



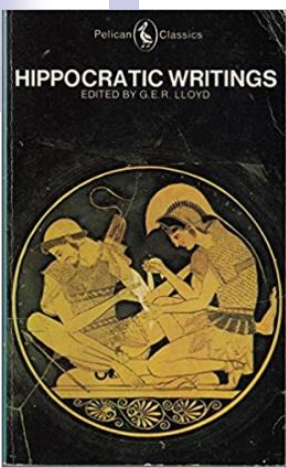
University
of Glasgow

Pitfalls in nutritional assessment in sick or critically ill paediatric patients

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Senior Lecturer in Clinical Nutrition-Dietitian

Col: Speaker fees, consultancy, travel & research grants, from Nestle and Nutricia



Malnutrition is not new!

“The flesh is consumed, the abdomen fills with water. The shoulders, clavicles, chest, and thighs, melt away. This illness is fatal.”



Hippocrates (460 BC)

Malnutrition Matters

Meeting Quality Standards in Nutritional Care

Ailsa Brotherton, Nicola Simmonds
and Mike Stroud
on behalf of the BAPEN Quality Group

2,500 years later....

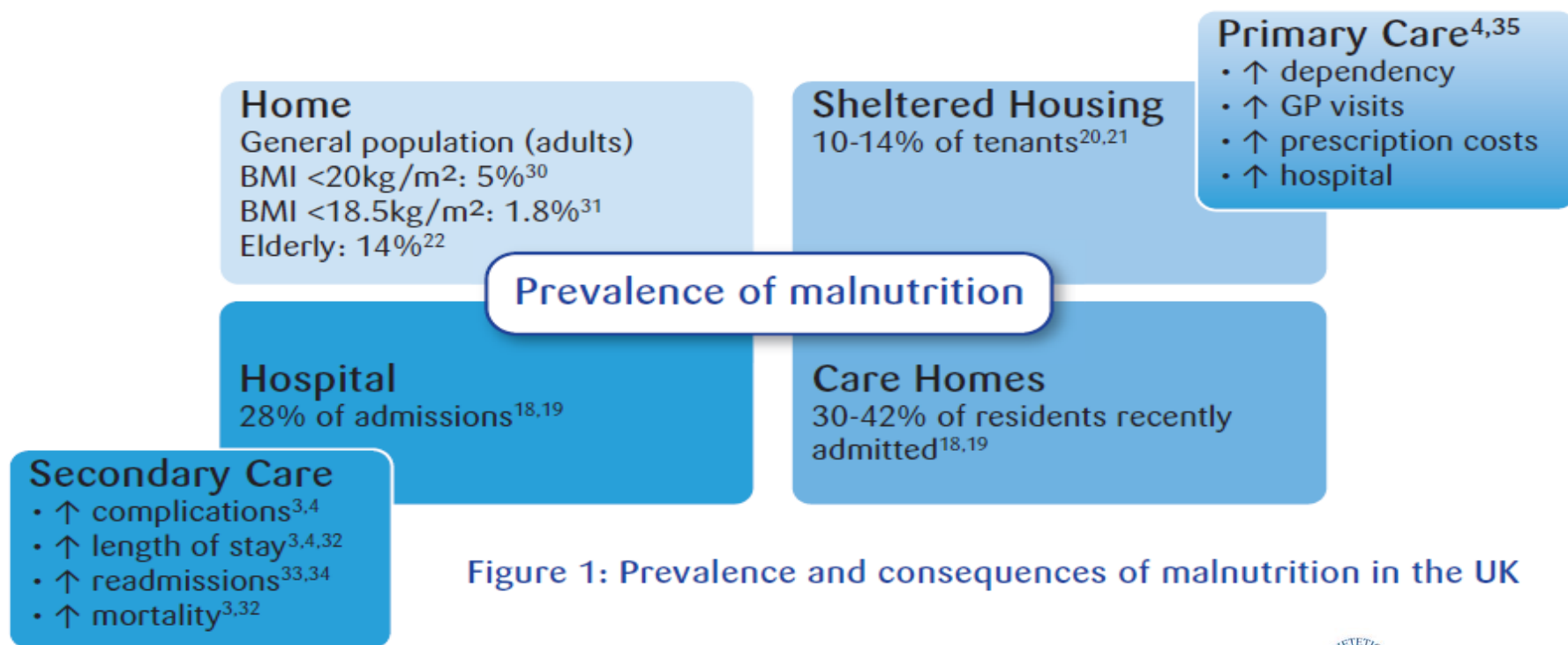


Figure 1: Prevalence and consequences of malnutrition in the UK

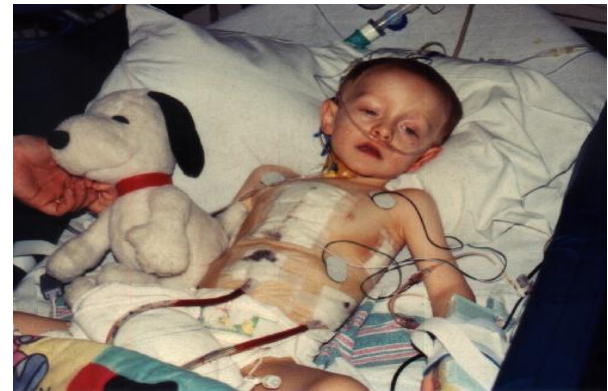
Which type of malnutrition?

Starvation-Associated Malnutrition



- Food security is **the** major cause
 - Low food availability & access
 - Unequal food provision
 - Poor hygiene
 - Inflammation secondary effect

Disease-Associated Malnutrition

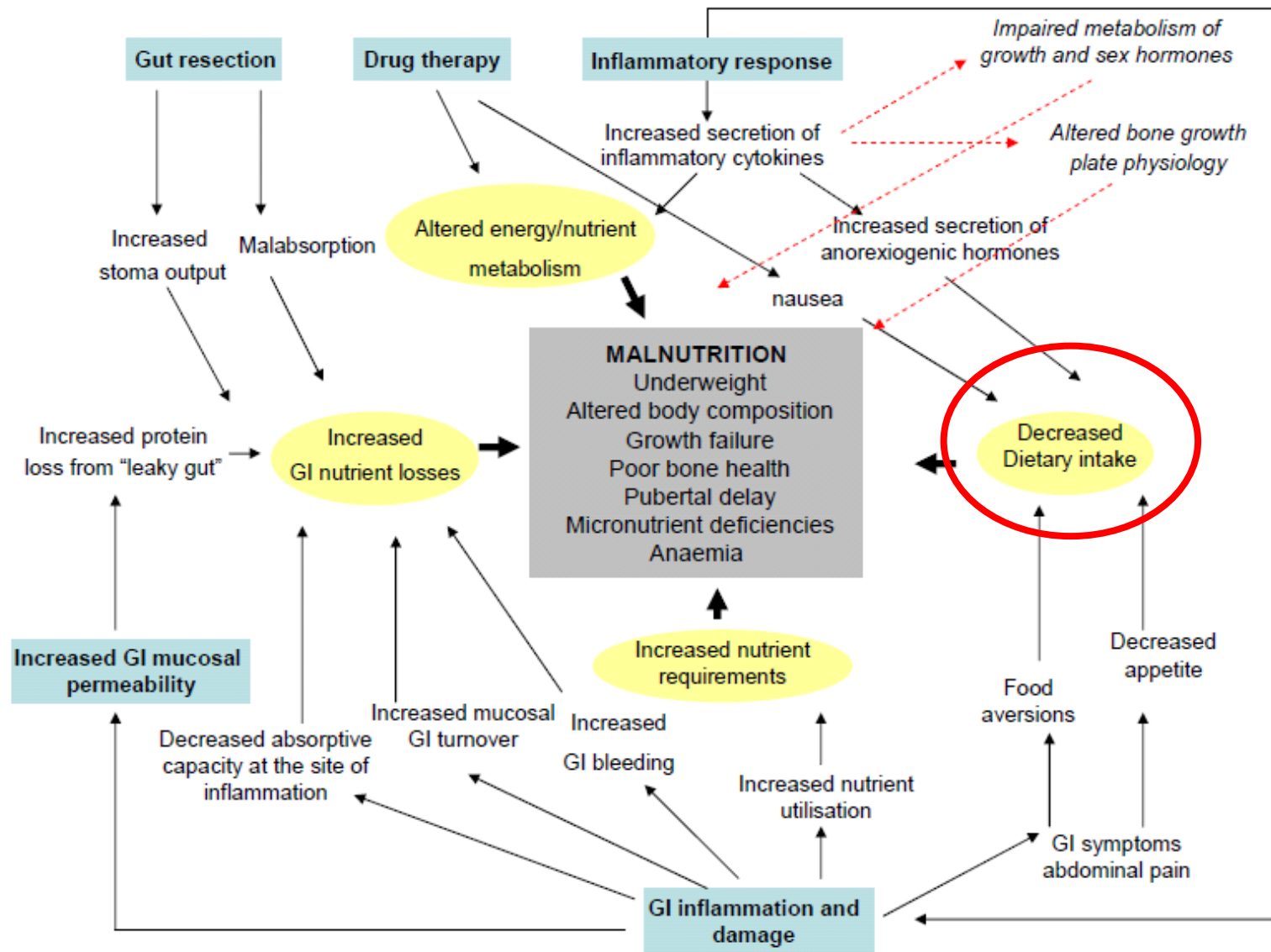


- Food security **not** a major issue

The impact of disease on:

- Appetite & food intake
- Energy/nutrient requirements
- Absorption/losses
- Inflammation primary effect

Malnutrition in Inflammatory Bowel Disease



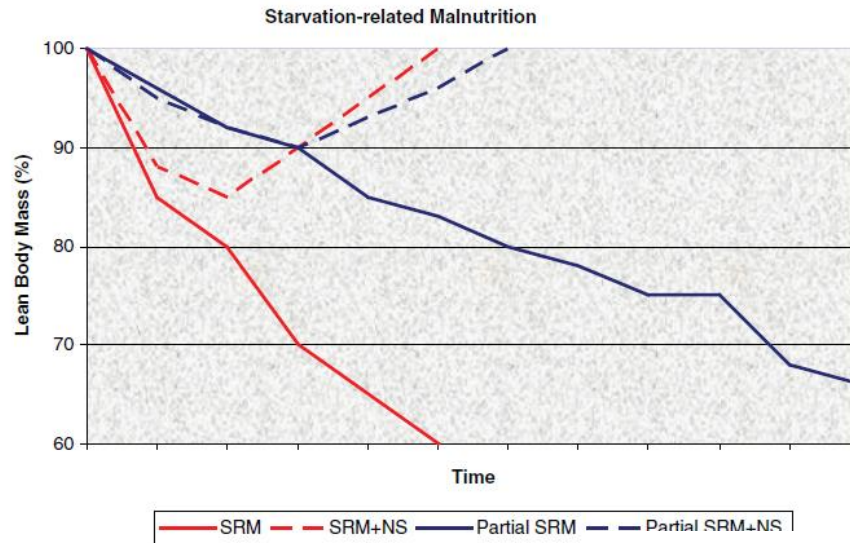
Dotted lines indicate non-nutrition associated factors in paediatric IBD malnutrition

Adult Starvation and Disease-Related Malnutrition : A Proposal for Etiology-Based Diagnosis in the Clinical Practice Setting From the International Consensus Guideline Committee

