Nutrition Following Traumatic Brain Injury: Recommendations for Education and Interventions

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Affiliations

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Diane Mortimer MD, MSN, FAAPMR: Medical Director of Outpatient TBI Rehabilitation at the Minneapolis VA Health Care System.
Objectives

1) Learners will list and discuss two of the most common post-TBI nutritional deficiencies.

2) Learners will discuss current evidence for potential supplementation with vitamin D and other vitamins following TBI.

3) Learners will discuss evidence-based paradigm, including diet, vitamins, and other supplements, to optimize overall nutrition following TBI.
Disclosures

We have no financial disclosures to report.

We are not speaking on behalf of the VA or federal government.

This presentation includes information regarding nutritional supplements which are not evaluated by the FDA.
TBI-Specific Nutritional Issues

TBI effects and sequelae can impact nutritional issues over the short-term and long-term:

- Hypermetabolic state during acute recovery
- Fluid and electrolyte abnormalities, such as sodium abnormalities
- Neurogenic bowel (constipation or diarrhea)
- Associated of gallbladder disease and pancreatitis
- Feeding tube issues, such as malfunction or malposition
TBI-Specific Nutritional Issues

TBI effects and sequelae can impact nutritional issues over the short-term and long-term:

- Behavioral issues surrounding eating
  - impulsivity; acting out
- Memory issues
  - not remembering to eat; forgetting that they already ate
- Altered sense of taste and smell
- Medication issues
  - can increase or decrease appetite
- Swallowing problems
Mr. B. is a 40 year old man who sustained a severe TBI in a motorcycle crash.

His injury included bilateral frontal bleeds. He was unresponsive for 2 weeks. He spent 3 weeks in the ICU and another 2 weeks in the hospital prior to coming to rehabilitation. During his acute care course, he underwent decompressive cranial surgery, tracheostomy placement and feeding tube placement.

He also required surgery for repair of a right lower limb musculoskeletal injury plus treatment of pneumonia and respiratory failure.

Upon admission to acute rehabilitation, he exhibits signs of agitation.
Nutrition Issues Following TBI
Calories

- Hypermetabolic & Hypercatabolic following acute TBI
  - Weeks to months depending on severity of injury

- Inadequate nutrition can lead to muscle wasting & wt loss of 15% per week!!!

- Providing adequate calories is essential
  - Providing excess of a patient's energy needs may result in complications such as hyperglycemia, hepatic steatosis, and pulmonary compromise
Early Feeding

- First 24 hours after injury
- Increased catabolic stress
- The likelihood of death for patients with TBI who were NOT fed within 5 days of injury was DOUBLE that of patients who were fed, and those not fed within 7 days had 4x greater likelihood of death (Hartl et al., 2008).
Estimating Calorie Needs

• Indirect Calorimetry
  – “Gold Standard”
  – Respiratory Quotient
    • CO2 production; O2 consumption

• Harris Benedict Equation (HBE)
  – Formula based on height, weight, sex, and age & activity

• Mifflin- St. Joer Equation
  – Recommended by A.S.P.E.N. guidelines but not validated for TBI patients

• Calories per kg body weight
  – 25-30 kcals/kg

* 2200-3700 kcals/day using above formulas!
Energy Expenditure

- Systematic Review of 24 studies by Foley et al. (Journal of Neurotrauma; December, 2008)
  - Energy needs increased & highly variable
  - Range from 87-200% of predicted value
  - Hyper-metabolism lasts for 30 days post injury

- Conclusion: formulas should not be used to estimate energy requirements for individual patients
Pattern of energy expenditure during first 30 days post-injury
Clinical Judgement

- Weight Loss
  - <10% of UBW not significant
  - Wt loss of up to 40% correlates with mortality!
  - On average, pts lose 15.6 lbs during acute hospitalization despite adequate nutrition support

- 24 hour UUN Test

- Watch for signs of Malnutrition!
Protein
Protein Needs

- 1.5-2.5 grams protein/kg
  - 200 lbs (91 kg) = 136-228 gms protein/day

- Is patient receiving adequate protein?!
  - Pre-albumin NOT a good indicator
    - Negative Acute Phase Reactant
      - CRP
      - Westergren
      - Liver disease
      - Corticosteriods
      - Nephrotic syndrome

- 24 hour Urine Urea Nitrogen Test
  - Nitrogen balance = (protein intake)/(6.25) – (UUN excretion + 3–5 g)
Protein Needs

- Positive nitrogen balance not achievable in TBI patients until 2-3 weeks post injury

