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ACUTE RESPIRATORY INFECTION DIAGNOSTIC AID: LEARNINGS AND NEXT STEPS

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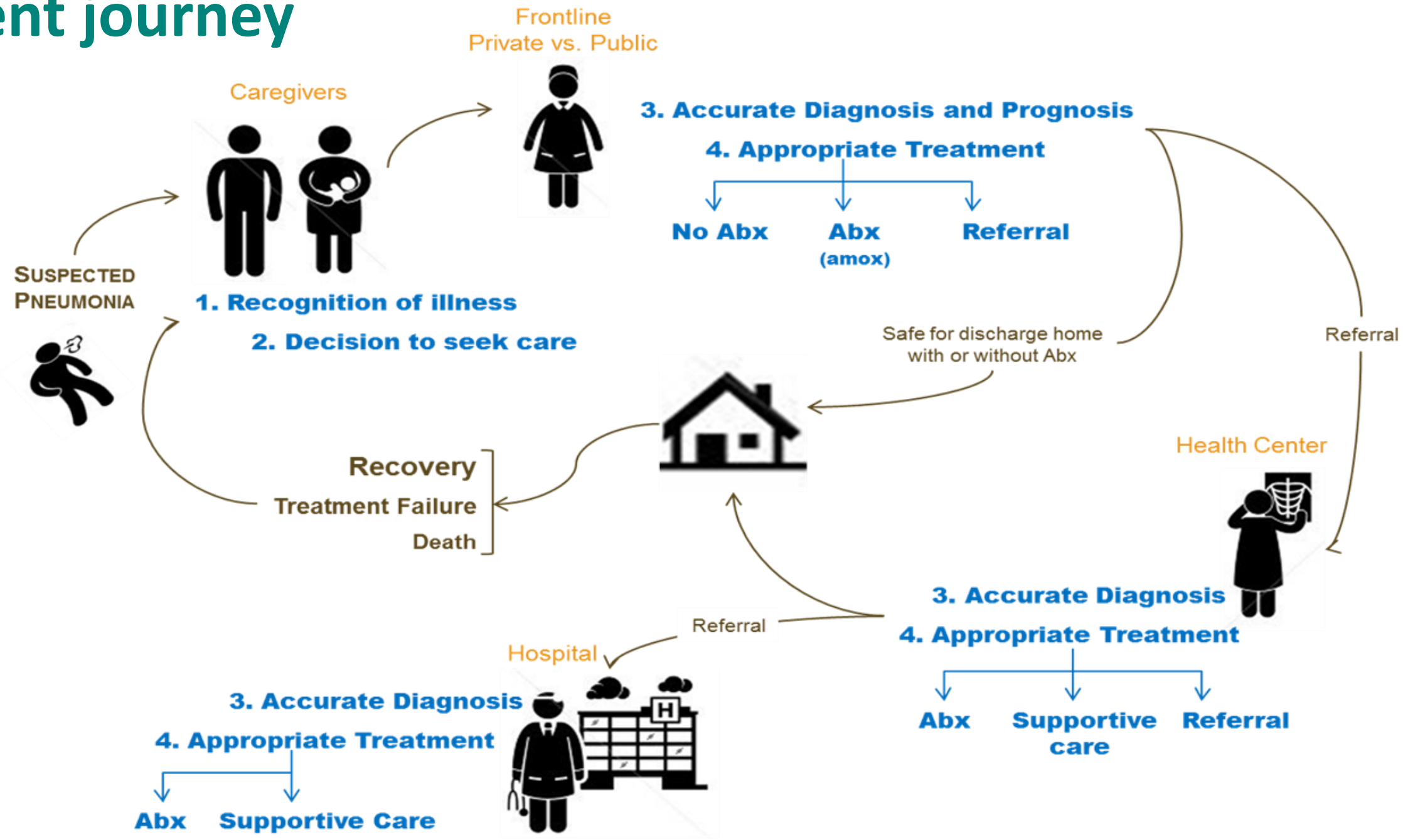
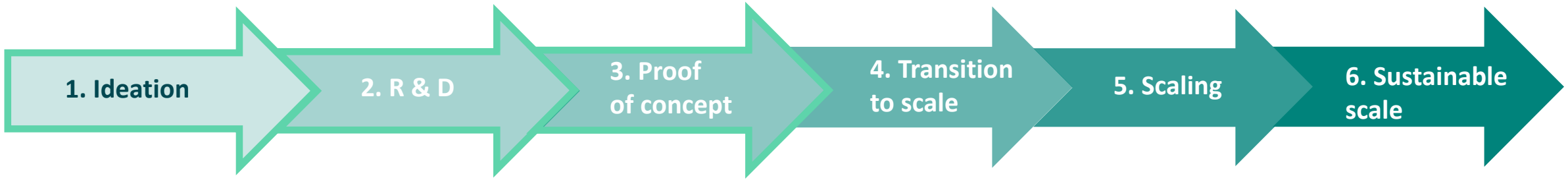
Patient journey



