Treatment of Young Infant Infection in Ntcheu District (TYIIN), Malawi

Presentation of preliminary findings

RAcE Multi-Country Dissemination Workshop, Abuja, Nigeria

October 24-27, 2017

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Overview

- Background
- Methods
- Preliminary results
- Conclusions

Study partners:

- *IMCI Unit in the Ministry of Health (MOH)*
- *Ntcheu District Health Office*
- *Save the Children*
- *World Health Organization*

Background

- Infections are a leading cause of newborn and young infant deaths in Malawi
- Full course of injectable antibiotic treatment for young infant infection is only available in inpatient setting at district/central level hospitals – out of reach for many families
- Where referral is not possible, simplified antibiotic regimens delivered in outpatient settings have the potential to save many lives (*WHO Joint Statement*)
- Implementation research is needed to demonstrate the feasibility and acceptability of providing treatment at first level health facilities in Malawi

Background

TYIIN Research objectives

Primary: To evaluate feasibility of treatment of possible serious bacterial infection (PSBI) and fast breathing as a single sign of illness for young infants delivered through first-level care facilities in Malawi

Secondary:

- To evaluate whether first-level health facilities can deliver quality care for PSBI and fast breathing cases
- To assess capacity of Health Surveillance Assistants to follow-up PSBI and fast breathing cases in young infants
- To assess the acceptability by families of PSBI and fast breathing treatment offered at first-level facilities

Study Site Description

NTCHEU district

Population: 588,038

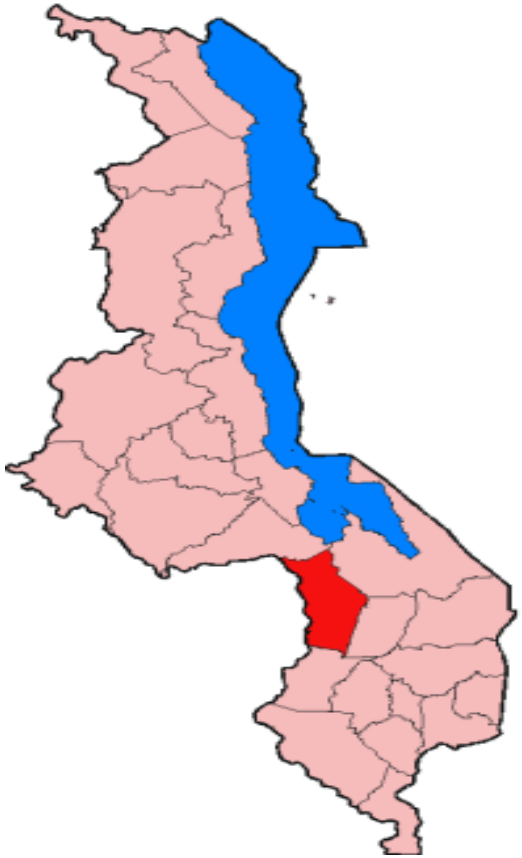
Annual live births: 22,444

Under-five children: 99,966

Health services: District Hospital (referral); 39 first level facilities (28 with maternity); Community village clinics

Study sites

- 12 health centers and their associated HSAs (~148)
- Catchment population ~200,000
- Health center selection was based on:
  - Facility workload and catchment population
  - proximity to the district hospital (ranging from 12-30 km)
  - Presence of facility based providers trained in IMCI
  - Presence of CBMNC trained HSAs



Ntcheu district, Malawi

Study Design

Study design

- Cohort only group design (no comparison group)
- Eligible sick young infants referred by HSAs or self-referrals at first-level facilities whose caregivers refuse or are unable to complete referral enrolled and followed up for 14 days
- Target sample size: 368 sick young infants (conservative, based on treatment completion at 80%)
- Study period:
  - IRB approval: September 2015
  - Pilot enrollment: December 2016 to February 2017
  - Full enrollment: February 22, 2017 to September 14, 2017

Definitions

Fast breathing: respiratory rate equal to or greater than 60 breaths per minute.

Signs of PSBI: not able to feed since birth or stopped feeding well or not feeding at all, convulsions, severe chest in-drawing, fever (temperature ≥ 38 °C), low body temperature (< 35.5 °C), movement only when stimulated or no movement at all, fast breathing (60 breaths per minute or more) in infants less than 7 days old.

