A stylized graphic on the left side of the slide. It features a large blue circle containing a white cross. Overlaid on the cross are several green and blue lines: a thick green line forming a leaf-like shape, a blue line forming a curved shape, and a white line forming a step-like shape. The background of the slide is a gradient of blue.

# Physical / Mechanical hazard: swallowing

Michael J. Kerins, PhD  
Toxicologist, Personal Health Care  
Procter and Gamble Company  
[kerins.mj@pg.com](mailto:kerins.mj@pg.com)  
March 2020

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# Consumer safety issue: dysphagia, choking

## Consumer safety issue: dysphagia, choking

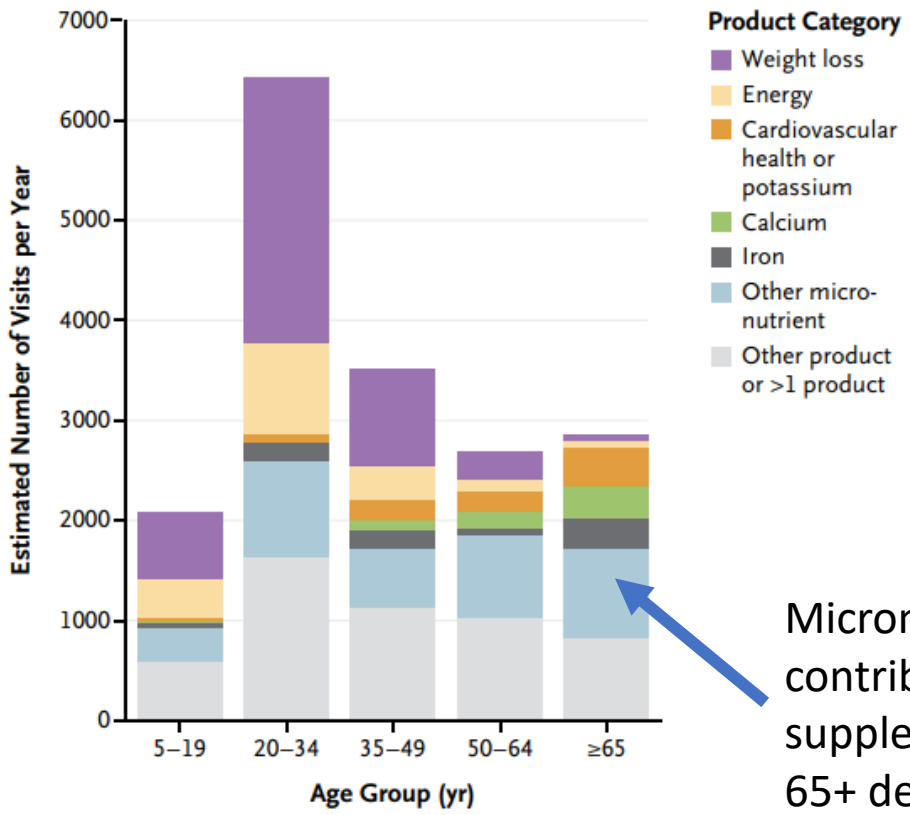
38% of supplement-related ER visits by elderly are for swallowing-related adverse events

“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”

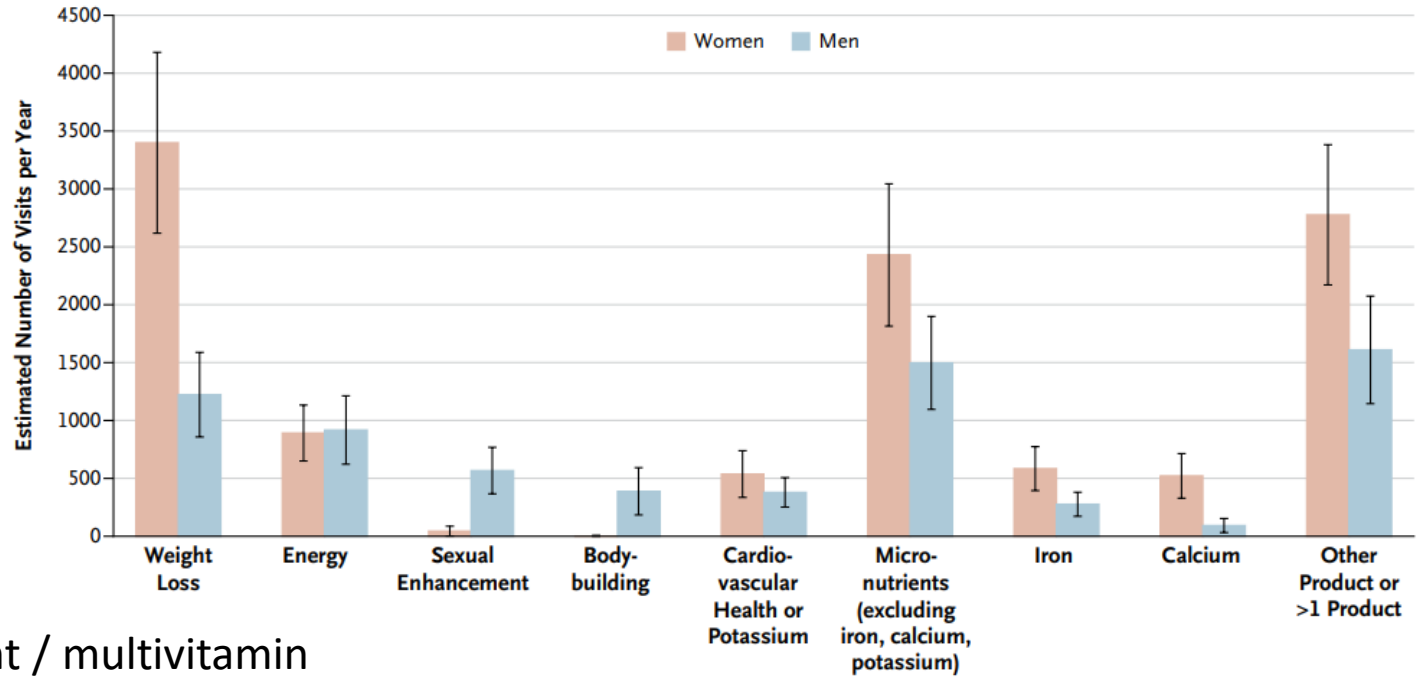


# Consumer safety issue: dysphagia, choking

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



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

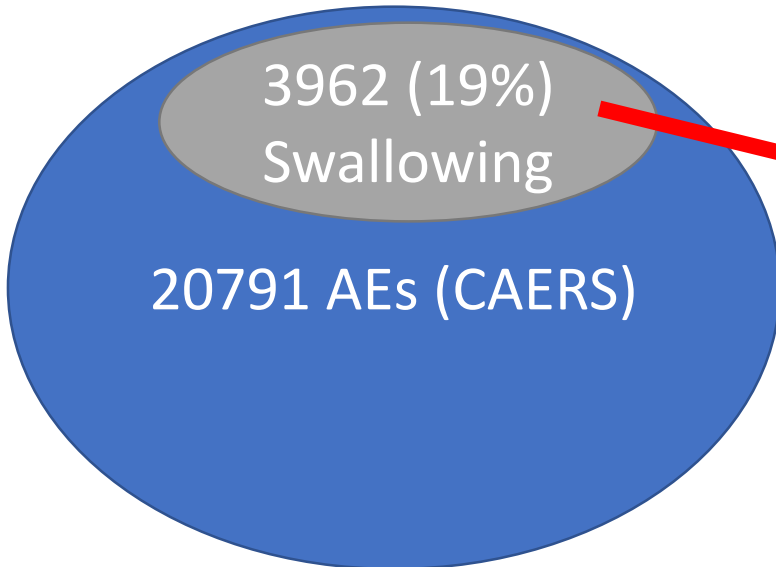


1. 40.6% mild allergy
2. 23.6% dysphagia
3. 19.4% choking



# Consumer safety issue: dysphagia, choking

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



- 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\*

Product Number	Product Description†	Reports Involving Swallowing Problems (n = 3962), n	PRR‡	Pill Dimensions, mm		
				Length	Width	Height
1	Multivitamin marketed to older women	1607	6.8	19.0	10.0	8.0
2	Multivitamin marketed to older adults	332	2.7	18.5	9.5	7.3
3	Multivitamin marketed to females	188	3.2	21.5	9.0	7.8
4	Calcium supplement	185	3.9	21.0	11.0	8.5
5	Calcium supplement	161	3.9	20.5	10.0	7.5
6	Multivitamin marketed to females	145	4.4	18.5	9.5	7.5
7	Multivitamin marketed to males	138	3.6	19.0	8.5	7.0
8	Multivitamin marketed to older women	99	4.1	19.5	10.0	7.5
9	Multivitamin marketed to older men	86	2.7	19.5	10.0	7.0
10	Calcium supplement	85	2.4	20.0	9.8	7.0
1-10§	All 10 products	3026	12.7	19.3	9.8	7.8

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]

Other deaths:

CALTRATE CHEWABLE – 2

NATUREMADE VIT C 1000MG – 1

METAMUCIL CAPSULES - 1

**NO DEATHS FROM  
SOFTGELS,  
CAPSULES**

Deaths	Product	# of AEs for product
4	CENTRUM SILVER WOMEN 50+ TABLET	1209
	CENTRUM SILVER ULTRA WOMEN'S MULTI TABLET	515
2	CITRACAL MAXIMUM COATED TABLET	439
	CITRACAL PETITES COATED TABLET	325
1	CENTRUM SILVER TABLET	240
2	CALTRATE600 PLUS D TABLET	204
1	CENTRUM SILVER ADULTS 50+ TABLET	198
	ONE A DAY WOMEN'S MULTIVITAMINS PLUS MINERALS COATED TABLET	183
	ONE A DAY WOMEN'S 50PLUS COATED TABLET	172
	ONE A DAY MEN'S HEALTH FORMULA COATED TABLET	138
	<b>Total</b>	<b>3623</b>