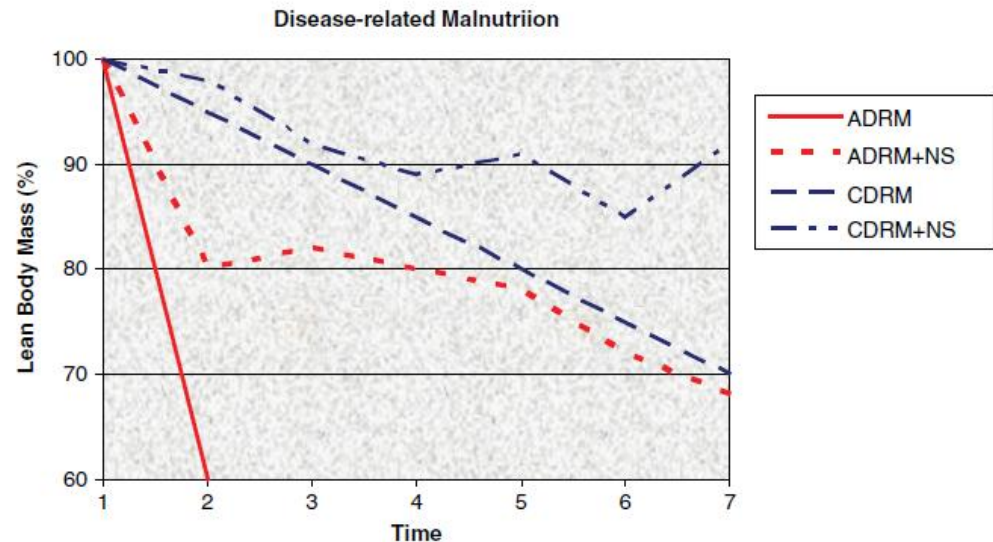
Gordon L. Jensen, Jay Mirtallo, Charlene Compher, Rupinder Dhaliwal, Alastair Forbes, Rafael Figueredo Grijalba, Gil Hardy, Jens Kondrup, Demetre Labadarios, Ibolya Nyulasi, Juan Carlos Castillo Pineda and Dan Waitzberg

JPEN J Parenter Enteral Nutr 2010 34: 156

DOI: 10.1177/0148607110361910



Which one to
prevent and treat
does matter



Suboptimal anthropometry at hospital admission



Prevalence of malnutrition and demographic aspects ($n = 2410$).

	Underweight ^a n (%)	p^b	Stunting ^c n (%)	Sum n (%)
Total group	167 (7%)		193 (7.9%)	322 (13.4%)
Moderate (-2 to -3 SDS)	120 (5%)		133 (5.5%)	241 (10.0%)
Severe (<-3 SDS)	47 (2%)		60 (2.5%)	97 (4.4%)
Age groups				
31 days-0.9 years	49 (10.8%)	<0.001	44 (9.7%)	79 (17.4%)
1-1.9 years	24 (8.3%)		31 (10.7%)	49 (17.0%)
2-5.9 years	24 (4.1%)		52 (8.8%)	73 (12.4%)
6-12.9 years	45 (6.9%)		42 (6.4%)	81 (12.4%)
13-17.9 years	25 (5.8%)		24 (5.6%)	40 (9.3%)
Sex				
Female	67 (6.1%)	0.188	81 (7.4%)	136 (12.5%)
Male	100 (7.6%)		112 (8.5%)	186 (14.1%)
Ethnic background				
Caucasian	142 (6.5%)	0.005	164 (7.4%)	280 (12.7%)
Non-caucasian	25 (11.8%)		29 (13.7%)	42 (19.9%)
Admission				
Acute	100 (7.9%)	0.038	103 (7.6%)	184 (13.7%)
Elective	67 (5.7%)		90 (8.3%)	138 (12.9%)
Chronic disease				
Yes	99 (9.2%)	<0.001	123 (11.4%)	195 (18.1%)
No	68 (5.1%)		70 (5.3%)	127 (9.6%)
Ward				
Surgical	33 (7.1%)	0.897	33 (7.1%)	59 (12.7%)
General	134 (6.9%)		160 (8.9%)	263 (13.5%)

^a Defined as body mass index <-2 standard deviation scores (SDS).

^b Chi²-test; comparison between the malnourished and not malnourished patients.

^c Defined as height/length for age <-2 SDS.



How to assess nutrition in routine clinical practice and which are the pitfalls?



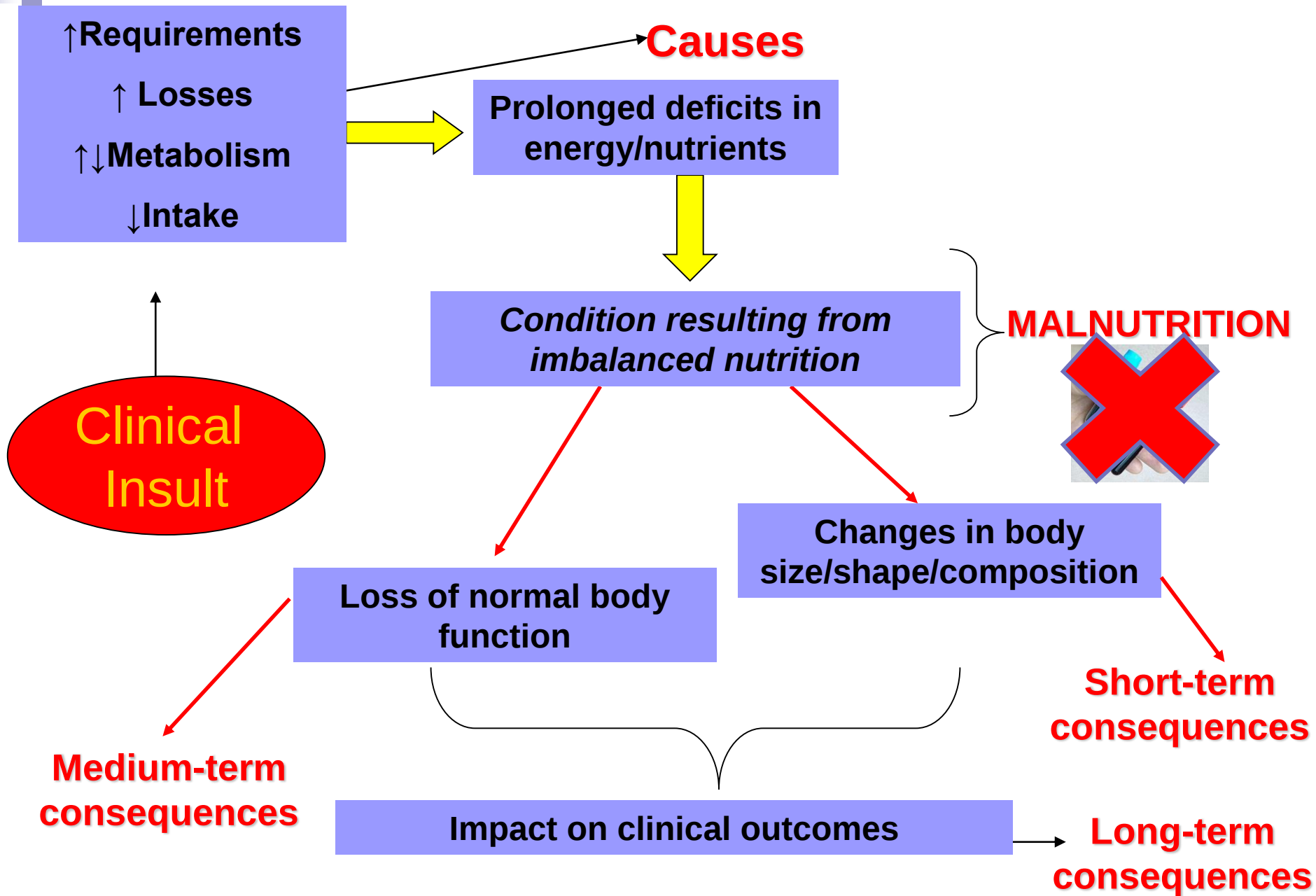
Malnutrition is not simply a measurement of anthropometry

“Undernutrition is a condition resulting from imbalanced nutrition which causes clinically meaningful adverse effects on tissue function, body size/composition with subsequent impact on health outcomes”

*Condition resulting from
imbalanced nutrition*

MALNUTRITION





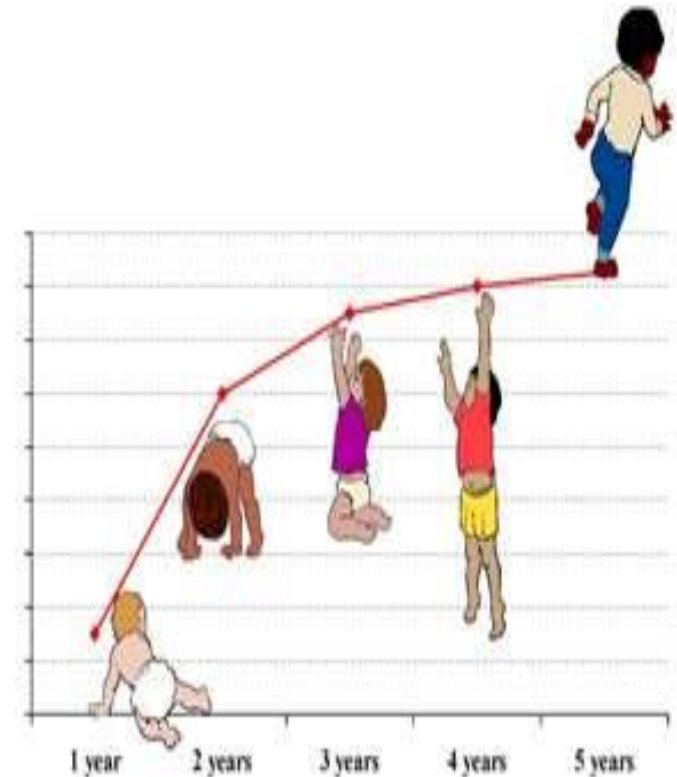
Mainstream approaches to assess nutritional status

- ☐ **A**nthropometric measurements
- ☐ **B**iochemical measurements
- ☐ **C**linical examination (“eyeballing”)
- ☐ **D**ietary intake
- ☐ **E**nvironment



