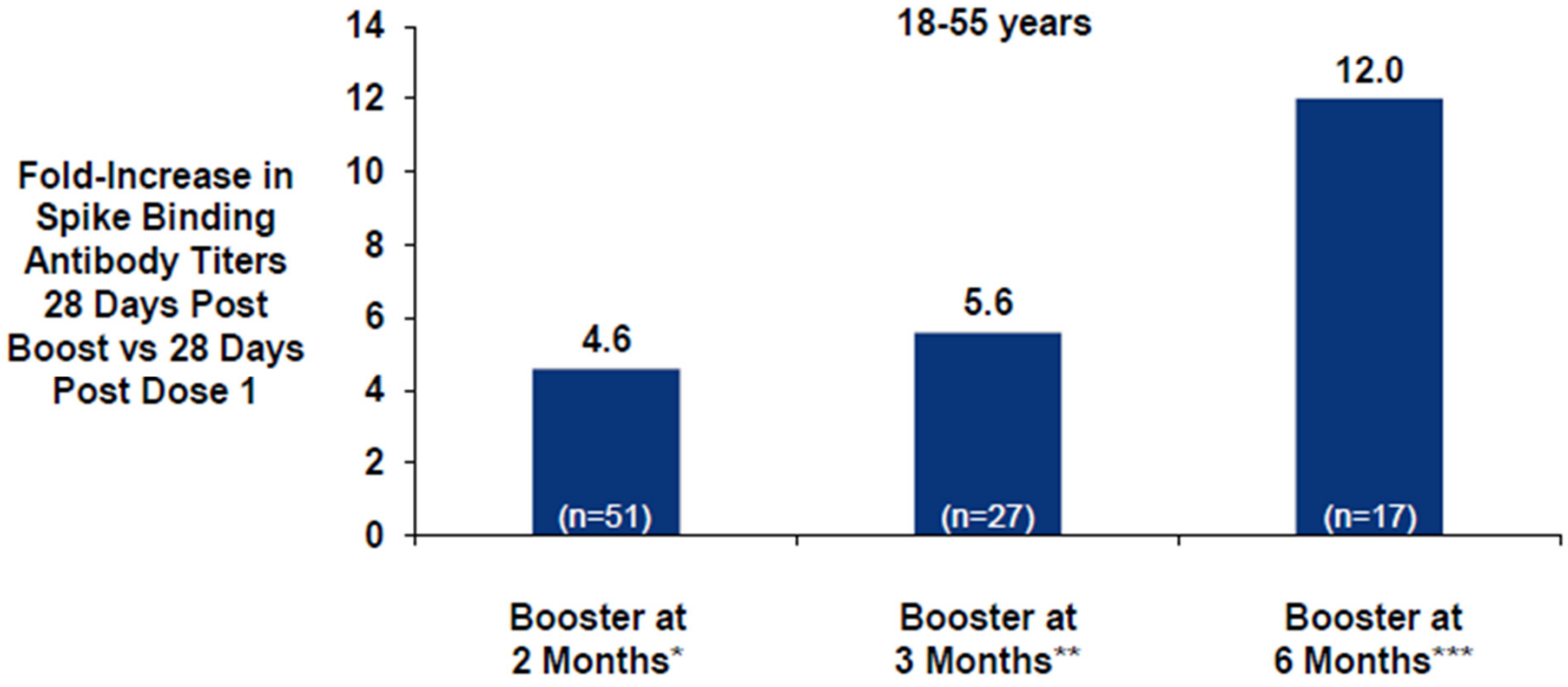
N	24	11	25	21	22	22	19
% Responders		100	96				
% Detectable antibodies				90	86	81	68

COV2001: Boost at 2 Months Increases Antibody Titers by 3.5- to 6.2-fold



N	52	52	54	54	53	52	50	N	29	28	29	29	29	28	27
% responders		86	96	96	100	100	98	% responders		64	93	97	100	100	96
% seropositive		89	98	98	100	100	100	% seropositive		64	93	97	100	100	96

COV1001 and COV2001: Benefit of Booster Dose Higher When Given at 6 Months or Later



J&J Ad26Cov2.S Phase 3 two-dose trial (COV3009)
Headline results (Sep 2020 - Jan 2021)

- 31,000 participants (9.6% seropositive); 1:1 randomisation; 2nd dose 2 months after dose 1
- US; Europe; Latin America; Philippines, South Africa
- 25% aged 60+ years
- Median follow-up-up after 2nd dose = 36 days
- Efficacy results 14+ days after dose 2

Endpoint	Cases in vaccine vs control	Vaccine efficacy (95% CI)
Symptomatic Covid-19	14 vs 52	75% (55,87)
Age 18-59y	*10 vs 41*	*78% (54,90)*
Age 60+y	*4 vs 11*	*66% (-14, 92)*
Severe-critical Covid-19	0 vs 8	100% (33,100)

J&J Ad26Cov2.S Two-dose and one dose results

Efficacy 14+ days after 2nd dose

Endpoint	Cases in vaccine vs control	Vaccine efficacy (95% CI)
Symptomatic Covid-19	14 vs 52	75% (55,87)
Severe-critical Covid-19	0 vs 8	100% (33,100)