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





# Consumer safety issue: dysphagia, choking

## Deaths attributable to solid-form supplement products

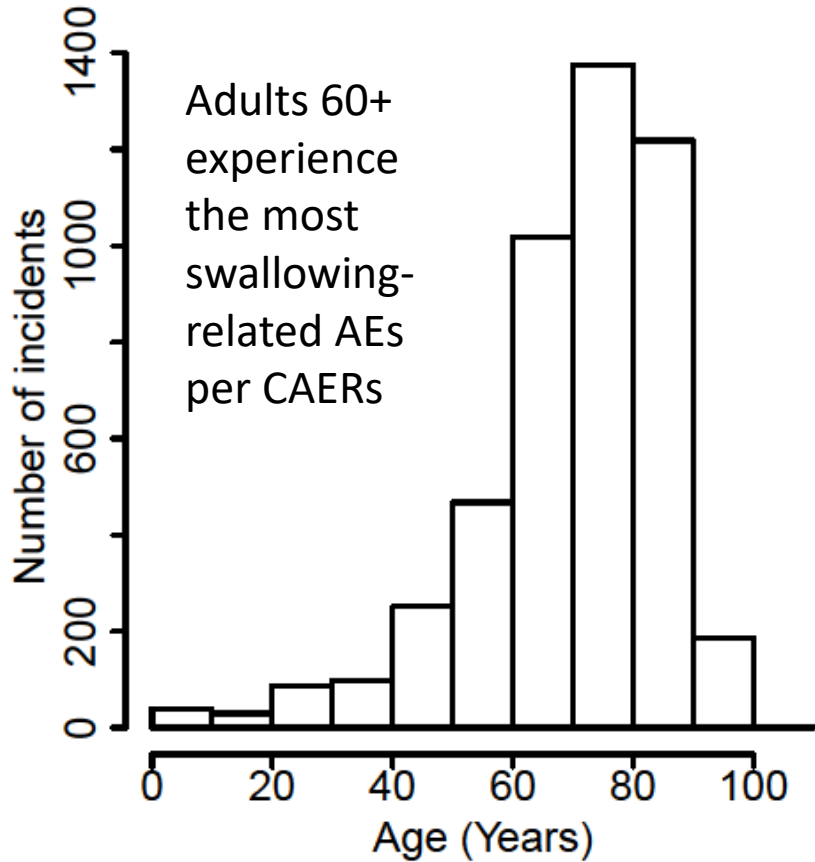
Product	Age	MedDRA Terms	Outcomes
CALTRATE600 PLUS D TABLET	NA	DYSPHAGIA	Death, Medically Important
CALTRATE600 PLUS D TABLET	NA	NEOPLASM MALIGNANT, DYSPHAGIA	Death
CALTRATE600 CHEWABLE TABLET	90F	RETCHING, DYSPHAGIA	Death
CALTRATE600 CHEWABLE TABLET	NA	DYSPHAGIA	Death, Medically Important
CENTRUM SILVER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

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

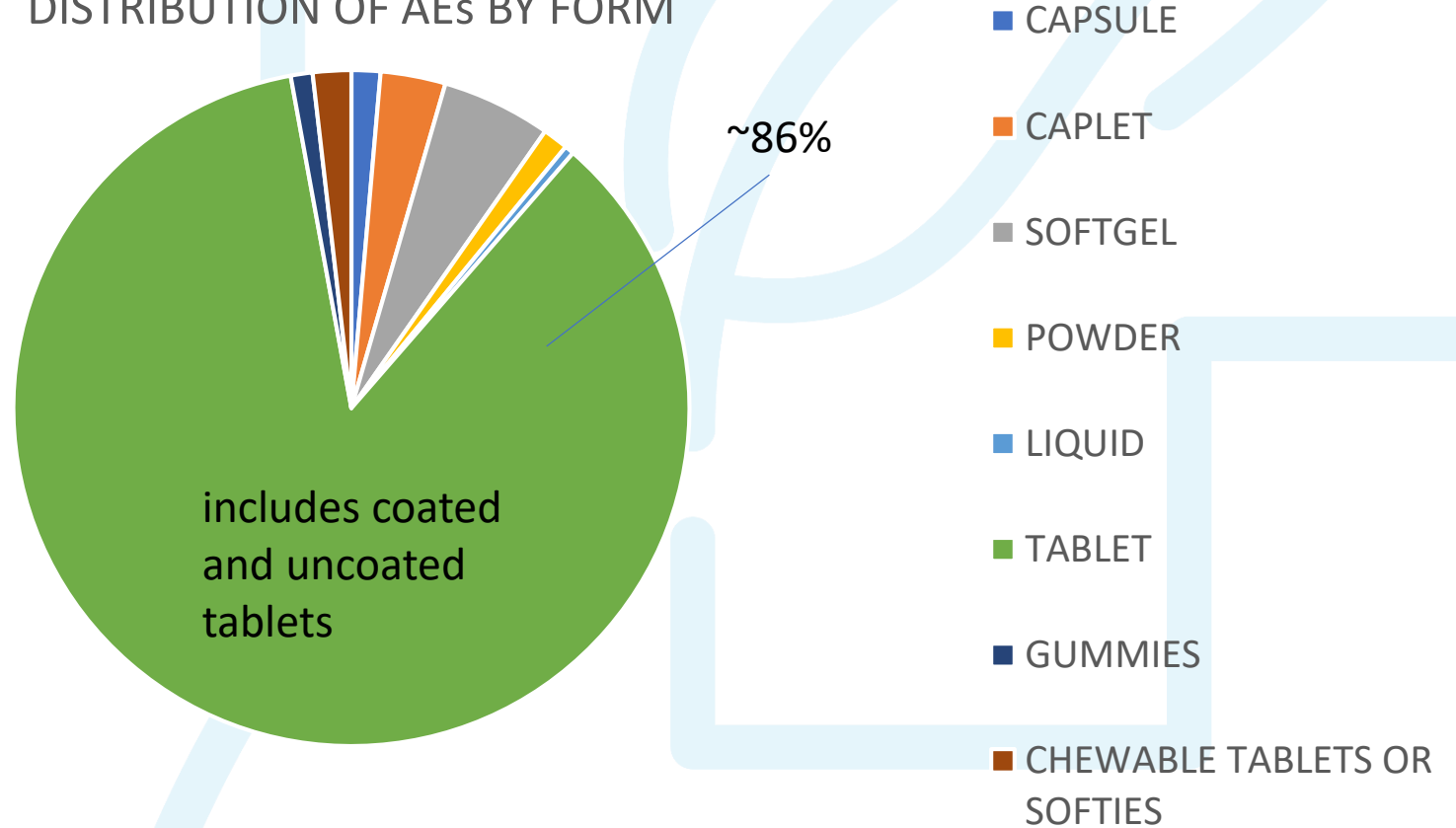


# Consumer safety issue: dysphagia, choking

## Tablets dominate the “product form” precipitating AEs



DISTRIBUTION OF AEs BY FORM



# 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%) → 42% of supplement users 55+ vs. 18% of users 18 – 34
- Capsule (19%)
- Gummy (16%) → 22% of supplement users 18 – 34 prefer gummies vs. 8% of supplement users 55+
- Soft gel (11%)
- Powder (4%) → 7% of male users vs. 2% of female users
- Soft chew (4%)
- Chewable tablet (4%)

