Tackling the burden of AMR

Mortality preventable by interventions

Strategies for reducing AMR burden

O’Neill Report (2016)

Context—the last generation of action plans

Public health actions to tackle AMR have a positive impact on population health...

The OECD has identified interventions that, for their impact on population health and heavy costs voided, could be defined 'best buys' to tackle AMR. The set of policies assessed are aligned with the WHO Global Action Plan on AMR and encompass:

> improving hygiene in healthcare facilities, including promotion of handwashing and better hospital hygiene;

> stewardship programmes promoting more prudent use of antibiotics to end decades of over-prescription;
>
> the use of rapid diagnostic tests in primary care to detect whether an infection is bacterial or viral;
>
> delayed prescription; and
>
> public awareness campaigns.

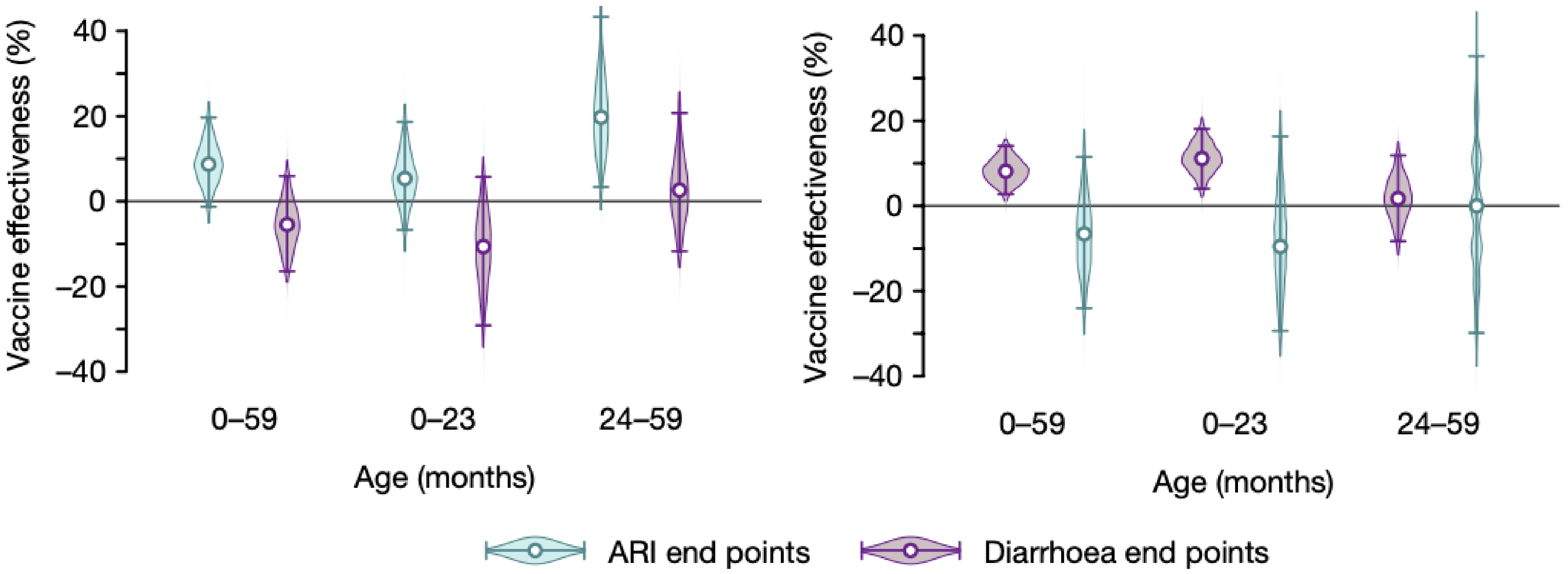
OECD 2018

Taking action amid competing priorities

- Little knowledge of the specific impact achievable through each intervention that has been recommended
  - Strength of evidence that the measure is effective?
  - Does that evidence connect the intervention to the actual outcome or just describe intermediate steps along the causal chain?
  - Magnitude of impact—how many deaths (etc.) preventable, if deployed?
  - Feasibility of implementation ***in all settings***?

- Interventions come at a cost: doing one thing means not doing something else
- Each of these must be known specifically to guide concrete action

Direct effects of PCV and rotavirus vaccines



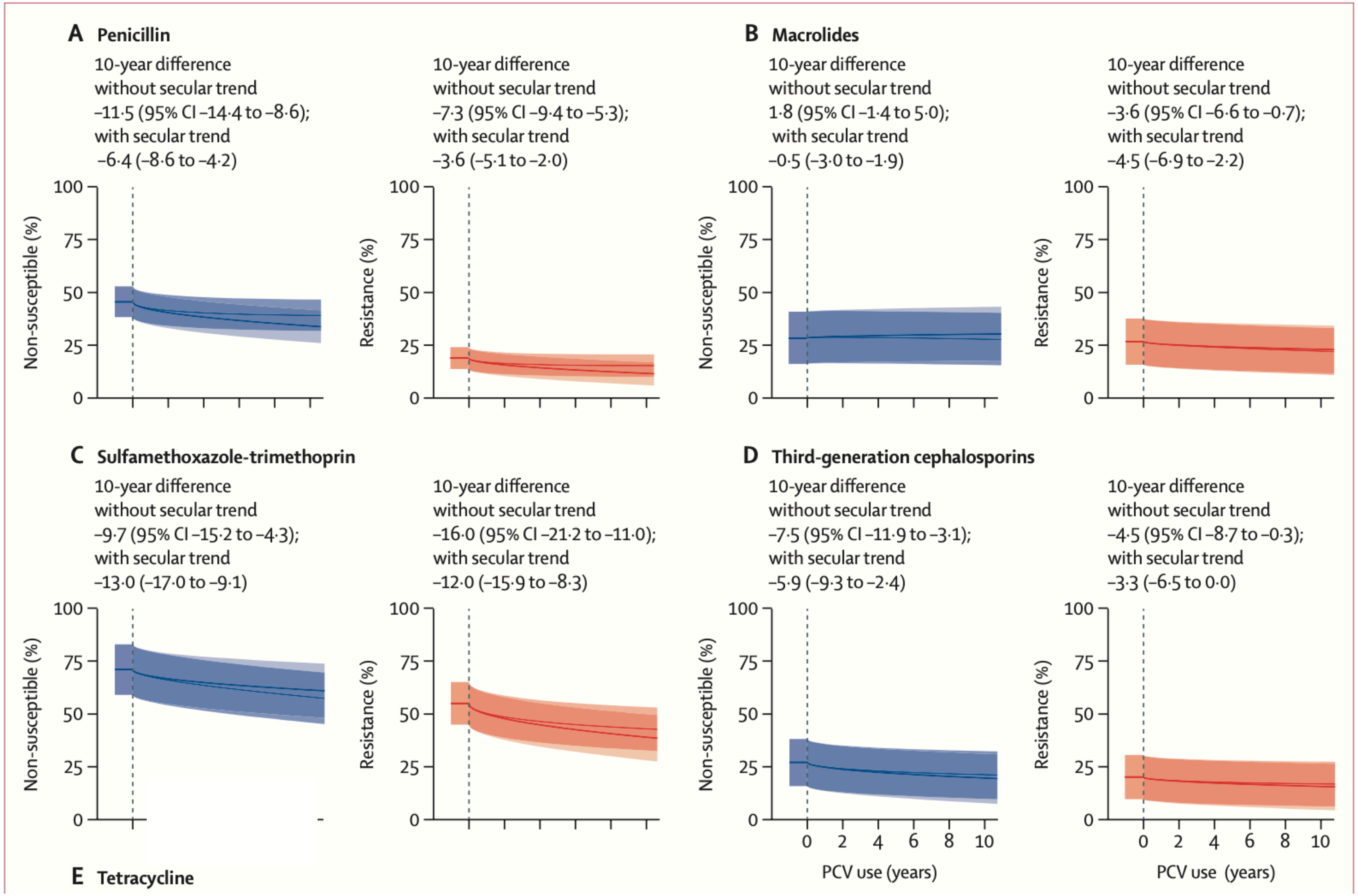
PCV effectiveness vs. antibiotic-treated disease episodes

