What is a breath?
Results from the BREATHE study to assess the reliability of using a video annotation tool as a reference standard for counting respiratory rate in children under five

Charlotte Ward, Senior Research Specialist
c.ward@malariaconsortium.org

ASHTM 68th Annual Meeting – November 23 2019
Pneumonia, respiratory infections and tuberculosis
BREATHE study background
(Breath recognition aid to health experts)
Background

- Pneumonia is the leading infectious cause of death in under-five children
- Community health workers (CHWs) currently count respiratory rate as a proxy sign for pneumonia.
- Manually counting respiratory rate is challenging:
  - It is hard to define what is and is not a breath
  - It is easy to lose count
  - Child may be moving, crying, breathing rapidly
  - External distractions
- Misdiagnosis of suspected pneumonia is common and can lead to over and under treatment with antibiotics and potential death
**Background**

- New, automated respiratory rate counters offer a potential solution
- To introduce new respiratory rate counters, their performance must first be validated
- Developing a **robust reference standard** for evaluating the performance of new respiratory rate counters is challenging and there is currently no gold standard.
- Previous studies have used contemporaneous counting by expert clinicians [1], retrospective review of video recordings by a panel of experts, [2, 3, 4] and other devices including capnography [1] as respiratory rate reference standards.
Timeline - respiratory rate counting and ARIDA field trials

1. Ideation
2. R & D
3. Proof of concept
4. Transition to scale
5. Scaling
6. Sustainable scale

1990s
- Pre-ARIDA: UNICEF and WHO developed ARI timer

2012
- UNICEF and MC field test ARIDA prototype

2014
- UNICEF published a target product profile for ARIDA
- First MC pneumonia diagnostic aid performance studies

2015
- ARIDA partnership formed

2016-2018
- ARIDA large scale pilot implementation
- BREATHE Study

2019
- UNICEF SPRINT
- UNICEF technical consultation

2019-2020
- UNITAID grant to PATH and Alima
- 2030 Sustainable Development Goals (Target 3.2: end preventable deaths of newborns and children under five)
Study methods
Study design and objectives

**Study design:** cross-sectional, mixed methods study

**Study objective:** To measure the reliability of manual video annotation

Primary outcome:

- The agreement between a group of five reviewers assessing the respiratory rate (RR) of selected subjects using a video annotation tool as measured by intra-class correlation coefficient $\rho$.

Secondary outcomes:

- Mean time taken to review a video
- The usability and acceptability of the video annotation tool to the video expert panel as measured by focus group discussion

**Study setting:** Hawassa, SNNPR, Ethiopia

**Data collection:** April-May 2019
Study population: Video Expert Panel

- Health officer or nurse
- 2 years working in health facility with pediatric experience and experience counting respiratory rate
- Excellent written and spoken English
- Certificate in basic computing
- Completed 4-day training:
  - Manual respiratory rate counting test – all within +/- 3 breaths per minute
  - Respiratory rate counting test with annotation tool:
    - all within +/- 2 bpm of each other for a video without distortion
    - 9/10 within +/- 3 bpm of each other for a video with distortion
Study population: Video sample of U5 children with cough/difficulty breathing

- Pool of n=98 videos of children from the previous ARIDA project (conducted at selected hospital in Ethiopia, i.e. Saint Paul’s Hospital and Millennium Medical College in Addis Ababa, Ethiopia).
- Pool of n=48 videos from the previous Pneumonia Diagnostics Project study (conducted at health facilities in Uganda, Ethiopia and South Sudan).
- 51 videos were selected from this pool of n=146 videos via stratified random sampling by video source and to ensure equal age distribution, powered for the primary outcome.
- Each video was reviewed by five randomly selected reviewers from a pool of ten.
Time taken to review a video

• Time taken was self-timed by the reviewer using a stopwatch.
• The length of the video varies by video source (ARIDA or PDP) which might affect the time taken to review the video.
• To account for this, standard time taken was calculated:

   Standard time taken = time taken (secs) / video duration (secs)
Movement period

• The total movement period for each video was calculated by summing up each period of movement between two normal breaths.
• The length of the video varies by video source (ARIDA or PDP) which might affect the duration of movement in the video.
• To account for this, standard movement was calculated:

\[
\text{Standard movement period} = \frac{\text{movement period (secs)}}{\text{video duration (secs)}}
\]
What did the reviewers annotate?

