Identifying children with a high risk of death in need of treatment – need of frequent screening

André BRIEND
University of Tampere (Finland)
University of Copenhagen (Denmark)
andre.briend@gmail.com

Malnutrition associated with about 50% of children's deaths in poor countries

Best approach to reduce this mortality: overall improvement of nutritional status with elimination of malnutrition

Interim strategy: focus nutritional interventions on most at risk children

Problem: how to identify these children?

Problems:

All nutritional indices are associated with the risk of death.
Which one to choose ?

Many possible cut-offs
Which one to choose ?

Two tools to these problems:

ROC Curves
Venn Diagrams

Receiver operating characteristics (ROC) curves

In practice, we need to identify for treatment a maximum of **children who would die in absence of treatment** (sensitivity)

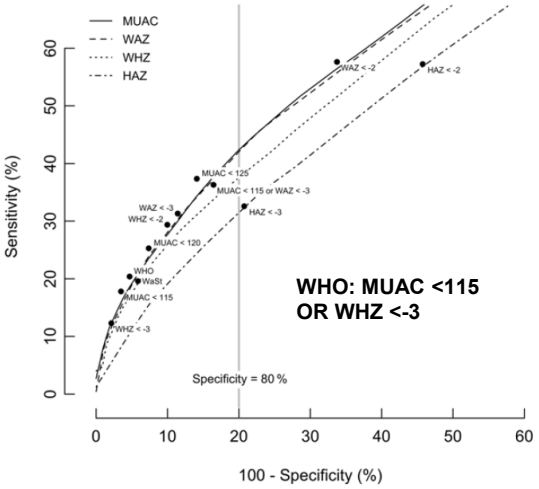
And a minimum of **children who would survive in absence of treatment** (false positives, or 1- specificity)

We need to maximise this ratio

This can be assessed by looking at the association between anthropometric indices and mortality in **cohorts of children with no treatment** programmes for malnourished children

To make programmes manageable, curves should be compared in the **high specificity region** (few false positives)

ROC curves in untreated 6-59 months children - 12 or 4 cohorts (MUAC)



MUAC and WAZ have the highest ROC curves, nearly identical

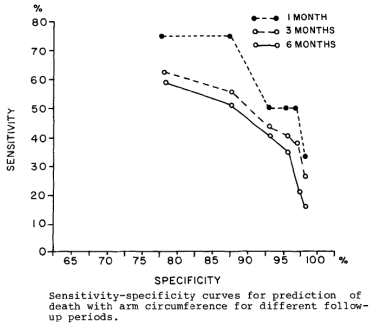
MUAC and WAZ capture the effect of wasting and stunting ?

Increasing cut-off increases sensitivity, but increases false positives

Combining indices also increases sensitivity, but increases false positives

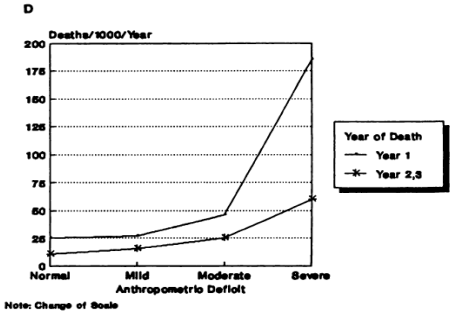
Khara T et al, Pub Health Nutr 2023

Effect of duration of follow-up: early findings



Sensitivity-specificity curves for prediction of death with arm circumference for different follow-up periods.

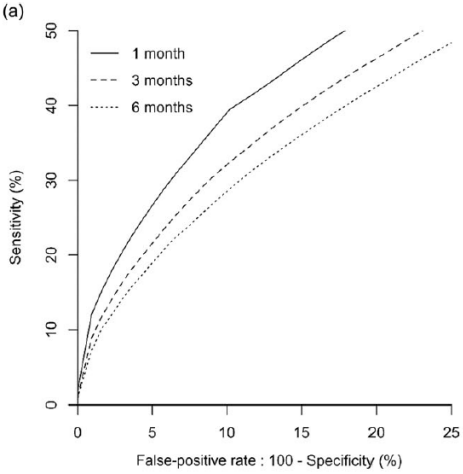
Briend A, Zimicki S, Nutr Res 1986



Pelletier D et al, J Nutr 1994

Effect of duration of follow-up difficult to explore as this requires very large sample sizes.

