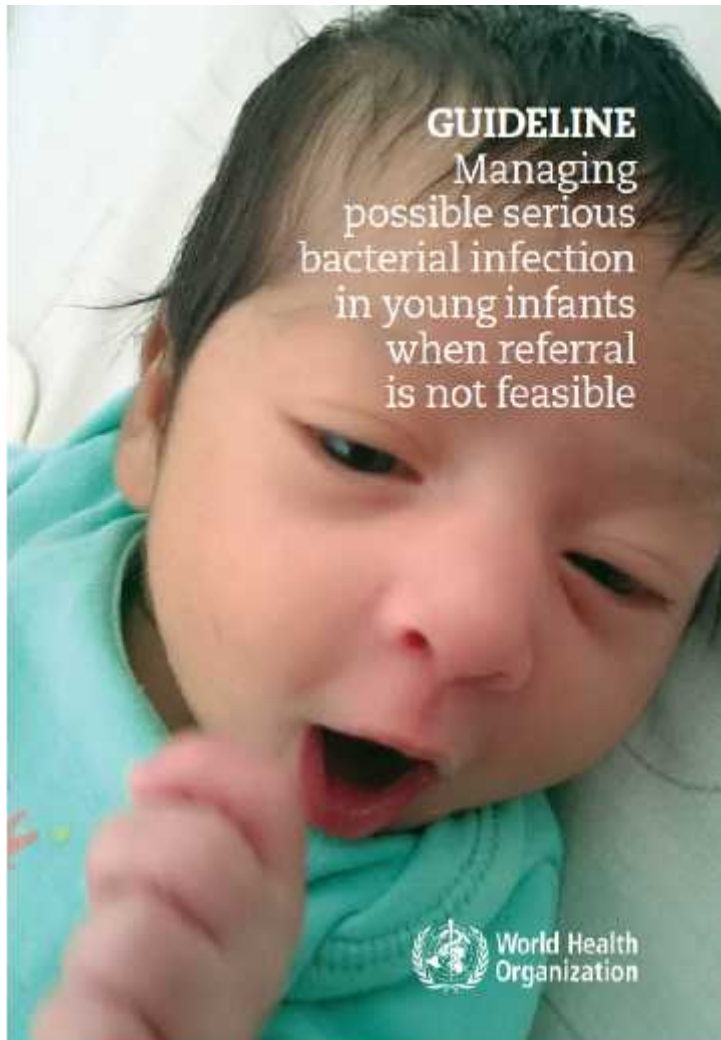




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GUIDELINE
Managing
possible serious
bacterial infection
in young infants
when referral
is not feasible



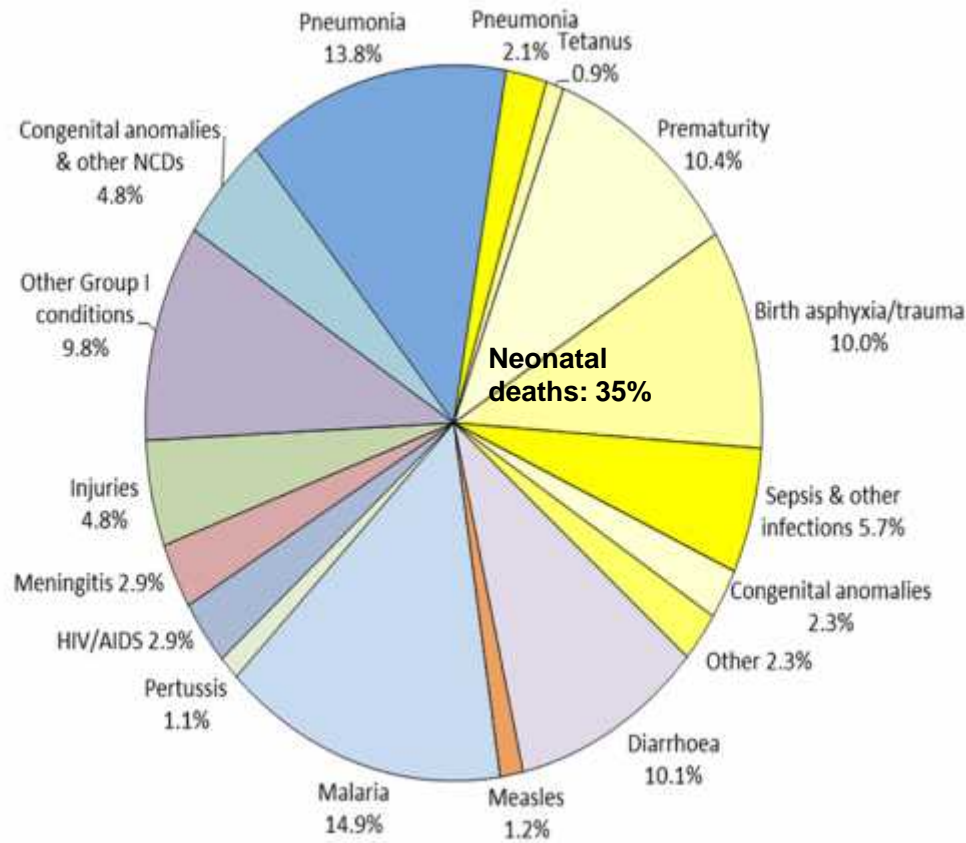
Guidelines for management of suspected sepsis in young infants where referral is not possible

