

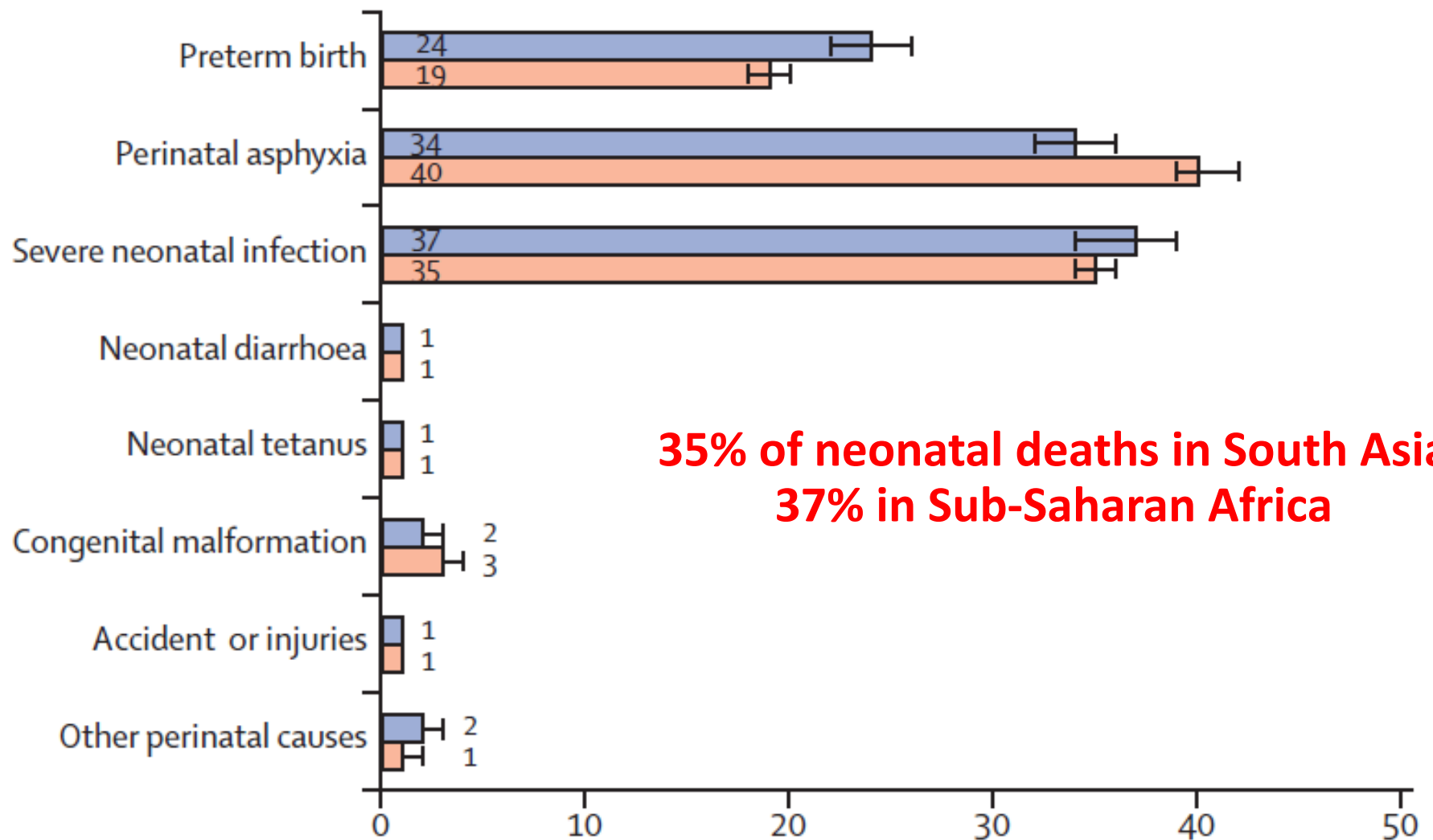
Management of Possible Serious Bacterial Infection: research to impact

