Optimized delay of the second COVID-19 vaccine dose reduces ICU admissions:

Making-of

Claudio José Struchiner[1]

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EPGE 2021

Cenário

Science

REPORTS

Cite as: Kissler *et al.*, *Science* 10.1126/science.abb5793 (2020).

Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period

Stephen M. Kissler[1]*, Christine Tedijanto[2]*, Edward Goldstein[2], Yonatan H. Grad[1]†‡, Marc Lipsitch[2]†‡

[1]Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, MA, USA. [2]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA.

Cenário

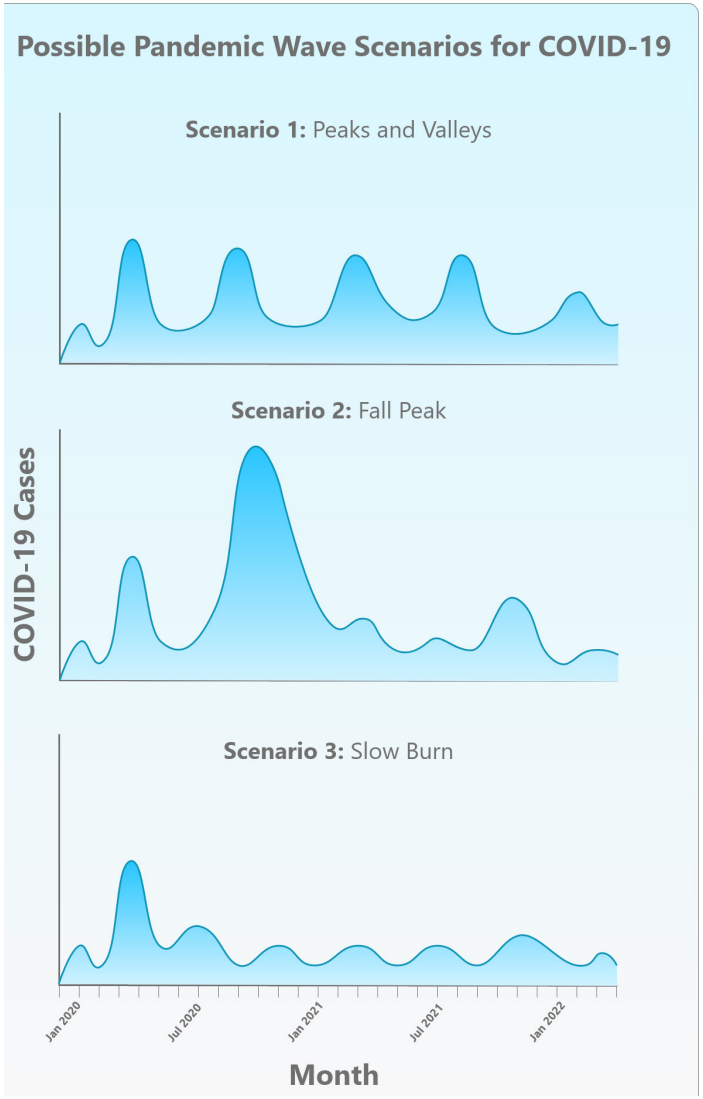


Figure 1

Cenário

Science

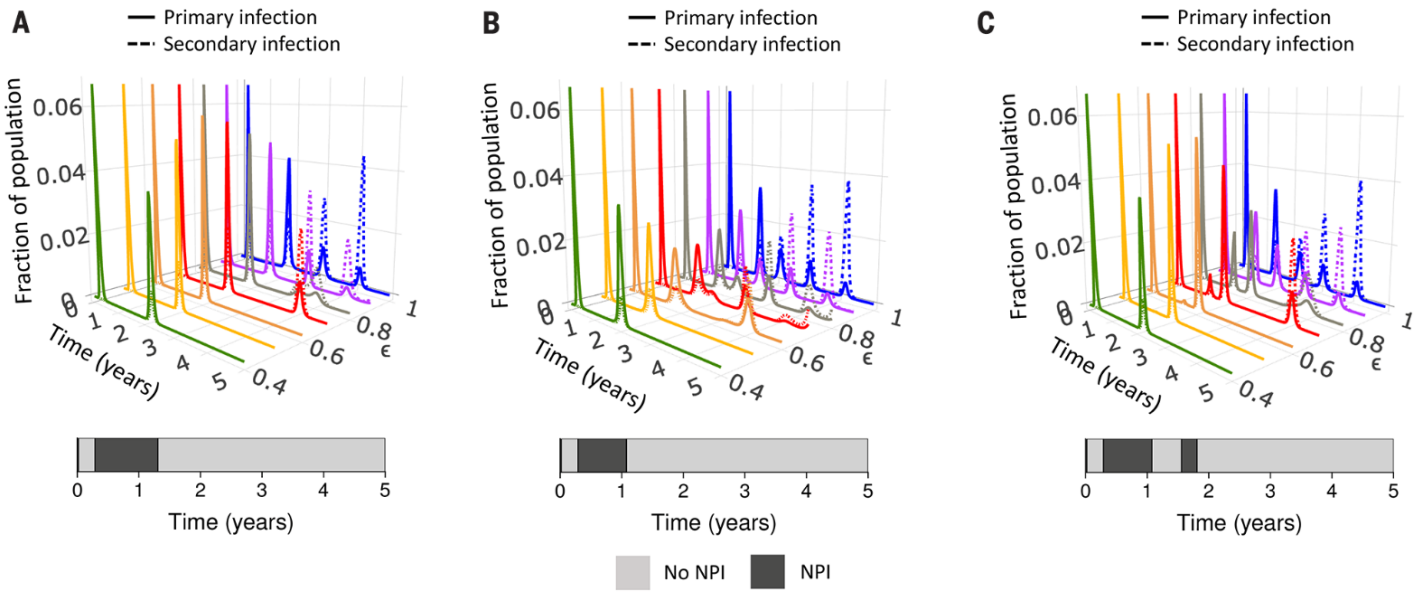
RESEARCH ARTICLES

Cite as: C. M. Saad-Roy *et al.*, *Science*
10.1126/science.abd7343 (2020).

Immune life history, vaccination, and the dynamics of SARS-CoV-2 over the next 5 years

Chadi M. Saad-Roy[1]*, Caroline E. Wagner[2,3,4]*, Rachel E. Baker[2,3], Sinead E. Morris[5], Jeremy Farrar[6], Andrea L. Graham[2], Simon A. Levin[2], Michael J. Mina[7], C. Jessica E. Metcalf[2,8], Bryan T. Grenfell[2,8,9]†

Cenário



Sazonalidade e NPI: infecção primária (linha contínua); infecção secundária (linha tracejada); ϵ - susceptibilidade relativa à infecção secundária (Saad-Roy, 2020)

Annals of Internal Medicine

IDEAS AND OPINIONS

A Public Health COVID-19 Vaccination Strategy to Maximize the Health Gains for Every Single Vaccine Dose

Ruanne V. Barnabas, MBChB, MSc, DPhil; and Anna Wald, MD, MPH

Annals of Internal Medicine

OBSERVATION: BRIEF RESEARCH REPORT

Speed Versus Efficacy: Quantifying Potential Tradeoffs in COVID-19 Vaccine Deployment

A. David Paltiel, PhD
Yale School of Public Health, New Haven, Connecticut

Amy Zheng, BA
Harvard Medical School, Boston, Massachusetts

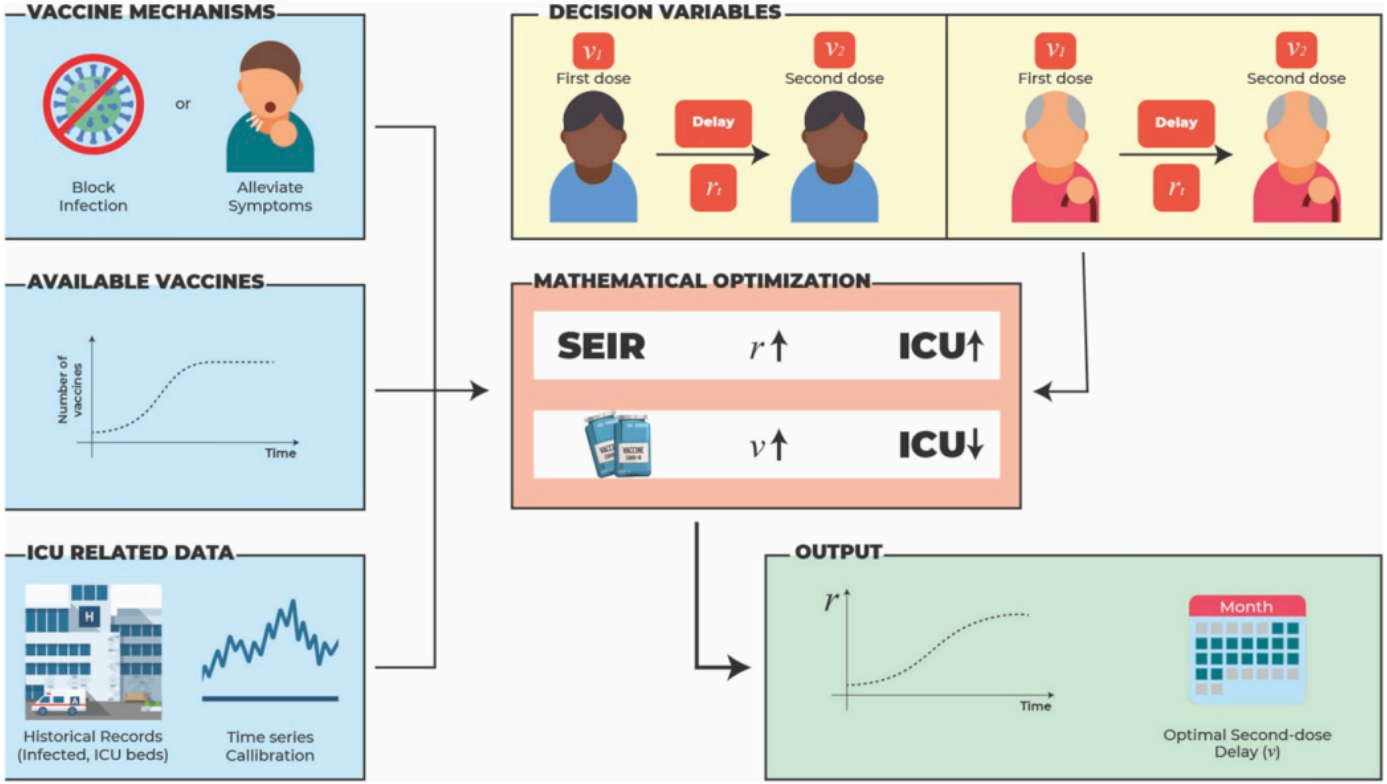
Jason L. Schwartz, PhD
Yale School of Public Health, New Haven, Connecticut

