MSD
INVENTING FOR LIFE

Evaluating the impact of universal varicella vaccination strategies on clinical burden of varicella and herpes zoster in England and Wales

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Background

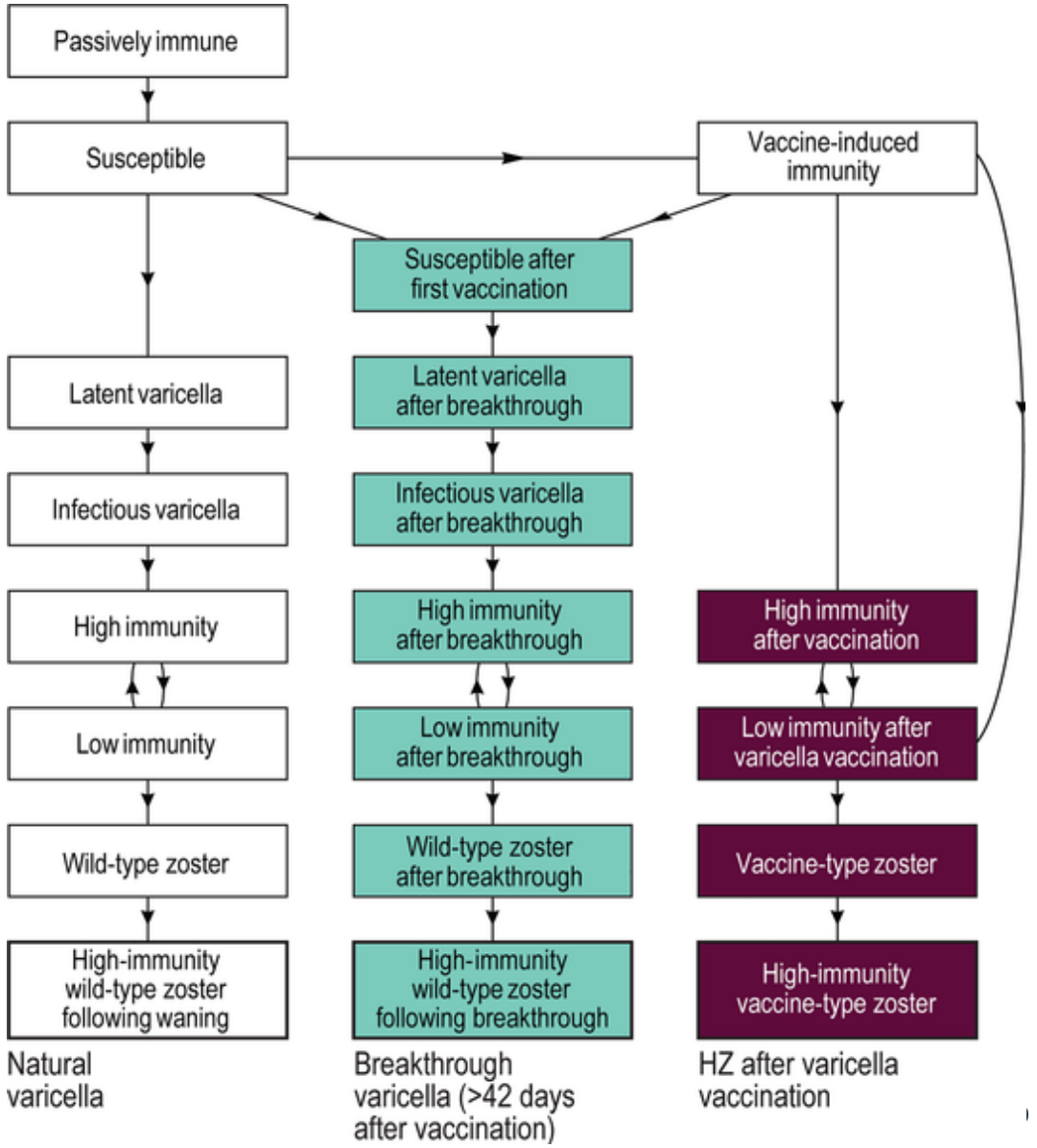
- Varicella (chicken pox) is a common infectious disease in children caused by the varicella zoster virus (VZV); it may reactivate later in adulthood as herpes zoster (HZ), or shingles
- In England, the average annual incidence of hospital admissions due to varicella was 7.6 per 100,000 during 2004-2013, and the average annual number of varicella-related deaths was 18.5[1]
- Varicella vaccines have been proven safe and effective:
  - One dose 85% effective and 2 doses 98% effective at preventing any form of varicella[2]
- Countries that have implemented universal varicella vaccination (UVV) have observed 80%-90% declines in varicella-associated morbidity and mortality[3-6]
- Currently, England and Wales have not implemented a UVV program primarily due to a hypothesized increase in zoster incidence, as vaccine may prevent re-exposure to wild-type virus (exogenous boosting)
- The current analysis assumes no benefit to the population from zoster vaccines in adults.

