Impact modelling of booster doses

WHO SAGE Meeting

7 December 2021

World Health Organization

Outline of Presentation

1. Relative benefits of boosters vs. primary series, comparing within and between risk groups

2. Transmission dynamic models of vaccine boosters: preliminary findings

Booster math: Cases averted by using vaccine as primary series vs. as booster, using conservative assumptions

Primary series effectiveness	Wanes to	Effectiveness after booster	Relative benefit of primary series
90%	90%	99%	5-fold
	80%	98%	2.5-fold
	70%	97%	1.7-fold
	60%	96%	1.3-fold
80%	80%	98%	2.2-fold
	70%	97%	1.5-fold
	60%	96%	1.1-fold

Assumptions

- Primary series is 2 doses
- Booster reduces risk 10-fold
- Similar risks of exposure/disease

i.e., within same risk group, primary series yields more benefit than booster

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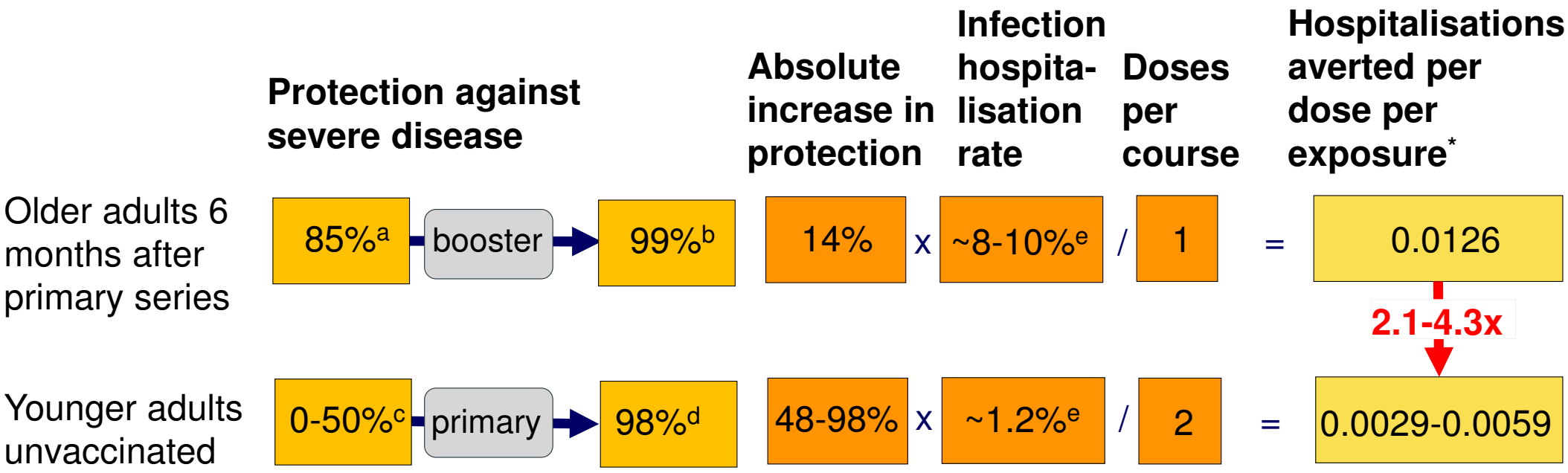
Krause P. "Synthesis of the evidence and next steps" WHO consultation on COVID-19 vaccines research: Emerging evidence on safety and the need for additional doses of COVID-19 vaccines. 25 Oct. 2021 https://www.who.int/news-room/events/detail/2021/10/25/default-calendar/who-consultation-on-covid-19-vaccines-research-emerging-evidence-on-safety-and-the-need-for-additional-doses-of-covid-19-vaccines

