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# Impact of TCV Introduction on Ileal Perforations in Pakistan: A Time Series (2016 – 2023)

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# Introduction

- Typhoid fever is a major health concern in Pakistan
- Typhoid-related ileal perforations are more prevalent in low-middle income countries and occur in 0.8%–39% of cases (*Qazi et al., 2020*)
- Pakistan introduced Typhoid Conjugate Vaccine in 2019
  - Mass campaign in November 2019
  - Routine immunization introduced in Sindh in 2019/2020
  - Routine immunization introduced in Punjab in 2021

# Rationale



- Current gap in knowledge
  - No existing assessments on the impact of TCV on typhoid-related ileal perforations
- Understanding burden
  - Lack of data on the burden of ileal perforations specifically linked to typhoid
  - Understanding how TCV influences the occurrence, burden, consequences, and surgical outcomes of typhoid-related ileal perforations



# Methods

- Pre-TCV data obtained from SEAP (Surveillance of Enteric Fever in Asia Project)
- Post-TCV data obtained from ITRIPP (Impact assessment of the Typhoid conjugate vaccine following introduction in the Routine Immunization Program of Pakistan)



# Methods

	<b>SEAP</b>	<b>ITRIPP</b>
<b>Study design</b>	Surveillance	Surveillance
<b>Duration</b>	Sept 2016 – Sept 2019	Mar 2022 – Sept 2023
<b>Sentinel Centers (Sind)</b>	<ul style="list-style-type: none"><li>• AKUH</li><li>• NICH (Children’s Hospital)</li><li>• JPMC (Feb 2018)</li><li>• KGH</li></ul>	<ul style="list-style-type: none"><li>• AKUH</li><li>• NICH (Children’s Hospital)</li><li>• JPMC</li></ul>
<b>Surveillance setting</b>	6 days a week	6 days a week
<b>Eligibility criteria</b>	<ul style="list-style-type: none"><li>• Hospitalized cases with a diagnosis of non-traumatic ileal perforation due to suspected typhoid.</li><li>• Ileal perforation due to tuberculosis and malignancy excluded.</li></ul>	



# Data Collection

- Data collection - eCRF
  - Structured questionnaires
  - Clinical information from medical records
  - Laboratory testing - IDRL at AKU
    - Histopathology, blood culture
- Outcomes documented at 6-week follow-up through phone calls in SEAP



# Sociodemographic Characteristics

<b>Sociodemographic variables</b>	<b>SEAP N=242 (%)</b>	<b>ITRIPP N=389 (%)</b>
<b>Age (in years)</b>		
≤ 15	115 (48)	96 (25)
> 15	127 (52)	293 (75)
<b>Gender</b>		
Male	180 (75)	317 (81)
Female	62 (25)	72 (19)
<b>Sentinel Centers</b>		
Aga Khan University Hospital	20 (8)	7 (2)
Kharadar General Hospital	1 (0)	-
National Institute of Child Health	103 (43)	76 (20)
Jinnah Post-graduate Medical Centre	118 (49)	306 (78)
<b>Area of residence</b>		
Rural	49 (20)	87 (22)
Urban	185 (76)	301 (77)