Objective

To evaluate the long-term clinical impact of UVV and exogenous boosting on varicella and HZ in a dynamic population for England and Wales

Methods: Dynamic Transmission Model

- Utilized age-structured, deterministic, dynamic transmission model using a dynamic population and adapted to England and Wales[7]
  - Based on MSEIRV (Maternal-Susceptible-Exposed-Infected-Recovered-Vaccinated) model
- Model features
  - Includes health states representing reactivation of VZV, potentially leading to HZ outbreaks
  - Differentiates between individuals who receive first or second vaccination dose
  - Uses Failure-Take-Waning structure of vaccine effectiveness[8]
  - Accounts for growing and aging population (dynamically changing population)



Methods: UVV program inputs

- Two intervals between 1st and 2nd dose
- Vaccines evaluated
  - Monovalent: V-MSD (VARIVAX®)
    V-GSK (Varilrix®)
  - Quadrivalent: MMRV-MSD (ProQuad®)
    MMRV-GSK (Priorix-Tetra®)
- Catch-up vaccination included and lasts two years during UVV program (for selected strategies)
- Coverage consistent with early childhood vaccination rates[9] and TdaP/IPV booster[10]
  - 12 and 18 months of age: 91%
  - 40 months of age: 88%
  - 13-14 years of age: 87%

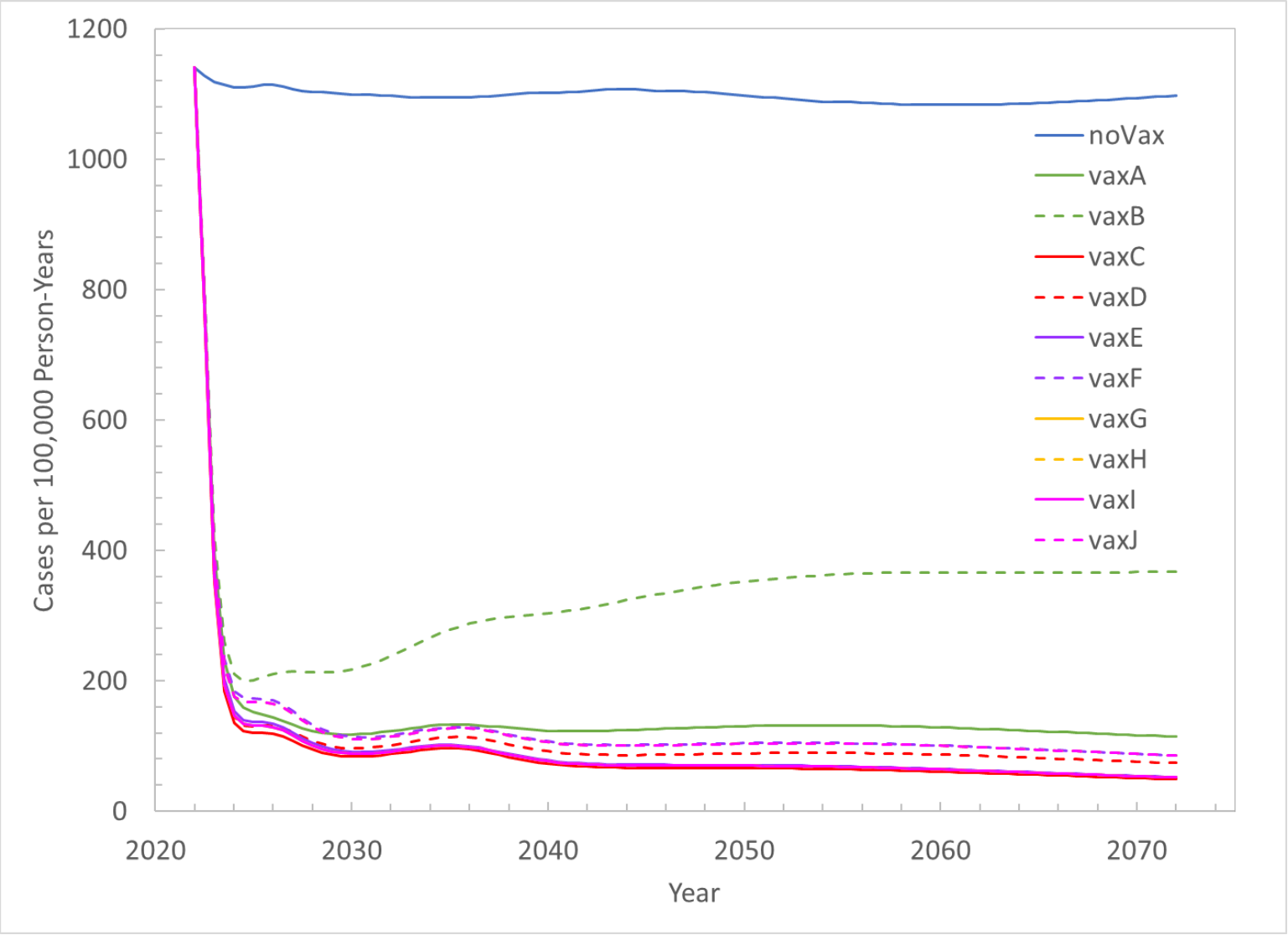
Strategy	Formulation		Age at vaccination (months)		2-dose Catch-up (13-14 years)
	1st Dose	2nd Dose	1st Dose	2nd Dose	
A	MMRV-MSD		18		
B	MMRV-GSK		18		
C	V-MSD	V-MSD	12	18	V-MSD
D	V-GSK	V-GSK	12	18	V-GSK
E	V-MSD	MMRV-MSD	12	18	
F	V-GSK	MMRV-GSK	12	18	
G	V-MSD	MMRV-MSD	12	40	V-MSD
H	V-GSK	MMRV-GSK	12	40	V-GSK
I	V-MSD	V-MSD	12	40	V-MSD
J	V-GSK	V-GSK	12	40	V-GSK