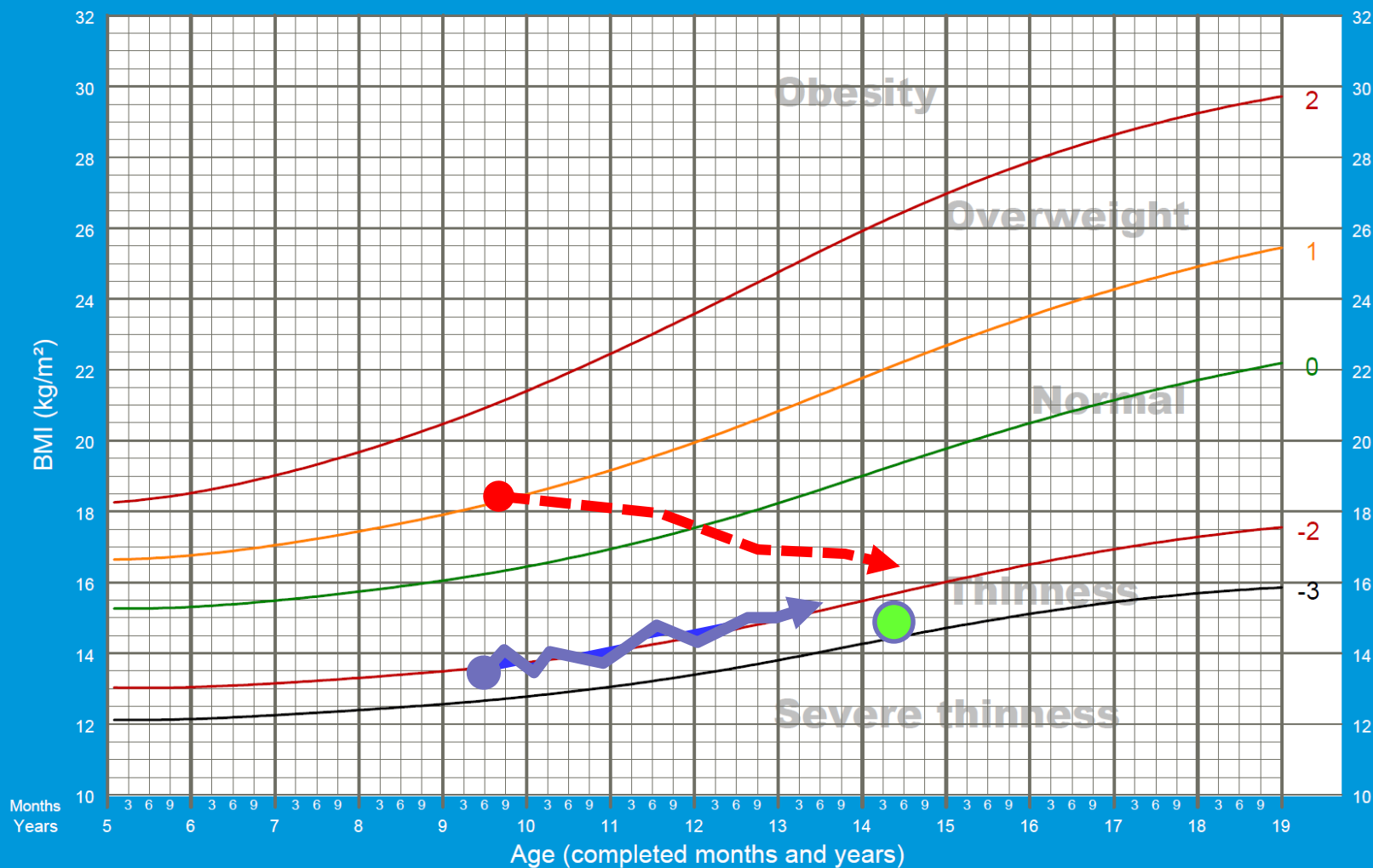
Anthropometry & growth charts

- The minimum and foremost minimum screening method
- Serial measurements more informative than a single/spot measurements
- Interpretation of patterns is important

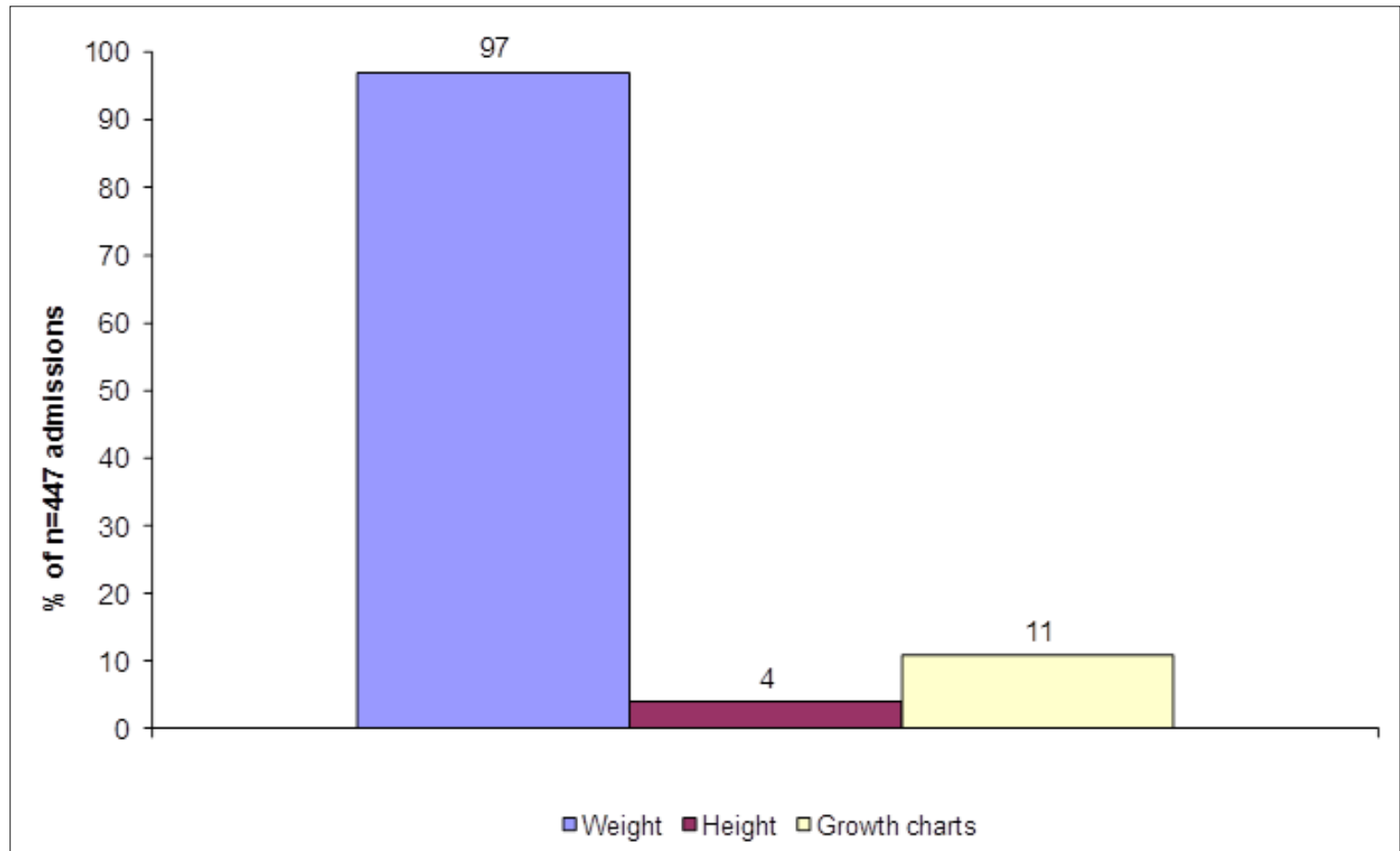


BMI-for-age BOYS

5 to 19 years (z-scores)



Opportunistic measurements of weight and height on admission



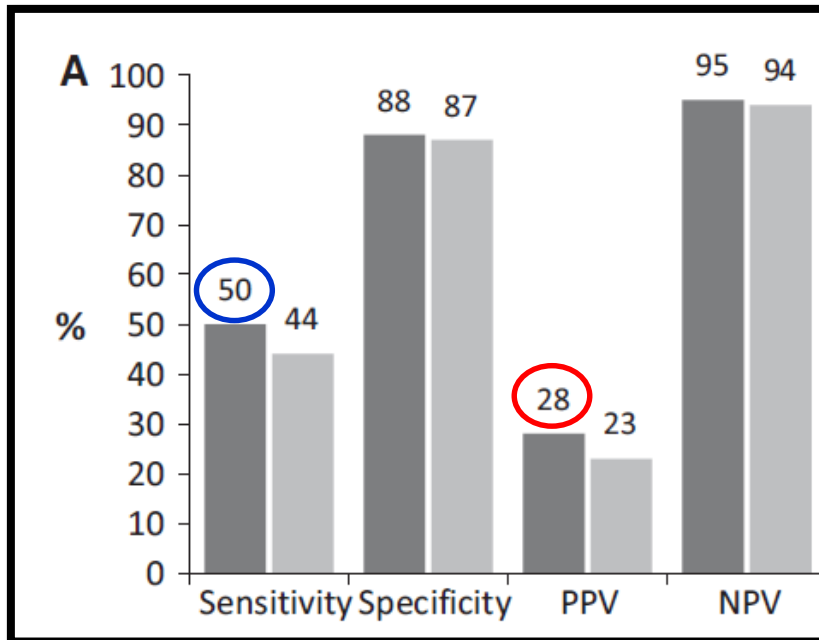
SHORT COMMUNICATION

Visual inspection is not a substitute for anthropometry in screening for nutritional status and growth in sick children

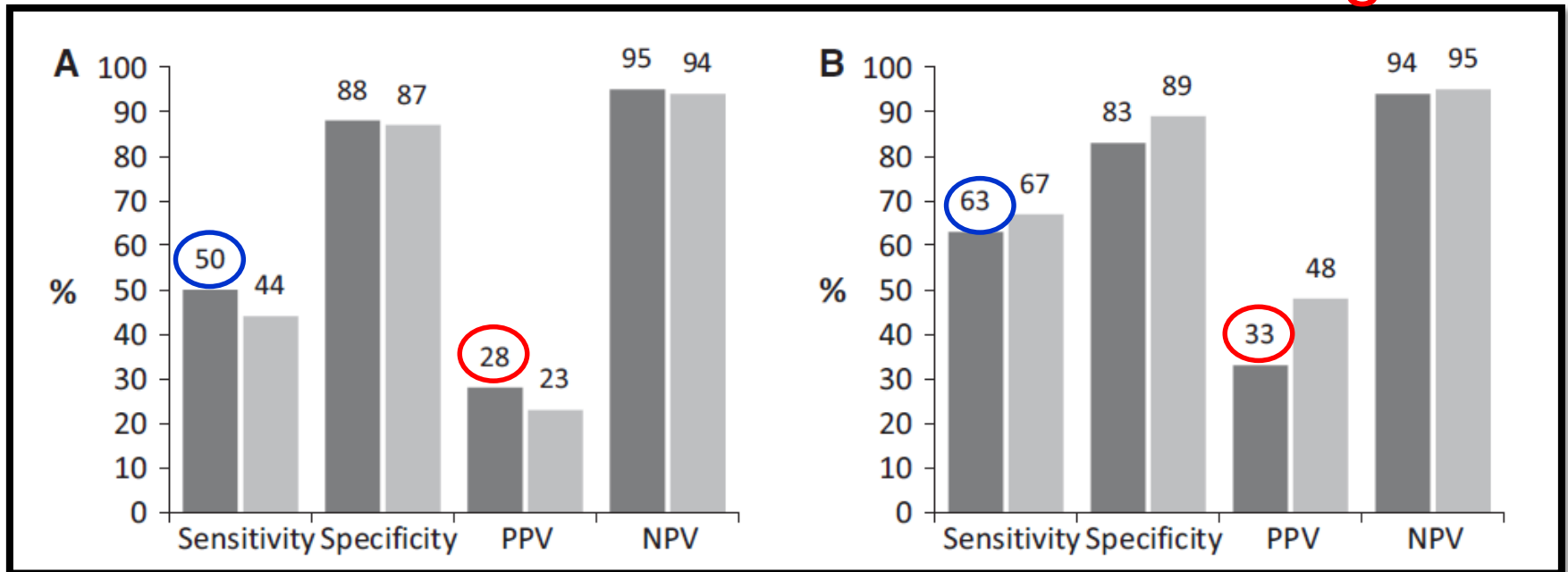
Jennifer McKechnie, Konstantinos Gerasimidis (konstantinos.gerasimidis@glasgow.ac.uk)

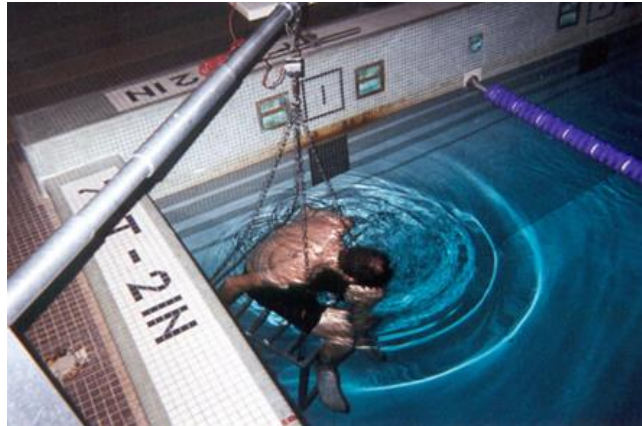
Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences, Glasgow Royal Infirmary, University of Glasgow, Glasgow, UK

