ARIDA field trials – update on ARIDA device agreement and acceptability studies in Ethiopia and Nepal

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Child Health Task Force – Implementation Science sub-group, September 26th 2018
Contents

1. Overview of pneumonia and ARIDA field trials

2. ARIDA diagnostic agreement study: ChARM
   - Methods, results and learnings

3. ARIDA acceptability study: ChARM and Rad-G
   - Methods and progress update

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Overview of pneumonia and ARIDA field trials

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Overview of pneumonia and ARIDA field trials

Problem

• Pneumonia is the leading cause of death from infectious disease in U5 children worldwide
• Pneumonia is under-diagnosed and inaccurately treated
• Pneumonia deaths are concentrated within poorest populations
• Investment in pneumonia R&D is low

Potential solutions

• Increase availability of improved tools to support frontline health workers diagnose pneumonia
• Improve access to treatment: antibiotics and oxygen therapy
Overview: Acute Respiratory Infection Diagnostic Aids

Image: Philips ChARM device: automated respiratory rate counter

Image: Masimo Rad-G device: fingertip pulse oximeter
Diagnostic agreement study: ChARM
St Paul’s Hospital Addis Ababa, Ethiopia, April – May 2017

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Diagnostic agreement study: ChARM

Study objectives:

- To assess the agreement* between the respiratory rate (RR) count of ChARM and the RR count of the reference standard, a video expert panel (VEP)

- To assess the agreement* between two ChARM devices counting RR for the same child at the same time

- To assess the agreement* between the on-the-spot RR count by an expert clinician (EC) and the RR count of the reference standard, a video expert panel (VEP)

- To assess the agreement* between two ECs counting RR for the same child at the same time

*Agreement is presented in terms of:
1) mean absolute difference in RR counts (root mean square difference);
2) binary classification of children to the ‘fast breathing’ and ‘normal breathing’ groups.
Diagnostic agreement study: ChARM

Reference standard:
Video expert panel (VEP)

60-second video of the child’s chest movements taken at the same time as the ChARM and EC evaluation

VEP respiratory rate (RR) compared to ChARM and EC RR

Image: Diagnostic agreement study pre-test – a child is being assessed by the ChARM device and by an expert clinician using the MK2 ARI timer. The assessment is being recorded on video
Diagnostic agreement study: ChARM

Inclusion criteria:
• Child aged 0-59 months presenting
• Parent or guardian consent
• Cough and/or difficulty breathing for 2-59 month olds

Exclusion criteria:
• Child with general danger signs
• Child with signs of severe pneumonia
• Child with IMNCI pink referral signs for severe disease
• Parent/guardian under 16 years
• Device manufacturer safety exclusion criteria

The study also enrolled a 3:1 ratio of fast:normal breathing cases
Diagnostic agreement study: ChARM

- Screened: 152
- Eligible: 128
- Consent: 128
- Eligibility confirmed: 124
- Children evaluated: 108
- Device readings: 106
- Paired readings: 101
- Per-protocol analysis: 98
- No device readings: 4
- Reference unavailable: 5
- Per-protocol exclusions: 3
- SAEs (all evaluations): 0
- ChARM device faults reported (all evaluations): 4
- ARI device faults reported (all evaluations): 0

- Lost to follow-up: 0
- Consent withdrawn: 1
- Change in eligibility: 2
- Unable to calm child: 13

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Results:

Table 1: ChARM and expert clinician agreement with video expert panel

<table>
<thead>
<tr>
<th></th>
<th>Root mean square difference</th>
<th>Positive percent agreement (%) (95%CI)</th>
<th>p-value</th>
<th>Negative percent agreement (%) (95% CI)</th>
<th>p-value</th>
<th>Kappa (interpretation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChARM agreement with VEP (n=98)</td>
<td>9.3</td>
<td>81.5 (68.6, 90.7)</td>
<td>1</td>
<td>84.1 (69.9, 93.4)</td>
<td>1</td>
<td>0.65 (moderate)</td>
</tr>
<tr>
<td>EC agreement with VEP (n=98)</td>
<td>5.3</td>
<td>92.6 (82.1, 97.9)</td>
<td>0.076</td>
<td>75 (59.7, 86.8)</td>
<td>0.3</td>
<td>0.69 (moderate)</td>
</tr>
</tbody>
</table>

Based on agreement between respiratory rate counts:
• the ChARM device agrees less with human experts than humans agree with each other (RMSD 9.3 vs. 5.3)