- STUDY:
  - 1.5 or 2.2 gms protein/kg to patients after TBI
    - 2.2 gms protein/kg: Positive nitrogen balance of +9.2
    - 1.5 gms protein/kg: Negative nitrogen balance of -31.2
Carbohydrates
Glucose

• Monitor glucose levels
  – Hyperglycemia has adverse impact in TBI
    • Increased mortality with blood glucose <60 mg/dL and >160 mg/dL
    • Worsened neurologic outcomes
    • Increase brain injury severity
  – Adjust insulin, tubefeeding or diet order accordingly
  – D5 should be avoided in TBI patients
  – Glucose administration rates should not exceed 3.5 g/kg/day to avoid complications associated with hyperglycemia
Fat
Fat

- Brain composed of 60% lipids by dry weight
  - DHA one of the most abundant fatty acids found in the brain
  - DHA potentially anti-inflammatory & may prevent or reduce traumatic axonal injury
  - Omega 3’s an Essential Fatty Acid (EFA)
- Docosahexaenoic acid (DHA) supplementation
  - Post TBI can promote cell survival and viability
  - Depletion of Omega-3 acids led to worsened motor and memory deficits & supplementation prior to injury lead to improvements in motoric ability & learning.
  - One clinical trial examining fish oil after injury found no improvements in mortality from brain injury
  - Anecdotal cases gave ~20 grams Omega-3 FA’s with good outcomes (Lewis, 2016)
FAT—Concerns?

• Omega 3 & bleeding risk?
  – No clinical data to support increased bleeding risk

• Immune Enhancing TF formulas (omega 3’s, L-arginine, Glutamine)
  – Mixed studies re: reduced length of stay or infectious complications compared with traditional formulas in patients with TBI
  – Area of research due to theoretical benefits

• EPA vs. DHA ratio
  – Goal of more DHA than EPA in a supplement
  – VA provided omega-3 contains 200 mg DHA & 300 mg EPA

• Heavy metal toxicity
  – www.consumerlabs.com

• Most clinical studies of DHA have used a dose of 2-6 g/d, and no consistent adverse events have been observed in humans consuming 1.0 -7.5g/d of DHA.
Immune Enhancing Nutrition (IEN)

Tubefeeding formulas that contain glutamine, arginine & Omega 3 FA’s

- 2015 study, 240 patients
- 2 groups: IEN vs. standard formula
- Showed pts with TBI who receive IEN more likely to have increased pre-albumin levels perhaps reflecting improved nutrition throughout their hospital stay

RESULTS:
- No change in UTI & pneumonia rates. Similar rates of mortality & LOS
- Some benefit in rates of infections, particularly in bacteremia
Malnutrition Diagnosis

• Pre-albumin NOT an indicator of malnutrition

• New Malnutrition Criteria since 2012
  – 6 General Guidelines (need 2 of 6 for Malnutrition dx)
    • Energy Intake
    • Weight Loss
    • Body Fat Loss
    • Muscle Mass Loss
    • Fluid Accumulation
    • Reduced Grip Strength
Inflammation Present?

NO

Mild to Moderate

Inflammatoty response

Chronic Disease-Related Malnutrition
(organ failure, pancreatic cancer, rheumatoid arthritis, sarcopenic obesity)

Acute Disease- or Injury-Related Malnutrition
(major infection, burns, trauma, closed head injury)

Starvation-Related Malnutrition
(pure chronic starvation, anorexia nervosa)

YES

Severe Malnutrition Diagnosis

**Table 4. Characteristics to Diagnose Severe Malnutrition.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Acute Illness or Injury Related Malnutrition</th>
<th>Chronic Disease Related Malnutrition</th>
<th>Social or Environmental Related Malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>&gt;2%/1 week</td>
<td>&gt;5%/1 month</td>
<td>&gt;5%/1 month</td>
</tr>
<tr>
<td></td>
<td>&gt;5%/1 month</td>
<td>&gt;7.5%/3 months</td>
<td>&gt;7.5%/3 months</td>
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<tr>
<td></td>
<td>&gt;7.5%/3 months</td>
<td>&gt;10%/6 months</td>
<td>&gt;10%/6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 20%/1 year</td>
<td>&gt; 20%/1 year</td>
</tr>
<tr>
<td>Energy intake</td>
<td>≤50% for ≥5 days</td>
<td>≤75% for ≥1 month</td>
<td>≤50% for ≥1 month</td>
</tr>
<tr>
<td>Body fat</td>
<td>Moderate depletion</td>
<td>Severe depletion</td>
<td>Severe depletion</td>
</tr>
<tr>
<td>Muscle mass</td>
<td>Moderate depletion</td>
<td>Severe depletion</td>
<td>Severe depletion</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>Moderate → severe</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td>Grip strength</td>
<td>Not recommended in intensive care unit</td>
<td>Reduced for age/gender</td>
<td>Reduced for age/gender</td>
</tr>
</tbody>
</table>

