UCSF Institute for Global Health Sciences

Existing Vaccines and Innate Immunity: A Neglected Tool for Pandemic Response?

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Old vaccines for new infections: Exploiting innate immunity to control COVID-19 and prevent future pandemics

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Study	Country; reference	Study design	Age groups covered	Reduction in mortality rate: after OPV campaigns vs before OPV campaigns
Community studies				
1	Guinea-Bissau; urban, 2002-2014 (22)#	Total population. Age and season adjusted mortality rate comparing after vs before OPV-only campaign. Adjusted for other health campaigns	1 day-35 months	25% (15-33%)
2	Burkina Faso; rural, 2012-2015 (24)	Age, season and sex adjusted mortality rate comparing after vs before any-OPV campaign - within an RCT of early MV	4-35 months	36% (6-56%)
3	Guinea-Bissau, rural; 2002-2003 (26); study 3 is partly overlapping with (25)*.	Age and season adjusted mortality rate comparing after vs before any-OPV campaign	0-11 months	10% (-17-31%)
4	Guinea-Bissau, rural, 2011-2015 (27)	Age, region and vaccination coverage adjusted mortality rate comparing after vs before any-OPV campaign - within a cluster RCT of MV-for-all vs restrictive MV vial policy	9-35 months	19% (-45-55%)
5	Guinea-Bissau, rural, 2017-2019 (28)	Age, region and vaccination coverage adjusted mortality rate comparing after vs before any-OPV campaign - within a cluster RCT of MV campaign vs no campaign	9-59 months	28% (6-45%)
6	Bangladesh, rural, 2004-2019 (29)	Age and period adjusted mortality rate comparing after vs before OPV-only campaign. Adjusted for other health campaigns	1 day-35 months	32% (10-49%)
	Combined effect in community studies			25% (18-31%)
Hospital studies				
6	Hospital CFR, 2001-2008 (30)	CFR for any cause; children exposed before admission to any-OPV campaign or not exposed	6 weeks to 8 months	28% (10-42%)

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One vaccine to counter many diseases? Modeling the economics of oral polio vaccine against child mortality and COVID-19

Angela Y. Chang[1,2]*, Peter Aaby[3,4], Michael S. Avidan[5], Christine S. Benn[1,3,4], Stefano M. Bertozzi[6,7,8], Lawrence Blatt[9,10], Konstantin Chumakov[10,11], Shabaana A. Khader[12], Shyam Kottilil[10,13], Madhav Nekkar[6], Mihai G. Netea[10,14,15], Annie Sparrow[16] and Dean T. Jamison[17]

Table 1. Comparing the characteristics of the two forms of immune response

Innate	Adaptive
Mediated by both myeloid and lymphoid (NK, T) cells	Involves lymphoid cells (B and T lymphocytes)
Based on direct phagocytosis and killing of microbes, release of cytokines and chemokines, NK-mediated killing of virus-infected cells	Mechanistically involve antibodies and specific T cells
Works almost immediately	Takes 1 to 2 wk to develop following exposure to a pathogen or vaccine
Present in all multicellular organisms	System is present in vertebrates but not in invertebrates or plants
Broadly specific, can be effective against groups of microorganisms	Specific to one microorganism or even strain

Chumakov *et al.* (2021)

Table 3. Existing LAVs and their characteristics

Criteria	Measles/MMR	OPV	Bacillus Calmette–Guérin
Route	Subcutaneous	Oral	Intradermal
Combination vaccines	MMR vaccine and MMR combined with Varicella vaccine	bOPV (OPV1 and OPV3)	Alone
Contraindications	Immunosuppression, pregnancy, HIV with CD4 T cell counts <15%	Immunosuppression, HIV, pregnancy	Immunosuppression, active tuberculosis, pregnancy
Adverse events	Serum sickness like arthralgias. Febrile seizures. Rare but severe allergic (anaphylactic) reactions.	Vaccine associated paralytic polio (VAPP) (1/million) only in unvaccinated children	Disseminated disease in immunosuppressed (CGD, IFN gamma defects)
Rare complication	SSPE (0.7/million)	VAPP (1/million) only in unvaccinated children	Bacillus Calmette–Guérin osteitis
Stimulation of innate immunity	Yes	Yes	Yes

Chumakov *et al.* (2021)

RESEARCH ARTICLE | APPLIED BIOLOGICAL SCIENCES |

BCG vaccine protection from severe coronavirus disease 2019 (COVID-19)

EClinicalMedicine. 2022 Jun;48:101414. doi: 10.1016/j.eclinm.2022.101414. Epub 2022 May 12.