Efficacy after one dose by time since vaccination

	Moderate and severe/critical COVID-19 VE% (95% CI)	Severe/critical COVID-19 VE% (95% CI)
Day 15-28	72.3% (62.1, 80.1)	65.5% (27.3, 85.0)
Day 29-56	61.7% (52.5, 69.2)	85.7% (71.0, 93.7)
Day 57-112	50.8% (40.2, 59.7)	67.8% (44.2, 82.2)
Day 113 to end DB Phase	45.2% (33.0, 55.3)	71.7% (51.4, 84.3)

Efficacy against variants (14+ days post dose 2)

(68% of cases sequenced)

	Ad26.COV2.S N=6024 Cases	Placebo N=5616 Cases	VE% (95% CI)
B.1.1.7 (Alpha)	1	16	75.2% (54.6, 87.3)
B.1.617.2 (Delta)	2	1	Not calculated
B.1.621 (Mu)	4	10	64.1% (-27.9, 91.6)

Janssen-Ad26.COV 2.S Vaccine Effectiveness (VE) of the Primary Series (1 dose): pre (non-) Delta and Delta

Of note: No VE data for 2 doses

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Non-Delta

Non-Delta Period Vaccine Effectiveness Studies

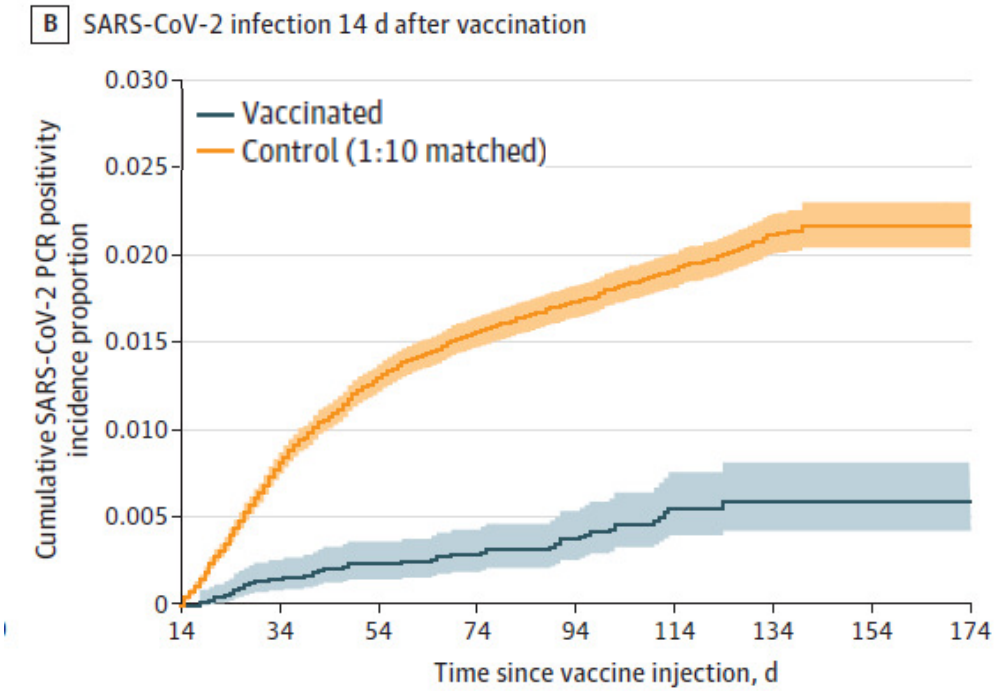
Variant	Author	Country	Study	Population	Infection	Disease	Hospitalization/ Severe disease	ROB
Alpha+ nonVOC	Polinski	USA	Cohort study	≥18 year olds	79 (77-80)		81 (79-84)	Serious
				<50 years	83 (81-85)		86 (80-90)	
				≥50 years	75 (74-77)		80 (77-82)	
				Immuno-compromised	64 (57-70)		68 (54-77)	
Alpha+ nonVOC	Thompson	USA	TND	≥50 year olds			68 (50-79)	Low-Moderate-Serious
Gamma	Ranzani	Brazil	TND	≥18 year olds		50.9 (35.5-63.0)	72.9 (35.1-91.1) 92.5 (54.9-99.6) (ICU) 90.5 (31.5-99.6 (death)	Moderate-Serious
Mu	Arregoces	Colombia	Cohort	≥60 year olds			80 (19.9-95.0) (Hospitalization without death)	Pending

TND=Test negative design case control study; VOC=Variant of Concern
References at end of slide deck

Mix of Variants (including Delta)

VE against infection in the US

- Propensity-score matched cohort study between February 27-July 22, 2021 in persons ≥18 years
  - Non-VOCs, Alpha, Delta
  - Median follow up of 111 days (IQR 102-131 days)
- VE against infection (95% CI) : 74.2% (64.9-81.6)
- Risk of Bias: Moderate-Serious