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



# 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

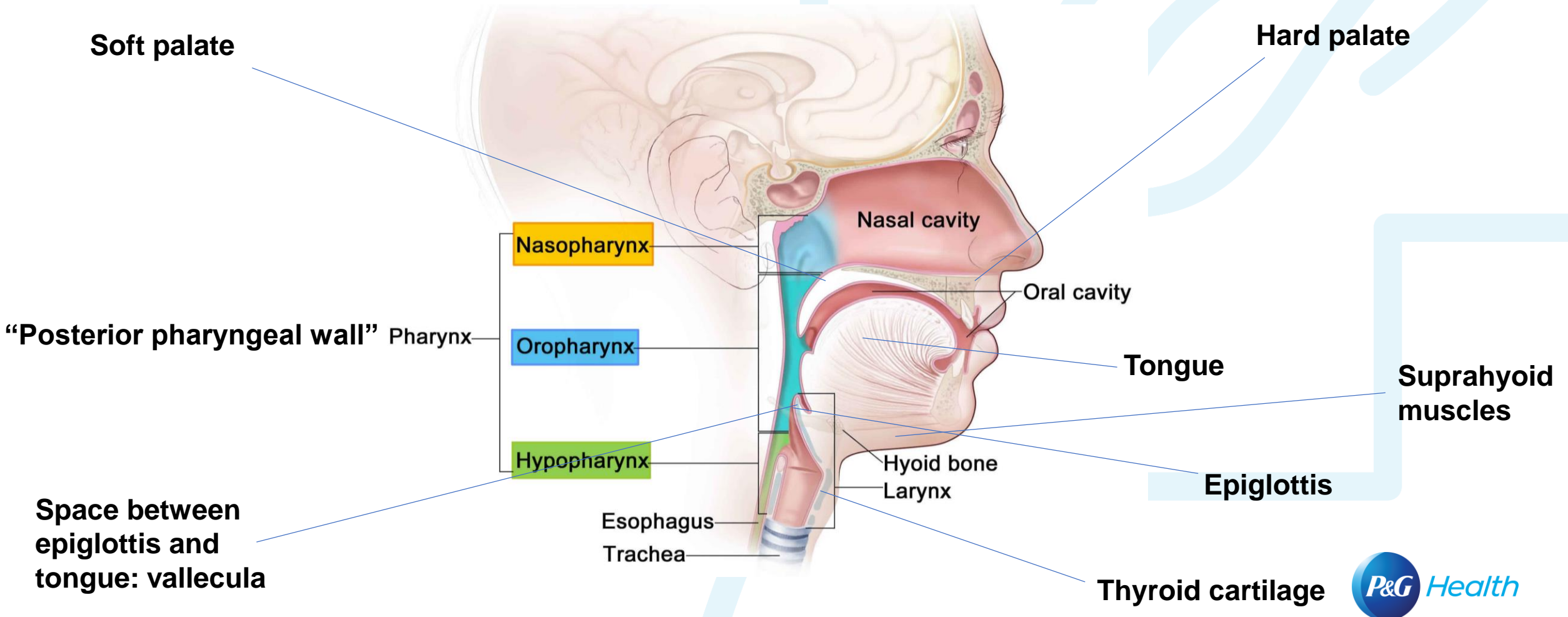
## APPROACH

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

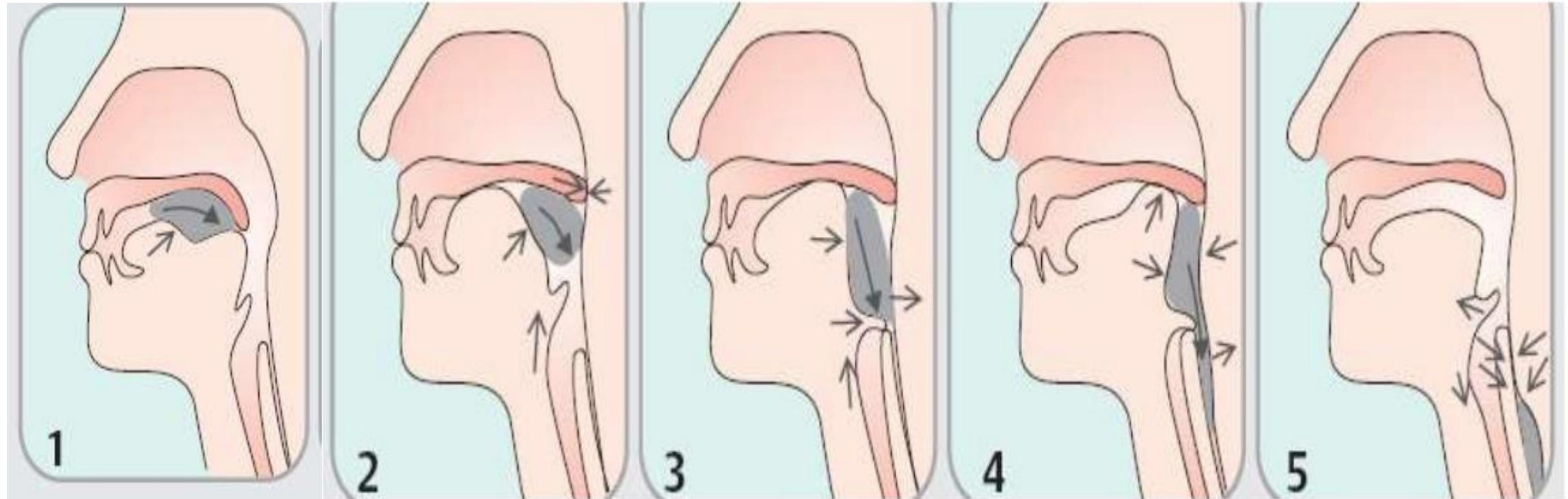
# Anatomy and physiology of swallow

## Anatomy of pharynx



# Anatomy and physiology of swallow

Deglutition (Swallowing) process is 3 phases



1  
ORAL  
(Voluntary)

2 3 4 5  
PHARYNGEAL  
(Involuntary)

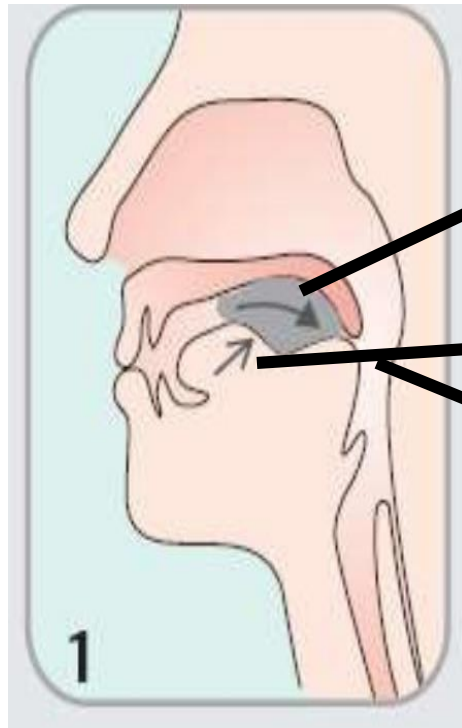
ESOPHAGEAL  
(Involuntary)





# Anatomy and physiology of swallow

## Deglutition



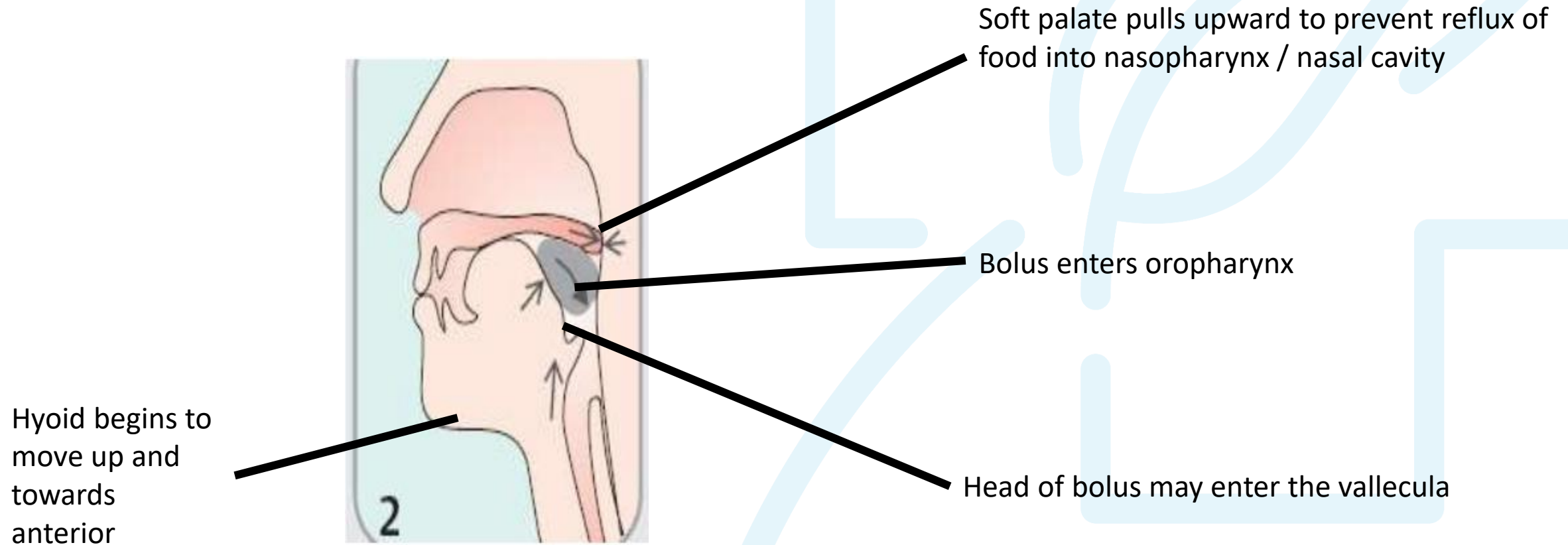
Bolus: bolus is moistened, masticated, etc., held against hard palate in anterior by tongue, and by tongue and soft palate in posterior

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

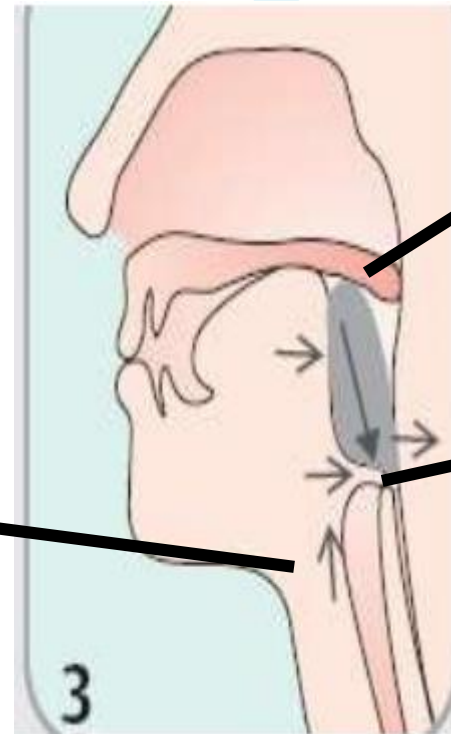
## Deglutition



# Anatomy and physiology of swallow

## Deglutition

Larynx and hyoid move up to most extreme position



Soft palate completely retracted upward

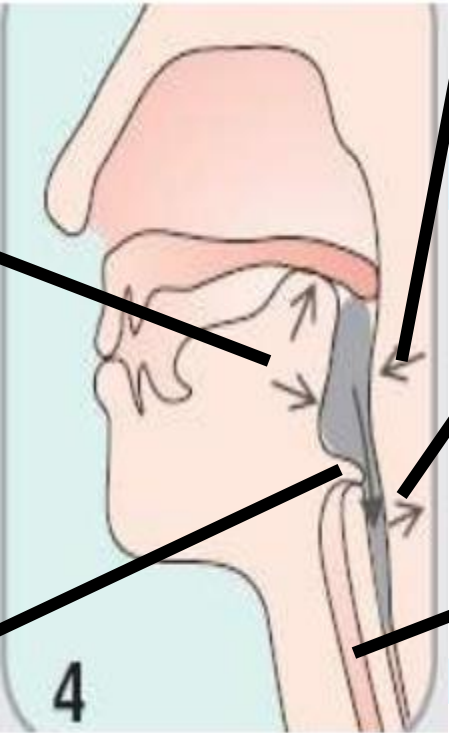
Epiglottis moves from upright to horizontal to fully inverted to protect trachea