Rotavirus vaccine effectiveness vs. antibiotic-treated disease episodes

1:3 matched case control study (country, age, sex season, wealth quintile, urbanicity, health access/utilization (receipt of pentavalent vaccine doses)

Lewnard et al., *Nature* 2020

Implications for resistance (pneumococci)



- Implementation of PCVs reduced prevalence of resistance/non-susceptibility among circulating pneumococci globally

Andrejko et al. *Lancet Microbe* 2021

RSV vaccine efficacy against antibiotic use

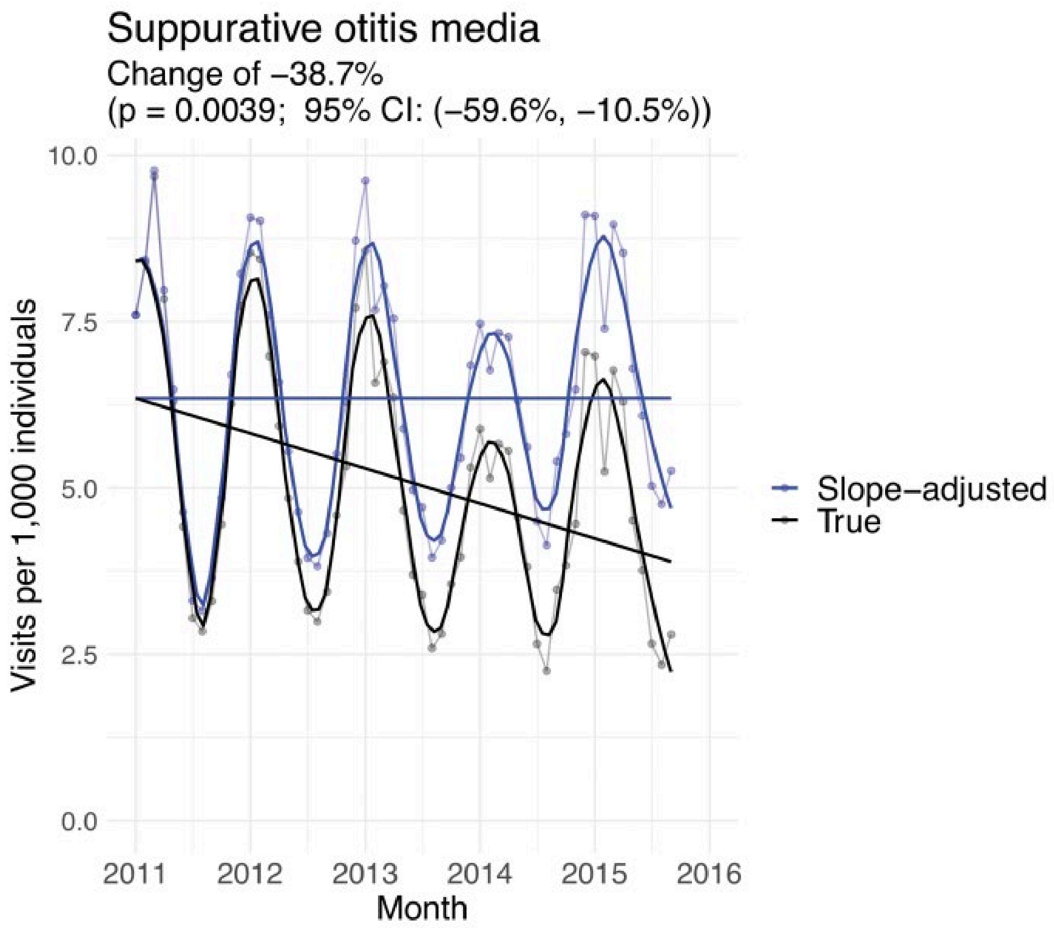
Table 2. VE against antimicrobial prescriptions among infants within the ITT population

