Malnutrition beim internistisch geriatrischen Patienten: die EFFORT Studie

Symposium Ernährungskommission Stadtspital Waid und Triemli Zürich, 3. Juni 2021

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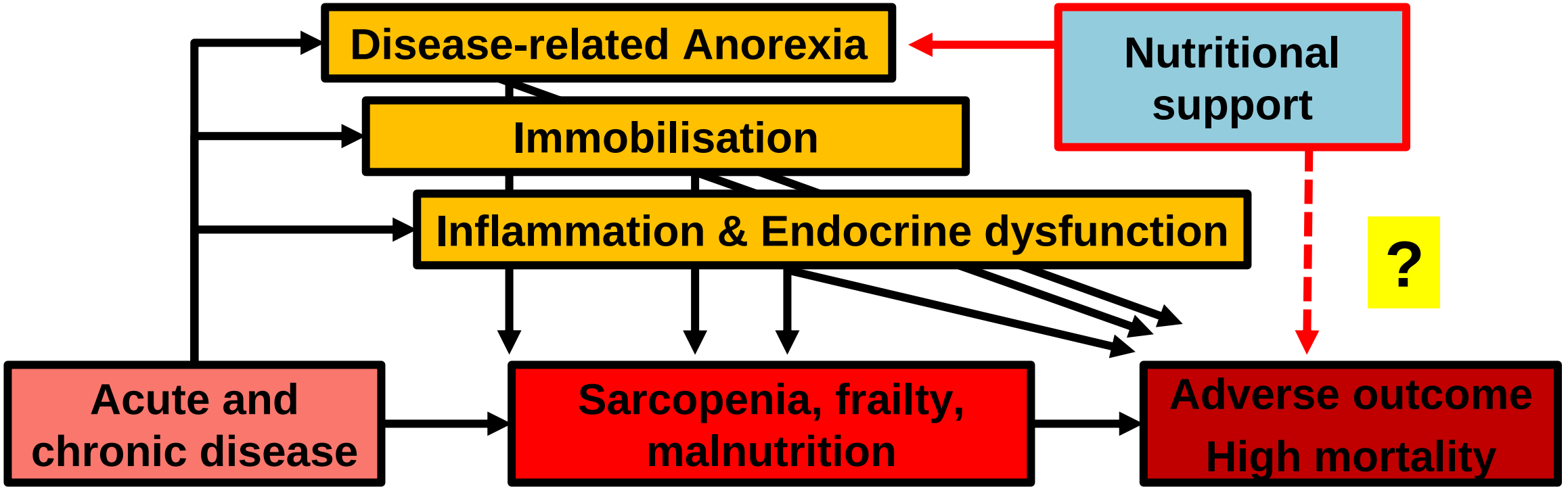
Pathophysiology of Malnutrition:
Our current concept



THE LANCET

Articles

Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial EFFORT Trial

Philipp Schuetz, Rebecca Fehr, Valerie Baechli, Martina Geiser, Manuela Deiss, Filomena Gomes, Alexander Kutz, Pascal Tribolet, Thomas Bregenzer, Nina Braun, Claus Hoess, Vojtech Pavlicek, Sarah Schmid, Stefan Bilz, Sarah Sigrist, Michael Brändle, Carmen Benz, Christoph Henzen, Silvia Mattmann, Robert Thomann, Claudia Brand, Jonas Rutishauser, Drahomir Aujesky, Nicolas Rodondi, Jacques Donzé, Zeno Stanga, Beat Mueller**

Summary

Background Guidelines recommend the use of nutritional support during hospital stays for medical patients (patients not critically ill and not undergoing surgical procedures) at risk of malnutrition. However, the supporting evidence for this recommendation is insufficient, and there is growing concern about the possible negative effects of nutritional therapy during acute illness on recovery and clinical outcomes. Our aim was thus to test the hypothesis that protocol-