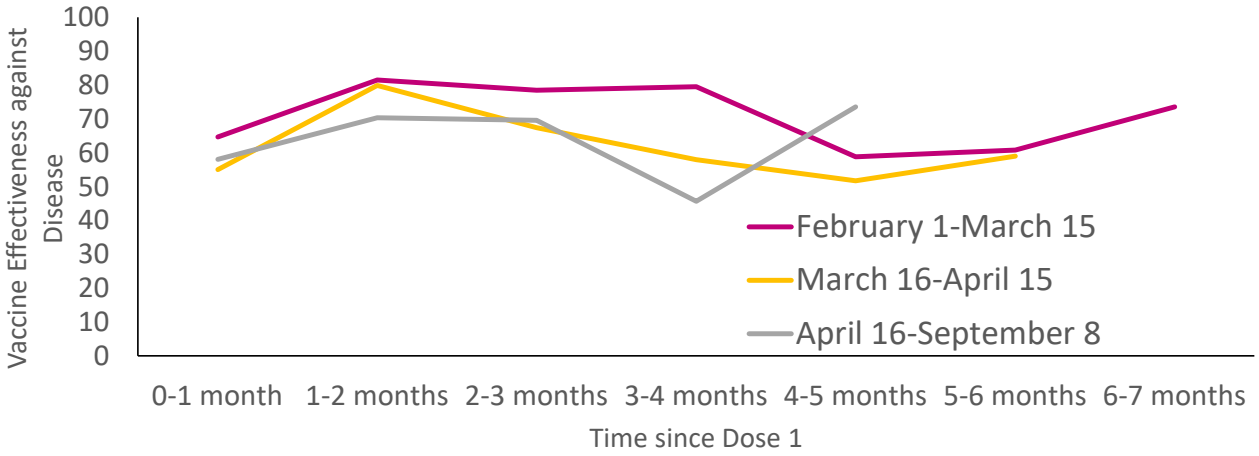


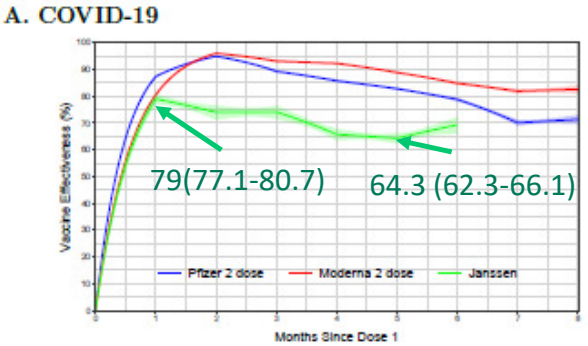
VOCs=Variants of Concern; IQR=Interquartile Range; VE=Vaccine Effectiveness; CI=Confidence Intervals

Corchado-Garcia, J., Zemmour, D., Hughes, T., Bandi, H., Cristea-Platon, T., Lenehan, P., Pawlowski, C., Bade, S., O'Horo, J. C., Gores, G. J., Williams, A. W., Badley, A. D., Halamka, J., Virk, A., Swift, M. D., Wagner, T., & Soundararajan, V. (2021). Analysis of the Effectiveness of the Ad26.COV2.S Adenoviral Vector Vaccine for Preventing COVID-19. *JAMA Network Open*, *4*(11), e2132540. https://doi.org/10.1001/jamanetworkopen.2021.32540

VE against infection in the US

- Cohort study using administrative data in North Carolina, USA between December 13, 2020 (March for JNJ)-September 8, 2021 among ≥18 years
  - VE against disease by time since vaccination similar by vaccine cohort→not due to Delta





Lin, D., Gu, Y., Wheeler, B., Young, H., Holloway, S., Sunny, S. K., Moore, Z., & Zeng, D. (2021). Effectiveness of Covid-19 Vaccines in the United States Over 9 Months: Surveillance Data from the State of North Carolina. *MedRxiv*, 2021.10.25.21265304. https://doi.org/10.1101/2021.10.25.21265304

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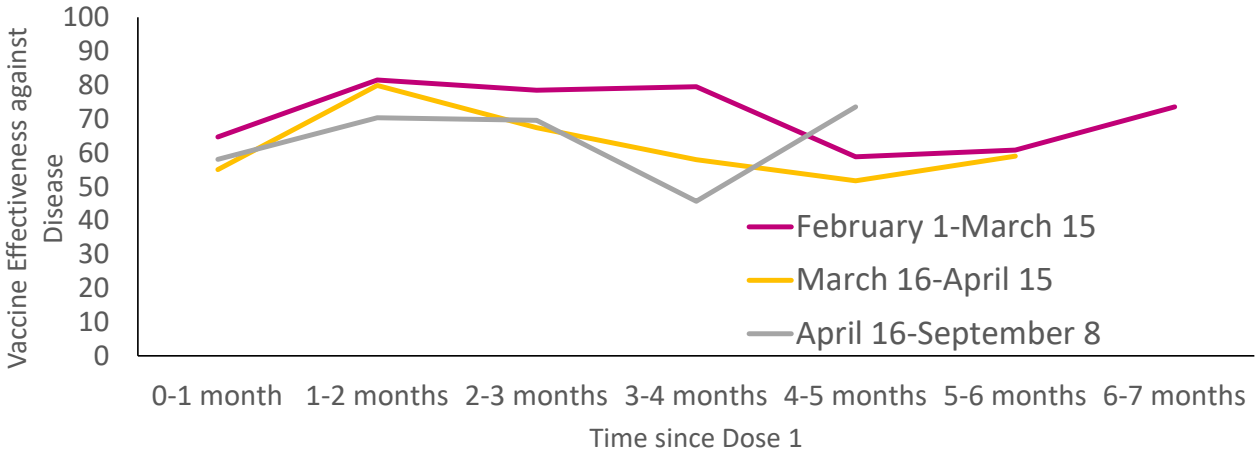