Methods: Key inputs/outputs

- Model used temporary/full immunity model of exogenous boosting to assess the impact on HZ
- Model calibrated to
  - Varicella transmission to seroprevalence data[11-14]
  - HZ reactivation to HZ incidence data[15-18]
  - Case fatality for varicella and HZ[18]
- Varicella consultation (outpatient care) and hospitalization fitted to UK data[1,19]
- Vaccine-related parameters shown in the table
- Exogenous boosting assumptions:
  - % of contacts leading to boosting: 33.4%
  - Duration of protection: 81.3 years
- Outcomes reported over 50-year time horizon
  - Varicella cases (total, outpatients, hospitalizations, deaths)
  - HZ cases (total, deaths)

Parameter	Dose	MSD	GSK
Vaccine failure rate	1st & 2nd	4%	5%
Dose take rate	1st	90.3%	61.7%
	2nd	69.0%	83.4%
Duration of temporary immunity when vaccine does not take	1st & 2nd	1.2 years	0.9 years
Waning period of high HZ immunity post vaccination	1st & 2nd	81.3 years	81.3 years

Results: Total varicella incidence by vaccination strategy (2022–2072)



Vaccination strategies

A: MMRV-MSD (18M)

B: MMRV-GSK (18M)

C: V-MSD (12M, 18M, catch-up)

D: V-GSK (12M, 18M, catch-up)

E: V-MSD (12M) + MMRV-MSD (18M)

F: V-GSK (12M) + MMRV-GSK (18M)

