Use of antibiotics for cholera chemoprevention: Example of Rann, Nigeria

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Médecins Sans Frontières / Epicentre

GTFCC Case management meeting, 2019

GLOBAL TASK FORCE ON
CHOLERA CONTROL

Technical Note
Use of antibiotics for the treatment and control of cholera
May 2018

6. Mass chemoprophylaxis is not recommended. There is currently insufficient evidence to evaluate the effectiveness of selective chemoprophylaxis (household contacts, enclosed communities). It is recommended that any use should be within the context of a prospective study specifically designed to measure effectiveness of antibiotic prophylaxis and development of antibiotic resistance in household contacts (i.e., sharing a meal) of a suspect cholera patient, as well as any impact of such strategy on outbreak evolution.

Key questions

- Rationale for household prophylaxis – household contacts at higher risk?

- Antibiotic use
  - Role of antibiotics in cholera
  - Effectiveness against cholera of household propyhlaxis at individual level
  - Impact on the epidemic?
  - Risk of antimicrobial resistance

- Feasibility during outbreak control interventions

Key questions: rationale for HH prophylaxis

Are household contacts at higher risk? Yes:

- Having HH contact with cholera – OR 2.9 (1.6-5.2) (1)
- Living within 50 m of the index case: RR 36 (95% CI: 23–56) within 3 days of the index case presenting to the hospital (2)
- Relative risk of next cholera case within 40 m distance to another case within days 0-4 (3):
  - Ndjamena: RR 32.4 (95% 25-41)
  - Kalemie: RR 121 (95% CI 90-165)

1) Richterman et al. Individual and Household Risk Factors for Symptomatic Cholera Infection: A Systematic Review and Meta-analysis. JID 2018
2) Debes et al. Cholera cases cluster in time and space in Matlab, Bangladesh: implications for targeted preventive interventions. Int J Epid 2016
3) Azman et al. Micro-hotspots of risk in urban cholera epidemics. JID 2018
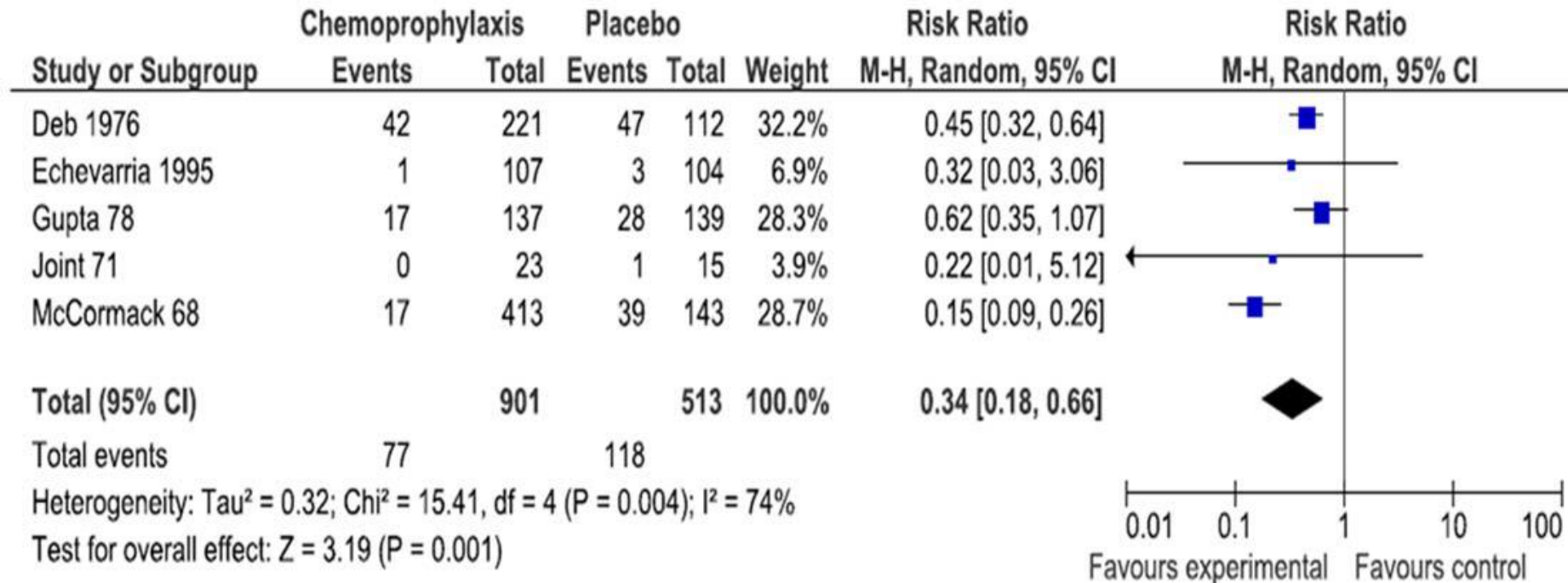
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Key questions: antibiotic use?

