Imperial College London

GASTRO

GASTROENTERITIS AGGRESSIVE VERSUS SLOW TREATMENT FOR REHYDRATION

Prof Kathryn Maitland
on behalf of the GASTRO team

KENYA MEDICAL RESEARCH INSTITUTE KEMRI

wellcome trust

MCRI

Gastroenteritis

- 2.5 billion cases worldwide in children under 5years
- Second biggest killer of children in this age group
- Children hospitalised in LIMC with GE are 8.5 times more likely to die than their non-GE counterparts
- 1/3rd of fatalities occurred <7 days following admission
- Are initial treatment recommendations working in practice?

GE fluid management: according to severity of dehydration

Table 12. Classification of the severity of dehydration in children with diarrhoea

Classification	Signs or symptoms	Treatment
Severe dehydration	Two or more of the following signs: ■ lethargy or unconsciousness ■ sunken eyes ■ unable to drink or drinks poorly ■ skin pinch goes back very slowly (≥ 2 s)	▶ Give fluids for severe dehydration (see diarrhoea treatment plan C in hospital, p. 131)
Some dehydration	Two or more of the following signs: ■ restlessness, irritability ■ sunken eyes ■ drinks eagerly, thirsty ■ skin pinch goes back slowly	▶ Give fluid and food for some dehydration (see diarrhoea treatment plan B, p. 135) ▶ After rehydration, advise mother on home treatment and when to return immediately (see pp. 133–4) ▶ Follow up in 5 days if not improving.
No dehydration	Not enough signs to classify as some or severe dehydration	▶ Give fluid and food to treat diarrhoea at home (see diarrhoea treatment plan A, p. 138) ▶ Advise mother on when to return immediately (see p. 133) ▶ Follow up in 5 days if not improving.

Kenya 13 hospitals report

- GE+ Severe dehydration : n=8562

➢ Mortality 9% (759 died)

➢ If shock present mortality =34%

➢ Indicated not getting fluid management risk factor: confirmation bias?

Lancet CAH 2018

CrossMark

Risk factors for mortality and effect of correct fluid prescription in children with diarrhoea and dehydration without severe acute malnutrition admitted to Kenyan hospitals: an observational, association study

oa OPEN ACCESS

*Samuel Akech, Philip Ayieko, David Gathara, Ambrose Agweyu, Grace Irimu, Kasia Stepniewska, Mike English, on behalf of the Clinical Information Network authors**

Rehydration guidelines: WHO Plan C

Current Guidelines (WHO 2013)

Severe dehydration

(only in a child with diarrhoea)

Diarrhoea plus any two of these signs:

- Lethargy
- Sunken eyes
- Very slow skin pinch
- Unable to drink or drinks poorly

DIARRHOEA PLUS

two signs positive

Check for severe malnutrition

- Make sure the child is warm.

If no severe malnutrition:

- Insert an IV line and begin giving fluids rapidly following Chart 11 and diarrhoea treatment plan C in hospital (Chart 13, p. 131).

If severe malnutrition:

- Do not insert an IV line.
- Proceed immediately to full assessment and treatment (see section 1.4, p. 19).

'Plan C'

100mls/kg Ringers Lactate

~ vol to *correct '10% dehydration'*

2-staged approach

2-rates according to age

Table 13. Administration of intravenous fluids to a severely dehydrated child

Age (months)	First, give 30 ml/kg in:	Then, give 70 ml/kg in:
< 12	1 h[a]	5 h
≥ 12	30 min[a]	2.5 h

[a] Repeat if the radial pulse is still very weak or not detectable.

The devil is in the detail....3 charts later.....

Severe dehydration

(only in a child with diarrhoea)

Diarrhoea plus any two of these signs:

- Lethargy
- Sunken eyes
- Very slow skin pinch
- Unable to drink or drinks poorly

DIARRHOEA PLUS

two signs positive

Check for severe malnutrition

- Make sure the child is warm.

If no severe malnutrition:

- Insert an IV line and begin giving fluids rapidly following Chart 11 and diarrhoea treatment plan C in hospital (Chart 13, p. 131).

If severe malnutrition:

- Do not insert an IV line.
- Proceed immediately to full assessment and treatment (see section 1.4, p. 19).

Chart 11. How to treat severe dehydration in an emergency after initial management of shock

For children with severe dehydration but without shock, refer to diarrhoea treatment plan C, p. 131.

If the child is in shock, first follow the instructions in Charts 7 and 8 (pp. 13 and 14). Switch to the chart below when the child's pulse becomes slower or capillary refill is faster.

- Give 70 ml/kg of Ringer's lactate (Hartmann's) solution (or, if not available, normal saline) over 5 h to infants (aged < 12 months) and over 2.5 h to children (aged 12 months to 5 years).

Chart 7. How to give intravenous fluids to a child in shock without severe malnutrition

- Check that the child is not severely malnourished, as the fluid volume and rate are different. (Shock with severe malnutrition, see Chart 8.)
- Insert an IV line (and draw blood for emergency laboratory investigations).
- Attach Ringer's lactate or normal saline; make sure the infusion is running well.
- Infuse 20 ml/kg as rapidly as possible.

Reassess the child after the appropriate volume has run in.

Reassess after first infusion:	• If no improvement, repeat 10–20 ml/kg as rapidly as possible. • If bleeding, give blood at 20 ml/kg over 30 min, and observe closely.
Reassess after second infusion:	• If no improvement with signs of dehydration (as in profuse diarrhoea or cholera), repeat 20 ml/kg of Ringer's lactate or normal saline. • If no improvement, with suspected septic shock, repeat 20 ml/kg and consider adrenaline or dopamine if available (see Annex 2, p. 353). • If no improvement, see disease-specific treatment guidelines. You should have established a provisional diagnosis by now.

Up to 3 boluses of 20mls/kg

WHO Plan C: management of severe dehydration

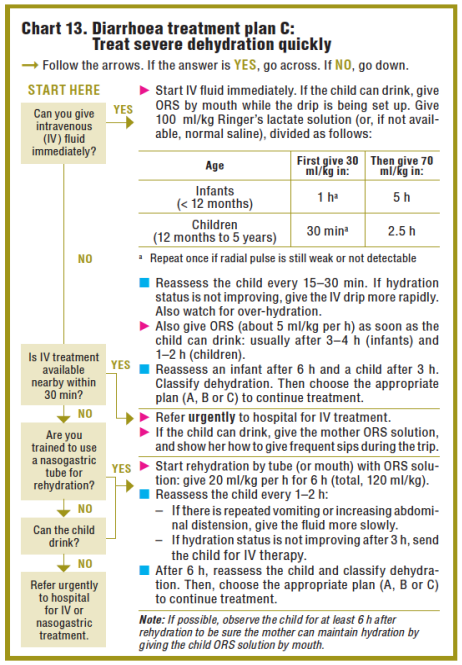


Chart 13. Diarrhoea treatment plan C: Treat severe dehydration quickly

→ Follow the arrows. If the answer is YES, go across. If NO, go down.