Reviewers were trained to annotate:
- **Certain breaths** (when child is calm and still)
- **Uncertain breaths** (very shallow breaths, incomplete cycles or breaths that are difficult to judge)
- **Distortions** (movement or another interruption)

Tool functionalities:
- Change speed
- Change brightness
- Zoom in/out
## Four possible ways to calculate respiratory rate

WHO integrated case management requirements [5] for counting respiratory rate: count the breaths in one minute, child must be calm

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>How the respiratory rate is calculated</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>[\text{Certain and uncertain breaths during calm} \times 60] (\frac{\text{Total annotation time} - \text{distortion time}}{\text{Total annotation time}})</td>
<td>Less conservative WHO case management guideline</td>
</tr>
<tr>
<td>3</td>
<td>[\text{Certain breaths during calm} \times 60] (\frac{\text{Total annotation time} - \text{distortion time}}{\text{Total annotation time}})</td>
<td>More conservative WHO case management guideline</td>
</tr>
<tr>
<td>2</td>
<td>[\text{Certain and uncertain breaths} \times 60] (\frac{\text{Total annotation time}}{\text{Total annotation time}})</td>
<td>Pragmatic* WHO case management guideline = human counting with ARI timer for 60 seconds</td>
</tr>
<tr>
<td>1</td>
<td>[\text{Certain breaths} \times 60] (\frac{\text{Total annotation time}}{\text{Total annotation time}})</td>
<td>Conservative pragmatic* WHO case management guideline = human counting with ARI timer for 60 seconds</td>
</tr>
</tbody>
</table>

*Assuming that children under five are rarely fully calm and still for 60 seconds in real practice

Annotation software “RR upper”

Annotation software “RR lower”
Quantitative results
Reviewers on the Video Expert Panel
# Characteristics of Video Expert Panel (VEP)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No.</th>
<th>Column %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of panel members</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>80</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Degree</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSC Nurse</td>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>BSC Public Health</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Public Health Officer</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Work place (facility type)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Centre</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Hospital</td>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>Health Centre &amp; Hospital</td>
<td>2</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>[95% Conf. Interval]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>29.9</td>
</tr>
<tr>
<td></td>
<td>27.24; 32.56</td>
</tr>
<tr>
<td>Years of experience in their role</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>5.92; 9.28</td>
</tr>
</tbody>
</table>

Abbreviations: BSc=Bachelor of Science, n=number of panel members with characteristic, 95% CI=95% confidence interval
Children/Video sample
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total No.</th>
<th>Column %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>51</td>
<td>100</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29</td>
<td>57</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>43</td>
</tr>
<tr>
<td><strong>Age group of child</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to &lt; 2 months</td>
<td>19</td>
<td>37</td>
</tr>
<tr>
<td>2 to &lt; 12 months</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>12 to 59 months</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethiopia</td>
<td>40</td>
<td>78</td>
</tr>
<tr>
<td>Uganda</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>South Sudan</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviations: ARIDA=ARIDA Diagnostic Agreement Study, PDP=Pneumonia Diagnostics Project, n= number of children in videos with characteristic, 95% CI=95% confidence interval
Intraclass correlation coefficient
ICC is the proportion of sample variance that can be explained by difference between videos

\[
\text{ICC} = \frac{\text{Between video variance}}{\text{Within video variance} + \text{Between video variance}}
\]

Classification (based on lower limit CI)

- ICC < 0.5: Poor reliability
- 0.5 - 0.75: Moderate reliability
- 0.75 - 0.9: Good reliability
- > 0.9: Excellent reliability
RR Lower Count: Good reliability