Optimized delay of the second COVID-19 vaccine dose reduces ICU admissions

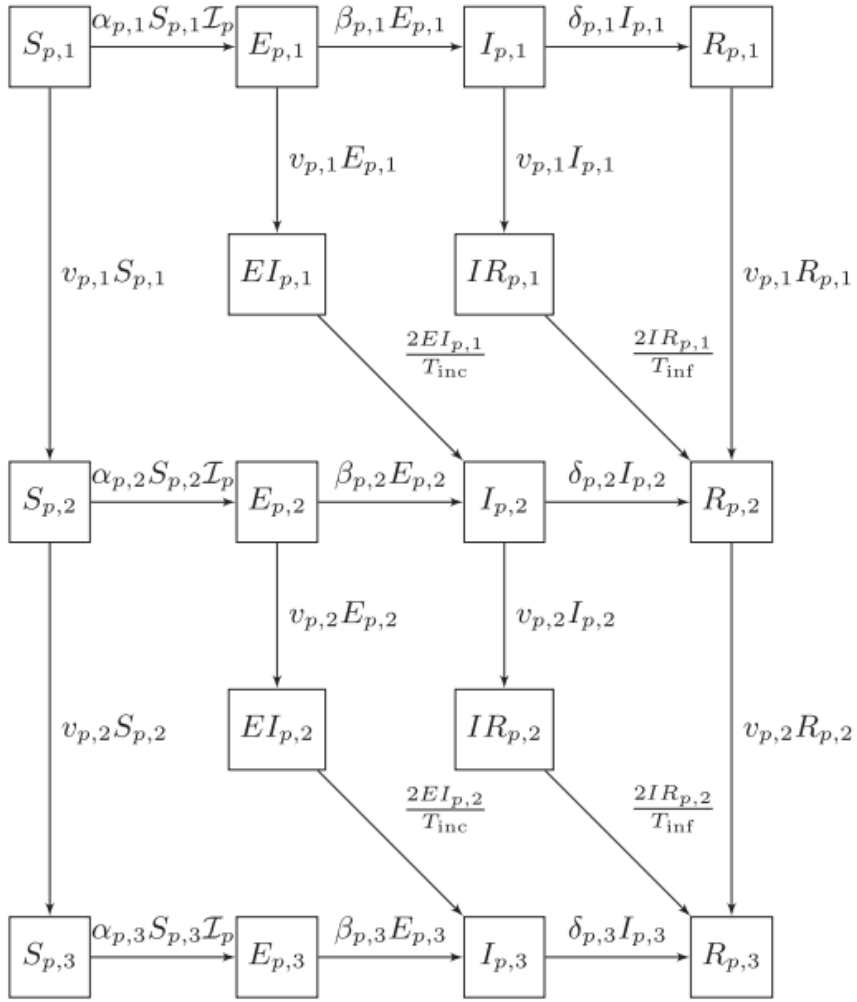
Paulo J. S. Silva[a], Claudia Sagastizábal[a], Luís Gustavo Nonato[b], Claudio José Struchiner[c], and Tiago Pereira[b,1]

[a]Instituto de Matemática, Estatística e Computação Científica, Universidade Estadual de Campinas, 13083-859 São Paulo, Brazil; [b]Instituto de Ciências Matemáticas e Computação, Universidade de São Paulo, 13566-590 São Paulo, Brazil; and [c]Escola de Matemática Aplicada, Fundação Getúlio Vargas, 22250-9 Rio de Janeiro, Brazil

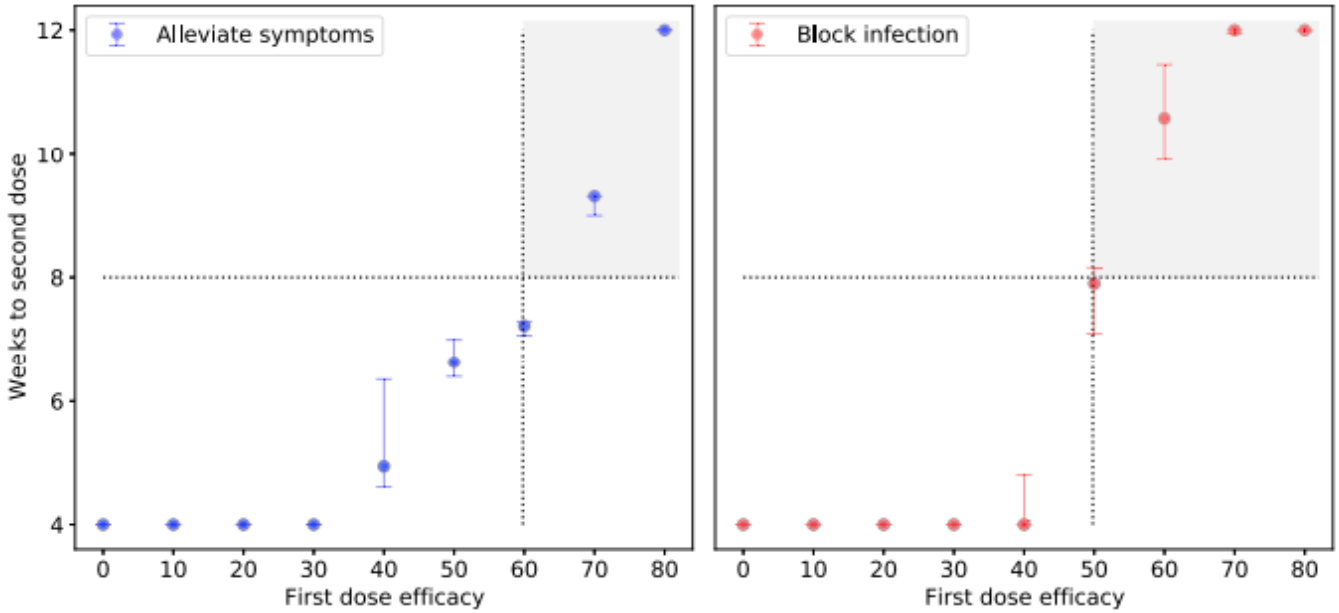
Edited by David L. Donoho, Stanford University, Stanford, CA, and approved July 8, 2021 (received for review March 12, 2021)



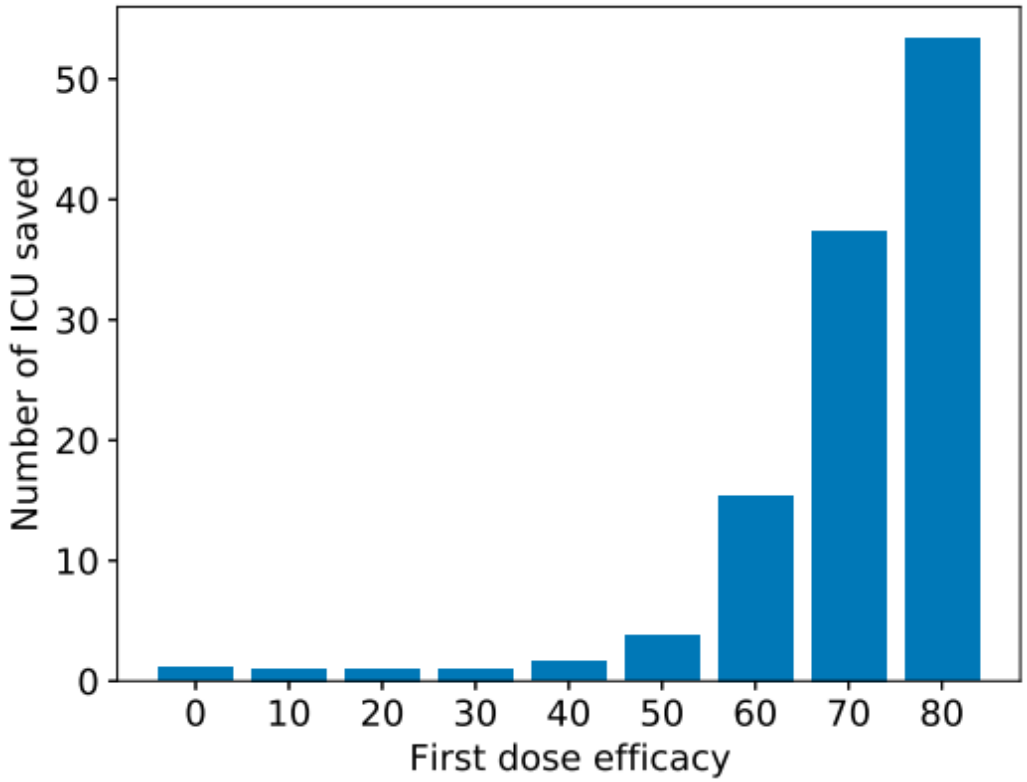
Data to obtain an optimal delay for administration of a vaccine second dose. The optimal second dose delay emerges from the solution of the optimization model. The model is solved using an optimization algorithm that considers multiple scenarios and iteratively adjusts the decision variables to find the optimal delay between the first and second vaccine doses and the target control reproduction number.