START HERE

Can you give intravenous (IV) fluid immediately? — YES →

- Start IV fluid immediately. If the child can drink, give ORS by mouth while the drip is being set up. Give 100 ml/kg Ringer's lactate solution (or, if not available, normal saline), divided as follows:

Age	First give 30 ml/kg in:	Then give 70 ml/kg in:
Infants (< 12 months)	1 h[a]	5 h
Children (12 months to 5 years)	30 min[a]	2.5 h

[a] Repeat once if radial pulse is still weak or not detectable

NO

- Reassess the child every 15–30 min. If hydration status is not improving, give the IV drip more rapidly. Also watch for over-hydration.
- Also give ORS (about 5 ml/kg per h) as soon as the child can drink: usually after 3–4 h (infants) and 1–2 h (children).

Is IV treatment available nearby within 30 min? — YES →

- Reassess an infant after 6 h and a child after 3 h. Classify dehydration. Then choose the appropriate plan (A, B or C) to continue treatment.

NO

- Refer **urgently** to hospital for IV treatment.
- If the child can drink, give the mother ORS solution, and show her how to give frequent sips during the trip.

Are you trained to use a nasogastric tube for rehydration? — YES →

- Start rehydration by tube (or mouth) with ORS solution: give 20 ml/kg per h for 6 h (total, 120 ml/kg).
- Reassess the child every 1–2 h:
  - If there is repeated vomiting or increasing abdominal distension, give the fluid more slowly.
  - If hydration status is not improving after 3 h, send the child for IV therapy.

NO

Can the child drink? — NO

- After 6 h, reassess the child and classify dehydration. Then, choose the appropriate plan (A, B or C) to continue treatment.

Refer urgently to hospital for IV or nasogastric treatment.

***Note:** If possible, observe the child for at least 6 h after rehydration to be sure the mother can maintain hydration by giving the child ORS solution by mouth.*

Integrated management of dehydration?

Chart 2 (Triage Page 6)

Chart 7 (Shock treatment Page 13)

Chart 8 (kids with SAM; Page 14)

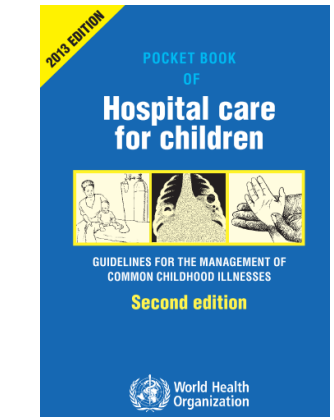
Chart 11 (Post shock Rx) Page 17

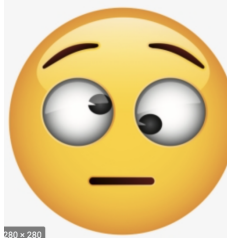
Chart 13 (WHO Plan C Page 141)

So lets do the Maths: Shock + Severe Dehydration

✓ Correctly followed 100-130mls/kg

➢ 'Incorrectly' followed 120-160mls/kg





Maths did not include this bit!

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[a] Repeat if the radial pulse is still very weak or not detectable.

Evidence for rehydration guidelines (worldwide!!)

Iro *et al. BMC Pediatrics*
DOI 10.1186/s12887-018-1006-1

BMC Pediatrics

RESEARCH ARTICLE Open Access

Rapid intravenous rehydration of children with acute gastroenteritis and dehydration: a systematic review and meta-analysis

M. A. Iro[1], T. Sell[1], N. Brown[2,3] and K. Maitland[4,5*]

Systematic review - 3 trials - total of 464 patients

- No trials conducted in LIMC settings
- In none of the 3 studies were there any deaths

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

ABSTRACT

Fast track; May 2011

Submitted to NEJM April 15th: **3 months after IDMC stop**

Unresolved questions arising from FEAST

FEAST TRIAL

Severe febrile illness (sepsis/septic shock)

Gastroenteritis (hypovolaemia)

Severe Malnutrition

RESUS trial

MAPS

GASTRO study

AFRIM study

CAPMAL study

Ovine Model Sepsis

GASTRO SAM Phase II trial: Starts 2019

Published Am J CCM 2018	PCCM 2022	BMC 2019	**Critical Care 2018**	Published JAMA Open 22nd March

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GASTROENTERITIS AGGRESSIVE VERSUS SLOW TREATMENT FOR REHYDRATION

What were the study hypotheses?

In children with diarrhoea and severe dehydration

1) Could the rehydration guideline be simplified?

2) As FEAST showed harm of fluid bolus therapy could this be extended to children with GE management by Plan C?