- Duration of diarrhea: median duration shorten for -36.77 hours (95% CI -43.51 to -30.03)
  - Mean duration in control group: 29-127 hours

- Stool volume reduction: 50% (95% CI 0.45 to 0.56)
  - Volume in control group: 13.5 liters in adults, 368 ml/kg in children

- Amount of rehydration fluids required reduced by 40% (95% CI 0.53 to 0.68)
  - Volume required in control group: 14 liters in adults, 374 ml/kg in children

- Fecal excretion of vibrios: median duration shorten for -2.74 days, 95% CI -3.07 to - 2.40)
  - Mean duration in control group: 2.97-6 days

Cochraine review. Antimicrobial drugs for treating cholera (2014)

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Efficacy of chemoprophylaxis: culture positive cholera

Culture positive cholera, 1414 participants;
RR 0.34 (95% CI 0.18 to 0.66)

Study or Subgroup	Chemoprophylaxis Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Deb 1976	42	221	47	112	32.2%	0.45 [0.32, 0.64]
Echevarria 1995	1	107	3	104	6.9%	0.32 [0.03, 3.06]
Gupta 78	17	137	28	139	28.3%	0.62 [0.35, 1.07]
Joint 71	0	23	1	15	3.9%	0.22 [0.01, 5.12]
McCormack 68	17	413	39	143	28.7%	0.15 [0.09, 0.26]
Total (95% CI)		901		513	100.0%	0.34 [0.18, 0.66]
Total events	77		118			

Heterogeneity: Tau² = 0.32; Chi² = 15.41, df = 4 (P = 0.004); I² = 74%
Test for overall effect: Z = 3.19 (P = 0.001)

Reveiz et al. Chemoprophylaxis in Contacts of Patients with Cholera: Systematic Review and Meta-Analysis. Plos One 2011.

Large-scale targeted chemoprophylaxis: feasibility and «impact»

- Duala, Cameroon, 2004 (5,020 patients Jan – Aug 2004)

- Doxycicline prophlyaxis to household contacts recommended

- Contact: same roof, table, food, water point, latrine

- Proportion of household contacts among cases:
  - 30% in January,
  - 0.2% at the end

- No change in *V. cholerae* sensitivity

Table 1. Distribution of antibiotics during the 2004 cholera outbreak in Douala.

Nombre de bénéficiaires (N)	Antibiotiques			
	Doxycycline orale (cp)	Amoxicilline orale (cp)	Amoxicilline sirop	Total
Malades	4 572	423	18	5 013
Contacts intrahospitaliers	15 484	118	26	15 628
Contacts communautaires	145 895	12 625	3 205	161 725
TOTAL bénéficiaires	**165 951**	**13 166**	**3 249**	**182 366**
Ratio Contacts/malade				*35,37*

Guevart et al. Large-scale selective antibiotic prophylaxis during 2004 cholera outbreak in Duala, Cameroon. Santé 2007

Guevart et al. Antibiotic susceptibility of Vibrio cholerae 01: evolution after prolonged curative and preventive use during the 2004 cholera epidemics in Douala (Cameroon)]. Med Mal Infect 2006