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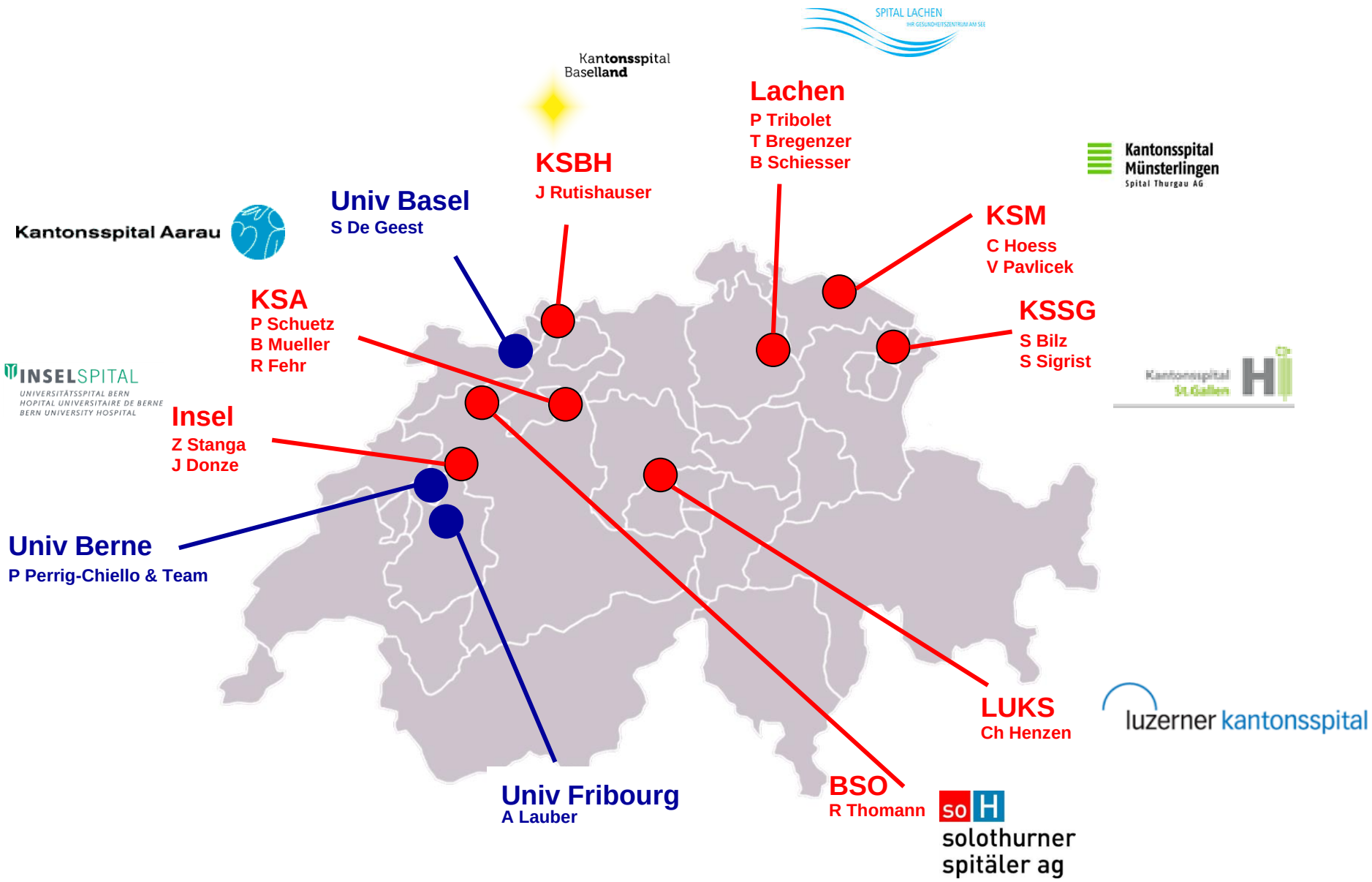
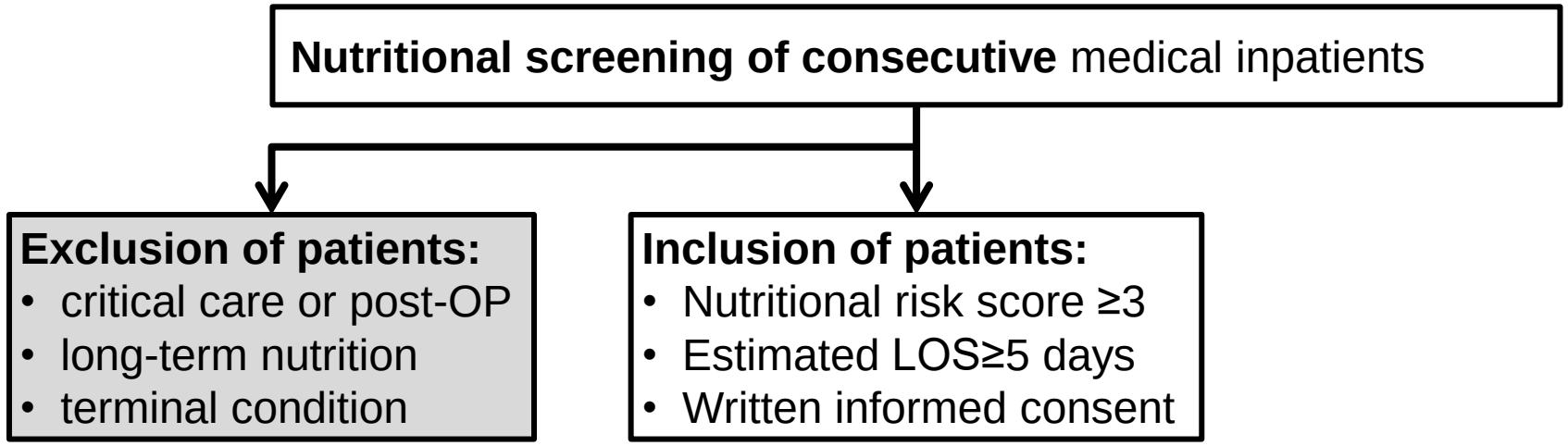
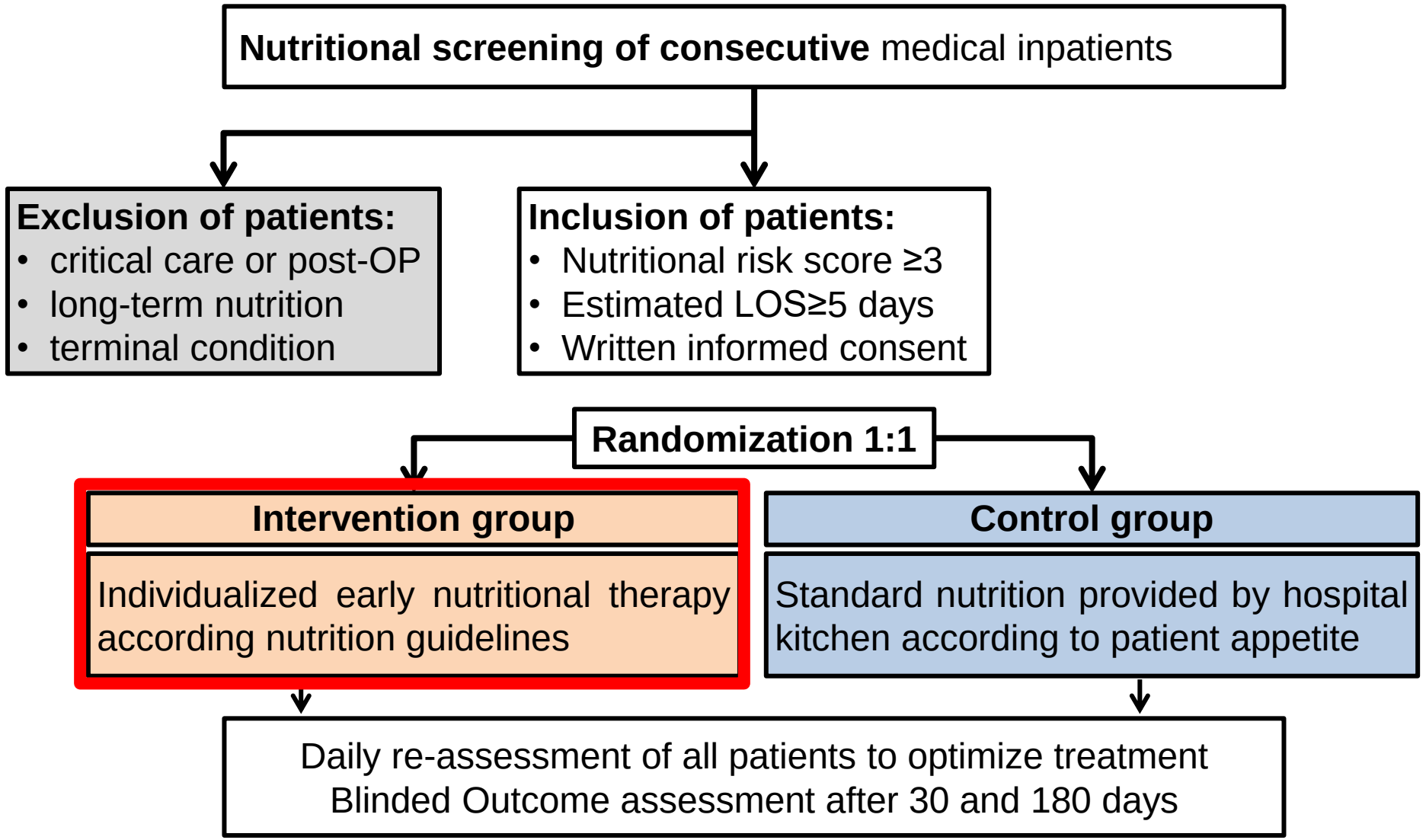
Swiss-wide network



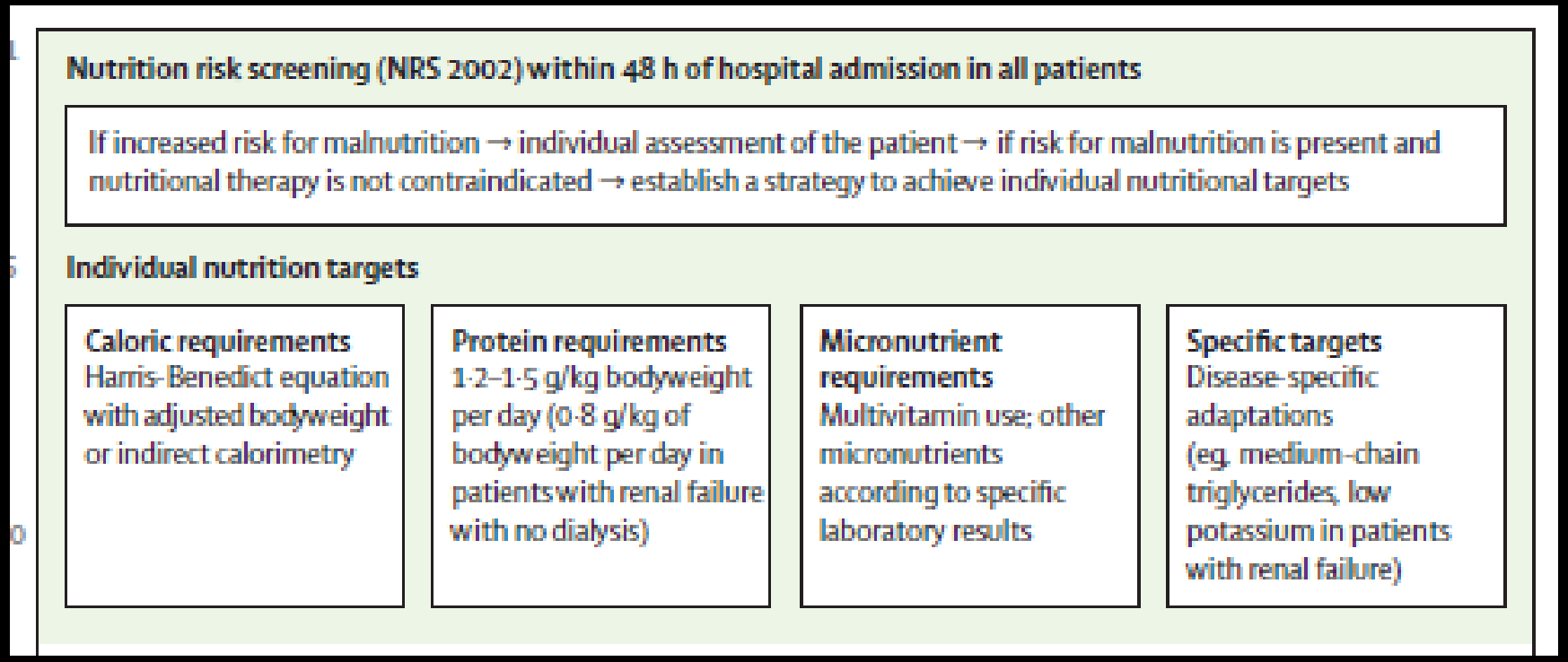
The EFFORT trial - study flow diagram (1/2)



