Hot or not?
Management of unclassified fever in children in sub-Saharan Africa

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Key messages
• Conditional follow-up of children with non-severe unclassified fever in a low-malaria endemic setting was non-inferior to universal follow-up advice through day 7.
• Allowing community health workers (CHWs) to advise caregivers to return only when a child has continued symptoms can be a more efficient use of resources.

Introduction
• More children seen by CHWs have unclassified fever, as a result of declining malaria prevalence and increased use of malaria diagnostic test.
• Caregivers of children seen with non-severe unclassified fever are advised to take the child to a CHW after two days for re-assessment.
• This study assessed the safety of conditional vs. universal follow-up of children with unclassified fever, hypothesising that the conditional arm does not have a higher treatment failure rate.

Methods
• This two-arm cluster-randomised controlled non-inferiority trial in Southwest Ethiopia randomised 25 health facilities, with 282 CHWs, to universal or conditional follow-up.
• CHWs enrolled children aged 2-59 months with fever and without malaria, pneumonia, diarrhoea or danger signs.
• Caregivers received advice to return after two days (universal arm), or to only come back if symptoms persisted (conditional arm).
• Clinical outcomes were assessed on day 7, and at day 14 and 28 if the child had not recovered; vital status of all children was assessed at day 28.
• Analysis was per-protocol with non-inferiority margin of 4% for treatment failure by day 7, using generalised linear models.

Results

Table 1: Comparison of the primary outcome between groups at day 7

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Conditional, n (%)</th>
<th>Universal, n (%)</th>
<th>Difference</th>
<th>Upper limit, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per-protocol</td>
<td>16 (0.80)</td>
<td>90 (4.61)</td>
<td>-3.81%</td>
<td>0.65%</td>
</tr>
<tr>
<td>Intention-to-treat</td>
<td>19 (0.89)</td>
<td>94 (4.57)</td>
<td>-3.67%</td>
<td>0.57%</td>
</tr>
</tbody>
</table>

*Any of: danger sign, admitted, child death, malaria, pneumonia, diarrhoea, reported fever

Discussion
• A strength of this study was the randomised controlled trial design and compliance to the study protocol was high among CHWs and caregivers.
• Insufficient clinical data was collected on children at enrolment to understand which other symptoms or diagnoses were present.
• However, most children were followed up until day 28. None of them died or were referred, indicating that no child deteriorated to a severe condition.
• We recommend that Ethiopian guidelines, which stipulate conditional follow-up of children with unclassified fever, remain unchanged as best practice in this context.

An independent assessor conducting a follow-up assessment on day 7

Figure 1: Trial profile

For more information
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