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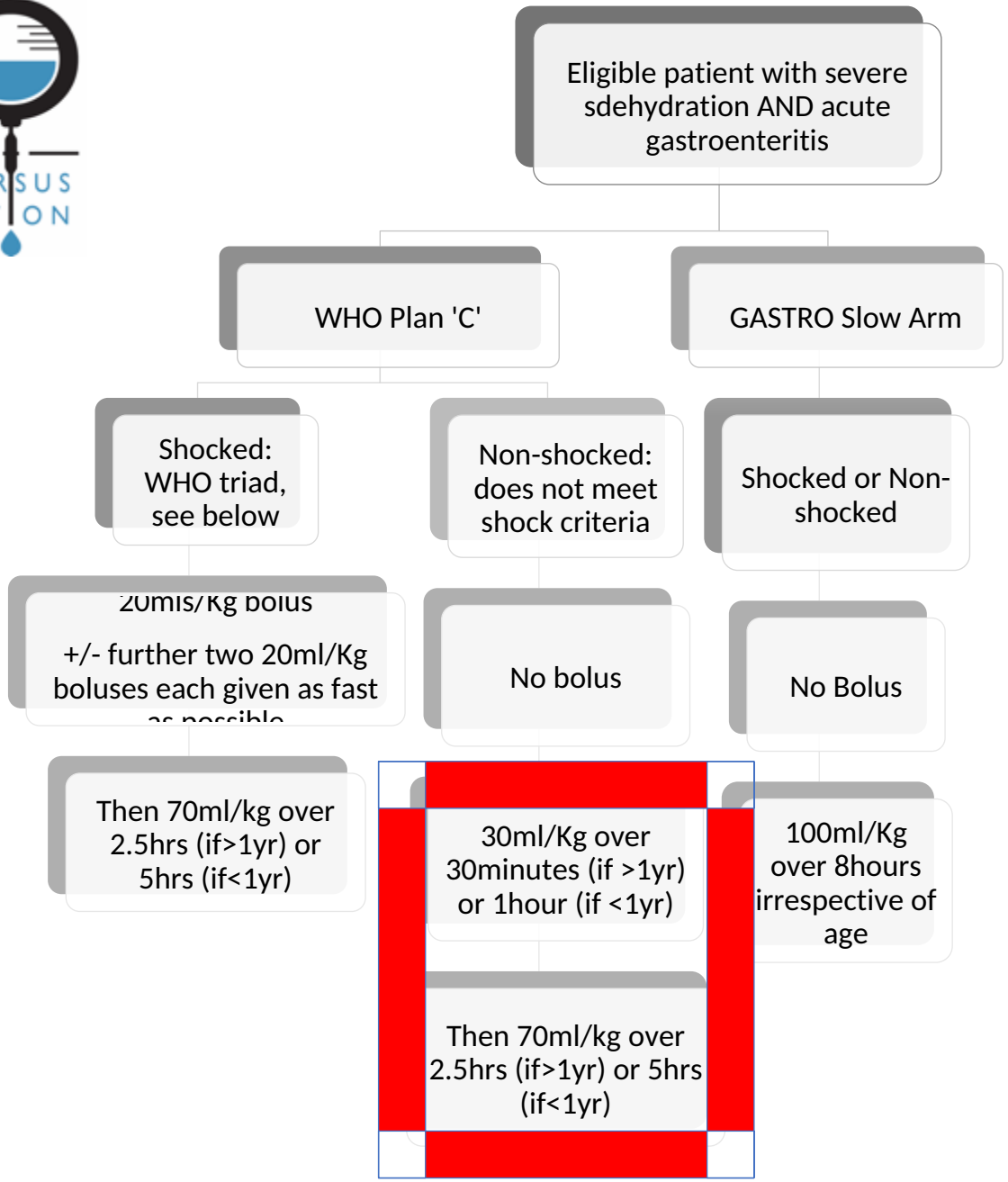
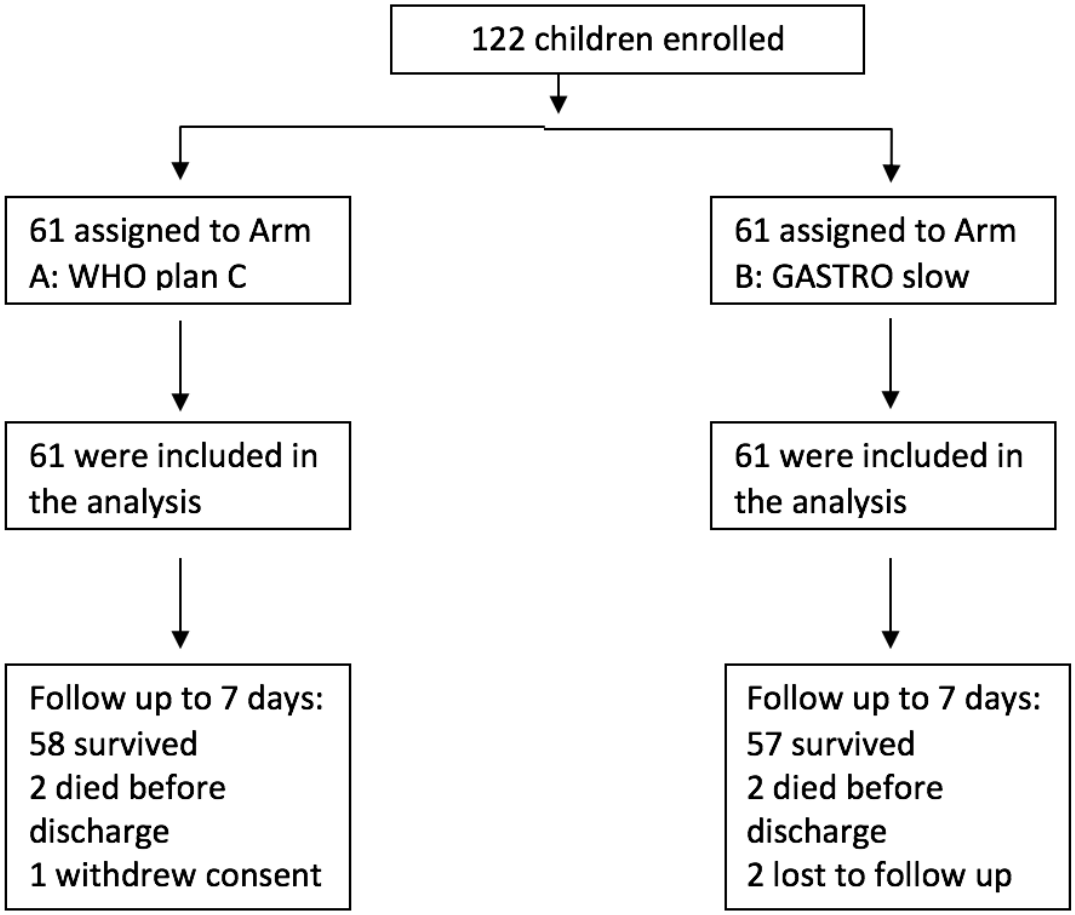
GASTROENTERITIS AGGRESSIVE VERSUS SLOW TREATMENT FOR REHYDRATION

- 120 children aged 2 mths to 12 yrs
- Kilifi, Kenya Mbale & Soroti Uganda
- Clinical, biochemical and physiological data during admission and at 7 day review
- Challenges implementing Plan C



Trial Flow


122 children enrolled
61 assigned to Arm A: WHO plan C
61 assigned to Arm B: GASTRO slow
61 were included in the analysis
61 were included in the analysis
Follow up to 7 days: 58 survived 2 died before discharge 1 withdrew consent
Follow up to 7 days: 57 survived 2 died before discharge 2 lost to follow up

