UPDATE ON MALNUTRITION, MUSCLE LOSS AND BODY COMPOSITION IN 2021

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The content of this program has met the (continuing education) criteria of being evidence-based, fair and balanced, and non-promotional.

This educational event is supported by Abbott Nutrition Health Institute, Abbott Nutrition.

Disclosures for Professor M. Cristina Gonzalez, MD, PhD include:

- Abbott Nutrition
- Nestlé
OBJECTIVES

1. Review key concepts related to malnutrition and muscle assessment
2. Discuss the clinical implications of associated malnutrition and low muscle mass
3. Examine recent advances in body composition assessment and their use in research and clinical practice

MALNUTRITION IS CAUSED BY REDUCED FOOD INTAKE & INFLAMMATION

- Starvation
- Aging
- Disease
- Injury
- Food intake
- Inflammation
- Biological function
- Muscle catabolism
- Altered body composition

MALNUTRITION IS ASSOCIATED WITH ADVERSE HEALTH OUTCOMES


↑ HOSPITALIZATION
↑ LENGTH OF STAY
↑ COMPLICATIONS
↑ COSTS
↑ COGNITIVE
IMPAIRMENTS
↑ COMORBIDITIES
↑ MORTALITY

OVERALL COSTS ARE GREATER IN PATIENTS WITH MALNUTRITION

Malnutrition → International Classification of Diseases (ICD-9 and ICD-10)

Malnutrition treatment reduces mortality rate

69,934 HOSPITALIZED PATIENTS WITH MALNUTRITION

Patients with malnutrition receiving vs. NOT receiving nutritional support
↓ In-hospital mortality rate
↓ 30-day readmission rate
↓ Discharge to a post-acute care facility

Figure 2. Kaplan-Meier Curve for Propensity Score-Matched Rate of All-Cause In-Hospital Mortality

Adjusted HR: 0.57; 95% CI: 0.44 to 0.74; P = .002
GLOBAL LEADERSHIP INITIATIVE ON MALNUTRITION (GLIM)

Global Consensus on Diagnostic Criteria to Support Benchmarking and Amend the Malnutrition Description in ICD-11

**PHENOTYPIC CRITERIA**
- Weight loss
- Low body mass index
- Reduced muscle mass
- Reduced food intake or assimilation

**ETIOLOGIC CRITERIA**
- Inflammation or disease burden
- Reduced food intake or assimilation


**PERFORMANCE CRITERIA**

Perform Nutrition Risk Screening with a Valid Tool

Check the Five GLIM Criteria Separately or from:
- Subjective global assessment
- Patient-generated subjective global assessment
- Mini nutritional assessment

Use GLIM Malnutrition Severity Grading

Apply GLIM Diagnostic Criteria

GLIM WITHIN NUTRITION CARE

GLIM is to be used alongside screening and nutritional assessment, it is not a replacement for these steps

MUSCLE LOSS
PATHOPHYSIOLOGY OF MUSCLE LOSS

• Insulin resistance
• Inflammation
• Oxidative stress
• Mitochondrial damage

MUSCLE WASTING

↑ Muscle protein degradation
↓ Muscle protein synthesis

Two Main Systems
- Proteasomal pathway
- Autophagic-lysosomal

MUSCLE LOSS: THE COMMON FEATURE AMONG DIFFERENT CLINICAL CONDITIONS

MALNUTRITION
- Weight loss
- Low BMI
- Reduced food intake
- Inflammation/disease

SARCOPENIA/FRAILTY
- Reductions in strength & performance

CACHEXIA
- Weight loss
- Reductions in muscle strength
- Fatigue
- Anorexia
- Inflammatory markers

MALNUTRITION, SARCOPENIA & FRAILTY: OVERLAPPING SITUATIONS IN HOSPITALIZED OLDER ADULTS

10 STUDIES, N=2427

Physical (pre-frailty) 49.7% (Risk of Malnutrition)

OR: 5.77 (95% CI: 3.88, 8.58), P<0.0001, I²=42.3%

7 STUDIES, N=2506

Sarcopenia 41.6% (Risk of Malnutrition)

OR: 4.06 (95% CI: 2.43, 6.80), P<0.0001, I²=71.4%

AGING
HORMONE DEFICIENCIES
OSTEOPOROSIS
VITAMIN D DEFICIENCY
DIABETES
OBESITY
ACUTE AND CHRONIC DISEASE

Muscle Loss

BMI - Body Mass Index

7 STUDIES, N=2506

OR: 5.77 (95% CI: 3.88, 8.58), P<0.0001, I²=42.3%

OR: 4.06 (95% CI: 2.43, 6.80), P<0.0001, I²=71.4%

Continuing interventions for preventing and treating muscle loss

MUSCLE GAIN

- ↓ Muscle protein degradation
- ↑ Muscle protein synthesis

Continuing interventions for preventing and treating muscle loss


MUSCLE WASTING

- ↑ Muscle protein degradation
- ↓ Muscle protein synthesis

Oxidative stress
Mitochondrial damage
Insulin resistance
Inflammation

Recent advances in muscle mass assessment

DXA
Anthropometrics
CT
Ultrasound
BIA

Overall performance of most commonly used techniques

DXA
Anthropometrics
CT
Ultrasound
BIA
PHASE ANGLE AS A MARKER OF LOW MUSCLE MASS AND ADVERSE CLINICAL OUTCOMES

Low phase angle was associated with higher risk of dysmobility. Phase angle was correlated with muscle area and radiodensity by CT. Among adult patients with cancer, those with low phase angle were 23% less likely to survive than those with high phase angle.

