Conflict of Interest

The author has declared no conflict of Interest.

Optimal mid-upper-arm-circumference (MUAC) based discharge criteria for community-based-management of Severe Acute Malnutrition (CM-SAM) in India: a randomized controlled non-inferiority trial

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BACKGROUND

- Of the **13.6 million** severely wasted children globally approximately **half** live in India
- No National Guidelines for Community Management of Acute Malnutrition (CMAM)
- In-patient treatment remains the primary treatment modality

BACKGROUND

WHO RECOMMENDATIONS FOR NON-OEDEMATOUS SEVERE ACUTE MALNUTRITION (SAM)

ADMISSION CRITERIA	DISCHARGE CRITERIA
Weight-for Height z-score (WHZ) **< -3 SD** And/or Mid-Upper Arm Circumference (MUAC) **< 115 mm**	Weight-for Height z-score (WHZ) **≥ -2 SD** And/or Mid-Upper Arm Circumference (MUAC) **≥ 125 mm**

MID-UPPER ARM CIRCUMFERENCE (MUAC)

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RATIONALE

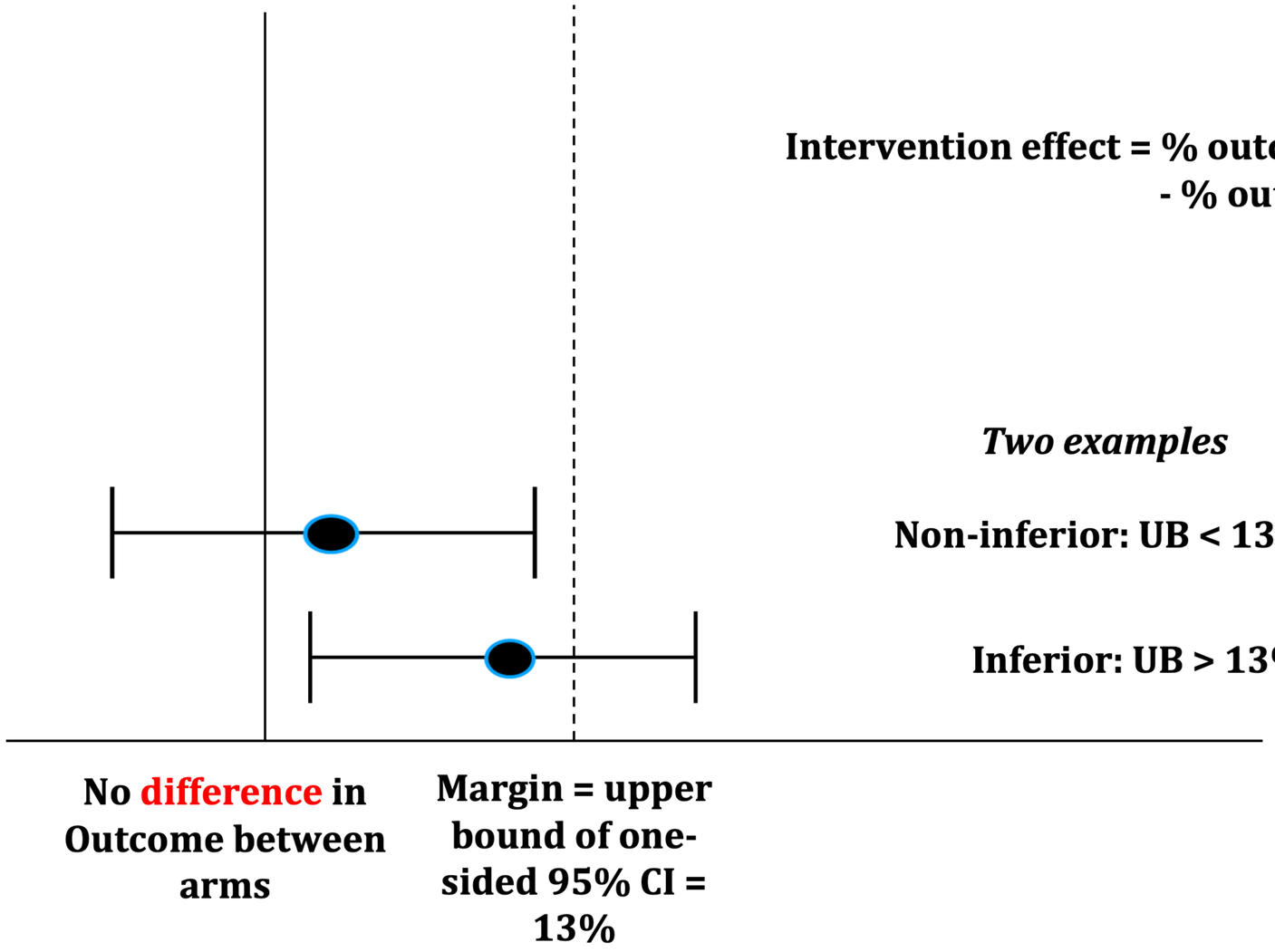
- Previous evidence from India suggest:
  - Severe Acute Malnutrition associated with lower morbidity and mortality
  - MUAC only programming targets those at highest risk of death
  - Alternative discharge criteria of MUAC ≥120 mm vs. MUAC ≥ 125mm results in similar long-term outcomes