ROC curves in untreated 6-59 months children for different follow-up periods – WAZ 12 cohorts

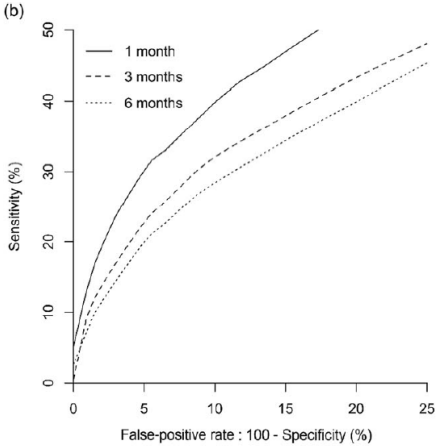


WAZ <-3

28% increase in sensitivity for follow-up of 1 month compared to 6 month

1,3% increase in false positive ratio

ROC curves in untreated 6-59 months children for different follow-up periods – WHZ 12 cohorts

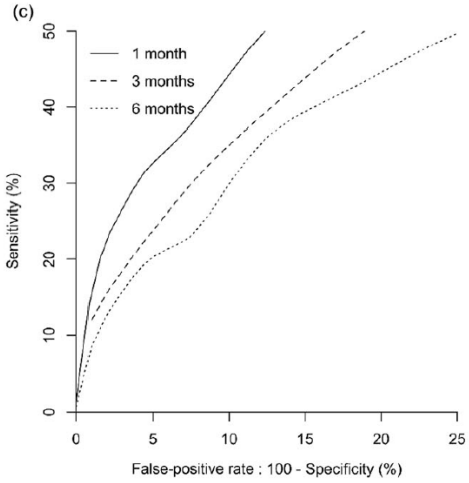


WHZ <-3

49% increase in sensitivity for follow-up of 1 month compared to 6 month

2,9% increase in false positive ratio

ROC curves in untreated 6-59 months children for different follow-up periods – MUAC 4 cohorts



MUAC < 115 mm

49% increase in sensitivity for follow-up of 1 month compared to 6 month

3,5% increase in false positive ratio

Improvement of ROC curves with shorter duration of follow-up quite expected

Nutritional status of children varies over time, with a strong random component.

Some deteriorate, and infrequent screening misses incident cases, which decrease the sensitivity of screening

Some improve, even without treatment, with a decreasing risk of death which decreases specificity of screening over time

Some children's nutritional status deteriorates: frequent incident cases

Table 1 Summary estimates of the incidence correction factor

Geographical area	N	K	95% CI	P value*
All available	352	3.5	(3.1 to 3.9)	<0.001
Western and Central Africa	197	3.6	(3.0 to 4.3)	<0.001
Burkina Faso	31	4.0	(3.4 to 4.6)	<0.001
Chad	26	14.7	(8.8 to 2.5)	<0.001
Democratic Republic of Congo	3	4.9	(1.9 to 12.6)	<0.001
Ghana	3	1.9	(1.0 to 3.9)	0.40
Liberia	15	5.9	(3.2 to 11.1)	<0.001
Mali	32	4.6	(3.7 to 5.6)	<0.001
Mauritania	2	5.0	(0.9 to 26.4)	0.002
Niger	16	8.4	(6.2 to 11.3)	<0.001
Nigeria	69	1.3	(1.0 to 1.6)	<0.001
Eastern and Southern Africa	99	3.7	(3.1 to 4.3)	<0.001
Angola	1	6.4	(3.1 to 14.5)	–
Burundi	1	30.1	(7.0 to 106.4)	–
Ethiopia	29	6.7	(5.3 to 8.4)	<0.001
Kenya	27	2.3	(1.6 to 3.2)	<0.001
Madagascar	8	8.5	(6.7 to 10.8)	0.13
Somalia	2	9.5	(0.7 to 134.6)	<0.001
South Sudan	5	2.6	(1.8 to 3.8)	0.015
Uganda	26	2.4	(1.9 to 2.9)	<0.001
Middle East and North Africa	35	2.8	(2.3 to 3.4)	<0.001
Yemen	35	2.8	(2.3 to 3.4)	<0.001
South Asia	16	2.3	(1.4 to 3.9)	<0.001
Afghanistan	16	2.3	(1.4 to 3.9)	<0.001
East Asia and Pacific	5	12.7	(5.7 to 28.4)	<0.001
Myanmar	5	12.7	(5.7 to 28.4)	<0.001

*P value for Cochrane's Q statistic assessing heterogeneity between K estimates within a geographical area.