CALF CIRCUMFERENCE

Most used tool for assessment of muscle mass component for sarcopenia assessment in clinical practice. High correlation with direct and indirect measures of skeletal muscle. Ability to capture age-associated muscle loss: muscles in the lower limbs are lost faster than in the upper limbs.
**KEY FACTORS AFFECTING CALF CIRCUMFERENCE MEASURES**

- **SEX**
- **RACE/ETHNICITY**
- **BMI**
- **EDEMA**

Cut-off values should be sex and population-specific.

Correction for edema: ♂ -2.0 cm  ♀ -1.6 cm

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**DIAGNOSIS OF REDUCED MUSCLE MASS – CALF CIRCUMFERENCE**

Adjustment factors* based on the BMI value:

- ≤ 18.5 kg/m²
- 18.5-24.9 kg/m²
- 25-29.9 kg/m²
- ≥ 30 kg/m²

Compare adjusted CC value to reference, sex-specific cut-off values.

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**CALF CIRCUMFERENCE CUT-POINTS: MARKER OF LOW MUSCLE MASS**

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>Cut-off values</th>
<th>Men</th>
<th>Women</th>
<th>Study</th>
</tr>
</thead>
</table>
THE USE OF ULTRASOUND FOR MUSCLE MASS ASSESSMENT

Comparison of ultrasound-derived muscle thickness with computed tomography muscle cross-sectional area on admission to the intensive care unit: A pilot cross-sectional study

Original Communications

Comparison of Ultrasound-Derived Muscle Thickness With Computed Tomography Muscle Cross-Sectional Area on Admission to the Intensive Care Unit: A Pilot Cross-Sectional Study

Kate J. Lambell, MNutrDiet; Audrey C. Tierney, PhD; Jessica C. Wang, MD; Vinodh Nanjaya, MD; Adrienne Forsyth, PhD; Gerard S. Goh, MD; Don Vicendese, PhD; Emma J. Ridley, PhD; Selina M. Parry, PhD; Marina Mourtzakis, PhD; and Susannah J. King, PhD

Original Communication

JPEN 2021;45:136-145

NOT ONLY IS MUSCLE MASS IMPORTANT...

Muscle: Site and age-related differences

Muscle wasting: 75% higher mortality risk

Myosteatosis: 40 studies (21,222 patients)

Primary myosteatosis: 5.5% lower mortality risk

Secondary myosteatosis: 75% higher mortality risk

Inflammation and Myosteatosis and Life Expectancy


Similar associations between mortality and body composition parameters from manual and automated CT segmentation


DAFS 3.0: Automated Analysis

Similar associations between mortality and body composition parameters from manual and automated CT segmentation

Do not hallucinate.
**Postmenopausal women (n=74)**
- Moderate correlations with lean mass measures by DEXA (r=0.50)
- Strong associations with physical function determined by SPPB (OR=5.24, 95% CI=1.40-19.58)

**Older men (n=903)**
- Positive associations with total protein (β=0.09, 95% CI=0.03, 0.14)
- Positive associations with non-dairy animal protein (β=0.09, 95% CI=0.03, 0.14)

**FINAL REMARKS**

- Malnutrition has been associated with unfavourable changes in body composition and several adverse health outcomes
- The GUM framework has been proposed to aid malnutrition diagnosis, and it should be used alongside screening and nutrition assessment
- Muscle loss is one of the most critical consequences of malnutrition — it is easier to prevent muscle loss than to rebuild muscle
- Several techniques have been proposed to assess muscle mass: research vs. clinical practice

**SUMMARY**
TAKE HOME MESSAGES

ASSESS/ESTIMATE MUSCLE MASS

IMPLEMENT MANAGEMENT STRATEGIES

GLIM

SURROGATE APPROACHES IN CLINICAL PRACTICE

Physical Examination
Anthropometry
Muscle Strength
Muscle Performance


THANK YOU

MALNUTRITION AND MUSCLE LOSS: IMMUNITY/COVID-19
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CATHOLIC UNIVERSITY OF THE SACRED HEART
CHIEF, GERIATRIC REHABILITATION UNIT
A. GEMELLI UNIVERSITY HOSPITAL
ROME, ITALY
The content of this program has met the (continuing education) criteria of being evidence-based, fair and balanced, and non-promotional.

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Disclosures for Francesco Landi, MD, PhD include:
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- Honoraria for speaking engagement from Abbott

LEARNING OBJECTIVES

1. Describe the relationship between COVID-19 and the nutrition status of patients
2. Review new data on COVID-19, and its implications for nutrition care - from hospital to home
3. Translate current knowledge for the nutritional management of COVID-19 patients into practical guidance for clinicians

Clinical Features

- The range of clinical presentations of COVID-19 disease have been described varying from asymptomatic infection to severe respiratory failure.
- The common clinical manifestations include fever, cough, fatigue, myalgia, shortness of breath, sore throat, and headache.
- In addition, patients may have also gastrointestinal symptoms, with diarrhea and vomiting.
- Some patients may have taste and smell disturbances, too.
- Interstitial pneumonia is present in most COVID-19 patients.