Introduction

- Community health workers (CHWs) across the world currently use respiratory rate (RR) as a proxy sign for pneumonia.
- Literature from Ethiopia has shown that manually counting breaths per minute is challenging (Spence et al 2018) as:
  - it is hard to define what is and is not a breath
  - it is easy to lose count
  - the child may be moving, crying and/or breathing rapidly.
- Ethiopia is among the 15 top under-five pneumonia high burden countries (JustActions 2018).
- Pneumonia is the single leading cause of death among under-fives in Ethiopia. It is estimated to affect 3,370,000 children and kill over 40,000 under-fives every year.

Timeline — RR counting and ARIDA field trials



Pre-ARIDA: UNICEF and WHO developed ARI timer

1990s

2012

UNICEF and MC field test ARIDA prototype

UNICEF published a target product profile for ARIDA

2013

2014

First MC pneumonia diagnostic aid performance studies

ARIDA partnership formed

2015

2016-2018

ARIDA field trials by MC

ARIDA large scale pilot implementation

2018

BREATHE Study

2019-2020

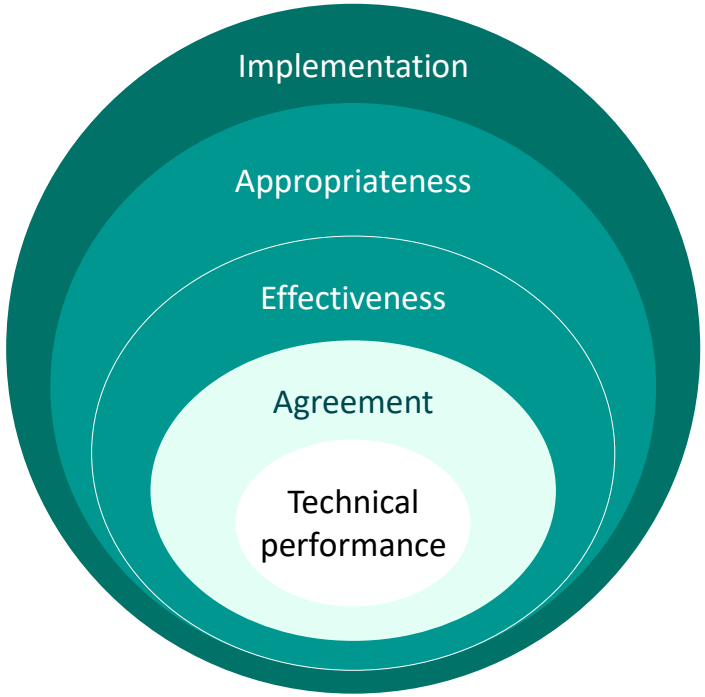
UNITAID/UNICEF SPRINT/etc. – more focus on diagnostics

UNICEF technical consultation

2030 Sustainable Development Goals (Target 3.2: end preventable deaths of newborns and children under five)

Stages of introducing a new technology

ARIDA project phases	Areas to address
Rollout	How should the technology be scaled up in this setting?
ARIDA acceptability study	Should the technology be implemented in this setting? Is it acceptable to health workers at different levels of the system and caregivers in this setting? Does ARIDA improve the correct classification of RR and pneumonia, and treatment of children under 59 months with cough and/or difficult breathing by CHWs?
Agreement study	Does ARIDA accurately measure RR in children under 59 months in a controlled setting?
ARIDA dossier review	Are there any concerns regarding whether the device meets the safety and technical specification required?