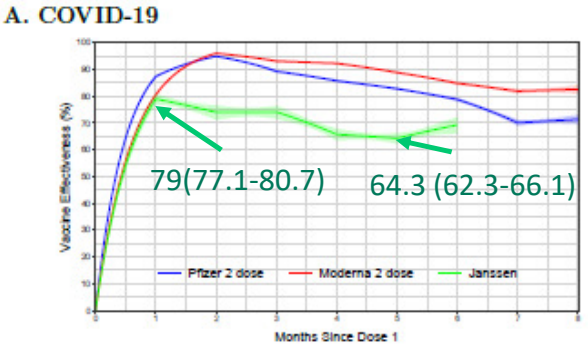

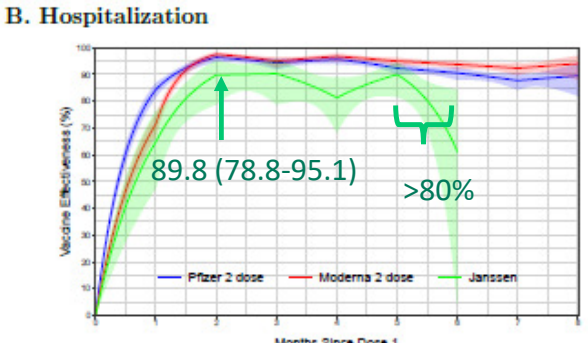

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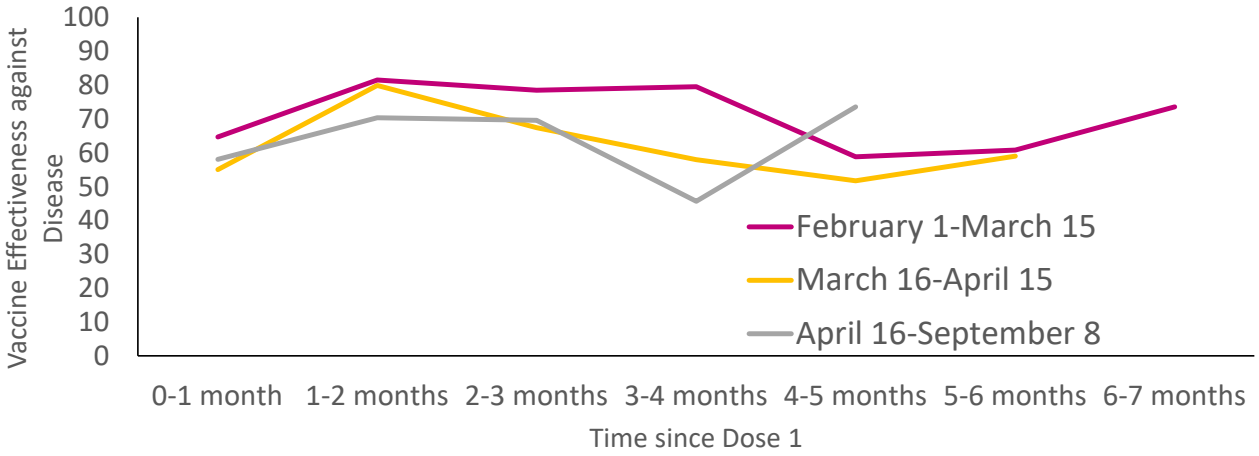