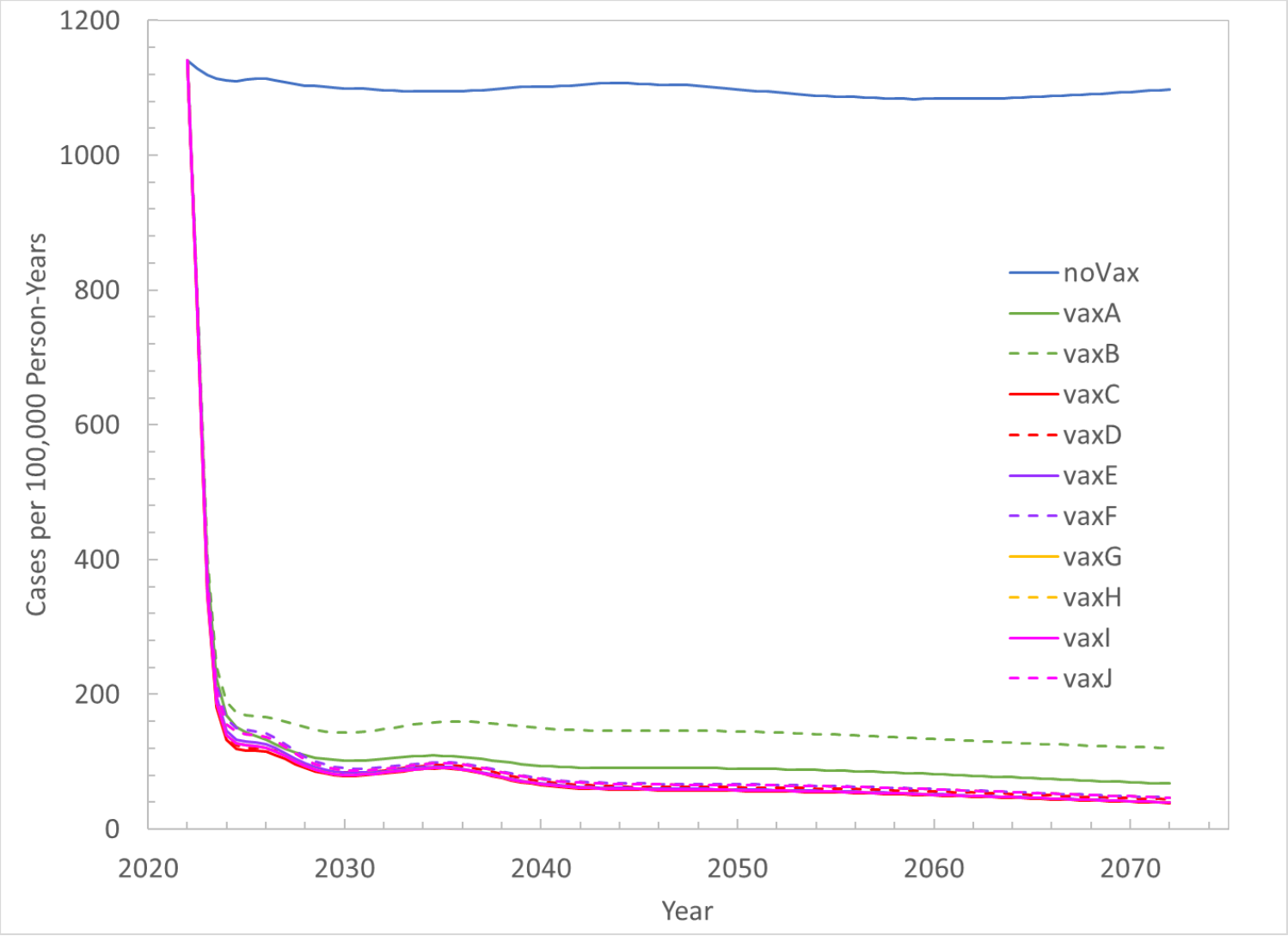
G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Natural varicella incidence by vaccination strategy (2022–2072)



Vaccination strategies

A: MMRV-MSD (18M)

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C: V-MSD (12M, 18M, catch-up)

D: V-GSK (12M, 18M, catch-up)

E: V-MSD (12M) + MMRV-MSD (18M)

F: V-GSK (12M) + MMRV-GSK (18M)