Safety and efficacy of BCG re-vaccination in relation to COVID-19 morbidity in healthcare workers: A double-blind, randomised, controlled, phase 3 trial

Distinctive features that are typical for nonpathogen-specific use of existing LAVs (but not for pathogen-specific vaccines):

- Effectiveness against multiple pathogens;
- More rapid elicitation of a protective immunity;
- Well-understood safety profiles;
- Population familiarity with and acceptance of many of the LAVs;
- Preexisting manufacturing capacity and licensing; and,
- Possibility that (current or future) vaccine stockpiles could be diverted to pandemic responses.

Table 4. Potential uses of live attenuated vaccines LAVs against COVID-19

Use	Population addressed
"Bridge" use (until SARS-CoV-2–specific vaccine becomes available)	General populations • Responders (medical, fire, police) • At-risk populations (hourly workers, gig workers, undocumented residents)
LAV incremental to SARS-CoV-2 specific vaccine	As an adjuvant concomitant to administration of a COVID-19 vaccine • To boost responses in elderly or individuals with comorbidity
Ring use (ring use will generally require single administration of vaccines in well-defined populations as a quick response to appearance of infection)	Quenching postpandemic flare-ups • Quenching prepandemic sparks • Institutionalized elderly and caretakers • Prisoners and guards • Other institutionalized groups
Therapeutic use (hypothetical)	• Infected individuals immunized early after detection of infection

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TABLE 1 Two immunization schedules adding OPV to COVID-19 vaccine.

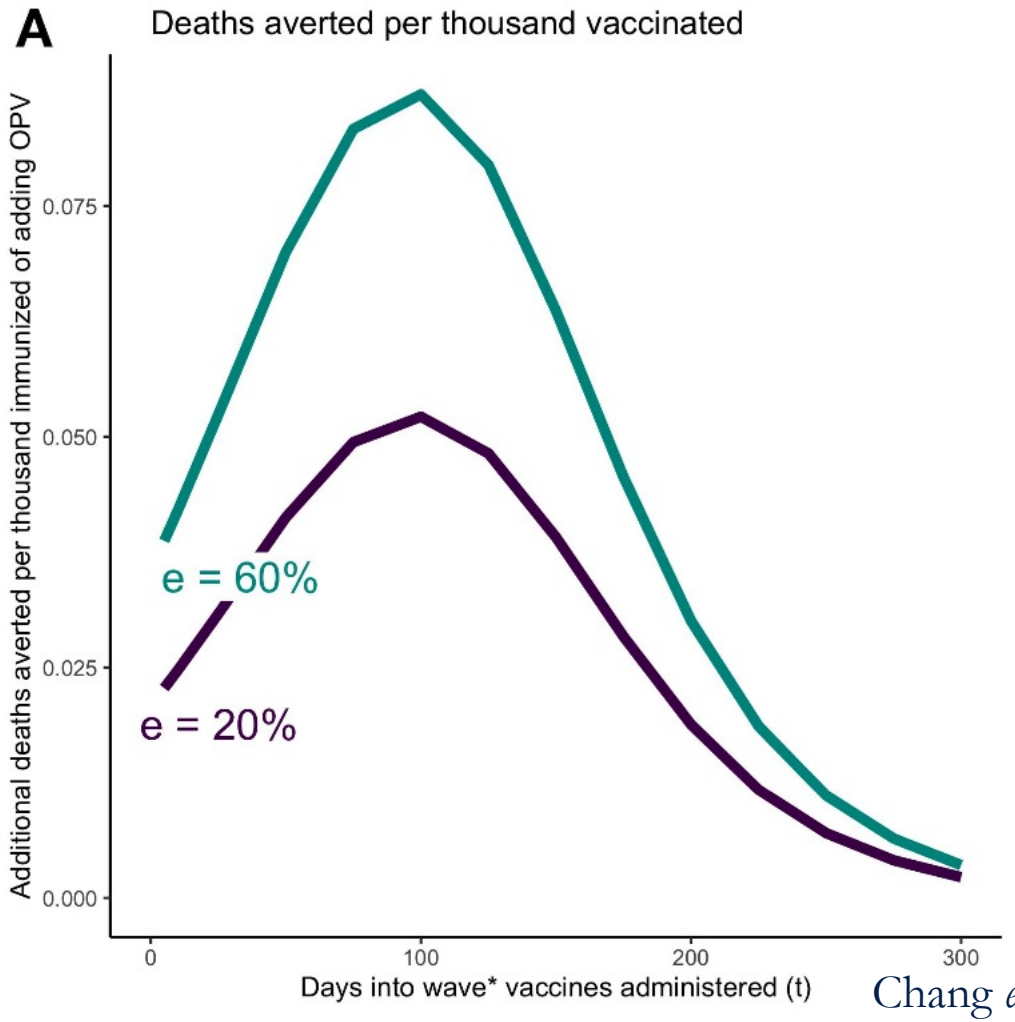
Schedule	Timing*
Simultaneous administration	COVID-19 vaccine and OPV both administered t days after beginning of a wave
COVID-19 vaccine delayed	OPV administered t days after beginning of wave and COVID-19 vaccine becomes available with a delay of d days after OPV administration (i.e., $t+d$ days after beginning of wave)