# 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)

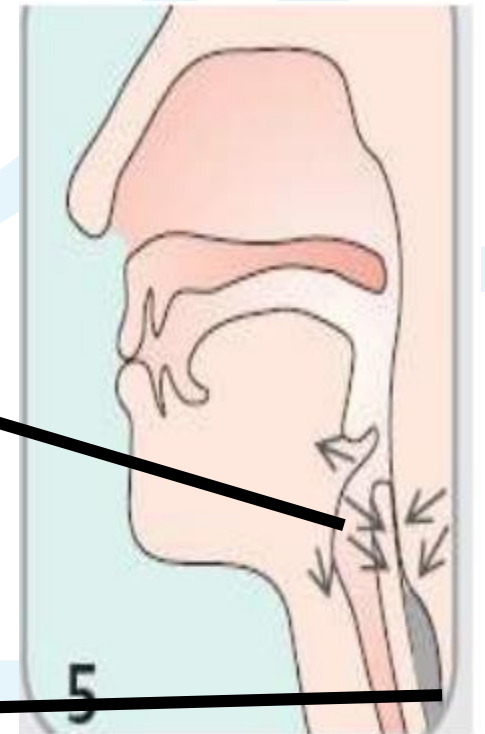


# Anatomy and physiology of swallow

## Deglutition

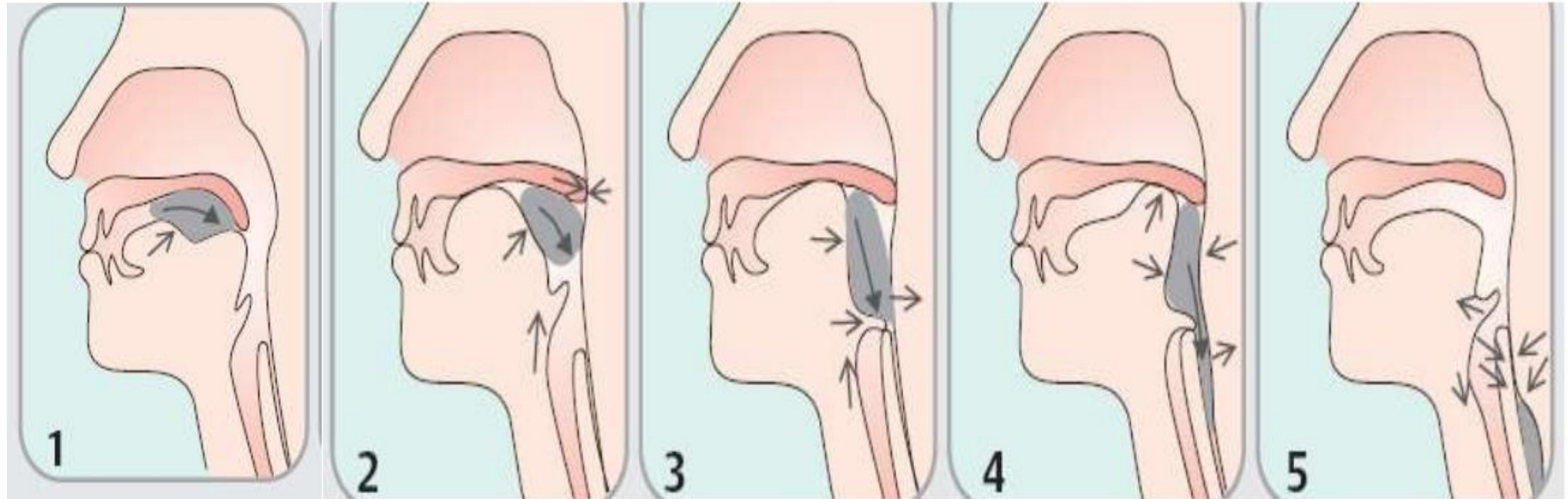
Nervous system forces muscle contractions/relaxations (peristalsis) of hypopharynx and forces food bolus into upper esophagus

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 3 4  
PHARYNGEAL  
(Involuntary)

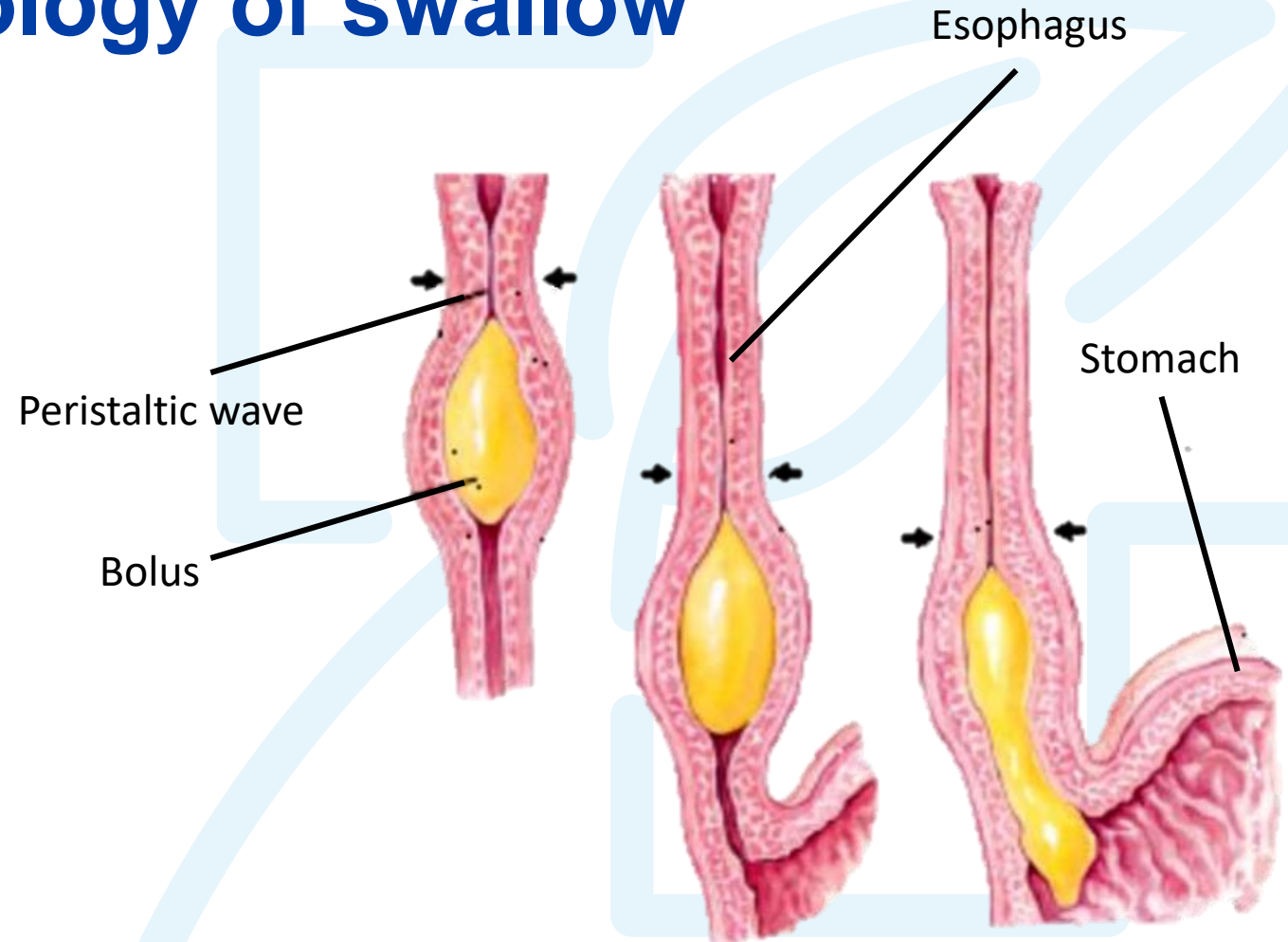
5  
ESOPHAGEAL  
(Involuntary)



# 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

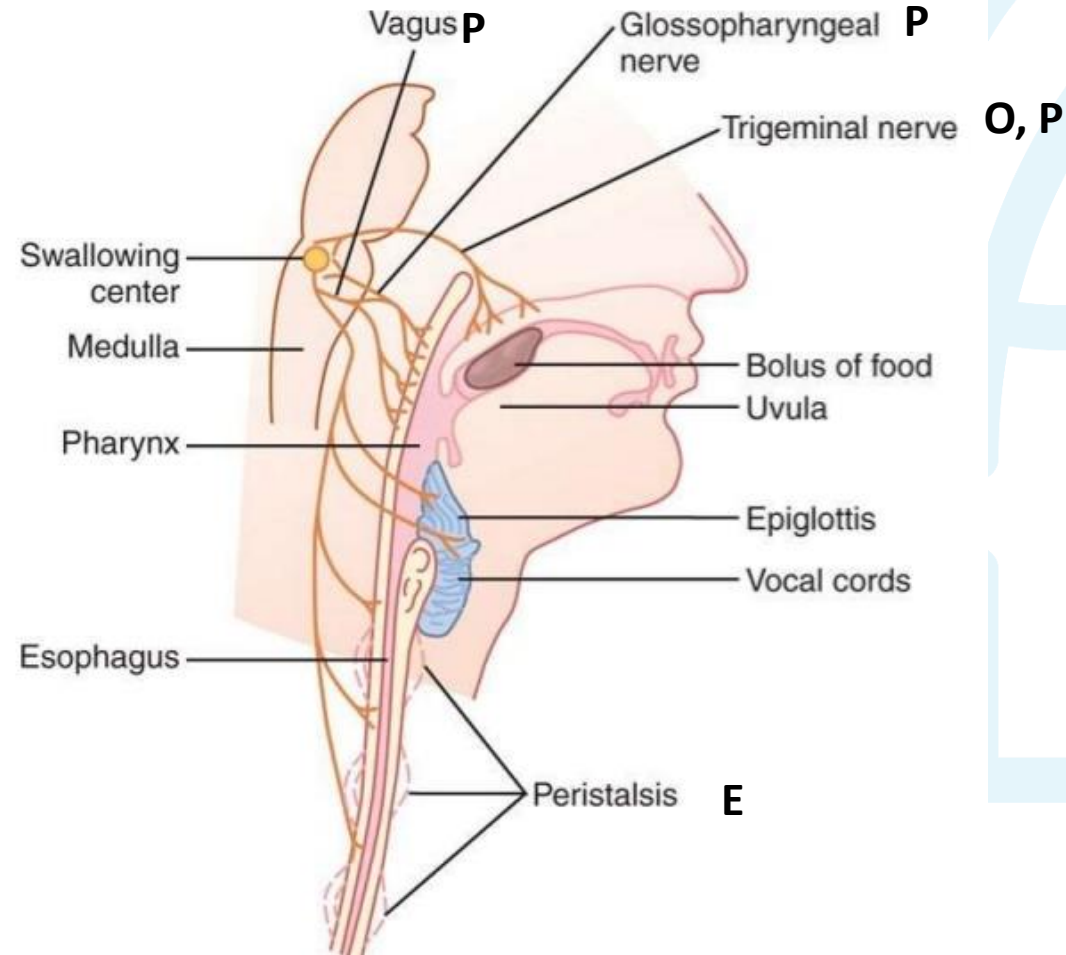


# Anatomy and physiology of swallow

## Nervous system controls deglutition

VOLUNTARY (VOLITIONAL)  
ORAL (O)

INVOLUNTARY (REFLEXIVE)  
PHARYNGEAL (P)  
ESOPHAGEAL (E)





# Anatomy and physiology of swallow

## Dimensions of pharynx and esophagus (mm)

AP: Anteroposterior  
LL: latolateral

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



Arana-Rueda, E., et al. (2009). "Electroanatomical mapping of the esophagus in circumferential pulmonary vein isolation." *Revista Española de Cardiología (English Edition)* **62**(10): 1189-1192.