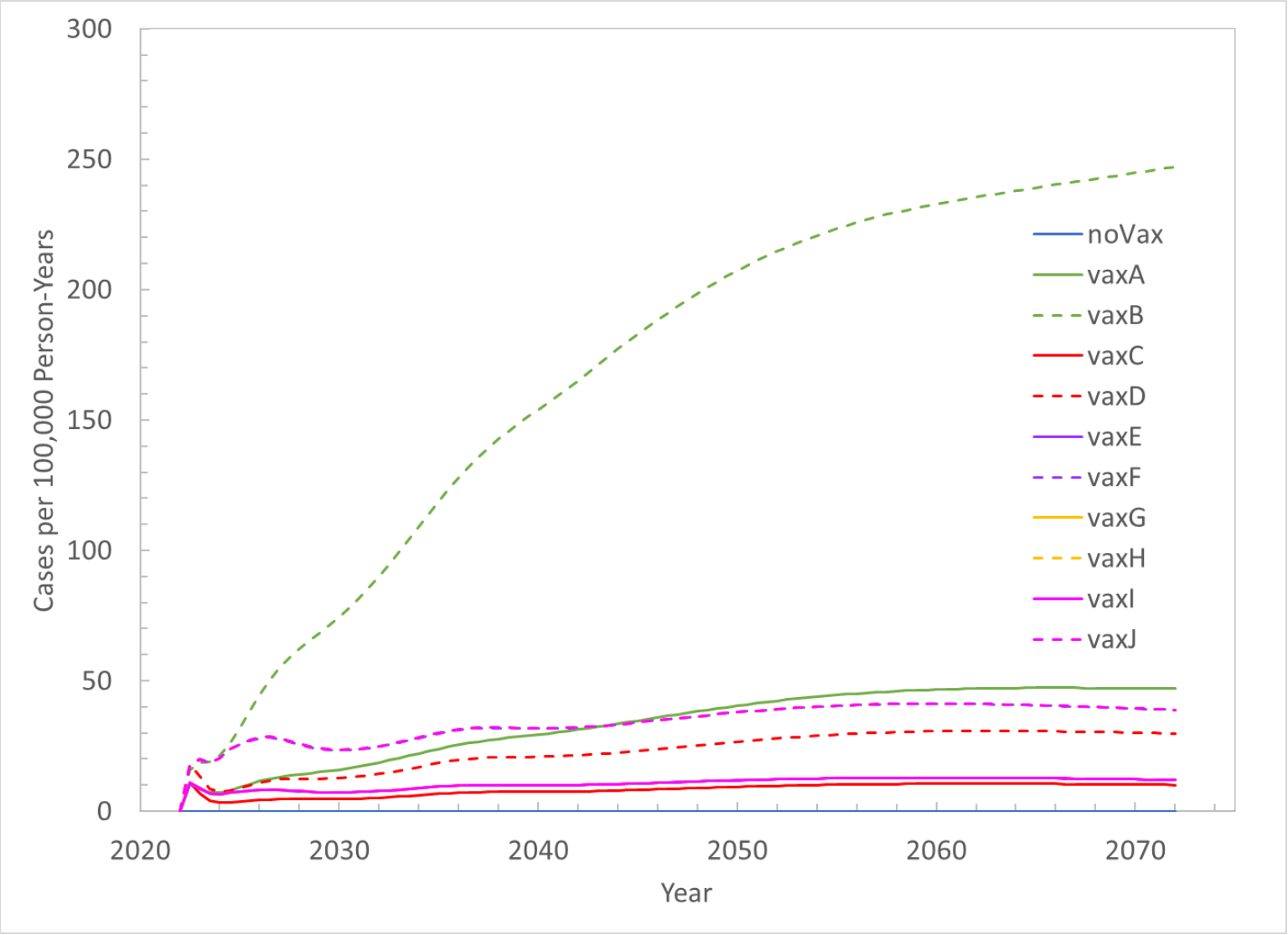
G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Breakthrough varicella incidence by vaccination strategy (2022–2072)



Vaccination strategies

A: MMRV-MSD (18M)

B: MMRV-GSK (18M)

C: V-MSD (12M, 18M, catch-up)

D: V-GSK (12M, 18M, catch-up)

E: V-MSD (12M) + MMRV-MSD (18M)

F: V-GSK (12M) + MMRV-GSK (18M)

