



UNLOCK: NUTRITION AND LOCOMOTORIC REHABILITATION IN LONG COVID

Study sponsor: Universitair Ziekenhuis Brussel (UZ Brussel)

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PI: Prof. Dr. Elisabeth De Waele

UNLOCK PILOT TRIAL

Rationale

- Fatigue, Post-exertional malaise (PEM) and muscle function ⇔ linked to energy metabolism¹⁻⁵
- COVID-19 and long COVID → ↑ Malnutrition and negative body composition changes⁶⁻¹¹
- Adequate & personalised nutrition:
 - Covers energy expenditure
 - Supports muscle retention/growth
 - Minimises GI symptoms
- **Multidisciplinary rehabilitation is necessary!**

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Pilot and Feasibility Studies

STUDY PROTOCOL

Open Access



Functional performance recovery after individualized nutrition therapy combined with a patient-tailored physical rehabilitation program versus standard physiotherapy in patients with long COVID: a pilot study

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Abstract

Background Long COVID is suggested to be present in 14 to 43% of COVID 19-survivors. Literature on this new condition states a need for a multidisciplinary approach including physical exercise and nutrition. The aim of the current pilot study is to investigate the feasibility of the proposed protocol to prepare for a randomized controlled study that addresses the effectiveness of a personalized multimodal treatment compared to standard physiotherapy.

Methods This is a protocol of the UNLOCK (Nutrition and LOComotoric rehabilitation in long COVID) study, a pragmatic, single center, randomized controlled pilot trial with two groups. Patients with persisting symptoms related to a SARS-CoV-2 infection will receive either standard physiotherapy or a personalized multimodal treatment for a period of 12 weeks, consisting of individualized physical exercise program combined with individualized nutritional therapy. They will be followed-up at 6, 12, and 18 weeks after randomization.

Discussion A multidisciplinary approach for dealing with long COVID is needed. Because of the lack of clear data and the fact that this is a very heterogenic group, we aim to prepare and optimize a randomized controlled study that addresses the effectiveness of a personalized multimodal treatment.

Trial registration ClinicalTrials.gov Identifier: NCT05254301 (since February 24, 2022).

Keywords Long COVID, Physical exercise, Nutrition, Rehabilitation

Aims:

- Assess **feasibility** of multimodal therapy
 - Assess **effectiveness** of multimodal therapy vs. standard physiotherapy
- prepare for RCT