CT shows diffuse ground-glass opacities, consolidation area, and both ground-glass opacities with consolidation.
ITALIAN EXPERIENCE

Practical Features
• New disease
• New department (ex. surgical units)
• Patient's isolation
• Protective Personal Equipment (PPE)
• Management of specific symptoms (nausea, diarrhea and vomiting)
• Drugs side effects
• Oxygen therapy

SARS-COV-2 INFECTION
IMPACT ON HEALTH OUTCOMES

WHO IS AT RISK OF NEGATIVE HEALTH OUTCOME?
WHO IS AT RISK OF NEGATIVE HEALTH OUTCOME?

- ACUTE CARE HOSPITAL
  - Slow loss over years
  - Isolation
  - Lock-down

- CHRONIC DISEASE
  - Interstitial pneumonia
  - Pulmonary fibrosis

LOSS OF MUSCLE MASS

- Acute loss due to immobilization
- Extreme muscle and weight loss

AGING AND MUSCLE: LOSS OF MUSCLE MASS AND STRENGTH IN THE HOSPITAL

Pre COVID-19

Assessment at Hospital/Discharge

- Hand Grip Strength
- Muscle Mass

- No Sarcopenia N=180
- Sarcopenia N=25

STUDY SAMPLE, N=394

Women=211; Men=183

- No Sarcopenia N=295
- Sarcopenia N=58

15%

No Sarcopenia N=41


SARS-COV-2 INFECTION

ASSESSMENT OF MALNUTRITION / MUSCLE LOSS
ASSESSMENT IN CLINICAL PRACTICE

FOCUS | REVIEW ARTICLE

JAMA

Age, mean (SD), y 56.1 (14.6)
Female sex, No. (%): 53 (37.1)
Pneumonia diagnosed 104 (72.7)
Length of hospital stay, mean (SD) 13.5 (9.7)
Oxygen therapy 77 (53.8)
Non-invasive ventilation 26 (14.7)
Mechanical ventilation 7 (16.9)
Only 12.6% were completely free of any COVID-19-related symptom, while 32% had 1 or 2 symptoms and 55% had 3 or more.


### Number of Symptoms

<table>
<thead>
<tr>
<th>Patients</th>
<th>Median Follow-up 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1343</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>50 (±17)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>665 (49.5%)</td>
</tr>
<tr>
<td>BMI</td>
<td>25.8 (±4.4)</td>
</tr>
<tr>
<td>Flu vaccination</td>
<td>300 (23%)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>107 (8%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>376 (28%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>108 (8%)</td>
</tr>
<tr>
<td>BPCO</td>
<td>105 (8%)</td>
</tr>
<tr>
<td>Number of drugs</td>
<td>2 (±2)</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>739 (55%)</td>
</tr>
<tr>
<td>ICU</td>
<td>161 (12%)</td>
</tr>
</tbody>
</table>

### Quality of Life EQ5D VAS

MALNUTRITION

ESFEN expert statements and practical guidance for nutritional management of individuals with SARS-Cov-2 infection

Table 1: Indications for nutritional intervention

<table>
<thead>
<tr>
<th>Indication</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt; 18.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent major surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay ≥7 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional performance ≤70% of predicted value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other serious chronic illness</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

According to Reduced BMI

- All
- Men
- Women
According to Reduced Muscle Mass (BIA)

- All: 0%
- Men: 5%
- Women: 10%

According to at Least One Phenotypic GLIM Criterion

- All: 0%
- Men: 5%
- Women: 10%

According to at Least One Phenotypic GLIM Criterion

- Hospitalized: 20%
- Not hospitalized: 10%
- > 65 years: 30%
- < 65 years: 15%
SARS-COV-2 INFECTION
THE IMPORTANCE OF ASSESSMENT

Screen/Assessment/Intervention

Screen/Assess

Mandatory in COVID-19 patients

Intervention

ASSESSMENT IN CLINICAL PRACTICE

Clinical Nutrition

A simple remote nutritional screening tool and practical guidance for nutritional care in primary practice during the COVID-19 pandemic.
ASSESSMENT IN CLINICAL PRACTICE: R-MAPP

R-MAPP: REMOTE CONSULTATION ON MALNUTRITION IN THE PRIMARY PRACTICE
A SIMPLE GUIDE TO ASSESSING PATIENTS BY VIDEO OR VOICE CALL

This graphic is intended for use in a primary care setting in order to identify patients at risk of malnutrition and improve prevention and treatment.