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### Table 5. Characteristics to Diagnose Nonsevere (Moderate) Malnutrition.4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Acute Illness or Injury Related Malnutrition</th>
<th>Chronic Disease Related Malnutrition</th>
<th>Social or Environmental Related Malnutrition</th>
</tr>
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<tbody>
<tr>
<td>Weight loss</td>
<td>1%-2%/1 week</td>
<td>5%/1 month</td>
<td>5%/1 month</td>
</tr>
<tr>
<td></td>
<td>5%/1 month</td>
<td>7.5%/3 months</td>
<td>7.5%/3 months</td>
</tr>
<tr>
<td></td>
<td>7.5%/3 months</td>
<td>10%/6 months</td>
<td>10%/6 months</td>
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<tr>
<td></td>
<td></td>
<td>20%/1 year</td>
<td>20%/1 year</td>
</tr>
<tr>
<td>Energy intake</td>
<td>&lt;75% for &gt;7 days</td>
<td>&lt;75% for ≥1 month</td>
<td>&lt;75% for ≥3 months</td>
</tr>
<tr>
<td>Body fat</td>
<td>Mild depletion</td>
<td>Mild depletion</td>
<td>Mild depletion</td>
</tr>
<tr>
<td>Muscle mass</td>
<td>Mild depletion</td>
<td>Mild depletion</td>
<td>Mild depletion</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>Grip strength</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
Case: Mr. B.

Prior to injury:
- Worked full-time at an office job.
- Ate 2-4 meals per day and did not follow any specific diet.
- Did not exercise regularly.
- 5’9”, UBW of 190-200 lbs per family.

Upon admission to acute rehabilitation:
- 157 lbs, BMI 23.3; 2 months out from injury (17% wt loss)
- Albumin 2.7 g/dL  L     (3.4-5)
- Pre-albumin 25.2 mg/dL (20-40)
- CRP 3.76   H
- Vitamin D 22 ng/mL  L     (Above 30)

After discharge: 197 lbs
Longitudinal Weight Changes

• 2014 Study
  – 107 patients (81 males/26 females) age 36 ± 13 yrs, baseline BMI 23
  – Followed for ~38 months
  – In ICU, lost a mean 11 ± 6 kg (24 lbs +/-13 lbs)

RESULTS:
  – Patients categorized in 3 groups: stable (30%), loss (28%) and gain (42%)
    • Factors related to wt gain were hyperphagia, dysexecutive syndrome
    • Factors related to wt loss were hypophagia, higher pre-TBI BMI
  – Over a median period of 38 months, 42% of TBI patients gained & 28% lost weight
Interventions

Patients with brain injury consume larger meals & more calories per day than controls

- Food Journal/Diary
- Limit Access to Food
- Schedule Meals
- Review Medications
Vitamin D Supplementation Following TBI
Illustrative Case: Mr. B.

Upon admission to acute rehabilitation, the following labs resulted:

- **Vitamin D (Vitamin D-OH, total)** was 22 ng/mL (normal is 30)
- **Calcium** 8.8 mg/dL (8.5-10.1)
- **Phosphorus** 2.9 mg/dL (2.3-4.5)
- **Albumin** 2.7 g/dL (3.4-5)
- **Creatinine** 0.6 mg/dL (0.7-1.2)
Vitamin D

- Fat soluble vitamin
- Found in many foods such as fish, egg yolk, fortified foods
- Vitamin D can also be manufactured on the skin through exposure to ultraviolet B rays from sunlight
Biologically inert and must undergo two hydroxylations for activation:

Supplementing Vitamin D

Vitamin D deficiency is defined as serum 1,25(OH)D less than 30 ng/ml.

Vitamin D likely has a regulatory role for many physiologic processes.

Vitamin D deficiency has been associated with

- Inflammatory problems
- Autoimmune problems
- Cardiovascular issues
- Neuromuscular problems
- Neurogenerative diseases
- Cancer.
Supplementing Vitamin D

- Population-based studies suggest that Vitamin D deficiency is associated with:
  - increased prevalence of Parkinson’s Disease
  - dementia
  - Alzheimer disease
  - increased stroke risk in the elderly

- More common in women than men (9.2% vs 6.6%), and pregnancy is known to represent a high-risk for Vitamin D deficiency (Scrimgeour et al).
Supplementing Vitamin D