Baseline parameters

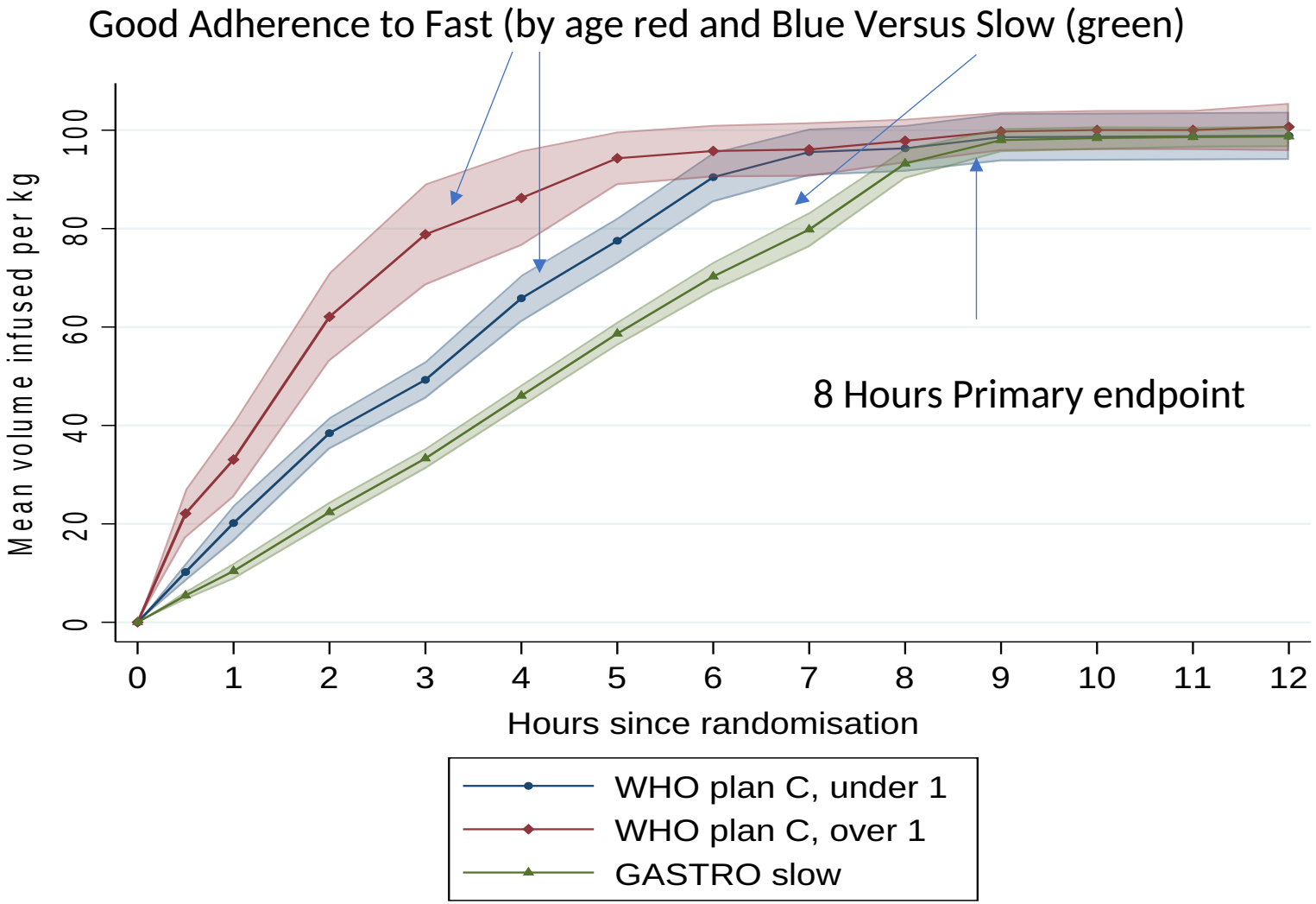
	WHO plan C	GASTRO slow	Total
Number	61	61	122
Female - n (%)	23 (38)	27 (44)	50 (41)
Age (months) - Median (IQR)	9 (6-12)	8 (6-12)	8 (6-12)
Weight (kg) -Median (IQR)	7.7 (6.8, 8.3)	7.3 (6.8,8.3)	7.5 (6.7-8.3)
Axillary temperature ℃ Median (IQR)	37.6 (37.0, 38.2)	37.8 (37.2, 38.3)	37.7 (37.0, 38.2)
<36 - n (%)	1 (2)	1 (2)	2 (2)
>37.5 - n (%)	32 (52)	37 (61)	69 (57)
Sunken eyes - n (%)			
Slightly sunken	17 (28)	18 (30)	35 (29)
Very sunken	44 (72)	42 (69)	86 (70)
Decreased skin turgor[a] - n (%)	32 (52)	34 (56)	66 (54)
Heart rate Median (IQR)	145.0 (138.5, 159.0)	149.5 (140.5, 160.5)	148 (139, 160)
Systolic blood pressure Median (IQR)	90 (85, 95)	89 (85, 96.5)	89 (85, 96)
Mod – severe hypotension – n (%)	3 (5)	5 (8)	7 (6)
Capillary refill time Median (IQR)	1 (1, 1)	1 (1, 1)	1 (1, 1)
≥3 - n (%)	5 (8)	3 (5)	8 (7)
No. with weak pulse n (%)	6 (10)	7 (11)	13 (11)
No. with temperature gradient n (%)	11 (18)	10 (16)	21 (17)
Respiratory rate Median (IQR)	40 (37, 48)	44 (40, 50)	43 (38, 49)
Respiratory distress - n (%)	5 (8)	9 (15)	14 (11)
Oxygen saturation Median (IQR)	98 (97, 99)	98 (97, 98)	98 (97, 99)
Conscious level n (%)			
Alert	12 (20)	16 (26)	28 (23)
Lethargic	35 (57)	30 (49)	65 (53)
Prostrate	13 (21)	13 (21)	26 (21)
Coma	1 (2)	2 (3)	3 (2)

[a]Recoil from skin pinch >2 seconds

Laboratory parameters

Admission Laboratory	Plan C	GASTRO slow	Total
N	53	50	103
Sodium Median (IQR)	139 (132, 149)	143 (137, 156)	142 (136, 154)
Hyponatremia (<135 mmol/L) - n (%)	16 (30)	8 (16)	24 (23)
Hypernatremia (>145 mmol/L) - n (%)	15 (28)	23 (46)	38 (37)
Severe hypernatraemia >150 mol/L- n (%)	11 (21)	16 (32)	27 (26)
Hypokalaemia (<3.5 mmol/L) - n (%)	11 (21)	8 (16)	19 (18)
High Creatinine (>74mmol/L) - n (%)	11 (21)	12 (24)	23 (23)
High Urea (>6.4 mmol/L) - n (%)	26 (49)	26 (52)	52 (50)
Glucose Median (IQR)	5.4 (4.9, 6.3)	5.3 (4.4, 6.9)	5.4 (4.7, 6.8)
Lactate[a] Median (IQR); N	1.2 (1.0, 2.1); 29	1.3 (1.1, 1.7); 27	1.3 (1.0, 1.7); 56
High Lactate >3 mmol/l - n (%)	4 (14)	0 (0)	4 (7)

Volumes and rates of fluid given by study arm



Primary Outcome: Safety Endpoints

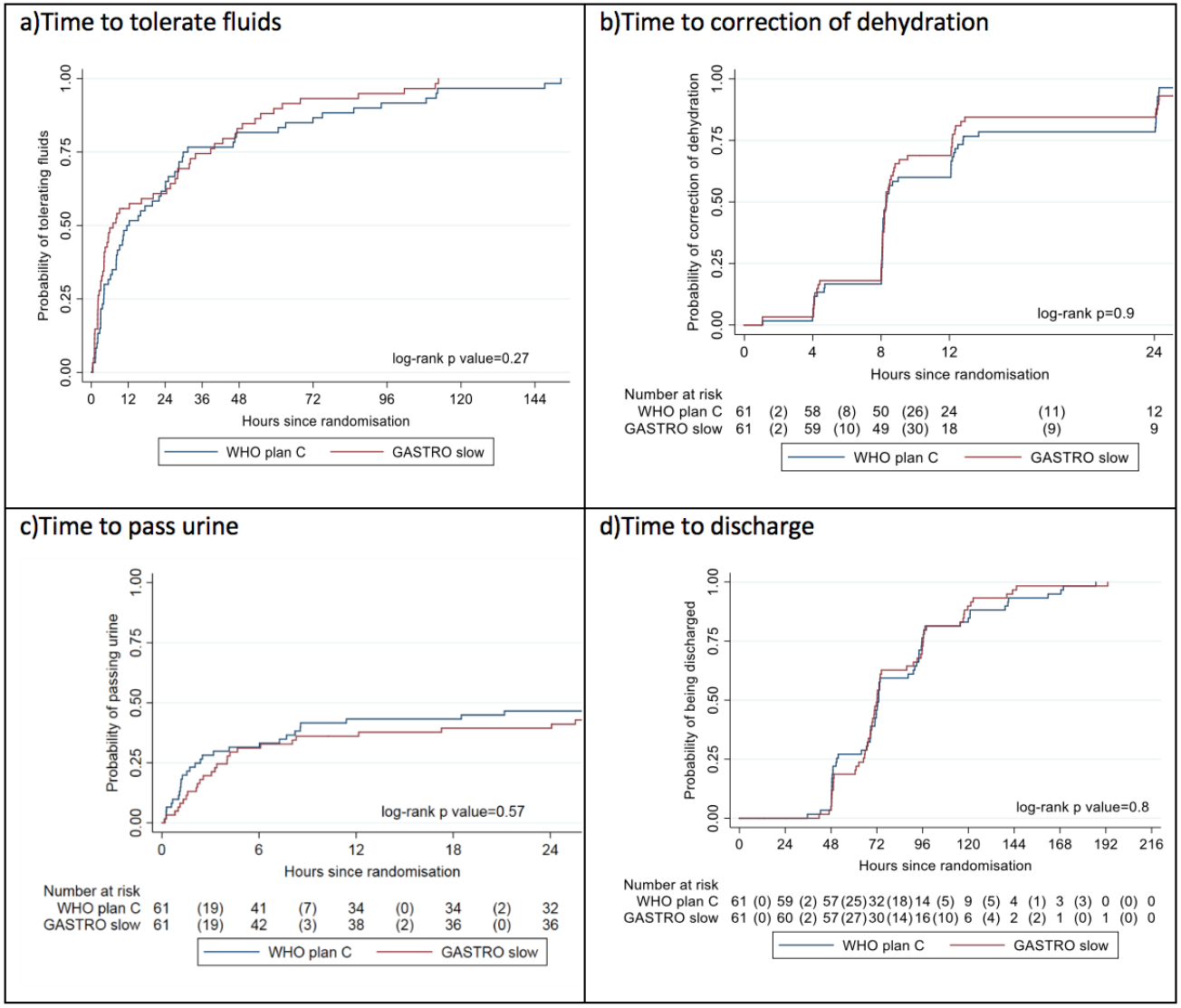
	WHO Plan C n = 61	GASTRO slow n = 61
Number of SAEs	3 (4.9%)	3 (4.9%)
Outcome of SAE		
Resolved	1	1
Died	2 (3.3%)	2 (3.3%)
Relationship to study fluid		
Unlikely to be related	2	3
Probably related	1	0
Nature of event		
Pulmonary oedema	0	1
Cardiovascular collapse	2	1
Other: **Seizures**	1	1