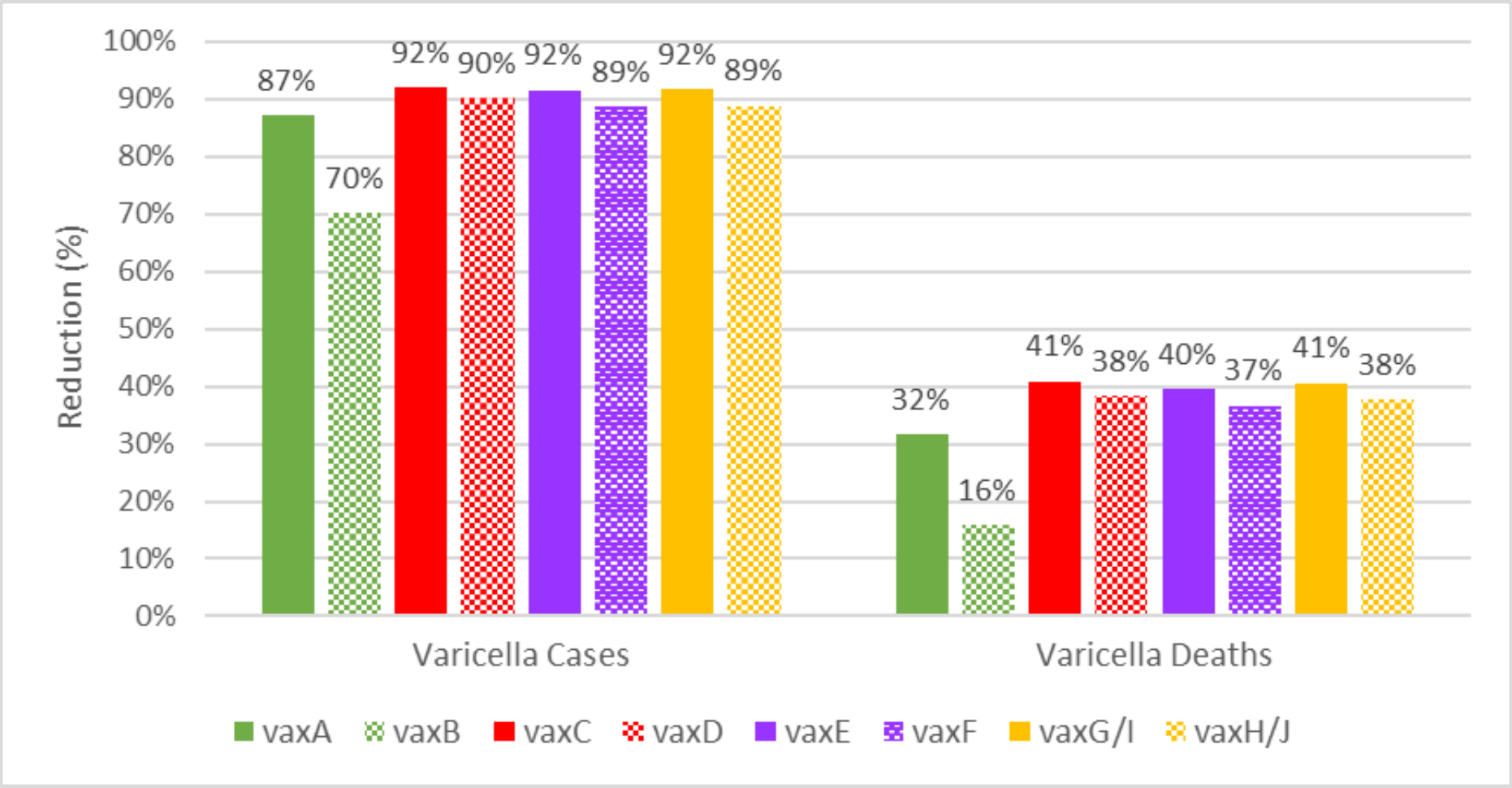
G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Reduction in total varicella cases and varicella deaths (2022–2072)



Vaccination strategies

A: MMRV-MSD (18M)

B: MMRV-GSK (18M)

C: V-MSD (12M, 18M, catch-up)

D: V-GSK (12M, 18M, catch-up)

E: V-MSD (12M) + MMRV-MSD (18M)

F: V-GSK (12M) + MMRV-GSK (18M)

