Physical / Mechanical hazard: swallowing

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March 2020
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Consumer safety issue: dysphagia, choking
Consumer safety issue: dysphagia, choking
38% of supplement-related ER visits by elderly are for swallowing-related adverse events

“Among adults 65 years of age or older, choking or pill-induced dysphagia or globus caused 37.6% of all emergency department visits for supplement-related adverse events; micronutrients were implicated in 83.1% of these visits”

Consumer safety issue: dysphagia, choking

Dysphagia and choking are 2nd and 3rd most common cause for ER visits from micronutrient supplements / multivitamins (after allergy)

Micronutrient / multivitamin contribute to most supplement-related ER visits in 65+ demographic

1. 40.6% mild allergy
2. 23.6% dysphagia
3. 19.4% choking

Consumer safety issue: dysphagia, choking
August 2019: FDA publishes study supplement-related adverse events and found women (age 50+) are most likely to choke

- 3962 (19%) Swallowing
- 20791 AEs (CAERS)

- 86% choking
- 77% adults 65+
- 86% females
- 14.3% were serious adverse events
- 73% multivitamins, 17% calcium supplements
- 3 deaths attributed to supplement-induced airway obstruction or aspiration (non-child)

**FDA previously released guidance:**
“We recommend that the largest dimension of a tablet or capsule should not exceed 22 mm”

Consumer safety issue: dysphagia, choking

Top 10 products precipitating swallowing problems are multivitamins and calcium supplements

Table 2. Pill Sizes of 10 Dietary Supplement Products Commonly Identified in Adverse Event Reports to the FDA Involving Swallowing Problems, 2006–2015*

<table>
<thead>
<tr>
<th>Product Number</th>
<th>Product Description†</th>
<th>Reports Involving Swallowing Problems ($n = 3962$), $n$</th>
<th>PRR‡</th>
<th>Pill Dimensions, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Length</td>
</tr>
<tr>
<td>1</td>
<td>Multivitamin marketed to older women</td>
<td>1607</td>
<td>6.8</td>
<td>19.0</td>
</tr>
<tr>
<td>2</td>
<td>Multivitamin marketed to older adults</td>
<td>332</td>
<td>2.7</td>
<td>18.5</td>
</tr>
<tr>
<td>3</td>
<td>Multivitamin marketed to females</td>
<td>188</td>
<td>3.2</td>
<td>21.5</td>
</tr>
<tr>
<td>4</td>
<td>Calcium supplement</td>
<td>185</td>
<td>3.9</td>
<td>21.0</td>
</tr>
<tr>
<td>5</td>
<td>Calcium supplement</td>
<td>161</td>
<td>3.9</td>
<td>20.5</td>
</tr>
<tr>
<td>6</td>
<td>Multivitamin marketed to females</td>
<td>145</td>
<td>4.4</td>
<td>18.5</td>
</tr>
<tr>
<td>7</td>
<td>Multivitamin marketed to males</td>
<td>138</td>
<td>3.6</td>
<td>19.0</td>
</tr>
<tr>
<td>8</td>
<td>Multivitamin marketed to older women</td>
<td>99</td>
<td>4.1</td>
<td>19.5</td>
</tr>
<tr>
<td>9</td>
<td>Multivitamin marketed to older men</td>
<td>86</td>
<td>2.7</td>
<td>19.5</td>
</tr>
<tr>
<td>10</td>
<td>Calcium supplement</td>
<td>85</td>
<td>2.4</td>
<td>20.0</td>
</tr>
<tr>
<td>1-10$</td>
<td>All 10 products</td>
<td>3026</td>
<td>12.7</td>
<td>19.3</td>
</tr>
</tbody>
</table>

Length of top 10 products < 22mm limit set by FDA ---- is limit wrong, or is size not a sufficient safety metric?

# Consumer safety issue: dysphagia, choking

We identified top 10 products curated in CAERS (Note: not adjusted for usage or sales volumes) [medDRA terms: aspiration, choking, swallow, dysphagia]

<table>
<thead>
<tr>
<th>Deaths</th>
<th>Product</th>
<th># of AEs for produc</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>CENTRUM SILVER WOMEN 50+ TABLET</td>
<td>1209</td>
</tr>
<tr>
<td></td>
<td>CENTRUM SILVER ULTRA WOMEN'S MULTI TABLET</td>
<td>515</td>
</tr>
<tr>
<td>2</td>
<td>CITRACAL MAXIMUM COATED TABLET</td>
<td>439</td>
</tr>
<tr>
<td></td>
<td>CITRACAL PETITES COATED TABLET</td>
<td>325</td>
</tr>
<tr>
<td>1</td>
<td>CENTRUM SILVER TABLET</td>
<td>240</td>
</tr>
<tr>
<td>2</td>
<td>CALTRATE 600 PLUS D TABLET</td>
<td>204</td>
</tr>
<tr>
<td>1</td>
<td>CENTRUM SILVER ADULTS 50+ TABLET</td>
<td>198</td>
</tr>
<tr>
<td></td>
<td>ONE A DAY WOMEN'S MULTIVITAMINS PLUS MINERALS COATED TABLET</td>
<td>183</td>
</tr>
<tr>
<td></td>
<td>ONE A DAY WOMEN'S 50PLUS COATED TABLET</td>
<td>172</td>
</tr>
<tr>
<td></td>
<td>ONE A DAY MEN'S HEALTH FORMULA COATED TABLET</td>
<td>138</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>3623</td>
</tr>
</tbody>
</table>