R&DBlueprint
Powering research to prevent epidemics

Boosters for older adults vs primary series for younger adults: illustration

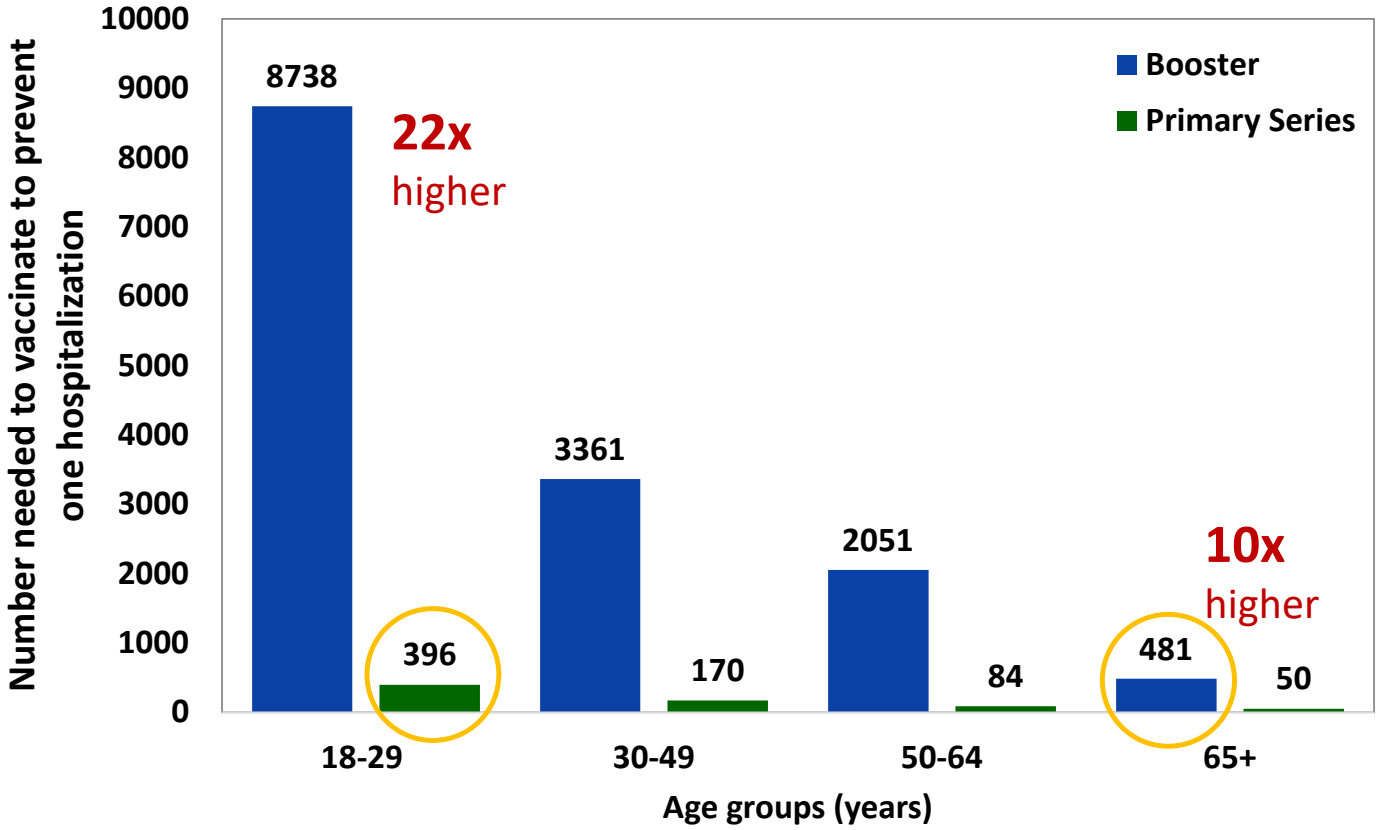


*assuming equal exposure for older and younger adults

(ratio lower if younger adults' exposure risk > older adults')

[a]based on 10% drop in VE against severe disease 6 months after initial protection of ~95% in older adults (systematic review, Feikin et al. 2021; UK data, Andrews et al. 2021); [b]booster dose effectiveness against severe disease in older adults compared with primary series (Israel data, Bar-On et al. 2021); [c]unvaccinated are assumed to be either unprotected or protected through naturally acquired immunity following infection (will depend on past epidemic in country); [d]initial effectiveness of primary series against severe disease in younger adults (UK data, Andrews et al. 2021); [e]based on age-specific IHR for France applied to LMICs (France data, Salje et al. 2020)

U.S. example: Number needed to vaccinate to prevent one hospitalization over 6 months, booster versus primary series (Pfizer-BioNTech COVID-19 vaccine)



Age group	% fully vaccinated (as of 10 Sep)	Pre-booster VE vs hospitalization
18-29	48%	90.7%
30-49	59%	90.2%
50-64	71%	91.1%
65+	84%	85.1%

Static model (constant VE and incidence over 6 months)

Direct benefits only

Assumed booster VE vs hospitalization = 95%

Source: Adapted from Dr. M. Wallace presentation to ACIP, 23 September 2021
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-9-23/02-COVID-Wallace-508.pdf

Caveat

Relative benefits will depend on:

- Past and future vaccine delivery and rollout timelines
- VE against severe disease and other outcomes
- Waning of protection against severe disease
- Potential impact of new variants on VE
- Country-specific hospitalization rates
- Differential exposure rates by age/risk group
- Complementary PHSM in use
- Indirect effects of vaccination

Individual-based model **(dynamic model)**

MRC Centre for Global Infectious Disease Analysis

Imperial College London

Approach

- Stochastic, individual-based model of SARS-CoV-2 transmission and vaccination mirroring compartmental model
- Key features:
  - Flexible dose and age prioritisation strategy options
  - Booster doses
  - Individual level antibody titre and decay linked to efficacy using a functional form (from Khoury et al *Nat Med* 2021*)
  - Individual variation in response to vaccination
  - Specific vaccine products modelled
  - Fast & extensible
- Fully open source as an R package: https://mrc-ide.github.io/safir/ (still in active development).
- **Safir** uses the "individual" package to specify and run the simulation (https://github.com/mrc-ide/individual; available on CRAN, published in JOSS**).

