Nutrition in ALS From Beginning to End

Edward J. Kasarskis MD PhD
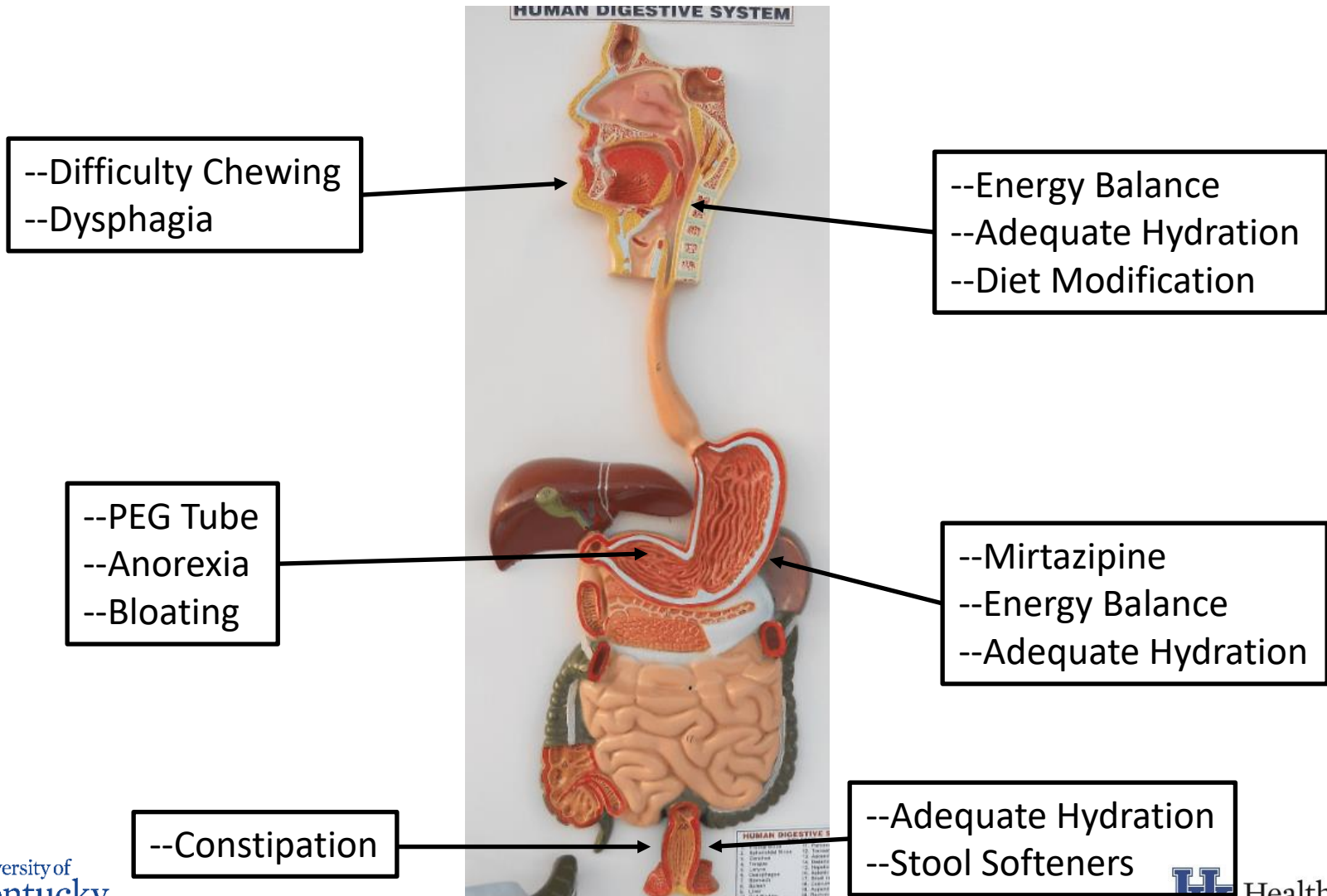
Professor, Neurology

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University of Kentucky

Lexington KY

University of Kentucky
College of Medicine

UK HealthCare
KENTUCKY NEUROSCIENCE INSTITUTE

Our Roadmap

--Difficulty Chewing
--Dysphagia

--Energy Balance
--Adequate Hydration
--Diet Modification

--PEG Tube
--Anorexia
--Bloating

--Mirtazipine
--Energy Balance
--Adequate Hydration

--Constipation

--Adequate Hydration
--Stool Softeners

Image from: Medilab Exports Consortium

Disclosures

- Grants: NINDS, ALS Association, Cynthia Shaw Crispen and Heidrich/Team 7 Endowments. Support as member of the ALS Healey Platform Trial group, Amylyx Pharmaceuticals, AB Science, Woolsey

Which Person Has ALS?

Person A

Person B

Goals

- At the end of this Grand Rounds you should be able to answer the question posed in the previous slide

- Understand how malnutrition may affect the course of ALS

- Consider an approach to determine the global energy (calorie) requirements for other neurodegenerative diseases.

- Answer the question, "Why should neurologists care?"

Case Presentation

Patient 1

- First seen on 06/27/2022 for second opinion on ALS

- 76-year-old right-handed female, housewife all her life, from rural Madison County

- Onset: November 2021 with slurred speech and elevated blood pressure

  - Stroke excluded at ED presentation

  - ENT physician considered ALS after observing tongue fasciculations

- ALS diagnosis supported by MRI scanning, EMG, and examination

Patient 1

- Progressive bulbar weakness with
  - progressive dysarthria to the point of anarthria
  - dysphagia and prolonged meal duration.
    - needed Heimlich maneuver once
- 25 lb weight loss (from usual adult weight of 163 lb.) as at first UK ALS Clinic visit
- Associated symptoms
  - sialorrhea
  - progressive weakness in the upper extremities
  - slowness of walking with 2 falls

- Medications
  - Glycopyrrolate
  - Riluzole
  - Losartan
- Medical history notable for hypertension & partial hysterectomy
- No cigarette, alcohol, or recreational drug use
- No family history of ALS

Patient 1

- BMI of 24.5, thin body habitus
- Bulbar
    - Functionally anarthric: communicating by writing on a dry-erase board.
    - Bilateral facial weakness with impaired jaw closure and lip seal.
    - Tongue weakness, atrophy and fasciculations
    - Pooling of saliva in oropharynx
- Generalized
    - Weakness of neck flexion and extension; Generalized limb weakness (3/5 – 4/5)
    - Diffuse fasciculations
    - Pathologically brisk upper extremities tendon reflexes with spread to fingers bilaterally associated with Hoffman signs
    - Extensor plantar response on RLE

Patient 1

- Assessment: Bulbar onset ALS with spread to the upper and lower extremities associated with significant weight loss