Other deaths:
- CALTRATE CHEWABLE – 2
- NATUREMADE VIT C 1000MG – 1
- METAMUCIL CAPSULES - 1

NO DEATHS FROM SOFTGELS, CAPSULES

Total events = 7234 → these top 10 account for ~50% of dysphagia/choking AEs

Analyzed by MJK. FDA CAERS. [https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers](https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers)
### Consumer safety issue: dysphagia, choking

Deaths attributable to solid-form supplement products

<table>
<thead>
<tr>
<th>Product</th>
<th>Age</th>
<th>MedDRA Terms</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALTRATE600 PLUS D TABLET</td>
<td>NA</td>
<td>DYSPHAGIA</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td>CALTRATE600 PLUS D TABLET</td>
<td>NA</td>
<td>NEOPLASM MALIGNANT, DYSPHAGIA</td>
<td>Death</td>
</tr>
<tr>
<td>CALTRATE600 CHEWABLE TABLET</td>
<td>90F</td>
<td>RETCHING, DYSPHAGIA</td>
<td>Death</td>
</tr>
<tr>
<td>CALTRATE600 CHEWABLE TABLET</td>
<td>NA</td>
<td>DYSPHAGIA</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td>CENTRUM SILVER TABLET</td>
<td>NA</td>
<td>DYSPHAGIA, DEATH</td>
<td>Death</td>
</tr>
<tr>
<td>CENTRUM SILVER ADULTS 50+ TABLET</td>
<td>NA</td>
<td>CHOKING</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td>CENTRUM SILVER WOMEN 50+ TABLET</td>
<td>NA</td>
<td>FOREIGN BODY TRAUMA, DYSPHAGIA, DEATH</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td></td>
<td>81F</td>
<td>PULMONARY OEDEMA, PNEUMONIA ASPIRATION, HYPERSENSITIVITY, CHOKING</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td></td>
<td>73F</td>
<td>RETCHING, MYOCARDIAL INFARCTION, DYSPHAGIA, COUGH, CHOKING, ANEURYSM RUPTURED, ANEURYSM</td>
<td>Death, Hospitalization, Medically Important</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>DYSPHAGIA</td>
<td>Death</td>
</tr>
<tr>
<td>CITRACAL MAXIMUM COATED TABLET</td>
<td>84F</td>
<td>RETCHING, DEATH, CHOKING SENSATION</td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>92F</td>
<td>DEATH, CHOKING</td>
<td>Death, Medically Important</td>
</tr>
<tr>
<td>METAMUCIL CAPSULES</td>
<td>NA</td>
<td>RESPIRATORY ARREST, FEELING COLD, CHOKING</td>
<td>Death, Hospitalization</td>
</tr>
<tr>
<td>NATUREMADE VITAMIN C 1000MG TABLET</td>
<td>NA</td>
<td>DYSPHAGIA, CARDIAC FAILURE</td>
<td>Death</td>
</tr>
</tbody>
</table>

**RED** colored boxes highlight cases with significant comorbidities

Analyzed by MJK. FDA CAERS. [https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers](https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers)
Consumer safety issue: dysphagia, choking
Tablets dominate the "product form" precipitating AEs

DISTRIBUTION OF AEs BY FORM

- CAPSULE
- CAPLET
- SOFTGEL
- POWDER
- LIQUID
- TABLET
- GUMMIES
- CHEWABLE TABLETS OR SOFTIES

Adults 60+ experience the most swallowing-related AEs per CAERs

includes coated and uncoated tablets

~86%

Number of incidents

0 200 400 600 800 1000 1400

Age (Years)

0 20 40 60 80 100

Analyzied by MJK. FDA CAERS. https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers
Consumer safety issue: dysphagia, choking

Tablets dominate the “product form” precipitating AEs, in contrast to usage survey which shows 42%

Top Delivery Form Preferences

- Tablet/Caplet (31%)
- Capsule (19%)
- Gummy (16%)
- Soft gel (11%)
- Powder (4%)
- Soft chew (4%)
- Chewable tablet (4%)

4% of supplement users indicated they don’t have a preference

2019 CRN Consumer Survey on Dietary Supplements
Consumer safety issue: dysphagia, choking

CURRENT GOAL

CRN approved the formation of a task force to explore the development of best practices or other potential activities in the area of swallowing and choking problems in women and older adults.