SET UP
Prepare yourself for service consultation:
- COVID-19
- Aging / Frailty
- Cancer
- COPD
- IBD
- Stroke
- Post-ICU
- Chronic kidney and liver disease
- Chronic wounds
- Diabetes
- Obesity
- Other chronic diseases

CONNECT
- Can see patient in photos or video:
  - Can you hear me?
  - Confirm patient's identity
  - Check patient's location

TGF-β
Transforming Growth Factor Beta
SARS-COV-2 INFECTION
THE IMPORTANCE OF FOLLOW-UP

POST ACUTE CARE ORGANIZATION

<table>
<thead>
<tr>
<th>First Day</th>
<th>Second Day</th>
<th>Third Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical History</td>
<td>Chest CT</td>
<td>Neurology</td>
</tr>
<tr>
<td>Performance tests</td>
<td>Pulmonary function tests</td>
<td>Psychiatry</td>
</tr>
<tr>
<td>ECG</td>
<td>Pneumology</td>
<td>Rheumatology</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>Gastroenterology</td>
<td>Angiology</td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>Otolaryngology</td>
<td>NUTRITIONIST</td>
</tr>
<tr>
<td>BIA</td>
<td>Dermatology</td>
<td>Internal medicine/ geriatrics</td>
</tr>
</tbody>
</table>
SUMMARY

- Risk for malnutrition affects a large proportion of the polymorbid medical inpatient population and it is important in COVID-19 patients.
- Sarcopenia and malnutrition are frequent in COVID-19 and have negative impact on short- and long-term outcomes.
- Screening with validated tools is effective to identify patients at risk who benefit from nutritional support.
- New multicenter trials provide high level evidence that early start of nutritional support is highly effective in reducing malnutrition-associated complications and mortality.
- Now it is time to ACT in all patients, health care settings and in COVID-19!

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Disclosures for Samuel TH Chew include:

• Honoraria for speaking engagement from Abbott

OBJECTIVES

1. Describe the effect of aging on muscle health, eating habits and nutrition knowledge among community-dwelling older adults

2. Compare and contrast conditions of sarcopenia and frailty, and describe assessment methods for each condition in the community setting

3. Explain the effects of nutrition intervention on muscle and strength over time (as observed in the SHIELD study)

RAPID POPULATION AGING IS A GLOBAL PHENOMENON

MORE THAN HALF OF THE WORLD’S OLDER PEOPLE LIVE IN ASIA

Asia: 2-Fold Increase in the Number of Older Persons

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Persons Aged 60 Years or Older in 2017 (Millions)</th>
<th>Number of Persons Aged 60 Years or Over in 2050 (Millions)</th>
<th>Percentage Change Between 2017 and 2050</th>
<th>Distribution of Older Persons in 2017 (Percentage)</th>
<th>Distribution of Older Persons in 2050 (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>962.3</td>
<td>2080.5</td>
<td>116.2</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Africa</td>
<td>68.7</td>
<td>225.8</td>
<td>158.1</td>
<td>7.1</td>
<td>10.9</td>
</tr>
<tr>
<td>Asia</td>
<td>549.2</td>
<td>1273.2</td>
<td>131.8</td>
<td>57.1</td>
<td>61.2</td>
</tr>
<tr>
<td>Europe</td>
<td>183.0</td>
<td>247.2</td>
<td>35.1</td>
<td>19.0</td>
<td>11.9</td>
</tr>
<tr>
<td>Northern America</td>
<td>78.6</td>
<td>122.8</td>
<td>74.2</td>
<td>8.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>76.6</td>
<td>122.8</td>
<td>74.2</td>
<td>8.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Oceania</td>
<td>6.9</td>
<td>13.3</td>
<td>92.6</td>
<td>0.7</td>
<td>0.6</td>
</tr>
</tbody>
</table>


SHIFTING THE FOCUS

Frail Inpatients
Healthy Community

FUNCTIONAL ABILITY OVER TIME: INTEGRATED CARE OLDER PEOPLE WHO 2017

High and stable capacity
Declining capacity
Significant loss of capacity

Functional ability
Intrinsic capacity
AETIOLOGY SARCOPENIA: CHANGE IN MUSCLE PROPERTIES AND MORPHOLOGY WITH AGING

Motor Units
- Slow (Type I Myosin)
  - Myoglobin
  - Mitochondria
- Fast (Type II Myosin)
  - Glycolysis
  - Large Cross Sectional Area (CSA)
  - 4X more power
  - Generates more reactive oxygen species and more mitochondrial damage and dysfunction
- Age related loss
  - 8% loss/decade: 40 to 70 years old
  - 15% loss/decade: >70 years old

ANOREXIA OF AGING

Anorexia of Aging
- Loss of appetite and/or decreased food intake in later life
- Unintentional decline in intake
- Altered satiety and hunger physiology (ghrelin vs leptin)
- Gastrointestinal motility changes
- Other physical, socioeconomic factors and impaired cognition
**EATING HABITS AND NUTRITION KNOWLEDGE**

- Factors related to better nutrition knowledge
  - Female
  - Able to access and understand nutrition information important
  - Media and social network most common source of information in Asian setting

- Impact of popular diet and misconceptions
  - Older people don’t need as much nutrition as young people
  - The lighter an older person is the better
  - Avoidance of “cold” and “heathy” food
  - Self-imposed “extreme diets”

- Impact of socioeconomic factors, lost of sense of smell and taste, and poor dentition

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**SARCOPENIA AND FRAILTY**

**CONTRAST AND ASSESSMENT**

- Physical Performance
  - Sedentary Lifestyle
  - Malnutrition/Anorexia
  - Low protein intake
  - Vitamin D