Daniel, M. M., et al. (2007). "Pharyngeal dimensions in healthy men and women." *Clinics* **62**(1): 5-10.

de Jong, J. R., et al. (2004). "The influence of laparoscopic adjustable gastric banding on gastroesophageal reflux." *Obesity surgery* **14**(3): 399-406.

Lee, J., et al. (2012). "Esophageal diameter is decreased in some patients with eosinophilic esophagitis and might increase with topical corticosteroid therapy." *Clinical gastroenterology and hepatology* **10**(5): 481-486.

Ize-Iyamu, I. (2016). "Pharyngeal dimensions in skeletal class I, II, and III orthodontic patients in a Nigerian population." *West African Journal of Radiology* **23**(2): 89-94.

# 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 1** Location of the foreign bodies (*n* = 100)

Foreign body location	<i>n</i> (%)
Esophagus	17 (17)
Oropharynx	8 (8)
Small intestine	6 (6)
Stomach	6 (3)
Trachea	2 (2)
Larynx	3 (3)
Colon	3 (3)
Undetermined location	1 (1)
Undetected	54 (54)

# Anatomy and physiology of swallow

## Resources

- <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
  - Matsuo, K., & Palmer, J. B. (2008). Anatomy and physiology of feeding and swallowing: normal and abnormal. *Physical medicine and rehabilitation clinics of North America*, 19(4), 691-707.
    - <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

Sura, L., et al. (2012). "Dysphagia in the elderly: management and nutritional considerations." *Clinical interventions in aging* 7: 287.

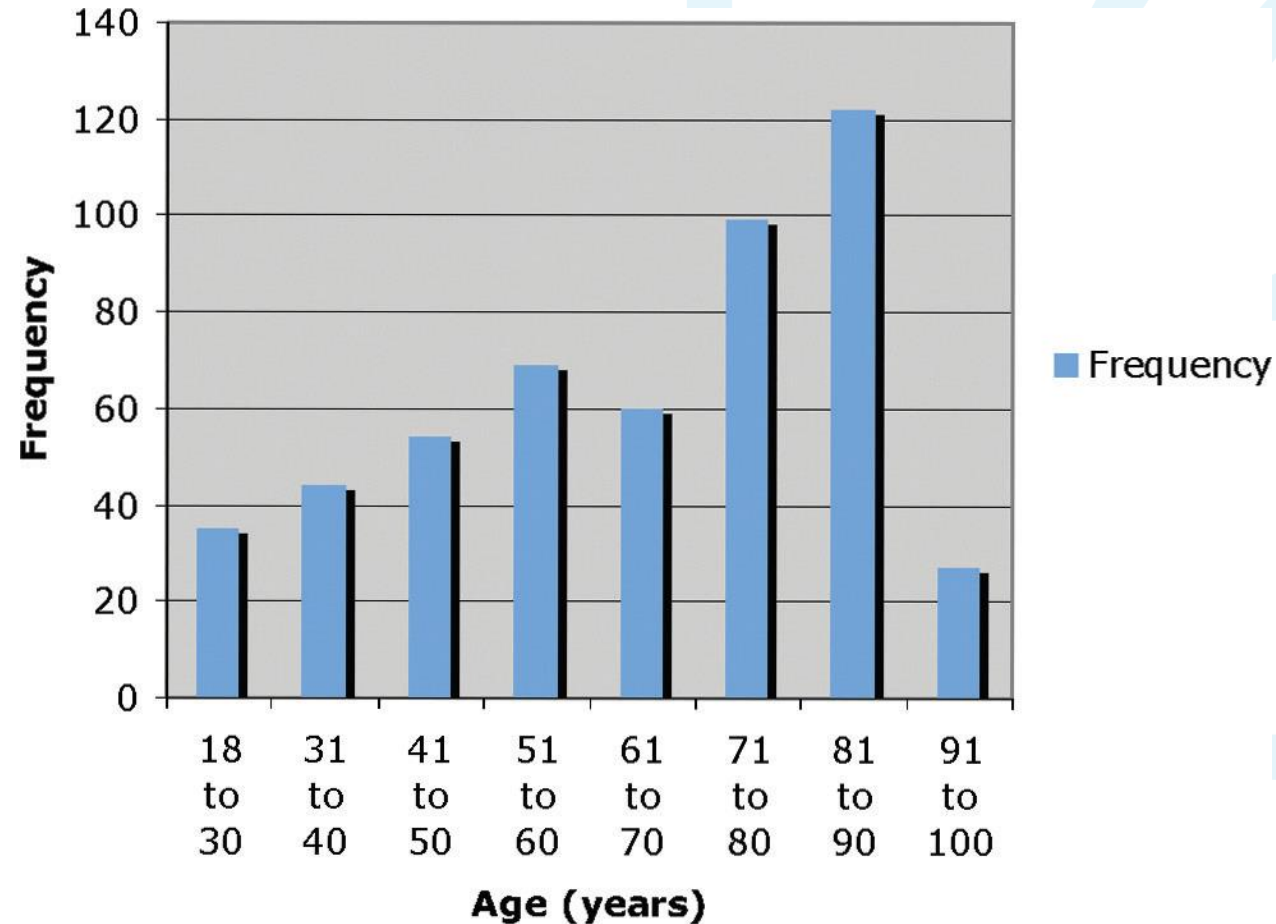
Wirth, R., et al. (2016). "Oropharyngeal dysphagia in older persons—from pathophysiology to adequate intervention: a review and summary of an international expert meeting." *Clinical interventions in aging* 11: 189.

Rofes, L., et al. (2010). "Pathophysiology of oropharyngeal dysphagia in the frail elderly." *Neurogastroenterology & Motility* 22(8): 851-e230

Strachan, I. and M. Greener (2005). "Medication-related swallowing difficulties may be more common than we realise." *Pharm Pract* 15(10): 411-414.

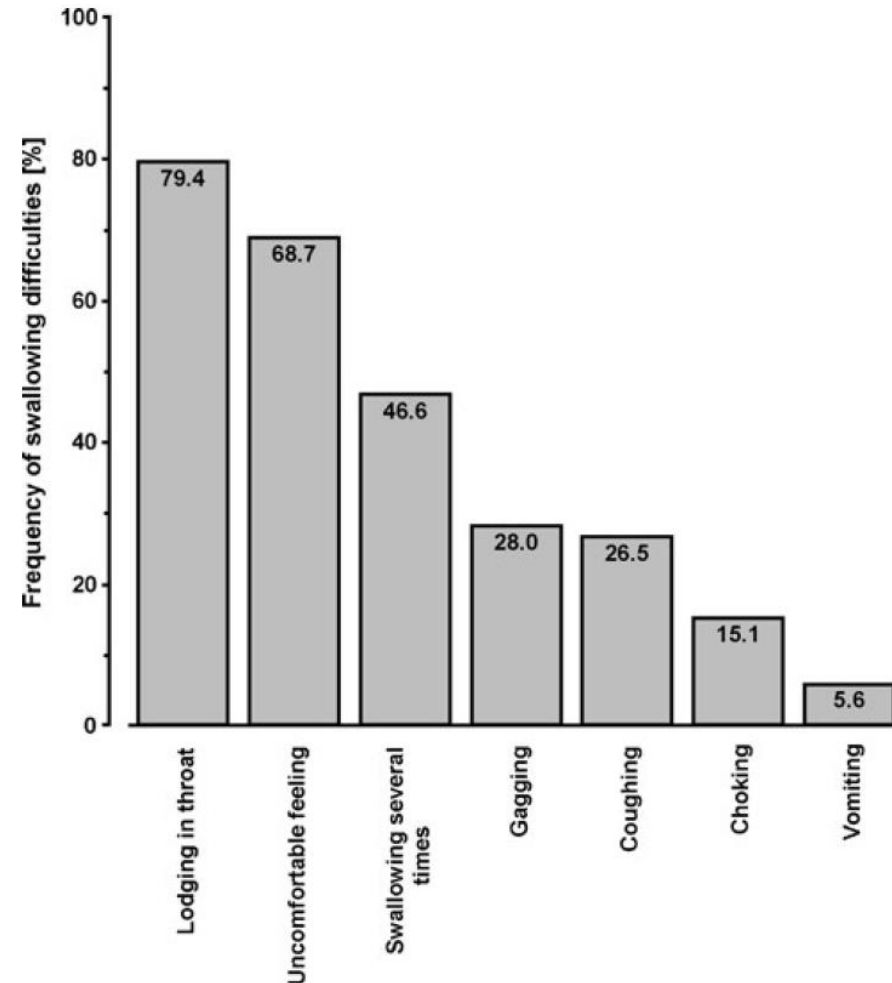
# Dysphagia in the elderly

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



# Dysphagia in the elderly

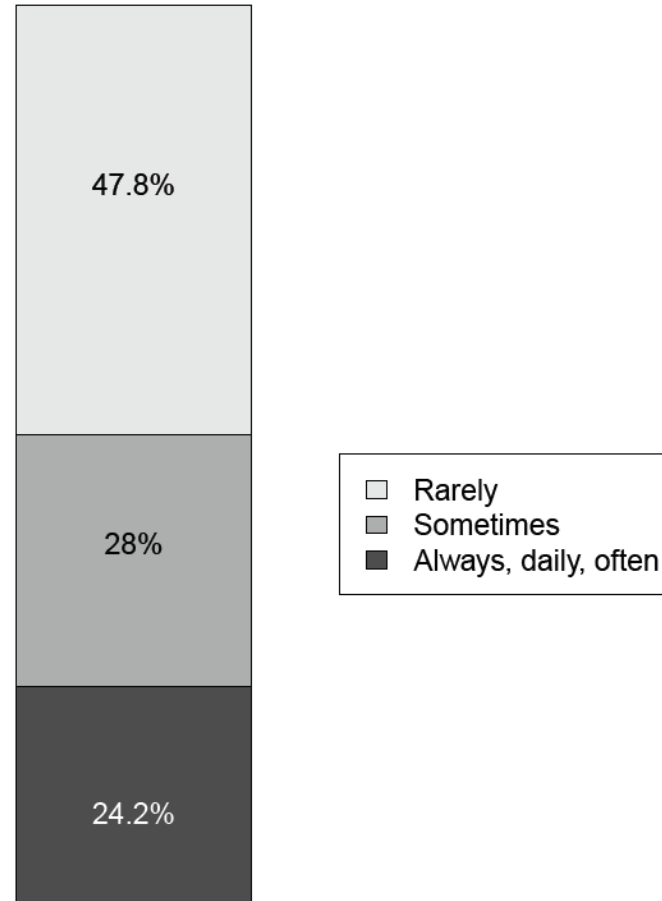
Swallowing difficulties have different descriptions from consumers



# Dysphagia in the elderly

Swallowing difficulties are experienced frequently

How often do you experience swallowing difficulties?