- Recommendations
  - hyoscyamine 0.125 mg twice daily
  - **feeding gastrostomy**

Patient 1

- Admitted to Neurology Floor on 08/19/2022 for increased fatigue and generalized weakness
  - ~40 lb. overall weight loss since symptom onset
  - PEG placed 08/23/2022 with oral thin liquids via spoon sips and head back for pleasure
- Neurology Clinic follow-up on 09/27/2022
  - Reduced velocity of weight loss
  - Only 1 fall since PEG placement and nutritional stabilization.
  - ALS Functional Rating Scale (revised) - 28

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Patient 2

- First seen on 07/13/2020 for second opinion on ALS
- Right-handed 60-year-old Caucasian female with no military background
- Onset: September of 2019 with progressive dysarthria and dysphagia (worse for liquids and pills), leading to 30 lb. unintentional weight loss.
- Associated symptoms
  - sialorrhea
  - muscle cramping in all extremities
  - No weakness in the extremities or falls

Patient 2

- Medical History:
  - Diabetes mellitus on oral glycemic agents.
  - Hyperlipidemia on atorvastatin
  - Hypertension: lisinopril.
  - Tubal ligation and endometrial ablation.
- No cigarette or illicit drug use. No significant alcohol use
- No known family history of ALS or neurological disorders

Patient 2

- Mild dysarthria with fully intelligible speech
- Tongue atrophy and fasciculations with tongue protrusion slightly to the right.
- Pooling of secretions in the oropharynx
- No muscle atrophy or fasciculations; normal muscle strength, normal reflexes
- Bulbar onset ALS without clinical evidence of spread to extremities
- However, EMG/NCS done March 23, 2020 already showed electrophysiological evidence of spread of disease to all extremities

- Riluzole therapy
- Consulted dietitian
  – Maintain nutritional intake with ultimate plan of feeding gastrostomy
- Consulted speech language pathologist
  – Possible voice banking
  – Diet: Solids: Mechanical Soft; Liquids: Thin
- Expiratory muscle strength training device

Patient 2

- August 2021: progressively worse speech, bilateral upper extremity weakness and unintended weight loss (27 lbs since first visit)

- September 2021: PEG tube inserted

- February 2022: anarthric, progressive weight loss now predominantly due to muscle atrophy; no falls

- July 2022: lost 7 lbs during hospitalization for pneumonia, returned quickly to previous weight thereafter

- October 2022: still independent in ADLs; good strength in all extremities with mild RUE weakness; weight 111 lbs (BMI 21)

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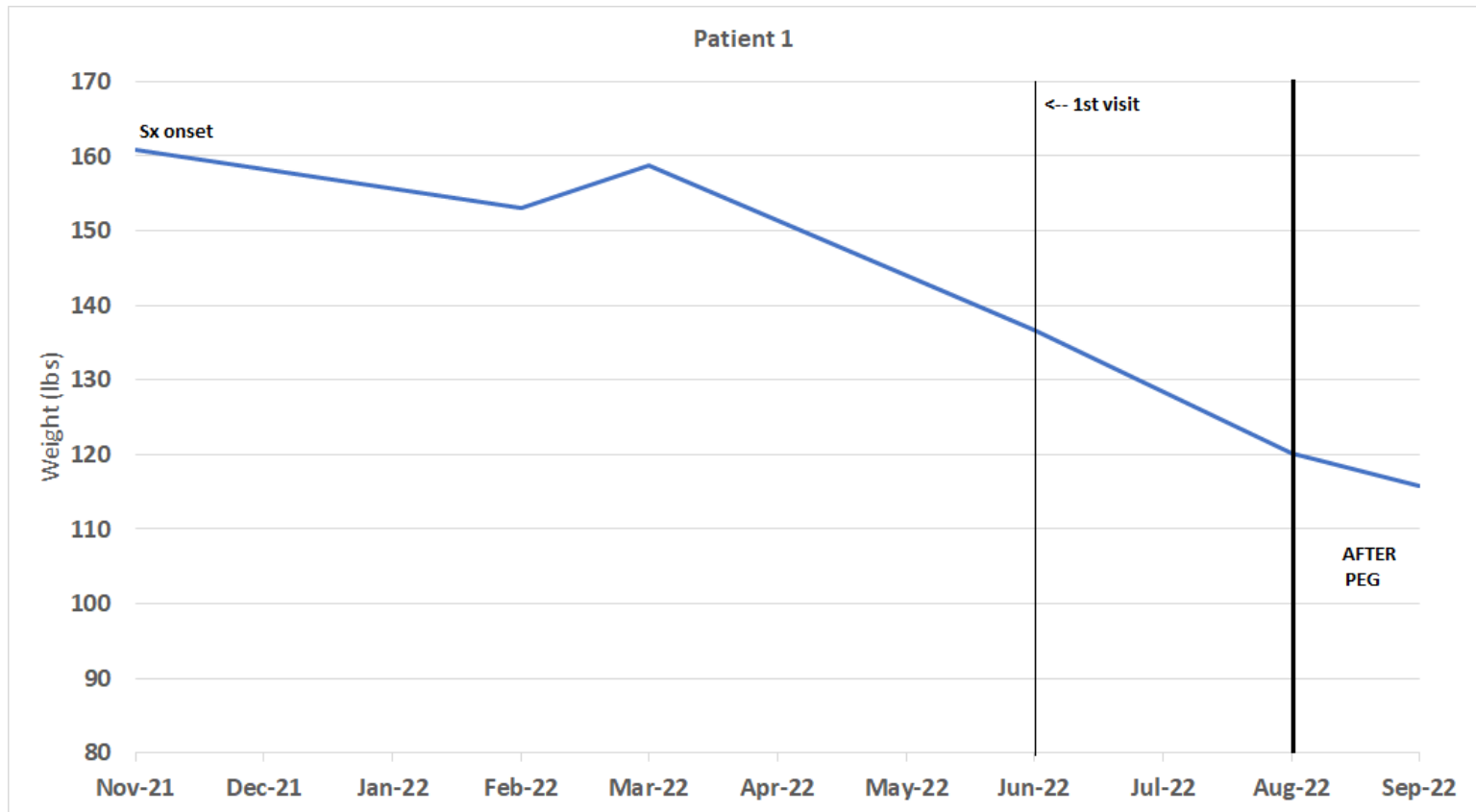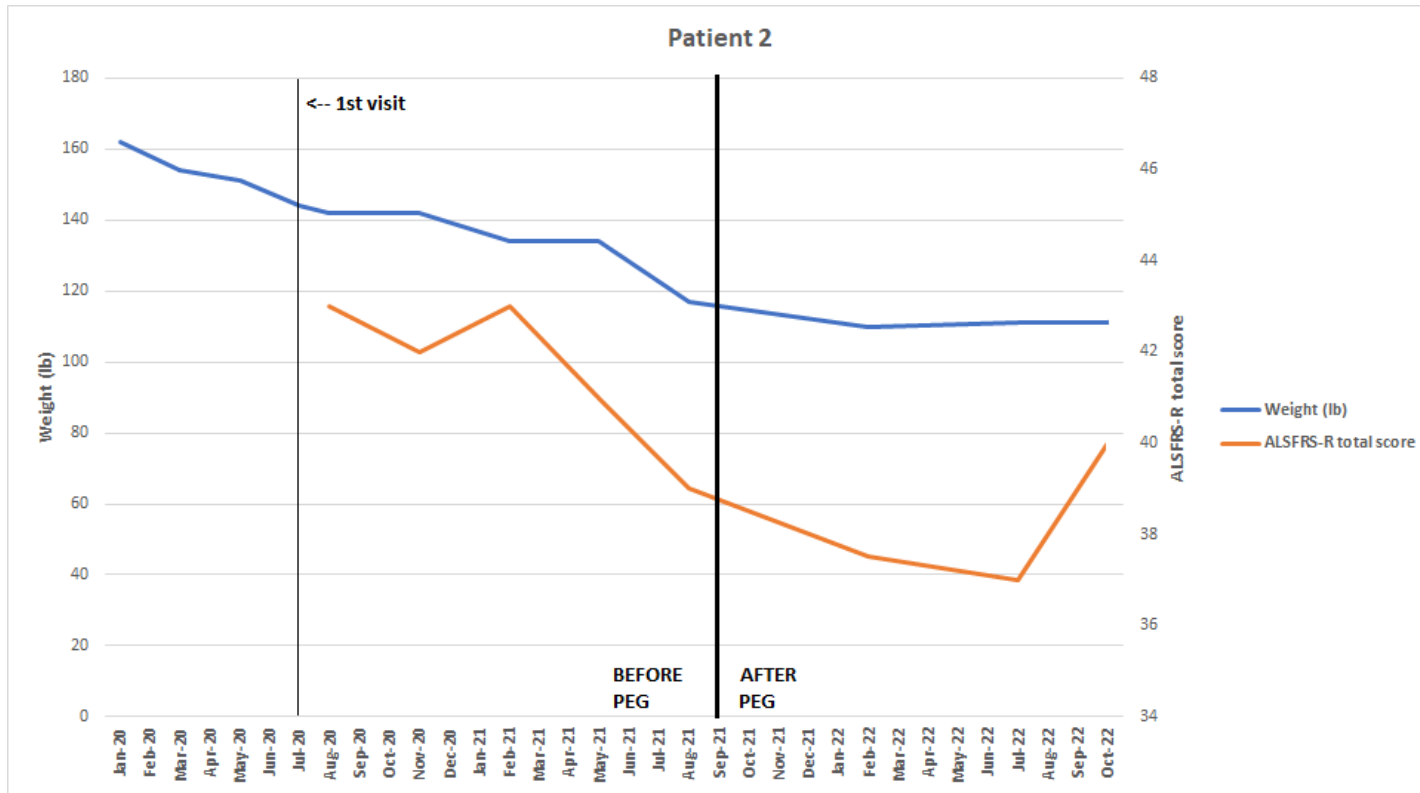
ALS Management: Problem #1