- Age-related Hormonal Changes
  - GH/IGF-1, testosterone, DHEAS, estrogens

- Illness/Injury

- Oxidative Stress

- Inflamm-aging

- Myostatin

- Alpha Motor Neurons

- Loss of Muscle Mass

- Muscle Strength

- Physical frailty
  - Mobility, Use of walking aids, reduced impairment

- Negative Health Outcomes
  - Mobility Disability

---

**CONTRAST AND ASSESSMENT**

- SARCOPENIA AND FRAILTY

- Sedentary Lifestyle

- Malnutrition/Anorexia

- Low protein intake

- Vitamin D

- Age-related Hormonal Changes
  - GH/IGF-1, testosterone, DHEAS, estrogens

- Illness/Injury

- Oxidative Stress

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SARCOPENIA VS FRAILTY

SARCOPENIA
- A disease
- Has ICD-10-CM code
- Diagnostic criteria established 1,2
  - EWGSOP
  - AWGS
- Targeted interventions 1,2
  - Muscle health (mass and function)
  - Nutrition
  - Fixed measurable targets
- Predicts adverse outcomes
  - Precedes frailty 2

FRAILTY 2
- A clinical state/syndrome
- Multiple models 2,3
  - Defined as a phenotype (Fried’s criteria) or
  - Defined as accumulation of deficits (Frailty Index) or
  - Defined as multi-dimensional construct
- May require further assessment to determine underlying causes
- Interventions are based on each of these causes
- Predicts adverse outcomes
  - Precedes disability

FRAILTY: SCREENING AND ASSESSMENT TOOLS

Clinical Frailty Scale
(1-2 mins)
- Easy, validated, reliable
- Summary of Frailty Index
- Non-frail (1-4), Mild-to-moderately frail (5-6), Severely frail (7-8), Terminally ill (9)
- A continuous scale

Fried’s Criteria/ Frail Phenotype
- 5 factors
  - Weight loss, exhaustion, sedentary, handgrip strength, gait speed
- Frail (≥3)
- A categorical scale

ASSESSMENT MUSCLE HEALTH

- Definitions:
  - Muscle health
  - Muscle Function + Muscle Mass
  - Muscle function
  - Muscle Strength +/- Performance

- Screening:
  - Malnutrition Universal Screening Tool (MUST) 3
  - SARC-F questionnaire 4

- Strength and Performance
  - Handgrip strength 1,4
  - 5-times Chair Stand Test (SCST) 2,3,5
  - 6-m Gait Speed / Short Physical Performance Battery 4,6

- Muscle Mass
  - Assessment of the Appendicular Skeletal Muscle Mass (ASM)
  - Bio-electrical Impedance Analysis
  - Dual-energy X-ray Absorptiometry (DEXA)
Possible/Probable Sarcopenia

• SARC F (≥4) + Low Muscle Strength (or Low Muscle Performance)

Sarcopenia Confirmed

• Low Muscle Mass + Low Muscle Strength (or Low Muscle Performance)

Severe Sarcopenia

• Low Muscle Mass + Low Muscle Strength + Low Muscle Performance

DIAGNOSIS OF SARCOPENIA

1,2


RESISTANCE EXERCISE TRAINING AND NUTRITION

RESISTANCE EXERCISE TRAINING (RET)

• First-line intervention older adults with sarcopenia

• Frequency, volume and duration dependent

  ▪ Increases strength, power, gait speed and muscle mass

  ▪ ≥3 months duration, ≥2 sessions per week

• 1-Rep Maximum (1-RM)

  ▪ Gold standard for assessment of muscle strength in non-laboratory settings

  ▪ 60% 1-RM

• Minimum muscle load for sustained long term improvement in strength and muscle mass

• Dose response relationship between volume and intensity of RET with muscle mass and muscle strength respectively
WHO GUIDELINES ON PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR
AND WHAT IT MEANS IN TARGETED PRACTICE

STRENGTHENING HEALTH IN ELDERLY THROUGH NUTRITION
(STHIELD) STUDY

Objective:
To determine the effects of oral nutritional supplement (ONS) containing beta-hydroxy-beta-
methylbutyrate (HMB) with dietary counselling on health outcomes, health status, and quality of life in community-
dwelling older adults at risk of malnutrition.

Community-dwelling older adults who were at risk of undernutrition were randomized to receive: (1) Placebo + Dietary Counseling, (2) ONS with HMB + Dietary Counseling. The study took place in 360 days total, with 180-day intervention and 180-day observation. The study was conducted in 5 visits: (1) Baseline, (2) Day 30, (3) Day 90, (4) Day 180 (Exit), (5) Day 360 (Follow up).

Primary Composite Outcome:
• Survival
• No hospital admission
• 5% weight gain

Secondary Outcomes:
• Mortality
• Malnutrition risk
• Anthropometric measurements
• Length of stay
• Energy and macronutrient intakes

Supportive Outcomes:
• Compliance to study products
• Biochemical indices
• Functional assessments
• Frequency of acute illness, falls, healthcare visits
• Micronutrient intake
• SF-36, Modified Barthel Index, Sleep

Exploratory Outcomes:
• Expenditure on healthcare visits
• Number of sick days
• Sensory and acceptance ratings
• PASE, Nutrition literacy questionnaire

All the outcomes at Day 360
4 IN 5 OLDER ADULTS AT RISK OF MALNUTRITION HAVE LOW MUSCLE MASS AT BASELINE\(^1\)

Low Appendicular Skeletal Muscle Mass Index (ASMI) is associated with multiple morbidities such as impaired immunity, decreased wound healing capacity, increased incidence of pneumonia, and mortality\(^2\).