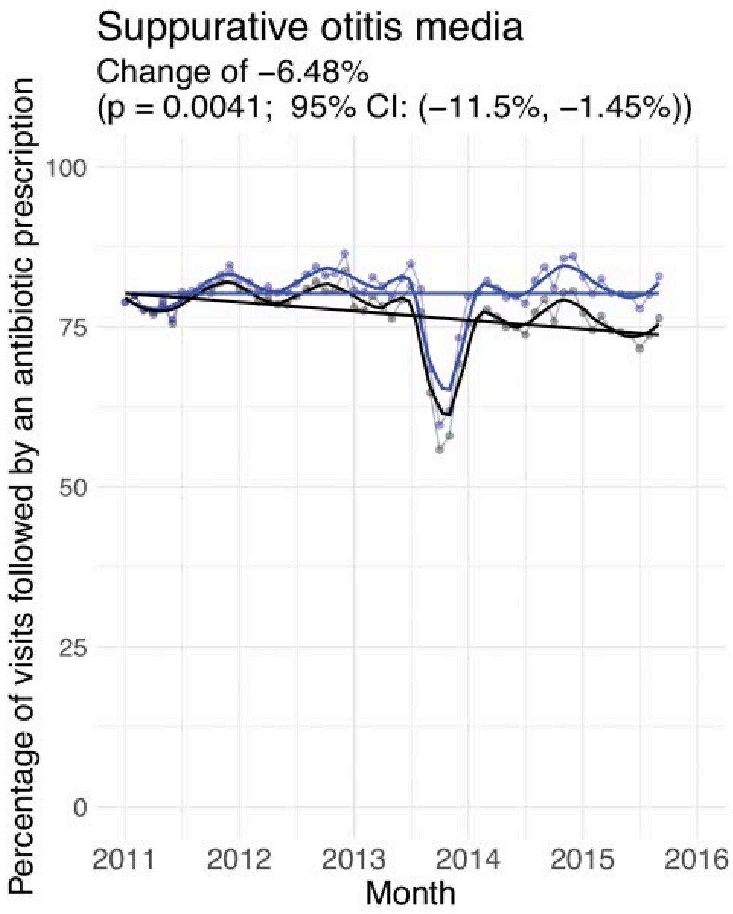
Setting and end point	Through 90 d from birth: RSV F vaccine, no. of events per 100 person-y (no. of events)	Through 90 d from birth: Placebo, no. of events per 100 person-y (no. of events)	Through 90 d from birth: VE (95% CI), %	Through end of follow-up: RSV F vaccine, no. of events per 100 person-y (no. of events)	Through end of follow-up: Placebo, no. of events per 100 person-y (no. of events)	Through end of follow-up: VE (95% CI), %
All countries, person-y	730	379		2,908	1,504	
All antimicrobial prescriptions	133.7 (976)	148.7 (563)	12.9 (1.3–23.1)	111.2 (3,234)	112.8 (1,696)	3.4 (−4.8–11.1)
All antimicrobial prescriptions for LRTI*	71.0 (518)	82.2 (311)	16.6 (1.4–29.4)	61.8 (1,797)	62.4 (939)	3.3 (−7.6–13.1)
HICs	242	132		953	516	
All antimicrobial prescriptions	55.8 (135)	72.2 (95)	20.2 (−10.1–42.2)	62.8 (599)	66.1 (341)	5.2 (−14.2–21.3)
All antimicrobial prescriptions for LRTI*	10.3 (25)	20.5 (27)	49.4 (3.5–73.5)	10.4 (99)	12.6 (65)	13.2 (−30.6–42.4)
LMICs	488	247		1,955	988	
All antimicrobial prescriptions	172.3 (841)	189.5 (468)	10.9 (−2.1–22.2)	134.8 (2,635)	137.1 (1,355)	2.8 (−6.5–11.3)
All antimicrobial prescriptions for LRTI*	101.0 (493)	115.0 (284)	12.8 (−3.6–26.7)	86.9 (1,698)	88.5 (874)	2.2 (−9.2–12.5)

Novavax fusion protein RSV vaccine in mothers prevented substantial proportion of antibiotic use in first 3 months of life in US and South Africa (among other countries). **Promising sign for higher-efficacy licensed vaccines.**