Adapted from 'Health technology assessment of medical devices' by WHO (2011) and 'Introducing new technology safely' by Mytton et al. (2010).

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ARIDA agreement study — ChARM in Ethiopia

ARIDA agreement study

- **Study design:** cross-sectional, prospective
- **Study setting:** St Paul's Hospital, Addis Ababa, Ethiopia
- **Data collection period:** April to May 2017
- **Main objective:** to assess the agreement between the RR count of ChARM and the RR count of the reference standard (a video expert panel)

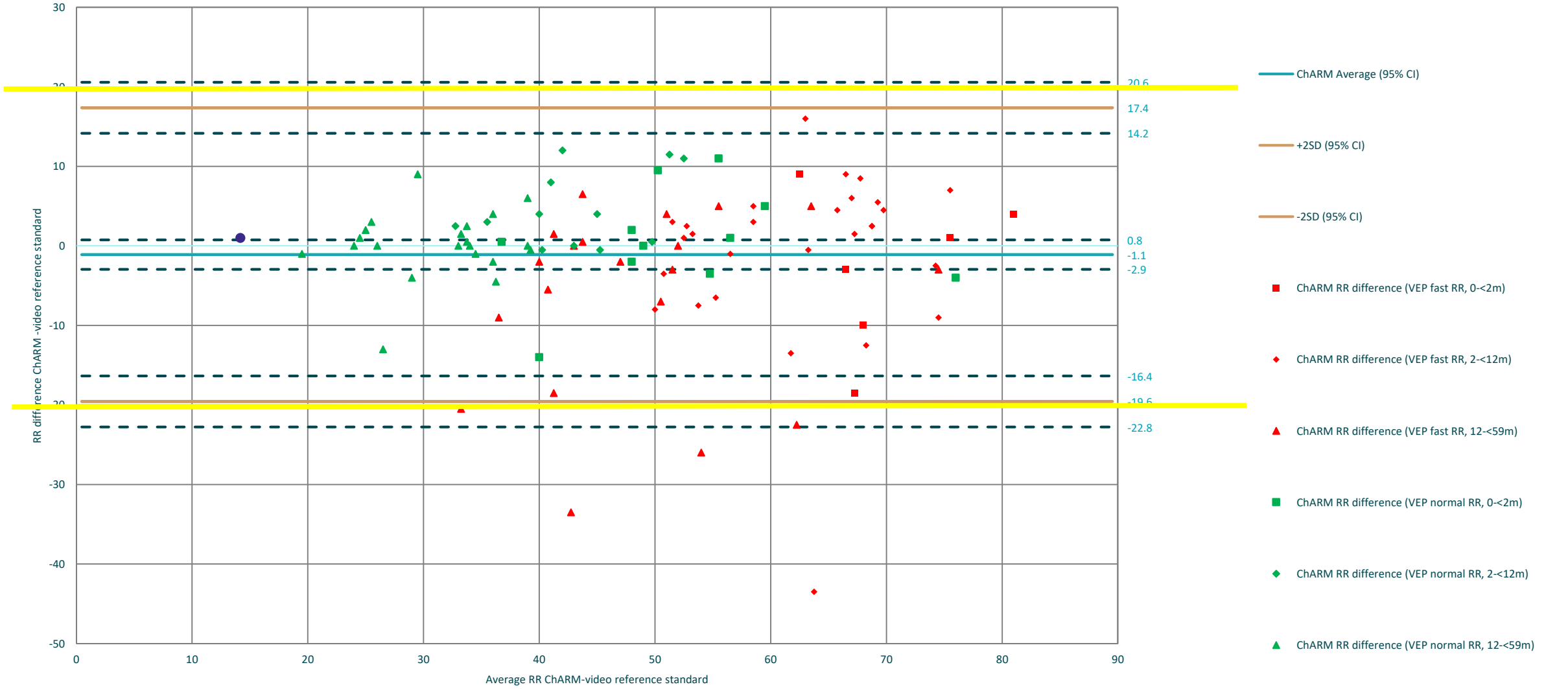
Study stopped early due to device programming fault