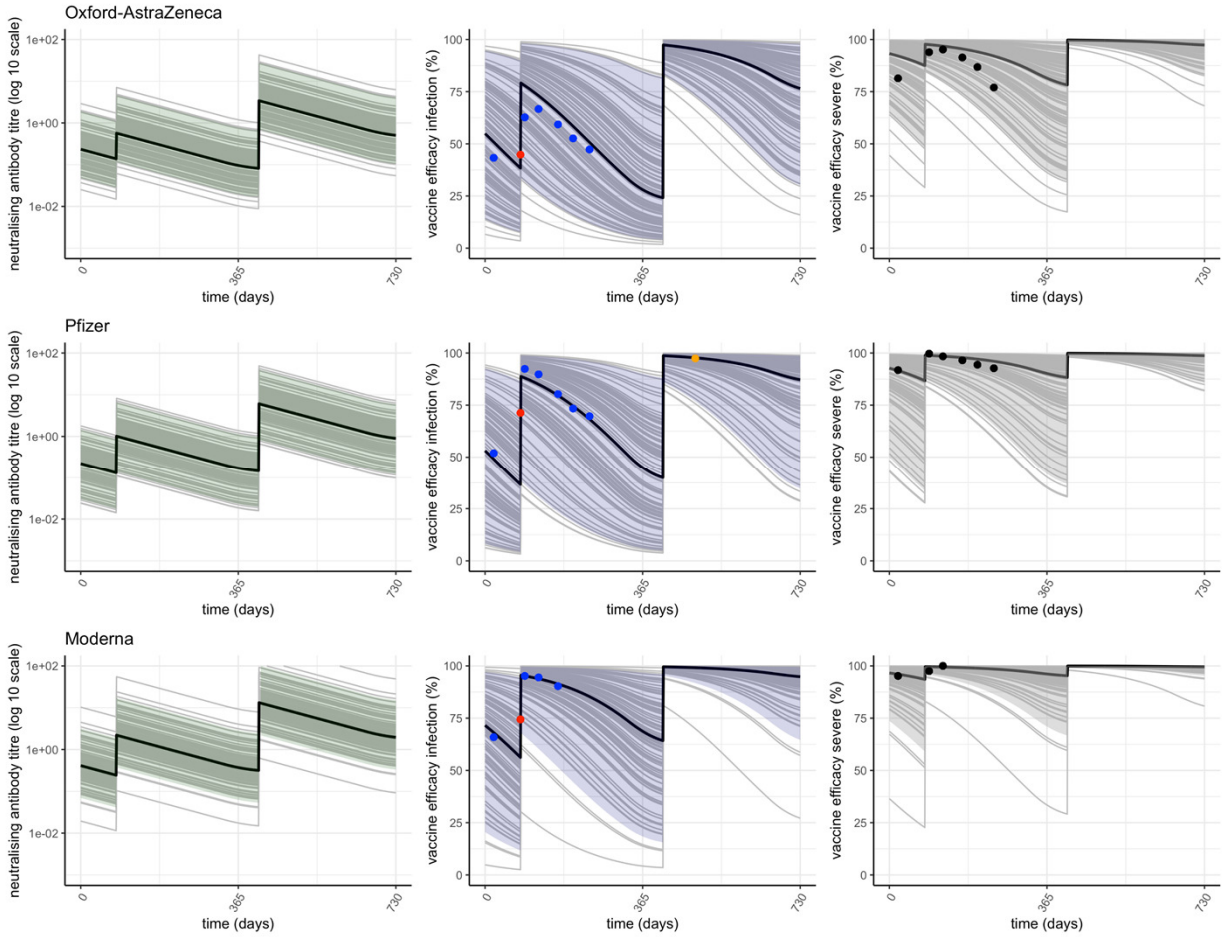
* https://www.nature.com/articles/s41591-021-01377-8; https://www.medrxiv.org/content/10.1101/2021.08.11.21261876v1.full.pdf

**individual: An R package for individual-based epidemiological models (theoj.org)

Source: Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 25 October 2021 and 15 November 2021.

Modified Relationship between Antibody Titre and Vaccine Efficacy

- Predicted vaccine efficacy against infection (purple) and severe disease (grey)
- Uses estimates of Ab titres at dose 1 and dose 2 from Phase II/III trials and 3rd dose from recent immunogenicity studies
- Blue/Red/Black points show UK data on effectiveness (PHE)
- Antibody titre appears to under-predict efficacy slightly for Moderna and Pfizer
- More substantial under-prediction for AZ
- Scaled estimates by varying dose 1/dose 2 antibody titre to match efficacy data



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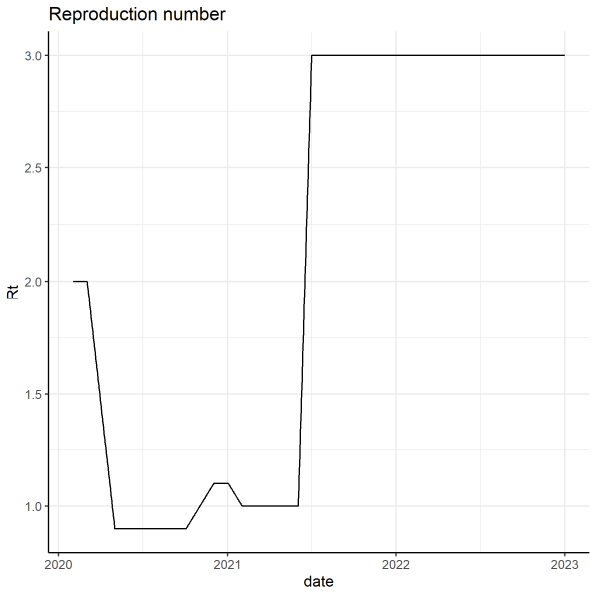
Country Settings