- Vitamin D has been shown to reduce the inflammatory response post-TBI
  - Lessens the severity of neuronal injury
  - Diminishes neuronal apoptosis
  - Improves functional outcomes
  - Minimizes neuronal calcium influx and excitotoxic glutamate release
  - Increases free radical scavenging
  - Promotes axonogenesis in traumatically injured axons
  - Upregulates neurotrophic growth factors

(Lawrence et al)
## Recommended Dietary Allowance for Vitamin D

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Pregnancy</th>
<th>Lactation</th>
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<tbody>
<tr>
<td>0-12 months*</td>
<td>400 IU</td>
<td>400 IU</td>
<td>400 IU</td>
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<tr>
<td></td>
<td>(10 mcg)</td>
<td>(10 mcg)</td>
<td>(10 mcg)</td>
<td>(10 mcg)</td>
</tr>
<tr>
<td>1-13 years</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
</tr>
<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
</tr>
<tr>
<td>14-18 years</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
</tr>
<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
</tr>
<tr>
<td>19-50 years</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
</tr>
<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
</tr>
<tr>
<td>51-70 years</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
<td>600 IU</td>
</tr>
<tr>
<td></td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
<td>(15 mcg)</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>800 IU</td>
<td>800 IU</td>
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<tr>
<td></td>
<td>(20 mcg)</td>
<td>(20 mcg)</td>
<td>(20 mcg)</td>
<td>(20 mcg)</td>
</tr>
</tbody>
</table>

* Adequate Intake (AI)

Source: National Institutes of Health Office of Dietary Supplements
Vitamin D Supplements

Active metabolite is 1,25-dihydroxyvitamin D (calcitriol)

Available in 2 forms:

1. **Ergocalciferol (Vitamin D2)**
   Vit D deficiency treatment (off-label): 50000 unit once weekly for 6-8 weeks to achieve 25(OH)D level > 30 mg/ml

2. **Cholecalciferol (Vitamin D3)**
   Vit D deficiency prevention 1500-2000 units daily to maintain 25(OH)D level > 30 mg/ml
Schnieders and Associates recently reported that 65% of patients with varying degrees of TBI were Vitamin D deficient, ie having a serum 25(OH)D level < 30 ng/ml (Scrimgeour et al).
Minneapolis VA Polytrauma Acute Rehab Center

Vitamin D 25-OH

- Number of patients w/ Vit D<30ng/ml
- Total

Year | Number of patients | Total
--- | --- | ---
2014 | 25 | 50
2015 | 30 | 50
2016 | 35 | 50
2017 | 40 | 55

2014-2017
<table>
<thead>
<tr>
<th>Year</th>
<th>Median Age (years)</th>
<th>Number of Patients with Vit D 25-OH Level less than 30ng/mL</th>
<th>Total Number of patients (Inpatient)</th>
<th>Percentage of patients with Vit D 25-OH Level less than 30ng/mL upon admit</th>
<th>Range of Low Vitamin D 25-OH values (in ng/ml)</th>
<th>Receive treatment with Vit D supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>48.5</td>
<td>28</td>
<td>52</td>
<td>53.9%</td>
<td>6-29</td>
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<tr>
<td>2015</td>
<td>57</td>
<td>36</td>
<td>47</td>
<td>76.6%</td>
<td>4-28</td>
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<tr>
<td>2016</td>
<td>49</td>
<td>34</td>
<td>50</td>
<td>68%</td>
<td>7-29</td>
<td>YES</td>
</tr>
<tr>
<td>2017</td>
<td>53</td>
<td>36</td>
<td>56</td>
<td>64.3%</td>
<td>6-29</td>
<td>YES</td>
</tr>
</tbody>
</table>

* Data Provided by Anders Westanmo, PharmD, BCPS, Minneapolis VA Pharmacoinformatics Specialist
** Excludes Hemodialysis Patients, Corrected Calcium >10.5mg/dl, CKD stage III and CKD stage IV patients.
*** One patient (24 year old male Veteran) declined treatment per chart review June 2014.
Cautions with Excessive Vitamin D

Vitamin D Toxicity

- Serum 25(OH)D levels above 50 ng/ml associated with increase all-cause mortality, greater risk of cancer and cardiovascular events, increase in falls and fractures among elderly population

- Symptoms
  - Anorexia
  - Weight loss
  - Polyuria
  - Heart arrhythmias
  - Hypercalcemia
Cautions with Excessive Vitamin D

Clinical Considerations

- Serum Calcium Level
  - Corrected Serum Ca = measured Ca + [0.8 x (4 - albumin)]
  - Check corrected calcium levels and avoid supplementing if calcium high
  - Serum calcium times phosphorus should not exceed 70 mg²/dL² to avoid ectopic calcification

- Renal issues
- Use caution if there are any parathyroid problems
Other Vitamins and Supplements
Case: Mr. B.