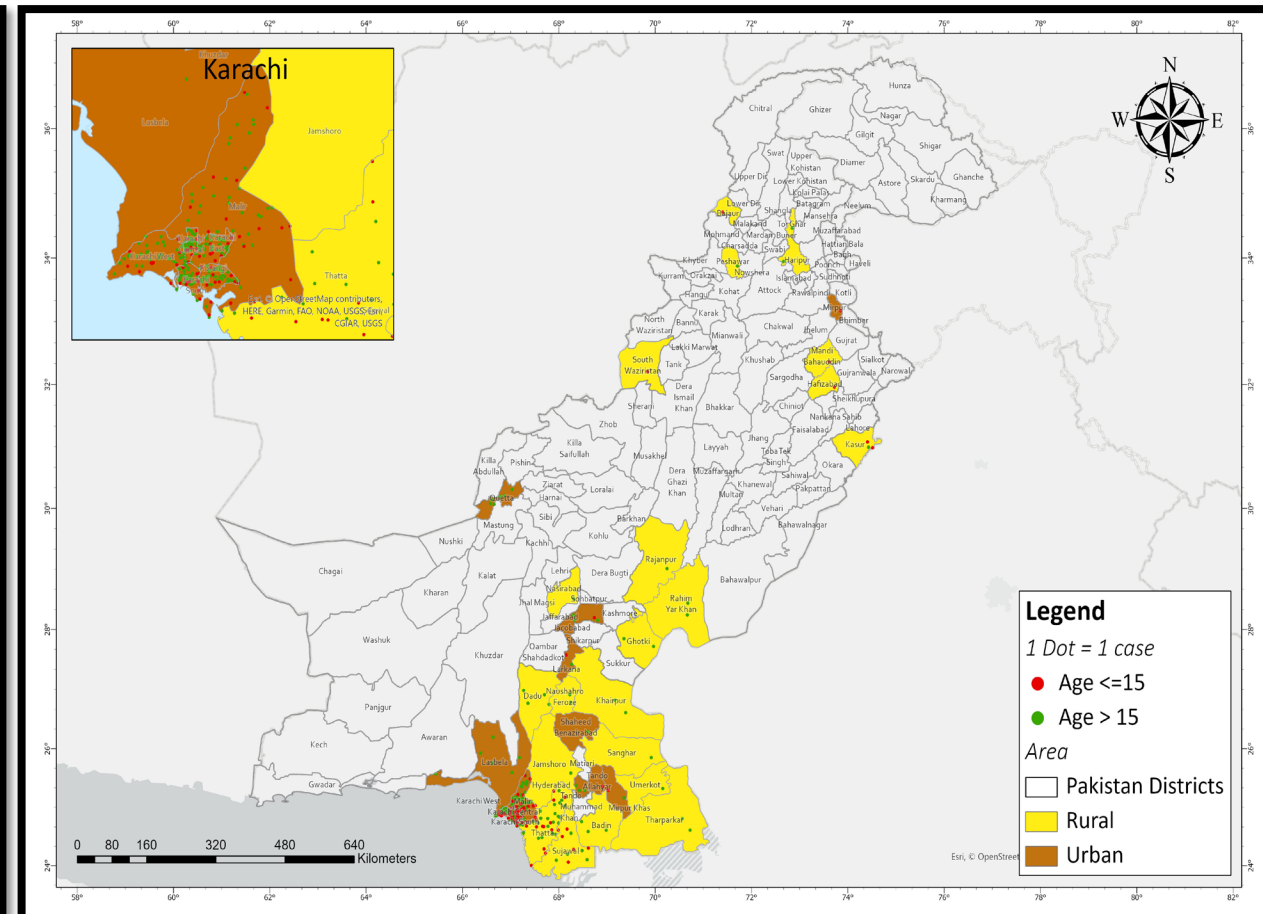