INTERVENTION GROUP HAD SIGNIFICANTLY GREATER WEIGHT GAIN\(^3\)

Weight loss in older adults is associated with increased morbidity and mortality\(^2,4\).


INTERVENTION GROUP 3X MORE LIKELY TO HAVE LOWER NUTRITIONAL RISK

Odds of having lower nutritional risk (MUST) = 2.68; \(P<0.001\)

Odds Ratio: Day 30 = 2.29, Day 90 = 3.35, Day 180 = 2.50; all \(P<0.001\)

Two servings of ONS provide 620 IU of vitamin D, which is 78% of the Recommended Dietary Allowance for adults aged >70 years.

**INTERVENTION GROUP HAD SIGNIFICANTLY HIGHER 25-HYDROXYVITAMIN D LEVELS**

![Graph showing 25-hydroxyvitamin D levels over time for intervention and placebo groups.](image)

**FEMALES IN INTERVENTION GROUP HAD SIGNIFICANTLY HIGHER HANDGRIP STRENGTH AT DAY 180**

![Graph showing handgrip strength over time for intervention and placebo groups.](image)

**INTERVENTION GROUP HAD SIGNIFICANTLY HIGHER LEG STRENGTH AT DAY 90**

![Graph showing leg strength over time for intervention and placebo groups.](image)

Handgrip strength is a powerful predictor of poor patient outcomes eg; longer hospital stay, increased functional limitations, poor health-related quality of life and mortality.

Low lower limb strength is associated with increased risk of disability, recurrent falls, hip fractures, increased hospitalization and mortality in the older adults.

INTERVENTION GROUP HAD SIGNIFICANTLY GREATER CALF CIRCUMFERENCE AT DAYS 90 AND 180 AMONG THOSE WITH LOW ASMI

Calf circumference is a known surrogate marker of lean muscle mass, which is related to multiple health outcomes and it can be used to screen for sarcopenia.1


SHIELD DIETARY DATA – TOTAL ENERGY AND PROTEIN INTAKE PER DAY

TOTAL ENERGY INTAKE PER DAY

TOTAL PROTEIN INTAKE PER DAY

COMPLIANCE TO STUDY PRODUCTS WAS RELATIVELY HIGH

Contrary to the widely perceived idea that Asian older persons are averse to milk-based nutritional supplements...
INTEGRATED RET AND NUTRITIONAL INTERVENTION

- Integrated interventions significantly better than nutrition alone
  - European and Asian cohorts\(^1\)\(^-\)\(^3\)
  - Including very old\(^4\)
- Muscle strength, muscle mass and function
- Strong effect preventing age related loss of muscle mass and strength
- Recommended by ICFSR 2018 and ESPEN 2019\(^5\)\(^-\)\(^6\)
  - Treatment for sarcopenia
  - Improve muscle health in older adults at risk or with malnutrition

SUMMARY

- Malnutrition, sarcopenia and frailty intimately linked
- Malnutrition key target for early identification and intervention
- Progressive resistance exercise training is first line in the treatment and prevention of sarcopenia
- Adequate energy, protein, vitamin D important for muscle health
- Targeted oral nutritional supplementation with HMB effective at-risk community dwelling older adults
- Paradigm change of maintaining and protecting function and muscle health with aging instead of living with frailty and disability in old age

FROM WAITING TO FAIL (FAIL), TO LIVING STRONG

Chen Jifang, 68-year-old grandmother from Shanghai, 2020
THANK YOU

INNOVATION: THE FUTURE OF NUTRITION INTERVENTION TO ADDRESS MALNUTRITION/MUSCLE LOSS

PROF. DR. PHILIP J AHERTON, PHD, AFHEA
CHAIR OF CLINICAL, METABOLIC, AND MOLECULAR PHYSIOLOGY SCHOOL OF MEDICINE
FACULTY OF MEDICINE AND HEALTH SCIENCES
UNIVERSITY OF NOTTINGHAM, DERBY, UK
DISCLOSURE
The content of this program has met the (continuing education) criteria of being evidence-based, fair and balanced, and non-promotional
This educational event is supported by Abbott Nutrition Health Institute, Abbott Nutrition
Disclosures for Prof. Dr. Philip J. Atherton include:
• Receipt of research funding and consultation/speaker fees for Abbott Nutrition and Fresenius Kabi

OBJECTIVES
1. Summarize available evidence on mechanisms that lead to loss of muscle mass, strength and physical function
2. Review data on existing interventions and novel nutrients/ingredients under investigation to support strength and physical function
3. Describe potential implications of nutrition interventions for public health programs and messages to support healthy ageing

SKELETAL MUSCLE: CENTRAL ROLE IN MOBILITY
HEALTH, PERFORMANCE AND AGING (age-dependent)
• Physical Function
• Physical Strength
• Posture and Balance
• Functional Limitations
• Falls
• Disability

ILLNESS, DISEASE AND TRAUMA
• Diabetes and Obesity
• Chronic Organ Failures
• Infections
• Chronic Lung Failure
• Critical Care/ICU
• Hospitalization
• Disability
• Mortality
• Cancers

COPD – Chronic Obstructive Pulmonary Disease
ICU – Intensive Care Unit
**METABOLIC ASPECTS: MUSCLE WASTING (“ANABOLIC RESISTANCE”)**