He continued to recover during his acute rehabilitation course.

Two weeks after admission, he was tolerating a regular diet and thin liquids. He was still confused.

His family asked if there were any nutritional supplements that might help his healing.
Sodium

Normal is 135-145 mmol/ L

Goal is individualized and may be high normal in some cases. Following TBI, it seems important to have normal sodium levels.

Interventions include salt tablets and high intake of salt.

Fluid restriction is also an option, but generally not as desirable due to risk of hypotension and fatigue.

In most cases, it seems to make more sense to have a balance of normal fluid intake and increased sodium intake.
Omega-3 Fatty Acids

Growing evidence regarding these

Most commonly administered one is Docosahexanoic acid (DHA)

Theory: DHA shunts prostaglandin production away from arachidonic acid and associated metabolites. This mitigates central inflammatory response and propagation of lipid peroxidation which occur in setting of ischemia and metabolic demand seen after TBI.
Branched Chain Amino Acids

Eg Glutamate, GABA

Important for
protein synthesis
Glucose metabolism
Oxidation of free fatty acids
Cerebral metabolism
Immune function

May have role in maintaining/ repairing learning circuit

Progesterone

Hormone that is normally present in the brain

Has role in lipid peroxidation and inhibiting free radical formation
Upregulates antioxidant enzymes like superoxide dismutase

Also acts as neurosteroid

Has been trialed in critical care (IV administration) and longer term

Appears safe but efficacy data remains inconclusive

Vitamin C

An antioxidant

Can be beneficial for wound healing
Vitamin E

Some evidence that Vitamin E can be beneficial for the brain

In Alzheimer’s Disease, supplementation has been shown to slow cognitive decline

Given as alpha tocopheral 2000 IU/ day

Dysken MW. Effect of vitamin E and memantine on functional decline in Alzheimer Disease. *JAMA* 2014. 31(1); 33-44.
Illustrative Case: Mr. B.

He recovered to the point where he could be discharged home with his family.

At his follow up appointment in clinic 6 weeks following discharge, he mentioned that his friend told him that probiotics and other supplements could be beneficial.
Green tea/ Caffeine

Stimulants are often used in combination with therapy and behavior plans to allow for optimal daytime function.

Need to monitor sleep and appetite, which can be negatively affected by stimulants.

Also, check for interactions with other medications and for contraindications involving a person’s health status (eg cardiac issues).
There is ample evidence that exercise is beneficial for the brain.

Many studies have demonstrated better-than-expected cognitive function in older adults who were physically active.

Animal studies are demonstrating improved neuronal functioning during and following exercise.

It follows that exercise is likely beneficial for the healing brain as well.

It is appropriate to recommend an individualized, appropriate exercise program.
Food as Medicine in TBI Recovery
Case: Mr. B.

Eight months later, Mr. B. has returned to work at his office job.

He has essentially resumed his pre-injury routine (with the exception that he is no longer riding a motorcycle).

At his clinic appointment, he reflects on all that he has experienced during the past year. He asks for advice and recommendations about optimizing his overall health going forward. He’d like to start with dietary changes.
Mr. B.

- Starts insulin, metformin, glipizide
- Dietary modifications

Hgb A1c 11.1%
Total Cholesterol 286
BP 136/66
Outline

• Individual dietary components

  - Fat
  - Cholesterol
  - Protein
• Individual dietary components
• Nurses’ Health Study
  - 121k + female nurses 30-55 yrs in 1976
  - Data collected 1980-2012
• Health Professionals Follow Up Study
  - 52k + male health care professionals 40-75 yrs in 1986
  - Data collected 1986-2012
• Food frequency questionnaire q2-4 yrs
• Participants grouped into quintiles of intake levels for each type of fat
### Table 2. Associations Between Total and Specific Types of Fat Intake and Total Mortality (Comparison Is Isocaloric Substitution for Total Carbohydrates) (continued)