One Metric (Body Weight; BMI)

But

Two Converging Pathophysiologies
- Weight loss due to neurogenic muscle atrophy
- Weight loss due to malnutrition

  - Step on the scale—weight loss is weight loss

- (Then a side order of dependent edema in persons with LE paralysis)

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ALS Management: Problem #2

- Meals and food itself has great symbolic value

But

- Completing a meal without choking ≠ Adequate nutrition

- A PEG tube ≠ an End of Life intervention

- Chronic malnutrition can cause accelerated loss of function

- Malnutrition in this context means failure to meet a person's energy (calorie) needs by the oral route

Frequently Asked Questions About Nutrition in ALS

- "How many calories does an ALS patient need?"

- "When does an ALS patient need a PEG?"

We now have scientific answers to these questions

Goal of Nutritional Intervention in ALS

Maintain Energy Balance

Energy (Food) Intake ≡ Total Daily Energy Expenditure (TDEE)

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Outline: 6 Questions

1. Why are ALS patients at risk for malnutrition? How do the risk factors change in ALS?

2. How do we measure Energy Expenditure (TDEE) in a research setting?

3. How did we move the TDEE research results into the clinical setting?

4. Strategies to identify the need for PEG.

5. We have an app for this.

6. Applicability for other neurodegenerative disorders.

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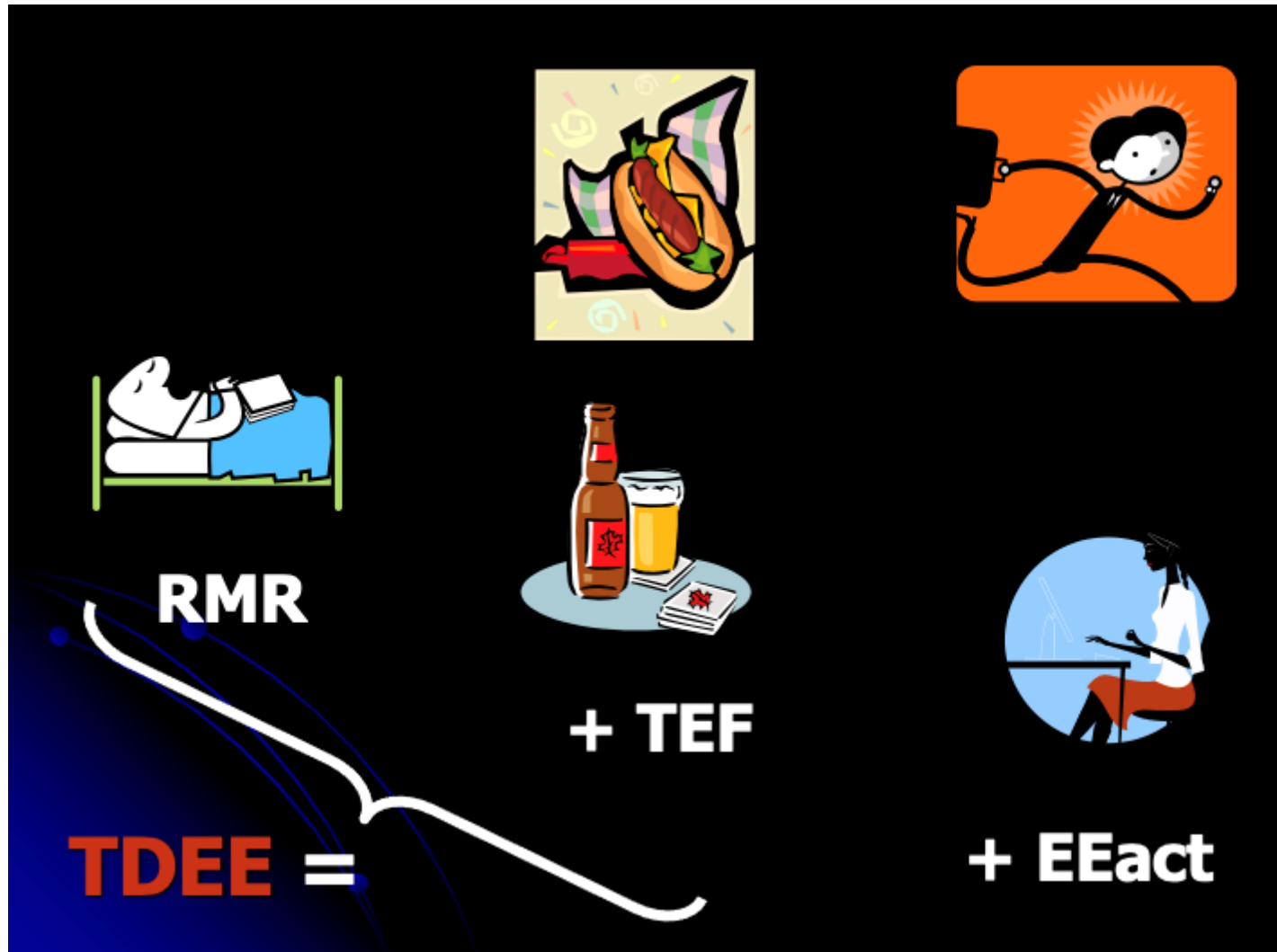College of Medicine