DESIGN UNLOCK PILOT TRIAL

Eligibility criteria

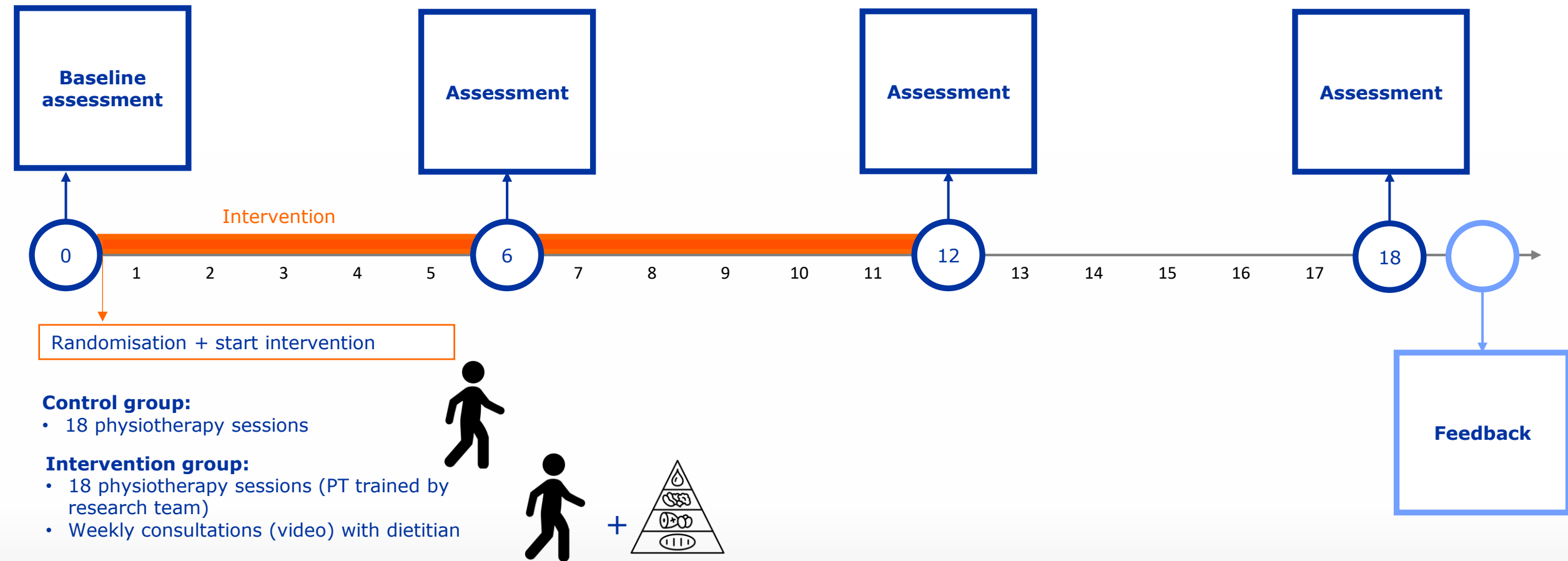
INCLUSION CRITERIA

1. Understands Dutch, French or English
2. ≥ 18 years
3. History of SARS-CoV-2 infection
4. **Functional difficulties (PEM/fatigue/muscle pain) > 12 weeks since infection**
5. Affiliated to Belgian social security system

EXCLUSION CRITERIA

1. Alternative diagnosis
2. Unable to undergo rehabilitation program due to comorbidities
3. >9 sessions of physiotherapy for long COVID in current calendar year
4. Metabolic disorders or severe gastro-intestinal conditions

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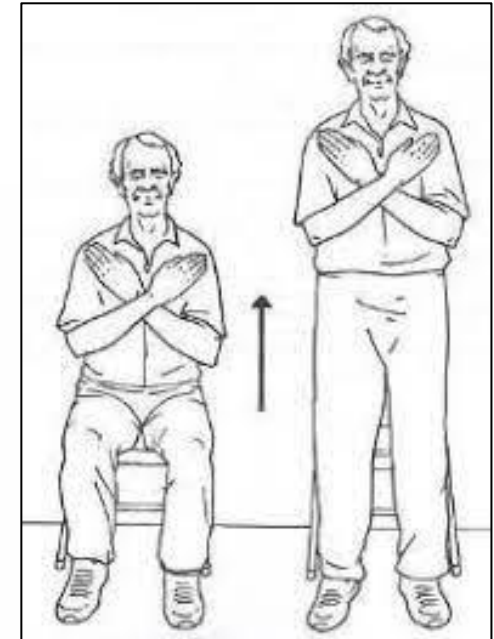


DESIGN UNLOCK PILOT TRIAL

Endpoints and outcomes

Primary endpoints

- Feasibility
 - Recruitment rate
 - Attrition rate
 - Participant study burden (Study Participant Feedback Questionnaire, section C)
- Effectiveness
 - Δ Functional performance after 12 weeks (1-minute sit-to-stand test, 1-MSTS)



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Endpoints and outcomes

Secondary endpoints	Outcomes
Fatigue	MFI-20
Quality of life	EQ-5D-5L
Functional status	PCFS
Work-related activities	WPAI
Mental health	HADS

EQ-5D-5L: EuroQoL group 5 dimensions 5 levels, HADS: Hospital Anxiety and Depression Scale, MFI-20: Multidimensional Fatigue Inventory, PCFS: Post-COVID-19 Functional Status Scale, WPAI: Work Activity and Productivity Impairment questionnaire

Explanatory endpoints	Outcomes
Participant characteristics	Sex, COVID-19 and long COVID outcomes
Illness perception	IPQ
Physical performance	6-MWT, handgrip strength, muscle strength
Nutritional status	REE, Feeding adequacy, body composition
Dyspnoea	mMRC
ADL	Barthel Index

6-MWT: 6-minute walk test, ADL: activities of daily living, IPQ: Illness Perception Questionnaire, mMRC: modified Medical Research Council dyspnoea scale, REE: Resting Energy Expenditure

