Single Cleansing of The Umbilical Cord Stump with Chlorhexidine to Prevent Severe Newborn Infections: A Randomized Controlled Trial in Uganda

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Acknowledgements: Study mothers, families and infants

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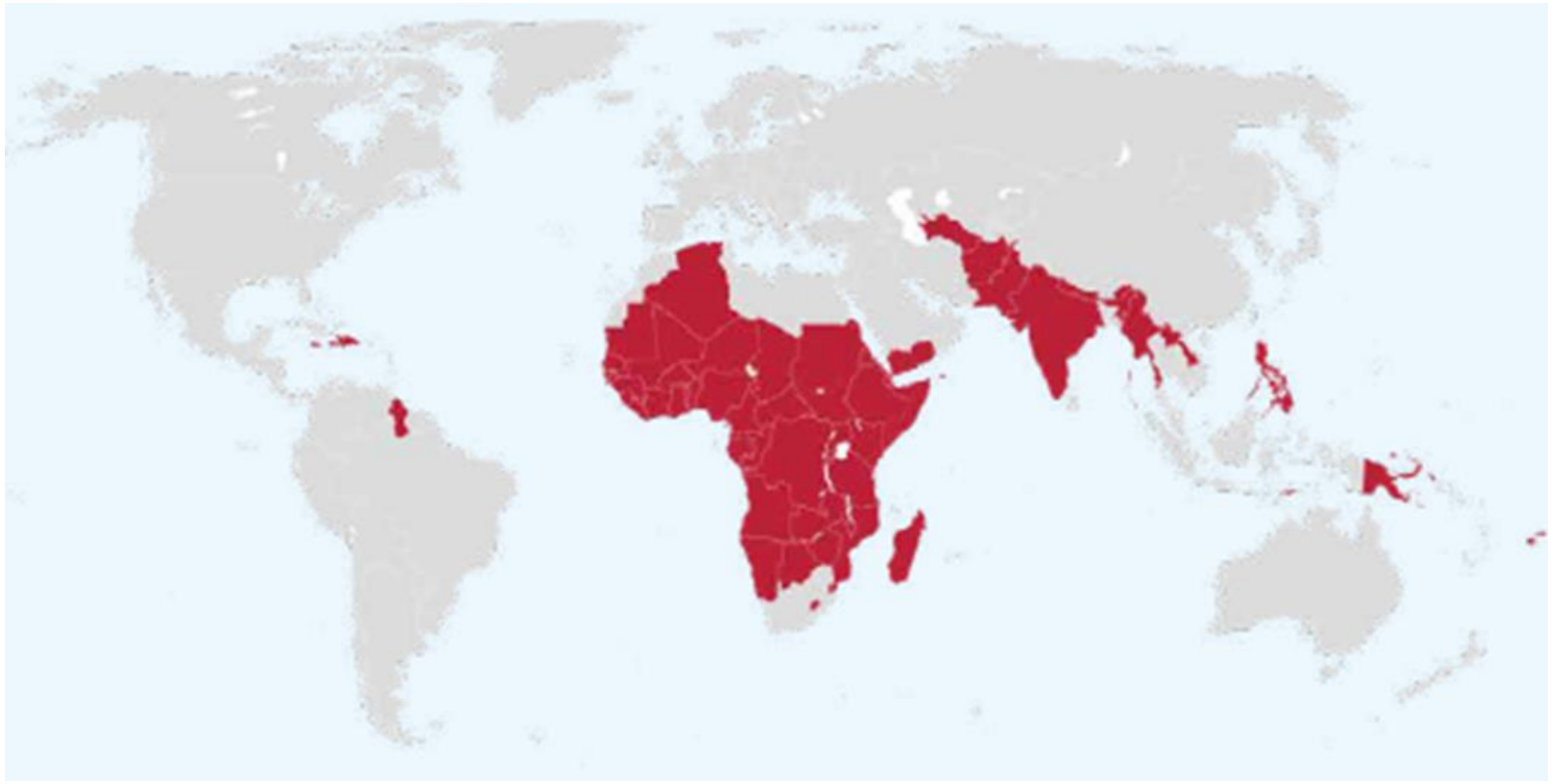
WORLD CONGRESS OF EPIDEMIOLOGY 2024



The unfinished agenda

- While ≈**60%** of the world's live births occur in sub- Saharan Africa (SSA) and Southern Asia, ≈**80%** under-five deaths occur here
- While ≈**30%** of the world's live births occur in SSA, almost **60%** of the deaths occur in here

Unicef, 2023

STUDY PROTOCOL Open Access

Efficacy of umbilical cord cleansing with a single application of 4% chlorhexidine for the prevention of newborn infections in Uganda: study protocol for a randomized controlled trial