Kenya Paediatrics Association Conference,
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Outline

- Background
- Evidence
- Guidelines development process
- Objectives of the guidelines
- Target audience
- Overall context
- Recommendations of the guidelines

Background - Why



Source: WHO. Global Health Observatory (http://www.who.int/gho/child_health/en/index.html)

- Almost a half of the world's 5.9 million under-five deaths are in the neonatal period: about 400,000 from possible severe bacterial infections
- In the Sub-Saharan region of the approximately 1 million newborn deaths 8% are due to infections.
- Current WHO - recommended option for management of sepsis in sick young infants entails hospitalization.

Background cont..

- Up to 60% of babies with signs of serious bacterial infection in resource-limited settings do not receive the recommended inpatient treatment.
- WHO with partners set up a research in 3 countries of the African Region (DRC, Kenya and Nigeria) to assess whether use of simplified antibiotics regimens to treat young infants with signs of severe infection was as efficacious as an injectable procaine benzylpenicillin-gentamycin combination for 7 days for situations in which hospital referral was not possible.

Summary of key findings

- Fast breathing as a single sign constituted about 40% of all infants referred based on WHO criteria for PSBI
- In infants with fast breathing only, treatment failure, clinical deterioration and deaths in those with oral amoxicillin was similar to that with procaine penicillin and gentamicin injections.
- Overall, in infants with clinical severe infection, treatment failure, clinical deterioration and death in those with 2, 4 or 7 antibiotic injections given with oral antibiotics, was similar to those with a regime that had 14 injections.

Conclusions

- Where referral is not possible, infants with fast breathing as a single sign can be safely and effectively treated as outpatient with oral amoxicillin under supervision
- Where referral is not possible, infants with severe infection can be safely and effectively treated as outpatients
- Community health workers can serve as a link between the families and health providers who provide outpatient treatment

Other research on PSBI

- In four urban hospitals and one rural field site in Bangladesh and Pakistan (Simplified Antibiotic Therapy Trials (SATT) studies) to determine whether two alternative antibiotics regimens with reduced numbers of injectable antibiotics combined with oral antibiotics had similar efficacy and safety to the standard regimen, which was also used as outpatient treatment.
- The result of the studies from the *AFRican NEonatal Sepsis Trial* (AFRINEST) and the 2 Asian countries SATT studies provided evidence for treatment of neonatal sepsis at outpatient level, in resource limited settings where referral is not possible
- WHO set up a steering committee to oversee the guidelines development.

Guidelines development process

- A guidelines development Group (GDG) comprising of 18 experts was convened by WHO to review and evaluate the quality of the available evidence.
- In October 2013 WHO staff and GDG reviewed the results of the studies and agreed there was adequate evidence to update the guidelines on management of PSBI in young infants with a focus on where families do not accept or cannot access referral.
- The GDG developed the priority questions and independent institutions were commissioned to conduct systematic reviews of each question

Priority Review Questions

- 1. Among all neonates 0–28 days old**, can home visits by CHWs compared to no home visits successfully identify newborns with serious illness and improve care seeking from a health facility?
- 2. Among neonates (0–6 days old) and young infants (7–59 days old) presenting with fast breathing as a single sign of PSBI**, are simpler antibiotic regimens, delivered at outpatient and/or community level, as effective as a combination of injectable penicillin and gentamicin for at least seven days as measured by rates of mortality and clinical deterioration within two weeks of starting treatment?