Muscle protein breakdown

Muscle protein synthesis

Muscle fiber atrophy

**NEUROMUSCULAR ASPECTS: MUSCLE WASTING**

**MICROVASCULAR ASPECTS: MUSCLE WASTING**

**A**

**B**

**C**

Responses to Food

Young

Old

**VEGF - Vascular Endothelial Growth Factor**
NUTRITIONAL REGULATION: MUSCLE ANABOLISM

WE TERMED THIS "MUSCLE FULL"

***Significant increase from postabsorptive values (repeated measures ANOVA with Tukey's post hoc test ***P < 0.0001

LEUCINE: A CENTRAL ANABOLIC AMINO ACID

*Increased phosphorylation versus control; # Indicates a greater response than all other EAA: P < 0.05; Data are presented as mean ± SEM

LEUCINE VS. B-HYDOXY-B-METHYLBUTYRATE: PROTEIN TURNOVER

Dashed line in A indicates intramuscular HMB concentration was below detection limit; Different from respective basal (a P < 0.05; aa P < 0.01)
CONSIDERATIONS:
• Digestibility?
• Protein "quality"?
• Matrix effects?
• Bio-activities?

ATTRIBUTES:
• Low protein
• High protein
• Low amino acids
• High amino acids
• High cysteine
• High threonine
• High isoleucine
• High methionine
• High lysine
• Low leucine
• Low tryptophan

PROTEIN SOURCES: EFFECTS ON MUSCULOSKELETAL OUTCOMES

HMB SUPPLEMENTS: EFFECTS ON MUSCLE

GOOD EVIDENCE TO SUPPORT HMB ALONE OR SUPPLEMENTS WITH HMB TO INCREASE MUSCLE STRENGTH
(SMD = 0.31; 95% CI: 0.12, 0.50; z = 3.25, p = 0.001)

Meta-analysis includes 20 randomized controlled trials using HMB alone or HMB + ONS or HMB + ONS + CPN (N = 1217)

CLINICAL EVIDENCE OF HMB ALONE IN OLDER ADULTS ACROSS CONTINUUM OF CARE

Improved strength, muscle mass and reduced inflammation

Reduced muscle breakdown

Recovery of muscle and strength following immobilization

Improved strength, function and muscle quality

Healthy Aging

■ HMB

Hospitalization

Anxie/Chronic disease

Improved strength, function and muscle quality

Reduced inflammation on COPD

Improved performance function COPD

Improved strength, function and muscle quality

Reduced adherence frailty

HMB
VITAMIN D AND SKELETAL MUSCLE

MECHANISMS

VITAMIN D SUPPLEMENTATION?

SUMMARY

Nutritional support with clinical outcomes among medical inpatients who are malnourished or at nutritional risk: An updated systematic review and meta-analysis

NOVEL "INGREDIENTS": LINKED TO MUSCLE HEALTH

WHAT CAN WE AFFECT?

- MASS
- FUNCTION
- BIOMECANICS
- VASCULAR
- OTHER SYSTEMS?

*Model 1 - Unadjusted; Model 2 - Adjusted for age; Model 3 - Model 2 plus adjusted for season, income, smoking status, physical activity, vitamin D supplement use, number of comorbidities, depressive symptoms, dementia, activities of daily living (ADL) disability, number of medications, white cell count, albumin, PTH eGFR; Model 4 = Model 3 plus 1,25D
CONCLUSIONS

MUSCLE IS CRITICAL IN HEALTH/ILLNESS

- Central role in strength and stability, critical role in metabolism
- Muscle dysfunction/atrophy involved in myriad non-infectious and infectious diseases
- Poor muscle health and/or outcomes linked to increased risk of morbidity and mortality

MECHANISMS LEADING TO MUSCLE DYSFUNCTION

- Dysregulated muscle protein turnover ("anabolic resistance") = fibre atrophy
- Motor neuron loss = fibre loss
- Reduced macro/microvasculature and mitochondrial function = bioenergetic failure

ESTABLISHED NUTRITIONAL AVENUES TO MITIGATE MUSCLE LOSS/DYSFUNCTION

- Protein-based = e.g., distinct sources, "quality", quantity and timing are critical to consider
- HMB as a leucine metabolite that increases MPS/decreases MPB
- Vitamin D, where deficiency is linked to muscle atrophy/dysfunction/sarcopenia

NOVEL INGREDIENTS/INTERVENTIONS TO IMPROVE MUSCLE HEALTH OUTCOMES

- Omega-3/anti-oxidants (myriad), nitrates (vascular), β-alanine/carnitine/creatine (bioenergetics)
- Maximizing anabolic efficiency: food matrix, protein timing and diurnal distribution
- Understanding specific patient needs and recognition of contractile activity to support outcomes

THANK YOU

JEROEN MOLINGER, MSC
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DUKE UNIVERSITY HOSPITAL, SCHOOL OF MEDICINE, DURHAM, NC, USA
ERASMUS MEDICAL CENTER UNIVERSITY ROTTERDAM, THE NETHERLANDS

INNOVATION: THE FUTURE OF BODY COMPOSITION TESTING: WHAT CAN BODY COMPOSITION REALLY TELL YOU? "DISSECTING THE SYSTEMIC CARDIOPULMONARY-METABOLIC PHENOTYPE AT RISK"
The content of this program has met the (continuing education) criteria of being evidence-based, fair and balanced, and non-promotional. This educational event is supported by Abbott Nutrition Health Institute, Abbott Nutrition.

