Vaccine Safety and Efficacy in Individuals with Down syndrome

From Evidence to Action

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The Dream Team

Learning objectives

- Describe the severe impact of (respiratory) infections on people with DS
- Summarize the important role of vaccines in protecting people with DS
- List reasons that impair uptake of vaccines in people with DS
- Explain that vaccines are safe and immunogenic in people with DS
- Outline opportunities to improve biologic response to vaccines in people with DS

Resource:

npj Vaccines https://doi.org/10.1038/s41541-026-01489-7

Article in Press

Vaccination in individuals with Down syndrome: immune vulnerability, safety, efficacy and opportunities

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Respiratory Infections: Deadly Impact in DS


Photo Credit: The Washington Post

- **Third highest cause of death** in people with DS.
- **10× mortality** versus individuals without DS.
- Leading cause of healthcare utilization, hospitalization, ICU admission
- High-risk pathogens include SARS-CoV-2, influenza, measles, pneumococcus, and RSV.

Respiratory Infections: Deadly Impact in DS

Influenza

10x mortality across lifespan

2nd leading cause of mortality

DS

No DS

Landes et al, *Disabil Health J* 2021

COVID-19

10x mortality

Begins 20 years earlier

No DS

DS

Hüls et al, *EClinicalmed* 2021

Measles

DS: 7% of all deaths ‘70-’83

Pneumonia most common cause

Deaths from measles in (a) previously normal and (b) previously abnormal persons, and deaths from subacute sclerosing panencephalitis 1970-83

Year	Total measles deaths	Ratio/10 000 notifications	(a) Previously normal (No %)	(b) Previously abnormal	Subacute sclerosing panencephalitis
1970	39	1·3	24 (62)	15	5
1971	25	1·9	17 (68)	8	9
1972	29	2·0	18 (62)	11	15
1973	27	1·8	18 (67)	9	15
1974	19	1·7	12 (63)	7	12
1975	13	0·9	10 (77)	3	14
1976	11	2·0	4 (36)	7	15
1977	18	1·0	5 (28)	13	18
1978	13	1·0	6 (46)	7	15
1979	14	1·8	7 (50)	7	15
1980	23	1·6	8 (35)	15	12
1981	12	2·3	3 (25)	9	15
1982	10	1·1	3 (30)	7	13
1983	17	1·6	9 (50)	8	2
	270	1·5	144 (53)	126	175

Miller CL, *Br Med J* 1985

“Milder Illness” and impact in people with DS

Even mild infections requiring outpatient care, emergency visits, or brief hospitalization can negatively impact individuals with DS

- Swabs, oxygen, IVs often required during these sick visits affect later participation in healthcare
- Missed therapies and school absences can **hinder skill development**.
- Missed workdays for caregivers, increasing **stress and financial burden**.