The EFFORT trial - study flow diagram (2/2)



Step 1: Screening and Assessment



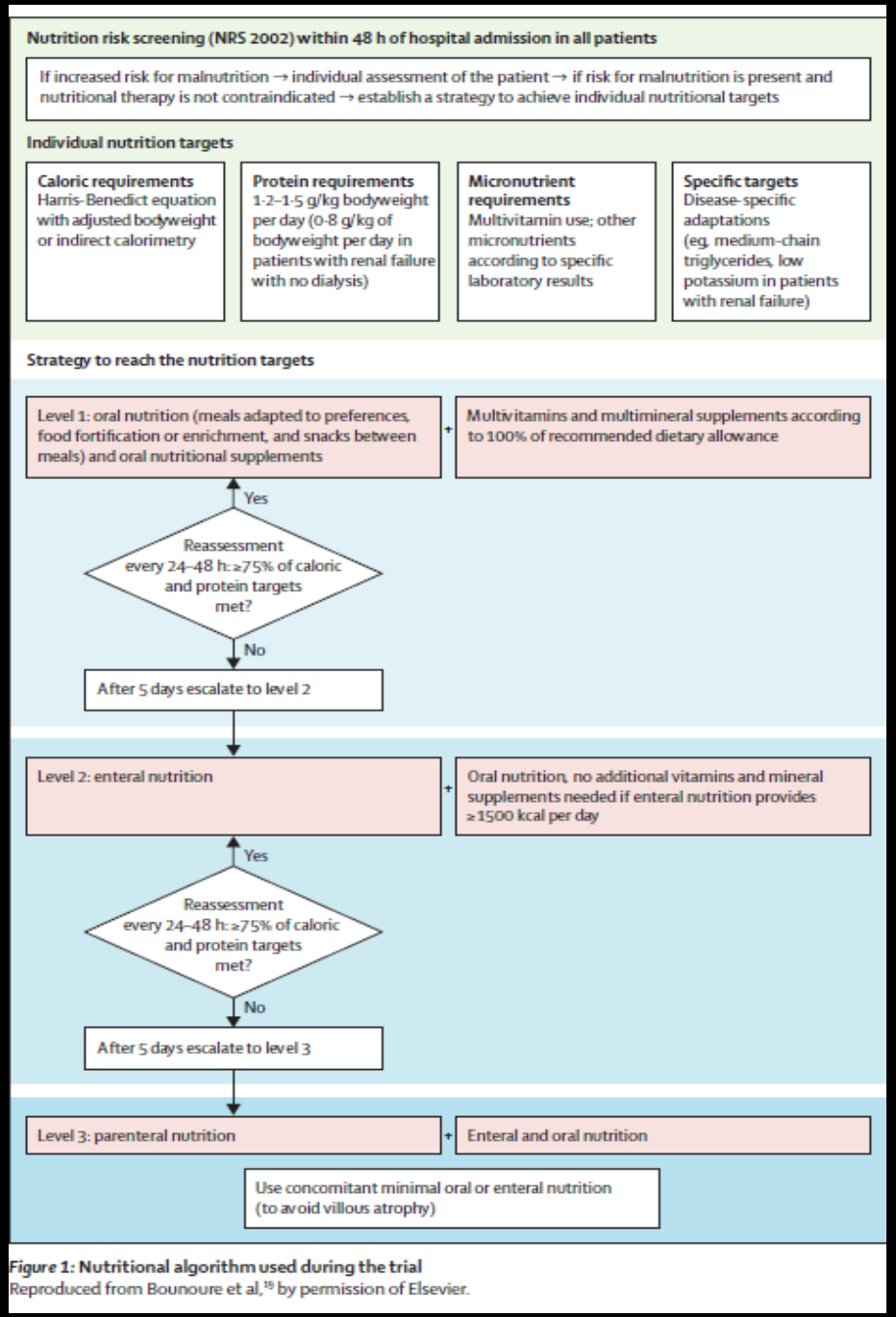


Figure 1: **Nutritional algorithm used during the trial**
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1. Malnutrition screening (NRS 2002)

2. Definition of individual nutritional goals

3. Individual nutritional intervention to reach goals

Oral

↓

enteral

↓

parenteral

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	Intervention group (n=1015)	Control group (n=1013)
Sociodemographics		
Mean age (years)	72·4 (14·1)	72·8 (14·1)
Age group		
<65 years	177 (17%)	178 (18%)
65–75 years	349 (34%)	322 (32%)
>75 years	489 (48%)	513 (51%)
Male sex	525 (52%)	539 (53%)
Nutritional assessment		
Mean body-mass index (kg/m²)*	24·9 (5·4)	24·7 (5·3)
Mean bodyweight (kg)	70·9 (16·4)	70·9 (16·4)
NRS 2002 score (%)†		
3 points	310 (31%)	314 (31%)
4 points	391 (39%)	384 (38%)
5 points	263 (26%)	261 (26%)
>5 points	51 (5%)	54 (5%)
Admission diagnosis		
Infection	298 (29%)	315 (31%)
Cancer	201 (20%)	173 (17%)
Cardiovascular disease	92 (9%)	113 (11%)
Failure to thrive	99 (10%)	95 (9%)
Lung disease	50 (5%)	75 (7%)
Gastrointestinal disease	96 (9%)	68 (7%)
Neurological disease	42 (4%)	53 (5%)
Renal disease	34 (3%)	34 (3%)
Metabolic disease‡	30 (3%)	32 (3%)
Other	30 (3%)	25 (2%)
Comorbidity		
Hypertension	557 (55%)	552 (54%)
Malignant disease	338 (33%)	329 (32%)
Chronic kidney disease	323 (32%)	318 (31%)
Coronary heart disease	287 (28%)	279 (28%)
Diabetes	215 (21%)	213 (21%)
Congestive heart failure	174 (17%)	179 (18%)
Chronic obstructive pulmonary disease	147 (14%)	156 (15%)
Peripheral arterial disease	80 (8%)	106 (10%)
Cerebrovascular disease	75 (7%)	87 (9%)
Dementia	39 (4%)	36 (4%)

Data are number of participants (%) or mean (SD). There were no significant differences between the groups at baseline, except for admission diagnosis of gastrointestinal disease and lung disease, and comorbidity of peripheral arterial disease.*The body-mass index is the weight in kilograms divided by the square of the height in metres. †Scores on nutritional risk screening range from 0 to 7, with a score of 3 or more identifying patients at nutritional risk and higher scores indicating increased risk. ‡Metabolic disease included, but was not limited to, hypoglycaemia, hyperglycaemia, ketoacidosis, electrolyte disturbances including hyponatraemia and hypernatraemia, hypokalaemia, and hyperkalaemia. NRS 2002=nutritional risk screening 2002.