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Neonatal infections mortality burden

AMANHI mortality study group, Lancet Global Health 2018



**35% of neonatal deaths in South Asia
37% in Sub-Saharan Africa**

Treatment of neonatal infections

- Initial diagnosis is based on clinical signs
- Hospital treatment with IV/IM antibiotics and supportive care
- Only 25% of these newborns receive hospital treatment in LMICs

AFRINEST and SATT studies (2010-2013):

- To find deliverable, safe and effective treatment for newborns with signs of severe infection where referral is not possible

Oral amoxicillin compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with fast breathing when referral is not possible: a randomised, open-label, equivalence trial

African Neonatal Sepsis Trial (ANNEST) group, Ankolabete Tabeju, Adrien Latiengala, Serge Ngaino, Cyril Engmann, Fabien Coumo, Peter Gilani, Adejumoke Idowu Ayede, Adegoke Gbodegehin Falade, Churud ussa A Adeniyigbe, Chibeme Henry Anyabolu, Robinson D Wammanda, Clara L. Ejembi, William N Ogala, Lu Grant, Simon Cousens

Lancet 2015

Lancet 2015

Simplified antibiotic regimens compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomised, open-label, equivalence trial

African Neonatal Sepsis Trial (ANNEST) group, Ankolabete Tabeju, Adrien Latiengala, Serge Ngaino, Cyril Engmann, Fabien Coumo, Peter Gilani, Adejumoke Idowu Ayede, Adegoke Gbodegehin Falade, Churud ussa A Adeniyigbe, Chibeme Henry Anyabolu, Robinson D Wammanda, Clara L Ejembi, William N Ogala, Lu Grant, Simon Cousens

Safety and efficacy of alternative antibiotic regimens compared with 7 day injectable procaine benzylpenicillin and gentamicin for outpatient treatment of neonates and young infants with clinical signs of severe infection when referral is not possible: a randomised, open-label, equivalence trial

Abdul Kadir H Baqui, Samira Saha, A S M Nawshad Uddin Ahmed, Mohammad Shahidullah, Jibbar Quasem, Daniel E Roth, A K M Samasromar, Wasir Ahmed, S M Shahnowar Bin Tabib, Dipali K Mishra, Nazma Begum, Mubashir Islam, Anif Mahomed, Mohammad Yefur Rahman, Muzammar Moin, Lubin C Mullany, Simon Cousens, Shams El Arifeen, Stephen Wal, Neal Brandes, Mahbubam Santoshang, Robert E Black, for the Projahnma Study Group in Bangladesh*