SEIR model for age group p with a two-dose vaccine that blocks infection



The shaded areas represent the first-dose efficacy that results in doubling the time to second dose from the baseline (4 wk). Left shows the second-dose delay when the vaccine alleviates symptoms; in this case, the best strategy delays the second dose for $\geq$ 8 wk when the first-dose efficacy is $\geq$ 70%. Right shows the second-dose delay when the vaccine blocks infection; here, the best strategy delays the second dose for $\geq$ 8 wk when the first-dose efficacy is $\geq$ 50%. For both vaccine types, the second-dose efficacy reaches 82.4%. The filled circles show the time to the second dose for r0 = 2.5, and the bars represent the variability across simulations when r0 is varied from 1.8 to 3 in 0.2 steps



Reduction in ICU occupancy using the optimized second-dose delay strategy compared with the standard delay strategy

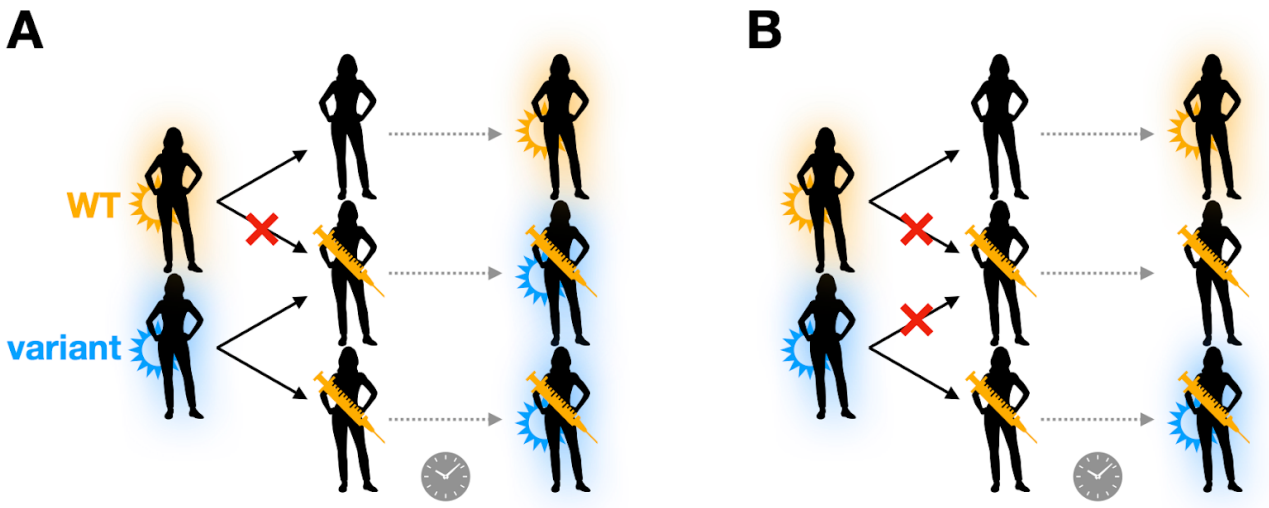
Variantes

Concerns about SARS-CoV-2 evolution should not hold back efforts to expand vaccination

Sarah Cobey[1]*, Daniel B. Larremore[2,3], Yonatan H. Grad[4], and Marc Lipsitch[4,5]

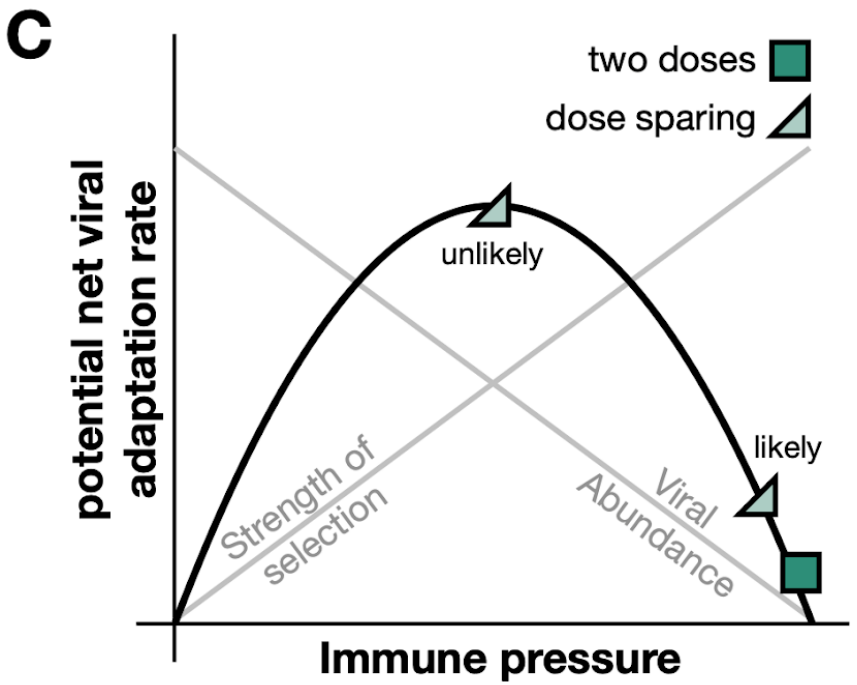
[1]Department of Ecology and Evolution, University of Chicago, Chicago, IL, USA
[2]Department of Computer Science, University of Colorado Boulder, Boulder, CO, USA
[3]BioFrontiers Institute, University of Colorado Boulder, Boulder, CO, USA
[4]Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[5]Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

Variantes



A - vacina confere vantagem para variante; B - proteção residual contra variante (Cobey, 2021)

Variantes



especulação: com apenas uma dose, a taxa de adaptação dentro do hospedeiro pode ser alta (triângulo no topo da curva) (Cobey, 2021)

Resistência a Vacinas vs Antibióticos

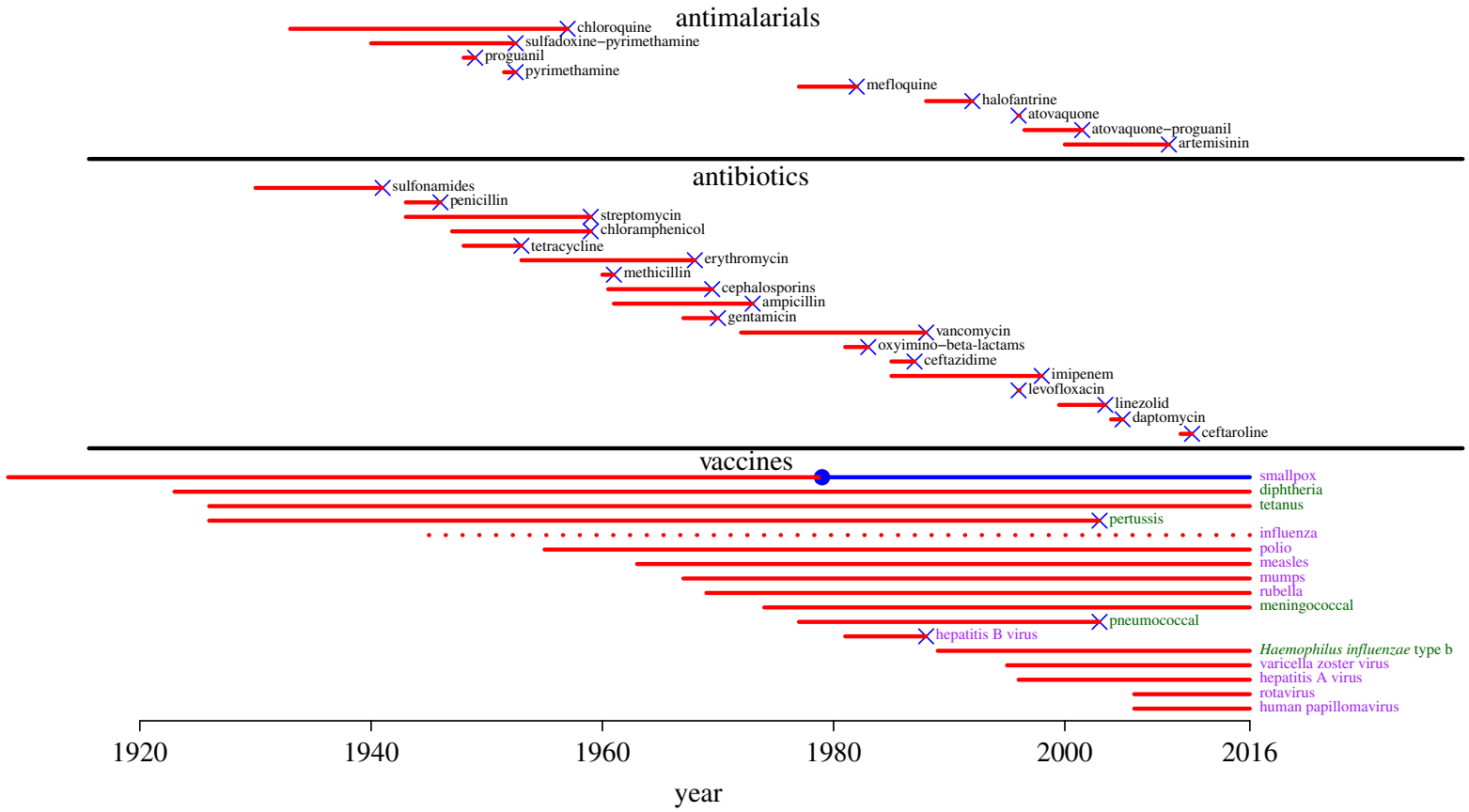
PROCEEDINGS B

rspb.royalsocietypublishing.org

Why does drug resistance readily evolve but vaccine resistance does not?