Based on the binary classification of children to the ‘fast’ and ‘normal’ breathing groups,
• ChARM is not significantly different from the EC at classification of RR in both fast (p=0.076) and normal (p=0.3) breathing cases.
• Overall agreement in classification with the VEP was moderate for both ChARM (K=0.65) and EC (K=0.69).
Results:

Table 2: Interrater agreement between two ChARM devices, two VEP members and two ECs

<table>
<thead>
<tr>
<th></th>
<th>Root mean square difference</th>
<th>Positive percent agreement (%) (95%CI)</th>
<th>Negative percent agreement (%) (95% CI)</th>
<th>Kappa (interpretation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChARM vs. ChARM</td>
<td>4.2</td>
<td>84.2 (60.4, 96.6)</td>
<td>100 (81.5, 100)</td>
<td>0.84 (strong)</td>
</tr>
<tr>
<td>(n=37)</td>
<td></td>
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</tr>
<tr>
<td>VEP 1 vs VEP 2</td>
<td>4.2</td>
<td>92.9 (82.7, 98)</td>
<td>91.8 (80.4, 97.7)</td>
<td>0.85 (strong)</td>
</tr>
<tr>
<td>(n=105)</td>
<td></td>
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</tr>
<tr>
<td>EC vs. EC</td>
<td>6.6</td>
<td>82.4 (56.6, 96.2)</td>
<td>100 (83.2, 100)</td>
<td>0.83 (strong)</td>
</tr>
<tr>
<td>(n=37)</td>
<td></td>
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</tbody>
</table>

Based on agreement between respiratory rate counts:
- **Human expert counters do not agree with each other perfectly**, but agree more when assisted with videos (RMSD=6.6 and 4.2 bpm)
- **Inter-ChARM agreement is similar to two VEP members** (4.2 bpm)

Based on the binary classification of children to the ‘fast’ and ‘normal’ breathing groups:
- Human inter-rater agreement and inter-ChARM agreement in RR classification is strong
Diagnostic agreement study: ChARM

Conclusions
- ChARM is not significantly different from the EC at RR classification - you can replace a human counter with this device.
- The findings from this study cannot support or challenge ChARM accuracy:
  - Large differences observed between human expert counters. Neither VEP or EC can be used as a reference standard.
  - ChARM measures a slightly different breath sequence (mean time taken for RR=79 seconds)
  - ChARM adjusts for non-breathing movement
- Further work is needed to refine reference standards for new RR devices
  - Video annotation software
  - Larger panel of experts
Acceptability study: ChARM and Rad-G
Acceptability study: ChARM and Rad-G

Conceptual framework of frontline health workers’ adherence to iCCM/IMCI guidelines, adapted from Adams et al., 2017
Acceptability study: ChARM and Rad-G

Specific objectives:
1. To determine if CHWs using an ARIDA adhere to iCCM algorithms and correctly assess and classify children under-five with cough and/or difficult breathing after two months of routine use.
Acceptability study: ChARM and Rad-G

Specific objectives:
2. To document the user experience of ARIDA in a sick child consultation.

- Number and type of errors made during the management of the sick child using ARIDA (assessment, classification, treatment, referral)
- Mean time taken to complete the sick child assessment
- Number of unsuccessful attempts and failures using ARIDA
- Number of children assessed by health workers with ARIDA during routine care
Acceptability study: ChARM and Rad-G

Specific objectives:
3. To explore the acceptability of the ARIDA to frontline health workers and caregivers
Acceptability study: ChARM and Rad-G

Methods

1. Health worker training on iCCM/IMCI and device
2. Quantitative evaluation 1
3. Routine device use for 2 months. Routine data collected.
4. Quantitative evaluation 2

Sample of caregiver exit interviews and SSI
Sample of health worker exit-interviews and SSI
Acceptability study: ChARM, SNNPR, Ethiopia
Acceptability study: Rad-G, SNNPR, Ethiopia

Image: mother and child waiting for the Rad-G assessment, Ethiopia, July 2018
Acceptability study: ChARM, Jumla, Nepal

Image: Female community health volunteer, Jumla district, Nepal, September 2018
Acknowledgements

• ‘la Caixa’ Banking Foundation – donor
• Federal Ministry of Health, Ethiopia
• SNNPR Regional Health Bureau, Ethiopia
• Ministry of Health, Nepal
• District Health Office, Jumla, Nepal
• HERD International – implementing partner in Nepal
• Research teams in Ethiopia and Nepal
Thank you