Photo Credit: Down Syndrome Alliance

Vaccines are safe and effective in the general population

Influenza
Typically >40%

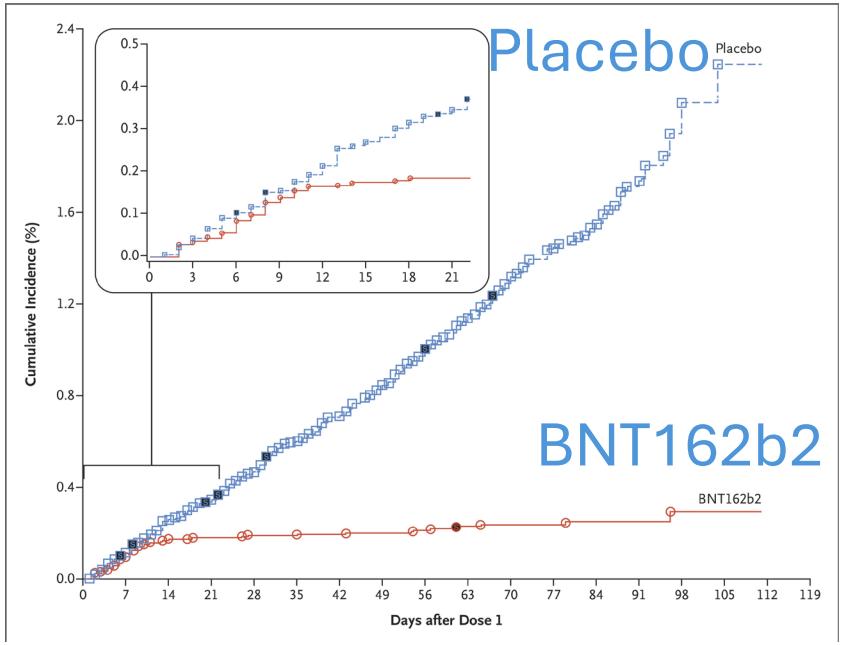
COVID-19
95% efficacy

Measles
~97% effective

2005

CDC

2025



Polack et al, *NEJM* 2020

TABLE VII

PROTECTION OF MEASLES VACCINE AGAINST "REGULAR" CASES OF MEASLES

Group	Approximate Time Post-vaccination	Attack Rate per 1,000			Effectiveness of Vaccine (%)	
		Placebo	KKK	KKL	KKK	KKL
I	4– 3 months	76.6	5.0	0	94	100
II	4–10 months	23.6	5.3	1.8	80	93
III	11–13 months	48.0	12.7	1.8	75	97

Guinee et al, *Pediatrics* 1966

Less utilization of vaccines in people with DS

- **Combined 7-vaccine series, up to date @19 mths:**
  - **58% of children with DS** vs 71% of typical children
- Caregivers: **42% feared serious side effects**.
- **Barriers of perception**
  - Vaccines vs “natural” immunity
  - Safety and utility specifically in people with DS
- **Barriers of biology**
  - Are vaccines equally immunogenic in people with DS?

Vaccines use natural biology

	Composition	Immune response	Side effect risk
Pathogen	Naturally occurring	Yes	High
Vaccines	Weakened Dead Subunits/Protein	Yes	Low

Vaccines: Developed against diseases with high risk of serious complications and death.

- Survivor immunity: High risk of these complications
  - Vaccines: Lower risk of these complications

Vaccines are **safe and immunogenic** in people with DS

Supplemental Table 1

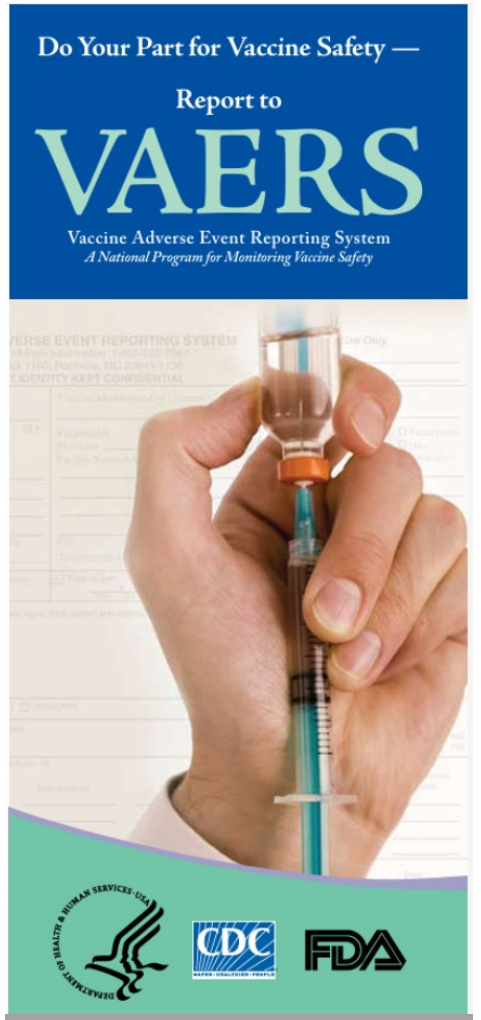
Table of vaccine safety and immunogenicity studies