RESULTS – BASELINE CHARACTERISTICS

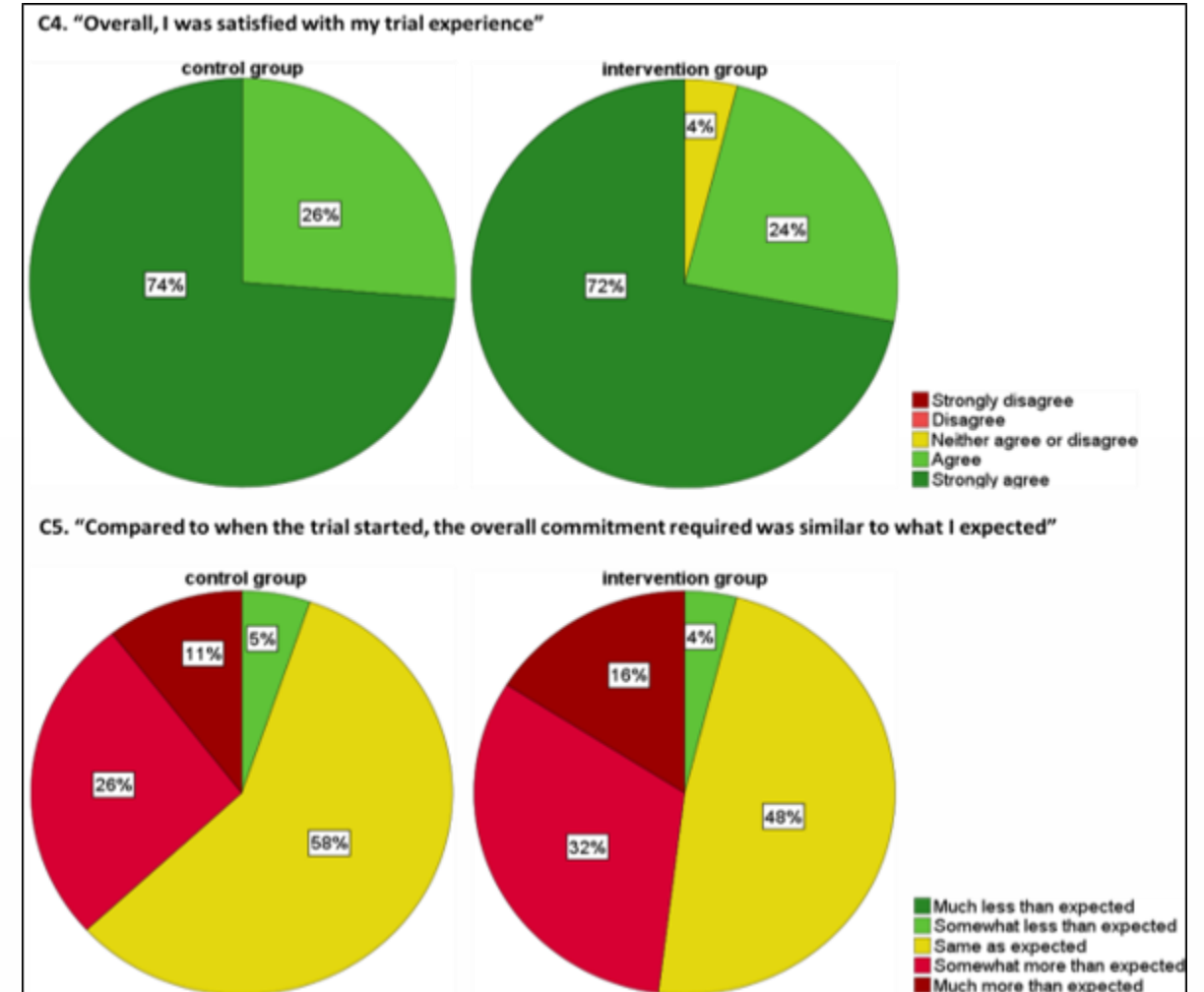
Table 4: Baseline characteristics of the study population

	Total	CG	IG
	n = 65	n = 33	n = 32
Age (years) (mean $\pm$ SD)	43 $\pm$ 10	44 $\pm$ 11	43 $\pm$ 11
Sex (% female)	64.6	63.6	65.6
Smoking (% yes)	4.6	9.1	0.0
Hospitalisation (% yes)	9.2	9.1	9.4
Length of hospitalisation (days) (mean $\pm$ SD)	16 $\pm$ 18	19 $\pm$ 24	13 $\pm$ 15
ICU admission (% yes)	3.1	3.0	3.1
Length of ICU stay (days) (mean $\pm$ SD)	20 $\pm$ 16	31 $\pm$ 0	9.0 $\pm$ 0
Long COVID duration (weeks) (mean $\pm$ SD)	78 $\pm$ 43	81 $\pm$ 44	75 $\pm$ 42
BMI (kg/m ²) (mean $\pm$ SD)	25.8 $\pm$ 4.1	26.0 $\pm$ 3.9	25.5 $\pm$ 4.3

BMI: Body Mass Index, ICU: intensive care unit, CG: control group, IG: intervention group, SD: standard deviation