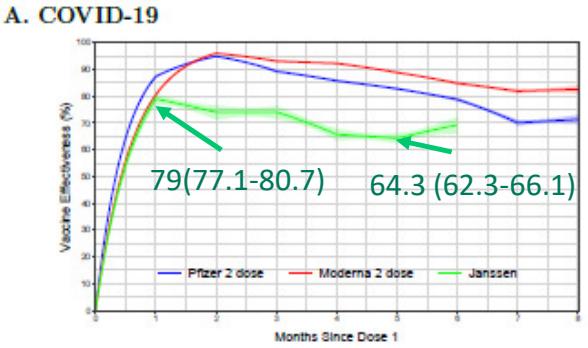

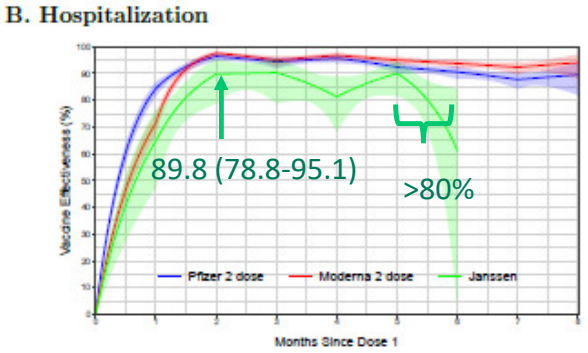

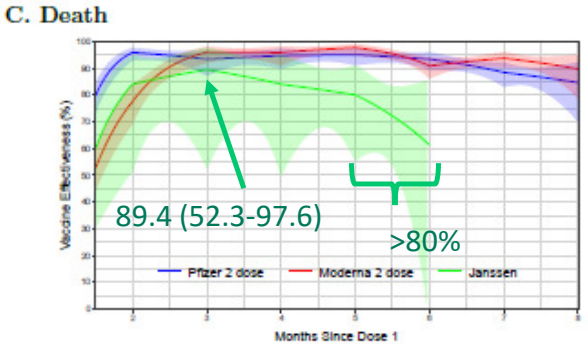

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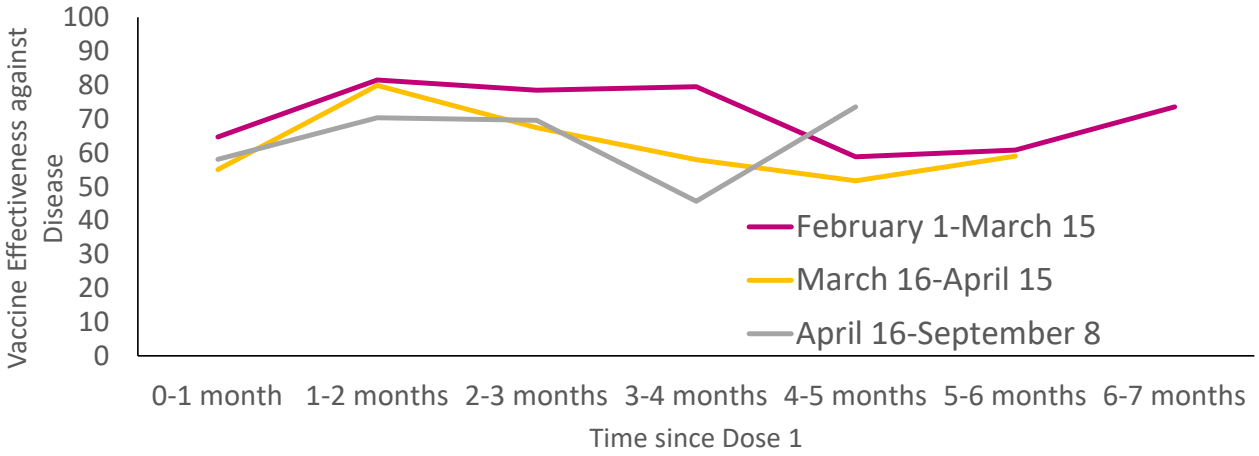
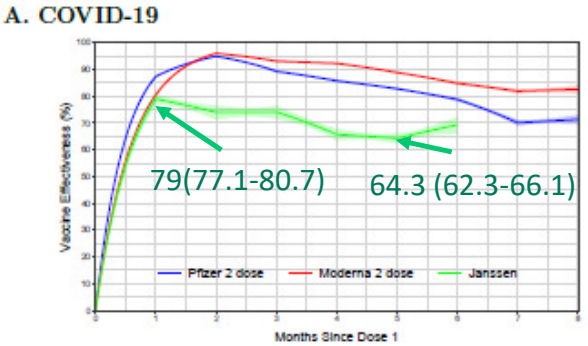
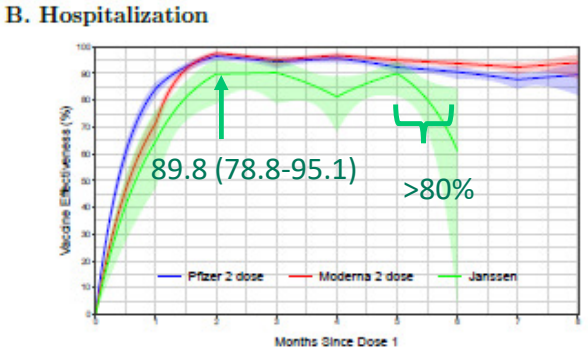
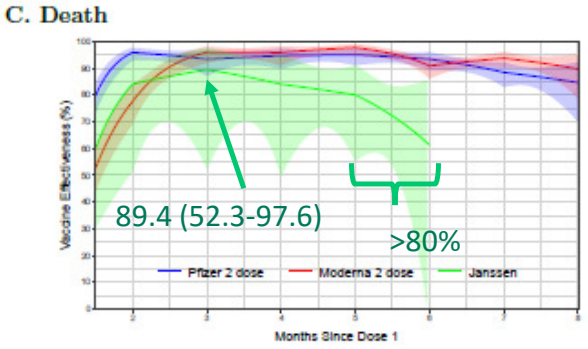