Disclosures for JEROEN MOLINGER, MSc include:
- Research funding from MuscleSound
- Honoraria for speaking engagement from Abbott

OBJECTIVES

1. Review current body composition testing techniques for use in research vs. clinical practice
2. Describe current ultrasound technology for measuring muscle mass
3. Examine new (ultrasound) technologies for testing body composition

BODY COMPOSITION vs. “BEING FIT” vs. “BEING AT RISK”? 
“BC; What you see is not always what you get”

A (new) metric of systemic mitochondrial (dys)function; beyond assessing kg/lbs only

WHAT YOU SEE IS NOT ALWAYS WHAT YOU GET (WYSINAWYG)

MUSCLE MASS MATTERS, BUT DOES MORE MASS MATTER MORE?
BODY COMPOSITION <-> WYSINAWYG ??

**WHY**
is body composition correlated to outcome?

**HOW**
is body composition correlated to outcome?

**WHAT**
is most correlated to outcome (mortality)?

---

PREDICTOR ALL-CAUSE MORTALITY: CARDIORESPIRATORY FITNESS

<table>
<thead>
<tr>
<th>VO_2max</th>
<th>11 MET: (3.5 ml/min/kg)</th>
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<tbody>
<tr>
<td>✔️ 13%</td>
<td>Mortality</td>
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**Meaning:** Cardiorespiratory fitness is a modifiable indicator of long-term mortality, and health care professionals should encourage patients to achieve and maintain high levels of fitness.

**CONCLUSIONS:** CRF was significantly related to longevity over the course of 4 decades in middle-aged, employed men free of CVD. The benefits of higher middle CRF extend well into the later part of life. (J Am Coll Cardiol 2018;72:987-95) In 2018 by the American College of Cardiology Foundation.

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DEFINING CARDIORESPIRATORY FITNESS

**FICK PRINCIPLE**

Cardiac-Output

\[ \text{VO}_2\text{\text{max}} = \text{O}_2 \text{ Consumption Muscles} \times \text{Cardiac-Output} \]
AEROBIC CAPACITY: VO₂MAX

MUSCLE TALK: MYOKINES

MUSCLE REGULATES METABOLISM

Skeletal Muscle Regulates Metabolism via Interorgan Crosstalk: Roles in Health and Disease
Josep M Argilés, PhD; Nefertiti Campos, PhD; José M Lopez-Pedrosa, MD; Ricardo Rueda, MD, PhD; Leocadio Rodríguez-Mañas, PhD

Skeletal Muscle
Bloodstream

Myokines

Malnourished State
Tissue Structure & Function
Organ Structure & Function
Immune Responses
Skin Integrity
Neural Function
"Intramuscular inflammation is associated with impaired anabolic recovery with lipid delivery observed as bioenergetically inert”

"Intramuscular lipid accumulation results in a dysregulated lipid oxidation”
MUSCLE AS A PROXY OF ALTERED SUBSTRATE UTILIZATION

Skeletal muscle quality as assessed by CT-derived skeletal muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients.


- Myosteatosis
- Systemic and/or local inflammation
- Lipid intermediates/high ceramide synthesis
- Lipolysis
- Blood flow
- Myokine secretion
- Differentiation
- Alteration in contractile fiber pennation angle
- Differentiation of muscle fiber type
- Activation of proteolytic systems
- Metabolic changes in the muscle
- Mechanical changes in the muscle

DIABETES/CVD

FUNCTIONAL DECLINE

MUSCLE AS A PROXY OF ALTERED CARDIORESPIRATORY FITNESS

Myosteatosis is associated with poor physical fitness in patients undergoing hepatopancreatico-biliary surgery.

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FUNCTIONAL DECLINE

MUSCLE AS A PROXY OF ALTERED CARDIORESPIRATORY FITNESS

Myosteatosis is associated with poor physical fitness in patients undergoing hepatopancreatico-biliary surgery.
MUSCLE ULTRASOUND; PROXY FOR MUSCLE STRENGTH
The intensity is associated with skeletal muscle power and concomitant
polymorphism in elderly men.


MUSCLE NEAR INFRARED SPECTROSCOPY (NIRS); PROXY FOR MUSCLE FUNCTION
In vivo assessment of muscle mitochondrial function in healthy men
in relation to parameters of aerobic fitness.


TSI - Tissue Oxygen Saturation Index

MUSCLE ECHO-INTENSITY ANALYSES
Validation of Musculoskeletal Ultrasound to Assess and Quantify Muscle Glycogen Content: A Novel Approach


MEASUREMENT OF INTRAMUSCULAR FAT BY MUSCLE ECHO INTENSITY

MSK ULTRASOUND – METABOLIC IMAGING

MUSCLESOUND RECTUS FEMORIS MUSCLE

MUSCLE METABOLIC IMAGING; CT VERSUS US
What you see is not always what you get; there is a need to address body composition (BC).

Muscle histology is a proxy of muscle strength and endurance.

Body composition, muscle histology and muscle metabolic profile are very much connected.

The imaging modality MSK ultrasound is able to assess BC in relation to muscle mass, intramuscular adipose fat (IMAT) / (muscle quality).

THANK YOU