ISRCTN16872570 https://doi.org/10.1186/ISRCTN16872570

# How long should young infants less than 2 months of age with moderate-mortality-risk signs of possible serious bacterial infection be hospitalized for?

**Submission date**
24/11/2020

**Recruitment status**
No longer recruiting

**Registration date**
20/01/2021

**Overall study status**
Completed

**Last Edited**
21/10/2025

**Condition category**
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

## Plain English summary of protocol

Background and study aims

The WHO Integrated Management of Childhood Illness (IMCI) algorithm classifies newborns and young infants up to 2 months old with clinically suspected sepsis as “Possible Serious Bacterial Infection (PSBI)”. WHO guidelines recommend that young infants with PSBI should be managed in a hospital with injectable antibiotics and supportive care. When referral to hospital is not feasible, the guidelines recommend further classification of these young infants into those who are critically ill and those who have clinical severe infection (CSI). Those with CSI, if referral is not feasible, can be managed on an outpatient basis with injectable gentamicin for 2 or 7 days and oral amoxicillin for 7 days. Implementation research on the above guidelines has demonstrated that outpatient treatment is safe and effective when hospitalization is not feasible. Overall a quarter to half of newborns in different settings are taken to a hospital. However, hospitalization has inherent risks, particularly that of nosocomial (hospital-acquired) infection with multi-drug resistant pathogens. Therefore, only those young infants with signs of PSBI who have a favourable benefit-risk ratio should be hospitalized. Studies have shown that infants with any sign of CSI had a higher mortality rate when they were hospitalized compared to when they received outpatient treatment. In contrast, the mortality rate was lower among those with any sign of critical illness who received inpatient treatment, compared to those who received outpatient treatment. This seems logical because critically ill young infants need supportive care in addition to antibiotics, whereas infants with CSI primarily need antibiotic treatment. The aim of this study is to find out whether the majority of infants with CSI who need hospitalization could be discharged early.

Who can participate?

Young infants under 2 months of age admitted to the study hospitals with moderate mortality risk signs of CSI

What does the study involve?

Infants will be discharged 48 hours after hospitalization for injectable antibiotic (gentamicin

once daily and ampicillin four times a day) and other supportive treattment, when they will be randomly allocated to either go home on oral amoxicillin for 5 more days (intervention) or continue inpatient hospital injectable antibiotic treatment and supportive therapy for a total of 7 days (control). Outcomes will be assessed on day 8 and 15 after the initiation of treatment.

What are the possible benefits and risks of participating?
The infant will receive treatment in hospital or as an outpatient. There may not be a direct benefit for the infant and society at this stage, but participation will bring benefit for future generations. If the finding of this study shows benefits for outpatient treatment, participants will have contributed to change the global recommendation on care for young infants with moderate signs of infection. If the finding of this study shows benefits for standard hospital treatment, it will be recommended for all other young infants presenting with moderate signs of infection.
It has been observed that the outpatient treatment for infants who do not have any signs of infection and have a negative laboratory test for infection after 2 days of hospital treatment for infection is associated with very low risk of mortality. However, in rare cases, the infant's condition may deteriorate despite treatment. In such rare eventuality, parents are encouraged to bring the infant back to the hospital immediately for prompt treatment and support. Additionally, parents are counselled on any danger signs that can appear in an infant while on treatment, so that they may recognize these in time and seek prompt care. The medicines being used in this study are used in infants throughout the world and are generally known to be safe, but they can rarely cause diarrhea, stomach ache or a skin rash. There is a very low risk of a serious allergic reaction, hearing problems or kidney damage. If the infant has a skin rash, diarrhea, or any other problem, the parents can always bring the infant back to the hospital for prompt treatment and support.

Where is the study run from?
World Health Organization (Switzerland)

When is the study starting and how long is it expected to run for?
January 2020 to December 2024

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Dr Yasir Bin Nisar
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# Contact information

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Public

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## Additional identifiers

### Protocol serial number
U1111-1251-1576

## Study information

### Scientific Title
Optimizing duration of hospitalization for young infants presenting with any moderate-mortality-risk sign of possible serious bacterial infection

### Study objectives
The main hypothesis is that the poor clinical outcome in young infants with any moderate-mortality risk sign or two or more signs of CSI who clinically improve 48 hours after initiation of treatment and have a negative C-reactive protein test, who are discharged and received oral amoxicillin for next 5 days will be non-inferior to the outcome of those who will continue inpatient hospital injectable antibiotic treatment for the next 5 days.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 12/06/2020, WHO Research Ethics Review Committee (20 Avenue Appia, CH-1211 Geneva 27, Switzerland; +41 (0)227912111; ercsec@who.int), ref: ERC.0003289

### Primary study design
Interventional

### Study design
Multi-country interventional randomized controlled trial

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Treatment of moderate-mortality-risk signs of possible serious bacterial infection in young infants <2 months old

### Interventions
Young infants <2 months of age with moderate mortality risk signs of possible serious bacterial infection (low body temperature [<35.5°C], not feeding well/stopped feeding well, movement only when stimulated or two or more low mortality risk signs) will be discharged 48 hours after hospitalization for injectable antibiotic (gentamicin injection once daily and ampicillin injection four times a day) and other supportive therapy, when they will be randomized to go home on oral amoxicillin for 5 more days (intervention) or continue inpatient hospital injectable antibiotic treatment and supportive therapy for a total of 7 days (control).