<table>
<thead>
<tr>
<th>Quintile of Dietary Fatty Acid Intake</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P Value for Trend</th>
<th>HR (95% CI)\textsuperscript{a}</th>
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<tbody>
<tr>
<td>Trans-fat intake</td>
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<td><strong>NHS</strong></td>
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<tr>
<td>Median, % of energy</td>
<td>0.9</td>
<td>1.2</td>
<td>1.5</td>
<td>1.9</td>
<td>2.5</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>No. of deaths</td>
<td>5747</td>
<td>5158</td>
<td>4268</td>
<td>3099</td>
<td>2042</td>
<td>NA</td>
<td>NA</td>
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<td><strong>HPFS</strong></td>
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<tr>
<td>Median, % of energy</td>
<td>0.7</td>
<td>1.0</td>
<td>1.2</td>
<td>1.4</td>
<td>1.9</td>
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<tr>
<td>No. of deaths</td>
<td>2511</td>
<td>2642</td>
<td>2683</td>
<td>2698</td>
<td>2456</td>
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<td>Age-adjusted model</td>
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<td>1.31 (1.27-1.35)</td>
<td>1.49 (1.44-1.54)</td>
<td>1.63 (1.57-1.69)</td>
<td>1.73 (1.66-1.80)</td>
<td>&lt;.001</td>
<td>2.31 (2.20-2.43)</td>
</tr>
<tr>
<td>MV-adjusted model</td>
<td>1 [Reference]</td>
<td>1.11 (1.07-1.15)</td>
<td>1.14 (1.10-1.19)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.13 (1.07-1.18)</td>
<td>&lt;.001</td>
<td>1.16 (1.09-1.24)</td>
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</table>
## Dietary Fat

### Polyunsaturated fat intake

<table>
<thead>
<tr>
<th></th>
<th>NHS</th>
<th>HPFS</th>
<th>Pooled</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Median, % of energy</td>
<td>Median, % of energy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.2</td>
<td>4.4</td>
<td>0.73 (0.70-0.75)</td>
</tr>
<tr>
<td></td>
<td>5.0</td>
<td>5.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>5.6</td>
<td>5.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.3</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>7.7</td>
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</tr>
<tr>
<td></td>
<td>No. of deaths</td>
<td>No. of deaths</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4423</td>
<td>2872</td>
<td>0.62 (0.59-0.65)</td>
</tr>
<tr>
<td></td>
<td>4380</td>
<td>2633</td>
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</tr>
<tr>
<td></td>
<td>3997</td>
<td>2513</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3829</td>
<td>2545</td>
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</tr>
<tr>
<td></td>
<td>3685</td>
<td>2427</td>
<td></td>
</tr>
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<td></td>
<td>Pooled</td>
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</tr>
<tr>
<td></td>
<td>Age-adjusted model</td>
<td>MV-adjusted model</td>
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</tr>
<tr>
<td></td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
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</tr>
<tr>
<td></td>
<td>0.91 (0.88-0.94)</td>
<td>0.97 (0.94-1.00)</td>
<td>0.81 (0.78-0.84)</td>
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<tr>
<td></td>
<td>0.85 (0.82-0.88)</td>
<td>0.91 (0.87-0.94)</td>
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</tr>
<tr>
<td></td>
<td>0.81 (0.78-0.84)</td>
<td>0.87 (0.84-0.91)</td>
<td>0.73 (0.69-0.77)</td>
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</table>

### Monounsaturated fat intake

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<tbody>
<tr>
<td></td>
<td>Median, % of energy</td>
<td>Median, % of energy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.4</td>
<td>8.9</td>
<td>1.16 (1.13-1.19)</td>
</tr>
<tr>
<td></td>
<td>11.4</td>
<td>10.8</td>
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</tr>
<tr>
<td></td>
<td>12.8</td>
<td>12.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.4</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.2</td>
<td>15.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No. of deaths</td>
<td>No. of deaths</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6241</td>
<td>2748</td>
<td>1.10 (1.06-1.14)</td>
</tr>
<tr>
<td></td>
<td>4769</td>
<td>2637</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3789</td>
<td>2622</td>
<td></td>
</tr>
<tr>
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<td>3191</td>
<td>2598</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2324</td>
<td>2385</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age-adjusted model</td>
<td>MV-adjusted model</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.05 (1.02-1.08)</td>
<td>0.95 (0.92-0.99)</td>
<td>0.90 (0.87-0.94)</td>
</tr>
<tr>
<td></td>
<td>1.10 (1.06-1.14)</td>
<td>0.93 (0.89-0.97)</td>
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</tr>
<tr>
<td></td>
<td>1.17 (1.13-1.21)</td>
<td>0.93 (0.89-0.98)</td>
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</tr>
<tr>
<td></td>
<td>1.22 (1.17-1.26)</td>
<td>0.89 (0.84-0.94)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.16 (1.13-1.19)</td>
</tr>
</tbody>
</table>
Highest Sources of Saturated Fat in U.S. Diet

Top Food Sources of Saturated Fats among U.S. Population, 2005–2006. NHANES.
Outline

• Individual dietary components

- Fat
- Cholesterol
- Protein
Cholesterol

- Individual dietary components
Cholesterol

Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths

Prospective Studies Collaboration*

• 61 observational studies
• 900k+ adults without previous disease
Dietary Sources of Cholesterol in U.S.