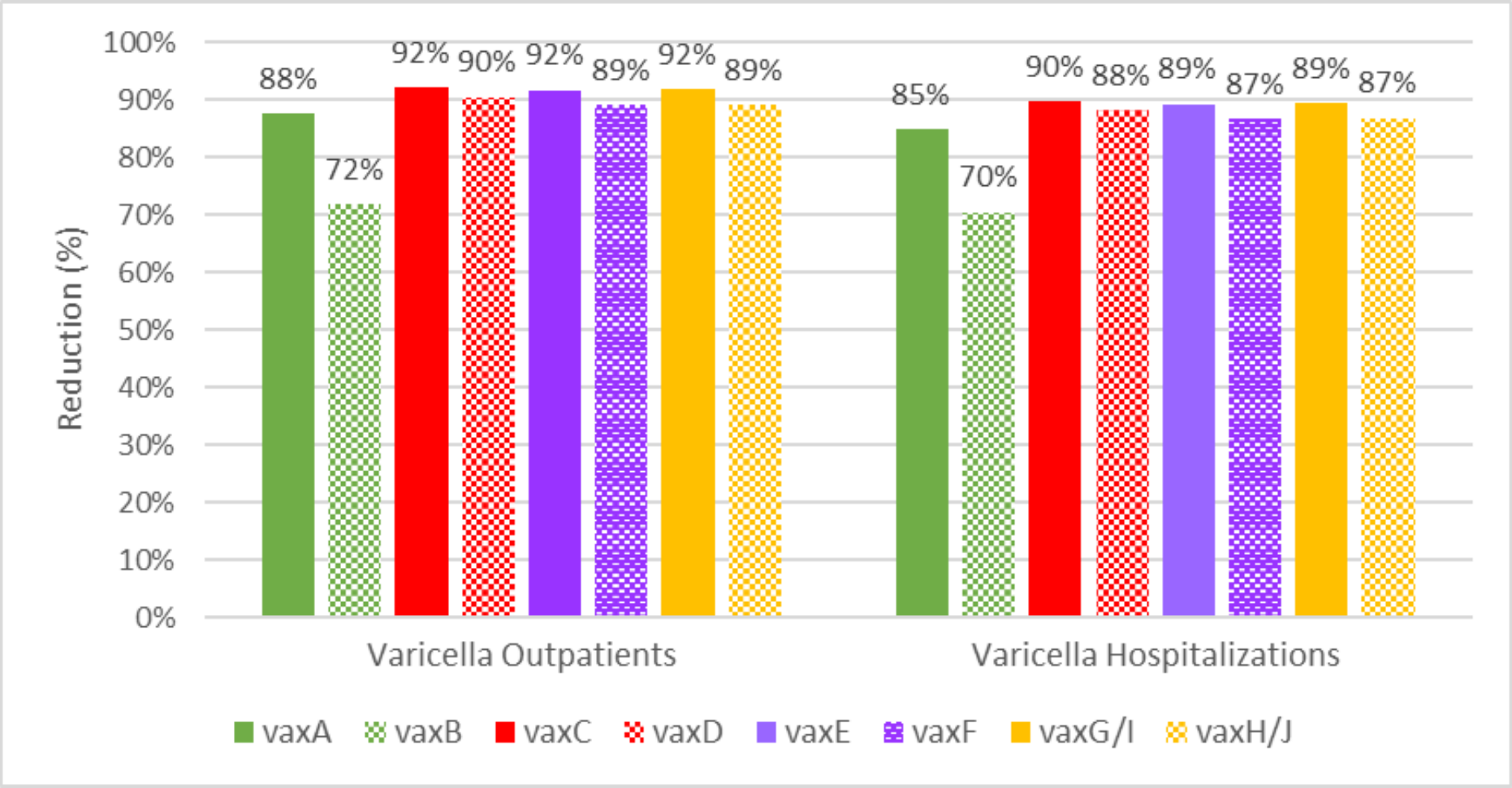
G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Reduction in varicella outpatients and hospitalizations (2022–2072)



Vaccination strategies

A: MMRV-MSD (18M)

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C: V-MSD (12M, 18M, catch-up)

D: V-GSK (12M, 18M, catch-up)

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F: V-GSK (12M) + MMRV-GSK (18M)