ARIDA agreement study — reference standard

Reference standard methods:

- two to four independent video reviewers
- all practising paediatricians with more than five years experience
- all passed a RR counting competency exercise
- 60 second videos of the child's chest
- stepwise review: 2+1+1
- mean RR between two closest reviewers was used as the reference standard.

Bland Altman — ChARM versus video expert panel reference



Yellow lines = acceptable performance

ChARM and expert clinician agreement with video expert panel

	Mean difference/bias (limits of agreement)	Positive percent agreement (95% CI)	p-value	Negative percent agreement (95% CI)	p-value	Kappa (interpretation)
ChARM agreement with VEP (n=98)	-1.1 (-19.6 to 17.4)	81.5 (68.6, 90.7)	[ref]	84.1 (69.9, 93.4)	[ref]	0.65 (moderate)
Expert clinician agreement with VEP (n=98)	1.8 (-8.2 to 11.9)	92.6 (82.1, 97.9)	0.076	75 (59.7, 86.8)	0.3	0.69 (moderate)

Based on agreement between **RR counts**:

- **ChARM agrees less with human experts than humans agree with each other** (LOAs).

Based on the binary **classification** of children to the 'fast' and 'normal' breathing groups:

- **ChARM's classification of RR is not significantly different from the expert clinician's (EC)** in both fast (p=0.076) and normal (p=0.3) breathing cases.
- Overall **agreement in classification with the video expert panel (VEP) was moderate** for both ChARM (K=0.65) and EC (K=0.69).

Summary of findings

Recent UNICEF-convened technical consultation in New York with 30 child health experts agreed that:

- there is no gold standard for evaluating RR devices and a consensus view on acceptable performance is required
- performance should be presented using Bland Altman plots
- an acceptable level of performance would be a plot with LOAs of ±20 breaths per minute.

Conclusions/recommendations:

- Results from the agreement study show an acceptable level of performance from ChARM.
- ChARM is not significantly different from the EC at RR classification level.
- The methods and results of the agreement study should be published.
- Meta-analysis to show performance across all studies (using same statistics) should be conducted.

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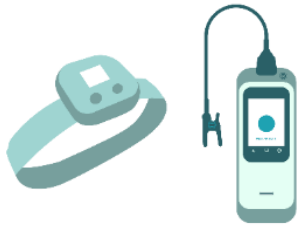
Testing ARIDA usability and acceptability

ARIDA usability and acceptability studies

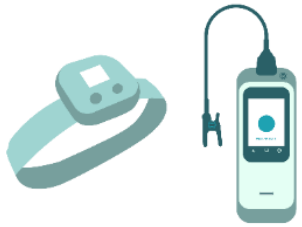


- **Study design:** cross-sectional, community-based
- **Study settings:** Southern Nations, Nationalities, and Peoples' Region (SNNPR), Ethiopia (ChARM and Rad-G) and Karnali region, Nepal (ChARM only)
- **Data collection period:** three studies implemented between May and December 2018

- **Main objectives:**
  1. Usability: to determine if CHWs* adhere to World Health Organization (WHO) requirements to assess fast breathing and device manufacturer instructions for use to assess and classify children under five with cough and/or difficult breathing using an ARIDA device.
  2. Acceptability: to explore the acceptability of the ARIDA devices to CHWs, first level health facility workers (FLHFWs) – Ethiopia only – and caregivers.