Critical Illness: convulsions, unable to feed at all, no movement on stimulation, unable to cry, bulging fontanelle and cyanosis.

Clinical severe infection: not feeding well, fever (temperature ≥ 38 °C), low body temperature (< 35.5 °C), severe chest in-drawing, movement only when stimulated.

Study Outcomes

Primary Outcomes

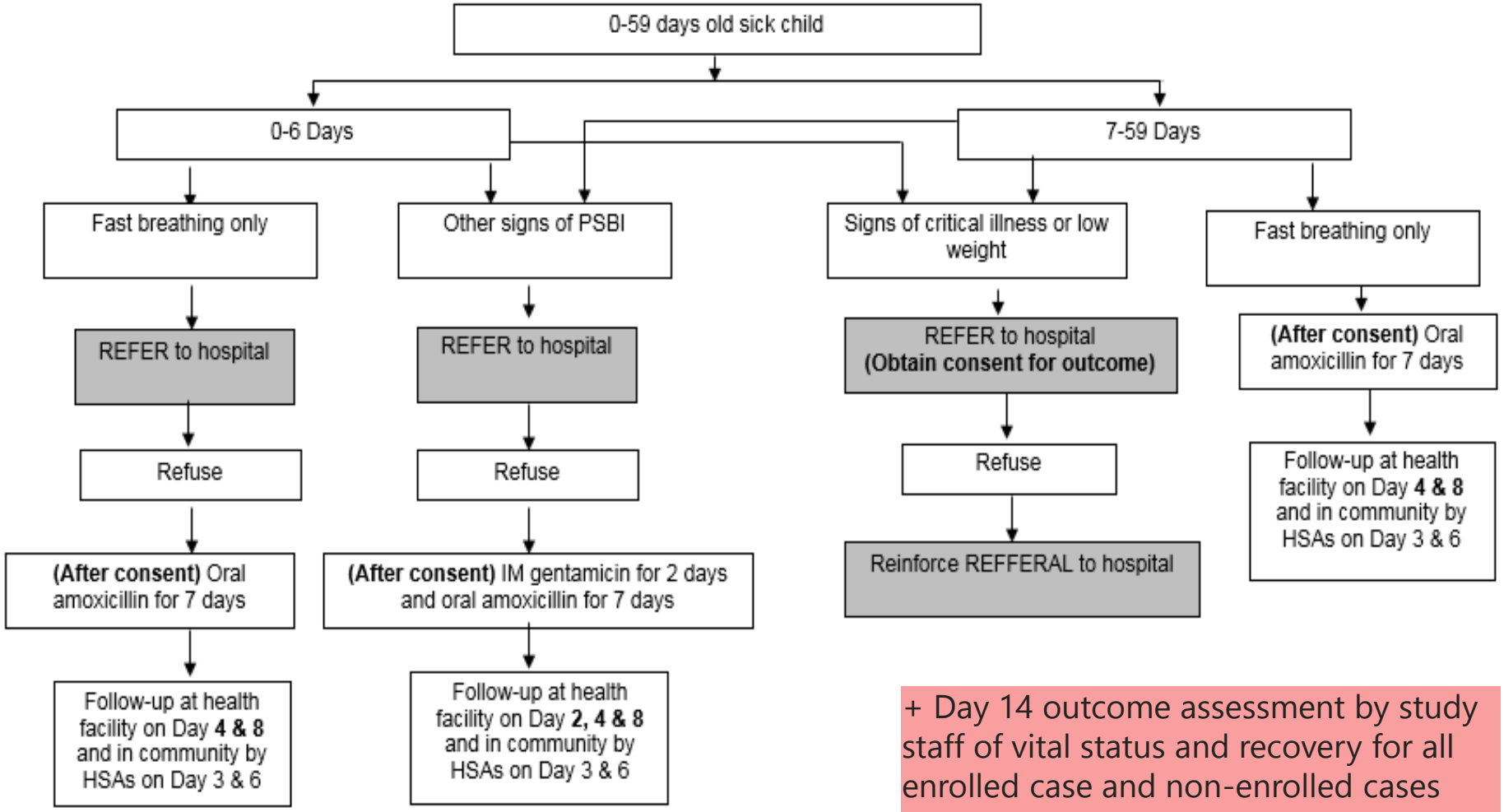
- Treatment failure:* proportion of enrolled cases who experienced clinical deterioration (additional sign of PSBI), serious adverse event (including death), or not cured by day 8 (presence of PSBI sign on Day 8) *[<8%]*
- Treatment completion: proportion of cases completing treatment as per protocol *[Target: >90%]*