Lewnard et al., *PNAS* 2022

The importance of preventing infections

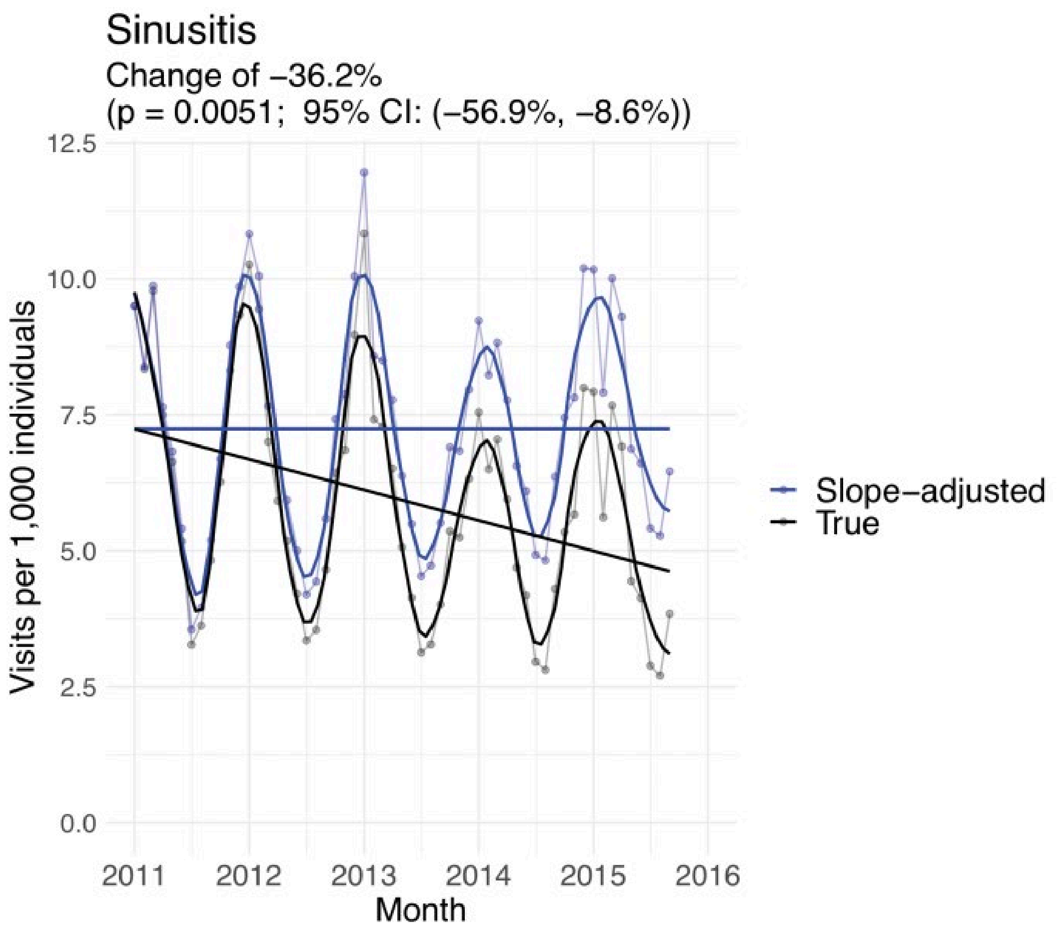


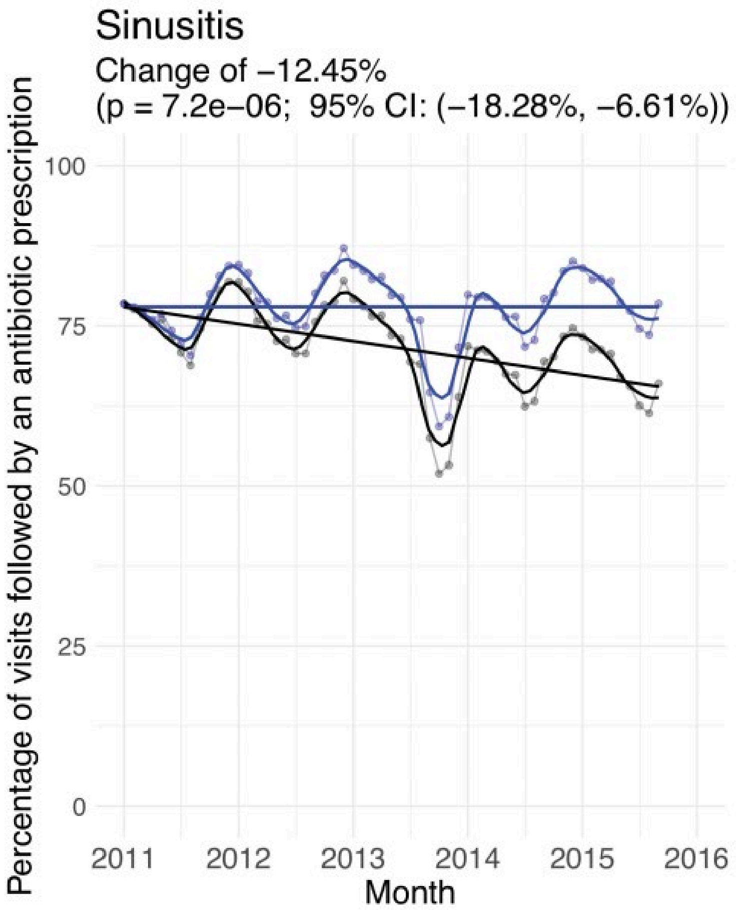


Although stewardship has been prioritized, greater share of recent reductions in antibiotic use is attributable to reduced incidence of infections rather than changes in prescribing

Kissler.& Grad, *Clin Infect Dis* 2021

The importance of preventing infections





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WASH interventions

	Improved source, not on premises	Improved source, on premises	Improved source, on premises, higher water quality*	Improved source, on premises, continuous supply†	POU chlorination	POU solar treatment	POU filtration
Unimproved							
RR (95% CI)	0·81 (0·70–0·94)	0·79 (0·60–1·03)	0·48 (0·26–0·87)	0·73 (0·37–1·44)	0·66 (0·56–0·77)	0·63 (0·50–0·80)	0·50 (0·41–0·60)
p value	0·0060	0·076	0·017	0·36	<0·0001	0·0002	<0·0001
Improved, not on premises							
RR (95% CI)	..	0·97 (0·75–1·25)	0·59 (0·32–1·07)	0·90 (0·46–1·77)	0·81 (0·68–0·95)	0·78 (0·63–0·96)	0·61 (0·49–0·75)
p value	..	0·79	0·081	0·75	0·012	0·023	<0·0001
Improved, on premises							
RR (95% CI)	..	..	0·61 (0·35–1·05)	0·93 (0·50–1·74)	..	..	..
p value	..	..	0·072	0·82	..	..	..

Results are adjusted for combined intervention (RR 0·89 [95% CI 0·74–1·08]). POU=point-of-use. RR=relative risk. *Based on two studies.[24,34] †Based on one study.[35]

Table 1: **Results of the meta-regression model for water supply interventions**

Recent evidence of the effectiveness of prevailing WASH interventions has been mixed (e.g., WASH Benefits Trials in Bangladesh & Kenya), underscoring the need for higher-quality interventions

However, large effect sizes of (successful) WASH interventions in preventing diarrhea, respiratory tract infections, and other acute antibiotic-treated conditions suggest possibility for reducing antibiotic use

Wolf et al., *Lancet* 2022

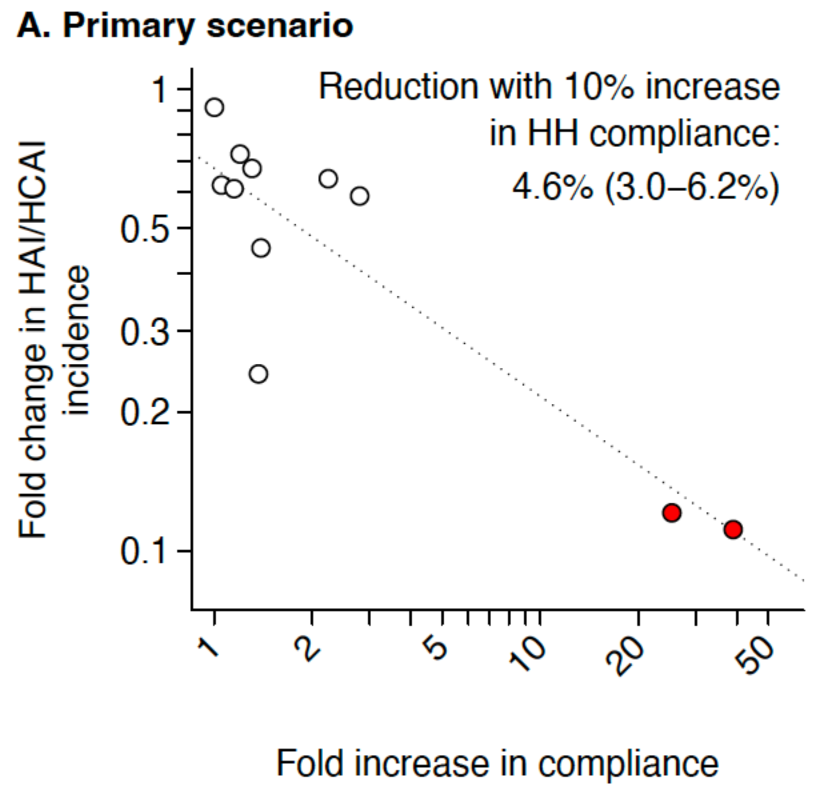
Wolf et al., *Lancet* 2023

	Prevalence of WASH minimum risk exposure counterfactual in 2019*	Association between WASH counterfactual and outcome (against lowest level of exposure)
Diarrhoea		
Safely managed drinking water	37·9% (27·1–49·9)	0·48 (0·26–0·87), p=0·017[4]
Basic sanitation connected to sewer	29·7% (23·9–36·1)	0·53 (0·30–0·93), p=0·030[4]
Handwashing with soap after potential faecal contact	26·4% (23·4–29·6)	0·7 (0·64–0·76), p<0·0001[4]
Acute respiratory infections		
Handwashing with soap after potential faecal contact	26·4% (23·4–29·6)	0·83 (0·76–0·90), p<0·0001[7]

Data are prevalence (95% CI) or relative risk (95% CI), p value. WASH=drinking water, sanitation, and hygiene. *Aggregated across included countries.