*Calculations assuming administration of vaccines on days t and $t+d$, and that this approximates gradual coverage growth centered on those days.

Chang *et al.* (2022)

OPV and COVID-19 vaccine simultaneously administered *t* days after beginning of epidemic wave

Incremental deaths averted per 1,000 individuals of adding OPV to COVID-19 vaccine only schedule



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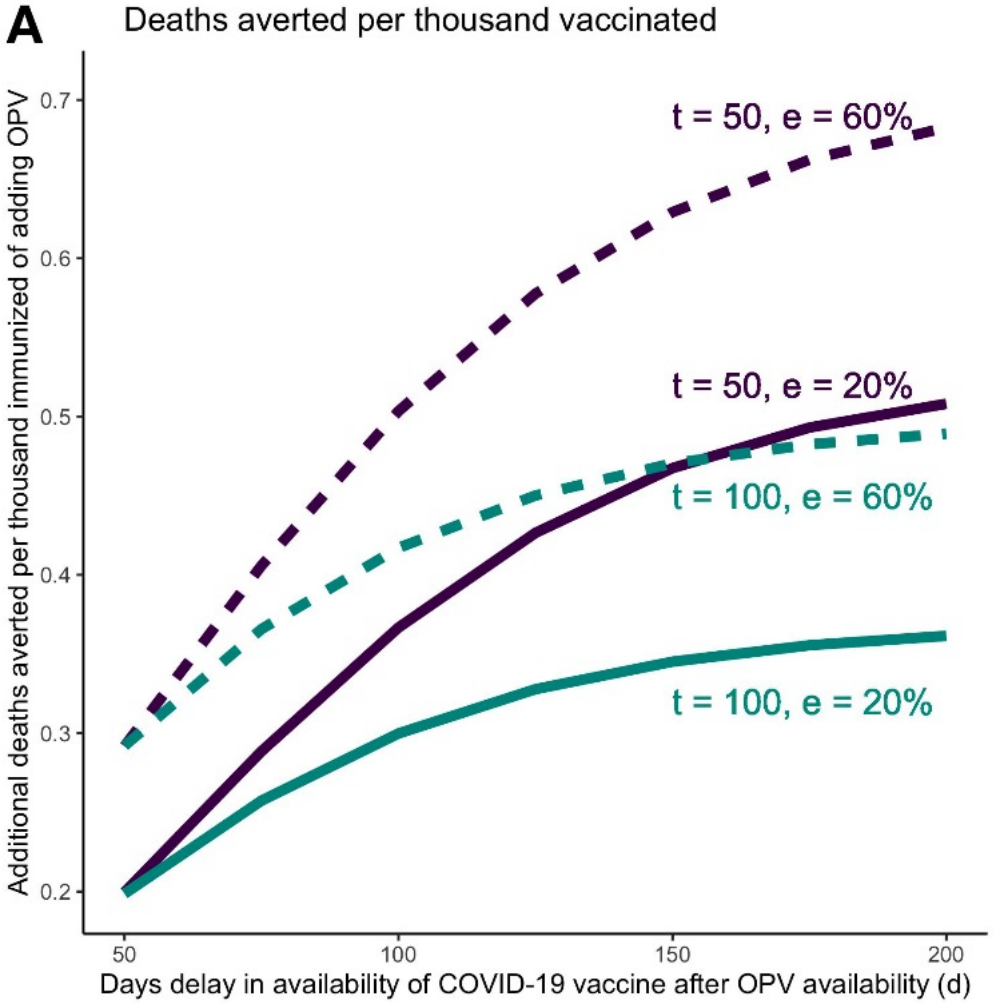
COVID-19 vaccine is delayed in a COVID-19 vaccine + OPV schedule