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Risk Factors for Malnutrition in ALS: Progression of Weakness + Hypermetabolism
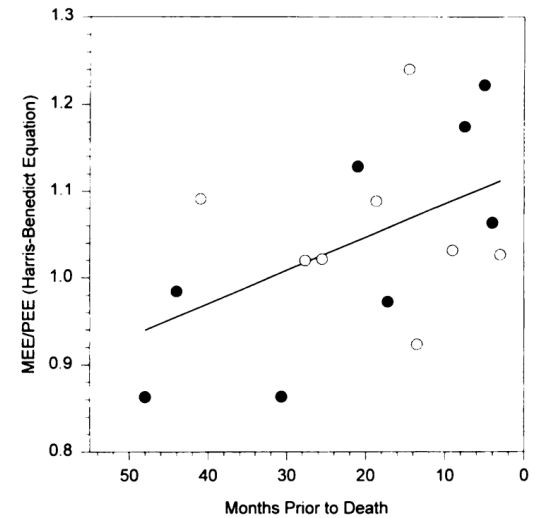
UE Weakness   Bulbar Weakness   Hypermetabolism

←   Energy Intake   →   ← Energy Expenditure →

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Components of Energy Expenditure

Current Approach to Estimating TDEE in Health and Disease

- Estimate Resting/Basal Metabolic Rate (RMR, BMR)
  - Predictive Equations
    - Harris-Benedict
    - Mifflin-St. Joer
    - Owen

- Add calories depending on physical activity

or

- Add calories depending on disease state

Doubly Labeled Water Method to Determine Total Daily Energy Expenditure (TDEE)

