Supplemental file 2. Algorithm for classifying children at risk of serious infection

Febrile patient meeting entry criteria for study
With available samples for biomarker discovery (RNA, proteomic, metabolomic)

Categorization of patients based on clinical data

**BACTERIAL syndrome**
- Tonic/shock syn
- LRTI/empyema
- Cellulitis
- empyema/Nec.
- fur, Pus/Pyo
- Pneumonia
- Pyomyositis

**Symptoms viral OR bacterial**
- Severe
- Neutropenia
- Neonates
- Lung infection
- Mucositis
- Scarlet fever
- Endocarditis
- Abscess
- Shock
- Fever
- LRTI
- No empyema
- Septic/septic

**VIRAL syndrome**
- Bronchiolitis
- Viral-induced whooping
- Group
- Varicella
- Herpes simplex
- Flu-like illness
- Hand-foot-mouth
- Rash
- Parotitis/measles
- Encephalitis
- Infection / pneumonia
- AKIS
- Adenitis

**Other febrile syndrome**
- Not bacterial or viral
- Infection without infection
- Other cause of fever

Review clinical investigation results
Bacteriology, virology, radiology, haematology, chemistry

- Sterile-site pathogenic bacteria, match syndrome
- Bacterial syndrome but no bacteria identified
- Uniliser features OR microbiology does not fit syndrome
- Viral syndrome but no virus identified
- Virus identified that matches syndrome
- Minor illness, & insufficient clinical information
- Other infection, eg malaria
- Uniliser features – infection or inflammatory syndrome
- Matches criteria for inflammatory syndrome

Definite Bacterial
Probable Bacterial
Bacterial syndrome low or no inflam, markers
Unknown bacterial or viral
Viral syndrome high or no inflam, markers
Probable Viral
Definite Viral
Trivial
Other infection
Infection or inflammation
Inflammatory syndrome

*CRP≥50 mg/L, neutrophils ≤12 ×10⁹/L

Legend:
Following discharge, clinical phenotypes were assigned after review of all available clinical and laboratory data including biochemistry, haematology, radiology and microbiology. CRP C-reactive protein

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