Incremental deaths averted per 1,000 individuals of adding OPV to COVID-19 vaccine only schedule



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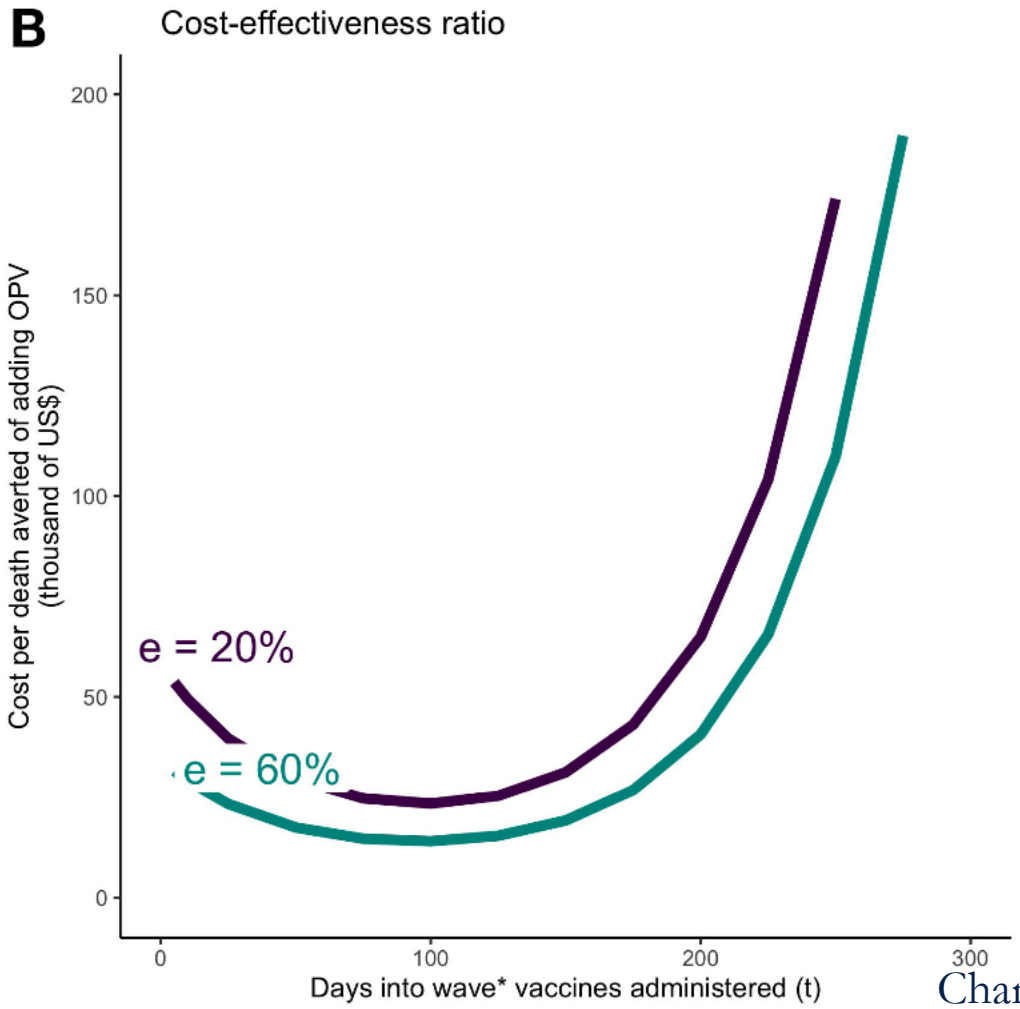
OPV and COVID-19 vaccine simultaneously administered *t* days after beginning of epidemic wave