Paper	PMID	Vaccine	N (DS)	Age	Variable	Immuno-genic?	Defect?	Safety
2022 James	35891309	flu	35 (18)	adults	Ab @0-52 wks	Y	Y	
2015 Valentini	26518399	flu x1	30 (15)	children	Ab @2 wks, B-SWM	Y	Y	
2012 Kusters	22986705	flu	48 (48)	children	Ab @3-38 wks	Y	Y	
2011 Joshi	21596078	flu TIV	24 (12)	children	Ab @4-6 wks	Y	Y	
1986 Philip	2419411	flu	20 (10)	both	PBMC proliferation, IL-2	Y	Y	
1978 Hawkes	148342	flu	188 (110)	adults, inst	Ab @6 wks	Y	N	
2023 Santoro	37864360	PCV13	55 (55)	both (mostly children)	Ab @XSxn	Y	UNK (we er in DS+Ifx)	
2015 Valentini	26518399	PCV13	30 (15)	children	Ab @2 wks	Y	N	
2013 Kusters	24200977	PCV7 x2 + PPSV23	18 (18)	(mostly children)	Ab @ 4 wks	Y	N	
2024 Martins	39053889	PPSV23	49 (49)	children	Ab @6 wks	Y	UNK (weaker n DS+Ifx)	
2011 Joshi	21596078	PPSV23	24 (12)	children	Ab @4-6 wks	Y	UNK	
2006 Costa-Carvalho	17160268	PPSV23	47 (17)	children	Ab @6 wks	Y	Y	
1982 Nurmi	6213331	PPSV14	52 (16)	adults, inst	Ab @3 wks	Y	Y	
2023 Valentini	36813120	CoV2	126 (126)	both	Ab @6 mths	Y	UNK (de v age)	
2023 Streng	38616780	CoV2	84 (44)	adults	Ab up to 6 mths, titer, IgG1 N-glycosylation	Y	Y	
2023 Esparcia-Pinedo	35869848	CoV2	88 (44)	adults	Ab up to 6 mths, Ag-T up to 6 mths	Y	Y	
2022 Valentini	35160144	CoV2	74 (38)	both	Ab up to 6 mths	Y	Y	no severe
2022 Streng	35748853	CoV2	253 (173)	adults	Ab up to 4 wks	Y	Y	
2022 Sali	35461998	CoV2	84 (42)	adults	Ab up to 6 mths	Y	Y	
1993 Oda	8365667	mumps	72 (36)	both	Ab @convenience	Y	Y	
1978 Hawkes	148342	mumps	188 (110)	adults, inst	Ab @7 wks	Y	Y	
2023 Familiar-Macedo	38155740	measles	58 (34)	children	Ab @up tp 61 mths	Y	N	
1993 Oda	8365667	measles	72 (36)	both	Ab @convenience	Y	Y	
1978 Hawkes	148342	measles	188 (110)	adults, inst	Ab @7 wks	Y	Y	
2023 Familiar-Macedo	38155740	rubella	58 (34)	children	Ab @up tp 61 mths	Y	Y	
1993 Oda	8365667	rubella	72 (36)	both	Ab @convenience	Y	N	
1978 Hawkes	148342	rubella	188 (110)	adults, inst	Ab @7 wks	Y	N	
1980 Hawkes	6300224	polio	18 (9)	children, inst	Ab @10 wks post-booster, OPV excretion	Y	Y	
2023 Santoro	37864360	tetanus	55 (55)	both (mostly children)	Ab @XSxn	Y	N	
2011 Kusters	21057373	tetanus	62 (22)	children	Ab @4 wks pos booster, avidity @4 wks post booster	Y	Y	
1986 Philip	2419411	tetanus	20 (10)	both	PBMC proliferation, IL-2	Y	Y	
1980 Epstein	6154538	tetanus	29 (15)	both	PBMC proliferation	N	Y	
1978 Hawkes	148342	tetanus	188 (110)	adults, inst	Ab @2 wks	Y	N	
2023 Santoro	37864360	diptheria	55 (55)	both (mostly children)	Ab @XSxn	Y	N	
1978 Hawkes	148342	diptheria	188 (110)	adults, inst	Ab @2 wks	Y	N	
2009 Ladhani	19580418	HiB	167 (3)	children	Ab	UNK	Y*	
2017 Eijsvoogel	28322457	HBV	227 (227)	both	Ab persistence up to 25 yrs	Y	Y	
2014 Nisihara	23952481	HBV	120 (120)	children	Ab @up to 6 mths	Y	Y	
1998 Vellinga	9892391	HBV	196 (10)	both, inst	Ab @up to 132 mths	Y	Y	
1993 Ahman	8460344	HBV	83 (83)	both, inst	Ab @up to 3 yr	Y	Y	
1992 Vajro	1533557	HBV	58 (29)	children	Ab @up to 2 yr	Y	Y	
1984 Heijtink	6235163	HBV	85 (23)	adults, inst	Ab @up to 6 mths	Y	Y	
1990 van Damme	2139285	HBV	275 (18)	both, inst	Ab @up to 2 yr	Y	Y	
1985 Troisi	2933533	HBV	62 (62)	both, inst	Ab @up to 1 yr	Y	N	
2004 Ferreira	15448421	HAV	127 (63)	children	Ab @up to 7 mths	Y	N (trend Y)	no SAE
2011 Kusters	21849866	Meningococcal ACWY	19 (19)	children	Ab @up to 1 yr	Y	Y	