IDENTIFY DATA AND RECOMMENDATIONS IN 2 AREAS:
• Product features to reduce swallowing hazards
• Tips for educating consumers on behavioral modifications
Consumer safety issue: dysphagia, choking

APPROACH

Dysphagia (difficulty swallowing) is common in older adults due to a variety of reasons; we must identify traits of pills and consumer behaviors that allow for easy passage of product from lips to stomach.
Anatomy and physiology of swallow
Anatomy and physiology of swallow

Anatomy of pharynx

- Soft palate
- Hard palate
- Hyoid bone
- Larynx
- Esophagus
- Trachea
- Epiglottis
- Thyroid cartilage
- Suprahyoid muscles
- Oropharynx
- Nasopharynx
- Oral cavity
- Nasal cavity

“Posterior pharyngeal wall”

Space between epiglottis and tongue: vallecula

Anatomy and physiology of swallow

Deglutition (Swallowing) process is 3 phases

1. ORAL (Voluntary)
2. PHARYNGEAL (Involuntary)
3. ESOPHAGEAL (Involuntary)

Anatomy and physiology of swallow

Deglutition

Bolus: bolus is moistened, masticated, etc., held against hard palate in anterior by tongue, and by tongue and soft palate in posterior

Tongue applies positive pressure to squeeze/roll bolus posteriorly into the pharynx by applying upward and backward pressure to the hard palate

Trigeminal, glossopharyngeal, and vagus nerves sense bolus and begin involuntary stages

Anatomy and physiology of swallow
Deglutition

- Soft palate pulls upward to prevent reflux of food into nasopharynx / nasal cavity
- Bolus enters oropharynx
- Head of bolus may enter the vallecula
- Hyoid begins to move up and towards anterior

Anatomy and physiology of swallow

Deglutition

- Soft palate completely retracted upward
- Epiglottis moves from upright to horizontal to fully inverted to protect trachea
- Larynx and hyoid move up to most extreme position

Anatomy and physiology of swallow

Deglutition

- Peristalsis of posterior tongue area
- Epiglottis completely occluding larynx opening to prevent passage of food into trachea
- Peristalsis of posterior pharyngeal wall
- Esophageal sphincter relaxes
- Trachea (to lungs)
Anatomy and physiology of swallow

Deglutition

Nervous system forces muscle contractions/relaxations (peristalsis) of hypopharynx and forces food bolus into upper esophagus

Esophageal peristalsis moves bolus along esophagus until lower sphincter into stomach opens, enters stomach

Anatomy and physiology of swallow

Deglutition (Swallowing) process is 3 phases: takes ~2 secs max

1. ORAL (Voluntary)
2. PHARYNGEAL (Involuntary)
3. ESOPHAGEAL (Involuntary)

Anatomy and physiology of swallow

Esophageal peristalsis

• Wave passes from the pharynx to the stomach
  • 3-5 seconds upright (gravity expedites)
  • 60-75x longer lying down

Anatomy and physiology of swallow
Nervous system controls deglutition

**VOLUNTARY (VOLITIONAL)**
- ORAL (O)

**IN VOLUNTARY (REFLEXIVE)**
- PHARYNGEAL (P)
- ESOPHAGEAL (E)

## Anatomy and physiology of swallow

### Dimensions of pharynx and esophagus (mm)

<table>
<thead>
<tr>
<th>Region</th>
<th>Women</th>
<th>Men</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>High retropalatal oropharynx</td>
<td>AP: 8.8 ± 1.9</td>
<td>AP: 8.6 ± 2.0</td>
<td>(Daniel, Lorenzi et al. 2007)</td>
</tr>
<tr>
<td></td>
<td>LL: 21.4 ± 4.1</td>
<td>LL: 19.7 ± 2.7</td>
<td></td>
</tr>
<tr>
<td>Low retropalatal oropharynx</td>
<td>AP: 5.8 ± 2.2</td>
<td>AP: 5.6 ± 1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LL: 18.0 ± 5.1</td>
<td>LL: 17.9 ± 5.4</td>
<td></td>
</tr>
<tr>
<td>Retrolingual oropharynx</td>
<td>AP: 11.9 ± 7.4</td>
<td>AP: 12.0 ± 2.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LL: 22.1 ± 5.4</td>
<td>LL: 22.1 ± 7.5</td>
<td></td>
</tr>
<tr>
<td>Lower pharynx</td>
<td>AP: 10.4 ± 3.1</td>
<td>AP: 11.3 ± 3.6</td>
<td>(Ize-Iyamu 2016)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>AP: 10.1 ± 1.5; LL: 18.7 ± 3</td>
<td>(Arana-Rueda, Pedrote et al. 2009)</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>Diameter (probably AP): 16.3 ± 3.6</td>
<td>(de Jong, van Ramshorst et al. 2004)</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>Diameter (probably AP): 16.5 ± 3.4</td>
<td>(Lee, Huprich et al. 2012)</td>
<td></td>
</tr>
</tbody>
</table>