ICC = 0.85 [0.79; 0.90]
RR Upper Count: Excellent reliability

Lowest within subject dispersion, highest ICC

ICC = 0.95 [0.93; 0.97]
## ICC by movement: ICC higher when less movement

<table>
<thead>
<tr>
<th>Movement tertiles</th>
<th>N</th>
<th>RR Lower Count ICC [95% CI]</th>
<th>RR Upper Count ICC [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>51</td>
<td>0.85 [0.79; 0.9]</td>
<td>0.95 [0.93; 0.97]</td>
</tr>
<tr>
<td>Lowest tertile</td>
<td>17</td>
<td>0.99 [0.98; 1]</td>
<td>0.99 [0.98; 1]</td>
</tr>
<tr>
<td>Medium tertile</td>
<td>17</td>
<td>0.92 [0.85; 0.96]</td>
<td>0.94 [0.89; 0.98]</td>
</tr>
<tr>
<td>Highest tertile</td>
<td>17</td>
<td>0.5 [0.28; 0.73]</td>
<td>0.86 [0.76; 0.94]</td>
</tr>
</tbody>
</table>

**Note:** Study not powered to detect significant differences between subgroups
Time taken (standard)
Time taken to review a video (standard)

Standard time taken - Based on observations (n=191)

<table>
<thead>
<tr>
<th>Source</th>
<th>Mean</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard time taken = timetaken (secs) / video duration (secs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Source</th>
<th>Mean</th>
<th>95% CI</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIDA</td>
<td>35.0</td>
<td>32.1-37.9</td>
<td>12.6</td>
<td>82.4</td>
</tr>
<tr>
<td>PDP</td>
<td>26.5</td>
<td>24.0-29.0</td>
<td>9.0</td>
<td>78.5</td>
</tr>
</tbody>
</table>
Standard Movement period
Movement period (standard)

Based on observations (n=255)

<table>
<thead>
<tr>
<th>Age group of child</th>
<th>mean</th>
<th>p50</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to &lt; 2 months</td>
<td>21%</td>
<td>14%</td>
<td>0</td>
<td>77%</td>
</tr>
<tr>
<td>2 to &lt; 12 months</td>
<td>20%</td>
<td>15%</td>
<td>0</td>
<td>74%</td>
</tr>
<tr>
<td>12 to 59 months</td>
<td>10%</td>
<td>4%</td>
<td>0</td>
<td>58%</td>
</tr>
<tr>
<td>Total</td>
<td>17%</td>
<td>12%</td>
<td>0</td>
<td>77%</td>
</tr>
</tbody>
</table>

On average across all videos, 17% of annotation period is annotated as movement.

There is less movement in children 12-59 months.

Standard movement period = movement period (secs) / video duration (secs) → Proportion of video with movement.
Qualitative results
Focus group discussion

• Two focus group discussions with the video panel reviewers were conducted to explore the usability and feasibility of the video annotation tool.

• Thematic analysis of the qualitative data was conducted using MAXQDA.
# Qualitative results

<table>
<thead>
<tr>
<th>Themes</th>
<th>Sub-themes</th>
<th>Associated Quotes</th>
</tr>
</thead>
</table>
| 1. Operational factors that facilitate usability | Keep training & practice to counter initial confusion and increase confidence | • "The big thing here is practice is mandatory. Unless you exercise repeatedly, even normal breathes may confuse you, you may consider normal breathe as uncertain. It takes time to do that. But through time, as you well understand the tool, it becomes easy to count."
| | Keep standard operating procedures | • "[talking about SOP] it is good if it is availed whenever we want to refer it."
• "How you can do something without SOPs! You do things by following it as states this is this and do this like this. You need it to refer even if you miss something. So, it was very important."
| | Keep easy to use functionalities | • "English is simple and easy because when you translate to Amharic, sometimes it puts us in confusion."
• "We practiced each of these things including how to manipulate [i.e. using tool functionalities]. It is not difficult thing."
| | Avoid using videos of insufficient quality and avoid hardware challenges | • "the quality of mouse and other devices is mandatory."
• "some videos were not clear to see respiration. So, it would be better if videos rerecorded by high quality HD cameras that shows clearly."