The nubmer of children to be treated each year is 3,5 times higher than suggested by prevalence data

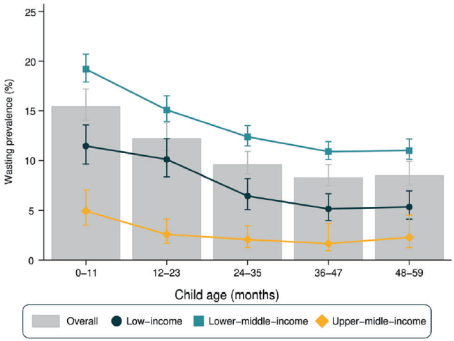
Isanaka et al, BMJ, 2021

Based on data from 352 sites in 20 countries

Some children's nutritional status improves: overall improvement of nutritional status over time

MUAC increases with age, reflecting normal growth

Wasting also decreases with age



Ricardo et al, Int J Obes 2021

Other evidence of spontaneous improvement over time: stability of WHZ SD even in crisis situations

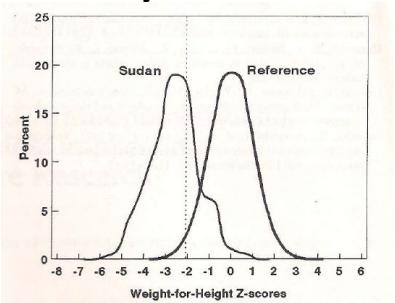


FIGURE 1 Comparison of weight-for-height distribution of children surveyed in Southern Sudan during famine in 1991 with that of international growth reference. The left shifted distribution indicating that all the children had significant weight loss.

Yip et Scanlon, J Nutr 1994

Summary of distributional parameters derived from 228 nutritional surveys.

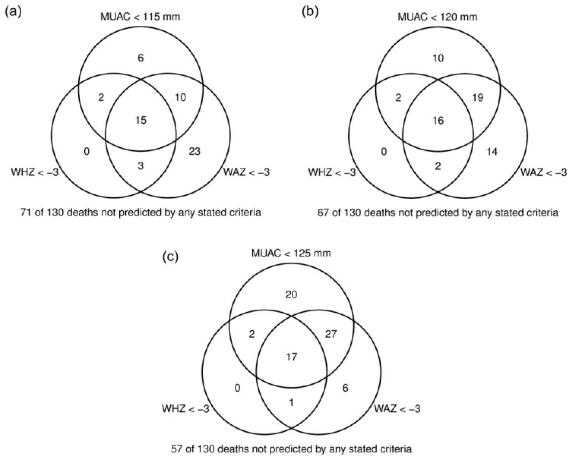
Statistic		Mean	± sd	2.5 & 97.5 centile		Normality*
mean	Z score	-0.63	± 0.48	-1.56	+0.36	NS
standard deviation	Z score	0.98	± 0.08	0.83	1.15	NS

Golden and Grellety, 2002

Within a population, if SD WHZ is constant, and some children deteriorate, then some other must improve.

Canalisation hypothesis: if they survive, children go back to their growth canal after an acute episode

Combining several indices with short follow-up (1-month) intervals



Venn diagrams among children who died within 1 month of assessment

MUAC <115mm OR WAZ <-3 detect all deaths associated with severe anthropometric deficits

WHZ <-3 not needed to detect high risk children

Increasing MUAC cut-off to 125 mm detects most WAZ<-3 deaths, but not all of them

Warning: increase of number of children to be treated when adding WAZ <-3, especially for programmes screening with MUAC <115mm

In practice: need for frequent nutritional screening +++

Family MUAC allowing a continousus screening a promising approach

Adding frequent WAZ measure is desirable, but may increase patient numbers