



International Conference

optimal
nutritional care
for all

MALNUTRITION: FROM AWARENESS TOWARDS CONTROL

A NUTRITIONAL CARE POLICY SUMMIT

Turin 6 & 7 June 2024



**Metrics that matter:
Transforming Nutritional Care Policies
Through
Data-Driven Paradigm Shifts**

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A2M, The Netherlands (<http://a2m.nl>)

June 7, 2024

**Malnutrition from awareness towards
control**



INTRODUCTION

Malnutrition

- What about the patient ?
- What is important for the patient ?



- What is important to us as professionals ?
- Is this consistent ? Are the differences too big or is there little or no overlap ?

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- Conference Turin 6 & 7 June 2024



INTRODUCTION

Malnutrition

- Access to nutritional care is essential for the patient
- Patient should receive nutritional care when medically necessary
- 1) prevention of at risk “malnutrition, 1) management of malnutrition



- Because we need optimal care in treatment of the disease

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INTRODUCTION

Malnutrition

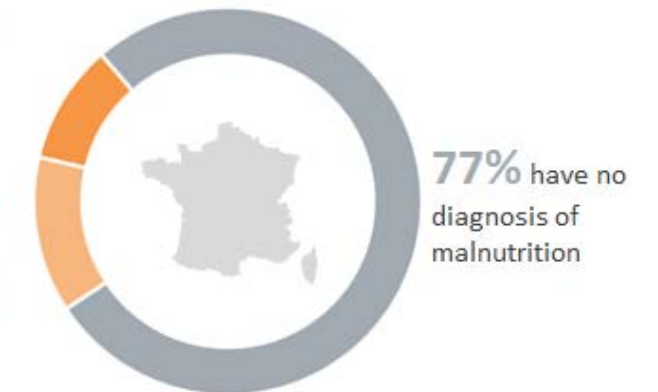
- **Screening: underdiagnosis of malnutrition (oncology) so no treatment.**
 - Increased risk of death and the risk of complications and reduced QoL.
 - Higher costs due to longer length of stay and the costs of treating complications.
- **Nutritionals should be part of basic insurance without co-payment.**

Cancer-related malnutrition is underdiagnosed and undertreated in Europe, and clinical nutrition is often used as an end-of-life intervention

While literature suggests **30-60%** of patients with cancer in France are **malnourished**, real-world data show that among patients with GI cancer:

10% are diagnosed with malnutrition at first hospitalization

13% are diagnosed with malnutrition after the first hospitalization



Abbreviations: GI, gastrointestinal; HPN, home parenteral nutrition.
<https://pubmed.ncbi.nlm.nih.gov/32110247/>

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INTRODUCTION

Malnutrition

- There is no consensus within the EU on nutrition reimbursement
- Access to nutritional care is essential for the patient



How can this be explained ?

- If everyone were convinced of the usefulness of nutrition, it would be reimbursed everywhere in the EU.
- The price cannot be the problem, because analyzes show that if the price for nutrition were 10 times higher, the use of nutrition is still efficient (cost-effective).

Table 1. Coverage of FSMP/MF reimbursement by country across different settings.

Country	Hospital	Outpatient	Community
Australia	Yes	Yes, limited to some disease conditions; might differ across provinces	
Belgium	Yes	Yes, limited to patients discharged from hospital	No
Brazil	Yes	Yes, limited to specific disease conditions and varies by state and municipalities	Yes, limited to some disease conditions
Canada	Yes	Yes, limited to some disease conditions; might differ across provinces	
China	No	No	No
France	Yes	Yes	Yes
Germany	Yes	Yes	Yes
Hong Kong	Yes	Yes, limited to low-income individuals*	No
Italy	Yes	No	Yes; might vary by region
Japan	Yes	Yes, limited to enteral tube feeding	
The Netherlands	Yes	Yes	Yes
Singapore	Yes	Yes, limited to low-income individuals [†]	Yes, limited to nursing homes
Spain	Yes	Yes	Yes
United Kingdom	Yes, limited to the public system under certain circumstances for malnourished patients		
United States Centers for Medicare & Medicaid Services	Yes, limited [‡]	Yes, limited [‡]	Yes, limited [‡]