Table 1: **Counterfactual and outcome association for diarrhoea and acute respiratory infections**

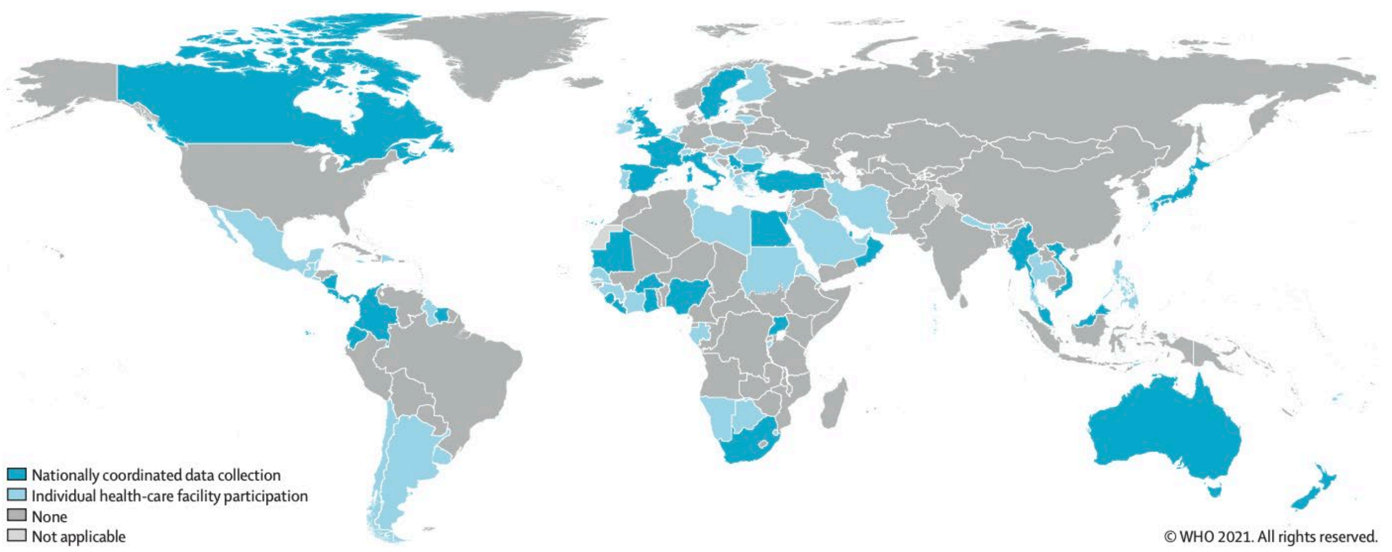
Improving IPC relative to current levels



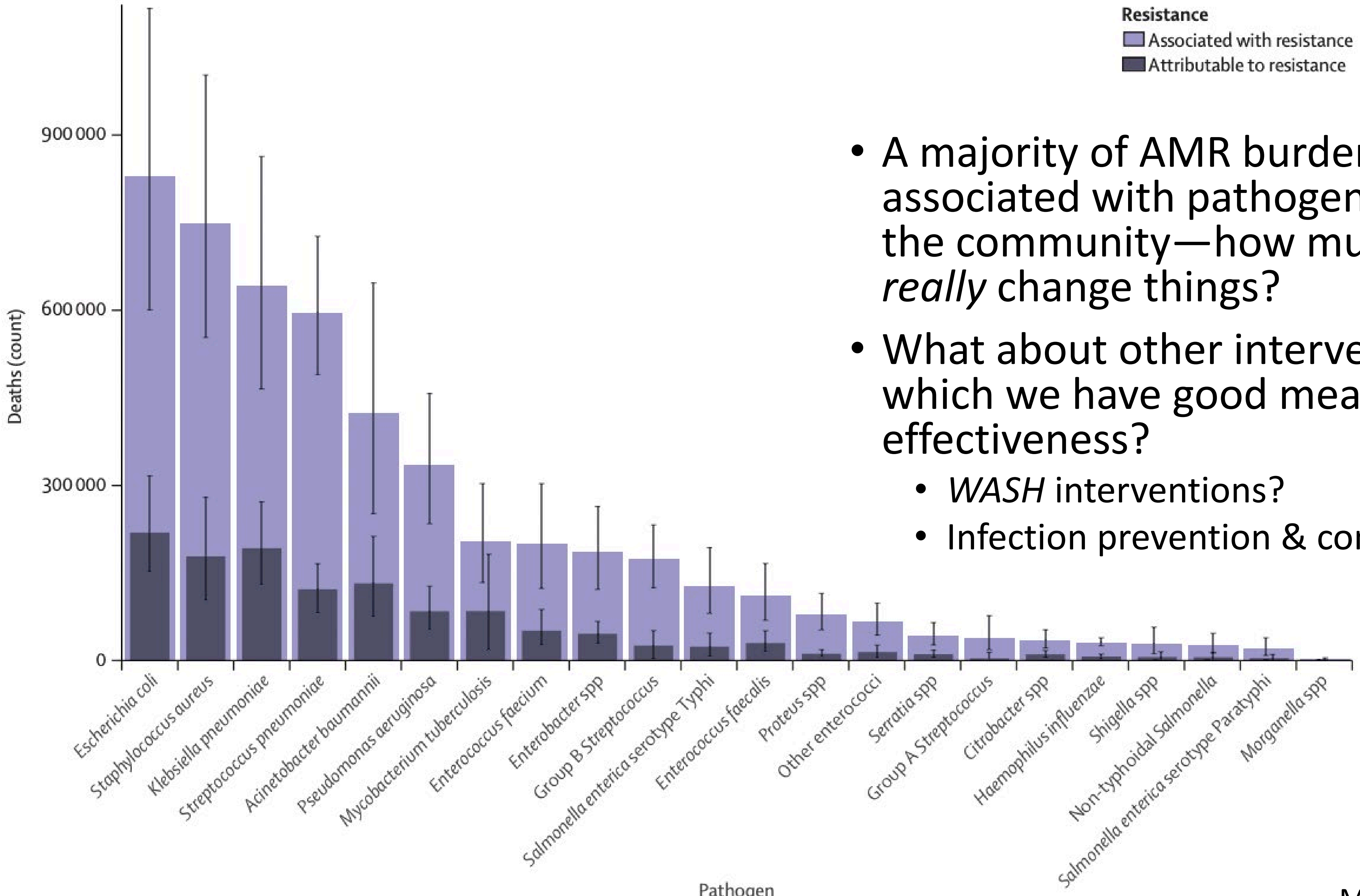
Meta-analysis: change in HAI/HCAI incidence with bundled IPC interventions in LMIC settings (Lewnard et al., *forthcoming*)

Implementation of hand hygiene in health-care facilities: results from the WHO Hand Hygiene Self-Assessment Framework global survey 2019

Marlieke E A de Kraker*, Ermira Tartari*, Sara Tomczyk, Anthony Twyman, Laurent C Francioli, Alessandro Cassini, Benedetta Allegranzi, Didier Pittet