- Eggs and egg dishes: 44%
- Chicken and chicken mixed dishes: 22%
- Beef and beef mixed dishes: 11%
- Burgers: 8%
- Cheese: 8%
- Sausage, franks, bacon and ribs: 7%

J, Krebs-Smith et al. *Am Diet Assoc* 2010
Outline

- Individual dietary components

- Fat

- Cholesterol

- Protein
Outline

• Individual dietary components
Dietary Protein

- Heart disease
- All cause mortality
- Diabetes
Association of Animal and Plant Protein Intake With All-Cause and Cause-Specific Mortality

Mingyang Song, MD, ScD; Teresa T. Fung, ScD; Frank B. Hu, MD, PhD; Walter C. Willett, MD, DrPH; Valter D. Longo, PhD; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD

- Nurses’ Health Study
- Health Professionals Follow Up Study
- Food frequency questionnaire q4 yrs
IHD mortality (33,744 deaths) versus usual total cholesterol

<table>
<thead>
<tr>
<th>Age at risk</th>
<th>1 mmol/L ↓ total cholesterol</th>
<th>15% ↓ risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>80-89</td>
<td>18% ↓ risk</td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td>28% ↓ risk</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>42% ↓ risk</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>56% ↓ risk</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
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</tbody>
</table>
### Table 2. Risk for All-Cause and Cause-Specific Mortality According to Percentage of Energy From Animal and Plant Protein Intake

<table>
<thead>
<tr>
<th>Protein Intake Category</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>HR (95% CI)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Intake category, % of total energy</td>
<td>≤10</td>
<td>&gt;10 to 12</td>
<td>&gt;12 to 15</td>
<td>&gt;15 to 18</td>
<td>&gt;18</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Median intake, % of energy</td>
<td>8.9</td>
<td>11</td>
<td>14</td>
<td>16</td>
<td>20</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>317,851</td>
<td>544,922</td>
<td>1,171,916</td>
<td>893,047</td>
<td>613,056</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>3770</td>
<td>6151</td>
<td>11,909</td>
<td>8401</td>
<td>5884</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1 [Reference]</td>
<td>0.97 (0.93-1.01)</td>
<td>0.97 (0.93-1.00)</td>
<td>0.98 (0.94-1.02)</td>
<td>1.01 (0.96-1.06)</td>
<td>1.03 (1.00-1.06)</td>
<td>.09</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1 [Reference]</td>
<td>1.01 (0.97-1.05)</td>
<td>1.03 (0.99-1.07)</td>
<td>1.03 (0.98-1.07)</td>
<td>1.03 (0.98-1.08)</td>
<td>1.02 (0.98-1.05)</td>
<td>.33</td>
</tr>
<tr>
<td>CVD mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>974</td>
<td>1,527</td>
<td>2,967</td>
<td>1,987</td>
<td>1,396</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Age-adjusted HR (95% CI)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1 [Reference]</td>
<td>0.94 (0.87-1.02)</td>
<td>1.01 (0.94-1.09)</td>
<td>1.07 (0.99-1.17)</td>
<td>1.19 (1.09-1.30)</td>
<td>1.20 (1.12-1.28)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1 [Reference]</td>
<td>0.98 (0.90-1.07)</td>
<td>1.05 (0.97-1.14)</td>
<td>1.06 (0.97-1.16)</td>
<td>1.09 (0.99-1.20)</td>
<td>1.08 (1.01-1.16)</td>
<td>.04</td>
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<td>Cancer mortality</td>
<td></td>
<td></td>
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**Table Title:**
Risk for All-Cause and Cause-Specific Mortality According to Percentage of Energy From Animal and Plant Protein Intake
### Table 2. Risk for All-Cause and Cause-Specific Mortality According to Percentage of Energy From Animal and Plant Protein Intake