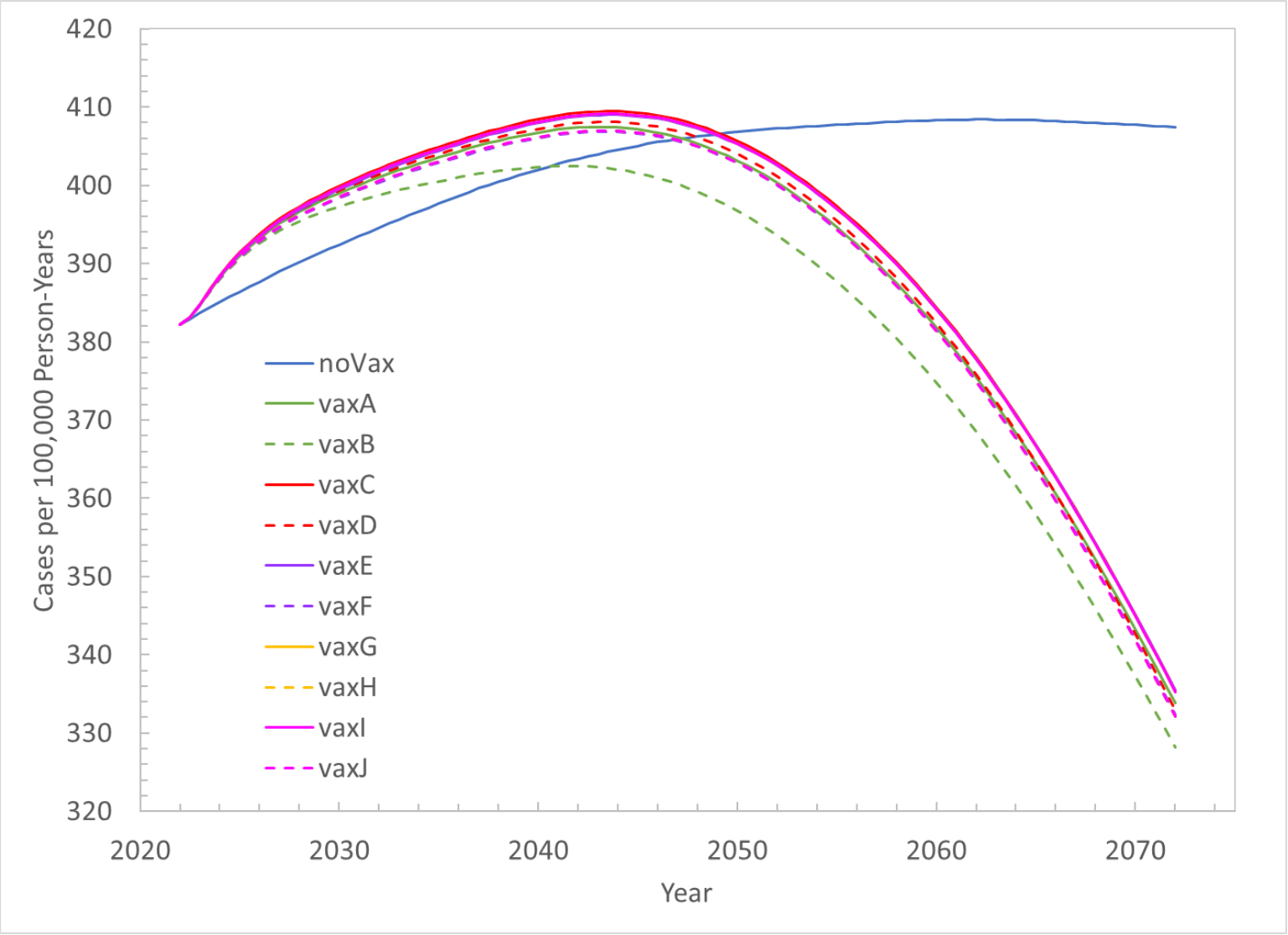
G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Herpes Zoster Incidence by Vaccination Strategy (2022 – 2072)



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H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Results: Total HZ cases and deaths by vaccination strategy (2022–2072)

Strategy	HZ cases		HZ deaths	
	Total	% Change	Total	% Change
noVax	13,168,468	–	4,757	–
A	12,740,377	-3.3%	4,935	3.7%
B	12,581,074	-4.5%	4,900	3.0%
C	12,800,974	-2.8%	4,948	4.0%
D	12,753,195	-3.2%	4,943	3.9%
E	12,791,341	-2.9%	4,946	4.0%
F	12,722,207	-3.4%	4,940	3.8%
G/I	12,793,067	-2.9%	4,947	4.0%
H/J	12,723,183	-3.4%	4,941	3.9%

Vaccination strategies

A: MMRV-MSD (18M)

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D: V-GSK (12M, 18M, catch-up)

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G: V-MSD (12M) + MMRV-MSD (40M) + V-MSD (catch-up)

H: V-GSK (12M) + MMRV-GSK (40M) + V-GSK (catch-up)

I: V-MSD (12M, 40M, catch-up)

J: V-GSK (12M, 40M, catch-up)

Limitations

- There is currently no paediatric vaccination visit at 18 months in the UK, which was the modelled timepoint for the one-dose MMRV strategies (A, B) and two-dose short interval strategies (C-F); this might have an impact on coverage rates
- While vaccines against HZ are available (e.g., Zostavax-MSD, Shingrix-GSK), these are not accounted for in this model, leading to conservative estimates for impact on HZ incidence
- We used the temporary immunity model to estimate exogenous boosting and its duration. There is also ongoing research on alternative modelling of the exogenous boosting mechanism such as progressive immunity[20]

Conclusions

- All UVV strategies are projected to substantially reduce varicella morbidity (70%-92%) and mortality (16%-41%) in England and Wales over the period from 2022–2072 compared with no vaccination
- In the absence of HZ vaccination, the UVV program had a modest impact on HZ cases (2.8%-4.5% reduction) and deaths (3.0%-4.0% increase) during this period compared with no vaccination
- Impact of UVV on HZ incidence is sensitive to the assumptions of exogenous boosting in this model. Our assumptions are based upon the latest real-world evidence data in the UK[21]
- Policy makers should consider including UVV in their childhood immunization program to reduce disease due to varicella
- Additional research is needed to assess the cost-effectiveness of UVV in England and Wales

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