RESULTS - FEASIBILITY

- Study burden = important limiting factor
 - Scening: average 9/month (141/16 months)
 - Attrition: 24.6%
- Feasibility intervention:
 - Physiotherapy: 14 sessions
 - Nutritional counselling (IG): 10 sessions
 - 70% continued with intervention past 12 weeks



RESULTS - EFFECTIVENESS

1-MSTS

Table 8: descriptive baseline results of the 1-MSTS

	Total (mean $\pm$ SD)	CG (mean $\pm$ SD)	IG (mean $\pm$ SD)
T0 repetitions	$n = 64$ 24 ± 8	$n = 33$ 24 ± 10	$n = 31$ 24 ± 6

Table 9: descriptive results of the 1-MSTS throughout the trial

	Total mean [95%CI]	CG mean [95%CI]	IG mean [95%CI]	Mean difference between IG and CG mean [95%CI]
Difference in repetitions T1-T0	$n = 52$ 2 [1, 3]	$n = 25$ 2 [0, 4]	$n = 27$ 2 [1, 4]	1 [-2, 3]
Difference in repetitions T2-T0	$n = 49$ 3 [2, 4]	$n = 33$ 3 [0, 5]	$n = 37$ 4 [2, 5]	1 [-2, 4]
Difference in repetitions T3-T0	$n = 47$ 4 [3, 6]	$n = 22$ 3 [1, 6]	$n = 25$ 5 [3, 8]	2 [-1, 6]

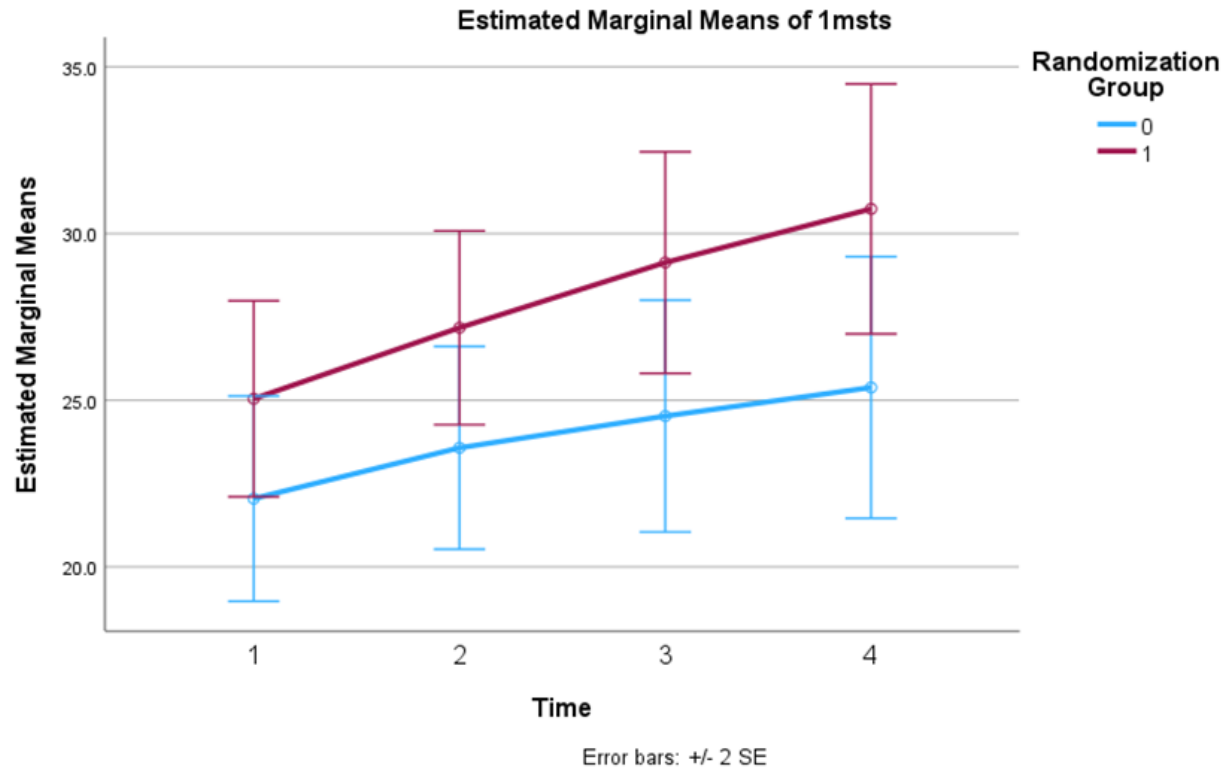
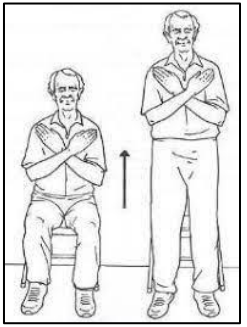
$d = 0.212$