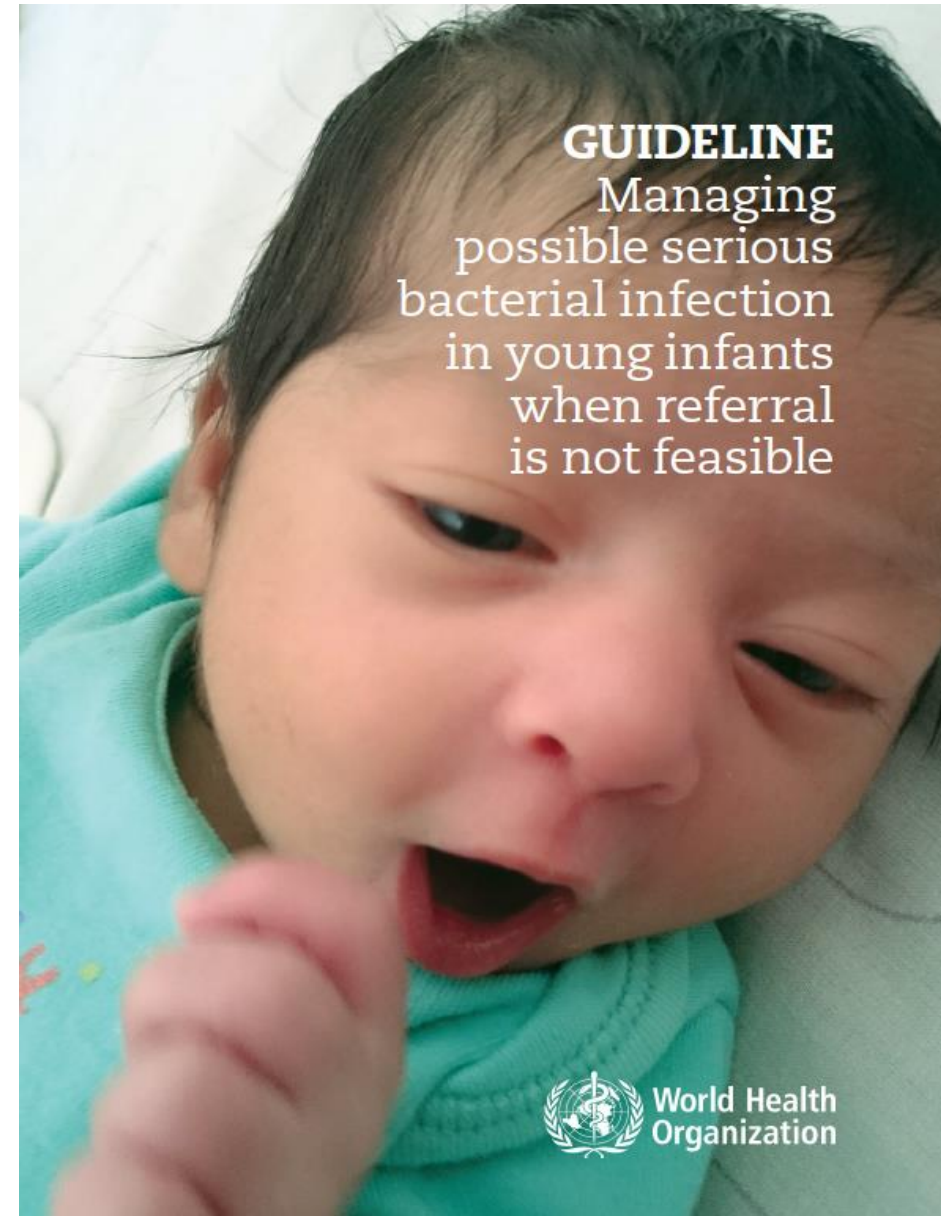
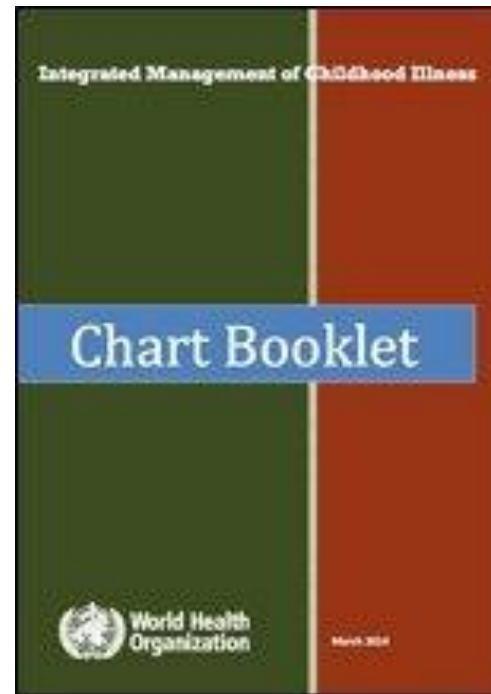
Lancet Global Health 2015

Lancet Global Health 2016

Simplified antibiotic regimens for treatment of clinical severe infection in the outpatient setting when referral is not possible for young infants in Pakistan (Simplified Antibiotic Therapy Trial [SATT]): a randomised, open-label, equivalence trial