Doubly Labeled Water to Measure TDEE

Steps

1. Patient drinks water sample containing non-radioactive isotopically labeled waters containing

$$^2H_2O \text{ and } H_2{}^{18}O$$

2. These forms of water equilibrate with total body water overnight

3. Obtain sample of body water (urine) in morning

4. Subject goes home for 10 days. Carries out normal ADLs.

5. Obtain 2nd urine sample at day 10.

6. Analyze ^2H **and** ^{18}O with isotopic mass spectrometry

What Do You Get??? This is It??
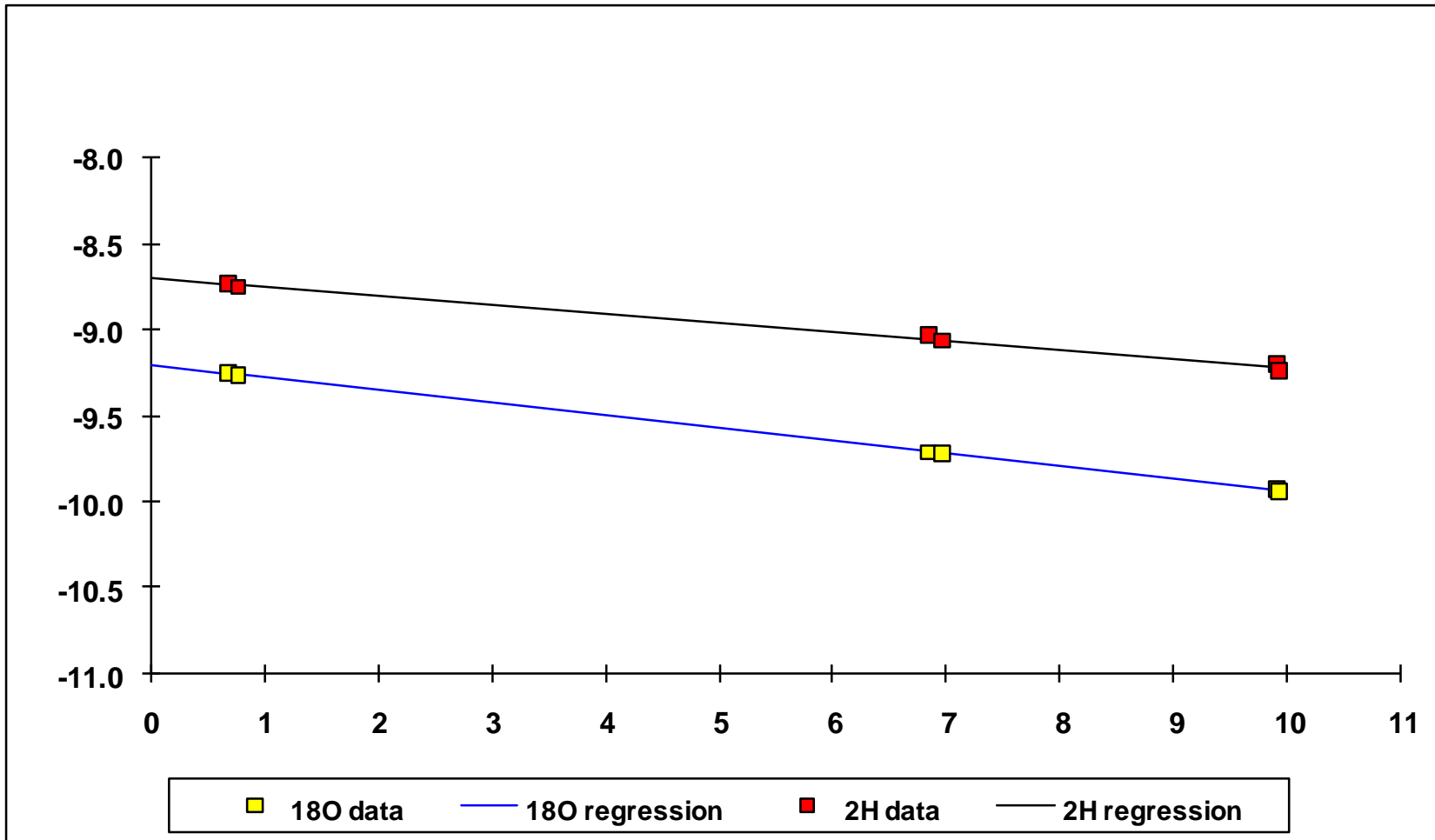
How Does the DLW Method Measure Energy Expenditure?
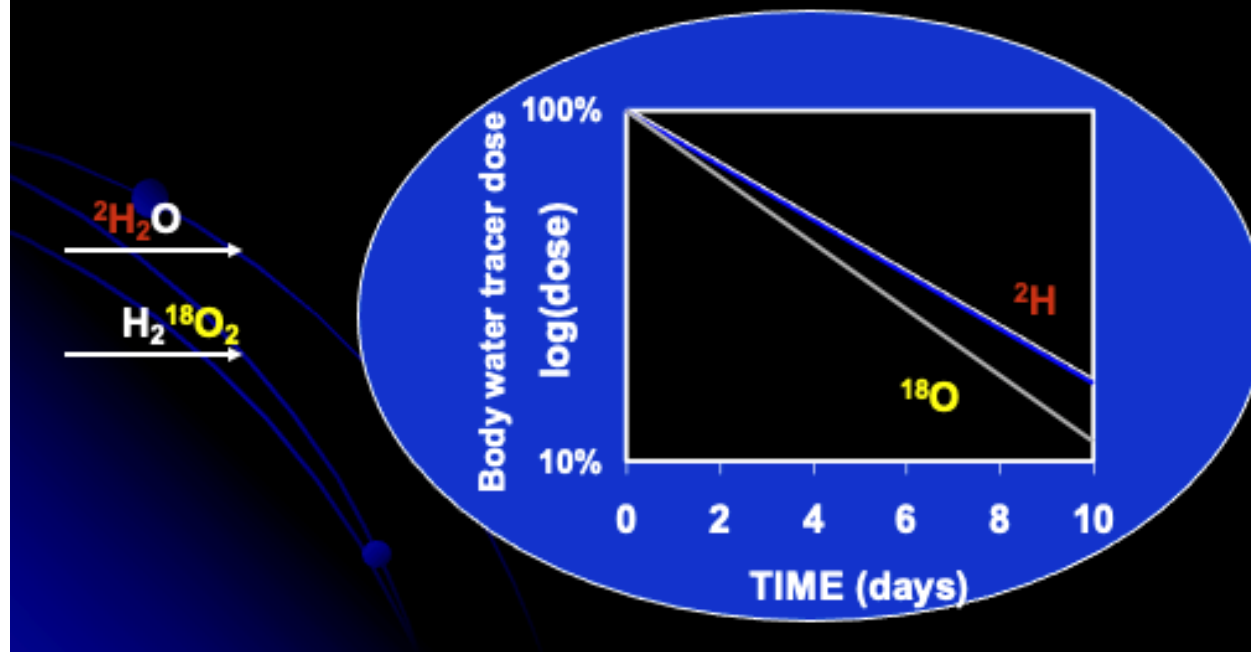
What Do You Get (continued)?

- At the end of this analysis, you find out your subject burned, as an example: 27,480 kCal over 10 days performing their normal ADLs, or 2,748 kCal/d.

- This is a rock solid number, not an estimate. This method will work for your pet cat or an elephant.

- Now what do we do with this?

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General Approach to Developing ALS-Specific Predictive Equation(s)

- Measure actual TDEE

- Measure factors that might possibly influence TDEE in ALS
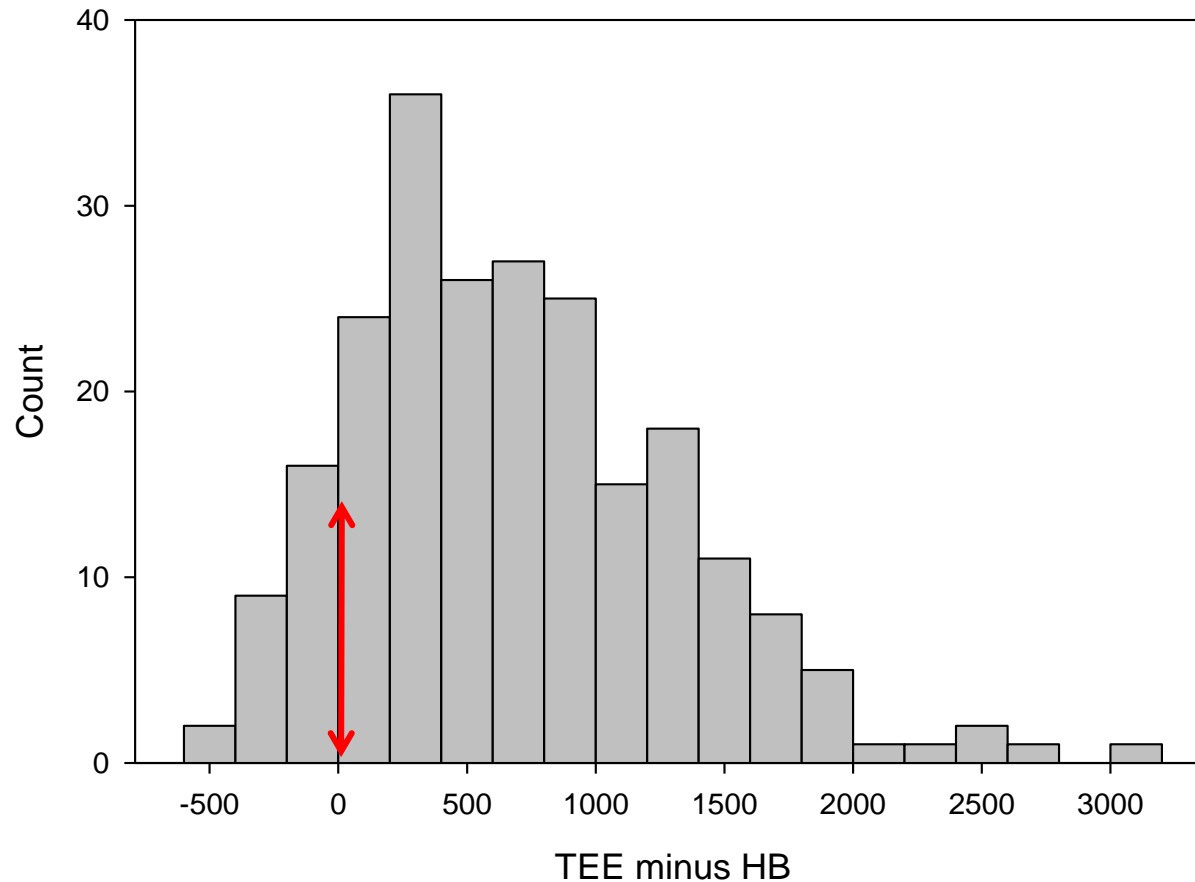
- Statistical Modeling