Table 1: **Characteristics of the patients at trial entry**

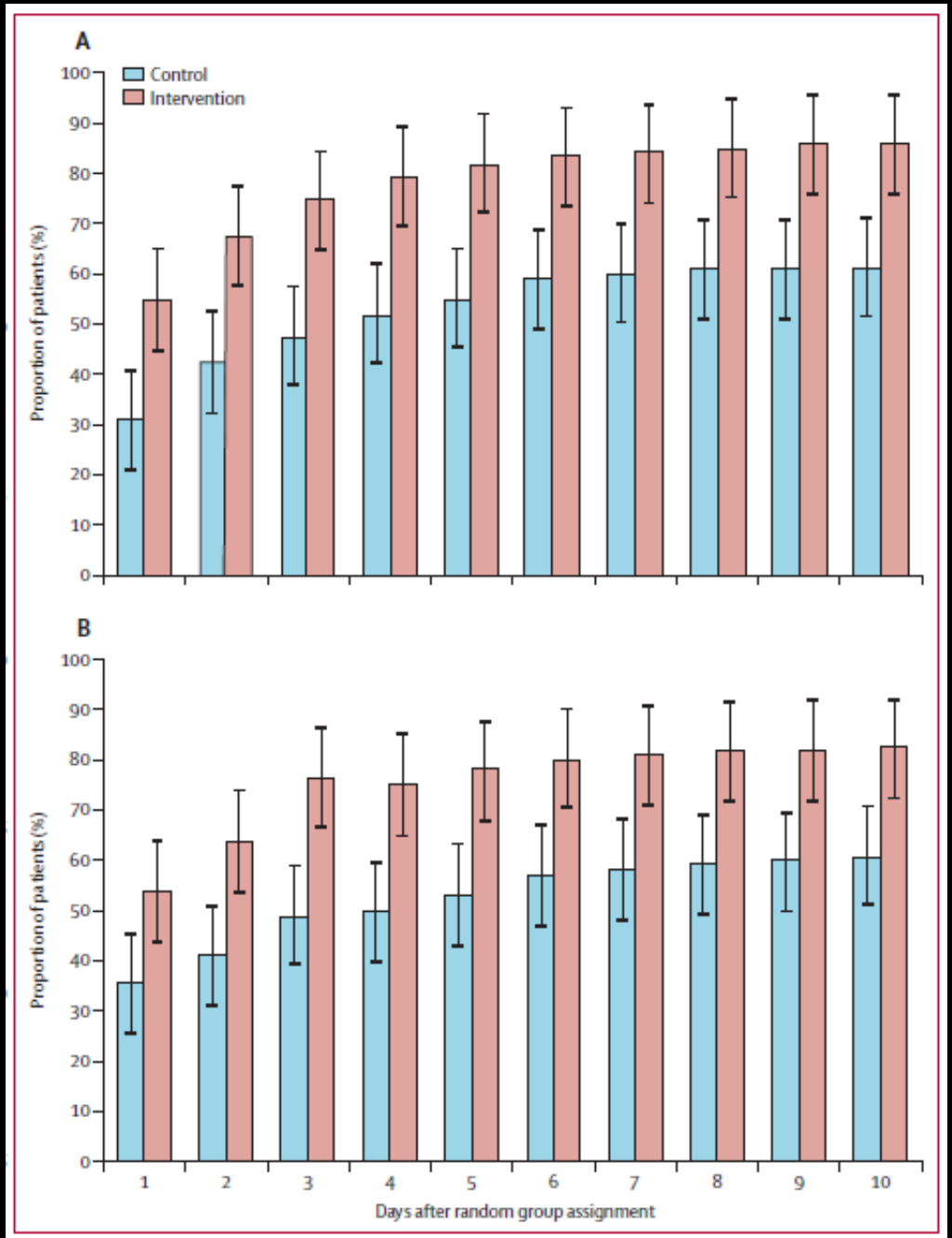

Figure 3: **Proportion of patients reaching caloric (A) and protein (B) requirements during the first 10 days after random group assignment**

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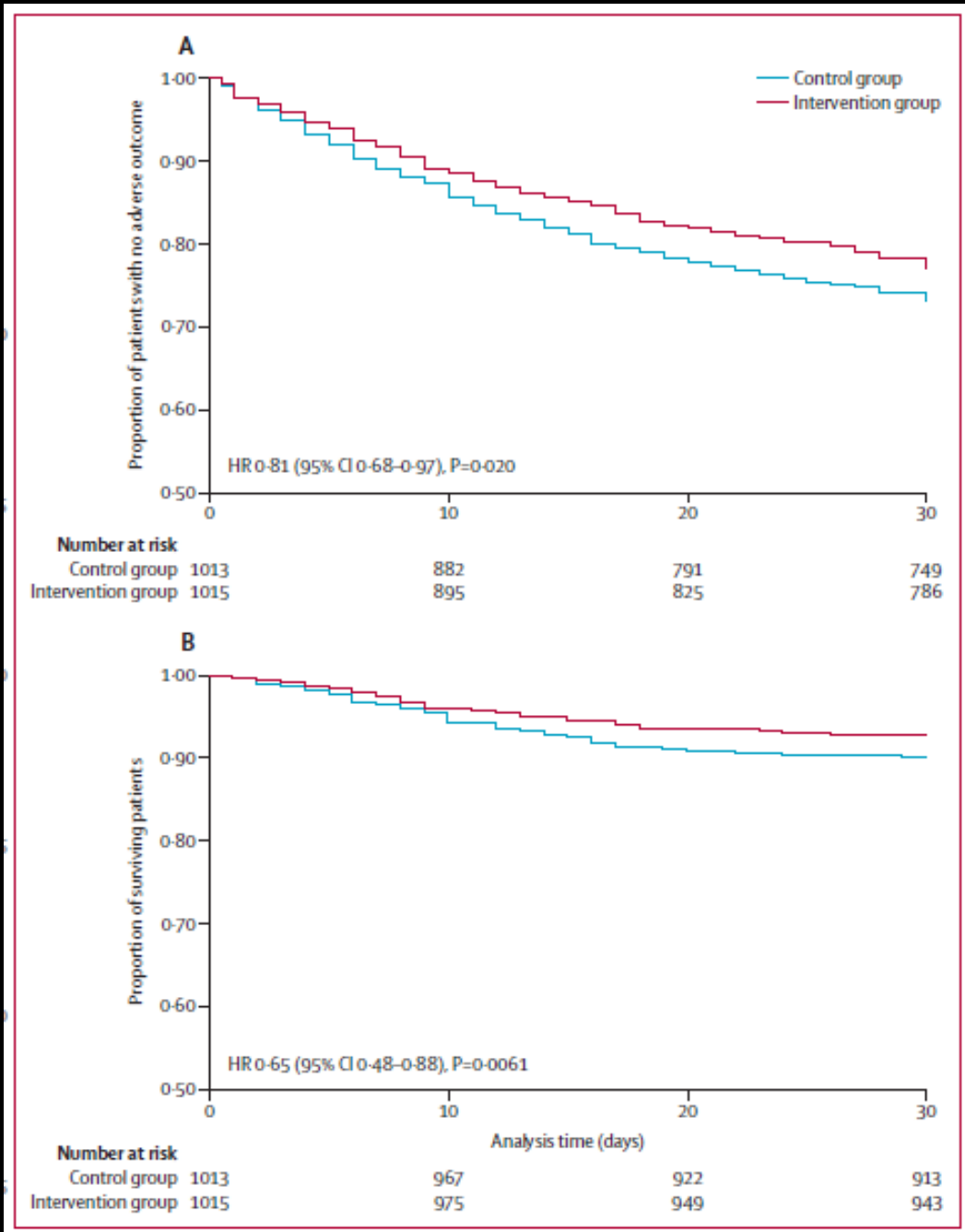

Figure 4: Kaplan-Meier estimates of the cumulative incidence of the primary endpoint and all-cause mortality
(A) Time to the first event of the composite primary endpoint (log-rank p value=0·035). (B) Time to death (log-rank p value=0·031).

Complications

26.9% (Controls) vs 22.9% (Intervention)
Number needed to treat (NNT): 25

Mortality

9.9% (Controls) vs 7.2% (Intervention)
Number needed to treat (NNT): 37

Schuetz P, et al. *Lancet*. 2019;393(10188):2312-2321.

	Intervention group (n=1015)	Control group (n=1013)	Odds ratio or coefficient (95% CI)	p value
Outcomes				
Primary outcome				
Adverse outcome within 30 days	232 (23%)	272 (27%)	0·79 (0·64 to 0·97)	0·023
Single components of primary outcome				
All-cause mortality	73 (7%)	100 (10%)	0·65 (0·47 to 0·91)	0·011
Admission to the intensive care unit	23 (2%)	26 (3%)	0·85 (0·48 to 1·51)	0·58
Non-elective hospital readmission	89 (9%)	91 (9%)	0·99 (0·73 to 1·35)	0·96
Major complications				
Any major complication	74 (7%)	76 (8%)	0·95 (0·68 to 1·34)	0·79
Nosocomial infection	40 (4%)	39 (4%)	1·01 (0·63 to 1·59)	0·98
Respiratory failure	14 (1%)	13 (1%)	1·06 (0·49 to 2·28)	0·89
Major cardiovascular event	8 (1%)	7 (1%)	1·11 (0·40 to 3·11)	0·84
Acute kidney failure	32 (3%)	31 (3%)	1·01 (0·61 to 1·69)	0·96
Gastrointestinal events	9 (1%)	15 (1%)	0·57 (0·25 to 1·31)	0·19
Decline in functional status of ≥10%*	35 (4%) of 942	55 (6%) of 913	0·62 (0·40 to 0·96)	0·034
Additional secondary outcomes				
Mean length of stay (days)	9·5 (7·0)	9·6 (6·1)	−0·21 (−0·76 to 0·35)	0·46
Mean Barthel score (points)*	88 (26)	85 (30)	3·26 (0·93 to 5·60)	0·006
Mean EQ-5D VAS (points)†	59 (26)	56 (29)	3·06 (0·53 to 5·59)	<0·0001
Mean EQ-5D index (points)	0·75 (0·32)	0·73 (0·34)	0·13 (0·09 to 0·17)	0·018
Side-effects from nutritional support				
All side-effects	162 (16%)	145 (14%)	1·16 (0·90 to 1·51)	0·26
Gastrointestinal side-effects	43 (4%)	40 (4%)	1·12 (0·68 to 1·83)	0·66
Complications due to enteral feeding or parenteral nutrition	5 (<1%)	3 (<1%)	1·63 (0·38 to 6·95)	0·51
Liver or gall bladder dysfunction	4 (<1%)	7 (1%)	0·54 (0·15 to 1·91)	0·34
Severe hyperglycaemia	48 (5%)	46 (5%)	1·06 (0·69 to 1·61)	0·80
Refeeding syndrome	86 (8%)	73 (7%)	1·21 (0·86 to 1·70)	0·27