Biochemistry over time

At 8 hours	Plan C	GASTRO slow	Total
N	50	52	102
Sodium Median (IQR)	142 (135, 147)	142 (138, 148)	142 (136, 148)
Hyponatremia (<135 mmol/L) - n (%)	12 (24)	6 (12)	18 (18)
Hypernatremia (>145 mmol/L) - n (%)	17 (34)	19 (37)	36 (35)
Severe hypernatraemia >150 mol/L - n (%)	7 (14)	10 (19)	17 (17)
At 24 hours			
N	41	45	86
Sodium Median (IQR)	142 (138, 154)	143 (138, 156)	143 (138, 155)
Hyponatremia (<135 mmol/L) - n (%)	7 (17)	5 (11)	12 (14)
Hypernatremia (>145 mmol/L) - n (%)	16 (39)	18 (40)	34 (40)
Severe hypernatraemia >150 mol/L - n (%)	12 (29)	16 (36)	28 (33)

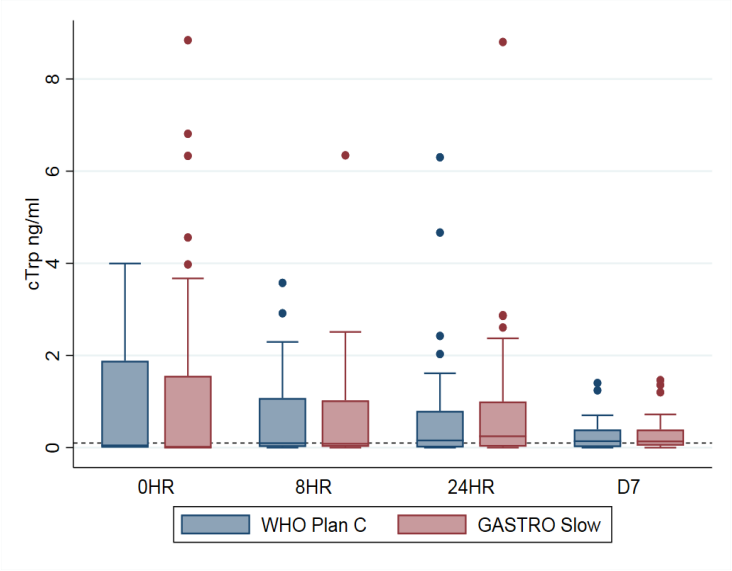
No statistical difference in any of the parameters

Secondary endpoints

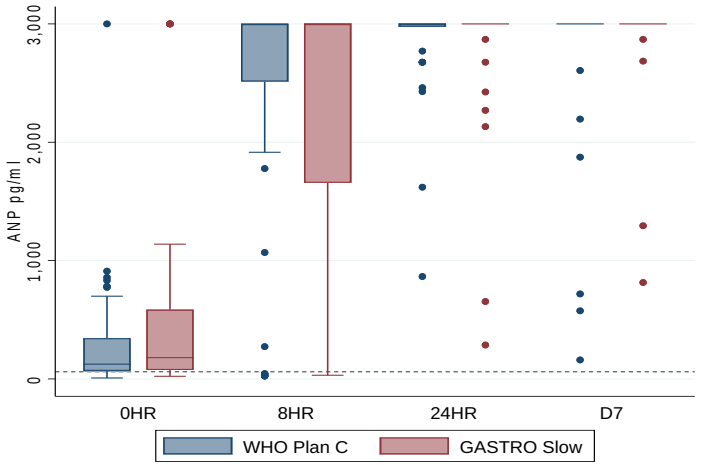


No statistical difference in any of 2^0 endpoints

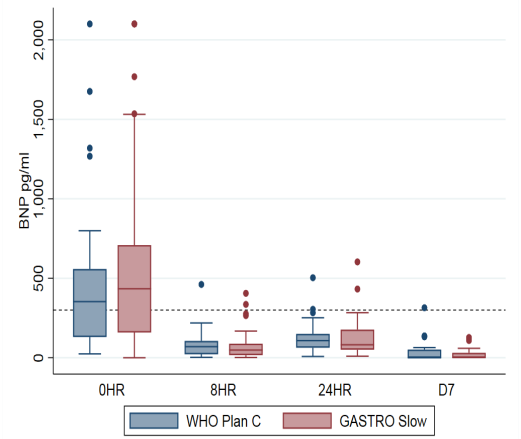
Troponin



Atrial Natriuretic Protein



Brain Natriuretic Protein



Accuracy of signs of severe dehydration (~10% loss)*

	WHO plan C	GASTRO slow	Total
N	58	57	115
Mean (sd)	6 (6)	7 (6)	7 (6)
Median (IQR)	6 (2, 11)	5 (3, 10)	6 (2, 11)
0-5% - n (%)	24 (41)	28 (42)	52 (45)
5-10% - n (%)	17 (29)	13 (23)	30 (26)
10% - n (%)	17 (29)	16 (28)	33 (29)

* Relevance

- On Day 7 all children (without on going losses) were reweighed.
- Day 7 weight was a proxy for pre-illness weight

Diagnostic accuracy of three clinical dehydration scales: a systematic review

Anna Falszewska, Hania Szajewska, Piotr Dziechciarz

What this study adds?

- The CDS provides a moderate-to-large increase in the post-test probability of predicting moderate-to-severe (≥6%) dehydration only in developed countries.
- The WHO and Gorelick Scales are not helpful in the assessment of dehydration both in developed and developing countries.