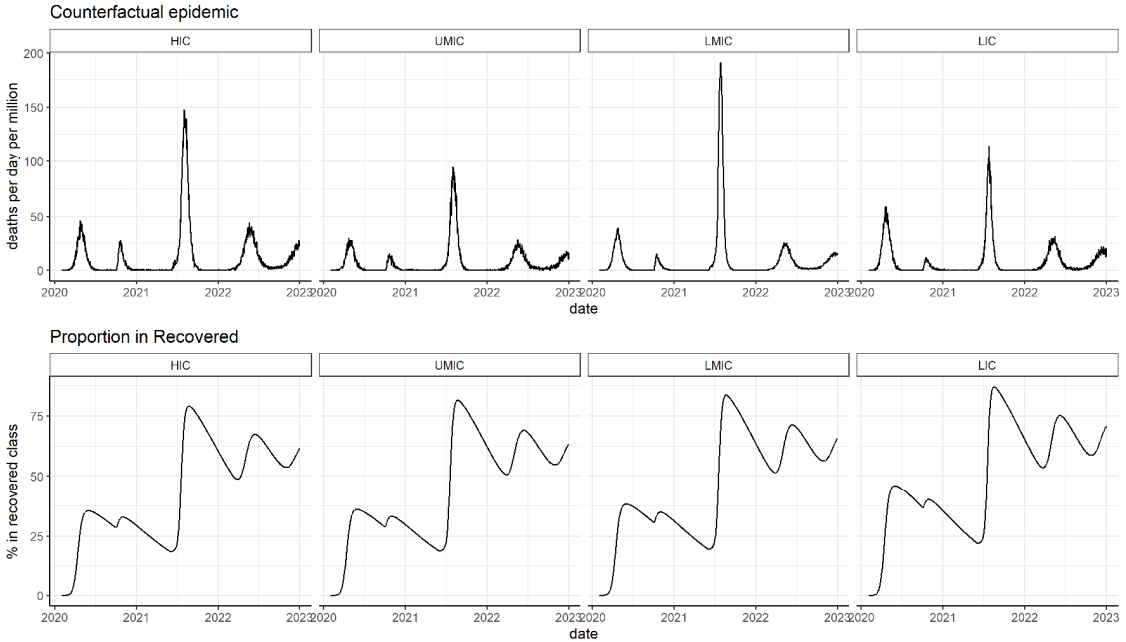
	HIC	UMIC	LMIC	LIC
Health system constraints	Unconstrained	Unconstrained	Constraints present	Constraints present
Contact patterns	HIC exemplar	UMIC exemplar	LMIC exemplar	LIC exemplar
Demography	HIC median	UMIC median	LMIC median	LIC median
Vaccine product	Pfizer	Pfizer	AstraZeneca	AstraZeneca
Vaccine start date	1 January 2021	1 January 2021	1 January 2021	1 January 2021
Vaccination rate	2.5% per week	2.5% per week	1.5% per week	1.5% per week

Source: Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 25 October 2021 and 15 November 2021.

Counterfactual

- Countries experienced 2 waves prior to vaccine introduction (2020), subsequent “delta” wave during vaccination program (2021).
- Incorporate lifting of NPIs during summer 2021 – in absence of vaccination this would have resulted in a sharply peaked epidemic in recent months





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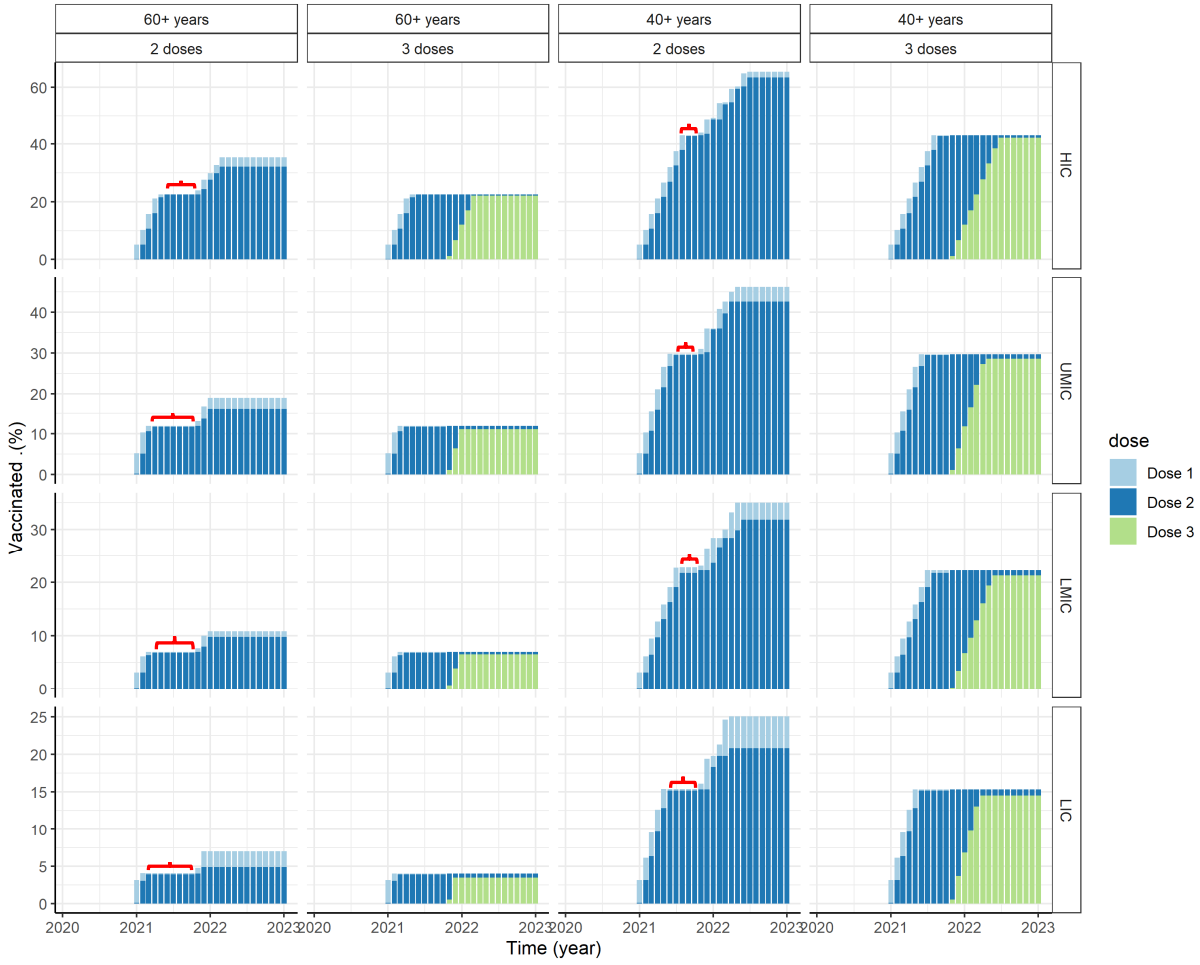
Vaccine Scenarios