Data are number of events (%), unless otherwise stated. All odds ratios were calculated with a logistic regression for binary data and linear regression for continuous data. Models were adjusted for predefined prognostic factors (initial nutritional risk screening score and baseline Barthel index) and study centre. *To estimate decline in functional status, we used the Barthel index (scores range from 0 to 100, with higher scores indicating better functional status) and compared initial scores on admission with scores at day 30; only surviving patients were included in this analysis. †To estimate quality of life we used the European Quality of Life 5 Dimensions index (EQ-5D; values range from −0·205 to 1, with higher scores indicating better quality of life) including the visual-analogue scale (EQ-5D VAS; scores range from 0 to 100, with higher scores indicating better health status).

Table 2: **Endpoints and adverse events**

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Is there a legacy effect inhospital nutrition after long term follow-up?

Clinical Nutrition xxx (xxxx) xxx

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Randomized Control Trials

Six-month outcomes after individualized nutritional support during the hospital stay in medical patients at nutritional risk: Secondary analysis of a prospective randomized trial

Nina Kaegi-Braun [a], Pascal Tribolet [a, b], Filomena Gomes [a, c], Rebecca Fehr [a], Valerie Baechli [a], Martina Geiser [a], Manuela Deiss [a], Alexander Kutz [a], Thomas Bregenzer [d], Claus Hoess [e], Vojtech Pavlicek [e], Sarah Schmid [e], Stefan Bilz [f], Sarah Sigrist [f], Michael Brändle [f], Carmen Benz [f], Christoph Henzen [g], Silvia Mattmann [g], Robert Thomann [h], Jonas Rutishauser [i], Drahomir Aujesky [j], Nicolas Rodondi [j, k], Jacques Donzé [j, l], Zeno Stanga [m], Beat Mueller [a, n], Philipp Schuetz [a, n, *]

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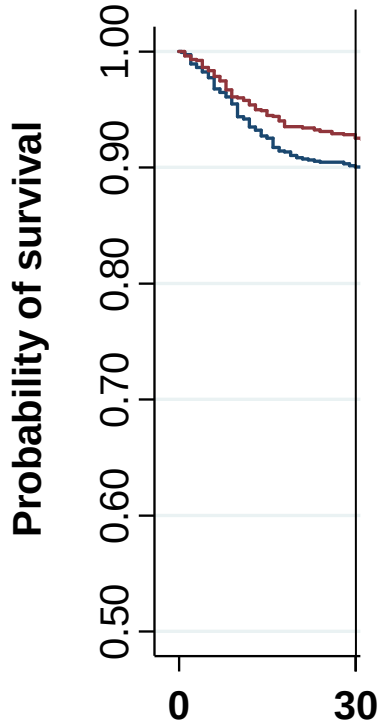
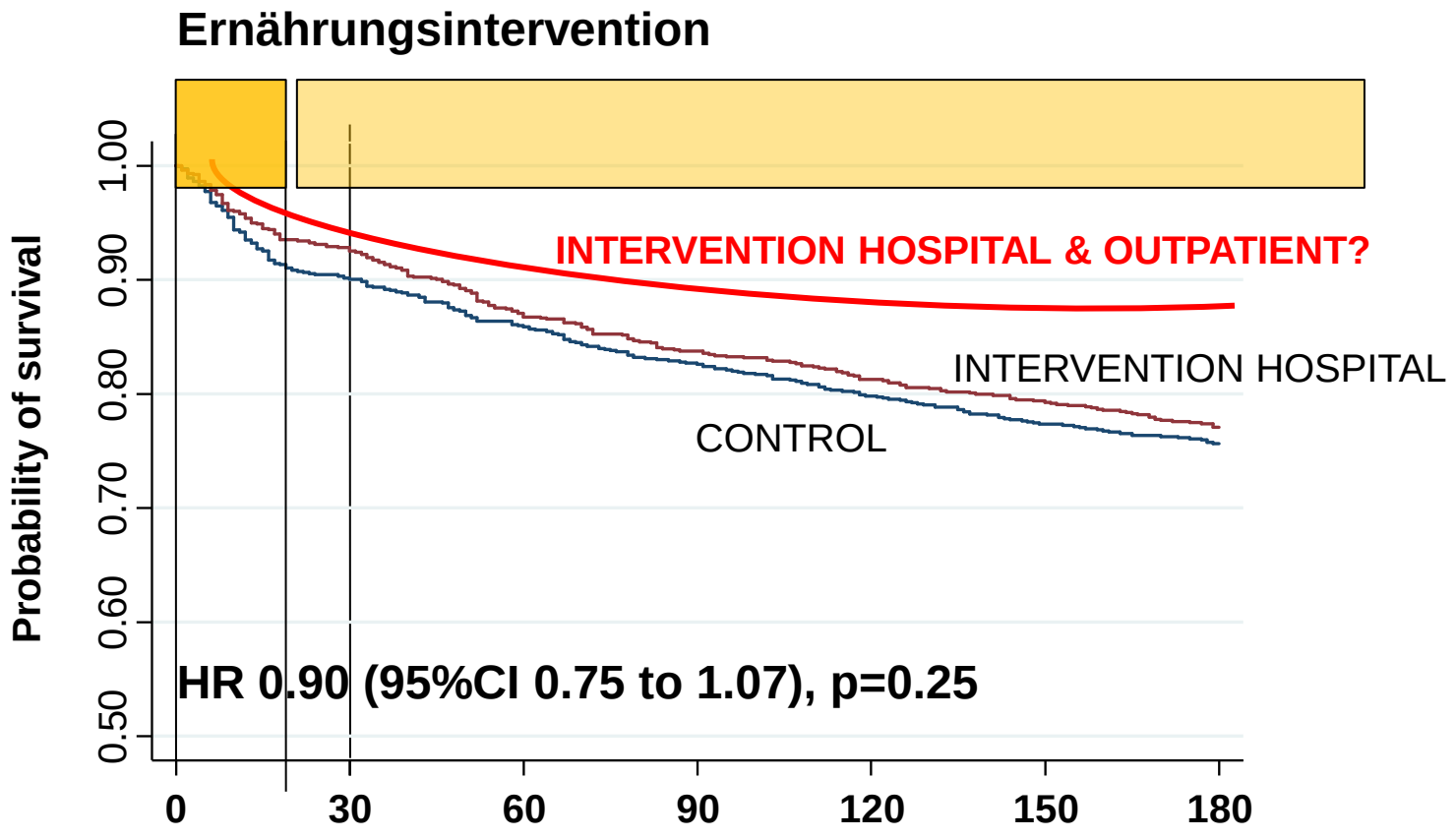
Shortterm - 30-day mortality



Number at risk		
CONTROL	1013	913
INTERVENTION	1015	942

Longterm - 180-day mortality



Number at risk							
CONTROL	1013	913	866	833	804	779	762
INTERVENTION	1015	942	873	840	815	796	773

Should we «individualize» nutritional support according to patient`s comorbidities?