Anatomy and physiology of swallow

Foreign bodies have been found in every anatomical swallow region

- Patients presented with “foreign body ingestion” to ER, mostly food in adults

- Complaints:
  - Difficulty swallowing: 53%
  - Pain in throat: 33%
  - Difficulty breathing: 6%
  - Foreign body sensation in throat: 2%
  - Coughing: 2%

<table>
<thead>
<tr>
<th>Foreign body location</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>17 (17)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Small intestine</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Stomach</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Trachea</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Larynx</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Colon</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Undetermined location</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Undetected</td>
<td>54 (54)</td>
</tr>
</tbody>
</table>

Anatomy and physiology of swallow

Resources

• [https://www.youtube.com/watch?v=SBbNxM7g2vg&t=2s](https://www.youtube.com/watch?v=SBbNxM7g2vg&t=2s)
  • Video
  • June 25, 2019
  • Bonnie Martin-Harris, PhD, CCC-SLP: speech language pathologist out of Northwestern University

• Good text resource
    • [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2597750/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2597750/)

Dysphagia in the elderly
Dysphagia in the elderly

Data indicate elderly are at risk for swallowing problems

- Dysphagia is defined as any disruption in the swallowing process, and can lead to aspiration (choking), aspiration pneumonia, and malnutrition
- Estimated point prevalence: 13% in total population
  - Potential major underestimate in many cases
- Dysphagia affects:
  - 68% of nursing home residents
  - 30% of elderly admitted to hospital
  - 64% of patients after a stroke

Dysphagia in the elderly
Paramedics responded to more foreign body airway obstructions in older adults than younger adults

Dysphagia in the elderly
Swallowing difficulties have different descriptions from consumers

Dysphagia in the elderly
Swallowing difficulties are experienced frequently

How often do you experience swallowing difficulties?

- Rarely: 47.8%
- Sometimes: 28%
- Always, daily, often: 24.2%

28.2% of patients were AFRAID to take tablets and capsules
8.7% of patients FEAR SUFFOCATION while swallowing tablets or capsules

Dysphagia in the elderly

Pills are the most frequent cause of airway obstructions in adults

<table>
<thead>
<tr>
<th>Item</th>
<th>Food</th>
<th>Other</th>
<th>Non-food solid items</th>
<th>Liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat (specified), 38</td>
<td>Soup, 8</td>
<td>Pills, 44</td>
<td>Secretsions, 11</td>
<td></td>
</tr>
<tr>
<td>Chicken, 33</td>
<td>Chips, 6</td>
<td>Plastic</td>
<td>Water, 6</td>
<td></td>
</tr>
<tr>
<td>Beef, 26</td>
<td>Apple, 6</td>
<td>Cough drops</td>
<td>Juice</td>
<td></td>
</tr>
<tr>
<td>Hotdog, 12</td>
<td>Rice, 6</td>
<td>False tooth</td>
<td>Metal</td>
<td></td>
</tr>
<tr>
<td>Pork, 11</td>
<td>Hard candy, 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamburger, 8</td>
<td>Potato, 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sandwich, 9</td>
<td>Grape</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone, chicken, 7</td>
<td>Toast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone, fish</td>
<td>Crackers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>Salad</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribs</td>
<td>Carrot</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pizza</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nut</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Pasta</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Corn</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Bagel</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Chocolate</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Cantaloupe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cinnamon roll</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Dysphagia in the elderly
Most swallowing-related supplement AEs (FDA CAERS) are in adults 60+

[Bar graph showing the number of incidents by age, with a peak in the 60-80 year range.]
Dysphagia in the elderly

Physiologic changes of aging increase risk for dysphagia

- Prolonged oral phase
- Reduced tongue pressure
- Delayed swallow reflex
- Delayed closure of larynx
- Decreased swallow volume
- Increased residual matter

Dysphagia in the elderly

Studies show quantitative decline in swallowing functions with age


![Graph showing vertical hyoid movement and laryngeal vestibule closure](image)

- Healthy volunteers
- Elderly
- Elderly with safe swallow
- Elderly with unsafe swallow

**Vertical hyoid movement**

**Laryngeal vestibule closure**
Dysphagia in elderly
Anatomical, physiological deficiencies that increase aspiration risk

- Delayed initiation of pharyngeal swallow
- Vallecular stasis
- Reduced hyoid and larynx elevation
- Deviant epiglottis, failed larynx closure