LIMC: Rwanda 2 studies – same authors

Findings

- Hypernatraemic dehydration is more common that considered in current guidelines: but appeared to safely managed in trial on same regime
- Accuracy of signs of dehydration: only 30% actually had equivalent of 10% loss
- Slow rehydration (no boluses) safe and easier to implement than Plan C
- Adherence to WHO Plan C required lots of training and monitoring

➢ Many en screened 'not eligible' as just qualified as severe malnutrition due to 10% dehydration (MUAC and WHZ) but once rehydrated no longer classified as SAM

Implications for evidence

- Emergency treatment (bolus) plus WHO Plan C may result in large volumes given over short period time (very low quality of evidence)
- Poor outcomes, low quality evidence base and new findings: rationale for a Phase III trial

GASTRO Trial RCT

BMC Medicine

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Research article | OPEN Open Peer Review | Published: 01 July 2019

Gastroenteritis aggressive versus slow treatment for rehydration (GASTRO): a phase II rehydration trial for severe dehydration: WHO plan C versus slow rehydration

Kirsty A. Houston, Jack Gibb, Peter Olupot-Olupot, Nchafatso Obonyo, Ayub Mpoya, Margaret Nakuya, Rita Muhindo, Sophie Uyoga, Jennifer A. Evans, Roisin Connon, Diana M. Gibb, Elizabeth C. George & Kathryn Maitland

BMC Medicine **17**, Article number: 122 (2019) | Download Citation

- ✓ Slower rehydration is safe and easier to implement than two stage WHO Plan C
- ✓ Need for Phase III RCT that includes both SAM and non-SAM

Severe malnutrition?

SAM: WHO guideline highlight cardiac compromise

Over the last 2 decades guidelines not changed/update suggesting:

- Heart is ‘shrunken’
- Unable to cope with volume (intravenous)
- Children with SAM are sodium overloaded
- IV infusions can precipitate heart failure (including severe dehydration)
- Children with kwashiorkor are particularly at risk
- At risk of refeeding syndrome (cardiac arrhythmias)
- Expert opinion; low quality of evidence AND NOT UPDATED with evolving research

JAMA Network | Open

Original Investigation | Global Health

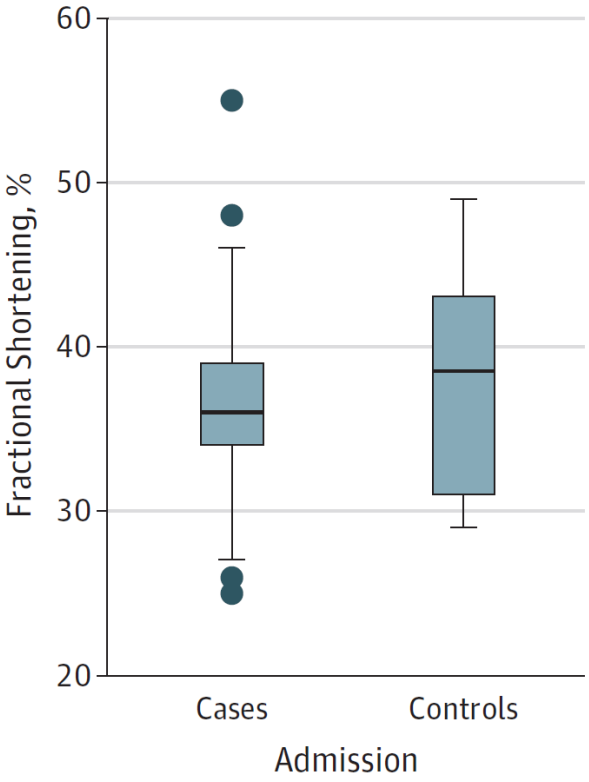
Assessment of Myocardial Function in Kenyan Children With Severe, Acute Malnutrition

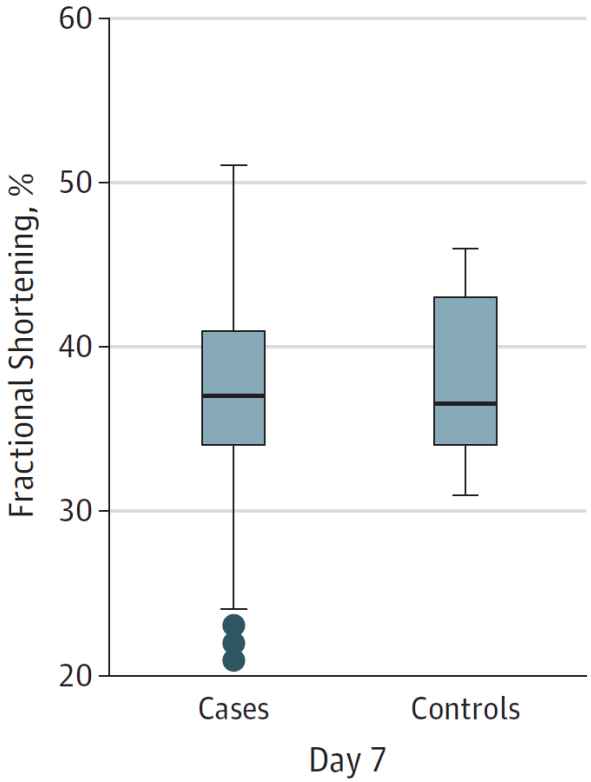
The Cardiac Physiology in Malnutrition (CAPMAL) Study

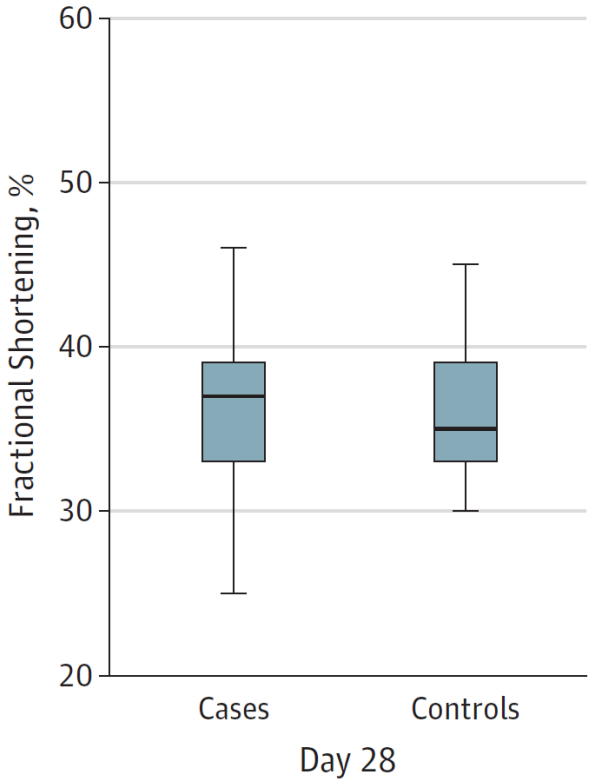
Bernadette Brent, MD; Nchafatso Obonyo, MB, ChB; Samuel Akech, MD, PhD; Mohammed Shebbe, DiplClinMedChir; Ayub Mpoya, MSc; Neema Mturi, MMed; James A. Berkley, FMedSci, MD; Robert M. R. Tulloh, MA, DM; Kathryn Maitland, FMedSci, PhD

Highly accessed and shared
by MSF and relevant agencies

Cases (severe malnutrition) vs controls:
no difference in SAM versus nonSAM (controls)