**Known as health extension workers (HEWs) in Ethiopia and female community health volunteers (FCHVs) in Nepal.*

Overview of the stages of the studies



132 CHWs and 20 FLHFWs trained on iCCM/IMNCI and using ARIDA device(s)*

→

Observation 1: CHWs using an ARIDA device on two children (after training**)

→

Routine ARIDA use for approx. two months. Frequency of ARIDA device use collected in patient registers

→

Observation 2: CHWs using an ARIDA device on two children (after approx. two months of routine use)

↑ Semi-structured interviews with a sample of caregivers

↓ Semi-structured interviews with a sample of CHWs and FLHFWs

**CHWs and FLHFWs completed pre and post-training tests that were designed to assess their understanding of the iCCM/IMNCI guidelines and ARIDA device(s).*

***Rad G only: a half-day refresher training was provided to CHWs on how to read and interpret the pleth wave form and ensure the signal is strong enough to get oxygen saturation (SpO2) and RR readings.*

Child consultation steps observed — ChARM

	Consultation step	Definition	Category
1	Correct child position	Back fully supported, either in the arms of the caregiver (younger child) or sat on the caregiver's lap with their back against the caregiver's front (older child) or lying on their back on a flat surface (older child).	Device manufacturer instructions for use
2	Correct device position	Device on the belly line in line with the nipple.	Device manufacturer instructions for use
3	Correct belt attachment	ChARM touching skin/clothing and belt not tangled.	Device manufacturer instructions for use
4	Correct age group	Age group selected by CHW on ChARM matches screening checklist.	WHO requirements to assess fast breathing
5	Correct child behaviour immediately before ChARM attempt	Calm: not actively crying or moving.	WHO requirements to assess fast breathing
6	Correct child eating/breastfeeding status during successful ChARM attempt	No eating/breastfeeding.	WHO requirements to assess fast breathing
7	Correct child behaviour during successful ChARM attempt	Calm: not actively crying or moving.	WHO requirements to assess fast breathing
8	Correct classification	According to iCCM/CB-IMNCI guidelines, based on screening age group and breathing status of the child	WHO requirements to assess fast breathing
9	Correct assessment and classification (stages 1-8)	FCHV correctly completed all steps 1-8	n/a
10	Correct referral guidance using ChARM classification and FCHV's assessment of other symptoms (yes/no?)	According to IMNCI guidelines, based on age group recorded during child screening, and breathing status of the child. N.B FCHV will not be marked as 'incorrect' if caregiver refused referral or other valid reason for no treatment recorded	n/a

CHWs had three attempts to obtain RR classification with ChARM. If they did not acquire a RR reading within these attempts, they moved onto using the ARI timer.

Child consultation steps observed — Rad-G

	Consultation step	Definition	Source of step
1	Child calm before assessment	Calm: not actively crying or moving	WHO requirements to assess fast breathing
2	Correct mode selected	Screening mode	Device manufacturer instructions for use
3	Correct age group	Age group recorded by HEW on Rad-G device matches screening checklist	WHO requirements to assess fast breathing
4	Correct probe position	Fully inserted	Device manufacturer instructions for use
5	Correct probe direction	Picture on top of finger or toe	Device manufacturer instructions for use
6	Child not eating/feeding during assessment	No eating/breastfeeding	WHO requirements to assess fast breathing
7	Child calm during assessment	Calm: not actively crying or moving	WHO requirements to assess fast breathing
8	Correct classification	According to iCCM guidelines, based on screening age group and breathing status of the child	WHO requirements to assess fast breathing
9	Correct assessment and classification (stages 1-8)	HEW correctly completed all steps 1-8	Device manufacturer instructions for use and WHO requirements to assess fast breathing
10	Correct treatment and referral guidance using RAD-G classification and HEW's assessment of other symptoms (yes/no?)	According to iCCM guidelines, based on age group recorded during child screening, and breathing status of the child. N.B HEW will not be marked as 'incorrect' if there was stock-out of antibiotics, caregiver refused treatment or other valid reason for no treatment recorded	WHO requirements to assess fast breathing

CHWs had three attempts to acquire RR and SpO2 classification with Rad-G. If they did not acquire RR and SpO2 readings within these, they moved to using the ARI timer.