Kasarskis et al. Am J Clin Nutr 99(4): 792-803 (2014)

Research Plan: Development of Empiric Equations

- TDEE using DLW

- Determine FFM (BIS, DXA)$\rightarrow$ BMR
- Determine spasticity, fasciculation, cramping
- Determine FVC
- Determine ALSFRS, ALS States Scale
- Determine Physical Activity (Bouchard, accelerometers)
- BMI, gender, age, clinical laboratory determinations

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The Magnitude of the Task

Histogram of (TEE - Harris-Benedict)

Results

- TDEE using DLW was available from 249 independent determinations in 80 subjects

- Mean number of observations per subject as 3.2 ± 1.2

- 82.5% of subjects had ≥2 sequential measurements of TDEE

$$TDEE(kcal/d) = [Harris\text{-}Benedict\ RMR\ (kcal)]$$
$$+ (55.96 \times ALSFRS\text{-}6\ score) - 168$$

In particular, the equation for men is

$$TDEE(kcal/d) = [66 + (13.7 \times weight\ in\ kg)$$
$$+ (5 \times height\ in\ cm)$$
$$- (6.76 \times age\ in\ y)]$$
$$+ (55.96 \times ALSFRS\text{-}6\ score) - 168$$

And the equation for women is

$$TDEE(kcal/d) = [655 + (9.6 \times weight\ in\ kg)$$
$$+ (1.8 \times height\ in\ cm)$$
$$- (4.7 \times age\ in\ y)]$$
$$+ (55.96 \times ALSFRS\text{-}6\ score) - 168$$

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Indications for PEG

1. If Energy Intake by the oral route is chronically less than

   Energy Expenditure

. . . And

2. You have a functioning gut

. . . Then

3. You need a PEG to maintain Energy Balance

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What Are the Current Recommendation for PEG in ALS?

- Basically, indirect risk factors for malnutrition

  - Weight loss

  - Length of meal times

  - Severity of dysphagia

  - Need for assistance with eating

# What Happens When An ALS Patient Loses Weight?
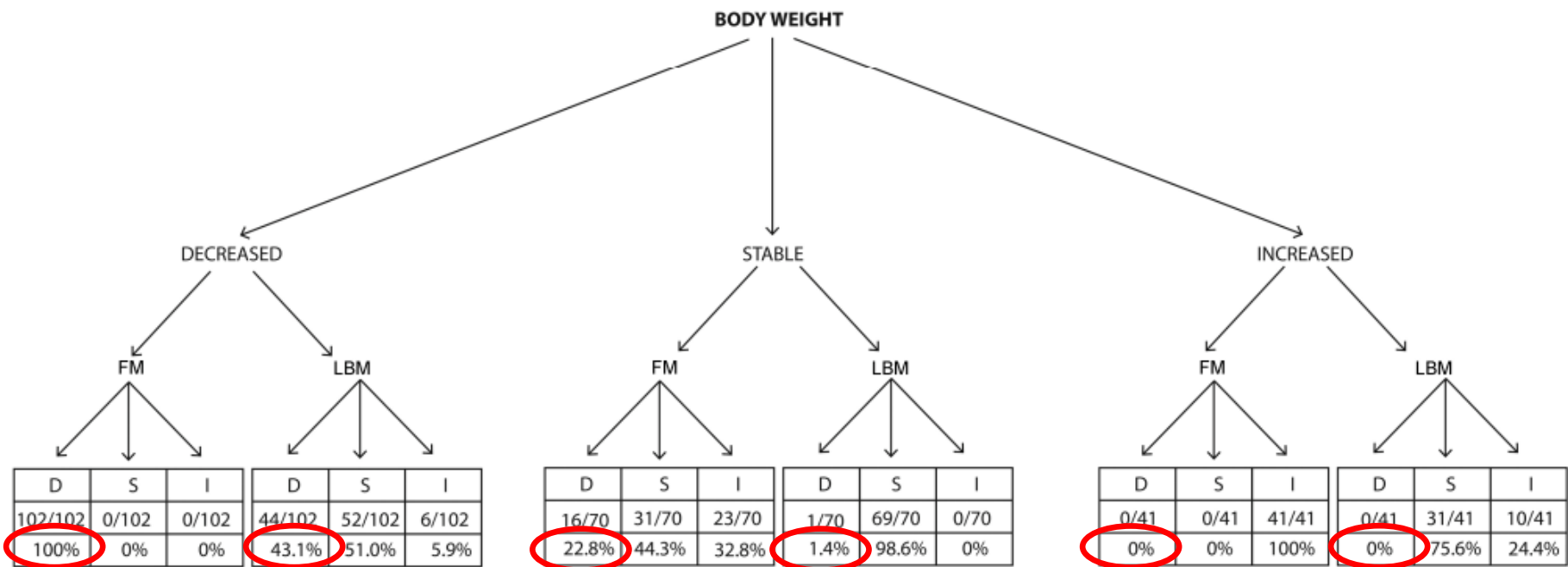
FIGURE 3 Relation between 6-mo change in weight and body composition computed using the ALS-specific equation in Cohort #3 ($n = 213$). D, decreased by >2.5%; FM, fat mass; I, increased by >2.5%; LBM, lean body mass; S, stable with <2.5% change in either direction.

Tandan et al. Am J Clin Nutr 2022;115:1378–1392.