Short

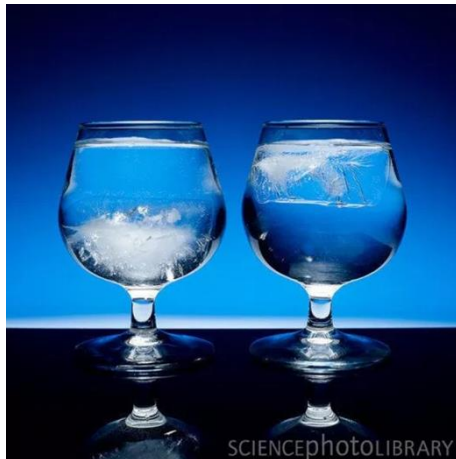


Underweight

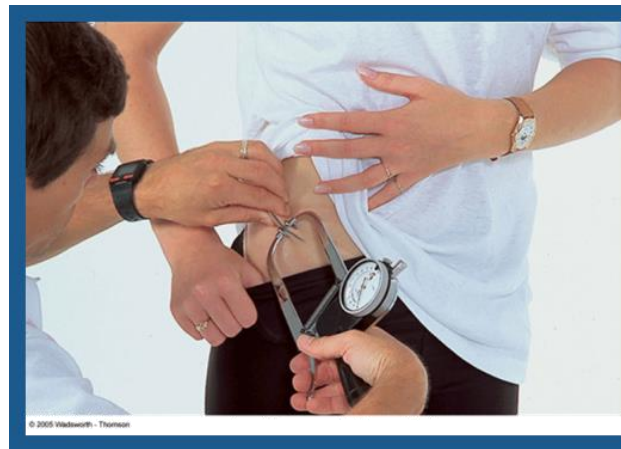




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SCIENCEPHOTOLIBRARY



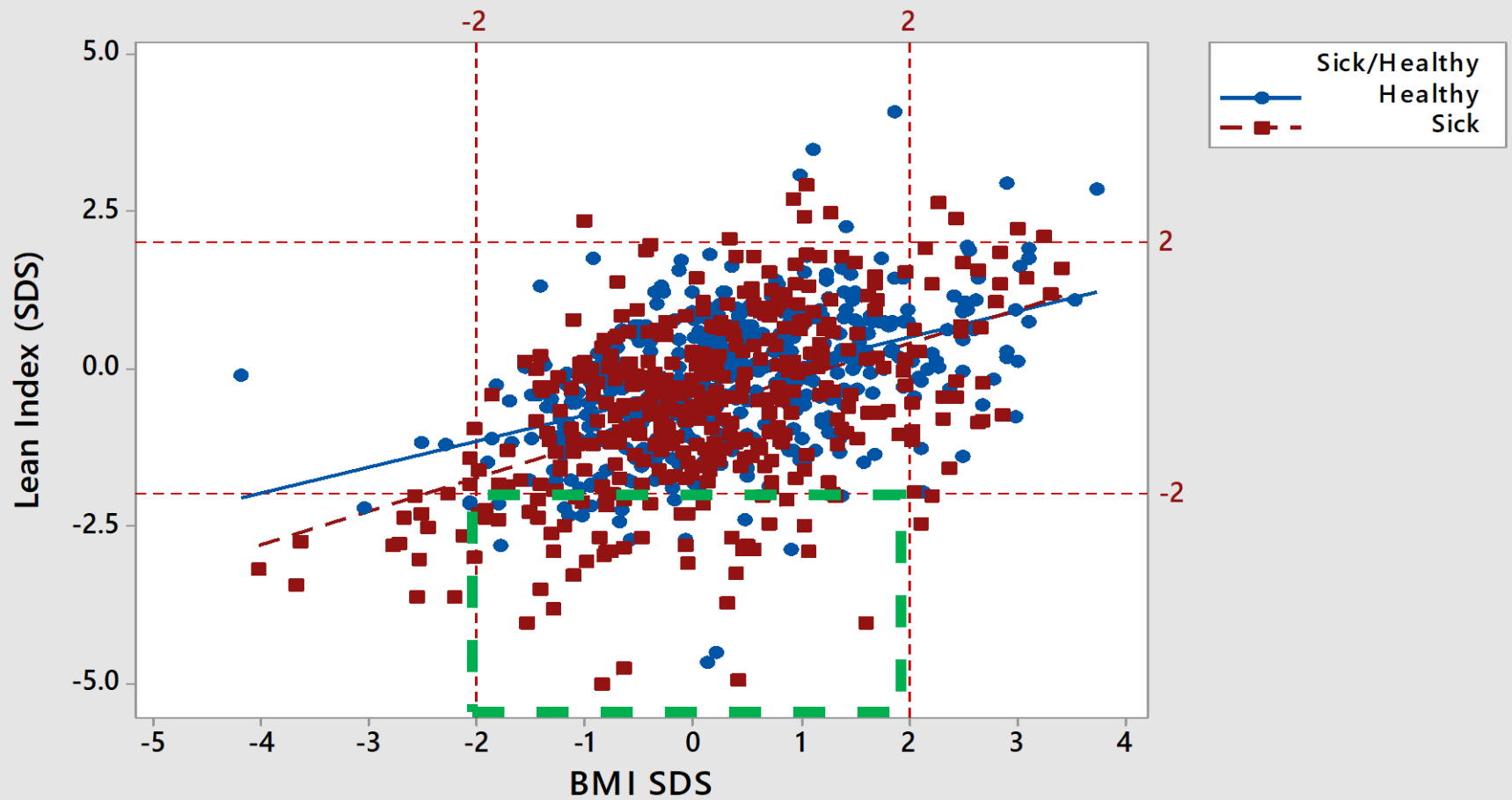
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Set-up shown is typical of ImpediMed devices intended for estimation of whole body composition



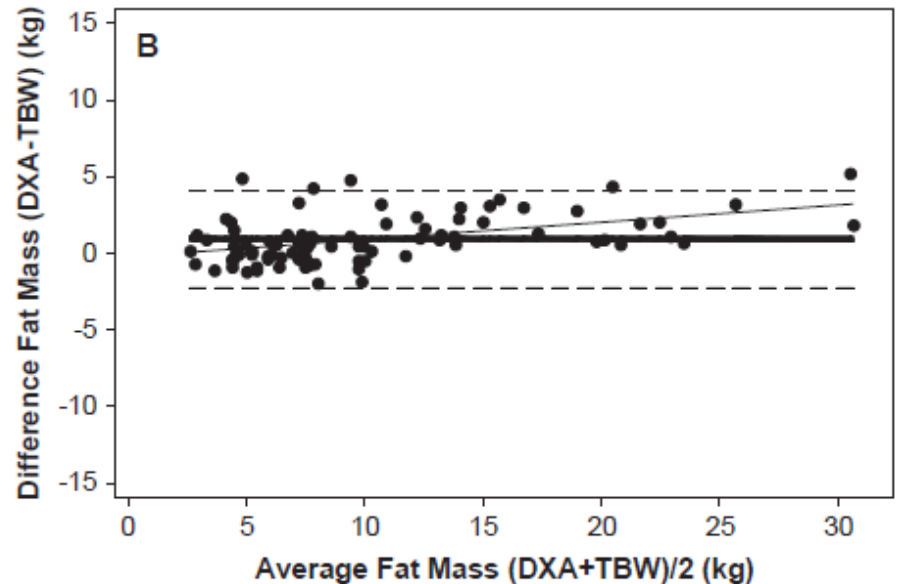
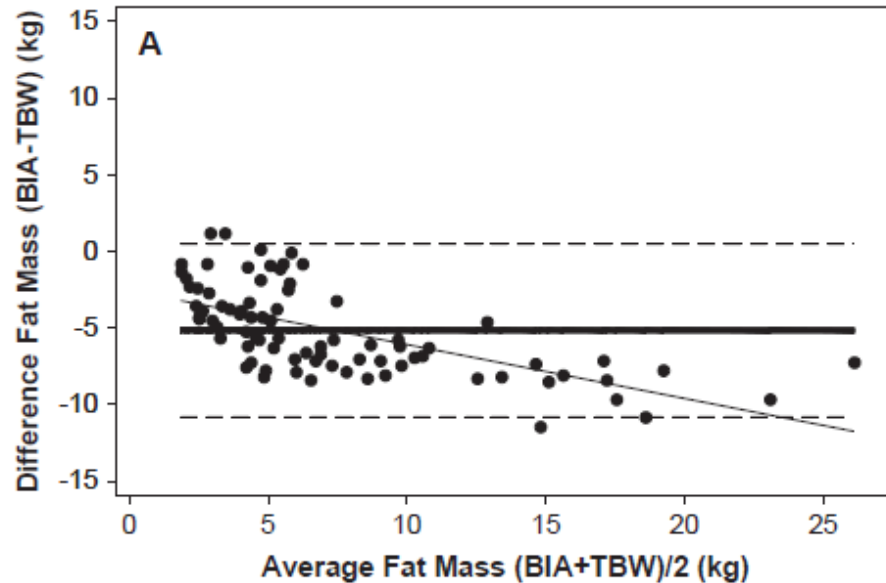
Scatterplot of Lean Index vs SDS_BMI



Validation of dual-energy x-ray absorptiometry and foot-foot impedance against deuterium dilution measures of fatness in children

JOHN J. REILLY¹, KOSTAS GERASIMIDIS¹, NATASA PAPARACLEOUS¹,
ANDREA SHERRIFF^{1,2}, AMANDA CARMICHAEL³, ANDREW R. NESS⁴ &
JONATHAN C. WELLS⁵

Bedside vs Reference methods



Estimation bias is random and unpredictable in healthy and patient groups

TABLE 5

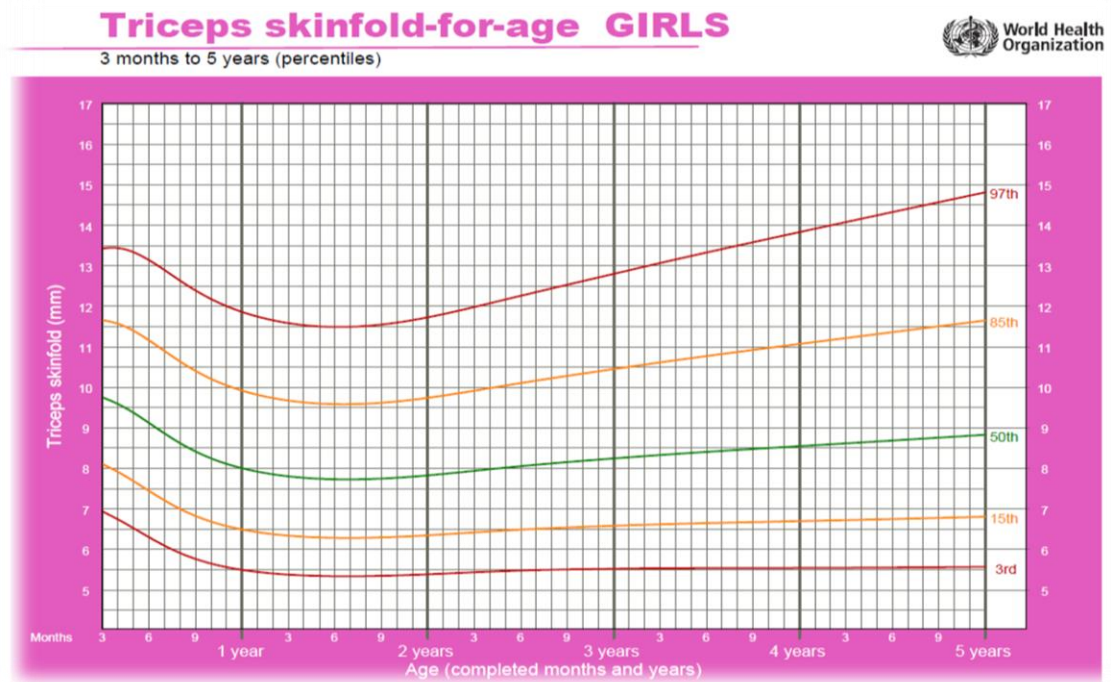
Bland-Altman analysis of mean bias in fat mass (FM), fat-free mass (FFM), weight, and percentage fat measured by dual-energy X-ray absorptiometry (DXA) compared with the 4-component model¹

	Absolute bias ²	Absolute 95% limits of agreement	Bias as a percentage of the mean ³	95% limits of agreement as a percentage of the mean	P for the bias from zero ⁴	r ⁵	P for the correlation
			%	%			
FM							
Adults							
Nonobese men (n = 26)	1.35	±2.82	12.4	±25.3	< 0.001	0.38	NS
Nonobese women (n = 44)	1.21	±2.29	6.19	±14.8	< 0.001	0.58	< 0.01
Obese women (n = 14)	1.58	±3.50	4.60	±11.0	< 0.01	-0.04	NS
Children							
Nonobese boys (n = 30)	-0.52	±1.17	-10.9	±23.8	< 0.001	0.10	NS
Nonobese girls (n = 22)	0.01	±1.24	9.72	±10.6	NS	0.46	< 0.05
Obese boys (n = 11)	0.93	±1.86	3.52	±7.06	< 0.01	-0.08	NS
Obese girls (n = 17)	0.46	±2.42	2.26	±9.39	NS	-0.24	NS
Boys with CF (n = 12)	-0.14	±1.83	0.38	±29.9	NS	-0.53	NS
Girls with CF (n = 14)	0.18	±1.42	0.77	±26.6	NS	0.48	NS
Boys and girls with GSD (n = 12)	-0.06	±2.28	-3.67	±22.6	NS	0.63	< 0.05

Which is the method of body composition to use in routine practice ?