- Compare two strategies
- First achieve specified level of coverage (80% of 60+ or 80% of 40+), then either:
  - Continue with rolling out first two doses to younger groups; or
  - Switch and give out boosters to the oldest groups that already received the primary series (60+ or 40+)
- Scenarios parameterised so that vaccine doses given out at the same rate in each strategy
- Fixed supply (volume equal to booster doses in green) to allocate for 1-dose booster or 2-dose primary series
- After primary series coverage target achieved (for 60+ or 40+), vaccination paused (red bracket) until booster decision point



Source: Adapted from Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 25 October 2021 and 15 November 2021.

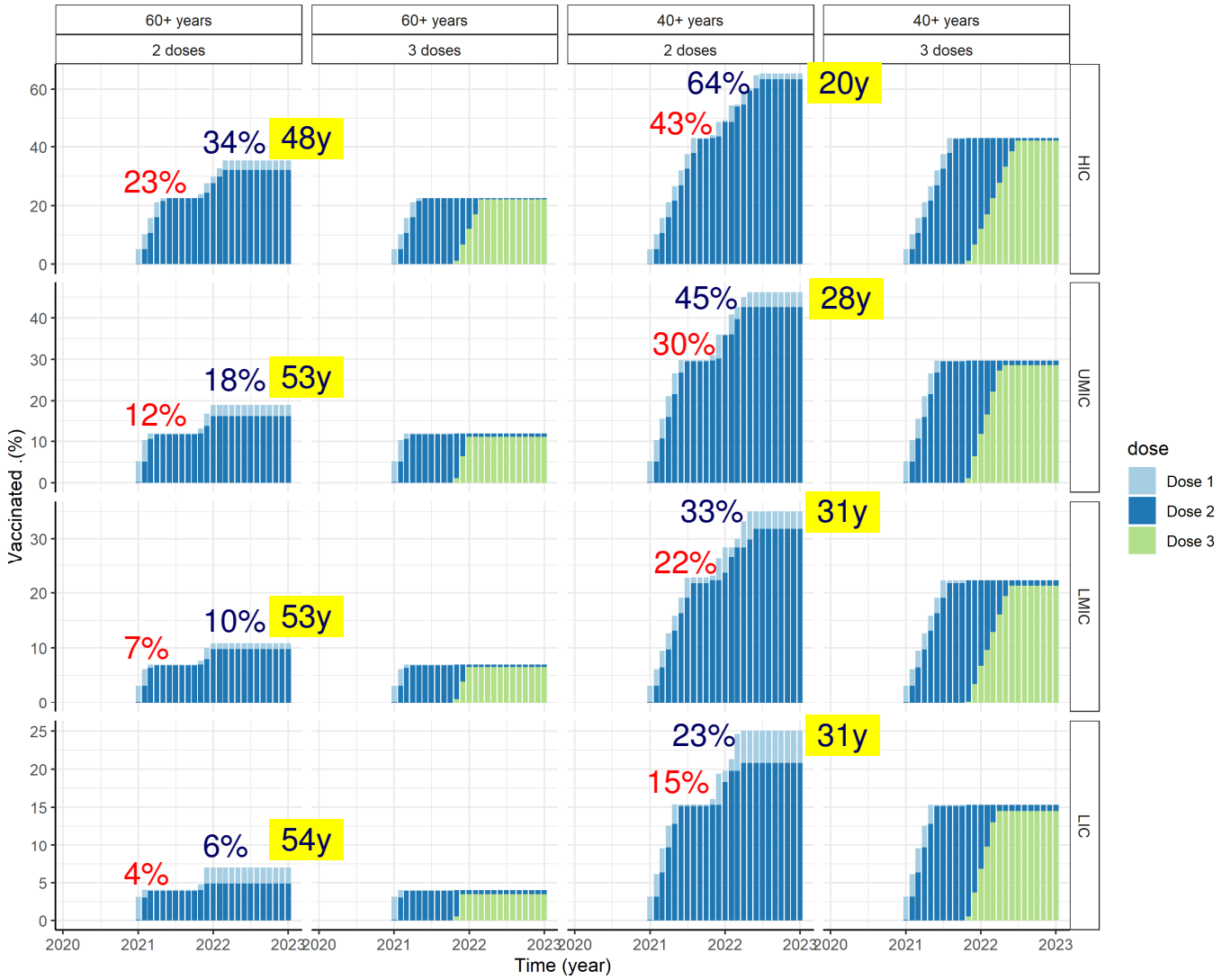
- Age groups reached and total population coverage achieved vary by country income group
- Greater vaccine supply for the 40+ scenarios than the 60+ scenarios
- Absolute vaccine supply varies across country income groups (due to older demographics in HICs/UMICs vs LMICs/LICs)
- Comparison can be made within a given country income group and vaccine supply strategy (60+ or 40+)