	Control group (n/N [%])	Intervention group (n/N [%])	Adjusted odds ratio (95% CI)	$p_{interaction}$
All patients	272/1013 (27%)	232/1015 (23%)	0·79 (0·64–0·97)	
Age				
<65 years	30/178 (17%)	34/177 (19%)	1·17 (0·68–2·02)	0·27
65–75 years	93/322 (29%)	82/349 (23%)	0·76 (0·54–1·07)	
>75 years	149/513 (29%)	116/489 (24%)	0·76 (0·57–1·01)	
Sex				
Male	157/539 (29%)	104/490 (21%)	0·78 (0·60–1·03)	0·74
Female	115/474 (24%)	128/525 (24%)	0·84 (0·62–1·14)	
Risk for malnutrition				
NRS 3 points	72/314 (23%)	69/310 (22%)	0·96 (0·66–1·40)	0·31
NRS 4 points	103/384 (27%)	83/391 (21%)	0·74 (0·53–1·02)	
NRS >4 points	97/315 (31%)	80/314 (25%)	0·77 (0·54–1·09)	
Body-mass index				
<20	48/198 (24%)	43/176 (24%)	1·01 (0·63–1·62)	0·28
20–25	107/372 (29%)	100/421 (24%)	0·77 (0·56–1·06)	
25–30	75/283 (27%)	61/254 (24%)	0·88 (0·59–1·30)	
>30	40/156 (26%)	27/157 (17%)	0·60 (0·35–1·04)	
Admission diagnosis				
Infection	70/315 (22%)	57/298 (19%)	0·83 (0·56–1·23)	0·85
Cardiovascular disease	36/113 (32%)	26/92 (28%)	0·84 (0·46–1·54)	0·90
Renal failure	9/34 (26%)	10/34 (29%)	1·16 (0·40–3·34)	0·50
Gastrointestinal disease	19/68 (28%)	23/96 (24%)	0·81 (0·40–1·65)	0·98
Cancer	62/173 (36%)	71/201 (35%)	0·98 (0·64–1·49)	0·26
Comorbidities				
Diabetes	[illegible]	[illegible]	[illegible]	[illegible]
Chronic kidney disease	115/318 (36%)	83/323 (26%)	0·61 (0·44–0·86)	0·045

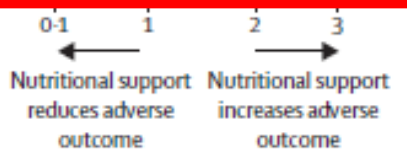


Figure 5: **Odds ratios for adverse outcome in prespecified subgroups**
The only significant interactions between group assignment and subgroup were for chronic kidney disease. The body-mass index is the weight (in kg) divided by the square of the height (in m). NRS=nutritional risk screening.

Schuetz P, et al. *Lancet*. 2019;393(10188):2312-2321.

Should we «individualize» nutritional support according to a patient`s inflammatory response?

JAMA Network Open

Original Investigation | Nutrition, Obesity, and Exercise

Association of Baseline Inflammation With Effectiveness of Nutritional Support Among Patients With Disease-Related Malnutrition

A Secondary Analysis of a Randomized Clinical Trial

Meret Merker, MD; Martina Felder, BMSc; Louise Gueissaz, BMSc; Rebekka Bolliger, MD; Pascal Tribolet, MSc; Nina Kägi-Braun, MD; Filomena Gomes, PhD; Claus Hoess, MD; Vojtech Pavlicek, MD; Stefan Bilz, MD; Sarah Sigrist, MD; Michael Brändle, MD; Christoph Henzen, MD; Robert Thomann, MD; Jonas Rutishauser, MD; Drahomir Aujesky, MD; Nicolas Rodondi, MD, MAS; Jaques Donzé, MSc; Zeno Stanga, MD; Beat Mueller, MD; Philipp Schuetz, MD, MPH

Abstract

IMPORTANCE Inflammation is a key driver of malnutrition during illness and is often accompanied by metabolic effects, including insulin resistance and reduction of appetite. However, it still remains unclear if inflammation influences the response to nutritional support among patients with disease-related malnutrition.

Key Points

Question Does nutritional support have a similar effect on 30-day mortality among patients with high inflammation compared with patients with low or moderate inflammation?

Figure 2. Kaplan-Meier Estimate for Time to Death Within 30-Days According to Inflammatory Status

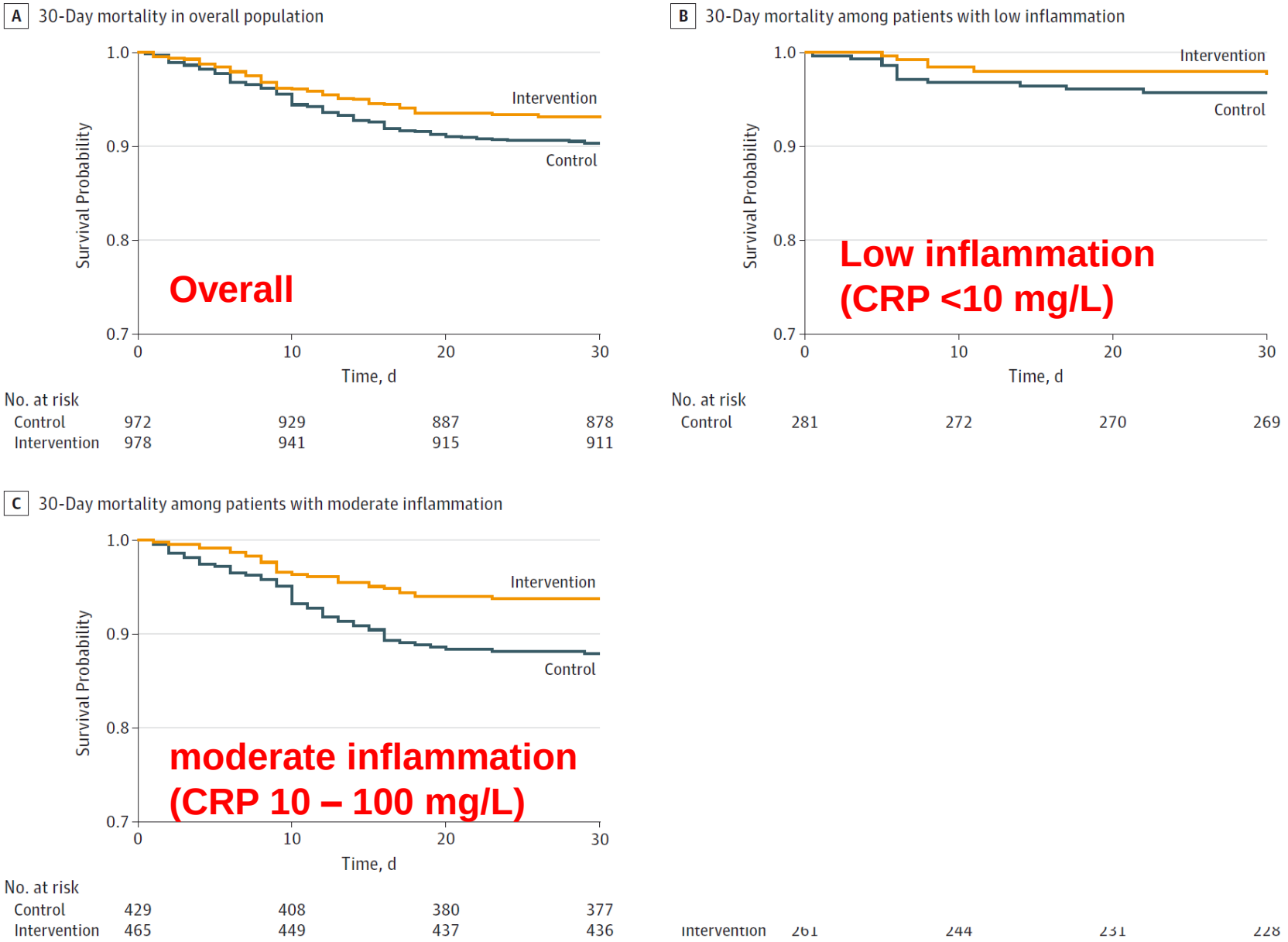
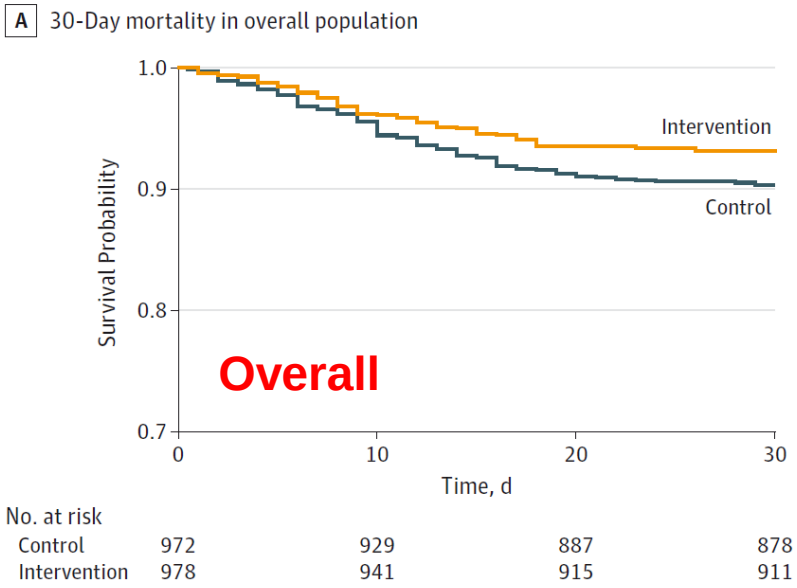
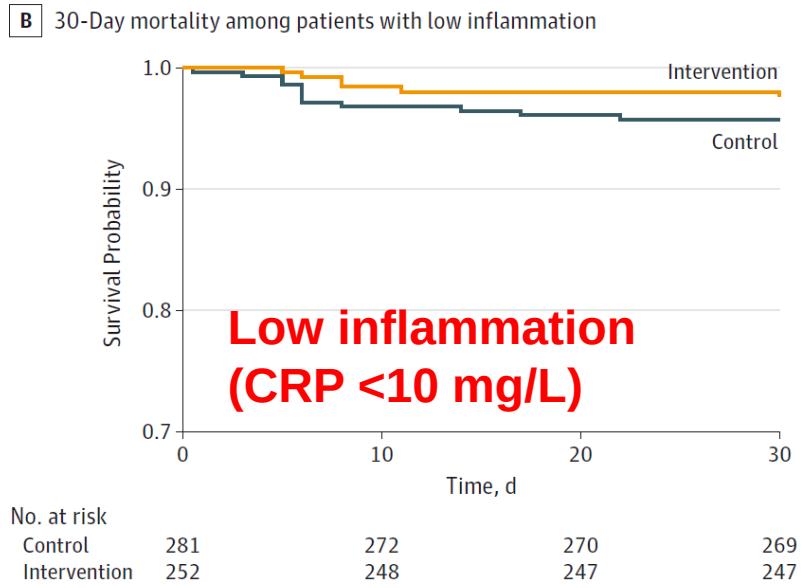
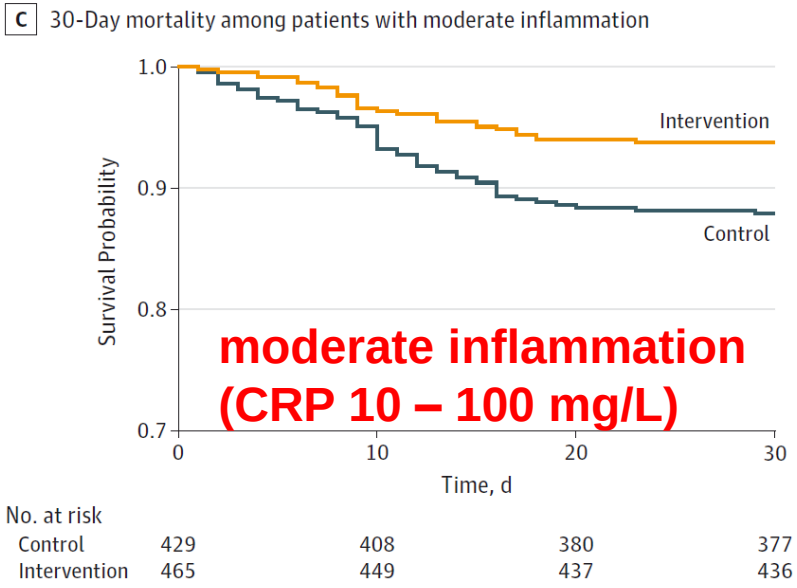
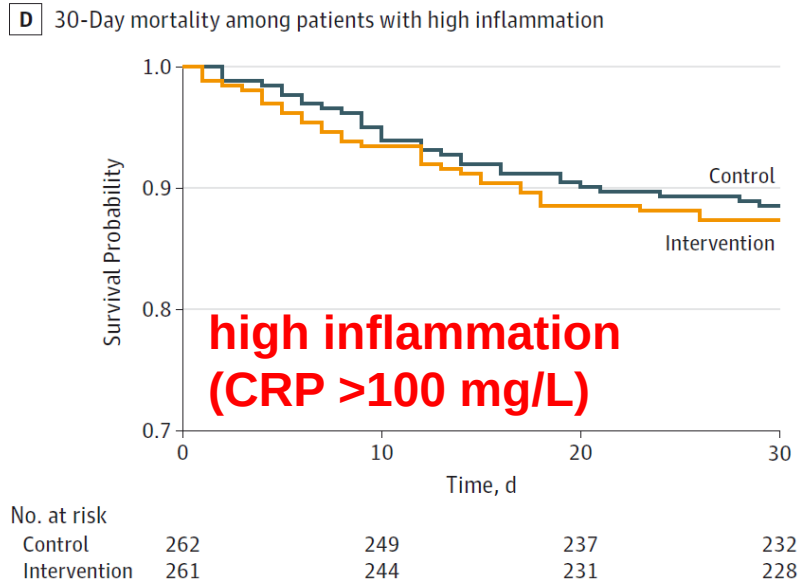