Which is the method of body composition to use in routine practice ?





Biochemical markers on malnutrition?

No biomarkers for protein/energy stores!

Serum albumin, prealbumin

- Expensive, time consuming, need blood
- Are **NOT** marker of malnutrition but disease activity index

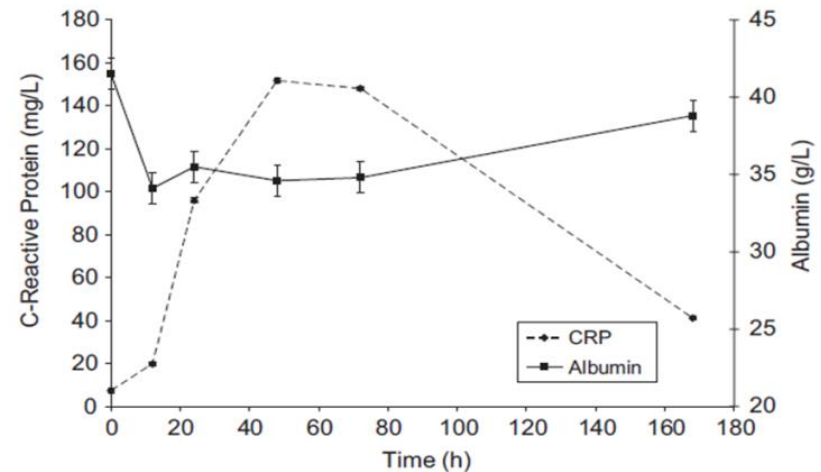


Fig. 1 The concentration changes of albumin and CRP (mean $\pm$ SE).

Serum Albumin

1023.e4

Table 1 Albumin and Body Mass Index (BMI)

Study (First Author)	Year	# of Subjects	Age (years)	Sex	Reason for Nutrition Restriction	Duration of Nutrition Restriction	BMI (kg/m ²) ± SD	Albumin (g/dL) ± SD
Nishida ¹³	2010	210	29.9 ± 5.31	F	BMI <18.5 but no anorexia nervosa		17.5 ± 0.78	4.49 ± 0.2
Rigaud ¹⁴	2000	118	32.9 ± 4.29	F	Self-reported wt loss >1 kg		20.7 ± 3.33	4.45 ± 0.21
		5	29.8 ± 9.3	F	Near-death anorexia nervosa		9.77 ± 0.1	3.35 ± 0.28
		16	25.2 ± 3.9		Anorexia nervosa		13.6 ± 1.1	4.05 ± 0.58
Chui ¹⁵	2008	63	21.3 ± 2.3	F	Anorexia nervosa	6.5 ± 1.7 years	21.8 ± 3.4	4.13 ± 0.28
Dostalova ¹⁶	2010	16	24.9 ± 1.34	F	Anorexia nervosa		15.7 ± 0.3	4.38 ± 0.112
Gendall ¹⁷	1999	152	25.9 ± 6.0	F	Bulimia nervosa	71.1 ± 65.6 months	23 ± 2.7	4.87 ± 0.34
Gentile ¹⁸	2011	298	19.8 ± 6.1	278 F, 20 M	Anorexia nervosa, eating		14.6 ± 2.1	4.8 ± 0.5

In these otherwise healthy subjects, serum albumin and prealbumin levels were not “markers of nutritional status.” The “markers” failed to identify subjects with severe protein-calorie malnutrition until extreme starvation (BMI <12 kg/m²)

Krantz ³¹	2005	1	52	F	Anorexia nervosa	20 years	17	4
Lawson ³²	2009	10	27.5 ± 2.4	F	Anorexia nervosa		18.3 ± 0.3	4.7 ± 0.1
		10	25.8 ± 1.1	F	Anorexia nervosa		18 ± 0.4	4.4 ± 0.1
		14	15.1 ± 2.56	F	Anorexia nervosa	9.4 ± 6.3 months	15.24 ± 1.71	4.51 ± 0.69
Nova ³³	2004	14	15.1 ± 2.56	F	Anorexia nervosa			
Olubodun ³⁴	1996	81	27.7 ± 5.9	M	Prisoners	229.1 ± 210.1 days	20 ± 2.7	3.66 ± 0.63
Rigaud ³⁵	2009	16	26 ± 9 (all)	115 F, 5 M (all)	Anorexia nervosa		11.1 ± 0.65	3.24 ± 0.51
		35			Anorexia nervosa		13.1 ± 0.5	4.02 ± 0.69
		35			Anorexia nervosa		15 ± 0.49	4.18 ± 0.63
		21			Anorexia nervosa		16.8 ± 0.51	4.34 ± 0.64
		13			Anorexia nervosa		19.5 ± 2.4	4.11 ± 0.72
Rock ³⁶	1995	13	26 ± 8	12 F, 1 M	Anorexia nervosa, Bulimia nervosa	6.4 ± 3.3 years	17.4 ± 2.9	4.1 ± 0.5
Smith ³⁷	1996	6	27.2 ± 2.36	F	Anorexia nervosa		15.35 ± 0.694	3.7 ± 0.193
Van Binsbergen ³⁸	1988	20	24.7	F	Anorexia nervosa	4.9 years	14.4	4.07

Medicine, Vol 128, No 9, September 2015

Nutrition Screening Tool (NST)

A step-by-step guide to using STAMP

Step 1 – Diagnosis
Does the child have a diagnosis that has any nutritional implications?

Response	Score
Definitely	3
Possibly	2
No	0

Step 2 – Nutritional intake
What is the child's nutritional intake?

Response	Score
None	3
Recently decreased/poor	2
No change/good	0

Step 3 – Weight and height
Use a growth chart or the centile quick reference tables to determine the child's measurements

Measurements	Score
> 3 centiles/columns apart (or weight < 2 nd centile)	3
> 2 centiles/columns apart	1
Similar centiles/columns	0

Step 4 – Overall risk of malnutrition
Add the scores from steps 1–3 together to calculate the overall risk of malnutrition

Risk Level	Score
High risk	≥ 4
Medium risk	2–3
Low risk	0–1

Step 5 – Care plan
Develop a care plan based on the child's overall risk of malnutrition

Risk Level	High risk	Medium risk	Low risk
High risk	- Refer to a Dietitian, nutritional support team or consultant - Monitor and review care plan weekly	- Monitor nutritional intake for 3 days - Repeat STAMP screening after 3 days - Amend care plan as required	- Continue routine clinical care - Repeat STAMP screening weekly while child is an in-patient - Amend care plan as required

Supported by Abbott Nutrition
Central Manchester and Manchester Children's University Hospitals
© 2008 Central Manchester and Manchester Children's University Hospitals

University of Glasgow
iNEWS
infant nutrition early warning score

NHS
Greater Glasgow and Clyde

Name: _____ Sex: _____
DOB: _____ Weight (to nearest 10g): _____ Ward: _____
Date of screening: _____ Hospital number: _____

Paediatric Yorkhill Malnutrition Score (PYMS)

NHS
Greater Glasgow and Clyde

Name: _____ Hospital No: _____ Date: _____
Surname: _____ CHI: _____ Nurse Signature: _____
DOB: _____ Weight: _____
Age: _____ Sex: F / M _____ Height: _____
Ward: _____ Consultant: _____ BMI: _____

1	Is the BMI below the cut-off value in the table overleaf?	NO	0		
2		YES	2		
3	Has the child lost weight recently?	NO	0		
4		YES	1		
5		- Unintentional weight loss - Clothes looser - Poor weight gain (if <2yrs)			
6	Has the child had a reduced intake (including feeds) for at least the past week?	NO	0		
7		Decrease of usual intake for at least the past week	1		
8		YES	2		
9		No intake (or a few sips of feed only) for at least the past week			
10	Will the child's nutrition be affected by the recent admission/condition for at least the next week?	NO	0		
11		For at least the next week	1		
12		- Decreased intake and/or - Increased requirements and/or - Increased losses			
13		YES	2		
14		No intake (or a few sips of feed only) for at least the next week			
15	Calculate total score (total of steps 1-14)	Total PYMS Score			

PYMS must be completed by a registered nurse

© Nutrition Tool Steering Group, Women and Children's Directorate, NHS Greater Glasgow and Clyde, 2009.

Step 2. Herkenning risico op ondervoeding met behulp van STRONG₁₈
De totaalscore van het screeninginstrument STRONG₁₈ geeft het risico op ondervoeding bij oprijdens opname aan.

Screening risico op ondervoeding met STRONG ₁₈	Score is gelijk antwoord U/A
Bij opname en vervolgens 1x per week bij kinderen van 1 maand - 18 jaar	
1) Is er sprake van een ziektebeeld met een verhoogd risico op ondervoeding (zie tabel hieronder)?	2
2) Verkeert op basis van uw klinische blik de patiënt in een slechte voedingstoestand: inschatting ingevallen gewicht en/of verlies subcutaan vet en/of verlies spijsmassa?	1
3) Is er sprake van 1 van onderstaande punten: - Overmatig diarree (>5x daags) dunnig ontlasting en/of vervoer (>3x daags) gedurende de laatste 1-3 dagen, en/of - Bestaande voedingsinterventie met toernik- of schrobvoeding, en/of - Budeijk verminderde innamen gedurende de laatste 1-3 dagen, en/of - Belemmering van voedselname door pijn?	1
4) Is er sprake van gewichtsverlies of stilstaan (<1 jaar) in groei/gewicht gedurende de laatste weken tot maanden?	1

Totaalscore risico op ondervoeding, advies voedingsinterventie en follow-up

Score	Risico	Interventie en follow-up
Score 0	laag	Geen voedingsinterventie nodig. Controleer gewicht regelmatig volgens ziekenhuisbeleid. Evalueer risico na 1 week.
Score 1-3	matig	Overleg voedingbeleid eventueel met diëtist. Controleer gewicht 2x per week. Evalueer risico na 1 week.
Score 4-6	hoog	Ga naar Step 3. Specifiek voedingsadvies in overleg met diëtist. Controleer gewicht 2x per week en evalueer voedingsadvies. Evalueer risico na 1 week.