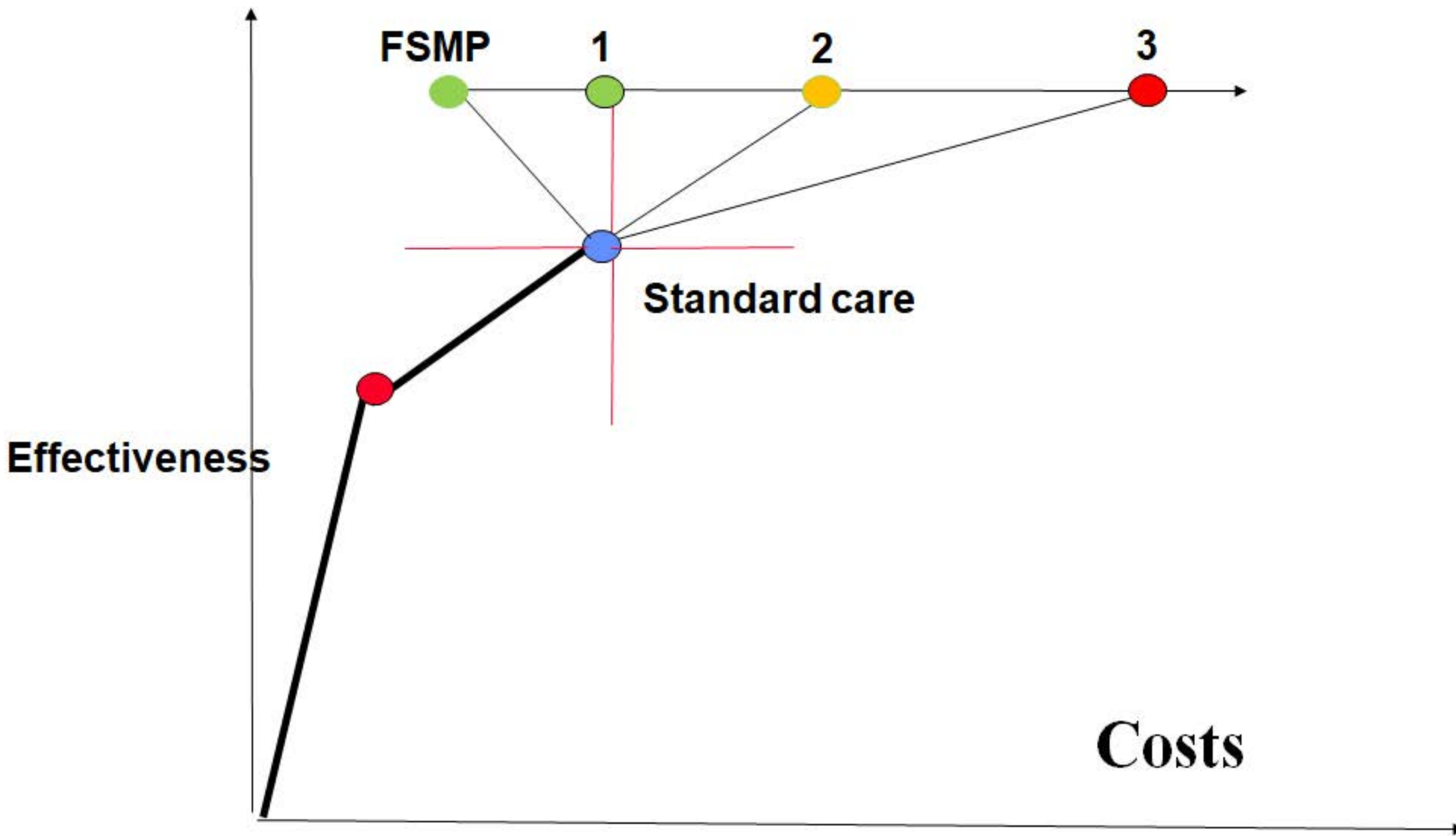
Note. Definition of the various settings according to ISPOR Nutrition Economics SIG publication on terminology and regulations.²⁸
 FSMP/MF indicates food for special medical purposes/medical food; GI, gastrointestinal; MN, medical nutrition; SIG, Special Interest Group.
 *Eligible individuals who qualify for Comprehensive Social Security Assistance will receive reimbursement.⁴⁶
[†]Individuals are means tested to determine eligibility, and approval is on a case-by-case basis.
[‡]Limited to a diagnosis of a functional GI impairment requiring enteral tube feeding through a prosthesis (feeding tube) for conditions deemed permanent (lasting at least 90 days per physician assessment). Flexible Spending Accounts and Health Spending Accounts may be used for the reimbursement of MN in the community, when justified with a letter of medical necessity.

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INTRODUCTION

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DILEMMA

Conclusion

- Lack of sufficiently convincing arguments.
- We do not provide the good and correct information.



- A lot of interesting scientific research, BUT:
 - What is benefit for the patient?
 - Do the results support the access to nutrition for patient?
 - Is the research at all relevant to daily practice?



DILEMMA

Conclusion

- Many time an effort in publications.
- Semantics of definitions, e.g. at risk of malnutrition
- Screening tools: numerous tools with similar sens/spec, but no consensus



- Priority on clinical evidence of treatment (DA . ONS) of malnutrition



- If no there is clinical evidence, screening has no clinical and economic value. (challenge)

	Prevalence MN	
Kruizenga (2016) Hospital	SNAQ 13,7%	MUST 14,9%
De van der Schueren (2022) nursing home	SNAQ 21,0%	MNA-SF 20,5%



DILEMMA

Clinical evidence

- **Cochrane review (2021) by Baldwin: pooled data - no evidence of an effect of any intervention on mortality, length of stay and re-hospitalization.**
 - **Grading of quality of evidence: very low to low.**
 - **No statistically significant results ($p > 0.05$).**
- **BUT: many single studies provide statistically significant results for clinical and economic outcomes.**

Schuetz (2019): mortality 7% v.s 10%:OR 0.65 ($p=0.011$) (n=2,088).



DILEMMA

Cochrane is very negative for use of nutritionals:

- Physicians cannot be convinced anymore to use nutritional support.
- Payers will not pay anymore, because Cochrane review shows that there is no or minimal effect of ONS.



Most important: no access to nutrition for patient



BUT:

- No action since 2021 that puts the negative outcomes of the Cochrane review in a broader perspective.
- No. critical review of applied methods in this Cochrane review, e.g. positive single studies were not included.



DILEMMA

Conclusion:

- We publish huge amount of clinical and economic data on malnutrition and nutritionals.
- BUT: We do not provide the right clinical data to convince decision makers of clinical value of ONS.
- IF no clinical data, then all published economic value of ONS drops to zero

- **No access to nutrition care for patients**



Is this optimal care for patient in its treatment?