Low BMI As a Risk Factor For Shorter Survival in ALS

Product–Limit Survival Estimates
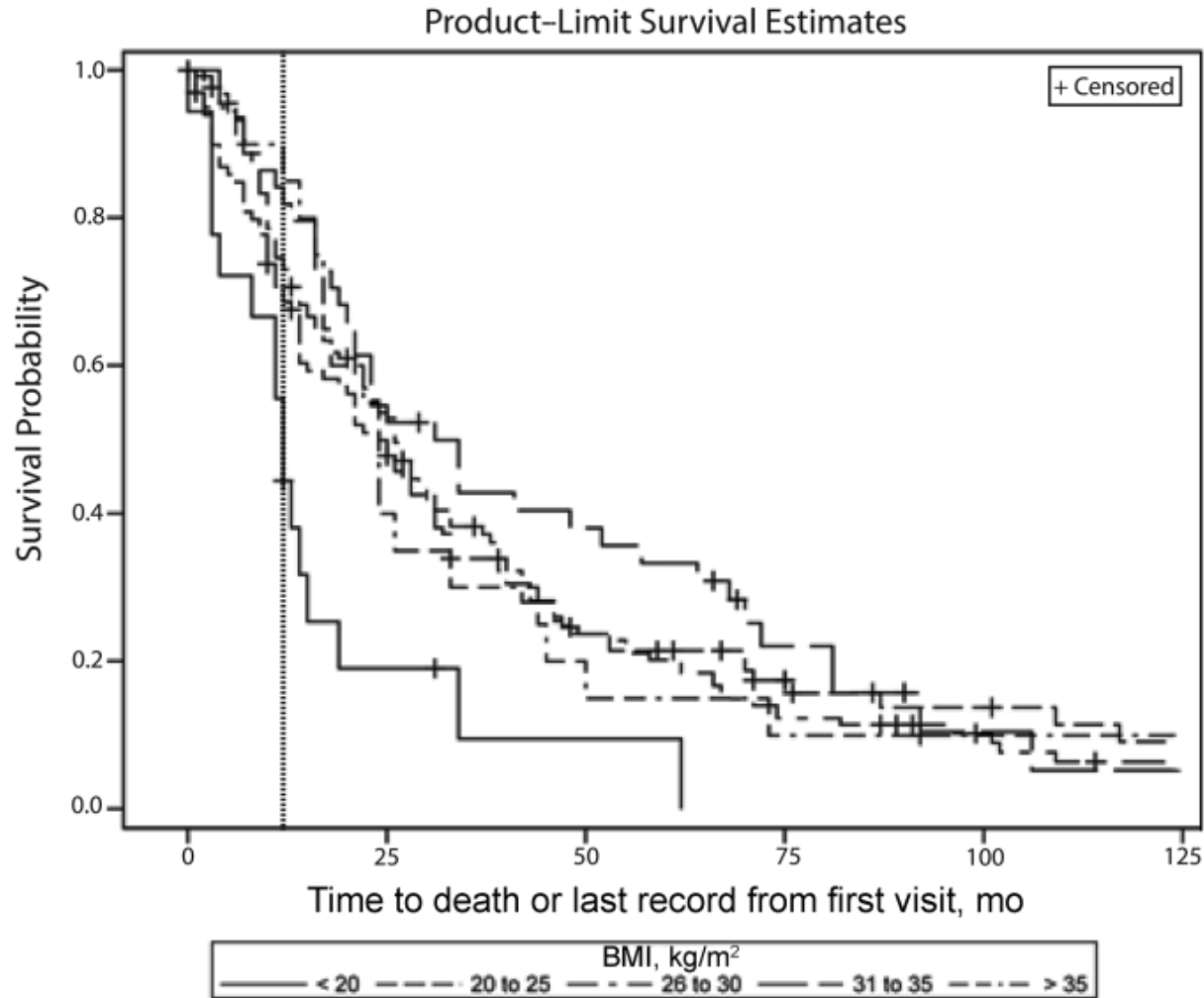
Effect of Loss of Fat Mass and Lean Body Mass on Survival in ALS
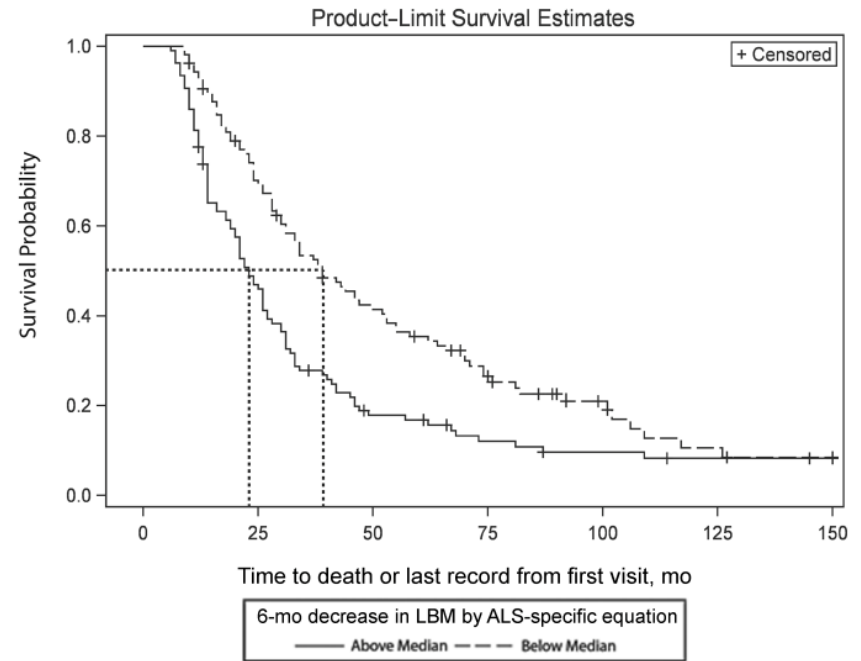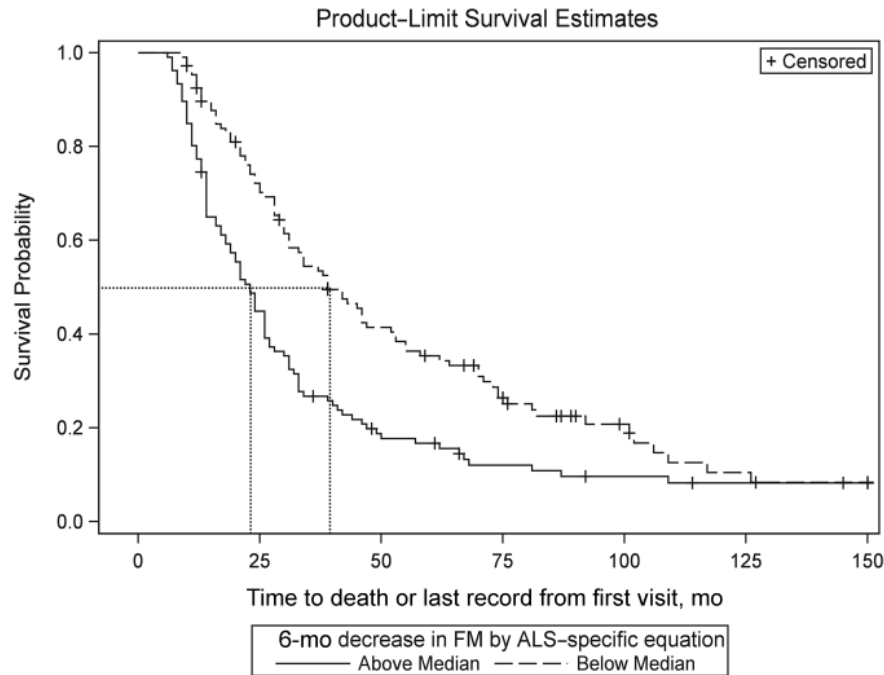
What Happens to Healthy Humans When They Starve?