Fatima Mir, Imran Nisar, Shiyam S Tikmani, Benazir Baloch, Sadia Shakoor, Fyezah Jehan, Imran Ahmed, Simon Cousens, Anita K M Zaidi

WHO guidelines on treatment of neonatal infections



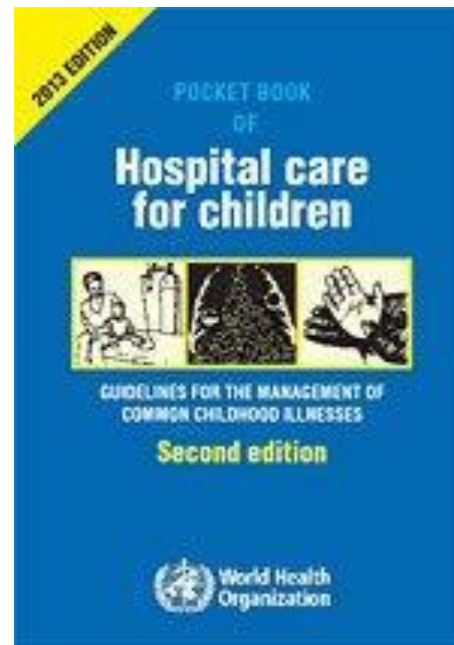
CARING FOR NEWBORNS AND CHILDREN IN THE COMMUNITY A TRAINING COURSE FOR COMMUNITY HEALTH WORKERS

Caring for the newborn at home



COUNSELLING CARDS

unicef World Health Organization



Home

Recommendation	Strength of recommendation	Quality of evidence
Community health workers and home visits for postnatal care At home visits made as part of postnatal care (2), community health workers should counsel families on recognition of danger signs, assess young infants for danger signs of illness and promote appropriate care seeking. ^a	Strong	Moderate

Danger signs for which baby should be taken to a health worker

- Not able to feed since birth, or stopped feeding well
- Convulsed or fitted since birth
- Fast breathing: two counts of 60 breaths or more in one minute
- Chest indrawing
- High temperature: 37.5°C or more
- Very low temperature: 35.4°C or less
- Yellow soles
- Movement only when stimulated, or no movement even on stimulation
- Signs of local infection: umbilicus red or draining pus, skin boils and eyes draining pus

First level health facility

Signs of Possible Serious Bacterial Infection

- Stopped feeding well
- Movements only on stimulation or no movements at all
- Fever, temperature $\geq 38.0^{\circ}\text{C}$
- Hypothermia, temperature $< 35.5^{\circ}\text{C}$
- Severe chest indrawing
- Fast breathing (0-6 days)
- Convulsions

Management

- Facilitate referral to hospital
- First dose of intramuscular ampicillin and gentamicin

Hospital

Management of serious bacterial infection

- Supportive care, as needed
- Intravenous/intramuscular ampicillin 8-12 hourly and gentamicin once daily for 10 days (3 weeks if meningitis)
- Cloxacillin instead of penicillin if extensive skin infection
- Second line antibiotic: third generation cephalosporin

When referral is not feasible

Re-classify possible serious bacterial infection into:

- Clinical severe infection
- Critical illness

Clinical severe infection: at first level or hospital outpatient facility:

- Combination of oral amoxicillin and gentamicin

Critical illness

- Facilitate referral again
- Treat with injections ampicillin and gentamicin at first level or hospital outpatient facility only as a last resort

Details on next slides

When referral is not feasible

Clinical Severe Infection* at outpatient facility

**Stopped feeding well, movement only when stimulated, severe chest in-drawing, temperature $\geq 38.0^{\circ}\text{C}$ or $< 35.5^{\circ}\text{C}$*