Priority Review Questions

3. **Among neonates and young infants (0–59 days old) with suspected/confirmed clinical severe infection**, can simpler antibiotic regimens, delivered at outpatient and/or community level, be as effective as a combination of injectable penicillin and gentamicin given for at least seven days in achieving comparable rates of mortality, clinical deterioration and persistence of signs of severe infection within two weeks of starting treatment?
4. **Among neonates and young infants (0–59 days old) with signs of critical illness**, are simpler antibiotic regimens delivered at outpatient and/or community level, as effective as a combination of injectable penicillin and gentamicin for at least seven days as measured by rates of mortality, clinical deterioration and persistence of signs of severe infection, within two weeks of starting treatment?

Additional priority questions

- Formulated to provide context and additional information on the possible treatments for outpatient care among infants whose families do not accept or cannot access referral care for treatment:
- 1. Among neonates and young infants (0–59 days old) who have signs of PSBI**, who are managed with simpler antibiotic regimens delivered at outpatient and/or community level, what are the total costs/cost-effectiveness of treatment with simpler effective antibiotic regimens (defined as having equivalent or better reductions in mortality, clinical deterioration, non-recovery and relapse), compared to a combination of injectable penicillin and gentamicin for at least seven days?
 - 2. Among neonates and young infants (0–59 days old) who have signs of PSBI**, who are managed with simpler antibiotic regimens delivered at outpatient and/or community level, compared with a combination of injectable penicillin and gentamicin for at least seven days, what are the feasible, acceptable, effective and cost-effective *models of service delivery* and what are the health system requirements for all these models?

Guidelines development process – cont.

- A systematic review was based on the following characteristics: population of interest, intervention, control and outcome (PICO).
- The quality of the evidence (outcome) for each question was assessed by the GDG using the GRADE* methodology - resulting in the draft recommendations.
- A Peer Review Group reviewed the draft recommendations and supporting documents developed by the GDG
- The draft recommendations underwent external peer review before they were approved by the GDG.
- The WHO Guidelines Review Committee (GRC) approved the guidelines on treatment of neonatal sepsis where referral is not possible on 14 July 2015 and they were published in August 2015

*Grading of Recommendations, Assessment, Development and Evaluation

Definition of quality of evidence using the GRADE system

Quality	Definition
High	Further research is unlikely to change confidence in the estimates of the effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of the effect and may change the estimate
Low	Further research is very likely to have an important impact on confidence of the effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Assessment criteria for the strength of the recommendation

Strength of recommendation	Rationale
Strong	The GDG is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects
Weak	The GDG concludes that the desirable effects of adherence to the recommendations probably outweigh the undesirable effects. However, the recommendation is only applicable to a specific group, population or setting OR where new evidence may result in changing the balance of risk to benefit OR where the benefits may not warrant the cost of resource requirements in all settings
No recommendation	Further research is required before any recommendation can be made.

Objectives of the guidelines

- Provide recommendations on the use of antibiotics for neonates and young infants (0-59 days old) with PSBI in order to reduce young infants mortality rates
- Seeks to provide clinical guidance on the simplest antibiotics regimens that are both safe and effective for outpatient treatment of clinically severe infection and fast breathing (pneumonia) in children 0-59 days old.
- Seeks to provide programmatic guidance on the role of CHW and home visits in identifying signs of serious illness in neonates and young infants

The population of interest

Neonates (0–28 days old) and young infants (0–59 days old) in resource-limited settings who have clinical signs of PSBI and whose families do not accept or cannot access referral care for treatment.

- Clinical signs of PSBI are defined as:
 - fast breathing (respiratory rate ≥ 60 breaths/minute)
 - severe chest in-drawing
 - fever (temperature ≥ 38 °C)
 - hypothermia (temperature < 35.5 °C)
 - no movement at all or movement only on stimulation
 - feeding poorly or not feeding at all
 - convulsions.

The population of interest – cont...

The guideline recommendations were categorized into two *subgroups of young infants with PSBI*, based on increasing clinical severity.

- **Fast breathing pneumonia:** A young infant (0–59 days old) with a respiratory rate of ≥ 60 breaths per minute as the only sign of possible infection.
- **Clinical severe infection:** A young infant (0–59 days old) with at least one sign of severe infection (i.e. movement only when stimulated, not feeding well on observation, temperature ≥ 38 °C or < 35.5 °C or severe chest in-drawing).

Outcomes evaluated

For each priority question **two critical** and **two important** outcomes were evaluated.

Critical outcomes

- 1) Death within two weeks of starting treatment for PSBI; and
- 2) Treatment failure by day 8 after starting treatment, (defined as clinical deterioration after starting treatment for PSBI including death, need for hospitalization/referral, need to change antibiotics, new signs of clinical infection or persistence of signs of illness).