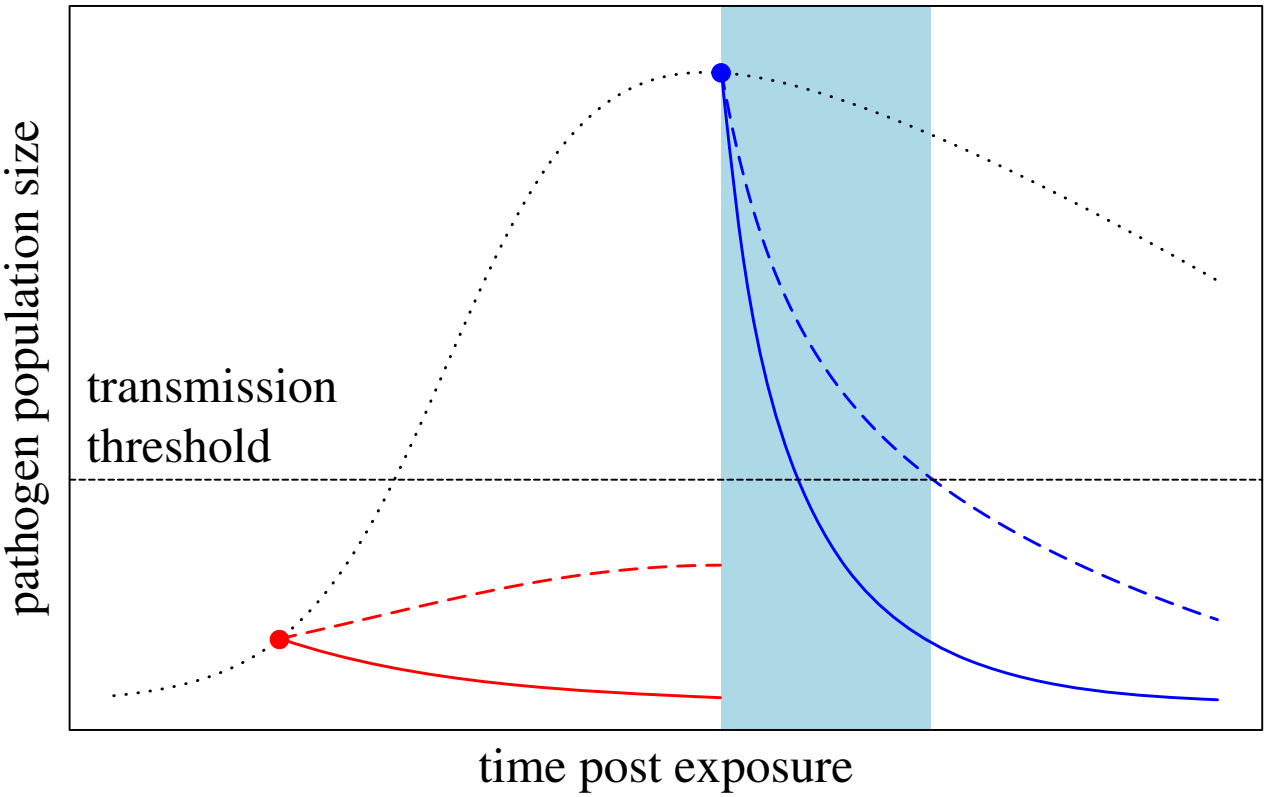
David A. Kennedy and Andrew F. Read

Resistência a Vacinas vs Antibióticos



roxo: vacinas virais; verde: vacinas bacterianas; X: relato de resistência; círculo azul cheio: erradicação; tracejado: evolução antigência mesmo na ausência da vacina (Kennedy, 2017)

Resistência a Vacinas vs Antibióticos



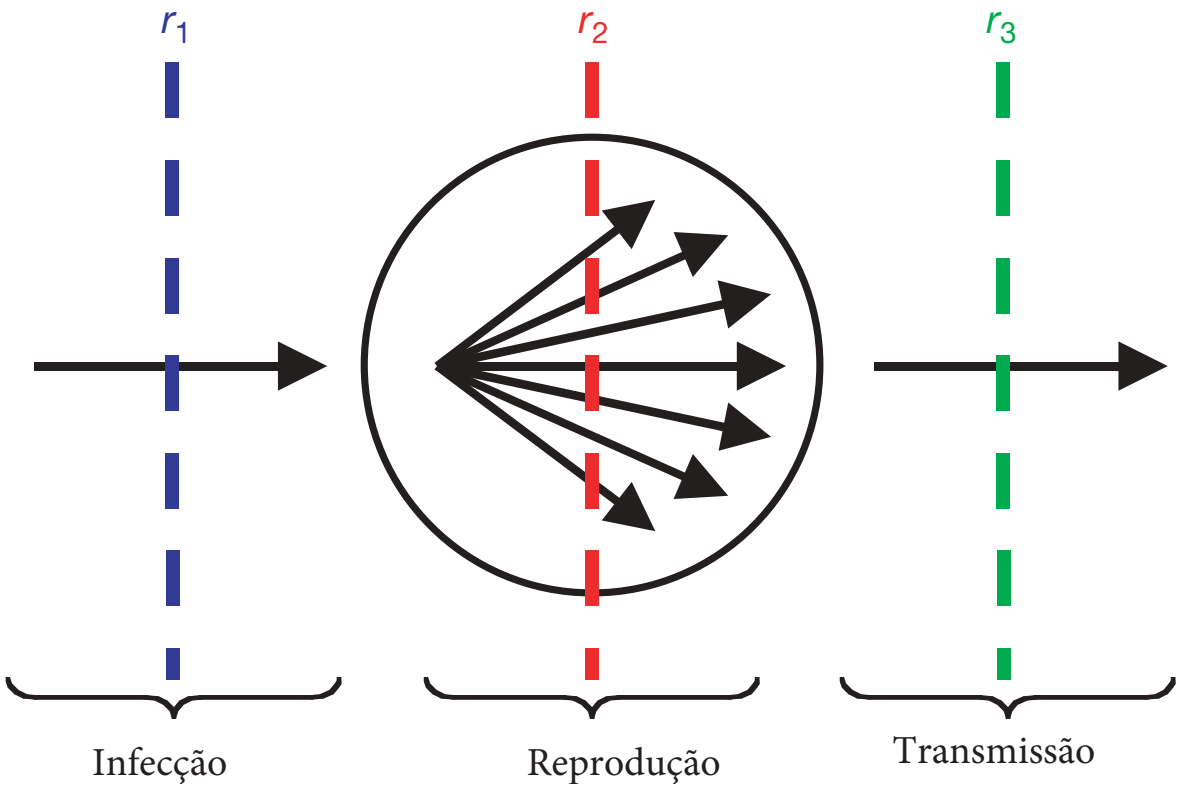
pontilhado: evolução natural; vermelho: cedo (profilaxia); azul: tarde (terapia); contínua: patógeno sensível; patógeno parcialmente resistente; horizontal: limiar de transmissão; sombreado: janela de oportunidade de seleção favorável (Kennedy, 2017)

Resistência a Vacinas vs Antibióticos

feature	origin	spread
early action (prophylaxis)	prophylaxis limits the accumulation of genetic diversity before intervention	pre-transmission clearance reduces opportunity for selection on partial resistance during spread
multiplicity of targets	combination-like effect reduces chance that resistance will appear	mosaic-like effect reduces the transmission advantage of resistance

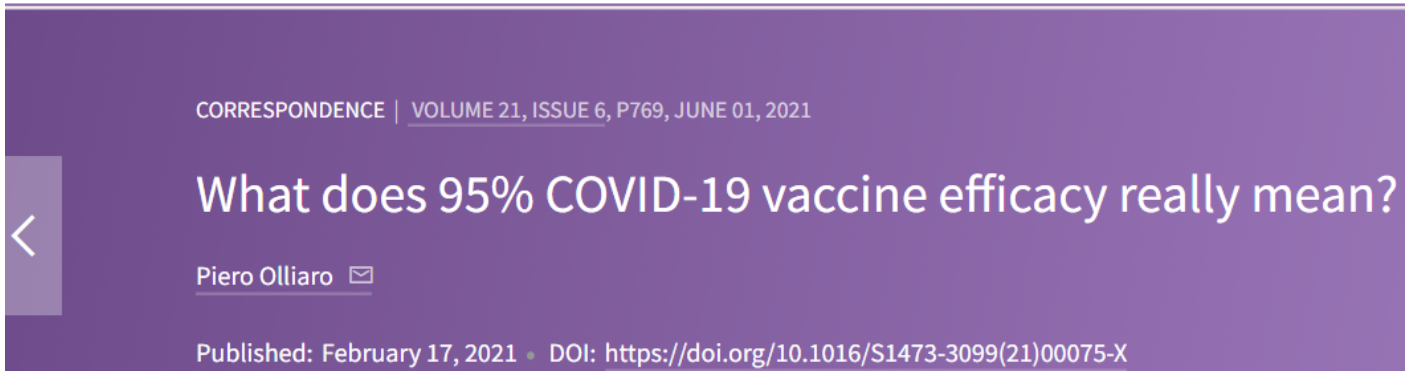
Vacinas agem precocemente e induzem imunidade que tem múltiplos alvos. Esses recursos reduzem a probabilidade de resistência se originar em primeiro lugar e reduzem a taxa de propagação da resistência se ela surgir. Vacinas tendem a funcionar profilaticamente, enquanto os medicamentos tendem a funcionar terapeuticamente. Vacinas tendem a induzir respostas imunológicas contra vários alvos, enquanto as drogas tendem a ter muito poucos. Conseqüentemente, as populações de patógenos geram menos variação para resistência à vacina do que para resistência aos medicamentos, e a seleção tem menos oportunidades de agir sobre essa variação. Quando a resistência à vacina evoluiu, essas generalidades foram violadas.(Kennedy, 2017)

Vacinas: mecanismos de ação



Fonte: Gandon et al., 2001

THE LANCET
Infectious Diseases



CORRESPONDENCE | VOLUME 21, ISSUE 6, P769, JUNE 01, 2021

What does 95% COVID-19 vaccine efficacy really mean?