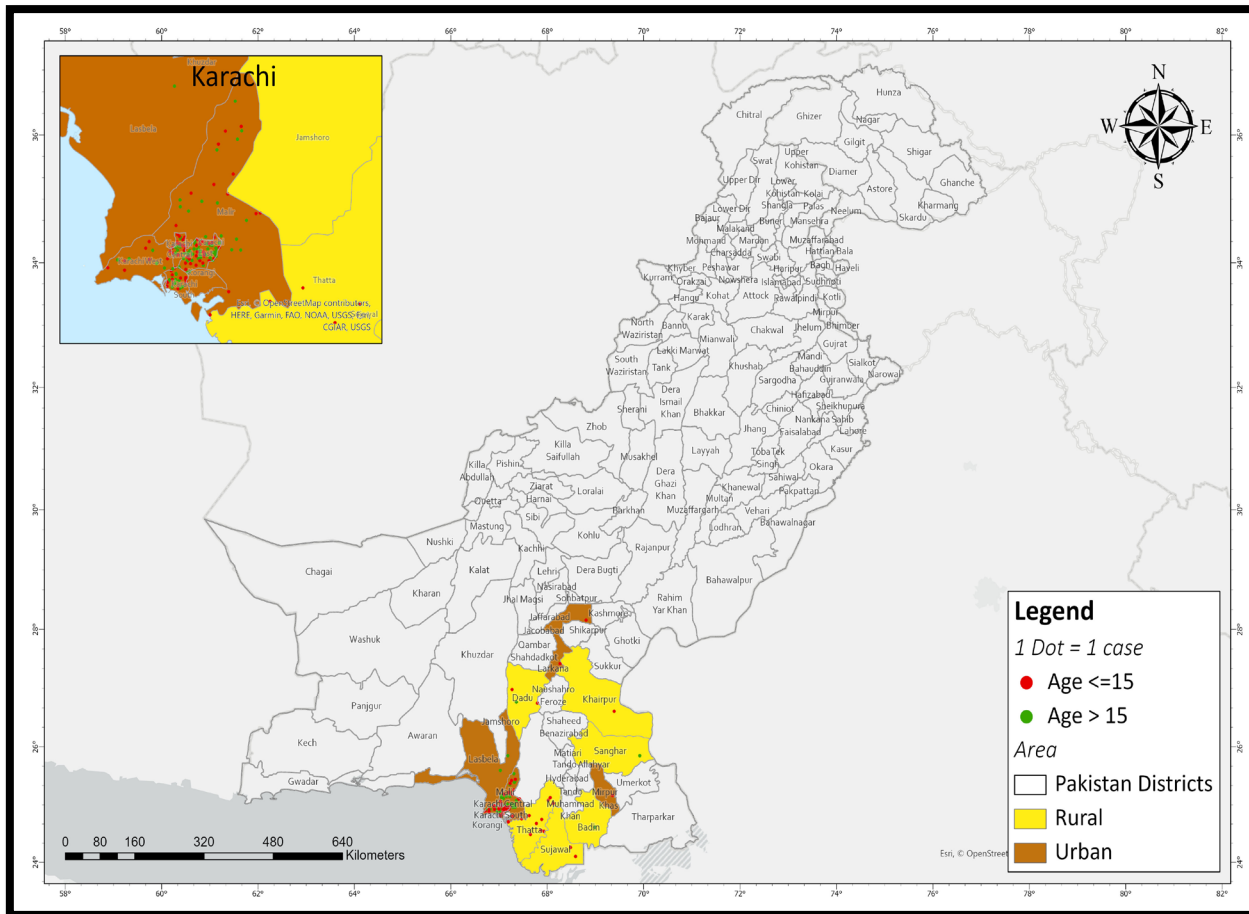