Secondary outcomes (selected)

- Proportion of cases identified at first-level facilities that accept outpatient treatment
- Proportion of under-treatment cases who complete mandatory Day 4 follow-up visit at the health facilities
- Proportion of under-treatment cases followed-up by HSAs

**Included as primary outcome to align with WHO-funded PSBI studies*

Intervention description – Patient flow



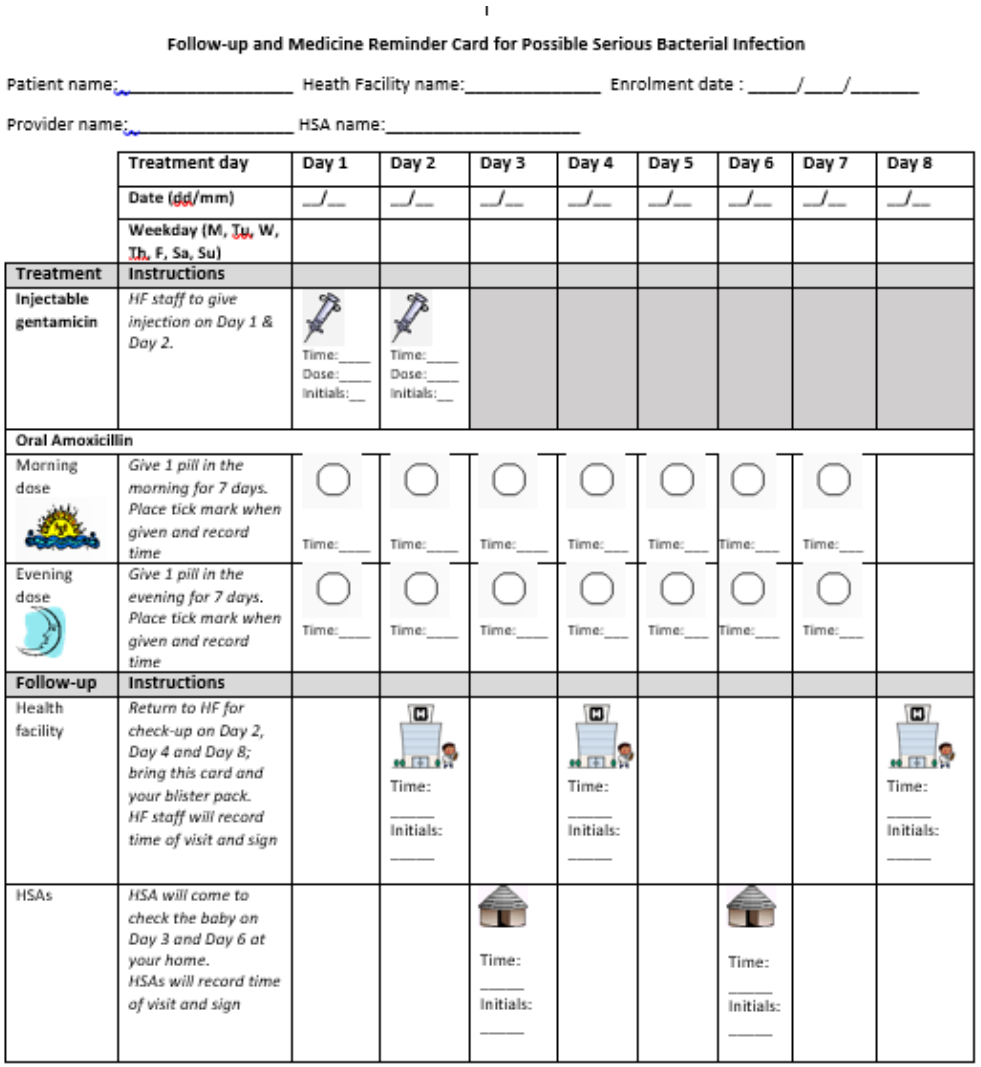
+ Day 14 outcome assessment by study staff of vital status and recovery for all enrolled case and non-enrolled cases accepting referral