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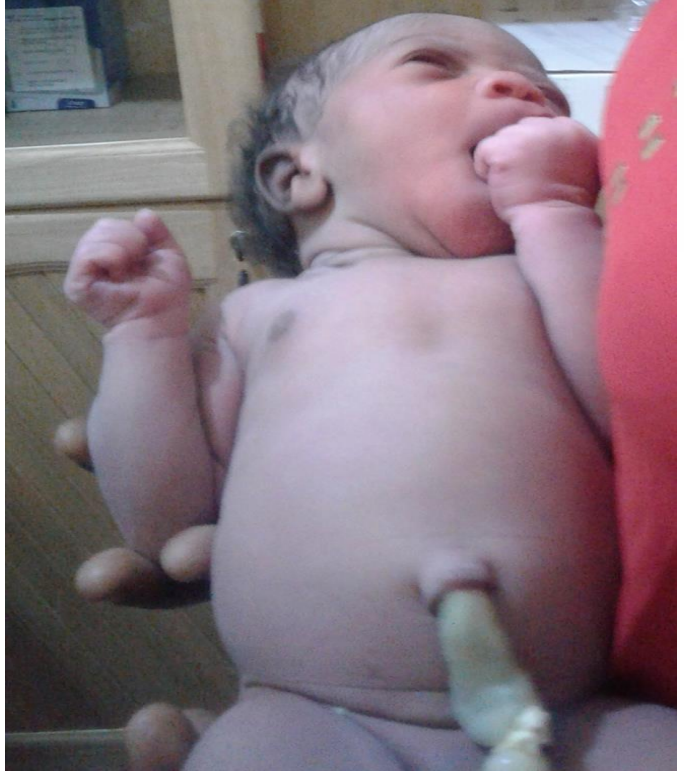
Abstract

Background: Yearly, nearly all the estimated worldwide 2.7 million neonatal deaths occur in low- and middle-income countries. Infections, including those affecting the umbilical cord (omphalitis), are a significant factor in approximately a third of these deaths. In fact, the odds of all-cause mortality are 46% higher among neonates with omphalitis than in those without. Five large randomized controlled trials in Asia and Sub-Saharan Africa (SSA) have examined the effect of multiple cord stump applications with 4% chlorhexidine (CHX) for at least 7 days on the risk of omphalitis and neonatal death. These studies, all community-based, show that multiple CHX applications reduced the risk of omphalitis. Of



The umbilical cord stump: A major entry point for pathogenic micro-organisms into the newborn

Chlorhexidine (CHX): An antiseptic commonly used for surgical procedures

Rationale for the Chlorhexidine (CHX) Study

1

Daily cleansing of umbilical cord stump (UCS) with CHX **for 7-10 days** at home to reduce neonatal mortality:

- Asia: Two RCTs with≈30% efficacy, one RCT with negligible efficacy
- SSA: Two RCTs combined: 0% efficacy

A ***single*** UCS cleansing with CHX to reduce neonatal mortality:

- Asia (Bangladesh): One RCT: 20% efficacy

2

3

Ugandan scientists and Health Ministry (+WHO-representatives): Need to estimate the effect of a ***single*** UCS cleansing with CHX in Ugandan birth facilities, because:

1. Bangladeshi trial showed promise
2. A single cleansing: Much simpler to implement

Methods

Primary objective

To estimate the efficacy of a single umbilical cord stump cleansing with 4% CHX at birth in facility-born babies on the risk of severe illness

Study design

Facility-based individually randomized controlled trial

Intervention

Single umbilical cord stump cleansing with 4% CHX at birth

Comparator

Dry cord care (current standard of care in facilities)