<table>
<thead>
<tr>
<th>Protein Intake Category</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>HR (95% CI)(^a)</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake category, % of total energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3 to 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&gt;4 to 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 to 6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median intake, % of energy</td>
<td>2.6</td>
<td>3.5</td>
<td>4.5</td>
<td>5.4</td>
<td>6.6</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>710</td>
<td>1060</td>
<td>929</td>
<td>550</td>
<td>290</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No. of deaths</td>
<td>6160</td>
<td>9661</td>
<td>10 235</td>
<td>6602</td>
<td>3457</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)(^b)</td>
<td>1 [Reference]</td>
<td>0.92 (0.89-0.96)</td>
<td>0.85 (0.82-0.89)</td>
<td>0.72 (0.69-0.76)</td>
<td>0.67 (0.63-0.70)</td>
<td>0.73 (0.70-0.75)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)(^b)</td>
<td>1 [Reference]</td>
<td>0.97 (0.94-1.01)</td>
<td>0.95 (0.91-0.99)</td>
<td>0.91 (0.86-0.96)</td>
<td>0.89 (0.84-0.96)</td>
<td><strong>0.90 (0.86-0.95)</strong></td>
<td>&lt;.001</td>
</tr>
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<td>CVD mortality</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of deaths</td>
<td>1260</td>
<td>2126</td>
<td>2638</td>
<td>1811</td>
<td>1016</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Age-adjusted HR (95% CI)(^b)</td>
<td>1 [Reference]</td>
<td>0.88 (0.82-0.95)</td>
<td>0.78 (0.72-0.85)</td>
<td>0.63 (0.57-0.69)</td>
<td>0.60 (0.53-0.67)</td>
<td>0.67 (0.62-0.72)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivariable-adjusted HR (95% CI)(^b)</td>
<td>1 [Reference]</td>
<td>0.93 (0.86-1.01)</td>
<td>0.90 (0.82-0.99)</td>
<td>0.83 (0.74-0.93)</td>
<td>0.85 (0.74-0.97)</td>
<td><strong>0.88 (0.80-0.97)</strong></td>
<td>.007</td>
</tr>
</tbody>
</table>

\(^a\) Adjusted for age, sex, and country.

\(^b\) Adjusted for age, sex, country, current smoking, alcohol use, educational attainment, physical activity, and diabetes.
Dietary Protein & Cardiovascular Health

• Iowa Women’s study: cohort study of post-menopausal women
  – Inverse association between plant protein and CVD mortality
  – Substituting plant protein for animal protein resulted in 30% reduction in mortality

• National Health and Nutrition Examination Survey III
  – Higher protein intake associated with increased all-cause mortality in respondents < 65 yrs.
  – Controlling for animal protein intake eliminated the association

• The China Study: nationwide study of dietary and lifestyle factors associated with disease mortality in 170 villages in mainland China
  – Consumption of red meat is associated with an increased risk of all-cause mortality and increased risk of CV mortality

Kelemen et al. Am J Epidemiol.. 2005
Levine et al. Cell Metab. 2014
Campbell Am. J. Cardiol. 1998
Unprocessed Red and Processed Meats and Risk of Coronary Artery Disease and Type 2 Diabetes – An Updated Review of the Evidence

Renata Micha • Georgios Michas • Dariush Mozaffarian
Summary

FAT

- Trans-fats and saturated fats all-cause mortality
- PUSF and MUSF all-cause mortality
- Most of the highest sources of saturated fats in the US diet are from animal products
Increased serum cholesterol increases ischemic heart disease mortality

- All of the highest sources of dietary cholesterol in the US diet are from animal products
Summary

PROTEIN

• For each 10% increment of total energy consumed from animal protein, there is an 8% increase in risk of cardiovascular disease mortality
• For each 3% increment of total energy consumed from plant protein, there is a 12% decreased risk of cardiovascular disease mortality
• Multiple large prospective studies have found increased risk of all-cause and cardiovascular specific mortality with animal protein consumption
Mr. B.

- **Jan**: Hgb A1c 11.1%
  - Total Cholesterol: 286
  - BP: 136/66
- **Feb**: Starts insulin, metformin, glipizide
- **Mar**: Dietary modifications
- **Apr**: Off insulin, glipizide, 2 anti-hypertensives
  - Health indices changes maintained
  
  
- **May**: Hgb A1c 6.3%
  - Total Cholesterol: 136
  - BP: 125/60
- **Jun**:
Recommendations Could Include:

- Limit saturated fats
- Optimize intake of fats and cholesterol from plant-based sources
- Consider transitioning to plant-based sources of protein
Nutritional issues are important for people who sustain TBIs of all severities.

Nutritional issues following TBI change over the course of recovery.

Common deficiencies include Vitamin D and protein.

Multiple other supplements have been trialed.

There is evidence that plant-based sources of fat, cholesterol and protein may have benefits for health over the long-term.

Interdisciplinary interventions need to be tailored to the individual’s needs and status.
Thank You!

Email: Diane.Mortimer@VA.gov
References

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- Lawrence DW. A review of the neuroprotective role of vitamin D in TBI with implications for supplementation post-concussion. *Journal of Brain Injury* 2016. 30(8); 960-968.
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• Campbell TC, Campbell TM II. The China study: the most comprehensive study of nutrition ever conducted and the startling implications for diet, weight loss and long-term health. Dallas, TX: BenBella Books; 2006 May 11.


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