Dysphagia in the elderly

**Diseases of aging increase risk for dysphagia**

**MEDICATIONS**

- Xerostomia (dry mouth)
  - Anticholinergics
  - Antihistamines (diphenhydramine)
  - Antiemetics
  - Antidiarrheal
  - Tricyclic antidepressants
  - CNS
    - Alcohol
    - Analgesics
    - Steroids
    - Benzodiazepines
    - Antiparkinsonian

**NEUROLOGICAL DISEASES**

- Neuronal degeneration
- Stroke
- Dementia
- Myasthenia gravis
- Polymyositis

**PROGRESSIVE DISEASES**

- Parkinson’s
- Huntington
- ALS
- Muscular dystrophy

**Diet**

- Mg deficiency
- Vitamin E deficiency
- Low caloric intake (correlation, not causation)

**CHRONIC HEALTH**

- Head/Neck surgeries
- COPD
- Chronic pain
- Cancer
- Obesity (BMI)
- Hyperthyroid

**RED** = Common in elderly, but others may still be present in elderly population


Dysphagia in the elderly
Supplements are recommended for sensitive population (stroke patients)

• WebMD indicates Fish Oil, Folic Acid, Potassium, and others may be effective for stroke
• “Intensive nutritional supplementation, using readily available commercial preparations, improves motor recovery in previously undernourished patients receiving intensive in-patient rehabilitation after stroke.”
Dysphagia in the elderly

Elderly may be given tips to maintain adequate nutrition

• Postural adjustments
  • Ex) Chin down technique = reduced aspiration

• Swallow maneuvers
  • Ex) Supraglottic swallow = reduced aspiration [image below]

• Diet modifications
  • Ex) Consumer takes a nutritional supplement to prevent malnutrition

• Food modifications
  • Ex) Take different food types (thickeners), cut into tiny pieces, etc.


Dysphagia in the elderly
Most GPs’ do not alter treatments based on swallowing issues

<table>
<thead>
<tr>
<th>GPs’ reaction after being informed about patients’ swallowing difficulties (n=54)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>GPs just changed drug</td>
<td>21 (38.9 %)</td>
<td></td>
</tr>
<tr>
<td>GPs just gave hints</td>
<td>8 (14.8 %)</td>
<td></td>
</tr>
<tr>
<td>GPs changed drug and gave hints</td>
<td>6 (11.1 %)</td>
<td></td>
</tr>
<tr>
<td>GPs did nothing at all</td>
<td>19 (35.2 %)</td>
<td></td>
</tr>
</tbody>
</table>

a  GPs: general practitioners

What do pill users think and do?
Patients think size and surface are more important than shape and flavor for swallowability, although all are important.
What do pill users think and do?
Quantifying behaviors reveals a variety of habits

• 1.1% of patients take pills without any fluid or food
• 57% of tablet users swallow multiple simultaneously
• 4.6% of patients who always/daily/often have swallowing problems take multiple pills at a time
• 54% of patients with swallowing problems tilt head back versus only 46% of patients without swallowing problems
• 27% take 5+ pills per day, 10% take 10+, 5% take 15+

What do pill users think and do?

Patients with swallowing difficulties frequently modify dosage form

What do pill users think and do?

Patients change behavior to ensure effective swallowing

What do pill users think and do?

Modification can impact bioavailability

• Modification of drugs can impact bioavailability, which may impact safety and efficacy due to improper dosing, product loss, etc.

<table>
<thead>
<tr>
<th>Measured Compound and Formulation</th>
<th>$AUC_{0-24}$ (ng·hr/mL)</th>
<th>$t_{\text{max}}$ (hr)</th>
<th>$C_{\text{max}}$ (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentoxifylline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400 mg intact</td>
<td>921 ± 367</td>
<td>2.55 ± 1.12$^b$</td>
<td>111 ± 40.0$^b$</td>
</tr>
<tr>
<td>400 mg crushed</td>
<td>1,447 ± 523</td>
<td>0.70 ± 0.35$^b$</td>
<td>1,316 ± 752$^b$</td>
</tr>
<tr>
<td>600 mg intact</td>
<td>1,614 ± 1080</td>
<td>2.25 ± 1.65$^b$</td>
<td>184 ± 86.0$^c$</td>
</tr>
<tr>
<td>600 mg crushed</td>
<td>2,201 ± 867</td>
<td>0.60 ± 0.32$^c$</td>
<td>1,789 ± 851$^c$</td>
</tr>
</tbody>
</table>

• Dosage form effects for nutritional supplements seem less clear


Known tablet and pill parameters affecting deglutition
Known tablet and pill parameters affecting deglutition