Figure 2. Kaplan-Meier Estimate for Time to Death Within 30-Days According to Inflammatory Status









How should we implement these data into clincial routine?

ANNALS FOR HOSPITALISTS

Annals of Internal Medicine

Inpatient Notes: Optimizing Inpatient Nutrition–Why Hospitalists Should Get Involved

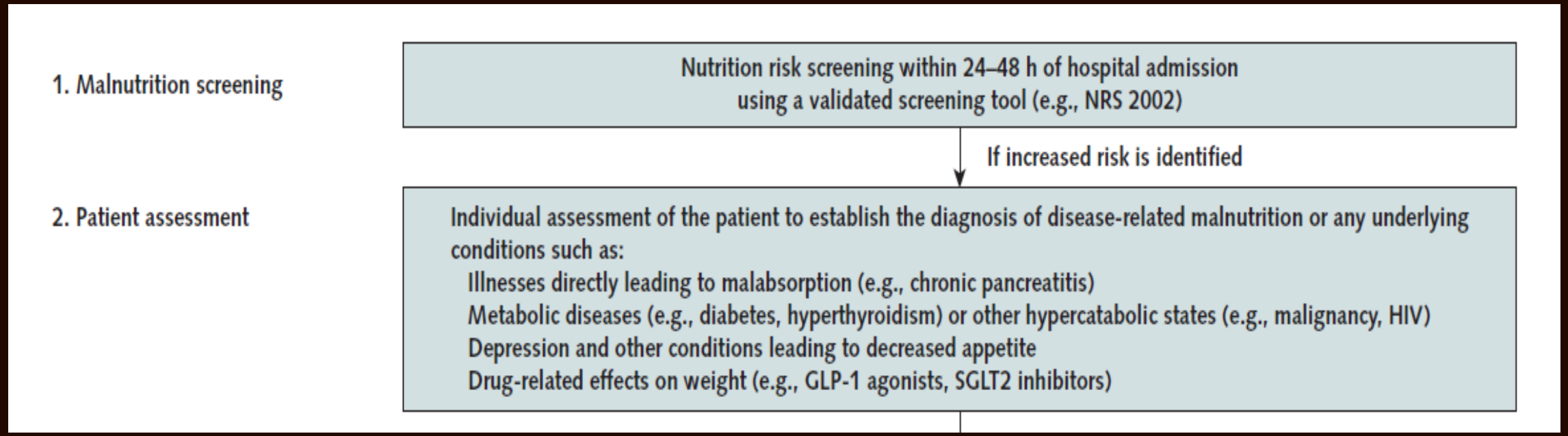
Philipp Schuetz, MD, MPH, and Jeffrey L. Greenwald, MD

Malnutrition is a common condition among newly admitted, medically complex inpatients. Emerging evidence demonstrates that malnutrition directly increases the risk for adverse clinical outcomes, including death, illness, and functional impairments, hospital length of stay, and the risk for hospital readmission (1). Moreover, nutritional status often further deteriorates during the hospital stay because of illness-related loss of appetite, fasting orders for diagnostic studies, or overall suboptimal nutritional management. Data from the United States and Europe show that about 1 in 4

number needed to treat of 25. The trial also found that nutritional support substantially reduced death, with a number needed to treat of 37. A similar positive effect on the risk for death (number needed to treat = 20) was also found in the placebo-controlled, 652-patient NOURISH (Nutrition effect On Unplanned Readmissions and Survival in Hospitalized patients) trial, which studied the effects of using a protein-rich oral supplement on clinical outcomes in malnourished, medical inpatients in the United States (3).

Schuetz P, et al. *Ann Intern Med*. 2020;172(4):HO2-HO3.