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CHALLENGE

Reversal in research:

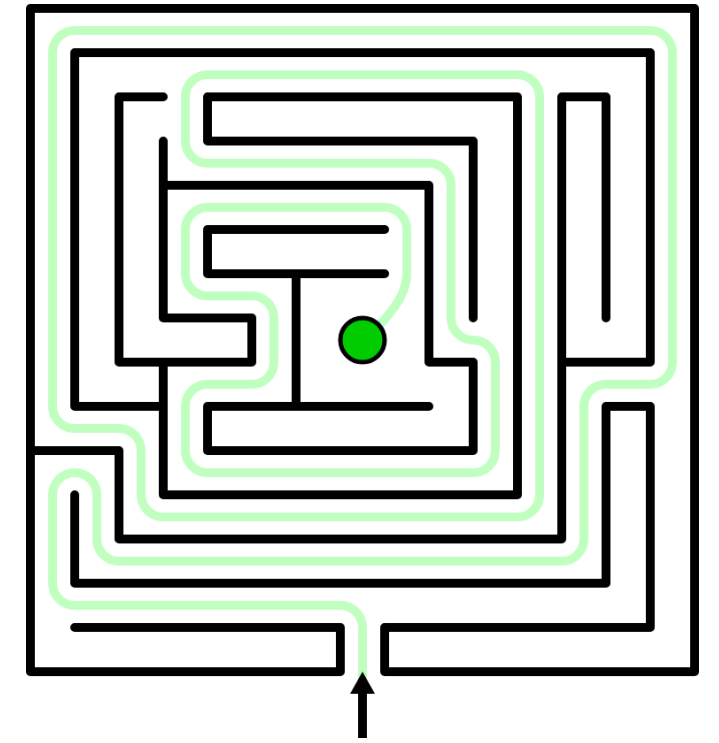
NOT- Take researcher perspective based on academic interests.

BUT:

Take patient perspective: define his data needs for convincing decision makers, and focus research on getting these data.



- Key clinical evidence
- Prevalence, economic data
- Opportunity costs (with and without Tx)



CHALLENGE

Considerations:

- Clinical trial (RCT) quality standards were developed primarily for clinical drug research.



BUT:

Food differs from drugs in many properties, and it is therefore not always practically possible to meet these clinical research standards for drugs.

- Adequate placebo for nutrition
- Blinding



Therefore, the prove of the clinical benefit of nutrition is not the real hurdle here, but mainly the need for a change of paradigm by HTA bodies and health authorities



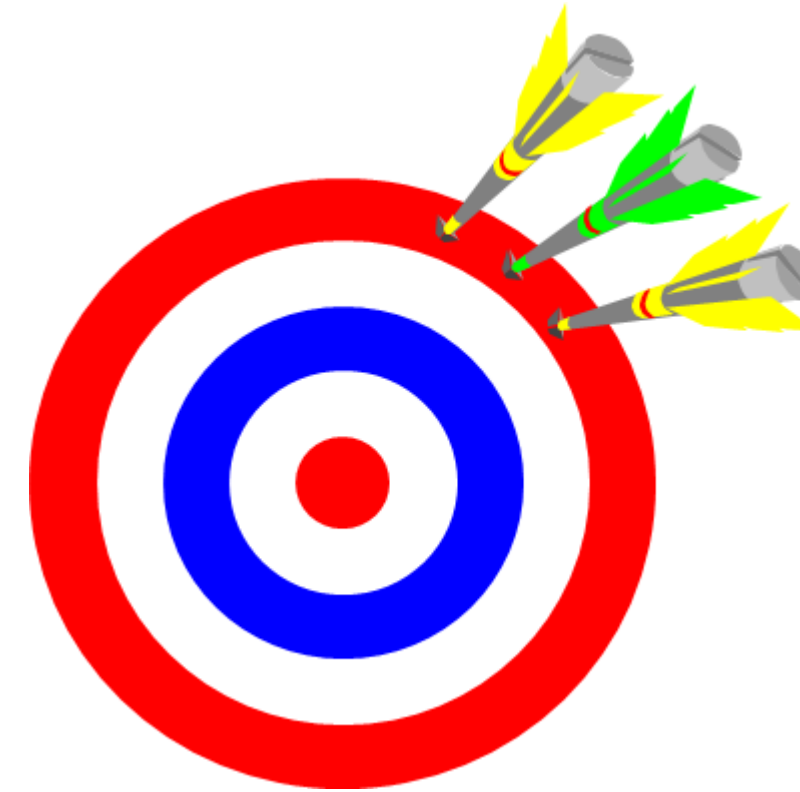
CHALLENGE

Internal validity

Drugs



Nutrition



- **Nutrition: more heterogeneity, multivariate nature of food and confounding effects.**
- **Even higher impact in meta-analysis like Cochrane – Quality of evidence**

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CHALLENGE

RCT:

- Old design when no knowledge of mechanism of action.
- Statistical model with prove only based on $p\text{-value} < 5\%$.
- No treatment for all patients through by inclusion and exclusion criteria – not representative.
- RCT limited number of patients: power problem for bias and confounding variables.
- RCT short duration < 2 years: sufficient to demonstrate a difference in intermediate outcomes (cholesterol reduction), but too short to demonstrate hard outcomes (mortality)