Incremental cost-effectiveness ratio per averted death of adding OPV to COVID-19 vaccine only schedule



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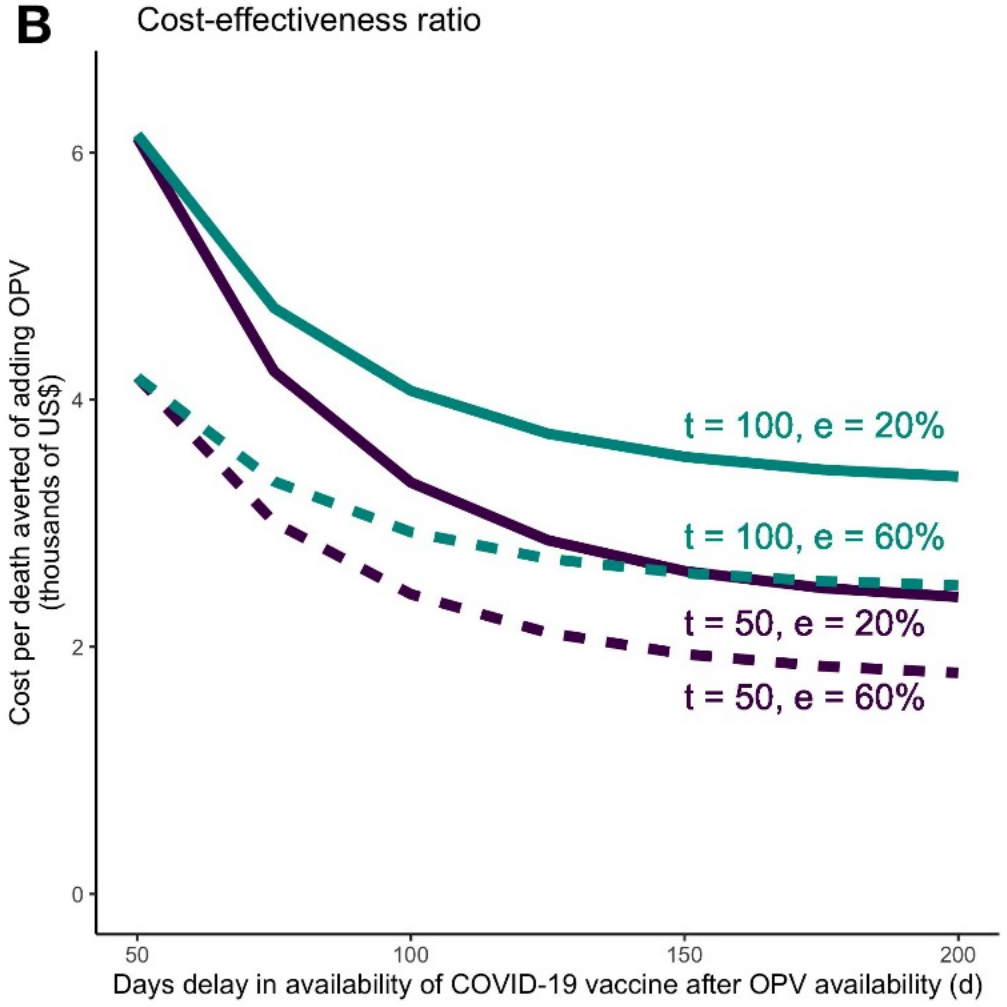

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Thank you