Khor et al, *npj Vaccines* 2026

Vaccines Are Safe for People with DS

- No signal of increased adverse events in people w/ DS
- Prospective trials **of hepatitis A and SARS-CoV-2 vaccines** in children and adults with DS found no increase in severe adverse events.
- Studies on **pneumococcal vaccine** confirm safety in people with DS
- Multiple studies also confirm that vaccines are safe in individuals with immune compromise.
- **Continued monitoring remains critical** to detect rare or unexpected adverse events
  - By the way, we looked as part of the review!



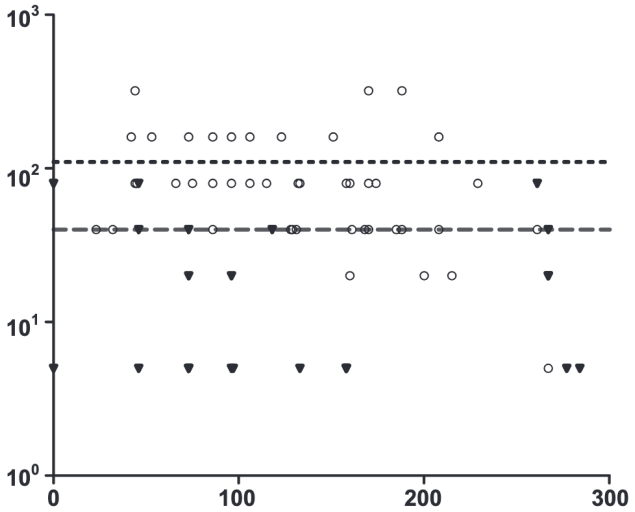
Source: HHS

Vaccines Are Immunogenic in People with DS

>95% of all studies show vaccines are immunogenic in people with DS

Influenza

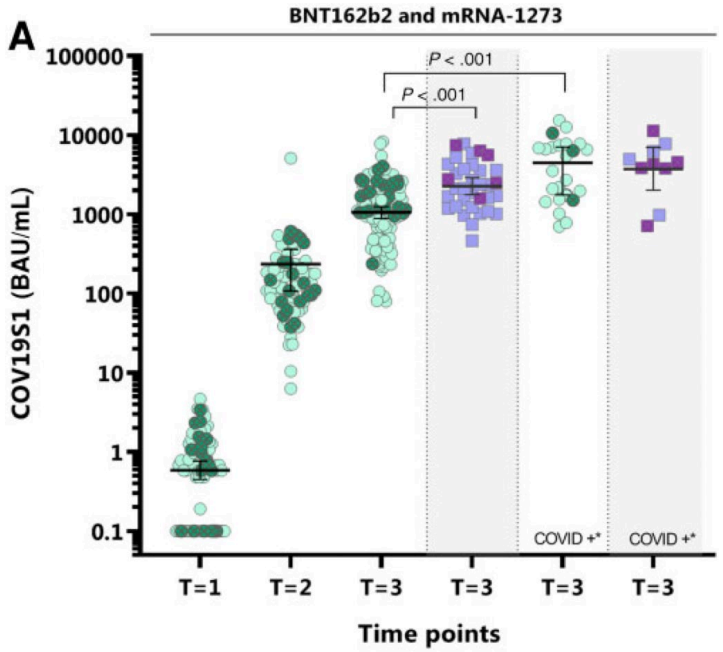
92% children >1:40 (EC_{50} in adults)