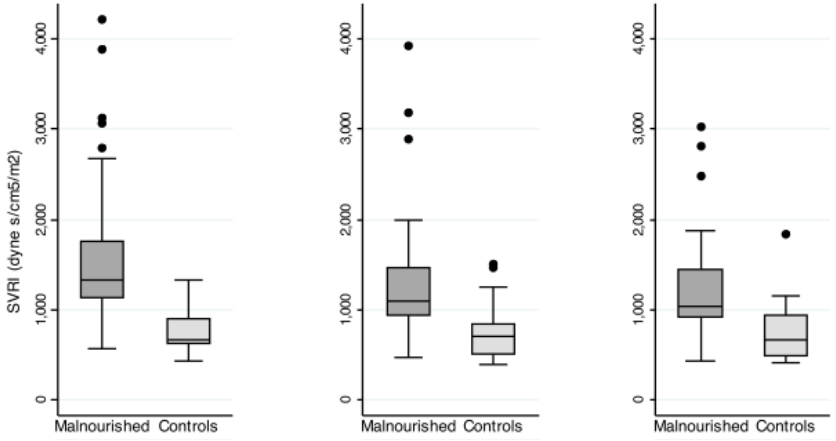




Systemic Vascular Resistance: marker of filling

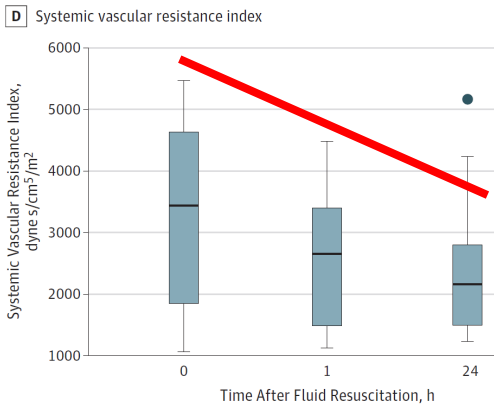
Higher levels of SVRI in SAM==evidence of underfilling

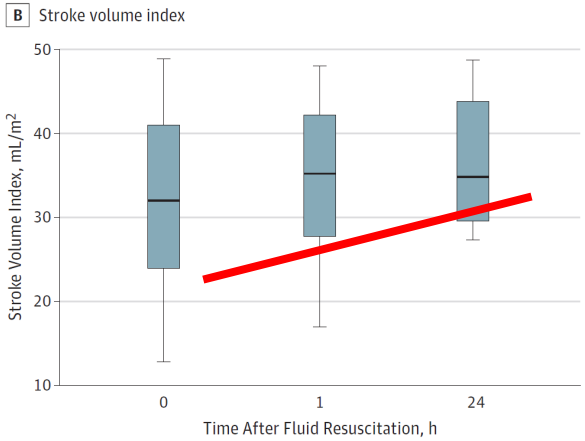
Admission Day 7 Day 28

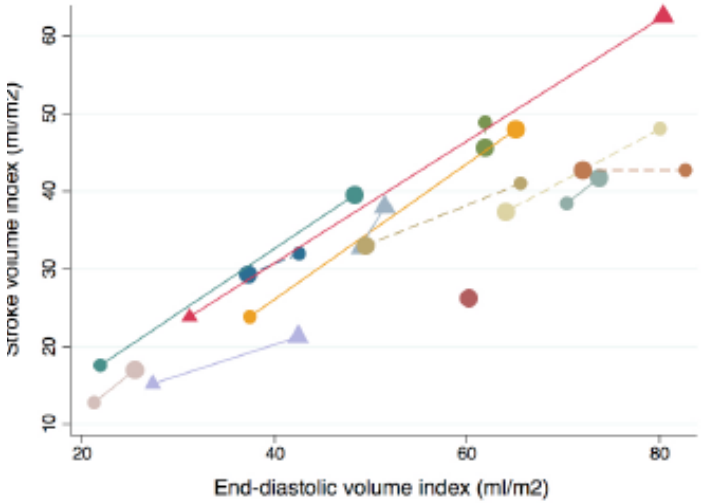


	SAM N=81	Control N=22	P value	SAM N=80	Control N=18	P value	SAM N=57	Control N=19	P value
Median (IQR)	1333 (1133, 1752)	677 (622, 910)	<0.001	1097 (939, 1472)	703 (510, 836)	<0.001	1043 (926, 1443)	674 (495, 944)	<0.001
High	28 (35%)	0 (0%)	0.002	11 (15%)	0 (0%)	0.084	7 (12%)	1 (6%)	0.495
Low	5 (6%)	13 (62%)	<0.001	6 (8%)	10 (56%)	<0.001	6 (11%)	9 (56%)	<0.001

Response to fluid rehydration therapy?







Over time SVRI improved/normalized; Stroke volume improved with iv fluids

Frank Starling Curves= Fluid responsive

Bottomline:

- ✓ No child developed cardiac overload or received diurectics:
- ✓ All cardiac parameters showed a positive response to fluids

In conclusion

- We found no evidence that children with SAM were more likely to have cardiac dysfunction or arrhythmias than matched controls,
- Nor that the cardiovascular profile of marasmus differed from kwashiorkor.
- No evidence for clinical cardiac failure or sudden death from arrhythmias in our study.
- Appropriate physiological response observed to IV fluids are better tolerated than current guidelines suggest

Largest study
of myocardial function
in SAM (n-272)

Original article

The effects of malnutrition on cardiac function in African children

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ABSTRACT

Objective Cardiac dysfunction may contribute to high mortality in severely malnourished children. Our objective was to assess the effect of malnutrition on cardiac function in hospitalised African children.

Design Prospective cross-sectional study.

Setting Public referral hospital in Blantyre, Malawi.

Patients We enrolled 272 stable, hospitalised children ages 6–59 months, with and without WHO-defined severe acute malnutrition.

Main outcome measures Cardiac index, heart rate, mean arterial pressure, stroke volume index and systemic vascular resistance index were measured by the ultrasound cardiac output monitor (USCOM, New South Wales, Australia). We used linear regression with generalised estimating equations controlling for age, sex and anaemia.

Results Our primary outcome, cardiac index, was similar between those with and without severe malnutrition: difference=0.22 L/min/m^2 (95% CI −0.08 to 0.51). No difference was found in heart rate or stroke volume index. However, mean arterial pressure and systemic vascular resistance index were lower in children

What is known on this topic

- Children hospitalised with severe acute malnutrition have a very high mortality rate.
- The effect of severe malnutrition on cardiac function is controversial.
- Fluid management in severely malnourished children is also controversial.

What this study adds

- Cardiac index is preserved in *stable*, hospitalised children with WHO defined severe acute malnutrition.
- When children are stratified by degree of wasting, cardiac index *increases* with worsening nutritional status, commensurate with a lower systemic vascular resistance index.

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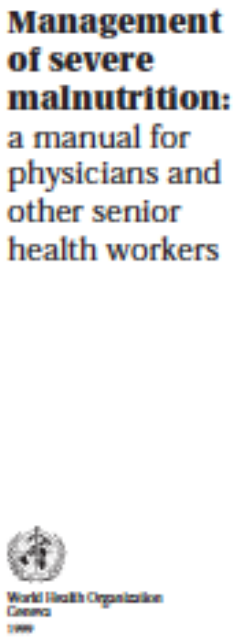
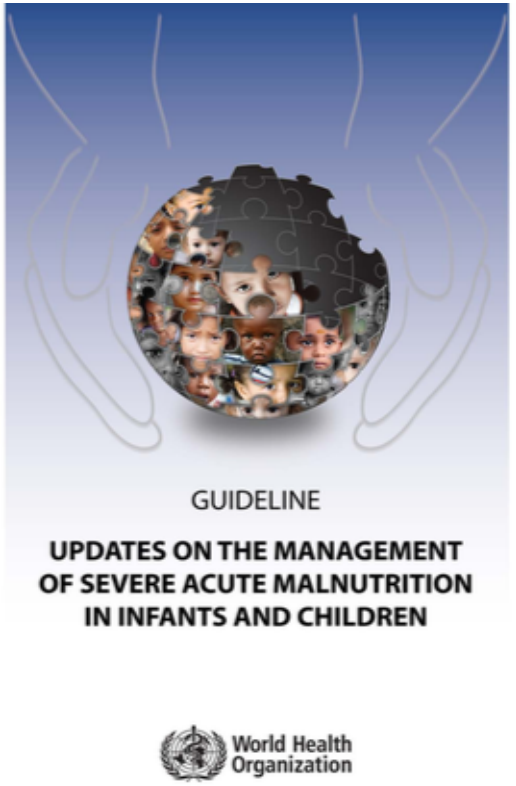


1999

2003



2012

Why does this matter?