Piero Olliaro

Published: February 17, 2021 • DOI: https://doi.org/10.1016/S1473-3099(21)00075-X

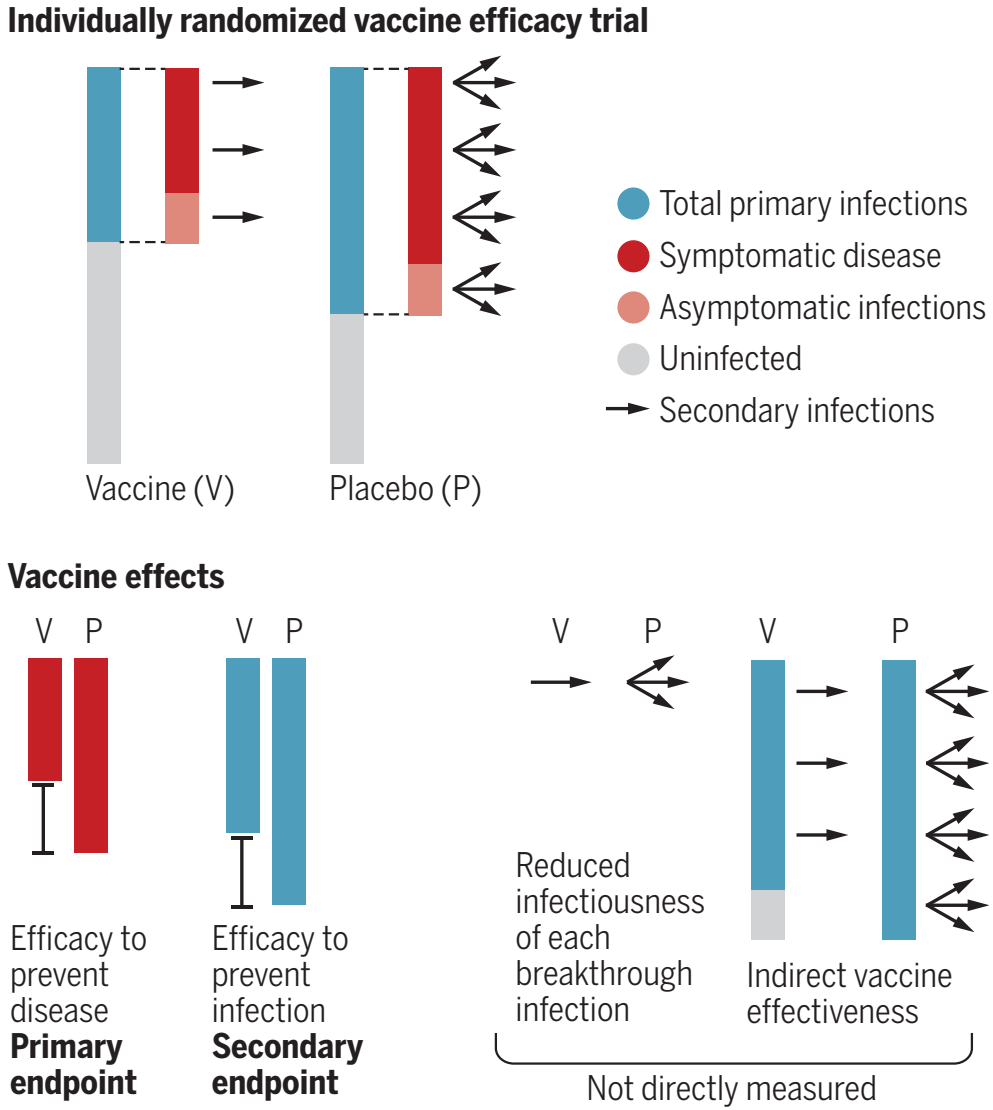
PERSPECTIVE | VIEWPOINT: COVID-19

Understanding COVID-19 vaccine efficacy

MARC LIPSITCH AND NATALIE E. DEAN

SCIENCE • 13 Nov 2020 • Vol 370, Issue 6518 • pp. 763-765 • DOI: 10.1126/science.abe5938

Vacinas: mecanismos de ação



Fonte: Lipsitch and Dean, 2020

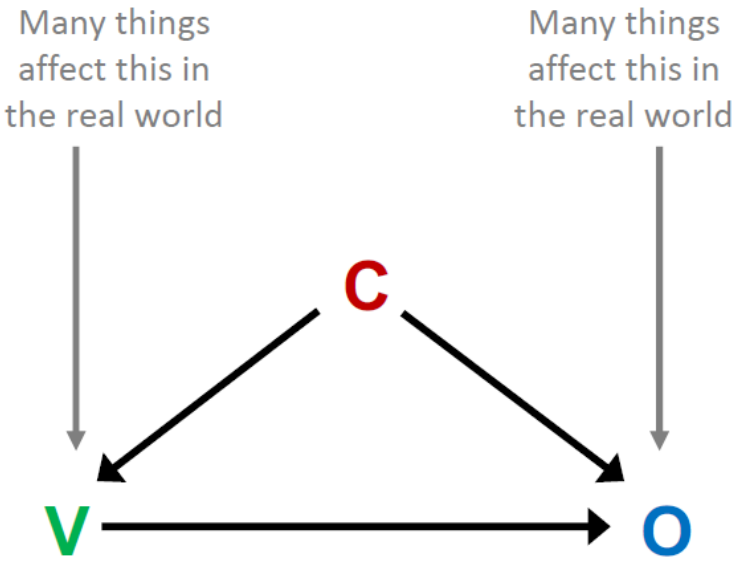
A case for RCT

Confounding occurs when there is a common cause (C) of BOTH

whether someone is vaccinated (V)

AND

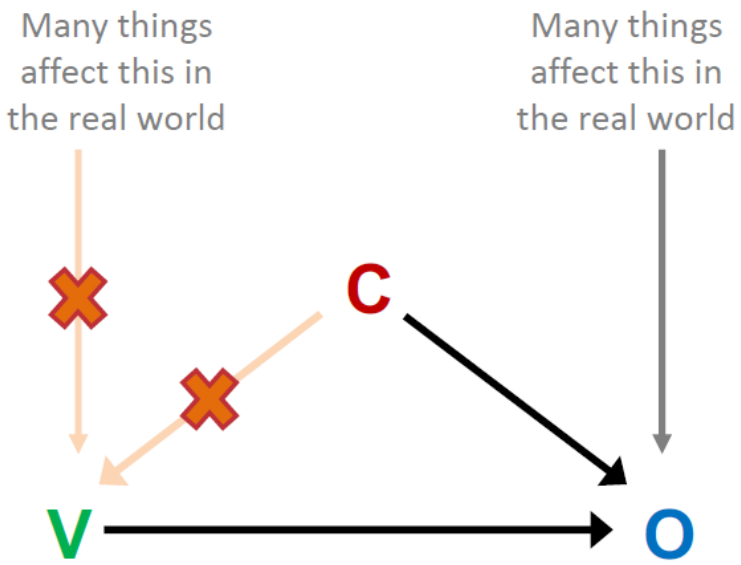
whether someone has an outcome event (O)



Source: Prof. Julian Higgins, University of Bristol, UK

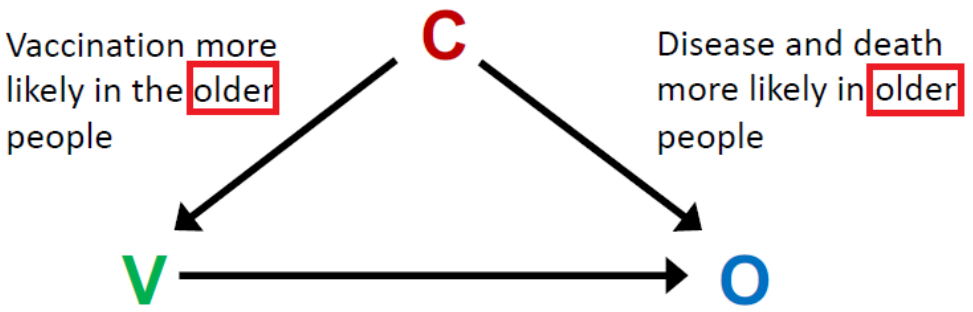
A case for RCT

Randomization removes these links by ensuring that only chance determines whether someone is vaccinated