Important outcomes

- 1) Clinical relapse (defined as emergence of any sign of infection within two weeks after the disappearance of all signs of clinical PSBI);
- 2) Adherence to treatment (defined as compliance or adherence to treatment as specified in the study methods).

Target audience

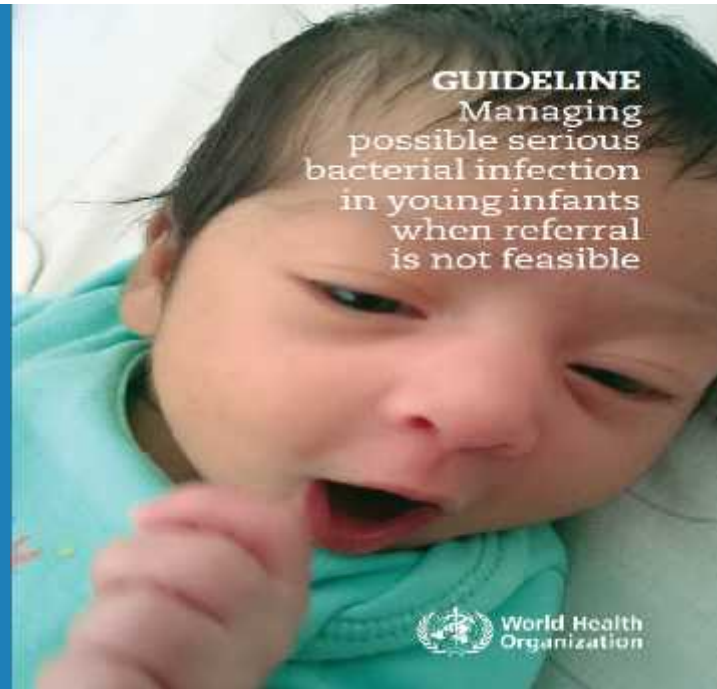
- For use in resource limited settings in situations where families do not accept or cannot access referral
- National policy-makers in health ministries, programme managers in child health, essential drugs and training institutions.
- Health care providers and clinicians managing sick children at various levels of health care including public and private
- Development partners supporting child health programmes

Will not replace the WHO-recommended inpatient management as a preferred treatment option.

Close follow-up is essential for young infants managed on an out-patient basis where referral is not possible.

Overall context

- These guidelines are for low resource settings in the context of primary health care only.
- The treatment guidelines are for use by professionally trained health workers, and not for lay community health workers.
- The health workers should be appropriately trained, supplied with necessary equipment and medicines and supervised for the identification of signs of illness, referral, treatment if referral is not accepted .
- Monitoring of the programme is needed for ensuring high quality of identification, treatment and follow up activities.
- These guidelines are expected to rationalize the use of antibiotics for young infants with suspected infection. Surveillance for antimicrobial resistance should be strengthened in all countries.



Recommendations for management of
suspected sepsis in young infants
where referral is not possible or
accepted

Fast breathing*

Recommendation	Strength of recommendation	Quality of Evidence
Young infants 7-59 days old with fast breathing as the only sign of illness should be treated with oral amoxicillin, 50 mg/kg per dose twice daily for 7 days, by an appropriately trained health worker.	Strong	Moderate
Infants 0-6 days with fast breathing as the only sign of illness should be referred to hospital. If referral is not accepted, they should also be treated with oral amoxicillin, 50 mg/kg per dose twice daily for 7 days, by an appropriately trained health worker.	Strong	Moderate

*Fast breathing 60 or more breaths per minutes

Clinical Severe Infection*

Recommendation	Strength of recommendation	Quality of Evidence
<p>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:</p>		
<p><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.</p>	Strong	Moderate
<p><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.</p>	Strong	Low

*Stopped feeding well, movement only when stimulated, severe chest in-drawing, Temperature 38.0°C or <35.5°C

Critical Illness*

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	(Current standard)

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

Postnatal Home Visits by CHWs

Recommendation	Strength of recommendation	Quality of Evidence
At home visits made as part of postnatal care, CHWs should counsel families on recognition of danger signs, assess young infants for danger signs of illness and promote appropriate care seeking.	Strong	Moderate

Summary

- The guidelines have the potential to transform the current limited access of young infants.
- The implementation of the guidelines:
 - Will contribute to the reduction of death of young infants due to PSBI
 - Has an opportunity to reduce the inequity in access to care in resource limited settings
 - Provide an opportunity to improve home visit for newborn
 - Needs to be within the context of the national health strategies, Every Newborn Action Plan and the available intervention packages – and not as vertical programme.



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Thank you
Merci
beaucoup