Sample size

4760 newborns

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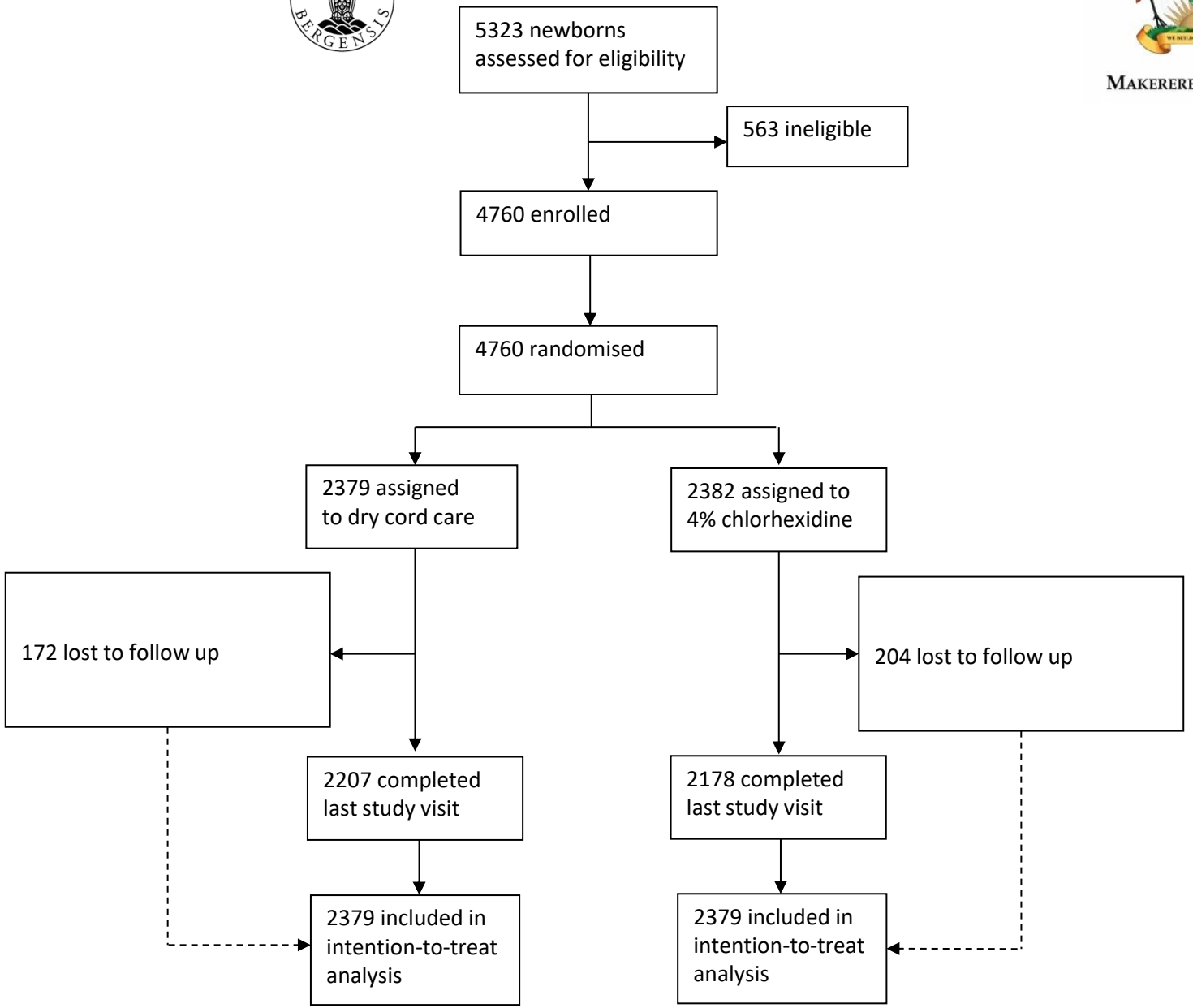
Follow up: >90%


5323 newborns assessed for eligibility
563 ineligible
4760 enrolled
4760 randomised
2379 assigned to dry cord care
2382 assigned to 4% chlorhexidine
172 lost to follow up
204 lost to follow up
2207 completed last study visit
2178 completed last study visit
2379 included in intention-to-treat analysis
2379 included in intention-to-treat analysis

	Dry Cord Care (Control) Arm N=2379	Chlorhexidine (Intervention) Arm N=2381
Birth weight (SD)	3.2 (0.4)	3.2 (0.4)
Mother's age in years (SD)	24.7 (4.8)	24.8 (4.9)
Number of people in household (SD)	3.6 (1.7)	3.7 (1.8)
Breast feeding initiation within 1 h. of birth		
Yes	2204 (92.6%)	2197 (92.3%)
No	175 (7.4%)	184 (7.7%)
Mother's education level		
None	38 (1.6%)	38 (1.6%)
Primary school	712 (29.9%)	714 (30.0%)
Secondary School	1418 (59.6%)	1411 (59.3%)
Certificate or Degree or Other	211 (8.9%)	218 (9.1%)
Electricity		
No	315 (13.2%)	337 (14.2%)
Yes	2064 (86.8%)	2044 (85.8%)

Baseline characteristics well balanced between arms

Results

Outcome	Infants	Cases	Risk	Efficacy
Mild omphalitis				
Chlorhexidine 4.0%	2381	347	146‰	28% (18%, 36%)
Dry cord care	2379	479	201‰	
Moderate to severe omphalitis				
Chlorhexidine 4.0%	2381	14	6‰	55% (15%, 76%)
Dry cord care	2379	31	13‰	

Results

Outcome	Infants	Cases	Risk	Absolute Risk Reduction (95%CI)	Efficacy (95%CI)
Severe illness					
Chlorhexidine 4%	2381	39	16 ‰	23 ‰ (13 ‰, 32 ‰)	58 % (39 %, 71 %)
Dry cord care	2379	93	39 ‰		

Number needed to prevent=**43!**

Comparison with Earlier Null African Trials

Our trial was:

- Used a single dose rather than daily doses for at least 7 days
- Different outcomes (Severe illness vs. Death)

Conclusion

This cheap and feasible intervention could substantially reduce the risk of severe illness in Ugandan and other LMIC children

Thank you