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

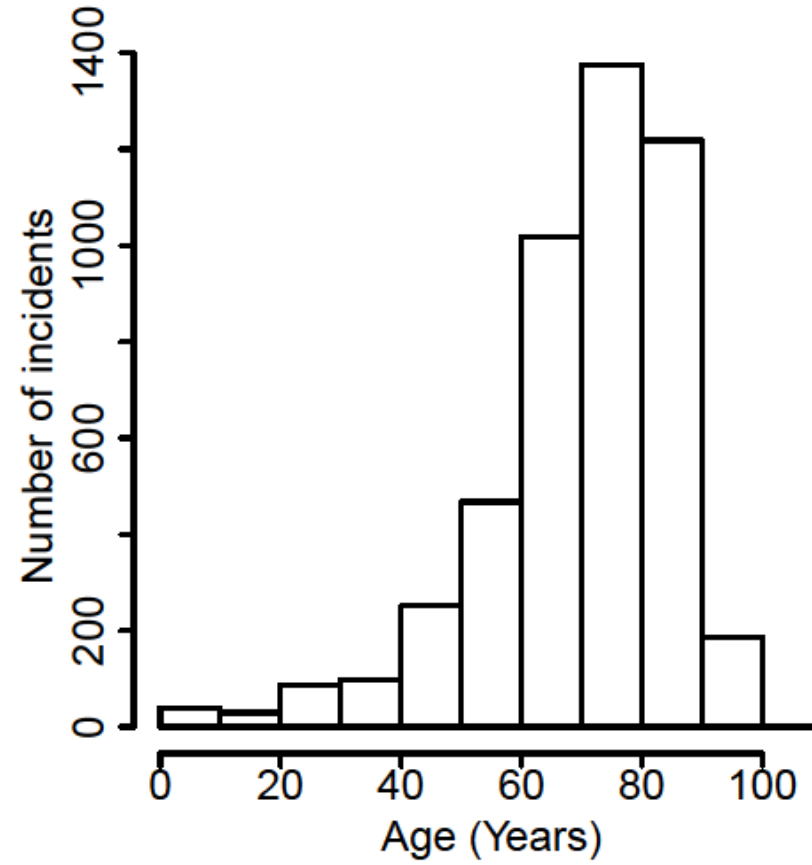
## Pills are the most frequent cause of airway obstructions in adults

TABLE 1. Items Causing Airway Obstruction in adults

Meat (30.6%)	Other Food (21.4%)	Non-food solid items (11.1%)	Liquid (4.7%)
Meat (unspecified), 38	Soup, 8	Pills, 44	Secretions, 11
Chicken, 33	Chips, 6	Plastic	Water, 6
Beef, 26	Apple, 6	Cough drops	Juice
Hotdog, 12	Rice, 6	False tooth	
Pork, 11	Hard candy, 6	Metal	
Hamburger, 8	Potato, 5		
Sandwich, 9	Grape		
Bone, chicken, 7	Toast		
Bone, fish	Crackers		
Fish	Salad		
Ribs	Carrot		
	Pizza		
	Nut		
	Pasta		
	Corn		
	Bagel		
	Chocolate		
	Cantaloupe		
	Cinnamon roll		