Source: Prof. Julian Higgins, University of Bristol, UK

Non-randomized

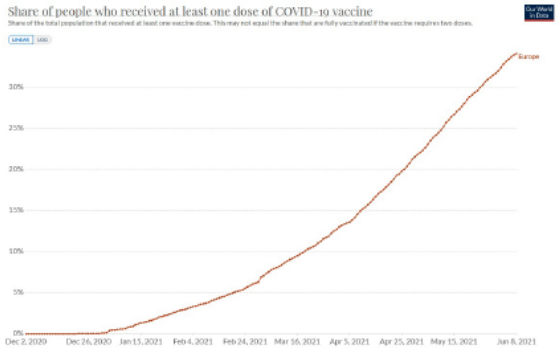


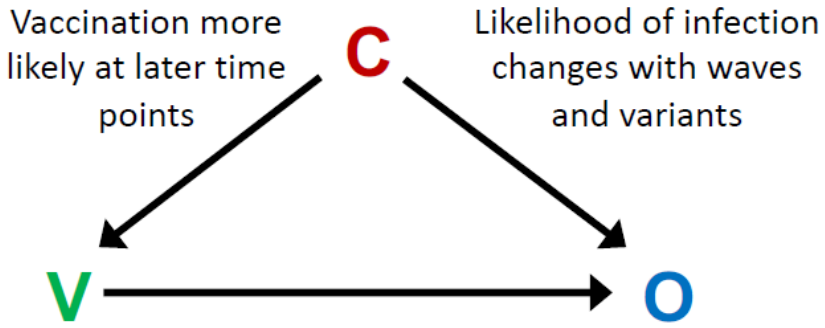
Leads to association between vaccination and disease even if the vaccine is ineffective

We can address this by *adjusting for age*

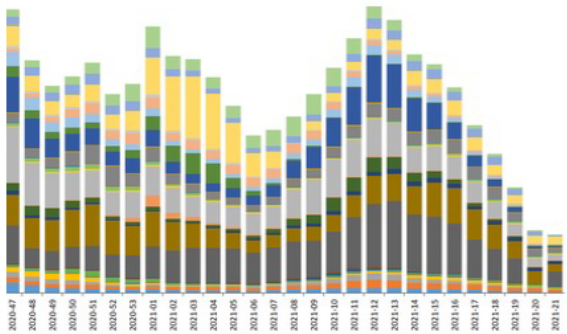
Source: Prof. Julian Higgins, University of Bristol, UK

Non-randomized





We can address this by taking calendar time into account in the analysis



Source: Prof. Julian Higgins, University of Bristol, UK

npj | Vaccines

www.nature.com/npjvaccines

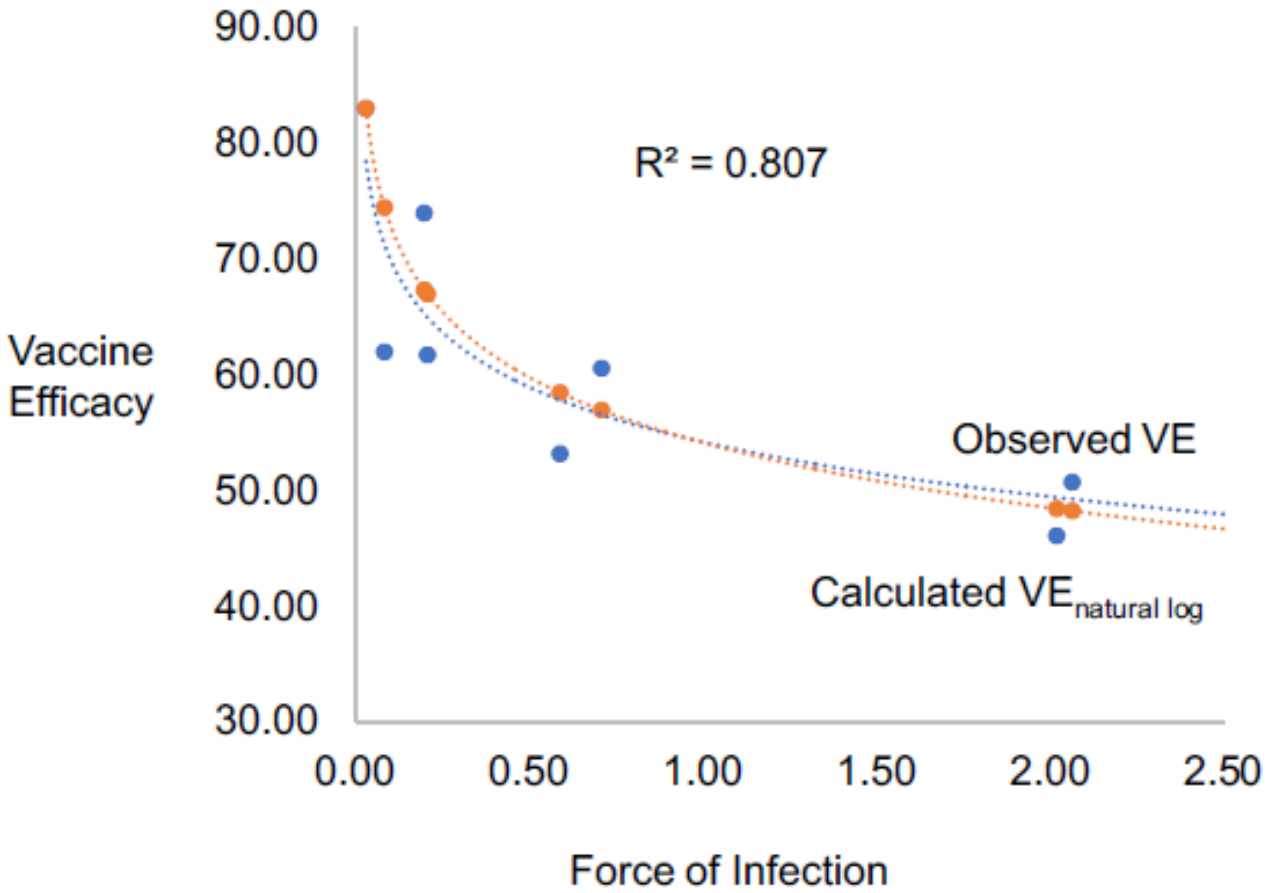
PERSPECTIVE OPEN

Check for updates

Force of infection: a determinant of vaccine efficacy?

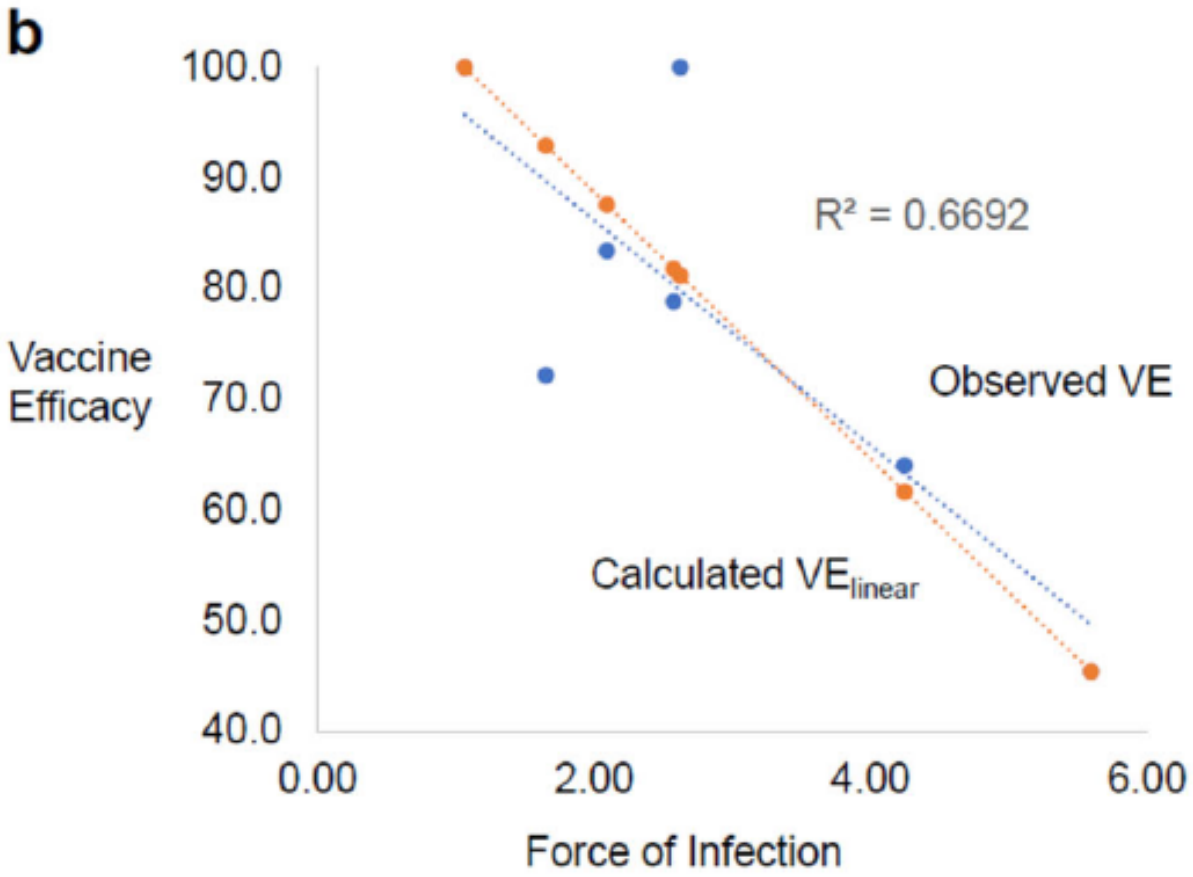
David C. Kaslow[1]✉

Does FoI "determine" VE? (malaria)