Sample size considering 24.6% attrition: 142 participants

T0: baseline, T1: 6-weeks, T2: 12 weeks, T3: 18 weeks

RESULTS - EFFECTIVENESS

Primary endpoint: Δ Functional performance (1-MSTS) after 12 weeks



No significant between-subject effect
($p = 0.067$)

However:

- Increasing mean difference between groups (at 18 weeks MD_{IG-CG} of 5 (SE: 3, $p = 0.055$))
- Significant (& clinically important) within-subject change in IG but not in CG

Repeated measures ANOVA ($n = 44$; 21 GC (0), 23 IG (1))

ADDITIONAL RESULTS

Nutritional intake at baseline: quantity



$\frac{\text{Intake}}{\text{Resting Energy Expenditure}} < 1$ in 50% of participants



ADDITIONAL RESULTS

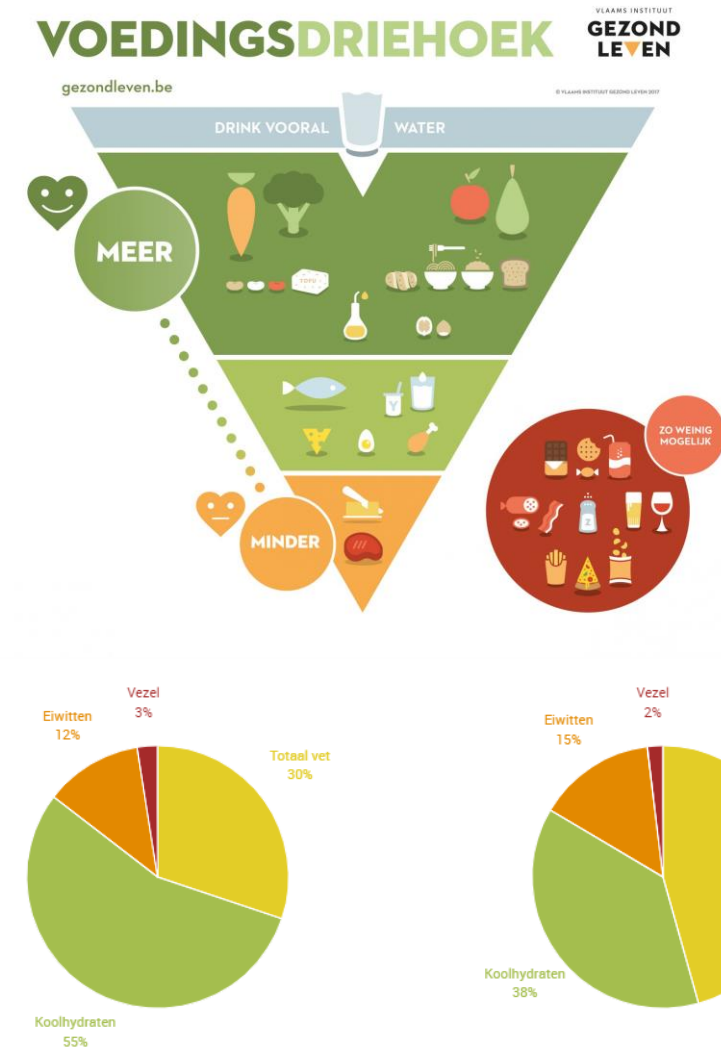
Nutritional intake at baseline: quality

Table: Mean daily macronutrient intake and quality compared to nutritional recommendations (n = 62)

	Protein	Carbohydrate	Fat
Mean ± SD	1.01 ± 0.37 g/kg	43 ± 7 En%	36 ± 7 En%
% within practical recommendations	55	16	42

Disbalanced macronutrient intake

→ Nutrition is a potential therapeutic target!



CONCLUSIONS

- Multimodal therapy (personalised nutrition + physiotherapy) = feasible
- No significant differences in functional performance between IG and CG
 - Positive trend within IG but not CG
 - Rationale for longer interventional period
- Powered RCT necessary to assess effectiveness
- Disbalanced nutritional intake can be a therapeutic target
 - Energy management
- Long COVID nutritional counselling: kaat.gerits@uzbrussel.be
 - CAVE: Without reimbursement RIZIV/INAMI

THANK YOU

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