Summary of findings

Outcome	Ethiopia ChARM Percent (95% CI)	Ethiopia Rad-G Percent (95% CI)	Nepal ChARM Percent (95% CI)
Adherence to all eight required guidelines after two months	74.6 (69.9–79.3) N=335	85.3 (80.2–89.3) N=238	52.8 (46.6–58.9) N=252
Change in adherence to required guidelines over two months	+18.6	+8.9	+2.8
Steps with lowest adherence to required guidelines after two months	1) Correct child position: 81.0 (76.8–85.2) 2) Correct device position: 94.7 (92.3–97.1) N=337	1) Correct age group: 95.0 (91.5–97.1) 2) Child calm before assessment: 95.8 (92.5–97.6) N=259	1) Child calm before assessment: 84.2 (79.1–88.2) 2) Correct child position: 85.0 (80.0–88.9) N=253

Outcome	Ethiopia ChARM Percent (95% CI)	Ethiopia Rad-G Percent (95% CI)	Nepal ChARM Percent (95% CI)
% Adherence to required guidelines after two months 1) Manufacturer instructions for use 2) WHO requirements to assess fast breathing	1) 76.9 (72.4–81.4) 2) 94.4 (91.9–96.8) N=337	1) 97.3 (94.4–98.7) 2) 80.3 (75.0–84.7) N=259	1) 79.1 (73.6–83.7) 2) 66.4 (60.3–72.0) N=253
% Adherence to required guidelines after two months 1) Fast breathers* 2) Normal breathers* *as determined by ARIDA and verified by source documents (screening checklist and ARIDA photo)	1) 79.6 (72.2–87.1) N=113 2) 72.1 (71.1–82.9) N=222	1) 68.6 (54.3–80.1) N=51 2) 89.8 (84.6–93.5) N=187	1) 24.2 (12.1–42.6) N=33 2) 57.1 (50.4–63.5) N=219

Outcome	Ethiopia ChARM	Nepal ChARM	Ethiopia Rad-G
% Adherence to required guidelines after two months (95% CI) 1) 0–<2 months 2) 2–<12 months 3) 12–59 months	1) 91.7 (85.3–98.1) N=72 2) 76.6 (69.6–83.6) N=141 3) 62.3 (53.7–70.9) N=122	1) 71.4 (21.5–95.8) N=7 2) 42.9 (32.1–54.3) N=77 3) 56.5 (48.9–63.9) N=169	1) 100.0 N=6 2) 87.3 (76.2–93.6) N=63 3) 84.0 (77.6–88.9) N=169
Mean time taken to complete the sick child consultation after two months (min, inter-quartile range (IQR), max) (minutes: seconds)	03:17 Min: 01:12 IQR: 02:26 to 03:45 Max: 15:13	04:26 Min: 01.15 IQR: 02:42 to 05:26 Max: 25:26	05:42 Min: 01:30 IQR: 03:40 to 06:26 Max: 22:31

Outcome	Ethiopia ChARM Number (percent)	Nepal ChARM Number (percent)	Ethiopia Rad-G Number (percent)
Number of attempts that were unsuccessful using ARIDA: 1) After training 2) After two months	1) 35 (11.9%) N=294 2) 34 (9.2%) N=369	1) 66 (20.1%) N=328 2) 56 (18.2%) N=308	1) 294 (60.1%) N=489 2) 94 (28.3%) N=332
Number of times no ARIDA reading could be obtained within three attempts: 1) After training 2) After two months	1) 3 (1.1%) N=262 2) 2 (0.6%) N=337	1) 2 (0.8%) 2) 1 (0.4%)	1) 69 (26.1%) N=264 2) 21 (8.1%) N=259

Usability

After two months, usability was different in each country due to their unique environments and populations of health workers.