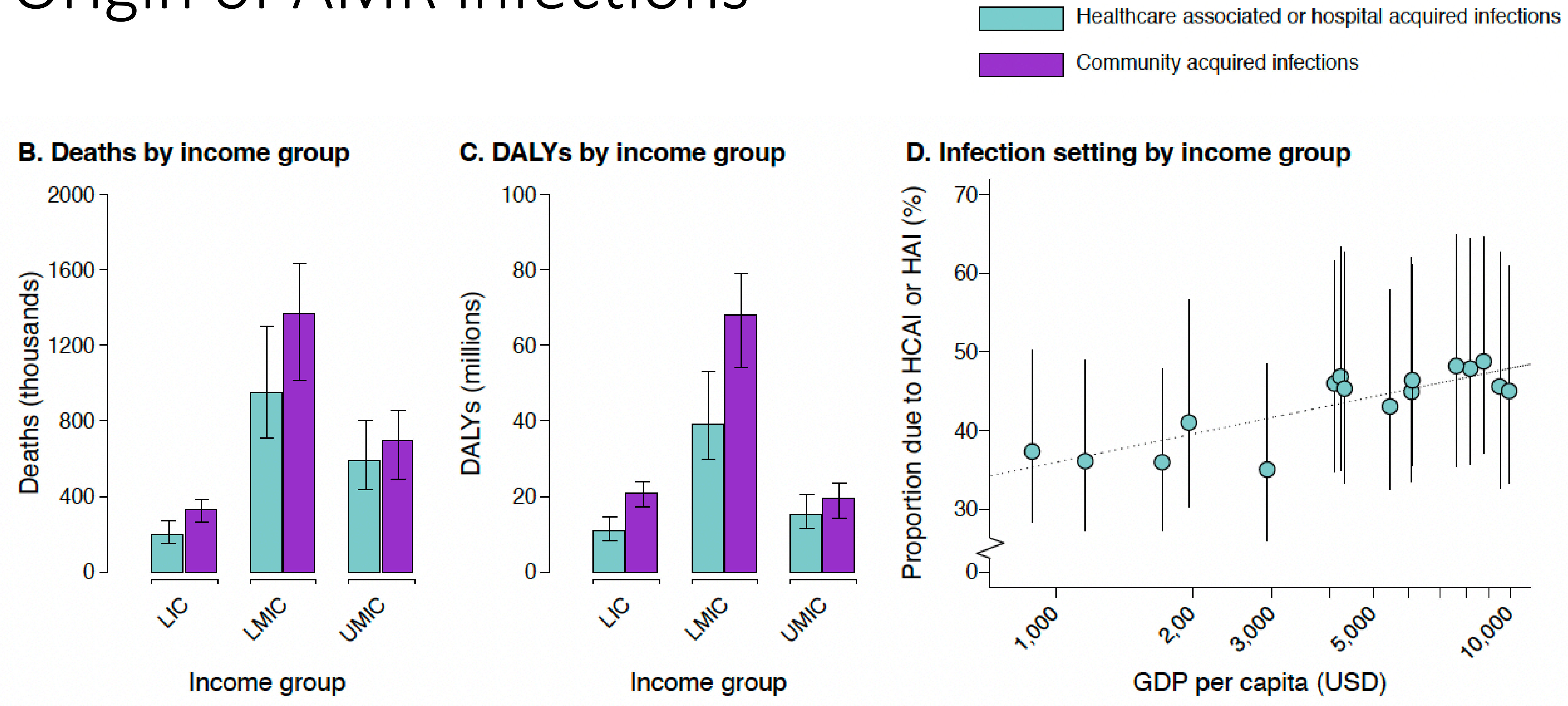
Lancet Infect Dis 2022



- A majority of AMR burden is not associated with pathogens acquired in the community—how much will vaccines *really* change things?
- What about other interventions for which we have good measures of effectiveness?
  - *WASH* interventions?
  - Infection prevention & control?