Kusters et al, *Pediatr Inf Dis J* 2012

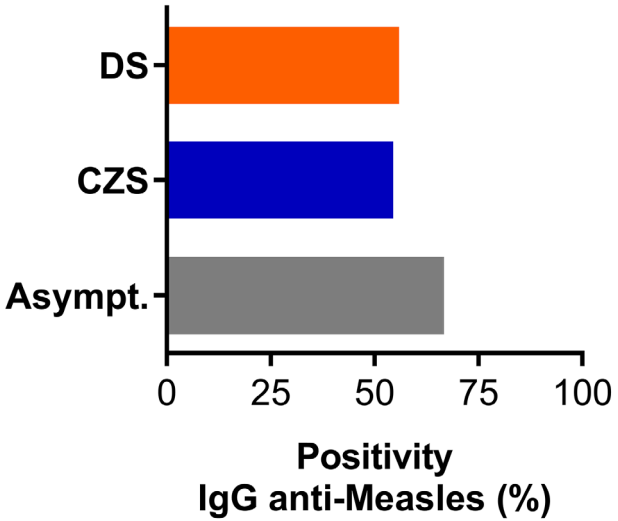
COVID-19

100% responders



Streng et al, *J Inf Dis J* 2022

Measles



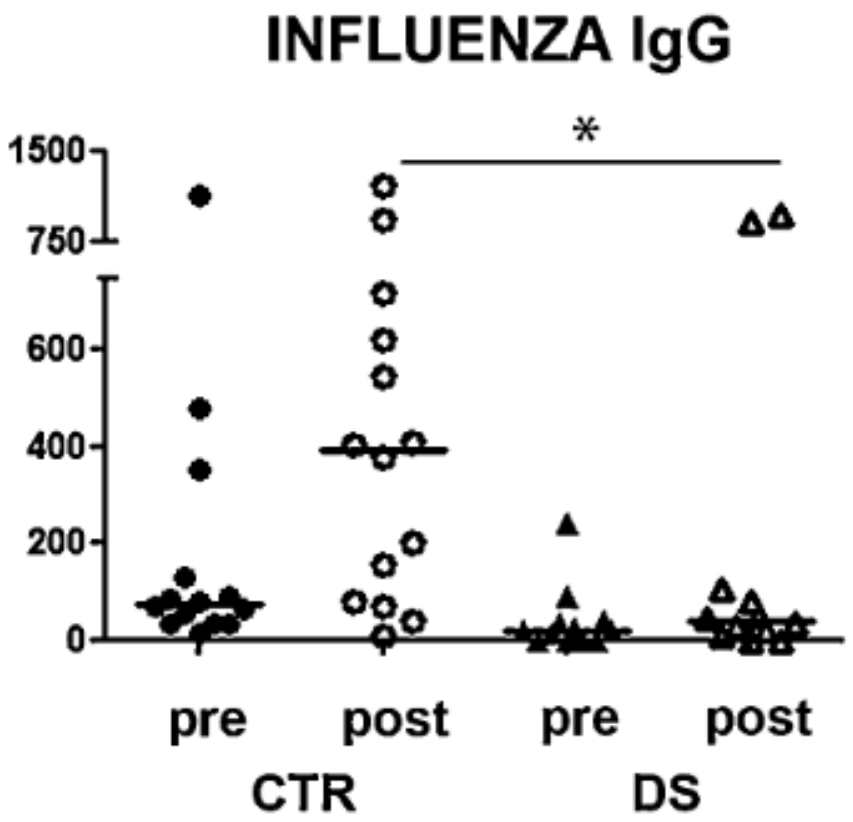
Familiar-Macedo et al, *Front Pediatr* 2023

Vaccination and Down Syndrome

- Vaccines are safe and immunogenic in people with DS.
- **The American Academy of Pediatrics recommends all children with DS receive routine immunizations, including influenza and RSV vaccines,** unless specifically contraindicated