Ethiopia:

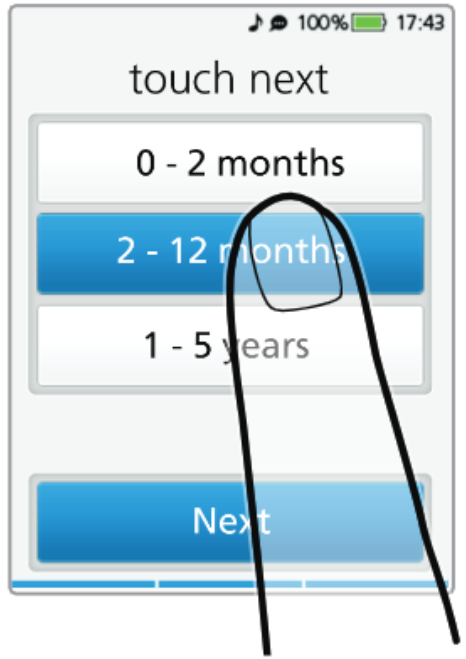
- Using the ChARM and Rad-G devices, CHWs in Ethiopia were able to adhere to WHO requirements to assess fast breathing and device manufacturer instructions for use.
- Practice improved their ability to take RR and SpO2 readings.
- HEWs found it more difficult to adhere to revised WHO required steps using Rad-G.
- The mean time taken to get a reading was over three minutes for both devices.

Across the three studies, there is not currently enough information to make recommendations in the youngest age group, in fast-breathing children or for the use of pulse oximetry in adhering to guidelines when referring hypoxemic children.

Acceptability

Frontline health workers:

- **preferred** ARIDA to their standard practice device
- felt that **practice** using the device was essential
- felt that ARIDA had increased the **credibility** of the service they provide and **encouraged care seeking behaviour**
- raised **Rad-G design issues** – motion detected, classification outcomes, probe fit and age groups
- reported that the **ChARM belt** was hard to adjust.



Caregivers:

- **accepted** the ARIDA devices and **demanded** for them to be available in future (Ethiopia)
- **initially feared the red light** produced by the Rad-G device.

Key messages from the ARIDA studies

- Some evidence exists on acceptable ChARM performance, but not on Rad-G.
- The ARIDA acceptability studies do not attempt to provide evidence of device accuracy; they were designed to determine usability and explore the acceptability of the devices to CHWs, FLHFWs and caregivers.
- HEWs had high adherence to guidelines and instructions for use for both ChARM and Rad-G.
- Both devices were acceptable to CHWs, FLHFWs and caregivers in Ethiopia, and CHWs felt that they provided support to classify, treat and refer children.
- ARIDA devices need to be introduced with comprehensive training, supervision and job aids.

Five papers are being published.

Recommendations from the usability and acceptability studies

Usability challenges should be considered:

- **Rad-G:** age categories are inconsistent with iCCM guidelines, not exclusive, and positioned too close together. In addition, a lot of concentration was required to use the device (outcomes are complex) and some children became distressed when seeing the red light.
- **ChARM:** HEWs said they sometimes struggled to adjust the ChARM belt, especially on older children.
- Further studies are needed on device performance in routine practice to assess fast breathing in children under five at different levels of the health system.
- Costing studies should be undertaken at country level before roll-out, to plan for costs of procurement, training, maintenance and replenishment.

Next steps and opportunities

1. ChARM – effectiveness study at the community level in Ethiopia to look at performance and cost effectiveness compared to standard practice.
2. Multimodal devices (Rad-G and Utech) – comparative agreement study (cost sharing on devices) to evaluate performance of this new class of devices.
3. Multimodal effectiveness study at health centre level to look at performance and cost effectiveness.
4. Investigate decision support tools to better support iCCM/IMCI delivery – e.g. Feebris.

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