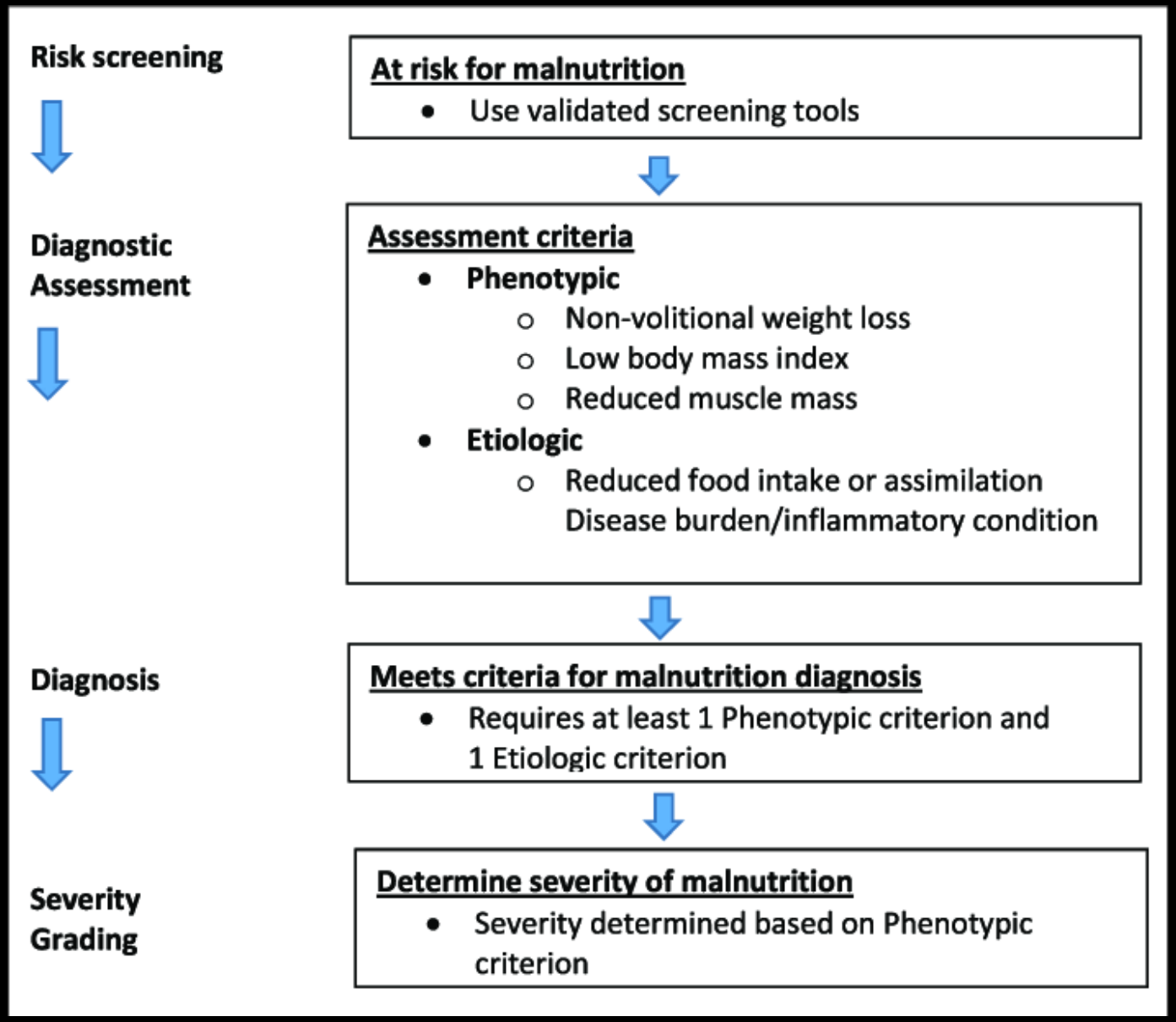
NUTRITIONAL SUPPORT ALGORITHM



EFFORT = Effect of early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial (1); GLP-1 = glucagon-like peptide-1; NRS 2002 = Nutritional Risk Screening 2002 (6); SGLT2 = sodium–glucose cotransporter-2.

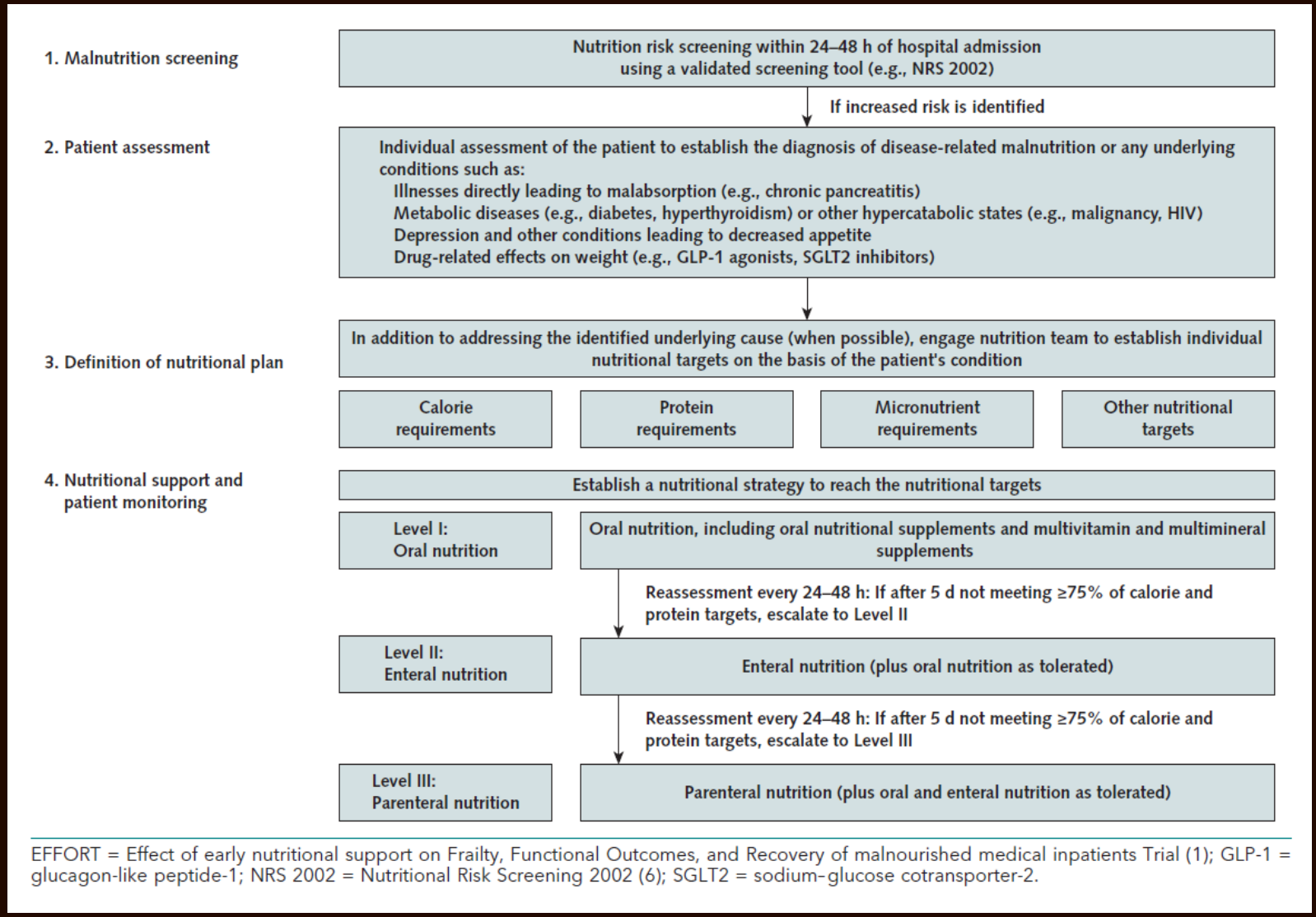
Schuetz P, et al. *Ann Intern Med*. 2020;172(4):HO2-HO3.

NUTRITIONAL ASSESSMENT: GLIM CRITERIA TO DIAGNOSE MALNUTRITION



Journal of Cachexia, Sarcopenia and Muscle 2019; **10**: 207–217

NUTRITIONAL SUPPORT ALGORITHM



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Schuetz P, et al. *Ann Intern Med*. 2020;172(4):HO2-HO3.

Summary

- There is increasing evidence that malnutrition is a modifiable risk factor for hospitalized patients with multiple illnesses
- Proactive screening of patients using a validated tool and start of nutritional support protocols should be implemented in the hospital setting to reduce mortality and complications of patients
- In the future, we may need to further individualize nutrition according to the specific situation of our patients including kidney function and inflammatory status
- **Internists should play an active role for early recognition and treatment of disease-related malnutrition**