Assessing the Global Risk of Typhoid Outbreaks Caused by XDR Salmonella Typhi

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Extensively Drug-Resistant (XDR) Typhoid Fever

- Ongoing outbreak in Pakistan since 2016
  - First identified in Karachi, Sindh region
  - Now common nationwide

- XDR = MDR + fluoroquinolone and cephalosporin resistance

- Few remaining treatment options
  - Oral: azithromycin
  - Intravenous: carbapenems
Travel-Associated XDR Cases Have Been Detected Worldwide

- 16 countries + Pakistan with confirmed XDR typhoid cases

*Traveler from India to UK (see Nair 2021)
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Which Countries are at Highest Risk for XDR Typhoid Outbreaks Going Forward?
XDR Introduction Associated with Air Travel from Pakistan

- XDR-detecting countries are among the most popular destinations for outgoing travel from Pakistan
  - 7 of the top 10 destinations have detected XDR cases

- Median Air Travelers from Pakistan (2019):
  - XDR Detected: ~85,000
  - XDR Not Detected: ~250

*Air Travel Data courtesy of the International Air Travel Association (IATA)
A Few Countries and Regions Account for Most of the International Air Travel from Pakistan

- ~3/4 trips bound for 5 countries: Saudi Arabia, UAE, Oman, UK, and US
- ~2/3 of trips bound for the Middle East, mostly Arab Gulf states
- Relatively little air travel from Pakistan to South Asia, Sub-Saharan Africa, and Latin America

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Overlapping Risk: Countries with Significant Typhoid Transmission and Travel from Pakistan

X-axis: Air Travel from Pakistan
- IATA data (2019)
- Proxy for risk of introduction

Y-axis: Typhoid Burden
- Median of IHME, Antillon et al., and Kim et al. model output
- Proxy for risk of onward transmission if XDR is introduced

- 10 high-burden countries receiving the most travelers from Pakistan:
  - 4 in South Asia
  - 4 in Southeast Asia
  - 2 in Africa
Conclusions

- Travel-associated XDR typhoid detected in 16 countries
  - Possibility of undetected introduction/transmission in additional countries

- Countries with strong travel connections to Pakistan are more likely to have imported XDR typhoid

- Identified a number of countries with efficient typhoid transmission and a relatively high volume of incoming travel from Pakistan
  - Highest risk of XDR outbreaks and sustained transmission
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