Risicovolte ziektebeelden

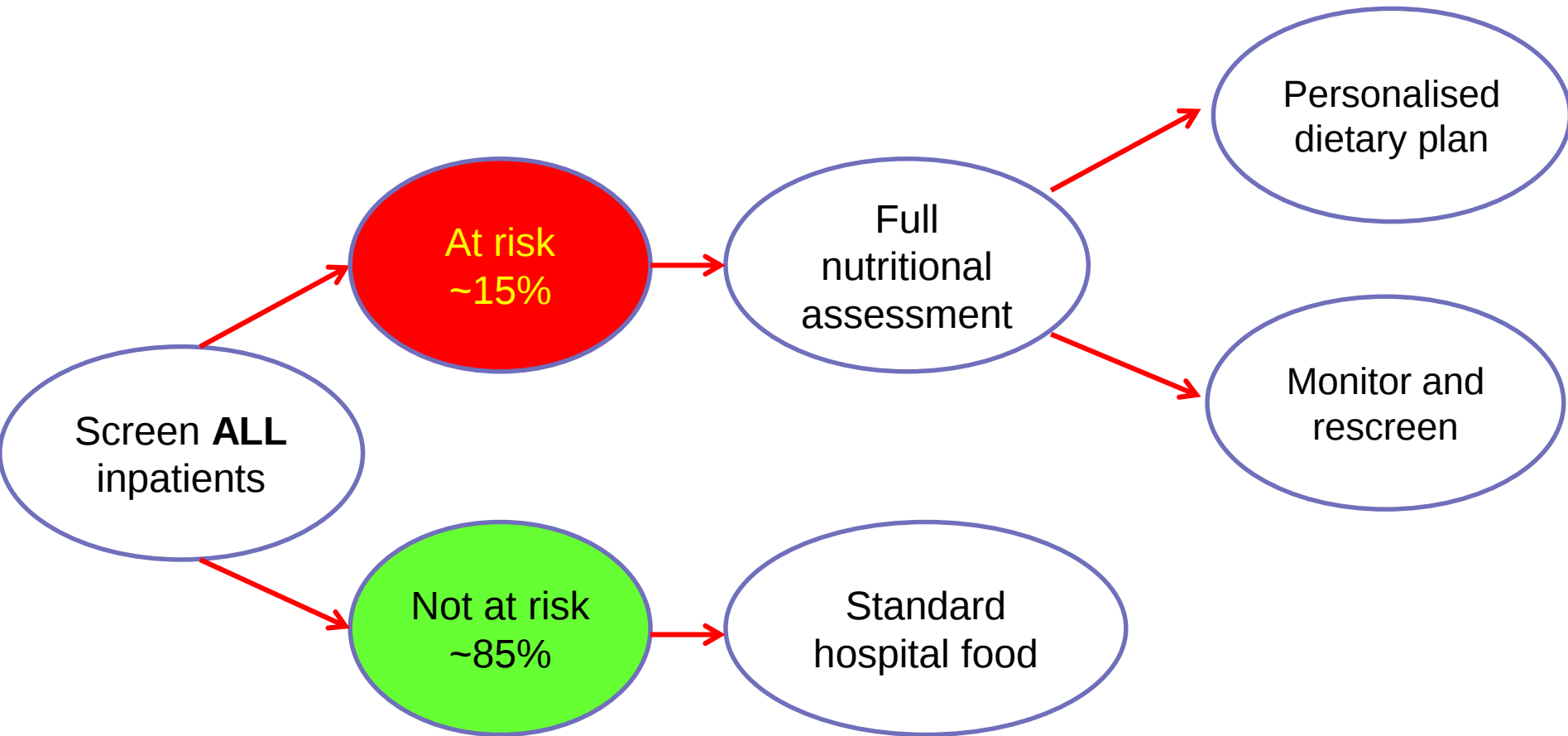
- Anorexia nervosa	- Dysmatuurspremautis (tot 6 maanden na term geboorte)	- Leverziekten, chronisch	- Sperziekten
- Brandwonden	- Hartziekten, chronisch	- Niet nacler gespeeld	- Spijsmissingsziekten
- Bronchopulmonale dysplasie	- Intestieziekten (acute)	- Pancreatitis	- Trauma
- (<2 jaar)	- Intestinale darmziekten	- Short bowel syndrome	- Verstandelijke handicap/retraite
- Cystische Fibrose	- Kanker		- Verwachte grote operatie

McCarthy *et al*, JHND 2012

Gerasimidis *et al*, BJN 2010
Gerasimidis *et al*, Clin Nutr 2011
Gerasimidis *et al*, Clin Nutr 2018

Hulst *et al*, Clin Nutr, 2010

NST are not malnutrition assessment methods but dietetic referral tools



Concurrent/criterion validity



PYMS vs STAMP vs STRONGkids

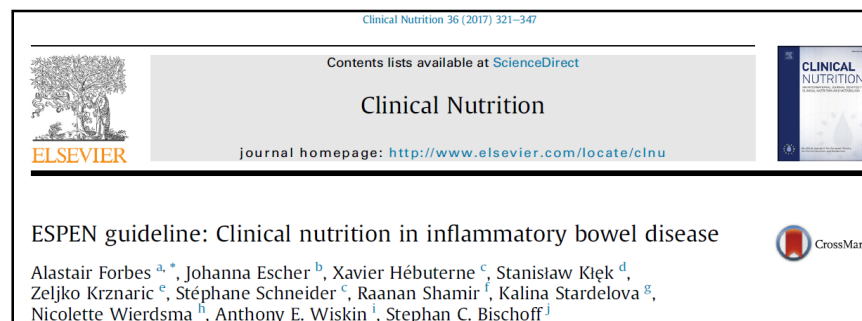
Characteristics of the “ideal” NST

■ Good diagnostic validity

- Identifies the majority of patients you want to treat (sensitivity)
- Equally important good positive predictive value (i.e. low false positive rate)

- Practical, quick, cheap, user friendly
- Can be implemented and perform well in clinical practice
- Does not waste resources and does not increase workload substantially
- Make a difference in patients' care

Micronutrient assessment in sick children



ECCO Topical Review

Research Gaps in Diet and Nutrition in Inflammatory Bowel Disease. A Topical Review by D-ECCO Working Group [Dietitians of ECCO]



Rotem Sigall-Boneh,^{a,*} Arie Levine,^b Miranda Lomer,^c Nicolette Wierdsma,^d Philip Allan,^e Gionata Fiorino,^f Simona Gatti,^g Daisy Jonkers,^h Jarosław Kierkuś,ⁱ Konstantinos H. Katsanos,^j Silvia Melgar,^k Elif Saritas Yuksel,^l Kevin Whelan,^m Eytan Wine,ⁿ Konstantinos Gerasimidis^o

Nutrition in Pediatric Inflammatory Bowel Disease: A Position Paper on Behalf of the Porto Inflammatory Bowel Disease Group of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition

^{*}Erasmus Miele, [†]Raanan Shamir, [‡]Marina Aloï, [§]Amit Assa, ^{||}Christian Braegger, [¶]Jiri Bronsky, ^{¶¶}Lissy de Ridder, ^{¶¶¶}Johanna C. Escher, ^{¶¶¶¶}Iva Hojsak, ^{¶¶¶¶¶}Sanja Kolaček, ^{¶¶¶¶¶¶}Sibylle Koletzko, ^{¶¶¶¶¶¶¶}Arie Levine, ^{¶¶¶¶¶¶¶¶}Paolo Lionetti, ^{¶¶¶¶¶¶¶¶¶}Massimo Martinelli, ^{¶¶¶¶¶¶¶¶¶¶}Frank Ruemmele, ^{¶¶¶¶¶¶¶¶¶¶¶}Richard K. Russell, ^{¶¶¶¶¶¶¶¶¶¶¶¶}Rotem Sigall Boneh, ^{¶¶¶¶¶¶¶¶¶¶¶¶¶}Johan van Limbergen, ^{¶¶¶¶¶¶¶¶¶¶¶¶¶¶}Gigi Veereman, and ^{¶¶¶¶¶¶¶¶¶¶¶¶¶¶¶}Annamaria Staiano



When to do it?



Who?



**IF YOU'RE
GOING TO
DO IT
THEN DO IT
RIGHT**

Conventional approaches to assess body micronutrient status



1. Clinical examination/symptoms
2. Dietary assessment
3. Lab biomarkers

Clinical symptoms

- Clinical relevance and needs clinicians
- Very rare in developed countries
- Present when stores are depleted
- Some specific some very unspecific (e.g. acne, tiredness, dry skin)
- Should be complemented by other assessments

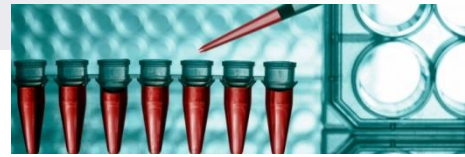




Dietary assessment of micronutrients

- Meet dietary references values=adequate body stores
- Micronutrient needs in disease=health?
- Requires dietitians and laborious dietary assessment (7-14d weighted diaries)
- Fairly imprecise at assessments per individual patient
 - Better for group averages
- Not to be used in isolation but complement other assessment

Laboratory biomarkers

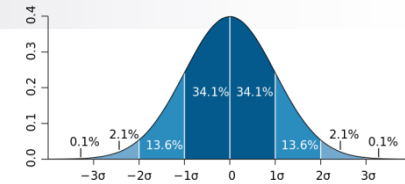


- Standard approach in routine clinical practice
- Two common methods
 - *Direct measurements of nutrient (blood, urine)*
 - *Functional markers (glutathione peroxidase, trankeolase activity)*



Caveats in the interpretation of micronutrient biomarkers

1) Reference range/values

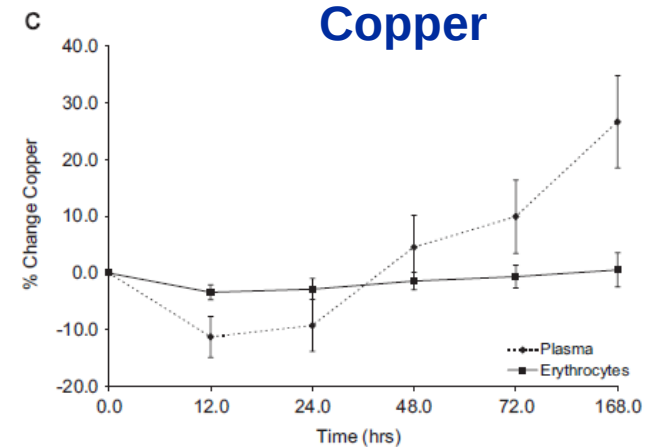
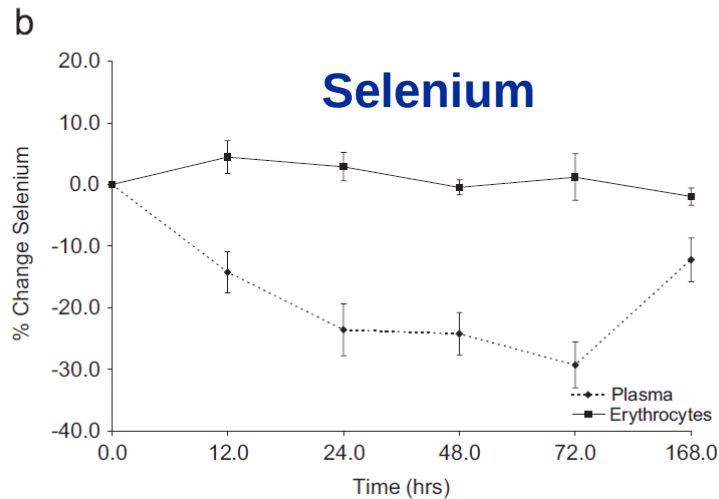
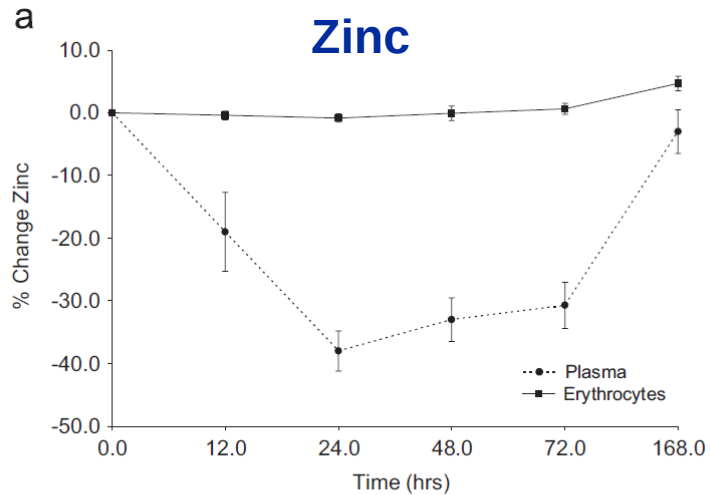