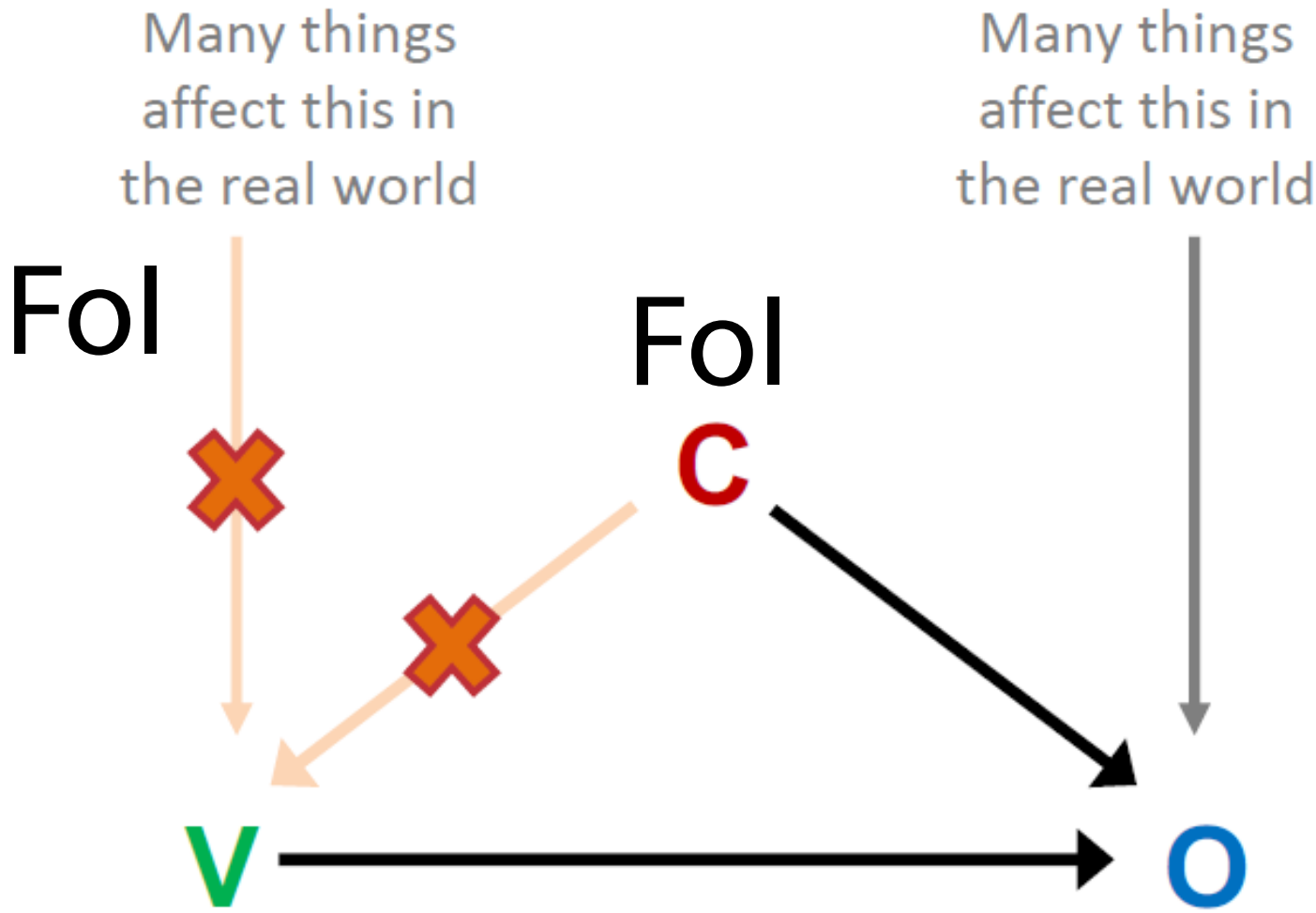
Source: Kaslow, 2021

Does FoI "determine" VE? (rotavirus)



Source: Kaslow, 2021

Does FoI "determine" VE?



Source: Modified from Higgins, 2021

Simplifying assumptions

- homogeneity in the population:
  - pathogen transmission
  - host susceptibility to infection and disease (be it genetic or acquired)
  - FoI over time in a specific setting
  - protective immunity as a result of vaccination across settings.
- implication: transportability problems

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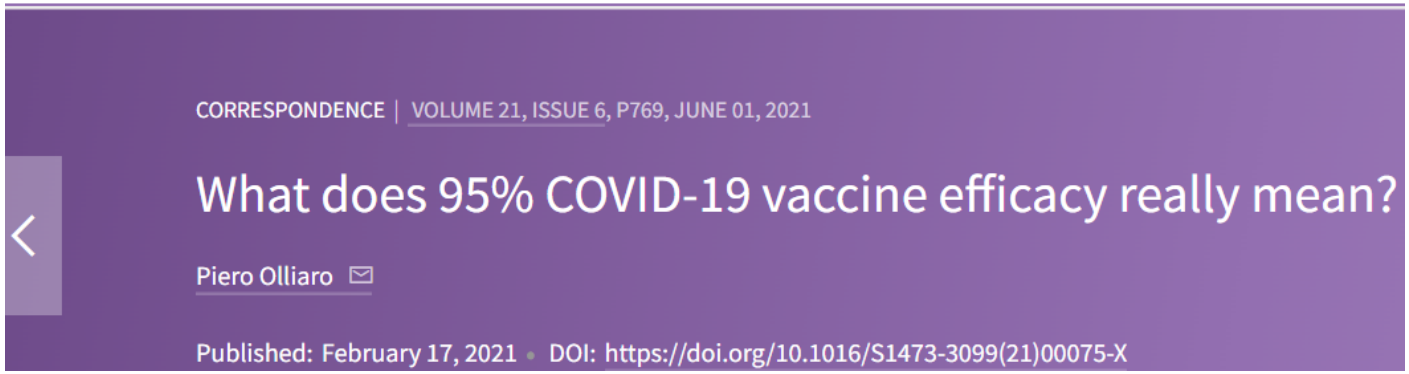

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Piero Olliaro

Published: February 17, 2021 • DOI: https://doi.org/10.1016/S1473-3099(21)00075-X

The Behaviour of Common Measures of Association Used to Assess a Vaccination Programme under Complex Disease Transmission Patterns—A Computer Simulation Study of Malaria Vaccines

CLAUDIO J STRUCHINER, MARY ELIZABETH HALLORAN ✉, JAMES M ROBINS, ANDREW SPIELMAN

International Journal of Epidemiology, Volume 19, Issue 1, March 1990, Pages 187–196, https://doi.org/10.1093/ije/19.1.187

Published: 01 March 1990 **Article history** ▾

Causal Inference in Infectious Diseases

Halloran, M. Elizabeth[1]; Struchiner, Claudio J.[2]

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[2]Escola Nacional de Saüde Pública, Fundacão Oswaldo Cruz, Rio de Janeiro, Brazil.

Epidemiology: March 1995 - Volume 6 - Issue 2 - p 142-151

Epidemiol. Infect. (2007), **135**, 181–194.
doi:10.1017/S0950268806006716 Printed in the United Kingdom

Randomization and baseline transmission in vaccine field trials

C. J. STRUCHINER[1]* AND M. E. HALLORAN[2]

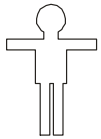
[1] *IMS/UERJ and Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil*
[2] *Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA, USA*

(*Accepted 8 March 2006; first published online 26 June 2006*)

Measure of intervention efficacy

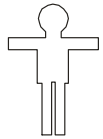
In the lab:

# of cases



V, E, PE
KC, UC

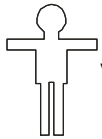
# of cases



NV, E,PE
KC, UC

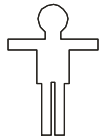
In the field:

# of cases



V, E?, PE?
KC, UC

# of cases



NV, E?, PE?
KC, UC

V, NV - treatment (vaccination)
E, PE - transmission level, previous exp
KC, UC - known and unknown covaritates