Recommendation	Strength of recommendation	Quality of Evidence
Young infants 0-59 days old with clinical severe infection whose families do not accept or cannot access hospital care should be managed in outpatient settings by an appropriately trained health worker with one of the following regimens: <u>Option 1</u> : IM gentamicin 5-7.5 mg/kg once daily for 7 days and twice daily oral amoxicillin, 50 mg/kg per dose for 7 days. Close follow up is essential. <u>Option 2</u> : IM gentamicin 5-7.5 mg/kg once daily for 2 days and twice daily oral amoxicillin, 50 mg/kg per dose for 7 days. Close follow up is essential. A careful assessment on day 4 is mandatory.	Strong	Moderate
	Strong	Low

Choice of option 1 vs option 2 dependent upon health system's ability to provide 7 vs 2 days injections

When referral is not feasible: **Critical Illness*** at outpatient facility

** unconscious, convulsions, inability to feed, inability to cry, apnoea, cyanosis, bulging fontanel, persistent vomiting, suspected meningitis*

Recommendation	Strength of recommendation	Quality of Evidence
Young infants 0-59 days old who have any sign of critical illness (at presentation or developed during treatment of clinical severe infection) should be hospitalized after pre-referral treatment.	Strong	Very low (Current standard)

* If referral not possible at all, treat with injection ampicillin twice daily plus gentamicin once daily

Implementation research in 7 countries

Newborn infections management strategy

- Improved identification of infants with PSBI by families and CHWs
- Treatment of fast breathing in 7-59d olds with oral antibiotics at first level health facilities
- Improved referral to hospital for other cases of PSBI
- If referral is not possible, provided outpatient treatment at first level health facilities

*Completed: Bangladesh, DRC, Ethiopia, Malawi, Nigeria and Pakistan.
Ongoing: India*

Implementation research in 7 countries

Steps in Implementation Research

- Orientation and Policy dialogue
- Informed decisions on treatment choices for early implementation in selected sites
- Establishment of early implementation sites and Technical Support Units
- Building capacity and creating a learning platform (TSU)
- Implementation, supervision, and monitoring

Implementation research in 7 countries

Implementation experience

	ETHIOPIA	MALAWI	NIGERIA	DRC	PAKISTAN	BANGLADESH
TSU role in implementation	Low	Low	High	High	Low	Low
Feasible/acceptable	yes	yes	yes	yes	yes	yes
Treatment completion	95%	94%	95%	96%	81%	56%
Day 4 follow up	95%	90%	98%	98%	90%	21%
No. treated year	10/HP, 32/HC	50/HC	51/HC	53/HC	110/BHU	29/UHC
Treatment failure	0.3%	4%	7%	9%	7%	4%
Treatment coverage (hospital + outpatient)	61%	58%	95%	88%	97%	27%

Implementation research in 6 countries:
Mortality among all identified PSBI cases

	% of PSBI cases	Deaths (CFR)
Fast breathing only (7-59d)	45%	1/1923 (0.1%)
Clinical severe infection	51%	68/2147 (3.2%)
Critical illness	4%	18/151 (11.9%)

Lessons from implementation research

- Implementation of the new PSBI treatment strategy is feasible in programme settings, and can result in high treatment coverage.
- When outpatient treatment was only available at very low (e.g. Bihar) or very high (e.g. Bangladesh) level facilities, treatment coverage was low.
- With outpatient treatment at appropriate facilities, postnatal home visits and a functional health system were critical for high treatment coverage.
- Technical support units played an important role in achieving high-quality implementation.
- Low treatment failure (4% to 9%) and mortality rates were achieved, which should motivate countries to scale-up the new PSBI treatment strategy.

Implementation research in 6 countries: Potential impact on mortality

Coverage: proportion of expected cases who received treatment (at hospital or outpatient facility)	75%
Case fatality: Proportion of deaths among the ~6000 total cases identified as PSBI (with new treatment strategy)	2%
Potential lives saved per year: <i>Assumption 1:</i> Sub-Saharan Africa and South Asia have 6 million PSBI cases <i>Assumption 2:</i> Scale up can achieve 75% coverage <i>Assumption 3:</i> Old strategy has 7% case fatality (previous prospective studies)	225,000

Questions?