- **Excellent “optimal/ideal” references for growth charts (WHO)**
 - Similar ranges for some micronutrients in children are lacking
- **Origin of micronutrient reference values is unknown**
 - Selective or random?
 - Lack of paediatric references and replace with adults
- **How much is the problem in an ‘normal’ population?**

2) Effect of systemic inflammatory response on blood micronutrient levels

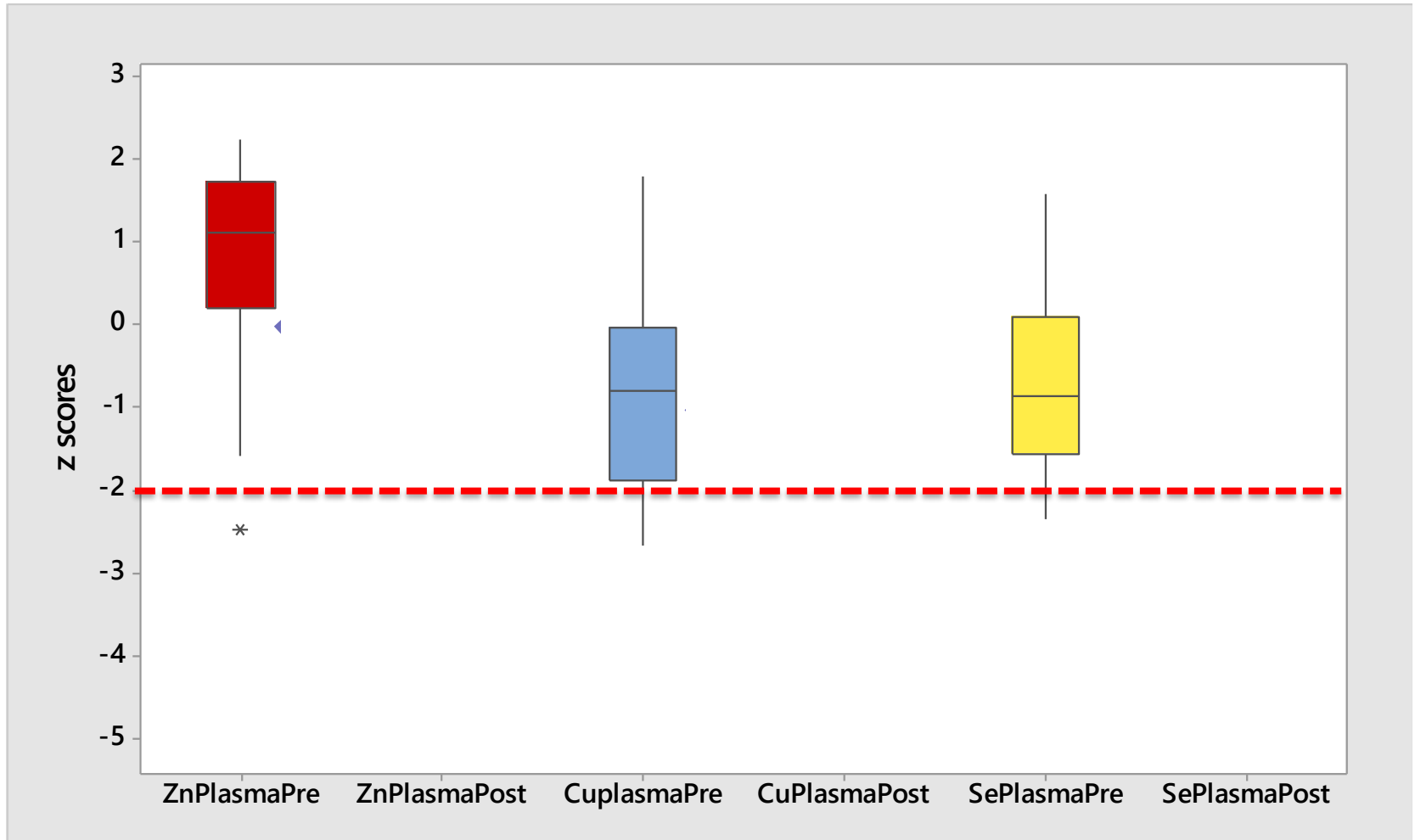
- Systemic inflammatory response (SIR) alters blood micronutrient status independently of actual body stores
 - Redistribution of nutrients to other tissues (liver)
 - Shifts in vascular fluids (dilution effect)
 - Loss of nutrient carrier protein (serum albumin, lipoproteins)
 - Increased excretion (urine)

Plasma micronutrients & acute phase response

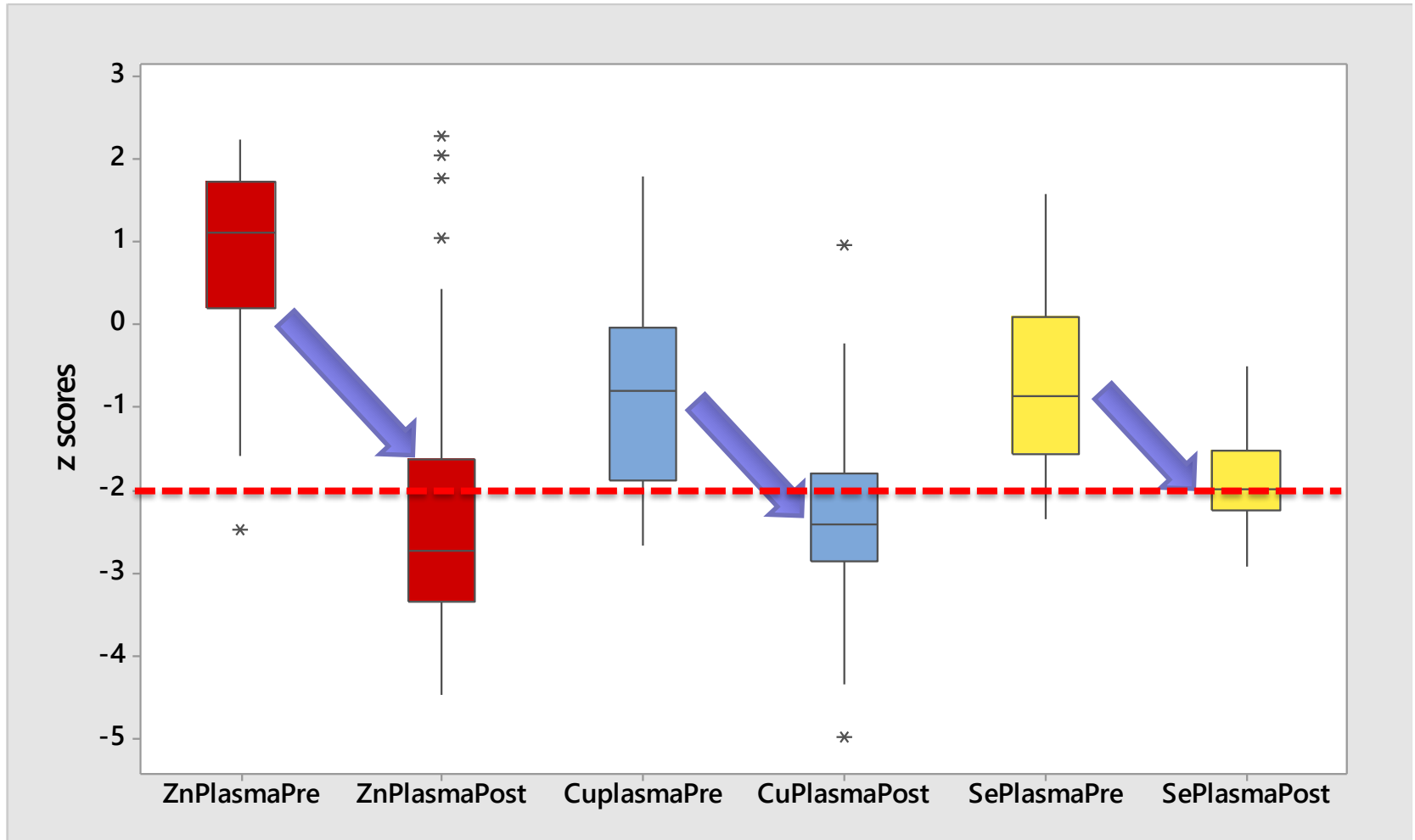


Serial %changes in serum and erythrocyte levels of well nourished healthy subjects who were admitted for elective hip surgery

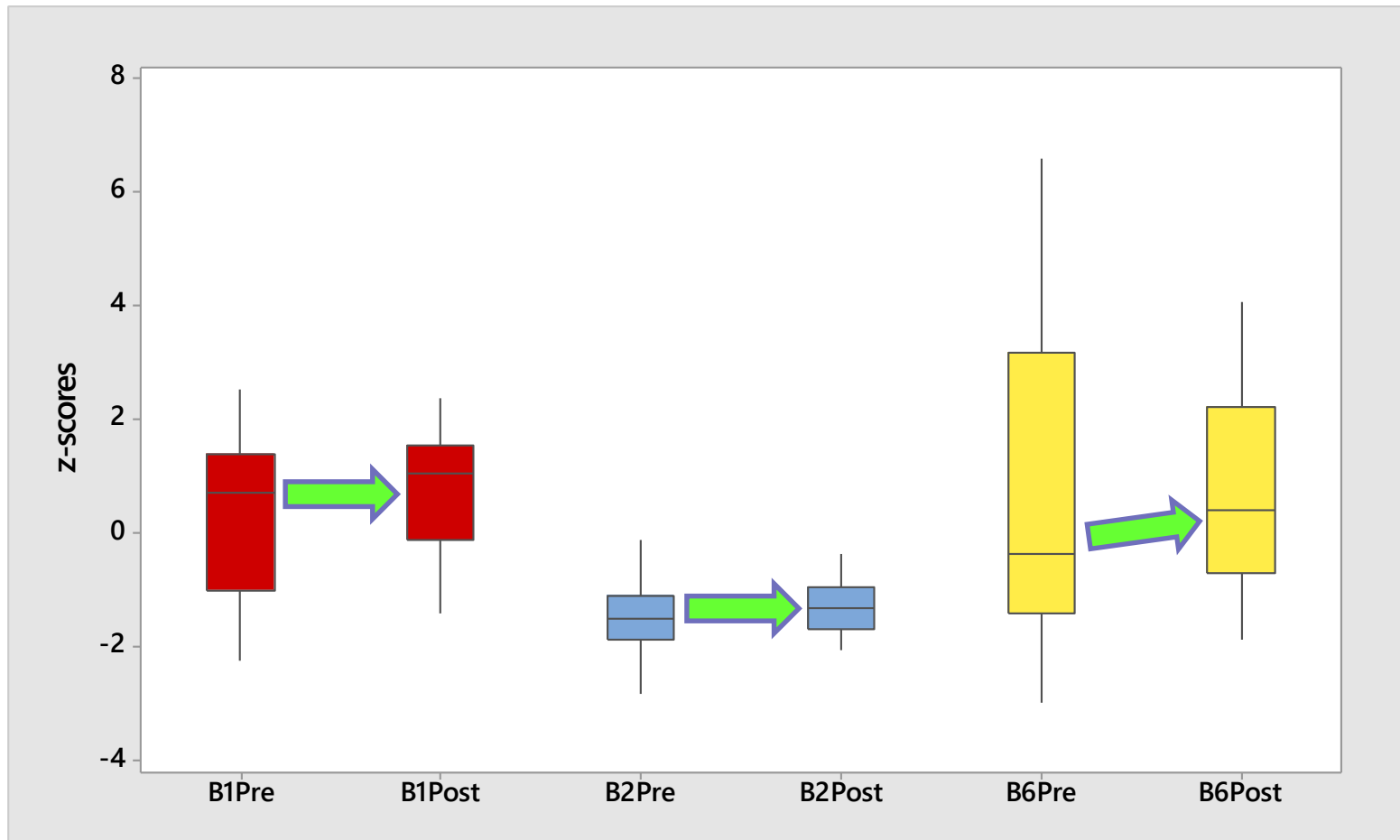
Children (n=50) with congenital heart defects pre-operatively (46% with BMI < 2nd centile)