Treatment and Follow-up by Day

Day	Treatment and Follow-up Protocol
Day 1 (Enrolment day)	PSBI: 1st dose injectable gentamicin given and 1st dose oral amoxicillin administration observed; told to take evening dose of amoxicillin and return Day 2 for second injection. FB-ONLY: 1st dose of oral amoxicillin administered and caregivers told to take evening dose. All cases - caregivers told to take amoxicillin twice a day for the next 6 days and return for mandatory follow-up on day 4; HF staff inform HSA for follow-up
Day 2	PSBI: 2nd dose injectable gentamicin given; caregivers told to continue taking amoxicillin as per schedule and return on Day 4 for mandatory follow-up
Day 3	HSA visits family and assesses treatment adherence and child's condition and reminds them to go to facility next day for mandatory Day 4 follow-up
Day 4 (Mandatory follow-up at HF)	Mandatory follow-up at HF- family returns to HF for assessment of status and treatment adherence (families asked to bring blister packs with them). If family misses Day 4 visit, study personnel will visit at home to assess condition of the child and check adherence.
Day 6	HSA contacts family and assesses treatment adherence and child's condition and reminds them to complete treatment and to return to the facility on Day 8.
Day 8 (Treatment & outcome assessment)	Family returns to HF for assessment of child's condition and to determine treatment adherence and completion. If family misses Day 8 visit, study personnel will visit at home to assess condition of the child and check adherence.
Day 14 (Vital status assessment)	Study staff conduct assessment of child's vital status and recovery status

Approaches to improve adherence

- Caregivers provided with a follow-up and medicine reminder card at enrollment
- Tailored to case type (CSI or FB-only)
- HSAs trained to conduct follow-up on Day 3 and Day 6 to reinforce treatment and follow-up
- Secret mothers oriented to support HSAs follow up by providing linkage



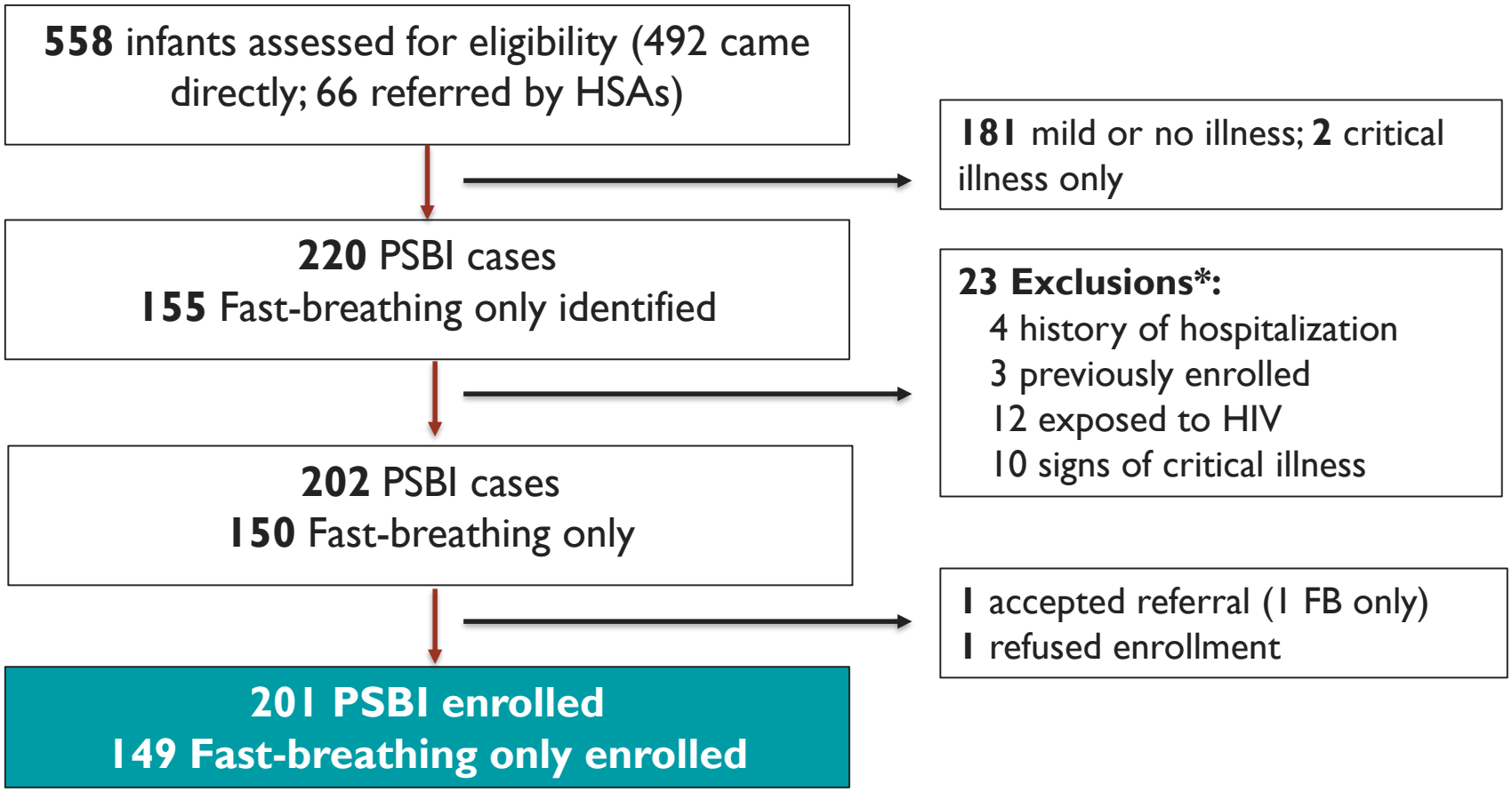
Follow-up and Medicine Reminder Card for Possible Serious Bacterial Infection