Shape

• Large oval tablet (14L x 9W mm) have shorter esophageal transit times than large round tablets (11 mm diameter)
• Older individuals have a harder time swallowing large round tablets compared to any size oval tablet or capsule
• 6 mm oval tablet near perfect swallow score
• Almond was equivalent to elongated; both were easier to swallow than round
• Round was perceived as easier to swallow than oval or diamond
• Round is best for SMALL tablets, while oval/oblong is best for medium to large tablets

EMPIRICAL SUMMARY (Worst to best): diamond < round < oval < oblong < irregular < almond
Known tablet and pill parameters affecting deglutition

Size

• Transit times for round tablets were shorter with smaller diameters: 5.5 mm < 8 mm < 11 mm
• 4% of 5mm round tablets vs 20% of 11mm round tablets arrested
• 6 mm oval tablet near perfect swallow score
• 4/5 consumers prefer 3 medium sized (6 mm) than 1 large (13+ mm)
• 4-5 mm may be too small
Known tablet and pill parameters affecting deglutition

Size+Shape

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean of tablets and capsules that caused difficulties</th>
<th>Mean of tablets and capsules that did not cause difficulties</th>
<th>Difference of the geometric means [%]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Round: Diameter [mm]</td>
<td>8.7±2.0</td>
<td>8.1±1.7</td>
<td>-7.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Round: Height [mm]</td>
<td>3.8±1.2</td>
<td>3.5±1.1</td>
<td>-6.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Oval: Length [mm]</td>
<td>15.0±4.4</td>
<td>13.2±3.3</td>
<td>-10.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oval: Width [mm]</td>
<td>7.4±1.8</td>
<td>6.6±1.4</td>
<td>-9.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oval: Height [mm]</td>
<td>4.5±1.5</td>
<td>4.6±1.3</td>
<td>+3.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>Oblong: Length [mm]</td>
<td>16.7±4.0</td>
<td>13.3±4.7</td>
<td>-22.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Oblong: Width [mm]</td>
<td>7.3±1.6</td>
<td>6.2±2.0</td>
<td>-16.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Oblong: Height [mm]</td>
<td>5.8±1.6</td>
<td>4.9±1.7</td>
<td>-18.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Irregular shapes: Diameter [mm]</td>
<td>9.4±1.1</td>
<td>8.8±1.4</td>
<td>-6.7</td>
<td>n.s.</td>
</tr>
<tr>
<td>Irregular shapes: Height [mm]</td>
<td>3.5±0.8</td>
<td>3.5±0.8</td>
<td>-1.2</td>
<td>n.s.</td>
</tr>
<tr>
<td>Irregular shapes: Length [mm]</td>
<td>7.3±0.5</td>
<td>8.1±1.5</td>
<td>+10.2</td>
<td>n.s.</td>
</tr>
<tr>
<td>Irregular shapes: Width [mm]</td>
<td>6.7±0.2</td>
<td>7.0±1.3</td>
<td>+2.1</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hard capsules: Diameter [mm]</td>
<td>6.8±1.4</td>
<td>6.4±1.2</td>
<td>-7.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hard capsules: Length [mm]</td>
<td>19.0±2.0</td>
<td>17.5±2.8</td>
<td>-9.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Soft capsules: Diameter [mm]</td>
<td>8.6±1.7</td>
<td>8.0±1.1</td>
<td>-7.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Soft capsules: Length [mm]</td>
<td>20.8±2.0</td>
<td>18.3±5.8</td>
<td>-16.7</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Size thresholds may exist for:
- Round, Oval, Oblong, Hard

Largest acceptable Size

- Round (8.1)
- Irregular (8.8)
- Oval (13.2)
- Oblong (13.3)
- Hard capsule (17.5)
- Soft capsule (18.3)

Known tablet and pill parameters affecting deglutition

**Weight**

- Heavier capsules have faster transit times than lighter capsules (less important than size/shape)
- Coated tablets had lower transit times than similarly-coated capsules (same size/shape, density tablet > capsule)

**Empirical summary:** Denser, heavier products are better.
Known tablet and pill parameters affecting deglutition

Composition and coatings

- Coated tablets show lower incidence of globus compared to uncoated tablets of same size
  - HPMC coating improved transit time in human subjects from 3.2 sec to 2.3 sec on a round tablet
- Eudragit L100-55 coated tablets had lower transit times than similarly-coated capsules (same size/shape, density tablet > capsule)
- Coatings universally improve ease of swallowing
- 50% prefer capsules to tablets (smooth, easy gliding), 50% prefer tablets to capsules (capsules too sticky, dissolve)
- Softgels perceived as easier to swallow
- Gelatin capsule was preferred over a coated tablet, which was preferred over an uncoated tablet

**EMPIRICAL SUMMARY (Worst to best):** tablet < gelatin capsule < soft gelatin = coated tablet
Known tablet and pill parameters affecting deglutition