CHALLENGE

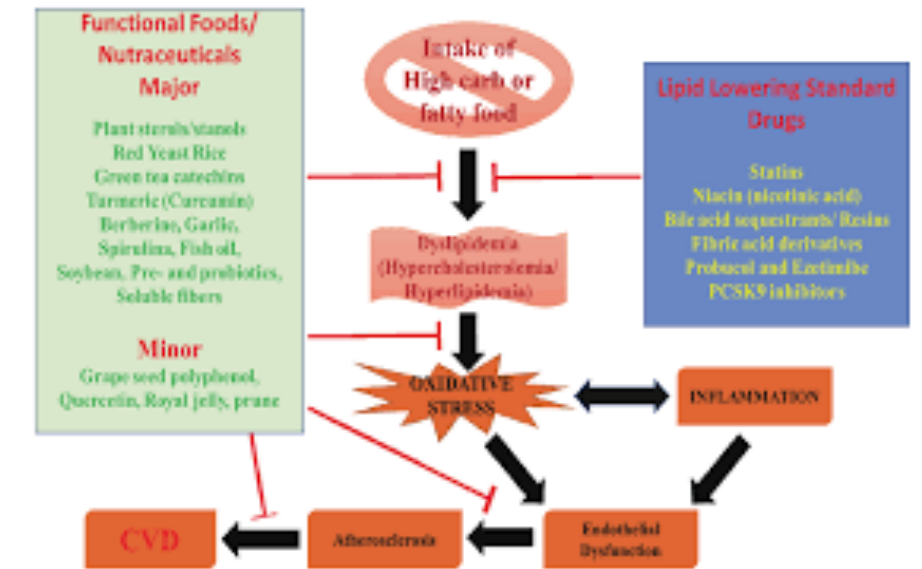
RCT: why still “gold standard” ?

- Mechanism of action: Real evidence of efficacy and no need for statistical evidence from RCT, especially nutritionals.
- Big data/AI solution constraints # number patients and follow-up time



Value-of Information concept.

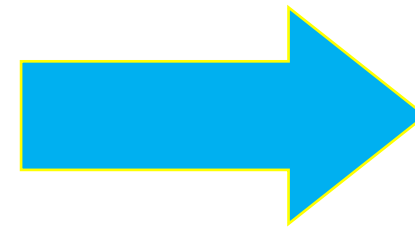
- Regression analyses: bias/confounding
- Learning curve effect
- Real life data - representative for daily practice



CHALLENGE

New paradigm

- Why stick to RCT, which old fashioned and not in line with 2024 developments in medicine:
 - Why ignore mechanism of action proof of evidence ?
 - Why ignore all non-RCT data, like big data and AI opportunities ?
- Both were not available 100 years ago and main reason for artificial RCT based on p-value.
- Believing in RCT is more religion and conflicting with value-based information concepts.



CHALLENGE

New paradigm digital health and AI - additions to RCTs:

- Which smart designs can improve validity and reliability, for example stepped wedge designs or cluster randomization ?
- Which real alternatives have been developed beyond RCTs, such as big data analysis or new forms of action research ?

TIP	Trials of intervention principles method
MOST	Multiphase optimization strategy trials
SMART	Sequential mutiple assignment randomised trials
CEEBIT	Continuous evaluation of evolving behavioural intervention technologies
I2	Intervention informatica
Realtime TA	Real time technology assessment
CEAR	Comparative effectiveness reserach



CHALLENGE – CALL TO ACTION

Call to action - Innovation task force Pan European project:

- **Step 1: A publication that puts the negative outcomes of the Cochrane review in a broader perspective.**
We recommend a methodological critical review of the applied methods in this Cochrane review.
- **Step 2: Development of new design for proving efficacy of medical innovation, e.g. nutritionals including, AI, Big Data, mechanism of action and other 2024 opportunities.**
- **Step 3: Change of HTA assessment criteria for nutritionals, e.g. clinical evidence.**
- **Step 4: Change of pricing policy from cost plus to value-based pricing.**

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Metrics that matter

Transforming nutritional care policies through data-driven paradigm shift

A workshop

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Disclosure

- **Honoraria for independent lectures at industry-sponsored events.**
- **Advisory board of Nutricia Oncology**
- **Board member, DNC.**
- **Consultant for BBraun, Fresenius Kabi, Nestlé Health Science, EO3.**





nutritionDay worldwide
benchmark & monitor your nutrition care



Worldwide (n=10702)

Patients defined by staff as malnourished: **13%**

Patients with weight loss: **48%** (40% unintentional + 8% intentional)

Food eaten before nD 2019

Patients eating 50% of usual or less: **33%**

Food eaten on nD 2019

Patients eating 50% of usual or less: **49%**

Patients on artificial nutrition (ONS, EN, PN): **30%**

Data from nD 2019



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**If we were in a market, what are we selling?
Which is our product?**



Our ultimate product is ...

- Health
- Efficacy of treatment
- Fitness
- Improvement of QoL
- Cost-efficiency

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Our setting is ...

- Prevention
- Treatment



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What is our testimonial?

- Survival
- PROMs
- Body composition
- Cost-efficiency

Microsoft Bing



The association of body composition phenotypes before chemotherapy with epithelial ovarian cancer mortality

Evan W. Davis MPH¹, Kristopher Attwood PhD², Joseph Prunier MS³, Gyorgy Paragh MD PhD⁴, Janine M. Joseph MS MBA¹, André Klein PhD⁵, Charles Roche MD⁶, Nancy Barone BS¹, John Lewis Etter PhD⁷, Andrew D. Ray, PT PhD^{1,8}, Britton Trabert PhD^{9,10}, Matthew B. Schabath PhD¹¹, Lauren C. Peres PhD¹¹, and Rikki Cannioto PhD EdD¹

Results: Overweight/obesity was associated with up to 51% and 104% increased mortality in EOC and HGSOC (HR=1.51, 95% CI: 1.05-2.19 and HR=2.04, 95% CI: 1.29-3.21).

Sarcopenia/overweight-obesity was associated with up to 66% and 67% increased mortality in EOC and HGSOC (HR=1.66, 95% CI: 1.13-2.45 and HR=1.67, 95% CI: 1.05-2.68).

Sarcopenia/cachexia was associated with up to 73% and 109% increased mortality in EOC and HGSOC (HR=1.73, 95% CI: 1.14-2.63 and HR=2.09, 95% CI: 1.25-3.50).