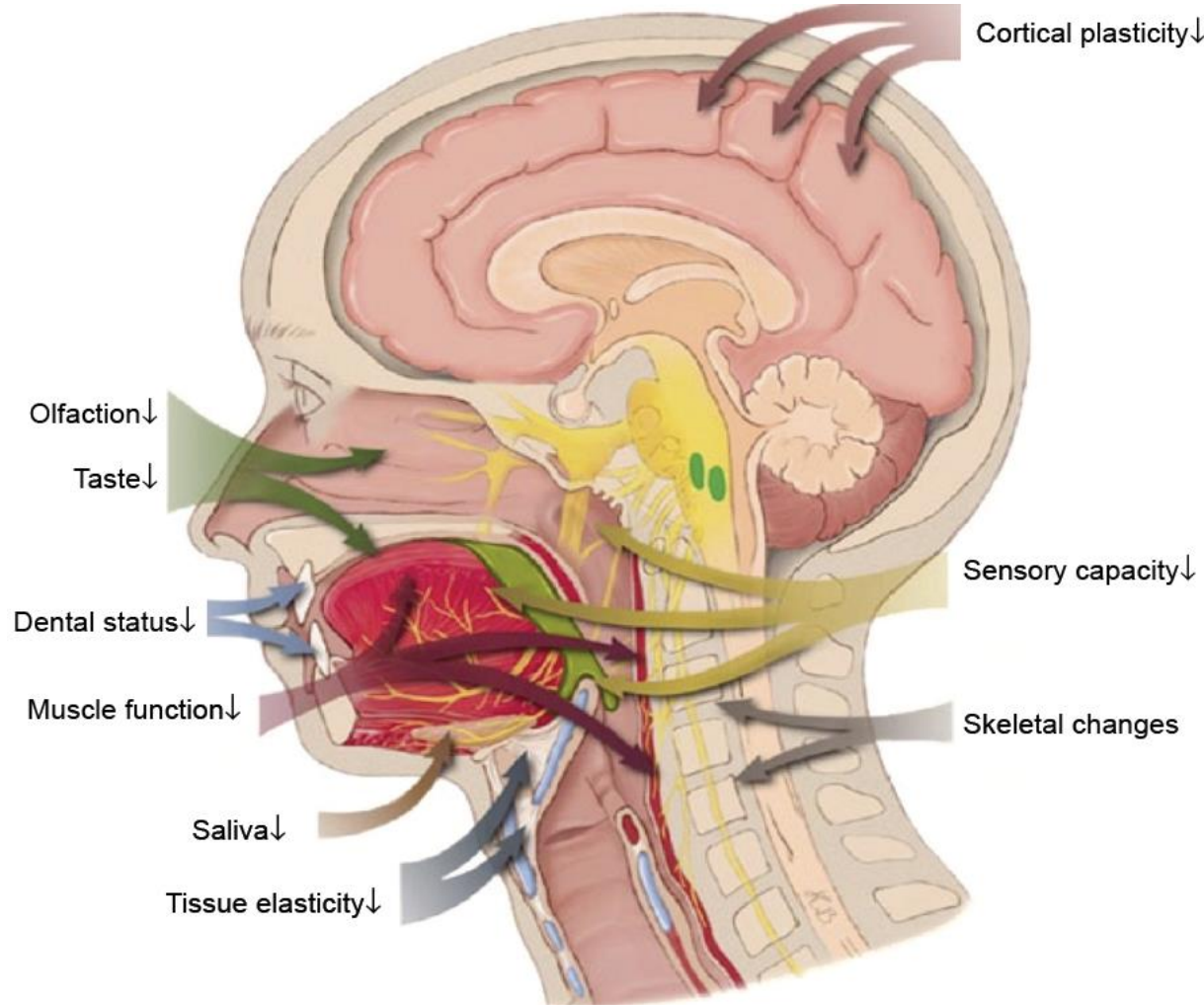
# Dysphagia in the elderly

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



# Dysphagia in the elderly

Physiologic changes of aging increase risk for dysphagia

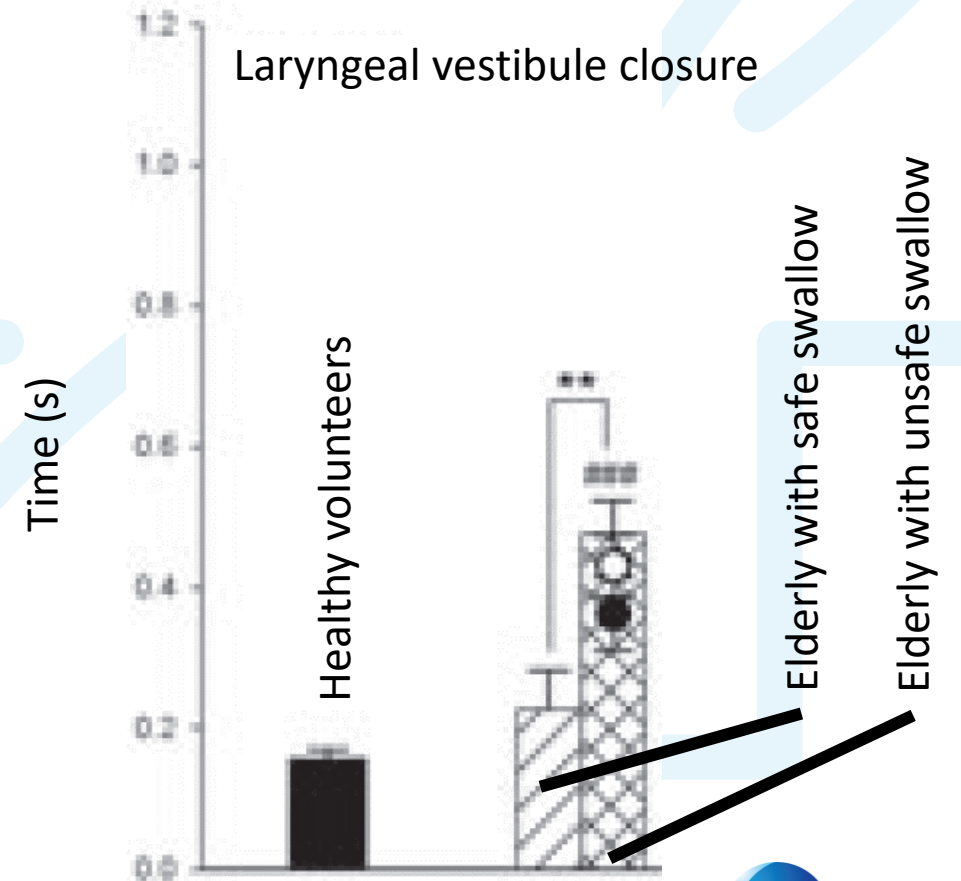
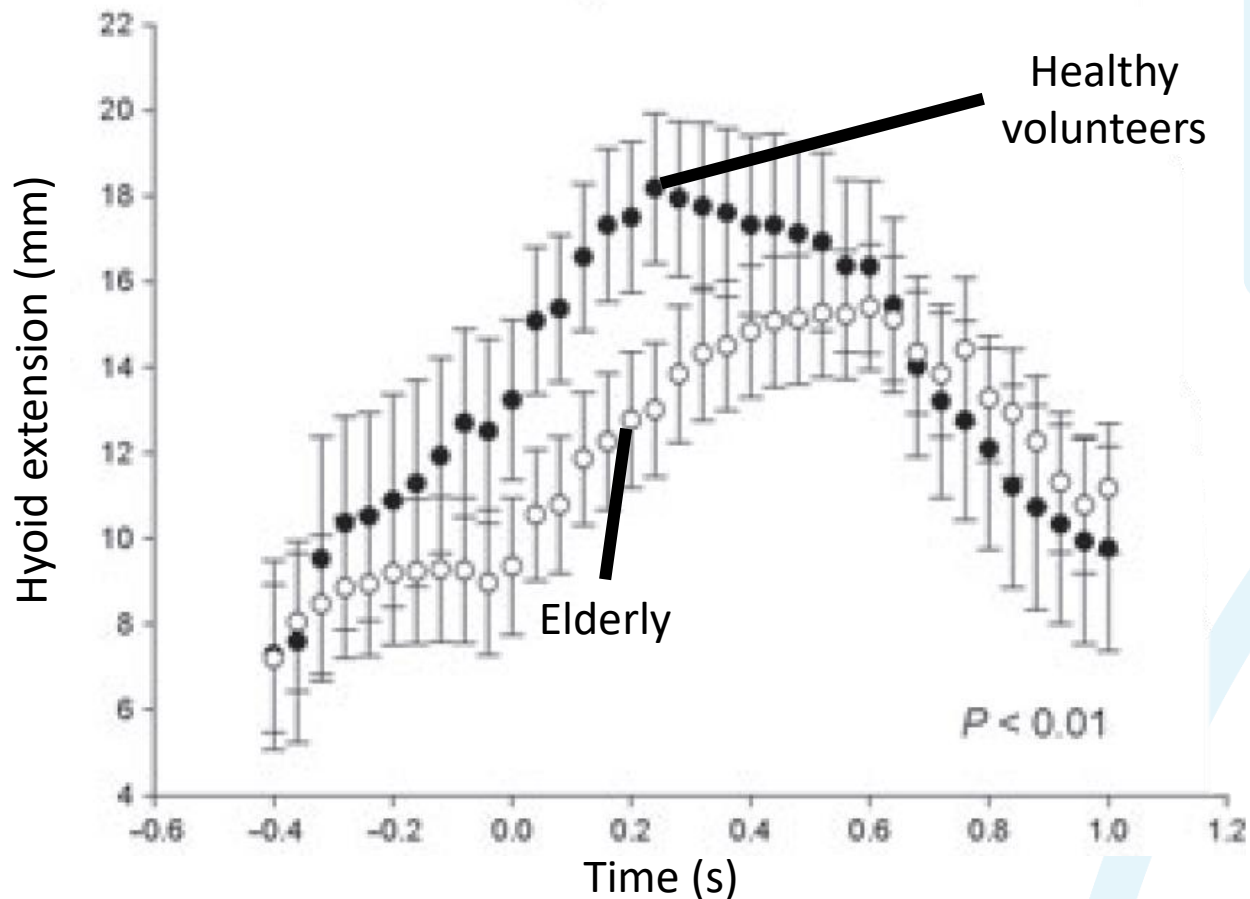


Prolonged oral phase  
 Reduced tongue pressure  
 Delayed swallow reflex  
 Delayed closure of larynx  
 Decreased swallow volume  
 Increased residual matter

# Dysphagia in the elderly

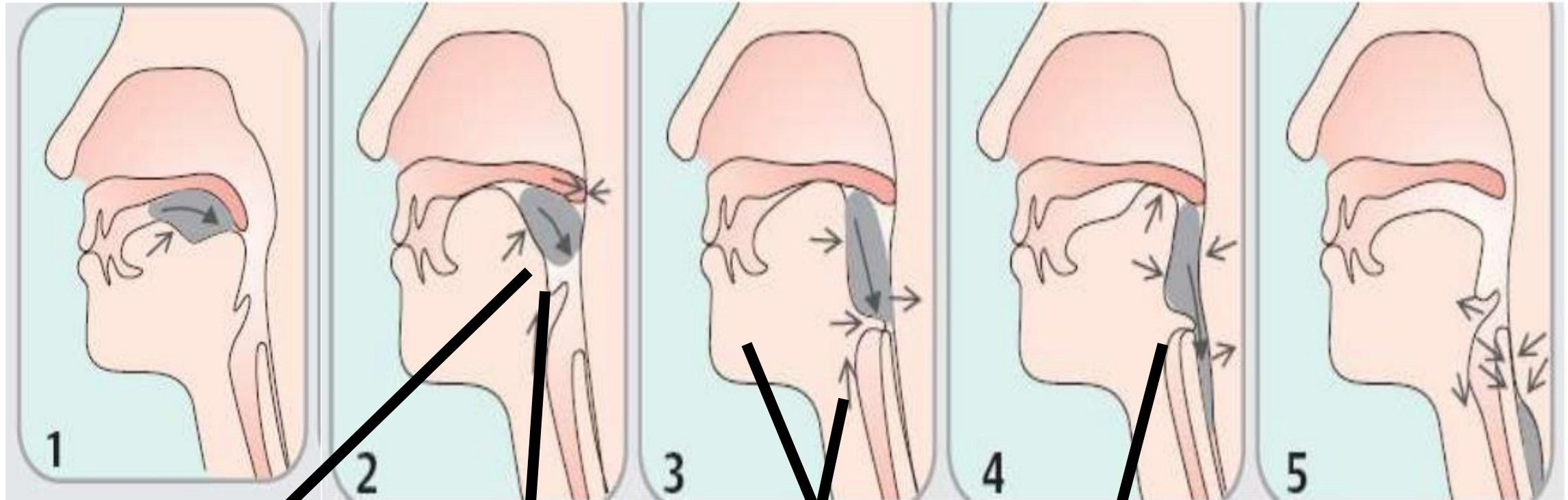
Studies show quantitative decline in swallowing functions with age

Vertical hyoid movement



# Dysphagia in elderly

Anatomical, physiological deficiencies that increase aspiration risk



1  
Delayed initiation  
of pharyngeal  
swallow

2  
Vallecular stasis

3  
Reduced hyoid and  
larynx elevation

4  
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

Antiparkinsonians

### 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

Schindler, J. S. and J. H. Kelly (2002). "Swallowing disorders in the elderly." *The Laryngoscope* **112**(4): 589-602.

Roy, N., et al. (2007). "Dysphagia in the elderly: preliminary evidence of prevalence, risk factors, and socioemotional effects." *Annals of Otolaryngology, Rhinology & Laryngology* **116**(11): 858-865.

Aslam, M. and M. F. Vaezi (2013). "Dysphagia in the elderly." *Gastroenterology & hepatology* **9**(12): 784.

Matsuo, K. and J. B. Palmer (2008). "Anatomy and physiology of feeding and swallowing: normal and abnormal." *Physical medicine and rehabilitation clinics of North America* **19**(4): 691-707.

Mann, T., et al. (2013). "The association between chewing and swallowing difficulties and nutritional status in older adults." *Australian dental journal* **58**(2): 200-206.

Maeda, K. and J. Akagi (2015). "Decreased tongue pressure is associated with sarcopenia and sarcopenic dysphagia in the elderly." *Dysphagia* **30**(1): 80-87.

# Dysphagia in the elderly

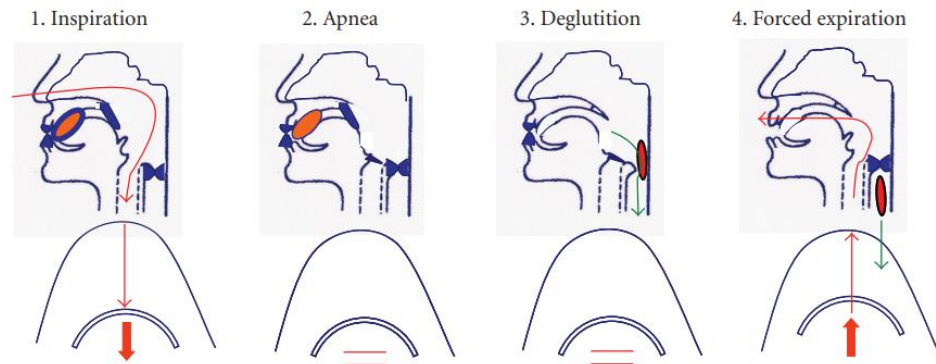
Supplements are recommended for sensitive population (stroke patients)

- WebMD indicates Fish Oil, Folic Acid, Potassium, and others may be effective for stroke
  - Therapeutic Research Faculty (2018). "Stroke." Vitamins and Supplements Center. 2020, from <https://www.webmd.com/vitamins/condition-1594/stroke>.
- “Intensive nutritional supplementation, using readily available commercial preparations, improves motor recovery in previously undernourished patients receiving intensive in-patient rehabilitation after stroke.”
  - Rabadi, M. H., et al. (2008). "Intensive nutritional supplements can improve outcomes in stroke rehabilitation." Neurology **71**(23): 1856-1861.