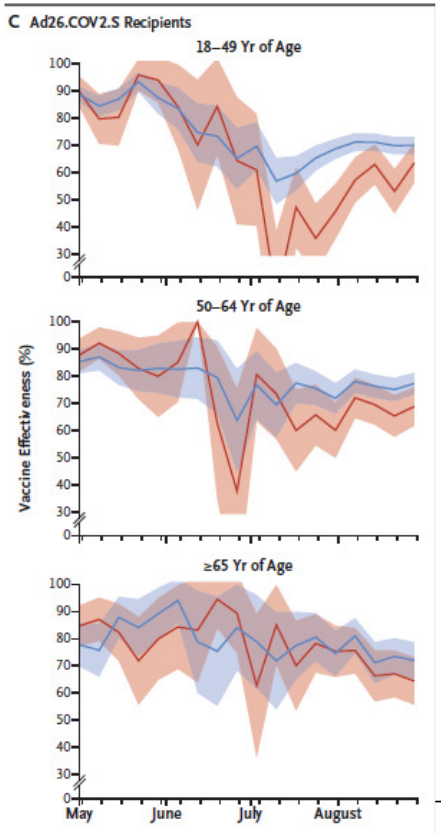
- Limitation: Missing death and hospitalization status on 60% and 40%, respectively
- Risk of Bias: Serious

Lin, D., Gu, Y., Wheeler, B., Young, H., Holloway, S., Sunny, S. K., Moore, Z., & Zeng, D. (2021). Effectiveness of Covid-19 Vaccines in the United States Over 9 Months: Surveillance Data from the State of North Carolina. *MedRxiv*, 2021.10.25.21265304. https://doi.org/10.1101/2021.10.25.21265304

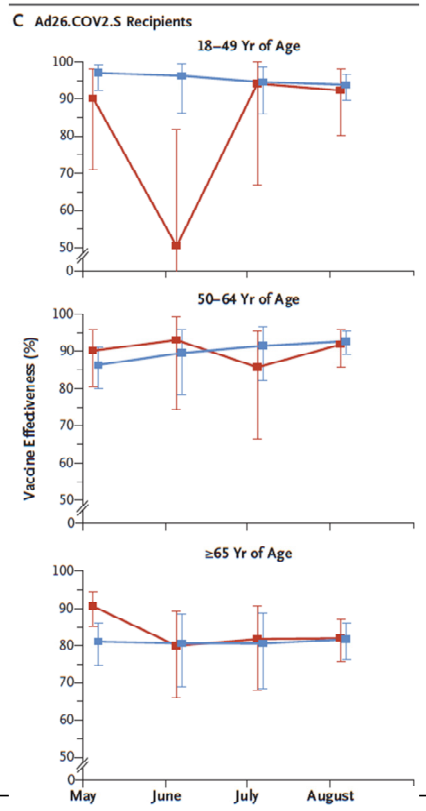
VE against infection and hospitalization in the US

- Cohort study using administrative data in New York, USA between May 1-September 3, 2021 among ~8.7 million ≥18 years Red=vaccinated in March Blue=vaccinated in April

Infection



Hospitalization



VE (95% CI) against Infection

Age group	Vaccine month	Week of May 1	Week of July 10	Week of August 28
18-49	March	89.7 (84.1-95.3)	13.8 (-10.9-38.4)	63.4 (56.1-70.7)
	April	88.8 (86-91.6)	56.8 (48.3-65.3)	69.9 (66.7-73.1)
50-64	March	87.8 (81.8-93.8)	73.4 (56.8-90.1)	68.8 (61.7-75.9)
	April	85.3 (81-89.7)	69.4 (57.5-81.3)	77.3 (73.3-81.3)
≥65	March	84.8 (77.3-92.3)	85.1 (70.3-99.8)	64.5 (55.7-73.3)
	April	77.8 (69.8-85.8)	71.9 (54.1-89.7)	72.0 (65.3-78.8)