STUDY OBJECTIVES

- To evaluate whether using a MUAC cut-off of ≥120 mm instead of MUAC cut-off of ≥ 125 mm in children 6 to 59 months for exit, from therapeutic feeding programs, results in a non-inferior relapse or death rate at 3 months post exit

- To summarize relapse rates by arm within enrolment MUAC strata of <110mm and 110-114mm.

WHAT DOES NON-INFERIORITY MEAN?



Intervention effect = % outcome in ≥120mm arm - % outcome in ≥125mm arm

Two examples

Non-inferior: UB < 13%

Inferior: UB > 13%

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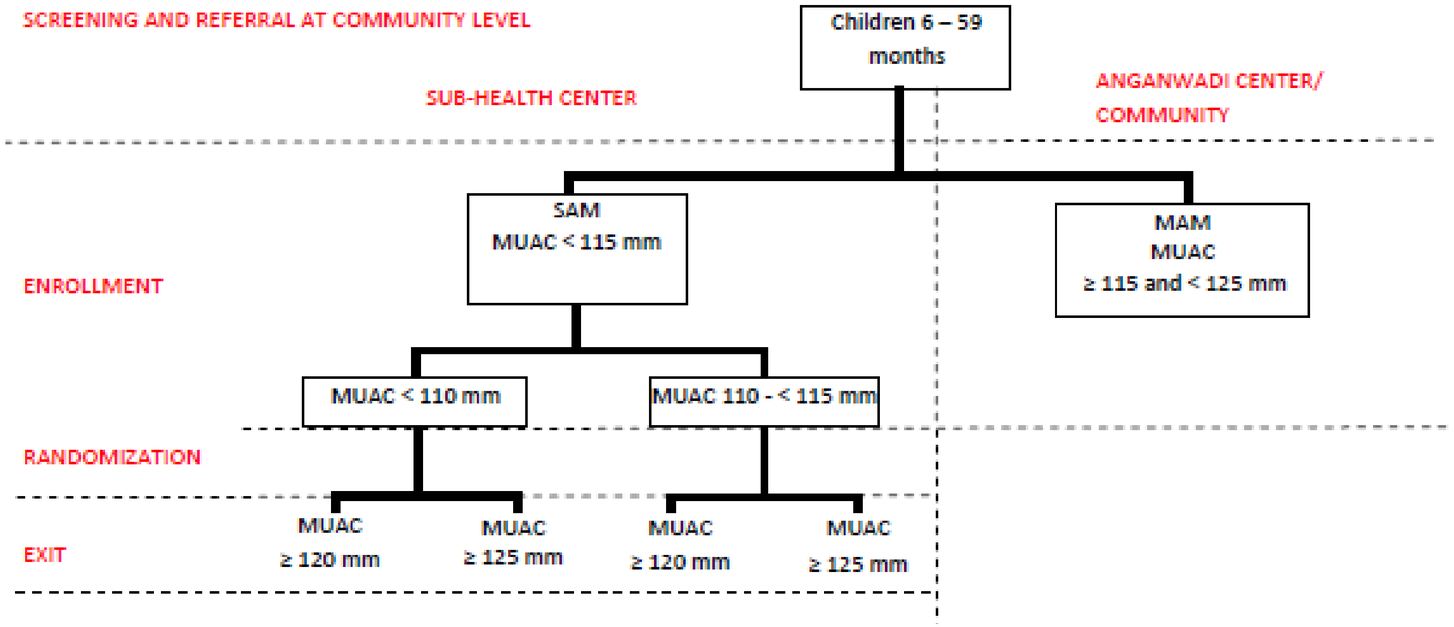
DEFINING THE MARGIN

Relapse if discharged with MUAC ≥125 mm	Relapse if discharged with MUAC ≥120 mm	Margin of non-inferiority
▸ Malawi study: 1.9% (155 children) at 3 months ▸ Bihar study: 2.8% (211 children) at 12-18 months ▸ Bihar study: 11.5% (52) children at 3 months ▸ MSF Guidelines: relapse rate < 5%	▸ Bihar study: 9.1% (253 children) at 3 months. Average of 3 food security period with relapse range between 3 – 13%	▸ 13 % margin is maximum allowable upper bound of CI around the difference in relapse or death rates ▸ Positive trade off: doubling coverage capacity, improved compliance.
≤5%	9-10%	13%