J Natl Cancer Inst 2024



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Is this enough?

Microsoft Bing





Barriers

- Lack of intervention studies
- Unrealistic targets
- Low rate of patients reporting
- Methodology
- Malnutrition does not attract





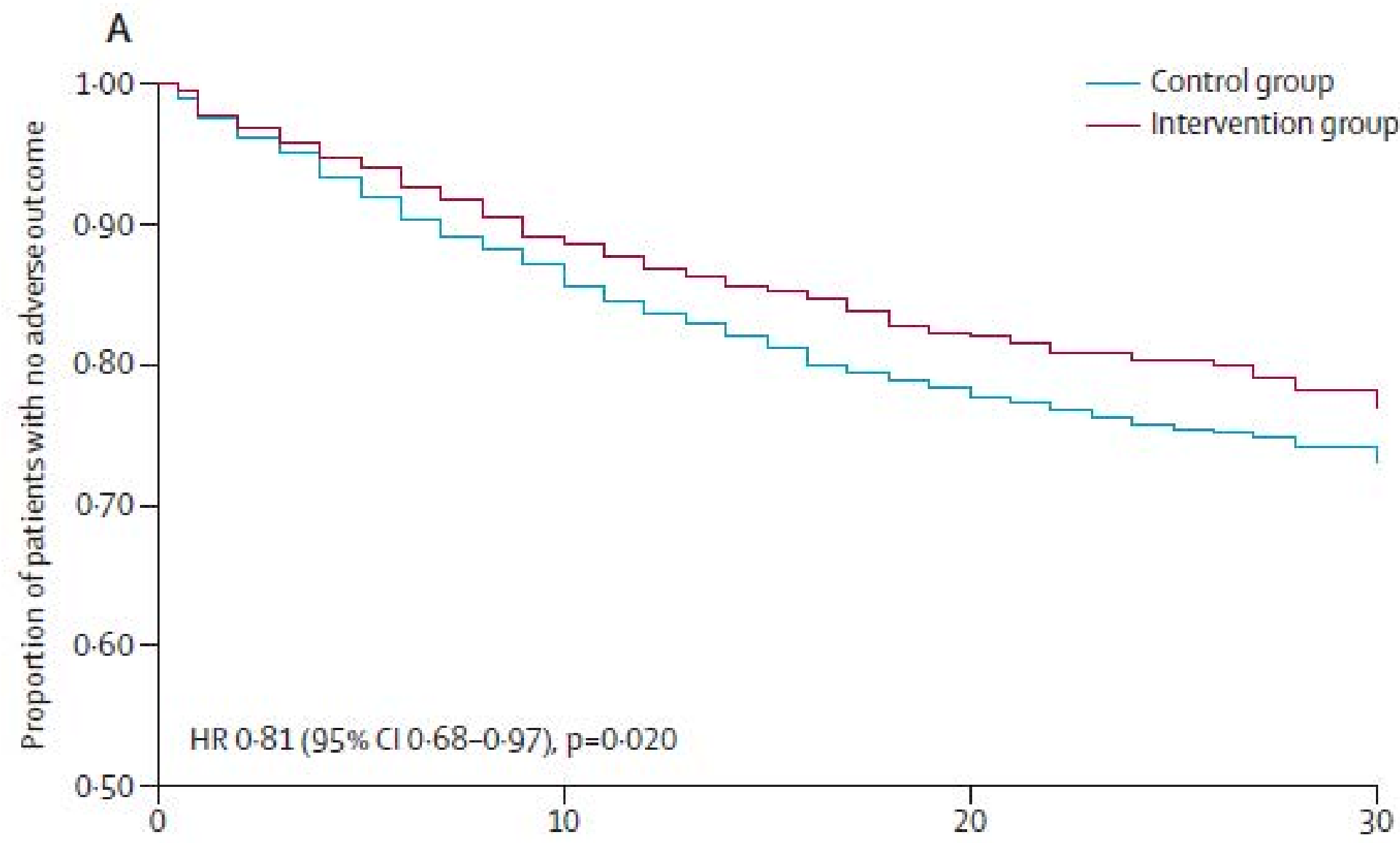
Barriers

- **Lack of intervention studies**
- Unrealistic targets
- Low rate of patients reporting
- Methodology
- Malnutrition does not attract



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

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Number at risk

	0	10	20	30
Control group	1013	882	791	749
Intervention group	1015	895	825	786

Lancet 2019; 393: 2312-21





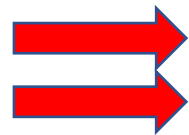
Barriers

- Lack of intervention studies
- **Unrealistic targets**
- Low rate of patients reporting
- Methodology
- Malnutrition does not attract



Supplementary Table 1: Additional outcomes regarding weight and nutritional intakes

	Control (N=251)	Intervention group (N=255)	p-value
Weight change during the hospital stay			
Mean bodyweight (kg) Day 1	72.8 (13.8)	69.7 (15.8)	0.043
Mean bodyweight (kg) Day 3	72.2 (13.6)	71.4 (17.0)	0.7
- Change in body weight (kg) , day 1 to day 3	0.1 (1.7)	0.9 (2.3)	0.006
Mean bodyweight (kg) Day 6	73.0 (14.1)	70.5 (15.8)	0.099
- Change in body weight (kg), day 1 to day 6	0.2 (2.4)	0.6 (2.2)	0.12
Nutritional intake during the hospital stay			
Mean caloric intake (kcal/24h) Day 5	1121.2 (581.6)	1364.9 (687.7)	<0.001
Mean protein intake (g/kg bodyweight/24h) day 5	44.8 (21.3)	53.6 (23.5)	<0.001
Mean caloric intake (kcal/24h) day 7	1141.6 (584.9)	1391.0 (682.6)	<0.001
Mean protein intake (g/kg bodyweight/24h) day 7	43.9 (22.6)	52.2 (24.8)	<0.001
Mean caloric intake (kcal/24h) day 10	1153.9 (584.8)	1410.7 (681.5)	<0.001
Mean protein intake (g/kg bodyweight/24h) day 10	44.2 (22.6)	52.7 (25.2)	<0.001
Mean caloric intake per kilogram per day	16.6 (9.0)	20.9 (10.4)	<0.001
Mean protein intake in grams per kilogram per day	0.6 (0.4)	0.8 (0.4)	<0.001