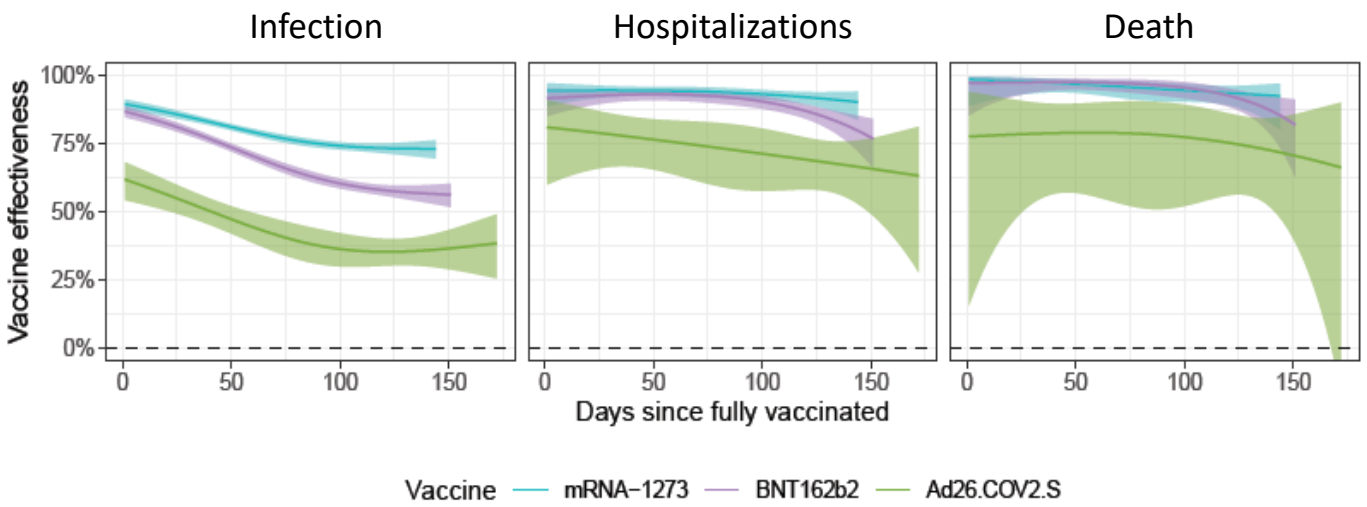
- Risk of Bias: Serious

Rosenberg, E. S., Dorabawila, V., Easton, D., Bauer, U. E., Kumar, J., Hoen, R., Hoefer, D., Wu, M., Lutterloh, E., Conroy, M. B., Greene, D., & Zucker, H. A. (2021). Covid-19 Vaccine Effectiveness in New York State. *New England Journal of Medicine*, 2021.10.08.21264595. https://doi.org/10.1056/NEJMoa2116063

VE against infection, hospitalization, death in Puerto Rico

- Cohort study in Puerto Rico using administrative data between December 15, 2020-October 15, 2021 among ≥18 years (for JNJ)

	Infection	Hospitalization	Death
VE at 2 weeks (99% CI)	62 (54-68)	81 (60-91)	78 (16-94)
VE after 144 days (99% CI)	36 (30-42)	67 (54-76)	72 (49-85)



- Unable to evaluate during pre-Delta versus Delta due to small #s
- Risk of Bias: Serious

Irizarry, R., Robles-Fontán, M., Nieves, E., Cardona-Gerena Irizarry, I. R., & Author, C. (2021). Time-Varying Effectiveness of Three Covid-19 Vaccines in Puerto Rico. *SSRN* https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3957118

Delta

VE against infection in Spain

- Cohort study of close contacts of cases identified as part of contact tracing
  - April-August 2021
  - Alpha and Delta specific VE estimates
  - Duration of protection
- Results

Variant	Timing since last dose	Infection	Disease	Hospitalization
Alpha+Delta	≥14 days	50 (42-57)	54 (45-62)	74 (43-88)
	<90 days	52 (44-59)		
	≥90 days	28 (-8-53)		
Alpha	≥14 days	77 (27-93)		
Delta	≥14 days	42 (18-59)		

- Risk of Bias: Serious

Martínez-Baz, I., Trobajo-Sanmartín, C., Miqueleiz, A., Guevara, M., Fernández-Huerta, M., Burgui, C., Casado, I., Portillo, M. E., Navascués, A., Ezpeleta, C., & Castilla, J. (2021). Product-specific COVID-19 vaccine effectiveness against secondary infection in close contacts, Navarre, Spain, April to August 2021. *Eurosurveillance*, *26*(39). https://doi.org/10.2807/1560-7917.ES.2021.26.39.2100894

VE against Infection, Emergency Department (ED) /Urgent Care Clinic (UCC) Visits and Hospitalizations in the US

- Matched test-negative design case-control in July 2021-August 2021

	ED/UCC	Hospitalizations
VE (95% CI)	65 (56–72)	60 (31–77)

  - Risk of Bias: Low-Moderate
- Test-negative design case-control without an immunocompromising condition in March 2021-August 2021 (Delta+nondelta)

	Hospitalizations
VE (95% CI)	71 (56–81)

  - Risk of Bias: Pending
- Cohort study in June-July 2021

	Infection	Hospitalizations
VE (95% CI)	78 (73-82)	85 (73-91)