Patient name:_____ Heath Facility name:_____ Enrolment date : ____/____/_____

Provider name:_____ HSA name:_____

	Treatment day	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
	Date (dd/mm)	__/__	__/__	__/__	__/__	__/__	__/__	__/__	__/__
	Weekday (M, Tu, W, Th, F, Sa, Su)								
Treatment	**Instructions**								
Injectable gentamicin	*HF staff to give injection on Day 1 & Day 2.*	Time:___ Dose:___ Initials:__	Time:___ Dose:___ Initials:__						
Oral Amoxicillin									
Morning dose	*Give 1 pill in the morning for 7 days. Place tick mark when given and record time*	Time:___	Time:___	Time:___	Time:___	Time:___	Time:___	Time:___	
Evening dose	*Give 1 pill in the evening for 7 days. Place tick mark when given and record time*	Time:___	Time:___	Time:___	Time:___	Time:___	Time:___	Time:___	
Follow-up	**Instructions**								
Health facility	*Return to HF for check-up on Day 2, Day 4 and Day 8; bring this card and your blister pack. HF staff will record time of visit and sign*		Time: ____ Initials: ____		Time: ____ Initials: ____				Time: ____ Initials: ____
HSAs	*HSA will come to check the baby on Day 3 and Day 6 at your home. HSAs will record time of visit and sign*			Time: ____ Initials: ____			Time: ____ Initials: ____		

Trial profile & study flow



**Some cases had more than one exclusion criteria*

Study Outcome: Treatment Failure

Indicator	PSBI cases (N=201)	FB-only cases (n=149)*	TOTAL (N=350)
Treatment Failure	**10 (5.0%)**	**6 (4.0%)**	**16 (4.6%)**
No improvement by Day 4	3 (1.5%)	0	3 (0.9%)
Appearance of new sign	2 (1.0%)	2 (1.3%)	4 (1.1%)
Inclusion sign Day 8	1 (0.5%)	3 (2.0%)	4 (1.1%)
Hospitalization	4 (2.0%)	1 (0.7%)	5 (1.4%)
Death/Other SAE	0	0	0
Missing *(did not complete Day 8)*	2 (1.0%)	4 (2.7%)	6 (1.7%)

*Only 3 cases 0-6 days so combined with 7-59 days

Study Outcome: Treatment Completion

Indicator	PSBI cases (N=201)	FB-only cases (n=149)	TOTAL (N=350)
Completed both doses injectable gentamicin	191 (95.0%)	--	--
Received all 14 doses of oral amoxicillin	180 (89.6%)	134 (89.9%)	314 (89.7%)
Received at least 12 doses amoxicillin	15 (7.5%)	10 (6.7%)	25 (7.1%)
Met criteria for treatment completion*	**185 (92.0%)**	**144 (96.6%)**	**329 (94.0%)**
Did not meet criteria for treatment completion¥	16 (8.0%)	5 (3.4%)	21 (6.0%)