Rann, Borno State, Nigeria 2018

- Around 48'000 people
- Difficult access+++
  - Arial bombing, insecurity –no permanent humanitarian presence
  - Flooding during rainy season
- No pre-emptive OCV campaign
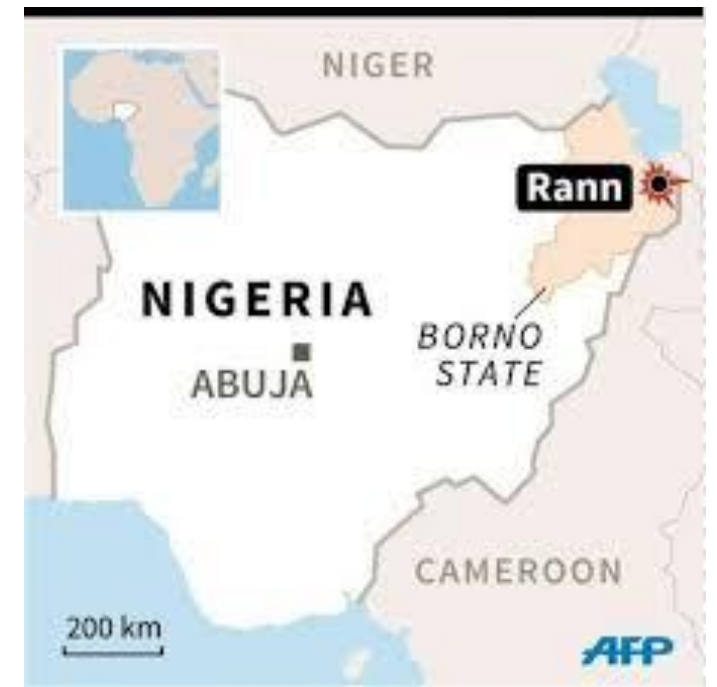
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DOCTORS WITHOUT BORDERS

Rann, Borno State, Nigeria 2018
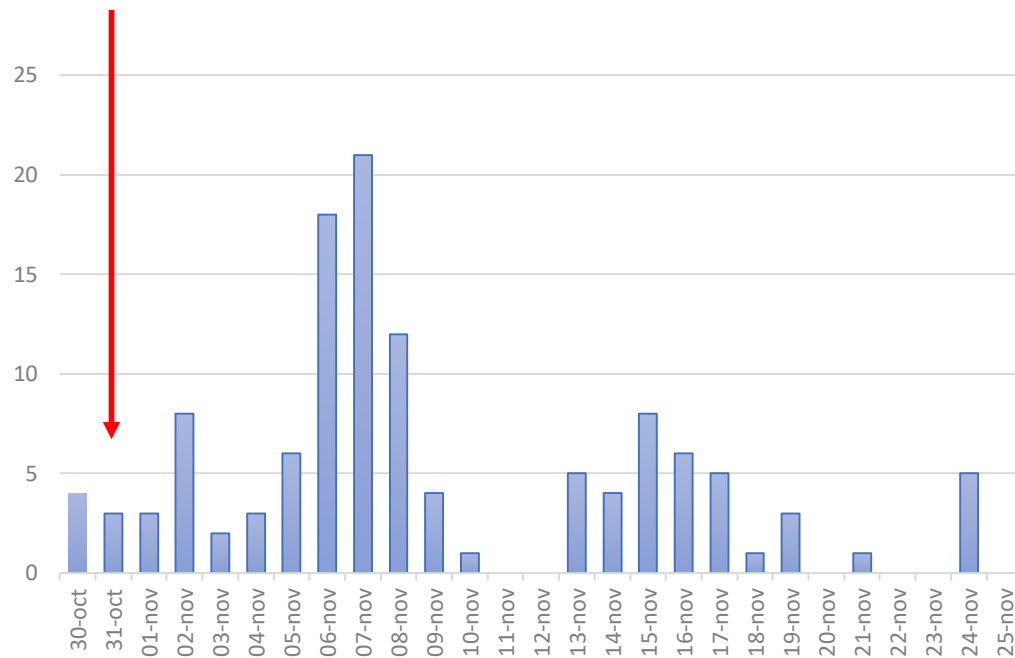
- Short explosive outbreak:
  - 129 cases, 13 deaths (half in community) – 10% CFR