Color

• Chinese consumers prefer white and yellow to red or blue (full ordering: White = yellow > green = pink = orange > red = blue) for swallowability, but colors had no impacts on US consumers or Colombian consumers
• For tablets, color preferences for swallowable tablets in Denmark were white > Gold > tan > orange > bright green > dark orange > grey > olive green > orange > turquoise > purple

Empirical summary: color may help but does not drive swallowing experience
Known tablet and pill parameters affecting deglutition

Taste/smell

• ~8% of people with swallowing difficulties have found bad taste and smell to be the cause of their swallowing disability

Empirical summary: more palatable pills are more swallowable
Known consumer behaviors affecting deglutition
Known consumer behaviors affecting deglutition

Postural position

- Esophageal times are 60-75x longer in supine than upright positions
- Delayed transit in supine position is so common that size and shape does not impact transit
- Large tablets should be taken standing, and should stay standing for at least 90 seconds

Empirical summary: always take pills while upright
Known consumer behaviors affecting deglutition

Head position

• Swallowing capsules is easier with the head tilted forward; if patients tilt their head back, they swallow the water first and leave the capsule lodged in the mouth or throat. Tilting head forward does opposite effect and helps water push capsule through to hypopharynx and esophagus
• Head down or head straight are preferred to head back as head back opens airway more readily
• Chin tuck is supported by literature to prevent aspiration in dysphagia

Empirical summary: look straight ahead or tuck chin
Known consumer behaviors affecting deglutition

Capsules and some soft gel oils float, tablets and some soft gel oils sink

Evening primrose oil, starflower oil

Capsule

Multivit tablet

Fish oil capsules, large and small

All tablets sink due to high density relative to water. Capsules float due to low density relative to water. Softgels will float or sink depending on their composition.

Conducted by MJK on commercial products.
Known consumer behaviors affecting deglutition

Fluid volume

- 17% of patients had esophageal lodging of gelatin capsule with 120mL fluid versus 61% of patients with 15mL fluid.

- 100mL fluid preferable to 25mL fluid in all cases, **but elderly had some problems swallowing 100 mL**

- Patients without swallowing difficulties more frequently used less than a half a glass of fluid compared to patients with swallowing difficulties who used half a glass or more

- 10-20mL fluid is necessary for peristalsis

- Subjects using 50mL water had faster, less variable, and less adherent swallowing activities than subjects using 30mL water (uncoated tablets)

- 40 mL was deemed to be the cutoff for acceptable amount of fluid for swallowing

**Empirical summary:** use 40-100 mL with a pill to best swallow pill
Known consumer behaviors affecting deglutition

Fluid habits

• The taking of small tablets should be followed by an additional drink of water

• Water should be cold to prevent premature tablet / gelatin capsule dissolution
  • https://www.statcrunch.com/reports/view?reportid=30915&tab=preview

• Take a quick drink before taking your pill to lubricate your throat
  • https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=1&contentid=501

• Take with a bolus of gelatinous food (applesauce) to help swallow reflex activate
  • https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=1&contentid=501
Known consumer behaviors affecting deglutition

Number of pills

• 4 out of 5 survey participants would rather take several medium-sized preparations as opposed to one jumbo sized

• 82.8% of patients preferred taking a small soft gel capsule 2x per day rather than 1 tablet once/day

• At least 2% of patients think swallowing too many tablets at once causes swallowing difficulties

Empirical summary: take 1 pill at a time, and take multiple pills per dose to achieve efficacy is preferred
Known consumer behaviors affecting deglutition

Mental

• Anxiety and negative associations with swallowing a pill likely contribute: you learn to chew solids, so it takes a mental shift to relax the throat and be able to swallow something that could choke you

• Some individuals have never been taught pill swallowing, so do not have proper knowledge

• Verbal praise, relaxation techniques, imitation, and repetition can improve pill-swallowing difficulties

Empirical summary: positive consumer mindset and knowledge can improve swallowing success
Known consumer behaviors affecting deglutition

Swallowing aids

• Pill-swallowing cups, pill-swallowing straws, pill coating devices, lubricating gels, and lubricant gels/sprays may help some individuals, although efficacy is unclear in most cases

• Pill coating devices potentially very efficacious
  - Amazing commercial for example product: https://www.medcoatusa.com/

Empirical summary: tools exist to aid swallowing
R&D methods of pill swallowing evaluation
Methods of pill evaluation

Shear stress measurements

• Pig oesophagus with simulated saliva

• Pig oesophagus not representative in 1 case: select model carefully

• Advanced in vitro model

Empirical summary: physical swallowing models exist but will require substantial investment and validation to be predictive.
Methods of pill evaluation

Mathematical modeling


• Studies are available on several parameters of different swallowing-related processes that could be incorporated into models, such as

Empirical summary: in silico models have been attempted, but are complicated to use and unvalidated
Conclusions to consider
Conclusions to consider

Interesting tidbits to further your knowledge on certain areas

• Verbatims on swallowing

• Review on several items that supports everything discussed so far: size, shape, coating, density

• Modification in a care setting

• General problems with pill-taking experience from start to finish (focus on medications but applicable everywhere)

• Difficulties swallowing pills is still prevalent in people *without* dysphagia
Conclusions to consider

Overall

Designing out swallowing problems will be impossible – problems often arise from underlying physiology and disease…older adults should have a discussion with their health care provider about their pill swallowing habits.