% total population coverage with primary series for initial age target group (80% of 60+ or 40+)

% total population coverage with primary series if supply used to expand primary series to younger adults rather than as boosters for initial age target group

Youngest age reached if supply used to expand primary series to younger adults rather than as boosters

Source: Adapted from Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 25 October 2021 and 15 November 2021.



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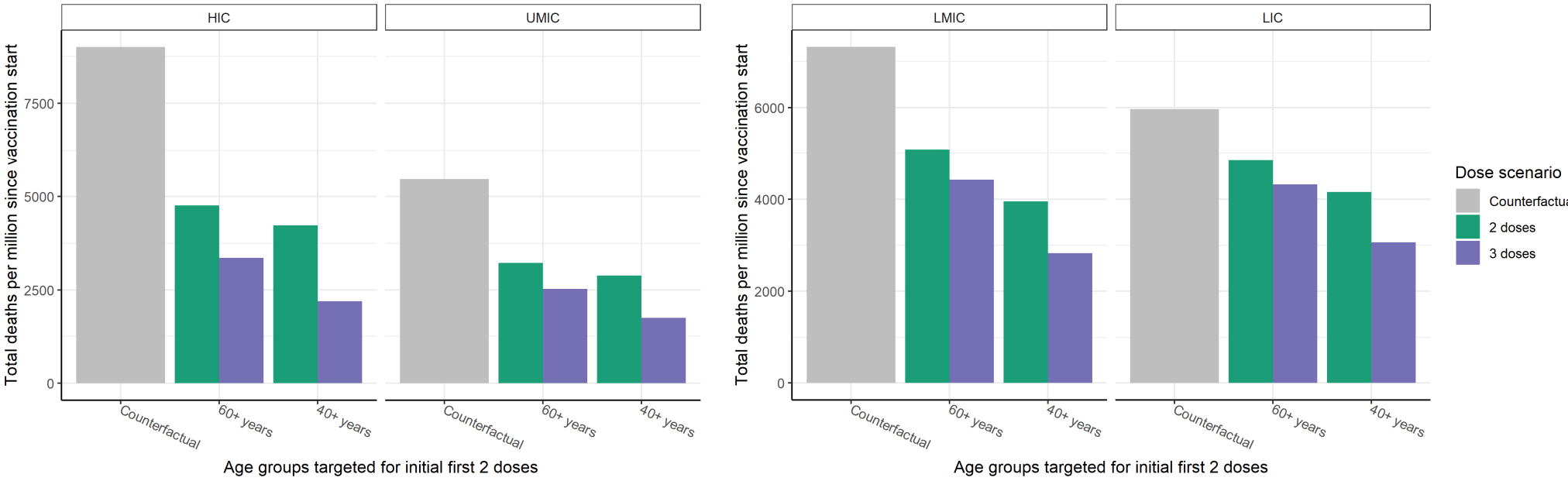
Vaccine Scenarios – Preliminary results

- Higher impact predicted by switching to booster doses in older adults rather than continuing into younger age-groups