Dose of amoxicillin: (dispersible tablet 250 mg), 1/2 tablet for 1.5 to 3.9 kg body weight, and 1 tablet for 4.0 to 5.9 kg body weight, twice daily.
Duration of amoxicillin: 5 days
Mode of administration of amoxicillin: oral

Outcome assessment will be carried out by an IOA. An IOA will visit all enrolled young infants in the control arm at the hospital or at home after discharge and intervention arm enrolees at home on Day 8 and 15 of initiation of treatment.

### Intervention Type
Mixed

### Primary outcome(s)
Poor clinical outcome defined as:
1. Death between randomization (day 3 of initiation of therapy) and day 15 of initiation of therapy, or
2. Presence of any sign of critical illness (no movement at all, unable to feed at all, or convulsions) or any sign suggestive of another serious infection, e.g. meningitis, bone or joint infection, on day 4 or day 8 of initiation of therapy, or
3. Presence of any sign of clinical severe infection (severe chest indrawing, high body temperature (>38°C), low body temperature [<35.5°C], not feeding well/stopped feeding well, movement only when stimulated, fast breathing [respiratory rate >60 breaths/minute in <7 days old]) or two or more of clinical severe infection signs on day 8 of initiation of therapy.

### Key secondary outcome(s)
There are no secondary outcome measures

### Completion date
31/12/2024

## Eligibility

### Key inclusion criteria

All patients (<2 months old at admission) admitted to the study hospitals with any moderate-mortality risk signs of clinical severe infection (CSI) at presentation (not feeding well, movement only on stimulation, low body temperature <35.5°C, two or more of the six signs of CSI) will be assessed for eligibility for this study 48 hours after initiation of treatment and considered for inclusion in the study if:
1. Clinically well on day 3 defined as the absence of all signs of critical illness (not feeding at all, no movement at all, convulsions) or CSI (not feeding well, movement only when stimulated, low body temperature (<35.5°C), high body temperature (≥38°C), severe chest indrawing, fast breathing in <7 days old)
2. C-reactive protein (CRP) test negative
3. Family lives within a catchment area where a follow-up of up to day 15 can be accomplished

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Child

### Upper age limit
2 Months

### Sex
All

### Total final enrolment
5252

### Key exclusion criteria
1. Weight <2 kg at the time of presentation (if age at screening is less than 10 days) or weight-for-age <-3z
2. Signs of critical illness on admission (no movement at all, unable to feed at all, or convulsions)
3. Appearance of any moderate-mortality risk sign or multiple low-mortality risk signs in the first 24 hours of life
4. Hospitalized for any illness in the previous 2 weeks
5. Prior use of injectable antibiotics for the same illness
6. Previously included in this study or currently included in any other study
7. Any other reason to stay in the hospital, as decided by the treating physician

### Date of first enrolment
24/06/2021

### Date of final enrolment
01/09/2024

## Locations

## Countries of recruitment
Bangladesh

Ethiopia

India

Nigeria

Pakistan

Tanzania

## Study participating centre
**Projahnmo Research Foundation (PRF)**
Block A, ABANTI, House 37, Road 27
Dhaka
Bangladesh
1213

## Study participating centre
**Tikur Anbessa Hospital, Addis Ababa University**
Addis Ababa University
Addis Ababa
Ethiopia
1000

## Study participating centre
**Center for Health Research and Development, Society for Applied Studies**
45, Kalu Sarai
New Delhi
India
110016

## Study participating centre
**Community Empowerment Lab (CEL), Lucknow**
26, 11, Wazir Hasan Road, Block I
Gokhale Vihar
Butler Colony
Lucknow
India
226001

**Study participating centre**
**Ahmadu Bello University Teaching Hospital, Zaria**
Ahmadu Bello University (ABU)
Zaria
Nigeria
1044

**Study participating centre**
**Aga Khan University**
National Stadium Rd
Aga Khan University Hospital
Karachi
Pakistan
74800

**Study participating centre**
**Muhimbili University of Health and Allied Sciences**
Dar-es-Salaam
Tanzania
65001

# Sponsor information

**Organisation**
World Health Organization

**ROR**
https://ror.org/01f80g185

# Funder(s)

**Funder type**
Charity

**Funder Name**
Bill and Melinda Gates Foundation

**Alternative Name(s)**

Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

### Funding Body Type
Government organisation

### Funding Body Subtype
Trusts, charities, foundations (both public and private)

### Location
United States of America

## Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

### IPD sharing plan summary
Other

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 20/10/2025 | 21/10/2025 | Yes | No |
| Protocol article | | 14/07/2023 | 17/07/2023 | Yes | No |