Engaging medical professionals (all specialties, but particularly GPs for dietary supplements) for discussion is worthwhile since they currently do not change treatment after knowing about swallowing problems.

Still, several PRODUCT DESIGNS and CONSUMER BEHAVIORS can REDUCE THE RISK. Only TABLETS were associated with death.
Conclusions to consider
Considerations for product design

- **Modeling**: Consider using physical models to estimate swallowability: HOWEVER, be sure the model is validated properly
  - In silico models, though imperfect, may be a cheaper substitute to further develop and studies with potential inputs abound
- **Shape**: Almond, oval, or oblong are better shapes for large pills than round/spherical
- **Size**: I could not identify literature reports at sizes 20+ mm, but generally:
  - 6 mm is the ideal target size, although this is like unreasonable for most supplements
  - Smaller is generally better to a point (~4); upper limits on an UNSAFE size are unclear
  - *Potential guideline* -- 22 mm for tablets, and +5 mm (27 mm) for softgel capsules?
- **Coatings**: Uncoated tablets are loathed: softgels, coated tablets much better
- **Density**: Heavy/dense pills are preferred over light pills due to faster transit and sink in water
- **Number of pills**: 2-3 medium pills are preferred over 1 large pill by consumers
- **Softgel vs tablet**: Softgels can be larger than tablets while not inhibiting swallowing
- **Taste**: Palatable taste can improve swallowing
- **Color**: Whites & yellows may improve swallowability, but more USA research needed
Conclusions to consider

Recommendations for consumer education & product labeling

• **Health care provider involvement:** If you have concerns swallowing, talk to a healthcare provider to better understand options available to you. Swallowing difficulties are common and treatable. Providers can help assess underlying causes of swallowing difficulties. You may be referred to a speech-language therapist who can provide advice specific to your situation.

• Speech-language pathologists may teach therapeutic maneuvers for specific dysphagia conditions, including but not limited to:
  - Supraglottic swallow
  - Effortful swallow
  - Super-supraglottic swallow
  - Mendelsohn maneuver
  - Chin tuck
  - ***Any therapeutic maneuvers should not be attempted without professional supervision***


Conclusions to consider

Recommendations for consumer education & product labeling

- **Attitude:** RELAX - anxiety can affect swallowing effectiveness. It’s not going to be a problem! This may be most relevant for large pills that are scary, even though size is not the only predictor of a safe swallow.
- **Body and head:** Always take pills upright with head looking straight ahead or chin tucked
- **Pre- and post-game:** Drink water both before and after the actual pill swallow
- **Water volume:** Take with appropriate volume of water: 40-100 mL (~1/4 cup)
- **Temperature:** Use cold water (note water may be preferred over other drinks since they can alter effective dose: for example, milk inhibits iron absorption while orange juice enhances it)
- **Number of pills:** Take 1 pill at a time
- **Modification:** Discuss with healthcare provider about modification strategies
  - Cut tablets to a more manageable size
    - Open capsules
    - Crush tablets
  - Dissolve in water
  - **Modification can alter pharmacokinetics: this is important to discuss with providers!**
- **Tools:** Choose alternate product forms (liquid, chewable gummies, etc.) OR consider obtaining a pill-swallowing aid, like a pill coater
Conclusions to consider

Labeling

• Manufacturers may want to consider labeling or posology instructions that include some of the aforementioned behaviors
• P&G’s Metamucil capsules (fiber supplement) have some features incorporated as an example:

Conclusions to consider

Labeling

• Manufacturers may want to consider labeling or posology instructions that include some of the aforementioned behaviors
• P&G’s Metamucil capsules (fiber supplement) have some features incorporated as an example:
Conclusions to consider

The perfectly SAFE label

“Relax! Take a deep breath and let it out slowly. While upright and looking straight ahead, take a small drink of water to lubricate your mouth and throat. Next, take one tablet with approximately a quarter cup of cold water. After swallowing, take a second drink of cold water to ensure the pill makes it all the way to your stomach. Repeat once daily. If you are worried about the swallowability of this pill, talk to your health care provider for tips to help you swallow. Also, see the Council for Responsible Nutrition guide: [url]”

--but that is long and unwieldy

The final question: how can we communicate this to consumers?