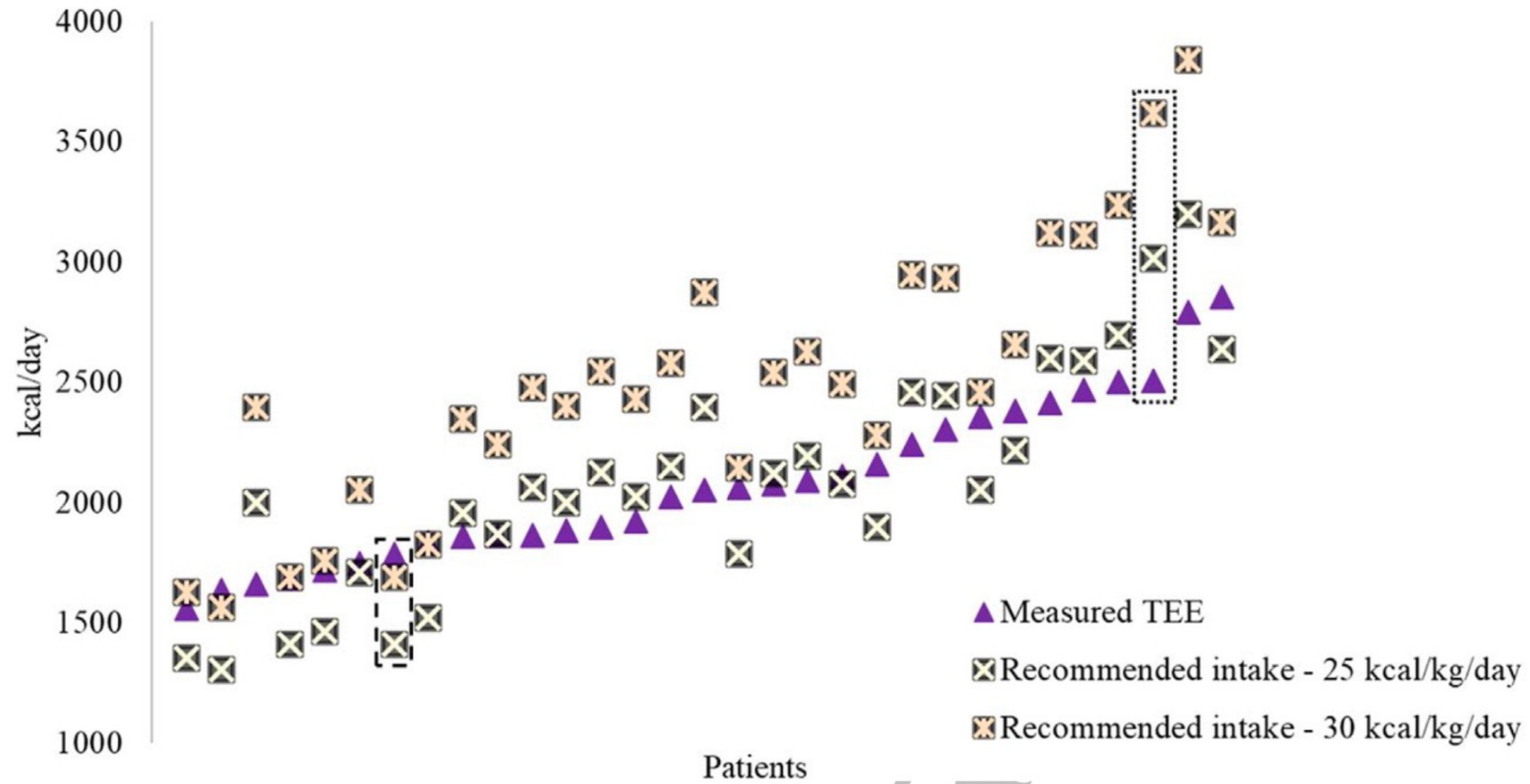


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L. Bargetzi et al. Ann Oncol 2021



Total energy expenditure assessed by 24-h whole-room indirect calorimeter in patients with colorectal cancer: baseline findings from the PRIME study