# Geospatial Distribution

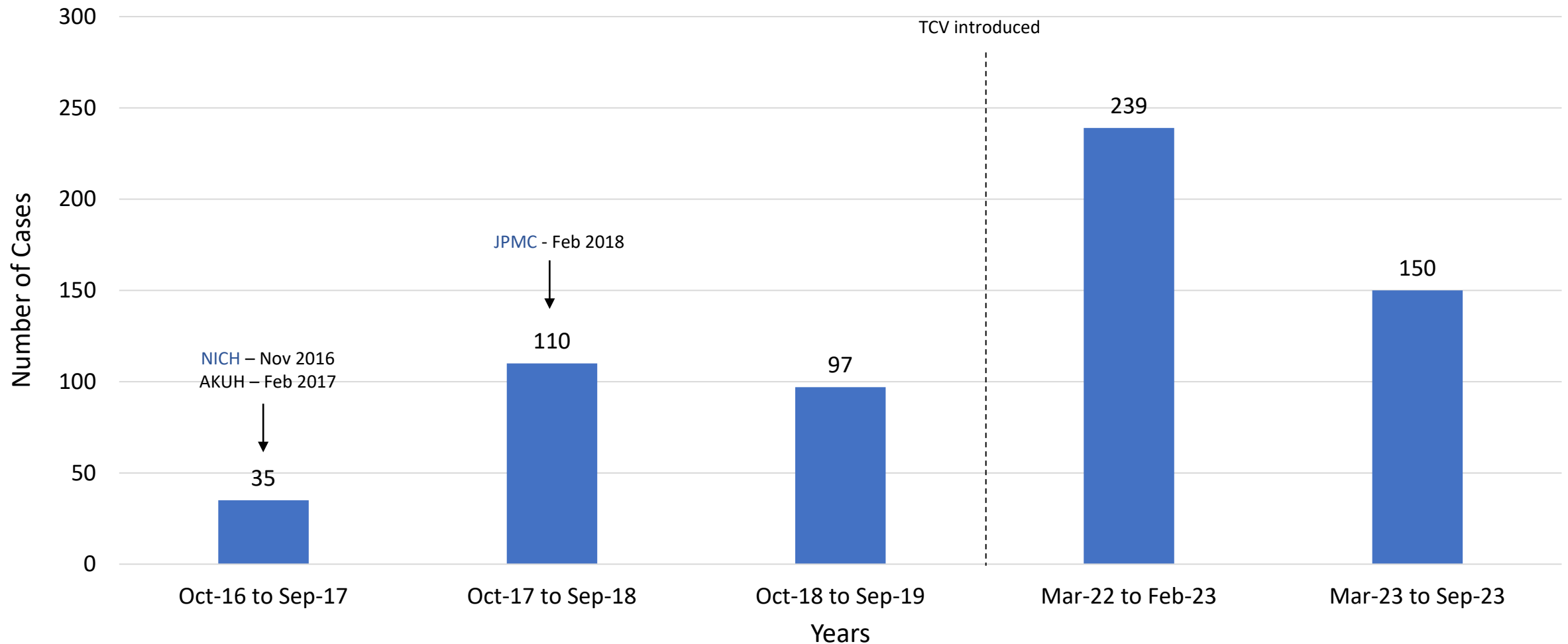


Pre-TCV (SEAP)

Post-TCV (ITRIPP)



# Yearly Status of Typhoid Ileal Perforation (2016 to 2023)



# Clinical Characteristics



<b>Clinical Characteristics</b>	<b>SEAP N=242 (%)</b>	<b>ITRIPP N=389(%)</b>
<b>Blood culture (samples collected)</b>	n=149 (62)	n=354 (91)
Positive for S. Typhi	7 (3)	27 (7)
MDR	0 (0)	7 (2)
XDR	6 (2)	13 (3)
Fluoroquinolone resistance	7 (3)	18 (5)
<b>Histopathology (samples collected)</b>	n=87 (36)	n=300 (77)
Ileal perforation with necrosis indicating TIPS	4 (5)	285 (73)
<b>Duration of hospitalization, Median (days)</b>	8	10
<b>Outcome</b>		
Death	16 (7)	53 (14)
Recovered	226 (93)	336 (86)



# Strengths and limitations

- Strengths:
  - The largest case data on TIPS with documented outcomes.
  - Availability of data pre and post TCV introduction
- Limitations:
  - Variation in surveillance across sites in SEAP and ITRIPP.
  - A limited number of laboratory samples were collected in SEAP
  - Post-discharge outcomes not documented in ITRIPP.
    - Most mortality documented in SEAP was at 6 weeks follow up.



# Key findings

- Ileal perforation rates are high in Pakistan
- High rates of ileal perforation in males greater than 15 years of age
- High referral rates from rural areas to urban centers
- High mortality rates following ileal perforation



# Way forward

- Strengthen routine immunization
- Making vaccine available for adults
  - TCV availability in the private market



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GATES  
*foundation*



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