- MSF team assessment 31/10/2018
- Initial proposal:
  - Standard response (re-enforcemnt of case management, HP, wash)
  - ORS points focus+++
  - Antibiotic prophylaxis (doxy): to all suspected cholera cases at CTU/ORS points
 - Investigation team sent to the HH – for HP, wash, doxy to contacts

Rann, Borno State, Nigeria 2018
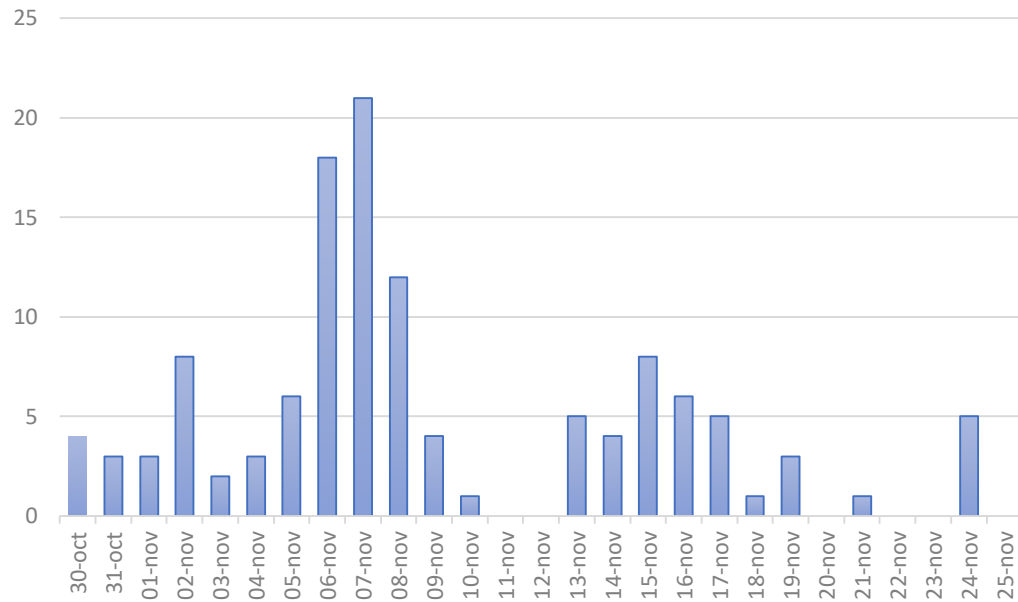
- Short explosive outbreak:
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- Intervention in reality
  - Standard response (re-enforcemnt of case management, HP, wash)
  - ORS points (11) + CTU
  - Antibiotics prophylaxis to cases >12 years old (and contacts?) presenting to CTU/ORS points, together with ORS and soap

Future

- Antibiotic prophylaxis already used in several countries, but not documented

- Rapid response teams

- Package interventions – wash + antibiotics + OCV around index case
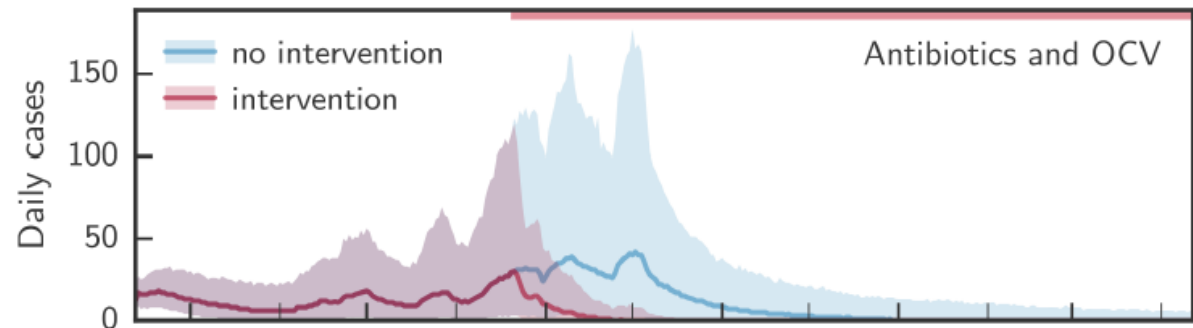
Azman et al. Case- area targeted interventions in response to cholera outbreaks. Plos Med 2018.