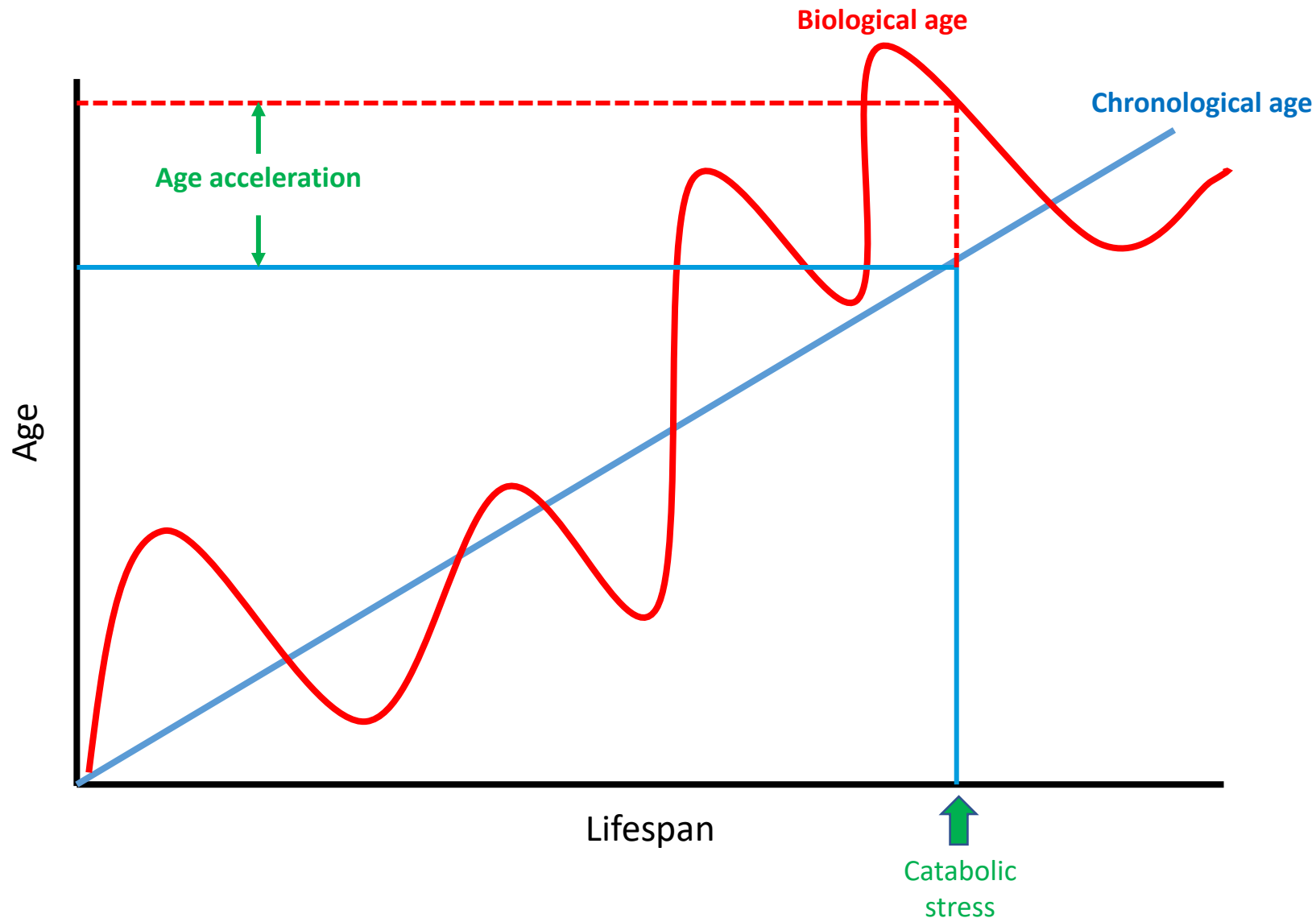


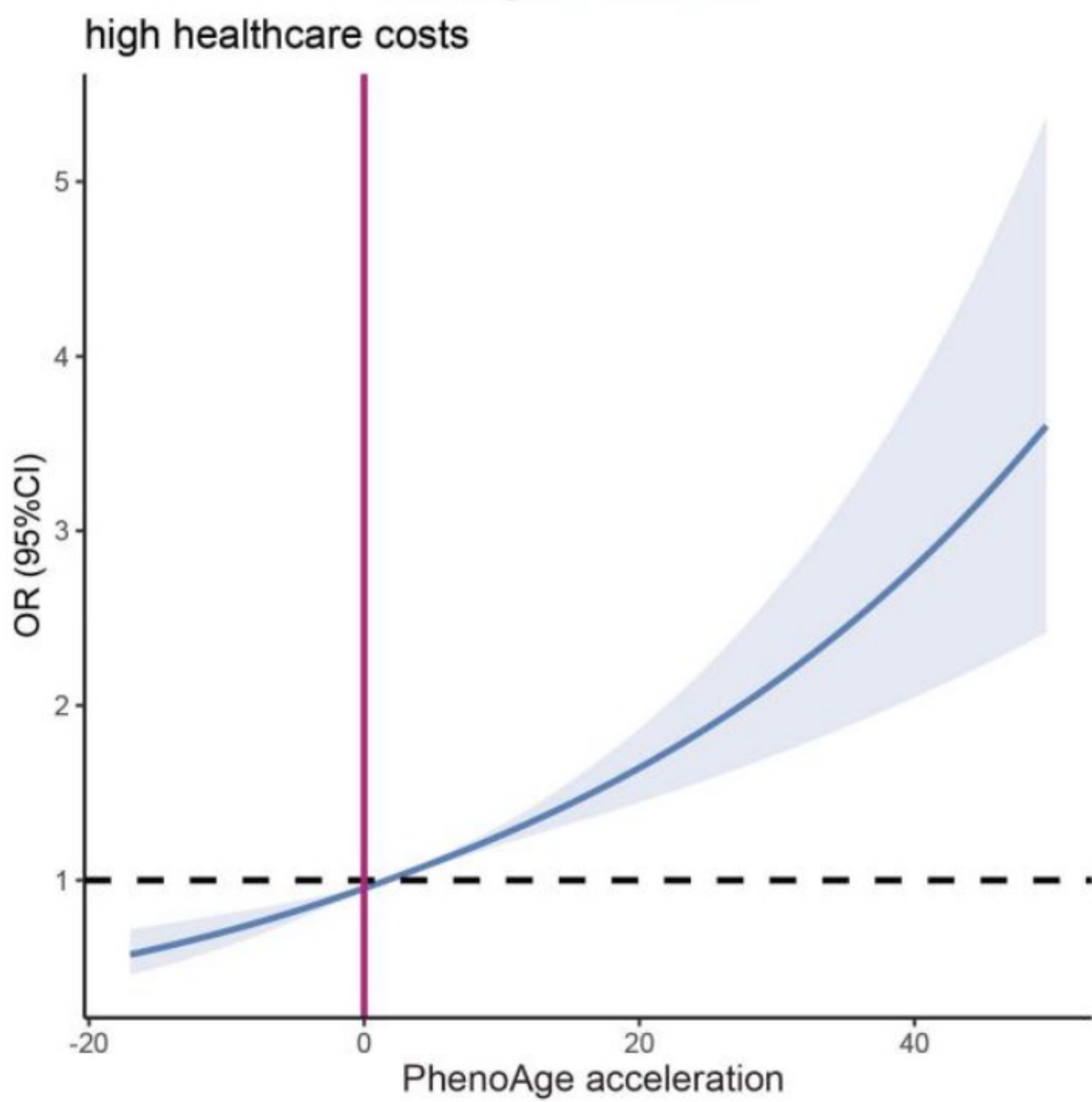
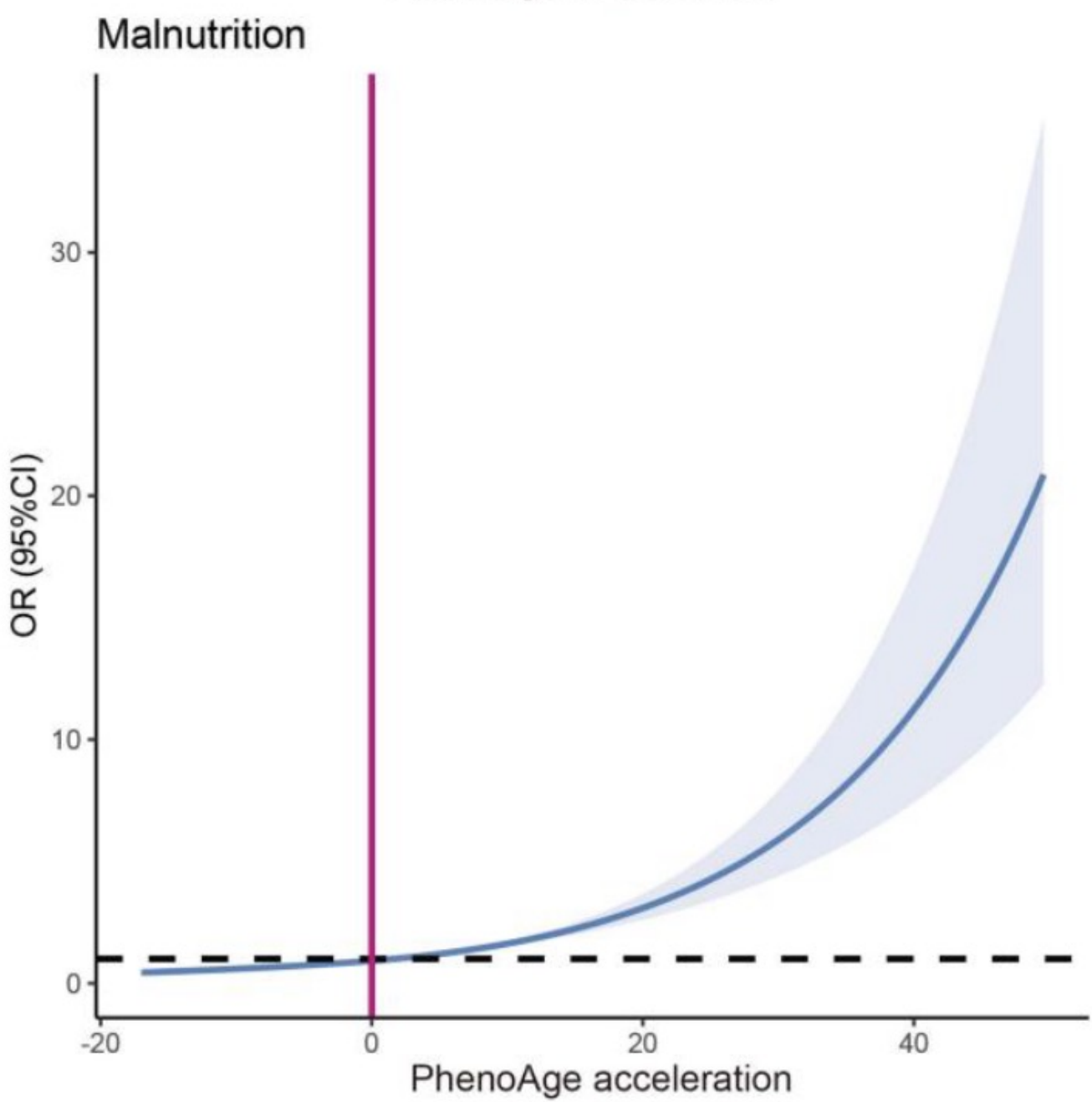
The American Journal of Clinical Nutrition



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Chronological vs biological age





Shi-Qi Lin et al. 2024 (submitted)



Conclusions (i.e., what's next?)

- **Healthy nutrition matters to individuals and patients (i.e., EU-funded European NHANES).**
- **Easily achievable information on nutritional status.**
- **More focus on PROMs rather than hard outcome measures or functional goals.**
- **Should we start thinking of a new wording for malnutrition?**