Murray et al., *Lancet* 2022

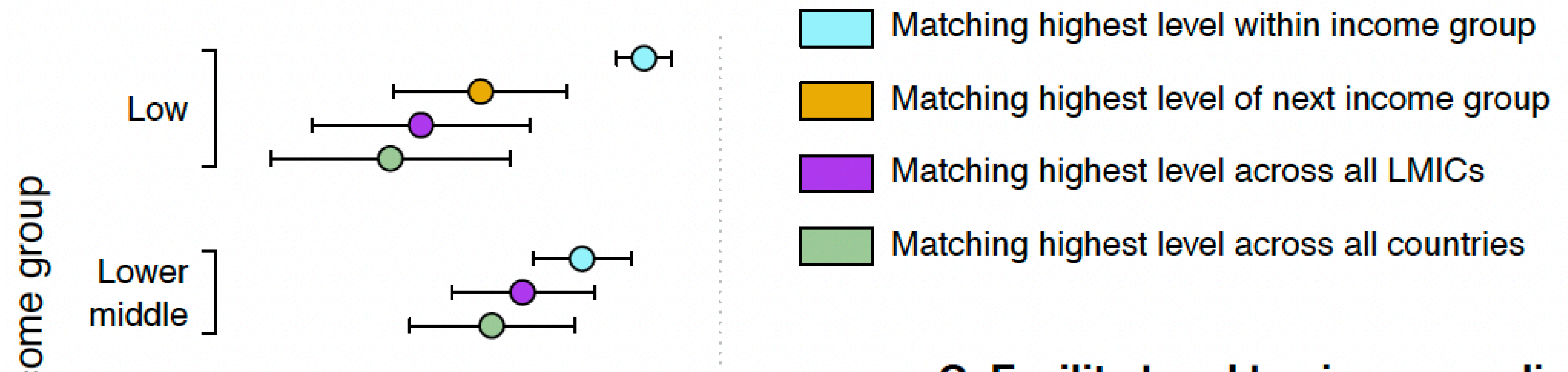
Origin of AMR infections



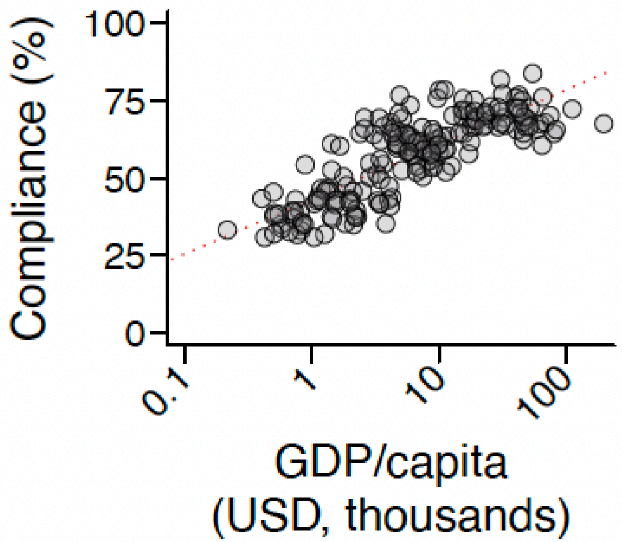
Murray et al., *Lancet* 2022

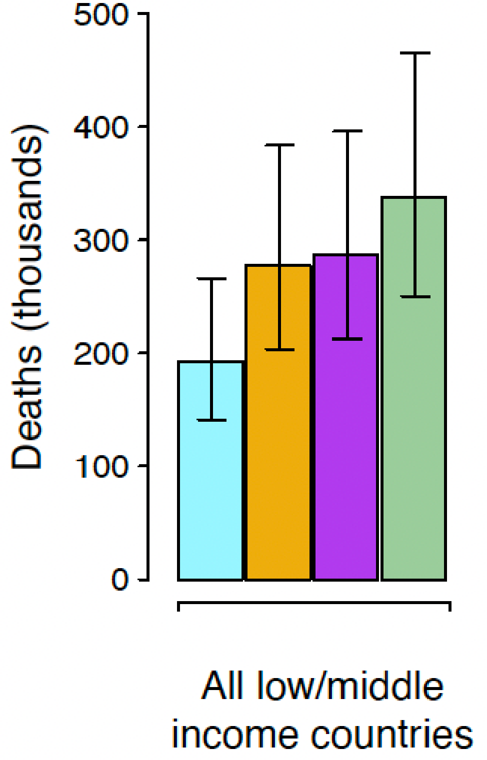
Improving IPC relative to current levels