*- ***PSBI cases receiving both doses injectable gentamicin and at least 12 doses oral amoxicillin. FB only cases receiving at least 12 doses oral amoxicillin;*** ¥ Includes 6 cases who missed Day 8 follow-up

Follow-up adherence – Health facility

Indicator	PSBI cases (N=201)	FB-only cases (n=149)	TOTAL (N=350)
Day 4 follow-up completed*	186 (92.5%)	143 (96.0%)	329 (94.0%)
Day 8 follow-up completed*	195 (97.0%)	144 (96.6%)	339 (96.9%)
Day 4 & 8 follow-up completed*	184 (91.5%)	140 (94.0%)	324 (92.6%)
Partial follow-up completed	13 (6.5%)	7 (4.7%)	20 (3.5%)
No follow-up	4 (2.0%)	2 (1.3%)	6 (1.7%)

**As evidenced by recorded respiratory rate, temperature, or information on child's condition*

Follow-up adherence – Community

Indicator	PSBI cases (N=201)	FB-only cases (n=149)	TOTAL (N=350)
Received HSA follow-up Day 3	109 (54.2%)	91 (61.1%)	200 (57.0%)
Received HSA follow-up Day 6	108 (53.7%)	90 (60.4%)	198 (56.4%)
Received both Day 3 & 6	108 (53.7%)	89 (59.7%)	197 (57.1%)
Did not receive any HSA follow-up	92 (45.8%)	58 (38.9%)	151 (43.0%)
Caregiver reported any HSA follow-up*	136 (67.7%)	104 (69.8%)	240 (68.4%)

**Caregiver reported HSA conducted follow-up (when asked by facility staff on Day 4 or Day 8)*

Qualitative findings: acceptability

Informal interviews with DHO staff (5), health facility staff (11), HSAs (8) and mothers (11)

Unanimous feedback that outpatient treatment was acceptable and should be expanded in Malawi

Reasons for acceptability and expansion included:

- Preferred to be treated closer to home
- Lower costs and greater family involvement in caring for child
- Reduced case load/congestion at district hospital
- Trained facility staff were able to manage cases according to protocol
- Families were completing treatment and follow-up as directed; improved treatment adherence

Qualitative findings: acceptability

"In the past caregivers were told that if you see your newborn is sick then you must go to the district hospital. This made communities to keep sick young infants (at home) in fear of going to the district hospital."
[Facility staff]

"There are a lot of people in the children's ward (up to four babies for one bed). But this treatment at the health center – we're getting treatment from home. Also, the saved money can be used to buy other things at home"
[Mother]

"The approach is good, we have seen change (reduction) in admission numbers and children are not dying. It is cost-effective. It gives caretakers the chance to do other work at home." *[DHO staff]*

Qualitative findings: challenges & recommendations

Challenges

- Poor referral systems (specifically lack of ambulances for transport)
- Lack of time/inadequate human resources
- Communication issues (network, airtime) with HSAs
- Distance for HSAs/large catchment areas; residency
- Challenges locating families/families residing outside CA (e.g. cases crossing border from Mozambique)
- Maintaining regular supply of equipment and medicines

Recommendations

- Train all staff in the protocol; consider intensive training to those involved in care provision (nurses; clinicians, HSAs)
- Referral notification and feedback to health facilities
- Continuous and consistent supervision of HF staff & HSAs
- Enhance support to and motivate HSAs (solar power, bicycles, etc)
- DHO to deploy more technical staff to health facilities and provide fuel/support for referral transport
- Reduce number of facility and HSA follow-up visits
- Reduce paperwork/forms to complete

Limitations

- Results are preliminary – data cleaning ongoing
- Completion of oral amoxicillin based on maternal report during facility follow-up visits and may be overestimated (although qualitative results support high adherence)
- Facility staff and HSAs received support for communication (airtime) and small incentives for completion of study forms
- **HSA follow-up was low under study conditions – likely to be lower without study support**
- Study team only had 2 clinical staff, limiting validation and in-person follow-up of cases

Conclusions

- Majority of families are unable to accept referral
- Health facility staff at first level facilities are able to treat sick young infants
- Treatment at first level facilities is more acceptable to mothers and their families
- Levels of adherence to treatment and follow-up were high
- DHO and facility staff and families are in strong support of expanding simplified treatment where referral is not possible