- ❖ Assuming 9% relapse or death in the ≥120mm discharge arm and conservatively assuming 1% relapse or death in ≥125mm discharge arm, 726 children would provide 90% power to determine non-inferiority within 13%
- ❖ No more than 13% inferior to the 125mm discharge arm determined to be sufficient in terms of resource saving

STUDY DESIGN

Randomized, controlled non-inferiority trial **Prospective observational cohort**



Follow-up at 3 and 6 months post exit for RCT, and post-recruitment for observational cohort

- This study was approved by the MSF Ethics Review Board and by the Ethical Review Boards of the Rajendra Institute of Medical Sciences, Ranchi and Jawaharlal Nehru University, New Delhi, India, and London School of Hygiene & Tropical Medicine, UK. Clinical Trials Registry – India number, CTRI/2017/12/010743

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RESULTS

PRIMARY OUTCOMES AT **3 MONTHS**

	Discharge ≥125mm (control)	Discharge ≥120mm
Randomized	**316**	**317**
Discharged Cured	194	236
Analysed (ITT) N	176	216
Died within 3 months of discharge, n (%)	0 (0.0, 95% CI: 0.0, 2.1)	1 (0.5, 95% CI: 0.0, 2.6)
Relapse to SAM or death at 3m, n (%, two-sided 95% CI)	14 (**8.0**, 95% CI: 4.4, 13.0)	31 (**14.4**, 95% CI: 10.0, 19.7)
Unadjusted difference in relapse (one-sided 95% CI UB)	**6.4% (11.6%)**	
Adjusted difference in relapse (one-sided 95% CI UB)	**4.6% (9.0%)**	

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RESULTS

SECONDARY OUTCOMES AT **6 MONTHS**

	Discharge ≥125mm (control)	Discharge ≥120mm
Analysed (ITT) N	174	218
Died within 6 months of discharge, n (%)	0 (0.0, 95% CI: 0.0, 2.1)	1 (0.5, 95% CI: 0.0, 2.5)
Relapse to SAM or death at 6m, n (%, two-sided 95% CI)	19 (10.9, 95% CI: 6.7, 16.5)	41 (18.8, 95% CI: 13.8, 24.6)
Unadjusted difference in relapse (one-sided 95% CI UB)	**7.9% (13.7%)**	
Adjusted difference in relapse (one-sided 95% CI UB)	**7.1% (12.7%)**	

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RESULTS

RELAPSE AT **3** AND **6 MONTHS** STRATIFIED BY ENROLMENT MUAC

	Outcome at 3 months		**Outcome at 6 months**	
	Discharge ≥125mm	**Discharge ≥120mm**	**Discharge ≥125mm**	**Discharge ≥120mm**
MUAC <110mm at enrolment:				
Analysed (ITT), N	46	61	42	63
Relapse or death at 3m, n (%, 95% CI)	4 (8.7, 95% CI: 2.4, 20.8)	16 (26.2, 95% CI: 15.8, 39.1)	7 (16.7, 95% CI: 7.0, 31.4)	17 (27.0, 95% CI: 16.6, 39.7)
Unadjusted difference in relapse (one-sided 95% CI UB)	**17.5% (29.0%)**		**10.3% (23.5%)**	
MUAC 110-114mm at enrolment:				
Analysed (ITT), N	130	155	132	155
Relapse or death at 3m, n (%, 95% CI)	10 (7.7, 95% CI: 3.8, 13.7)	15 (9.7, 95% CI: 5.5, 15.5)	12 (9.1, 95% CI: 4.8, 15.3)	24 (15.5, 95% CI: 10.2, 22.2)
Unadjusted difference in relapse (one-sided 95% CI UB)	**2.0% (7.5%)**		**6.4% (12.7%)**	

CONCLUSION

- MUAC ≥120mm as discharge criterion suitable in children admitted with MUAC 110-114mm, but lack of evidence in those with MUAC<110mm.
- 75 % of children are admitted with MUAC 110-114 and early discharge may result in an increased coverage capacity which is especially important in a country such as India with a high burden and limited resources.

LIMITATION

- Lower than expected sample size;
  - Trial still powered for primary analysis due to less conservative relapse rate than assumed in control arm
  - Trial not powered to stratify by food security periods

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- London School of Hygiene & Tropical Medicine, UK

THANK YOU

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