# Qualitative results

<table>
<thead>
<tr>
<th>Themes</th>
<th>Sub-themes</th>
<th>Associated Quotes</th>
</tr>
</thead>
</table>
| 2. Benefits of the tool     | Ability to consider new elements                     | • "this video annotation tool can identify normal breathe, uncertain breathe and distortion or other movements [...]. So, [...] the tool helps us to accurately count [...] respiratory rate of a child."  
  • "when health workers count respiratory rate, it is subjective and differs from person to person. So, the tool is to standardize it by using software" |
|                             | Tool functionalities support marking breaths in more difficult children | • "By changing color, we can see whether the movement is normal breath or shallow or distortion."  
  • "when there is distortion, we change brightness it shows movement more clearly"  
  • "When you see uncertain shallow breath, you may zoom from 1cm to 2cm and can see it." |
### Qualitative results

<table>
<thead>
<tr>
<th>Themes</th>
<th>Sub-themes</th>
<th>Associated Quotes</th>
</tr>
</thead>
</table>
| 3. Limitations of the tool     | Videos with lots of distortions, movement and uncertain breaths are difficult to annotate | • "It was difficult to me to mark because you can’t calm children as actual patient. And you can’t seek help from other."
• "when child is restless and crying, the abdomen becomes rigid and breathing can’t be seen."
• "I may miss some breathes in the mid of distortion."
|                                | Even though functionalities help annotating "difficult" videos, using them takes time and attention | • "If child is severely sick, RR increases and marking many breathes is time consuming. I remember a video took 63 minutes from me. And spending such time on single video is a little challenging."
• "if there is distortion or shallow breathing, it consumes time when you go forward and backward and changing brightness etc. It can take up to 50 minutes or an hour."
• "To find [respiration in mid of distortion] you go forward and backward. Because you should annotate it. It is that time challenging."

## Qualitative results

<table>
<thead>
<tr>
<th>Theme</th>
<th>Associated quotes</th>
</tr>
</thead>
</table>
| **4. Trust in the tool** | - "if difference [between result of annotation tool and other device] occurs, I will use the result of the video annotation tool because I trust my count."  
- "Probably I can consider as good. Of course, nothing is perfect. But relatively it is good as compared to others that we have been using to count respiratory rate because it considers something that previous tools did not consider."
- "To set reference, normal videos should be assessed to set reference for normal breathing. For videos with distortion, the tool should be revised [to 1) software that automatically detect distortion or 2) train experts only on distortion and test for distortion separately]"
- "what if distorted area is skipped from video. [...] I think it is better to consider area where there is minimal distortion and it may improve accuracy."
- "In the cases of differences, I may redo it up to three times with attention. When you redo repeatedly, you become confident and choose your own results." |
Conclusion, limitations and recommendations
Conclusion, limitations and further work

Conclusion
• Video annotation has potential as a reliable reference standard, if marking of breaths in the distorted period can be improved.
• Video annotation allows reviewers to consider new elements when counting respiratory rate and the tool’s functionalities supported the reviewers in marking these elements, but it is time consuming.

Limitations
• Visual reference standards have inherent limitations due to human subjectivity:
  • Humans do not always mark breaths in the same way, particularly when there is distortion
  • Operational considerations, for example: time taken to review, professional videographer required

Further work:
• Consensus building around which elements to include in the calculation of respiratory rate when using video annotation as a reference standard is required.
Acknowledgements

• St Paul’s Hospital, Addis Ababa, Ethiopia
• Yrgalem District Hospital in Ethiopia
• Mpigi Health Centre IV in Uganda
• Aweil General Hospital in South Sudan
• Reviewers on the video expert panel
• Colleagues at Malaria Consortium: Dr Kevin Baker and Ann-Sophie Stratil
• Senior Scientist at Philips Research who provided the video annotation software and technical support
References


Thank you

www.malariaconsortium.org
About Malaria Consortium

Malaria Consortium is one of the world’s leading specialist non-profit organisations. Our mission is to improve lives in Africa and Asia through sustainable, evidence-based programmes that combat targeted diseases and promote child and maternal health.