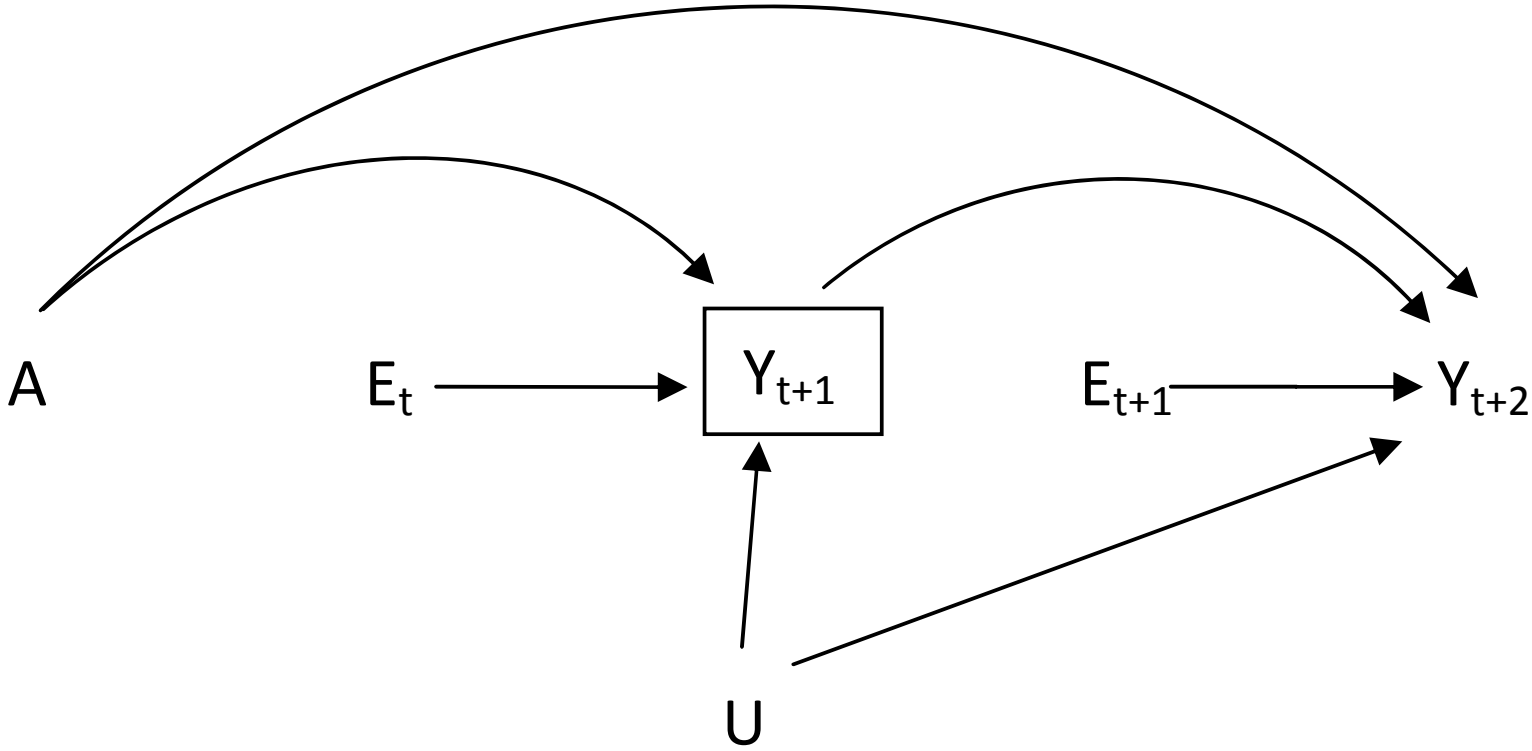
Estimating the Per-Exposure Effect of Infectious Disease Interventions

O'Hagan, Justin J.[a,b]; Lipsitch, Marc[a–c]; Hernán, Miguel A.[a]

Author Information

Epidemiology: January 2014 - Volume 25 - Issue 1 - p 134-138

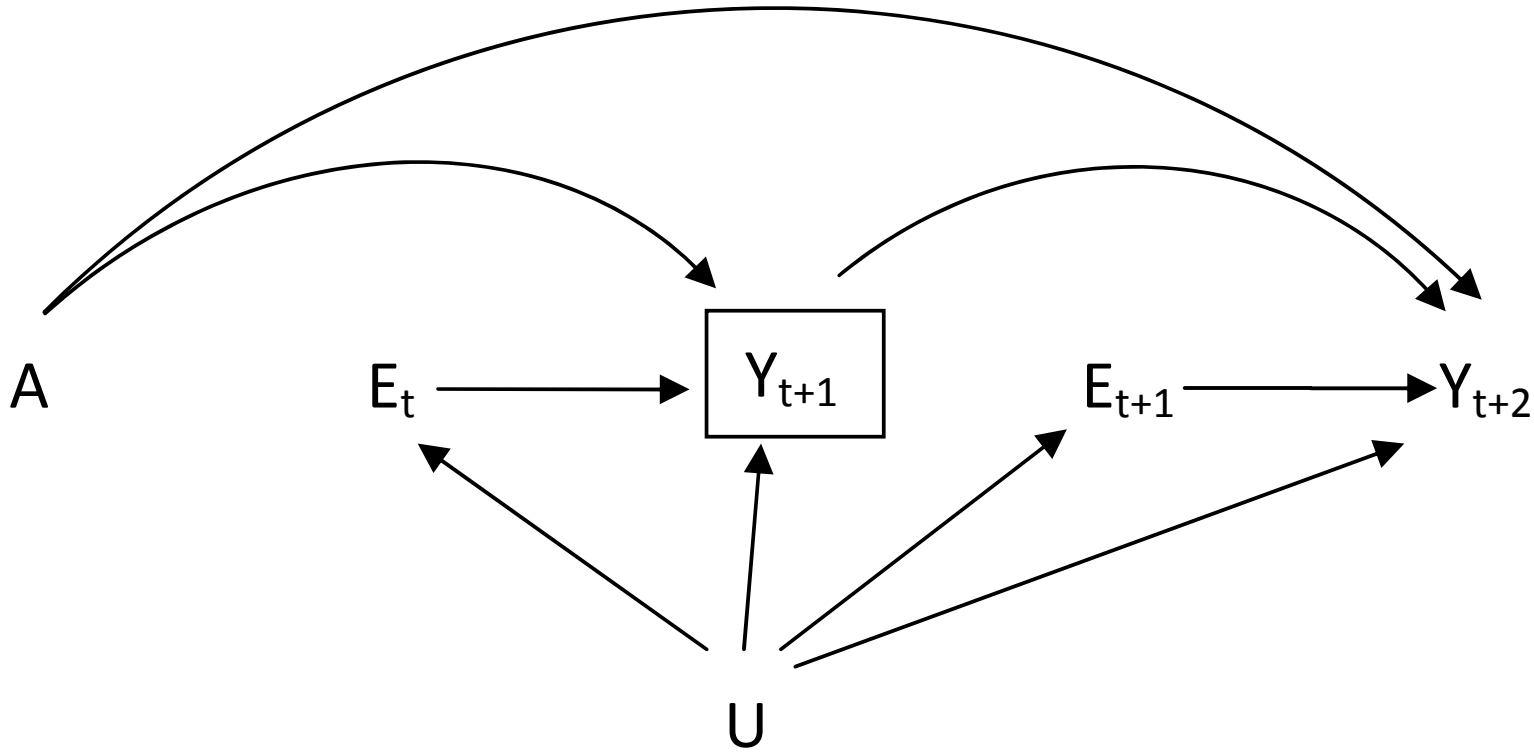
DAG: RCT and challenge



Causal diagram for a double-blind randomized trial of a Chlamydia vaccine A and Chlamydia infection Y. E (FoI) represents exposure to infection and U unmeasured risk factors for infection. The subscripts denote time period. For simplicity, only two time periods are shown (O'Hagan, 2013).

selection bias (conditioning on a collider): $A \rightarrow \boxed{Y_{t+1}} \leftarrow U \rightarrow Y_{t+2}$

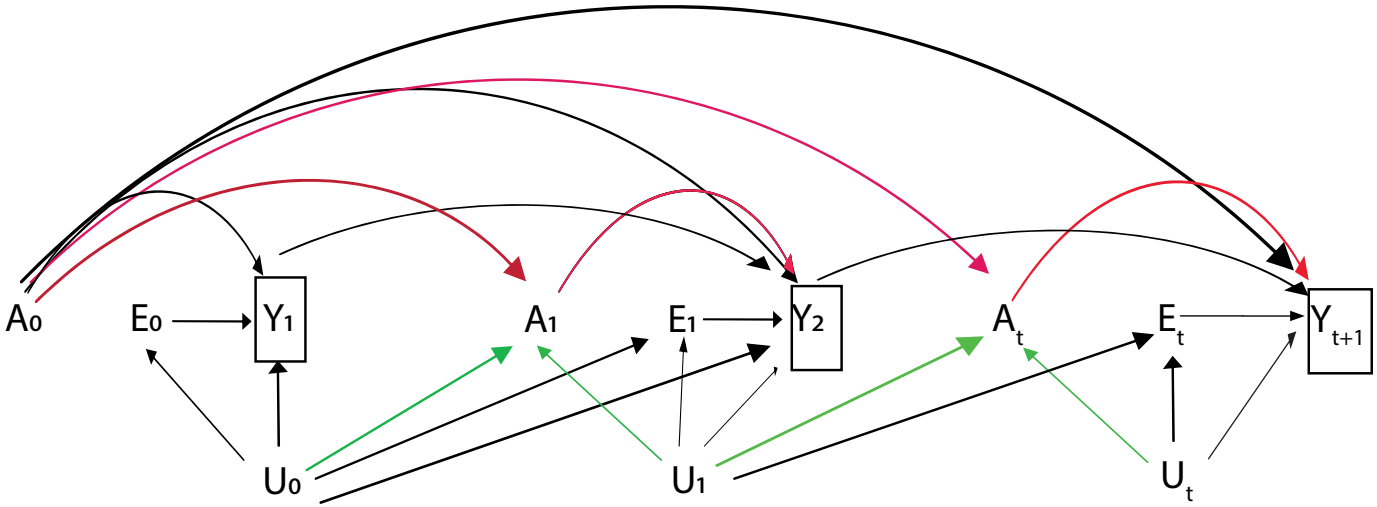
DAG: RCT, challenge and confounding



Causal diagram for a double-blind randomized trial of a Chlamydia vaccine A and Chlamydia infection Y. E represents exposure to infection and U unmeasured risk factors for infection. The subscripts denote time period. For simplicity, only two time periods are shown. Risk factors U affect exposure E (O'Hagan, 2013).
The per-exposure effect is a joint effect of A and E_t and therefore, its unbiased estimation requires no unmeasured confounding for the effect of both A and E_t at all times t.

confounding due to U for the effect of E_t on Y_{t+1}.

DAG: RCT, challenge, and time-dependent confounding and efficacy



Causal diagram for a double-blind randomized trial of vaccine A and infection Y. E represents exposure to infection and U unmeasured risk factors for infection. The subscripts denote time period. Risk factors U affect exposure E, VE is time-dependent (red arrows) and risk factors U are no longer indepedent of A (green arrows) since randomization takes place at time zero (modified from O'Hagan, 2014).