The Biology of
HUMAN STARVATION

by

ANCEL KEYS
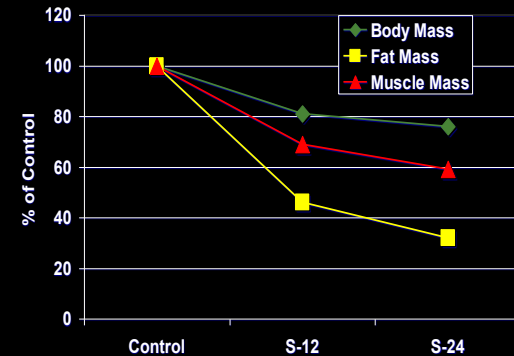
JOSEF BROŽEK   AUSTIN HENSCHEL

OLAF MICKELSEN

HENRY LONGSTREET TAYLOR

WITH THE ASSISTANCE OF

Ernst Simonson, Angie Sturgeon Skinner, and Samuel M. Wells

OF THE LABORATORY OF PHYSIOLOGICAL HYGIENE
SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF MINNESOTA

The Minnesota Experiment:
Change in Body Composition

Sam Legg before the experiment (left) and during it (right)

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Does Nutritional Supplementation Via PEG Have Benefit in ALS?
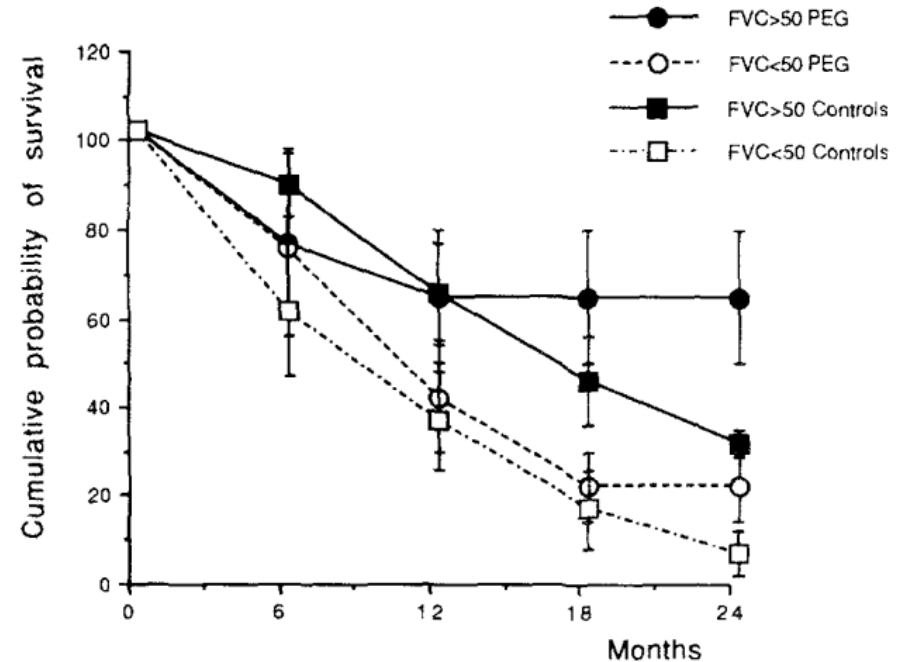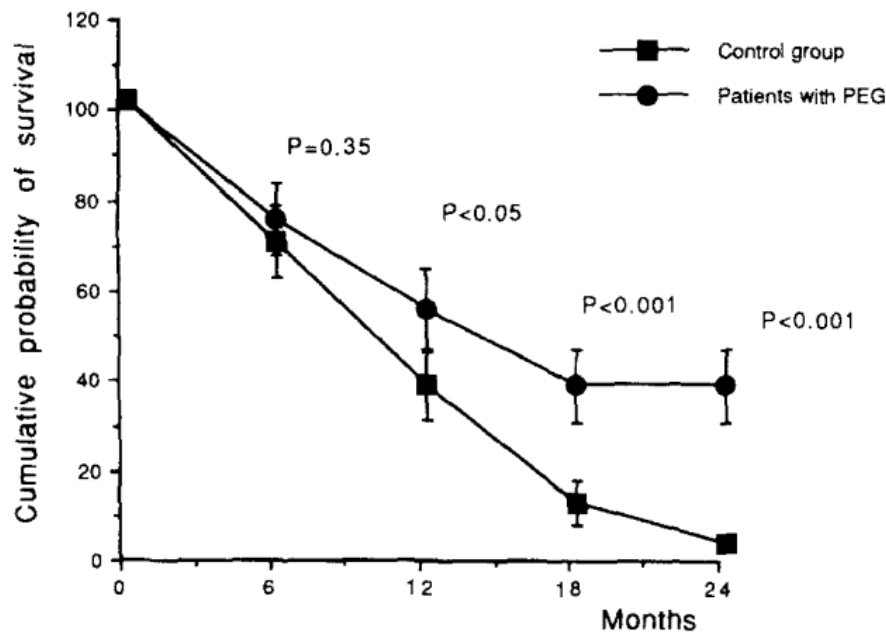
Mazzini et al. J Neurol 242:695-8 (1995)

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App to Compute Body Fat, Lean Body Mass, and Energy Requirements in ALS

https://alsnutrcalc.ukhc.org/

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Which Person Has ALS?

Person A

Person B

Special Thanks

- Dick Kryscio
- Marta Mendiondo
- Jody Clasey
- Lan Chi Luu

- Rup Tandan
- Terry Heiman-Patterson
- Mike Sherman

- Megan Thompson
- Stephen Wells
- Susan Vincent-Rawn
- Margaret (Sundquist) Healey
- Marsha Sams
- Kathie Vanderpool
- Christie Shrestha