WHO Guidelines:

- "**Giving iv fluids put SAM children at risk of overhydration and complications like heart failure**". ?

- SAM Children with acute diarrhoea and severe dehydration are not given IV fluids, only those with signs of decompensated shock.

- 15mls/kg Half strength Ringers lactate, half strength Darrow's solution in 5% dextrose or 0.45% saline are the recommended solutions

Observational Study : indicates high risk group diarrhoea & dehydration

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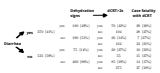
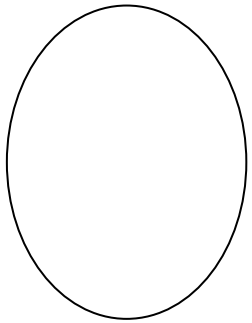
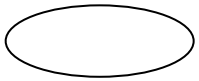
OPEN ACCESS Freely available online PLOS MEDICINE

Children with Severe Malnutrition: Can Those at Highest Risk of Death Be Identified with the WHO Protocol?







Maitland PLoSMed 2006

Contradicts WHO indicate that diarrhoea of ‘minor consequence

Wellcome Open Research

Wellcome Open Research 2017, 2:65 Last updated: 03 OCT 2017

Check for updates

SYSTEMATIC REVIEW

Intravenous rehydration of malnourished children with acute gastroenteritis and severe dehydration: A systematic review [version 1; referees: 3 approved]

Kirsty A. Houston[1,2], Jack G. Gibb[1,2], Kathryn Maitland [1,2]

4 studies were identified = 883 children conducted in low resource settings.
2 were RCT 2 two observational cohort studies, 1 incorporated assessment of myocardial function (AFRIM).

No evidence of fluid overload or other fluid-related adverse events,
In African children Mortality was high overall, particularly in children managed on WHO protocol (day-28 mortality 82%).

There was no difference in safety outcomes when different rates of intravenous rehydration were compared.
Conclusions: The current 'strong recommendations' for conservative rehydration of children with SAM are not based on emerging evidence.

Obonyo *et al. Critical Care* (2017) 21:103
DOI 10.1186/s13054-017-1679-0

Critical Care

RESEARCH Open Access

Myocardial and haemodynamic responses to two fluid regimens in African children with severe malnutrition and hypovolaemic shock (AFRIM study)

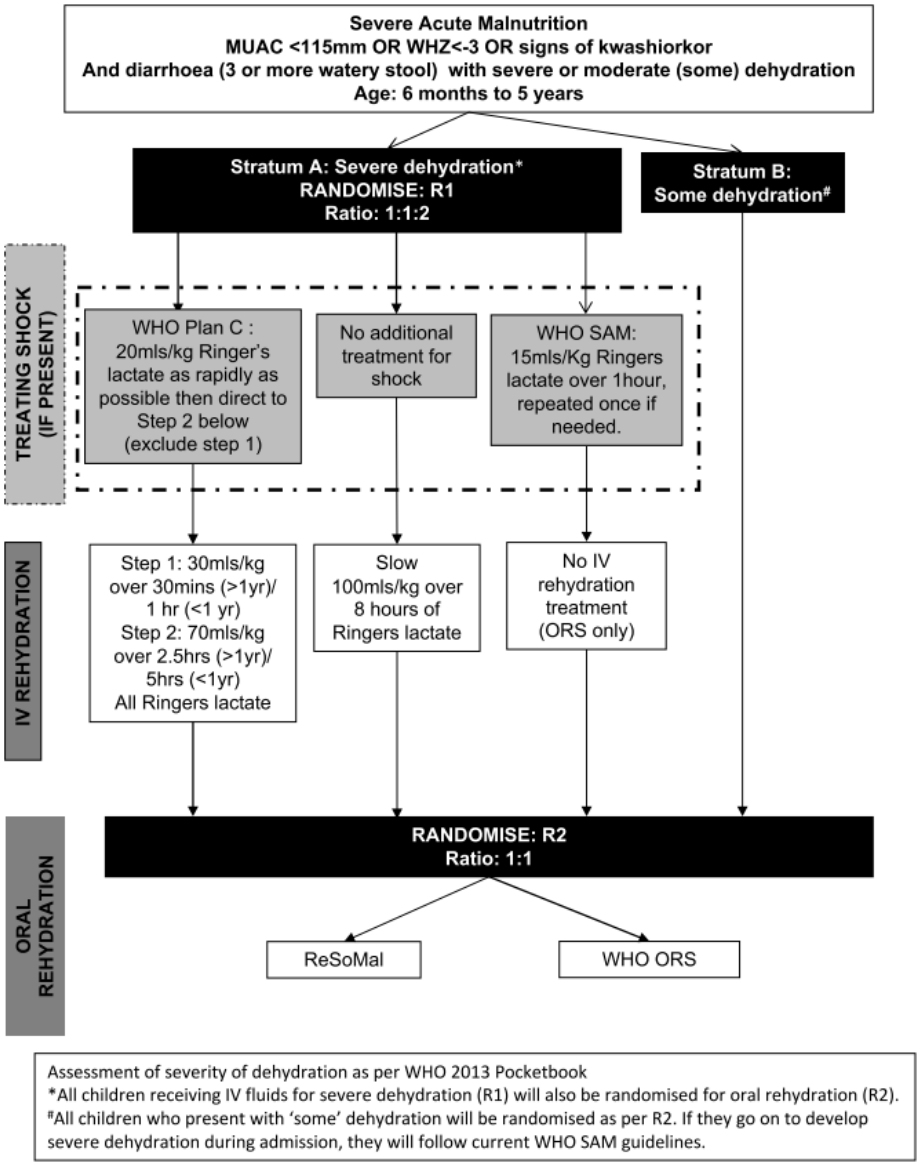
Nchafatso Obonyo[1,3,6], Bernadette Brent[1,2], Peter Olupot-Olupot[3], Michael Boele van Hensbroek[4], Irene Kuipers[4], Sidney Wong[5], Kenji Shiino[6,7], Jonathan Chan[6,7], John Fraser[6,7], Job B. M. van Woensel[4†] and Kathryn Maitland[1,2*†]

Conclusions

- Mortality – High overall including those children managed using WHO recommendations.
- No evidence of fluid overload found in any of the studies
- Neurological compromise not reported
- Cardiovascular compromise
  - Persistent low systolic BP and weak pulse associated with increased mortality
  - No evidence of biventricular heart failure found

GASTRO SAM

Started enrolment
August 2019



Funded by MRC JGHT 2018