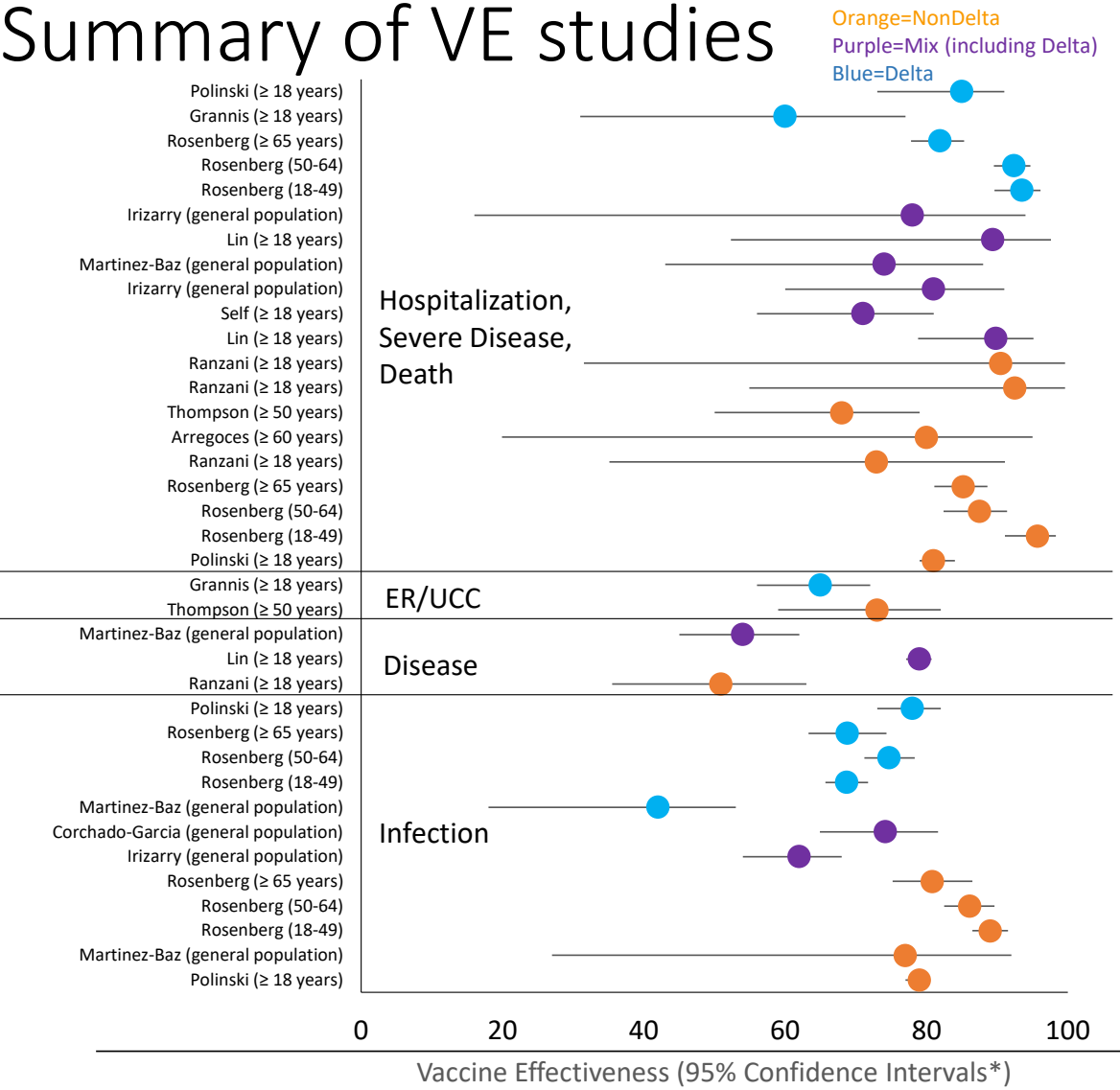
  - Risk of Bias: Serious

Grannis, S. J., Rowley, E. A., Ong, T. C., Stenehjem, E., Klein, N. P., DeSilva, M. B., Naleway, A. L., Natarajan, K., & Thompson, M. G. (2021). Interim Estimates of COVID-19 Vaccine Effectiveness Against COVID-19–Associated Emergency Department or Urgent Care Clinic Encounters and Hospitalizations Among Adults During SARS-CoV-2 B.1.617.2 (Delta) Variant Predominance — Nine States, June–August 2021. *MMWR. Morbidity and Mortality Weekly Report*, *70*(37). https://doi.org/10.15585/mmwr.mm7037e2

Polinski, J. M., Weckstein, A. R., Batech, M., Kabelac, C., Kamath, T., Harvey, R., Jain, S., Rassen, J. A., Khan, N., & Schneeweiss, S. (2021). Effectiveness of the Single-Dose Ad26.COV2.S COVID Vaccine. *MedRxiv*, 2021.09.10.21263385. https://doi.org/10.1101/2021.09.10.21263385

Self, W. H., Tenforde, M. W., Rhoads, J. P., Gaglani, M., Ginde, A. A., Douin, D. J., Olson, S. M., Talbot, H. K., Casey, J. D., Mohr, N. M., Zepeski, A., McNeal, T., Ghamande, S., Gibbs, K. W., Files, D. C., Hager, D. N., Shehu, A., Prekker, M. E., Erickson, H. L., … Arter, O. G. (2021). Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March–August 2021. *MMWR. Morbidity and Mortality Weekly Report*, *70*(38). https://doi.org/10.15585/mmwr.mm7038e1

Summary of VE studies



*99% CI for Irizarry estimates

- Few studies on the VE of 1 dose especially in the context of Delta
  - Delta studies need to be considered in the context of waning immunity
- Most studies from the US
- VE against infection 80-90% during alpha and 70-80% during Delta
- VE against severe outcomes
  - More variable with wide confidence intervals
  - 70-90% with minimal impact of Delta
- Lower vaccine effectiveness in older persons, immunocompromised