Children with congenital heart defects *24h post-operatively*



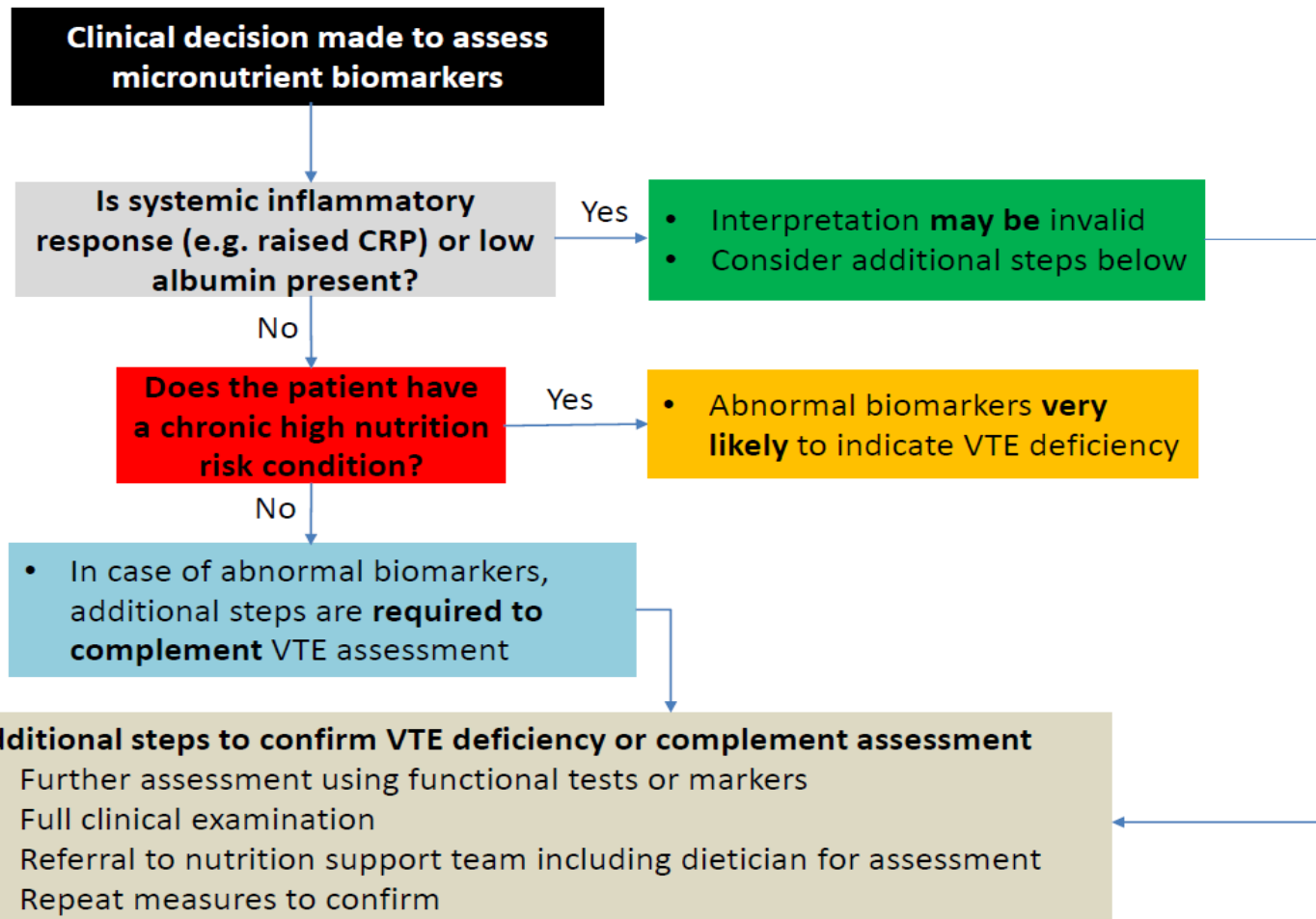
B-complex vitamins pre and post-operatively in erythrocytes



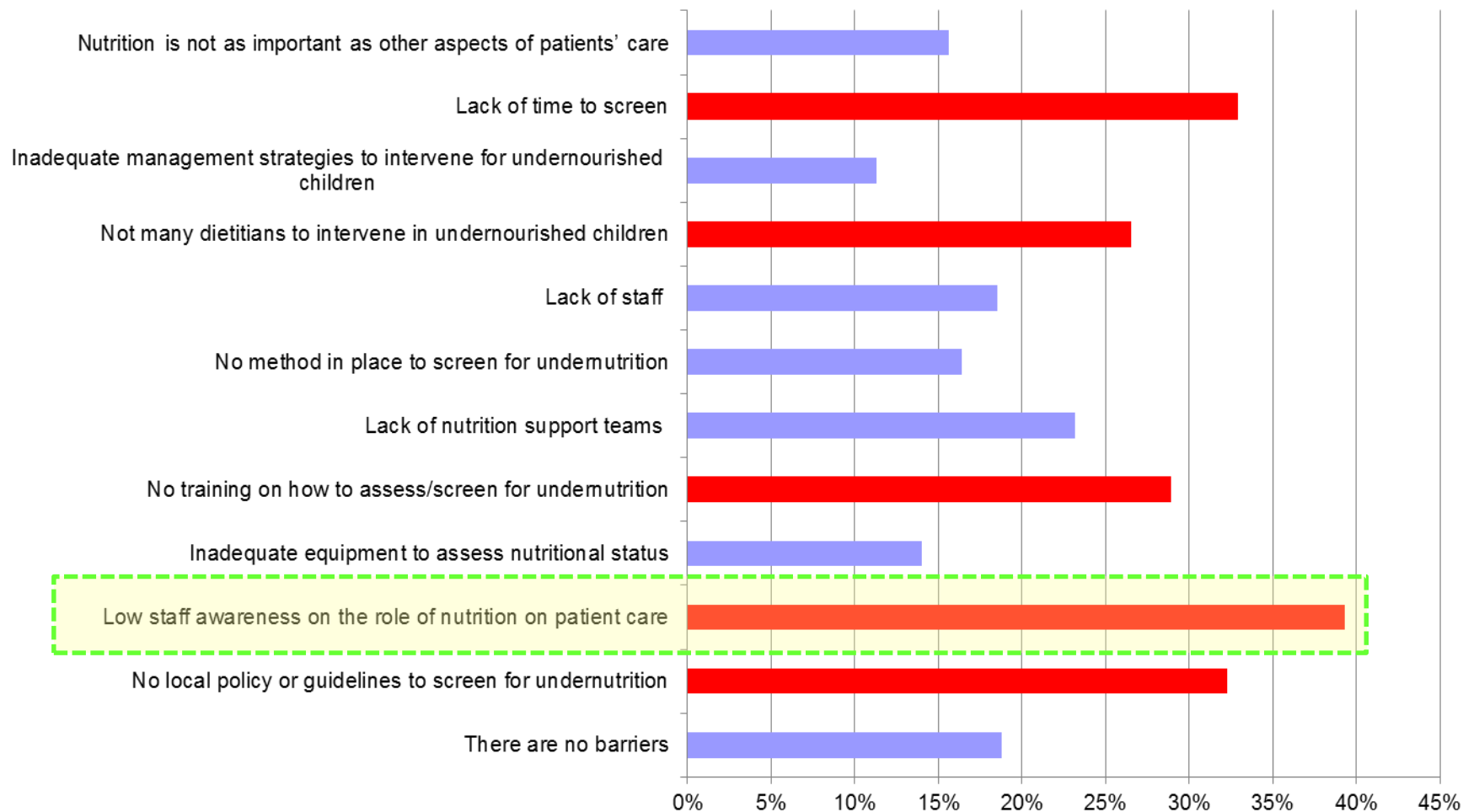
Which micronutrients are affected?

Micronutrient	Lowest reported	Highest reported
Zinc	-10	-40
Selenium	-20	-65
Copper	10	15
Vitamin A	-10	-65
Vitamin D	0	-40
Vitamin E	0	-10
Vitamin B2	-10	-60
Vitamin B6	0	-70
Vitamin B12	0	-25
Vitamin C	0	-75
Lutein	-40	-75
Lycopene	0	-95
α -carotene	-20	-80
β -carotene	-20	-90

Decision tree to evaluate micronutrient status using laboratory biomarkers



Barriers of nutritional screening/assessment





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Is supplementation effective in the presence of systemic inflammatory response?

Table 1 Characteristics and B complex vitamins of normal subjects and critically ill patients.

	Normal subjects	Critically-ill patients		ANOVA, <i>P</i> -value
	No supplementation (<i>n</i> = 49)	No supplementation (<i>n</i> = 18)	Supplementation (<i>n</i> = 23)	
Age (yr)	57 (35–72)	65 (23–85)	60 (22–82)	0.697
Sex (M/F)	26/23	10/8	14/9	0.824
Apache II		24 (13–38)	25 (10–42)	0.298
Predicted mortality (%)		38.6 (5.8–78.9)	57.4 (5.6–93.9)	0.028
Day of sampling (Day 0/1/2/ 3/4/5/ ≥ 6)		11/2/1/1/1/0/2	0/3/4/2/2/2/10	0.002
C-reactive protein (mg/l)	< 10 (< 10–< 10)	140 (20–290)	134 (16–255)	< 0.001
Albumin (g/l)	42 (37–49)	22 (13–33)	25 (10–31)	< 0.001
Red cell haemoglobin (g/l)	261 (231–324)	269 (240–310)	270 (230–310)	0.961
Red cell TDP (ng/gHb)	437 (294–647)	600 (320–1252)	906 (390–2420)	< 0.001
Plasma FAD (nmol/l)	94 (63–159)	38 (22–76)	44 (16–74)	< 0.001
Red cell FAD (nmol/gHb)	2.1 (1.10–3.70)	2.6 (1.3–4.7)	2.8 (0.9–4.6)	0.010
Plasma FAD/red cell FAD	45.9 (26.9–80.0)	15.4 (4.9–39.2)	15.7 (8.6–56.7)	< 0.001
Plasma PLP (nmol/l)	43 (26–154)	13 (3–63)	20 (2–121)	< 0.001
Red cell PLP (pmol/gHb)	371 (278–774)	363 (209–883)	1000 (267–8491)	< 0.001
Plasma PLP/red cell PLP	0.121 (0.082–0.199)	0.035 (0.009–0.165)	0.020 (0.002–0.157)	< 0.001

Median (range).