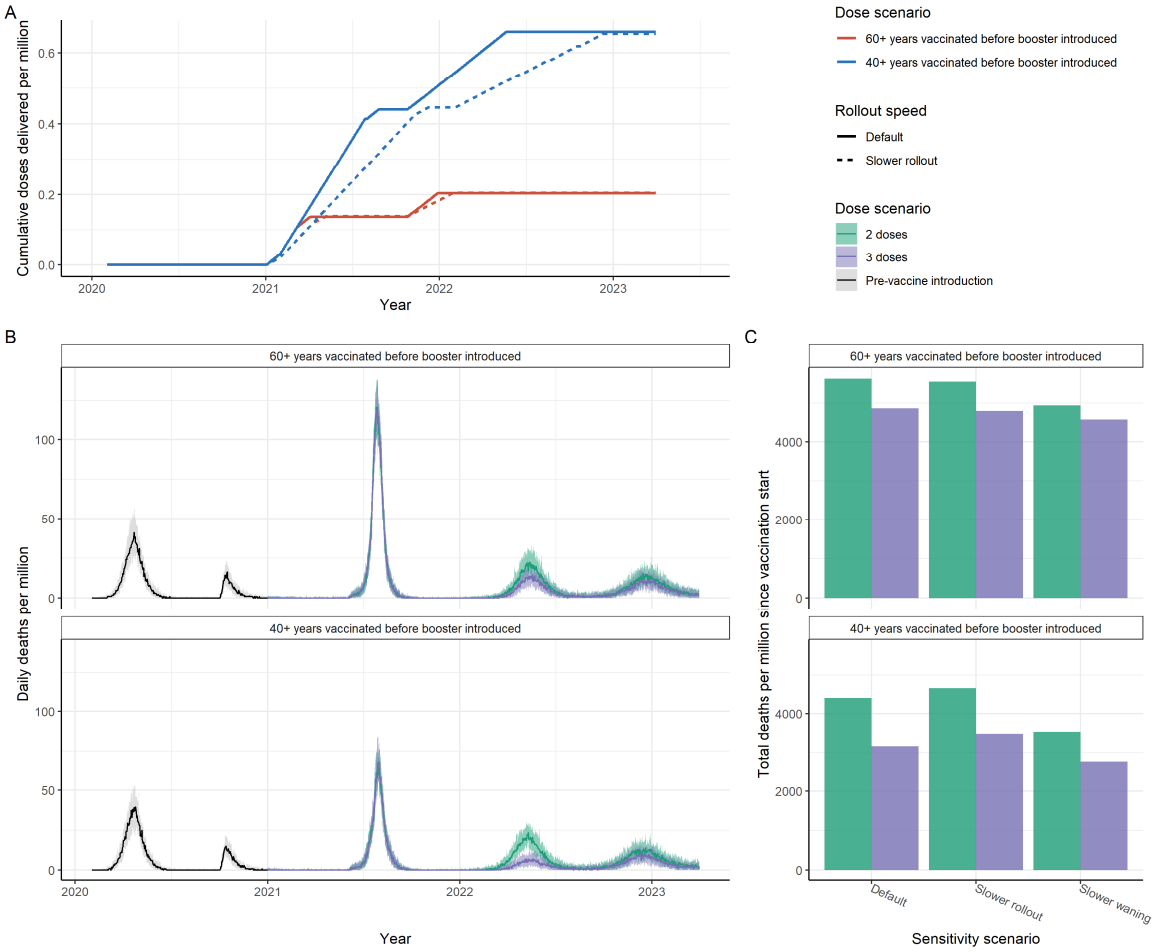


Note: more doses delivered in 40+ years strategy compared to 60+ years strategy

Source: Adapted from Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 25 October 2021 and 15 November 2021.

Central scenarios – LMIC

- Higher impact predicted by switching to booster doses in older adults rather than continuing into younger age-groups
- Robust to slower roll-out and slower waning of vaccine-induced immunity

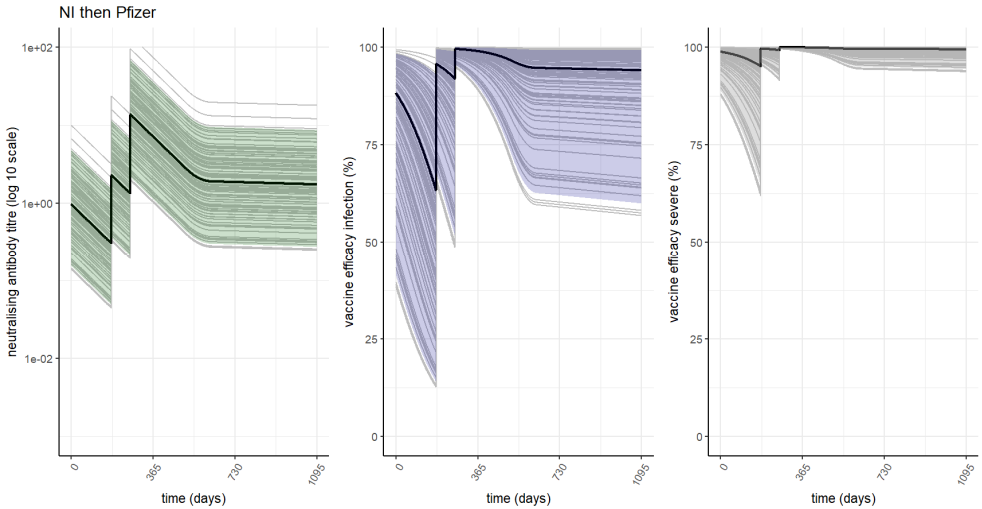


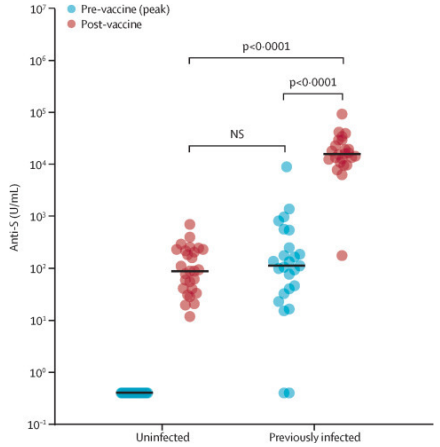
Source: Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 15 November 2021.

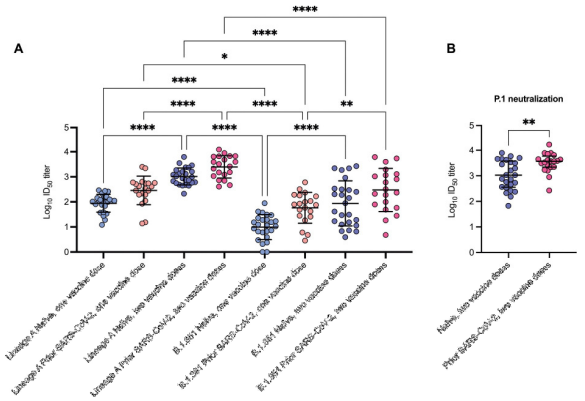
Impact of Pfizer following natural infection

- Assume vaccine dose 1 given 180 days after natural infection
- Predict 93% (71%-99%) vaccine efficacy against infection after first dose
- Predict 99% (96%-100%) vaccine efficacy after second dose