B. Modifiable risk of HAI/HCAI, by intervention target and country income group



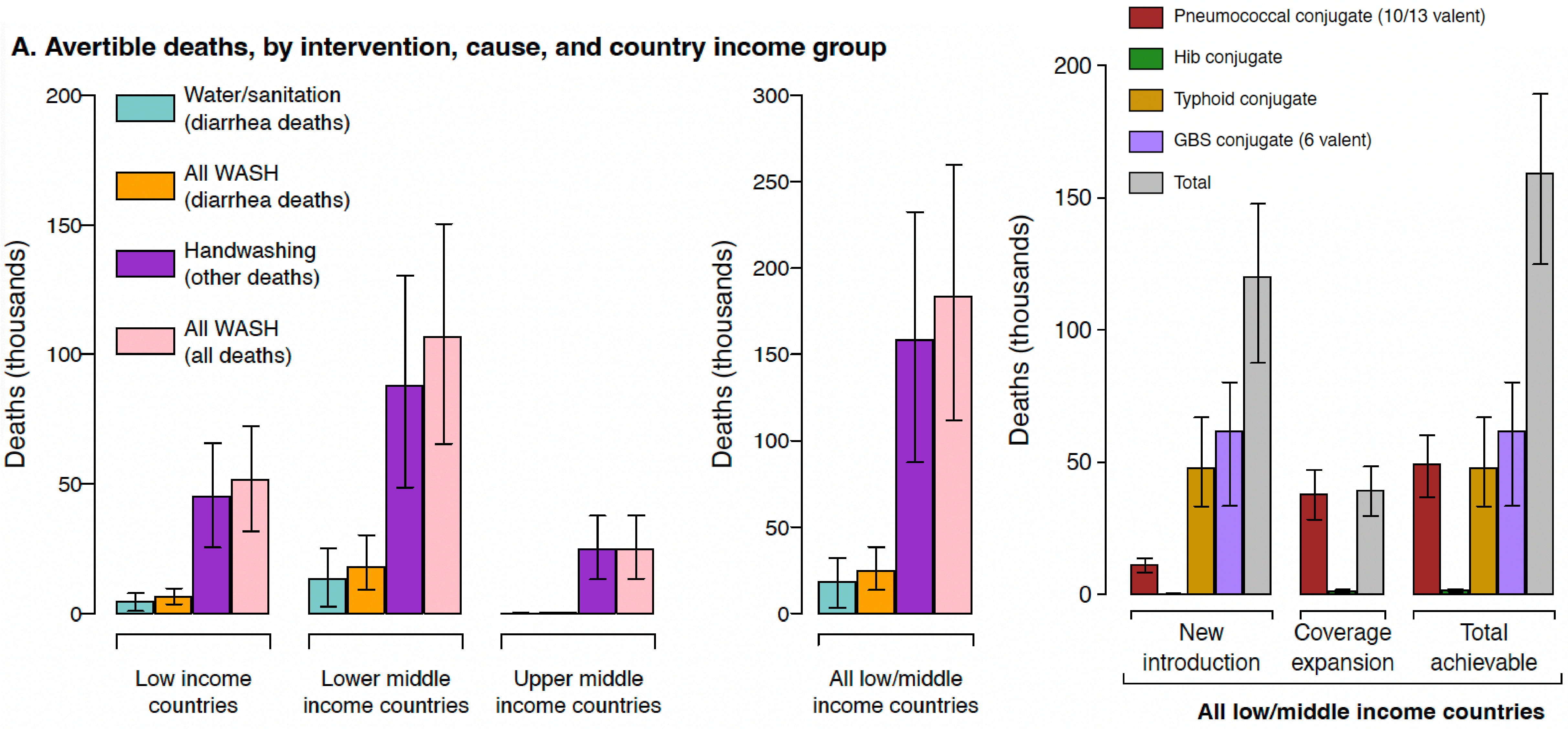
C. Facility hand hygiene compliance





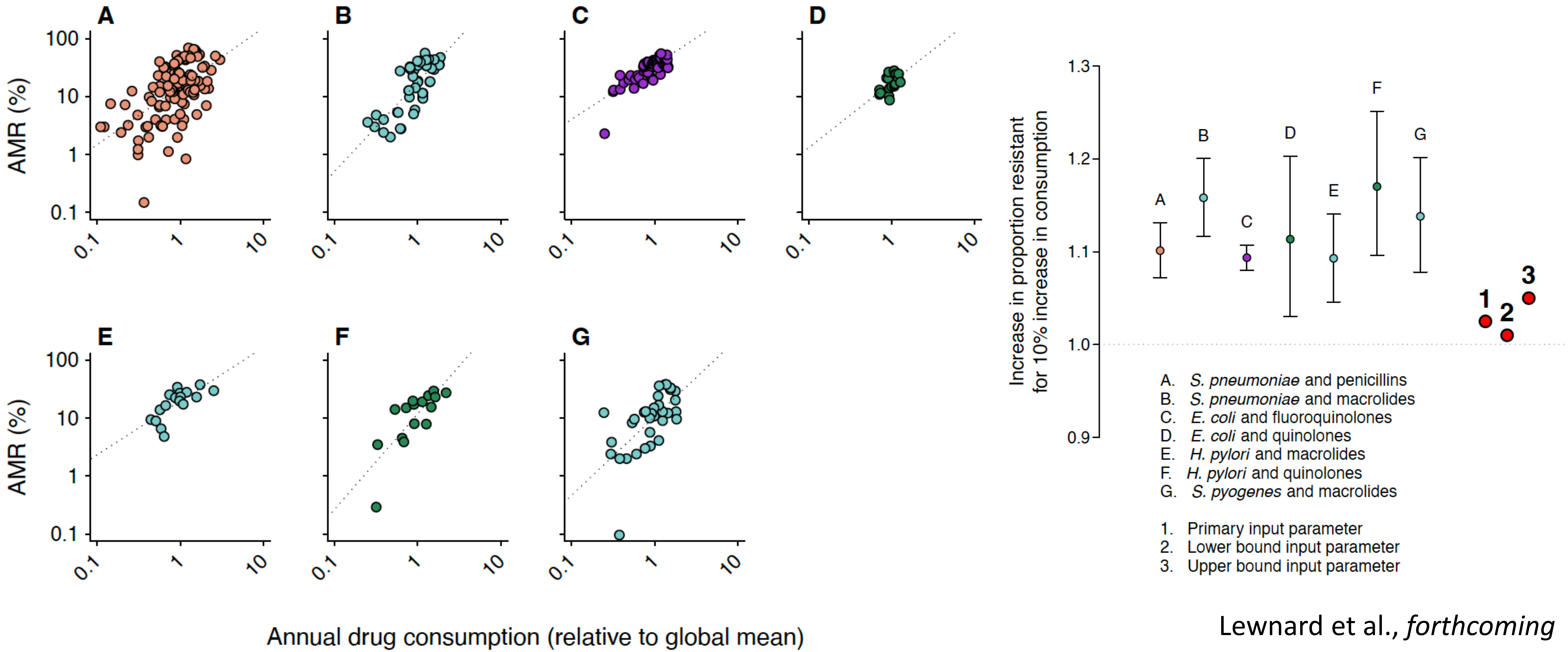
Lewnard et al., *forthcoming*

WASH and vaccines: "direct" prevention



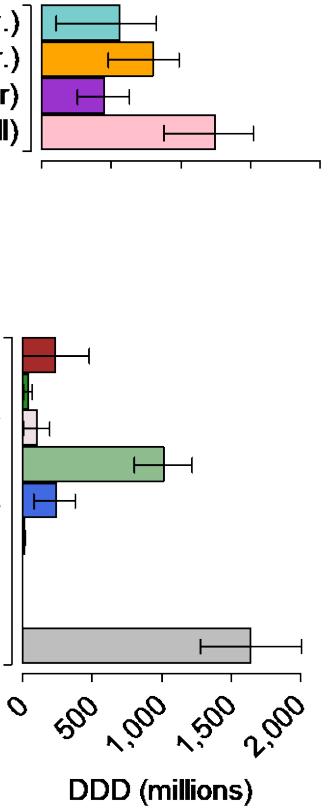
Lewnard et al., *forthcoming*

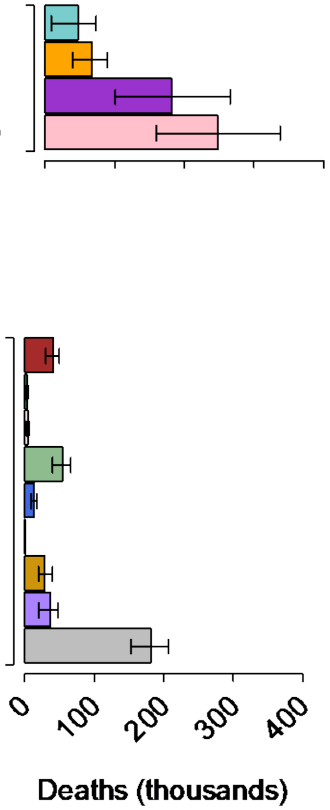
WASH and vaccines: reducing antibiotic use and direct prevention of infections



Lewnard et al., *forthcoming*

WASH and vaccines: accounting for antibiotic use





	DDD averted by intervention: Total (millions)	DDD averted by intervention: Prop. (<5y, %)	Deaths averted by intervention: Total (thousands)	Deaths averted by intervention: Prop. (%)	DALYs averted by intervention (thousands)
WASH interventions					
Water/sanitation (diar.)	562.6 (105.0–823.2)	5.2 (1.0–7.6)	47.7 (9.0–73.3)	1.1 (0.2–1.7)	2,738 (528–4,166)
All WASH (diar.)	799.8 (478.8–985.3)	7.4 (4.4–9.1)	66.8 (39.3–89.1)	1.5 (0.9–2.1)	3,799 (2,247–4,981)
Handwashing (other)	451.7 (258.5–631.2)	4.2 (2.4–5.8)	181.7 (100.9–265.9)	4.2 (2.3–6.3)	9,651 (5,461–13,993)
All WASH (all)	1243.2 (875.2–1518.4)	11.5 (8.1–14.0)	247.8 (160.0–337.8)	5.7 (3.7–8.0)	13,403 (8,867–17,967)
Total achievable					
Pneumococcal conjugate	233.2 (0.0–479.8)	2.2 (0.0–4.4)	40.4 (30.6–49.9)	0.9 (0.7–1.2)	3,024 (2,353–3,685)
Hib conjugate	38.5 (10.4–66.9)	0.4 (0.1–0.6)	3.3 (2.4–4.2)	0.1 (0.1–0.1)	180 (135–226)
RSV	104.5 (7.0–195.0)	1.0 (0.1–1.8)	4.6 (2.7–6.4)	0.1 (0.1–0.2)	209 (126–293)
Seasonal influenza	1014.7 (803.3–1219.7)	9.4 (7.4–11.3)	54.6 (39.7–66.0)	1.3 (0.9–1.6)	2,494 (1,947–2,948)
Oral rotavirus	239.0 (81.8–377.1)	2.2 (0.8–3.5)	13.2 (9.1–17.2)	0.3 (0.2–0.4)	563 (402–719)
RTS,S	14.9 (7.9–19.8)	0.1 (0.1–0.2)	0.8 (0.6–1.0)	– –	55 (41–68)
Typhoid conjugate	– –	– –	28.7 (20.0–40.1)	0.7 (0.4–1.0)	2,146 (1,454–3,051)
GBS conjugate	– –	– –	37.0 (20.0–48.1)	0.9 (0.5–1.2)	3,309 (1,776–4,297)
Total	1637.1 (1279.5–2004.8)	15.1 (11.8–18.5)	181.5 (153.4–206.8)	4.2 (3.4–5.1)	11,924 (10,010–13,623)

Lewnard et al., *forthcoming*

Thank you

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