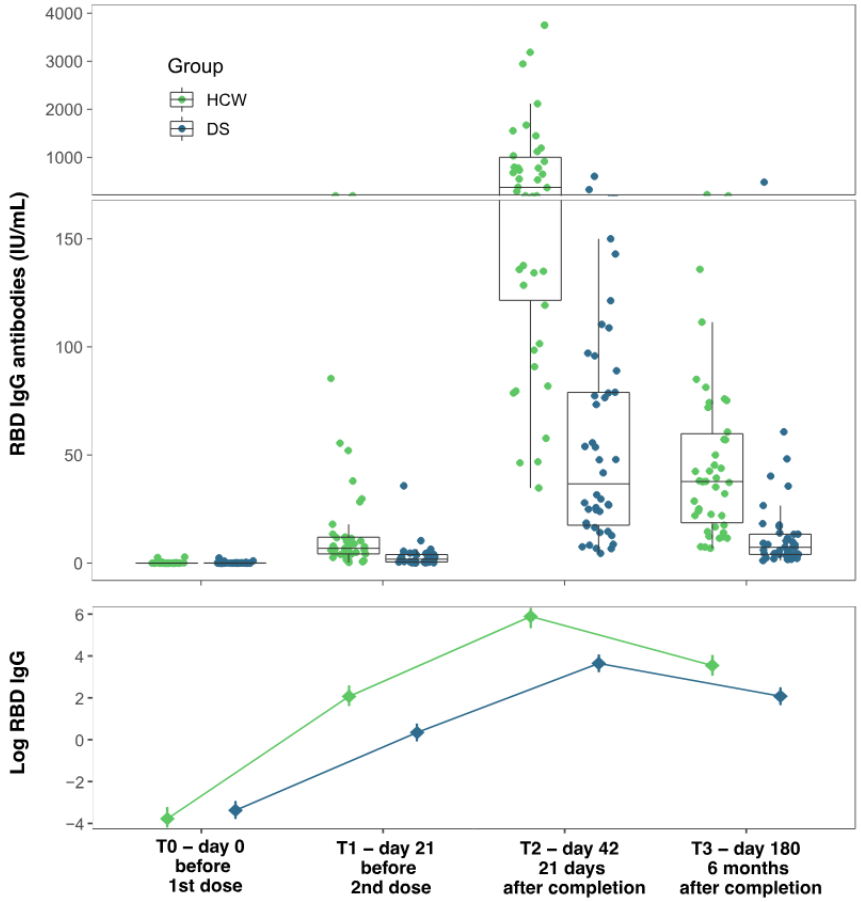
Vaccines in People with DS: Immunogenic, but impaired

Influenza



Valentini et al, *Vaccine* 2015

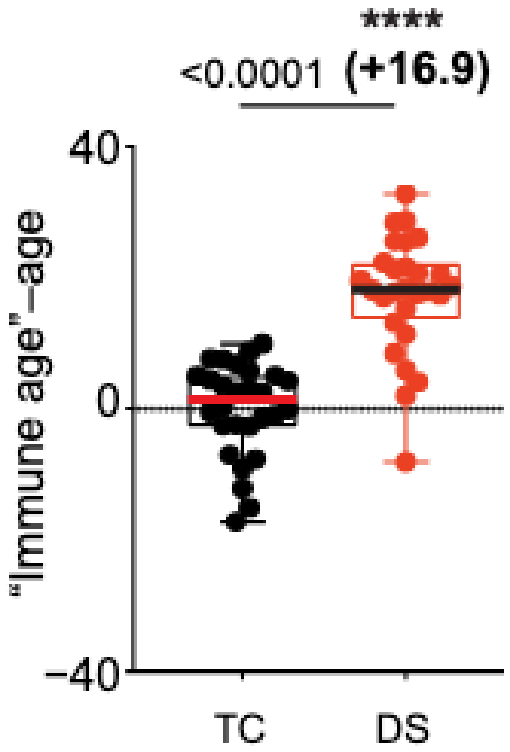
COVID-19



Sali et al, *J Clin Microbiol Inf* 2022

Impaired vaccine response in people with DS: Immune contributors

Immune aging



Lambert et al, *Sci Transl Med* 2022

Innate immune

- ↑ Inflammatory cytokines
- ↓ phagocytosis
- ↓ pathogen clearance
- ↓ mannan-binding lectin
- ↑ Interferon signaling

Adaptive immune

- ↓ IgG/IgM/IgE
- ↓ switched B memory
- Thymic hypoplasia
- ↓ T naive
- ↑ T exhaustion
- ↑ Interferon signaling

Khor et al, *npj Vaccines* 2026

Impaired vaccine response in people with DS: Available and emerging solutions

Available now:

Utilization of existing vaccines

Prioritization for boosters, especially influenza and SARS-CoV2

Near term, to be evaluated:

High-dose influenza vaccine

Adjuvanted influenza vaccine

Potential longer-term candidates:

JAK inhibitors

Metformin

Rapalogs

Senolytics

Khor et al, *npj Vaccines* 2026

Summary

- People with DS are susceptible to respiratory infections
- Vaccines are a key component of care for people with DS
- Lower vaccine utilization in DS: A major opportunity
- DSMIG team review: A key resource for conversations
- Vaccines are **safe** and **immunogenic** in people with DS
  - Continue to monitor safety in studies and postmarketing surveillance
- **Recommend**
  - All standard vaccinations for typical individuals of same age
  - Prioritization for boosters and additional specific vaccines
  - Continued research to improve vaccine response in people with DS

npj Vaccines https://doi.org/10.1038/s41541-026-01489-7

Article in Press

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