Consistent with studies suggesting one dose in seropositive is similar to 2 doses in naïve





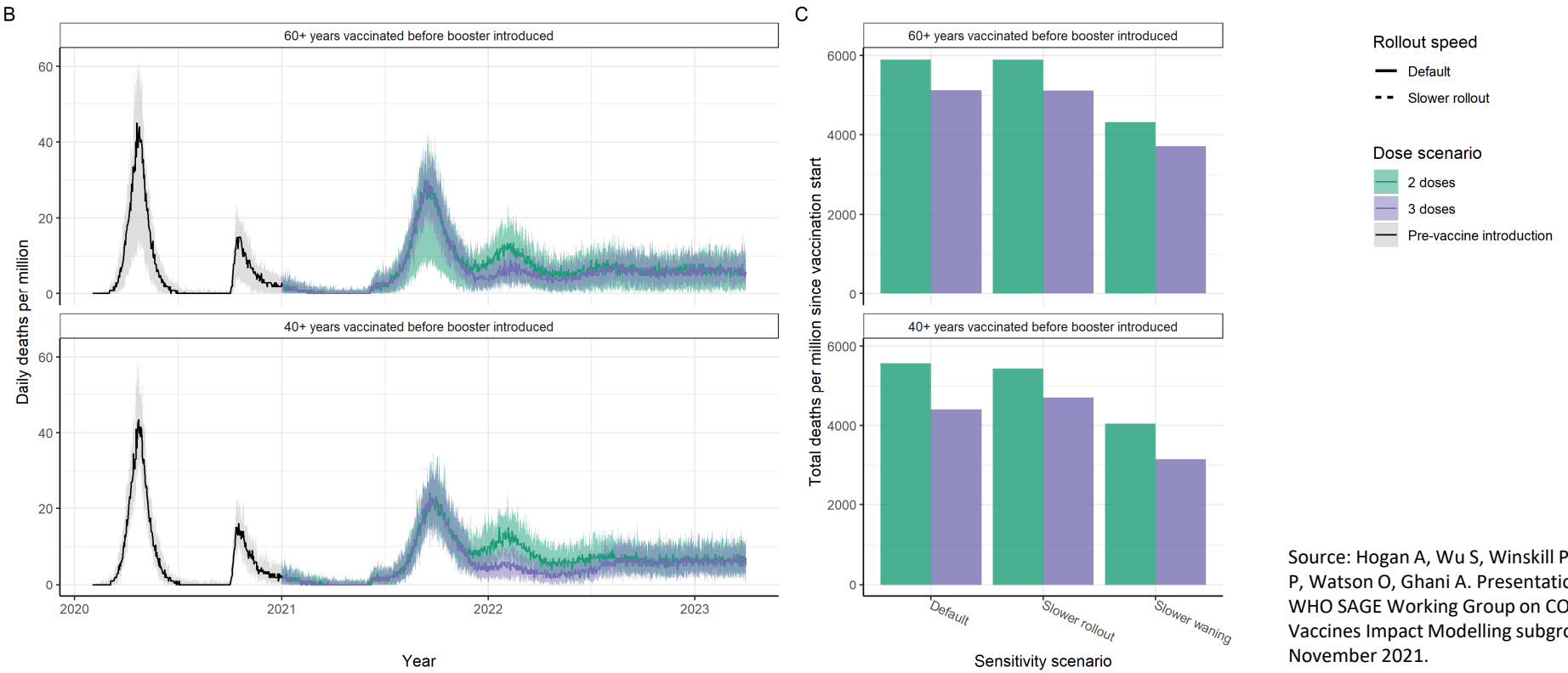


Source: Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 15 November 2021.

New natural immunity model – LMIC

- Different dynamics predicted with NAT model for natural immunity & interaction with vaccine-induced immunity
- Conclusions on booster doses unchanged

PRELIMINARY RESULTS



Source: Hogan A, Wu S, Winskill P, Doohan P, Watson O, Ghani A. Presentation to WHO SAGE Working Group on COVID-19 Vaccines Impact Modelling subgroup, 15 November 2021.

Summary

- Limited modeling of booster dose impacts, especially for MICs/LICs; work ongoing. Available modeling suggests that:
  - **Within the same risk group, primary series vaccination will have greater impact** than booster doses;
  - **Across risk groups, the benefits of booster doses for higher risk groups vs. primary series for lower risk groups may be a relatively close tradeoff that depends on country conditions**, including supply and rollout timelines, past epidemic dynamics and naturally-acquired immunity, vaccine product, estimated effectiveness and waning of protection.
  - **When high primary series coverage has been achieved among groups at higher risk** of severe disease and death (e.g., older adults)**, booster doses for higher risk groups** (e.g., older adults) **may yield greater reductions in severe disease and death than use of equivalent vaccine supply for primary series vaccination of lower risk groups** (e.g., the next youngest adult age group)
    - Assuming an age-descending vaccination rollout, this finding holds even when:
      - Total population vaccination coverage is very low (<10%)
      - Vaccination rollout is slower (e.g., due to delivery system constraints or vaccine hesitancy)
      - Waning of vaccine-induced immunity is slower
      - Vaccination provides additional protection to previously infected individuals
  - **Achieving high primary series coverage among the groups at highest risk of severe disease and death remains a critical priority** to optimize impact of available COVID-19 vaccine supply.