# 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.



Sura, L., et al. (2012). "Dysphagia in the elderly: management and nutritional considerations." *Clinical interventions in aging* 7: 287.

Rofes, L., et al. (2011). "Diagnosis and Management of Oropharyngeal Dysphagia and Its Nutritional and Respiratory Complications in the Elderly." *Gastroenterology research and practice* 2011.



# Dysphagia in the elderly

## Most GPs' do not alter treatments based on swallowing issues

---

GPs' reaction after being informed about patients' swallowing difficulties ( $n=54$ )

---

GPs just changed drug	21 (38.9 %)
GPs just gave hints	8 (14.8 %)
GPs changed drug and gave hints	6 (11.1 %)
GPs did nothing at all	19 (35.2 %)

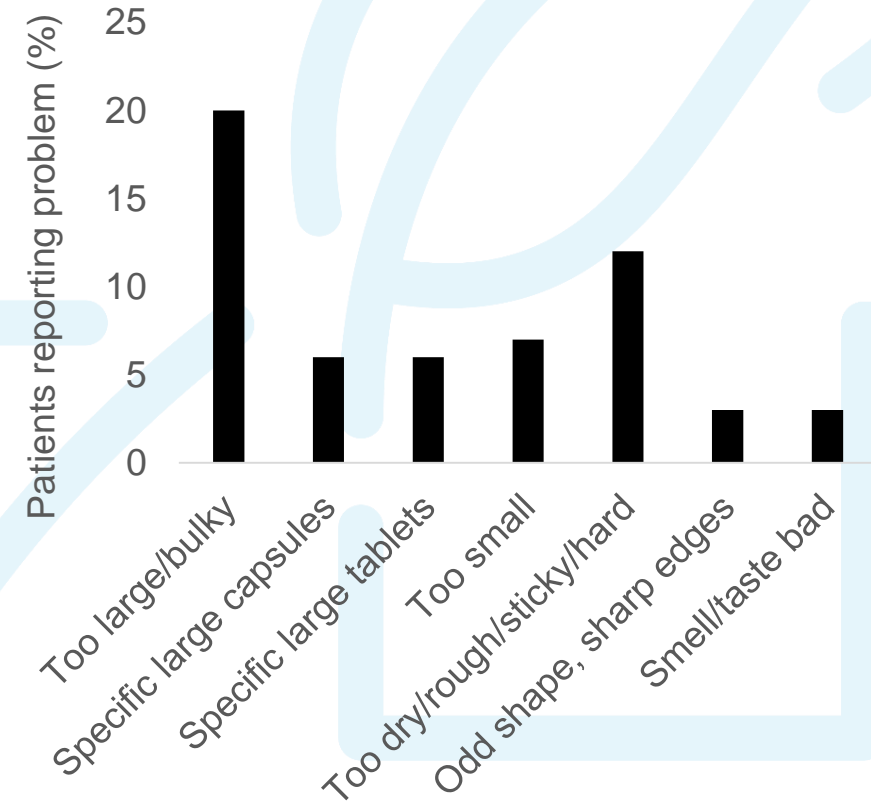
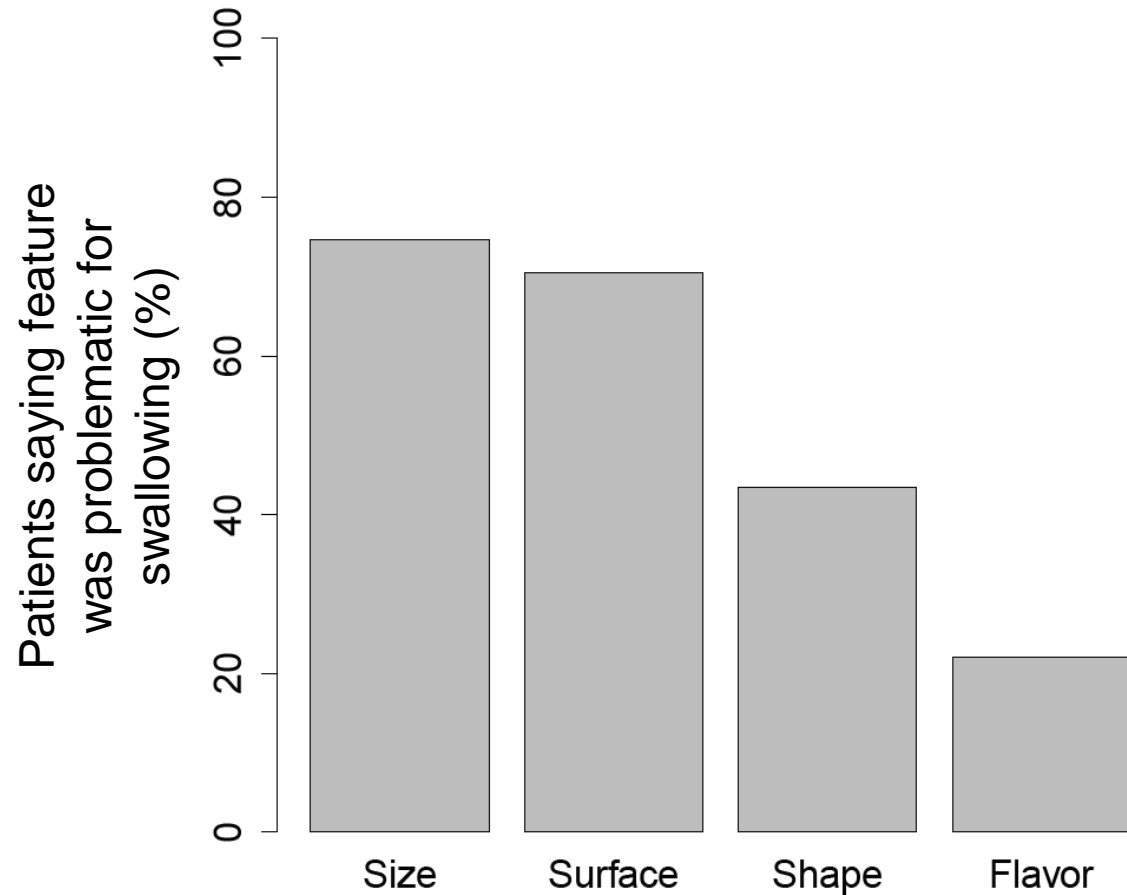
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<sup>a</sup> GPs: general practitioners

# What do pill users think and do?

# What do pill users think?

Patients think size and surface are more important than shape and flavor for swallowability, although all are important



Adapted by MJK from Schiele, J. T., et al. (2013). "Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms." *European journal of clinical pharmacology* **69**(4): 937-948.

Adapted by MJK from Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." *Current Therapeutic Research* **77**: 79-82.

# 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+

Bar-Shalom, D., et al. (2016). "The Quest for Easier-To-Swallow Tablets." Tablets and Capsules.

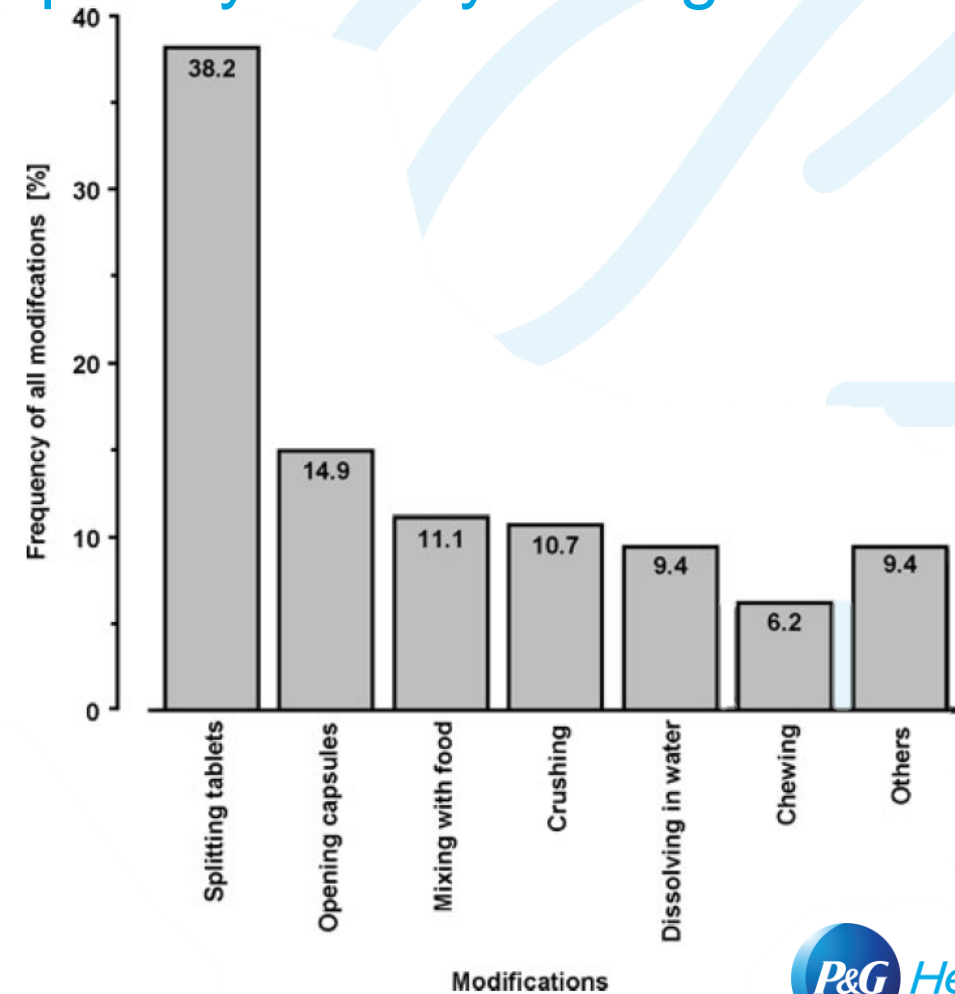
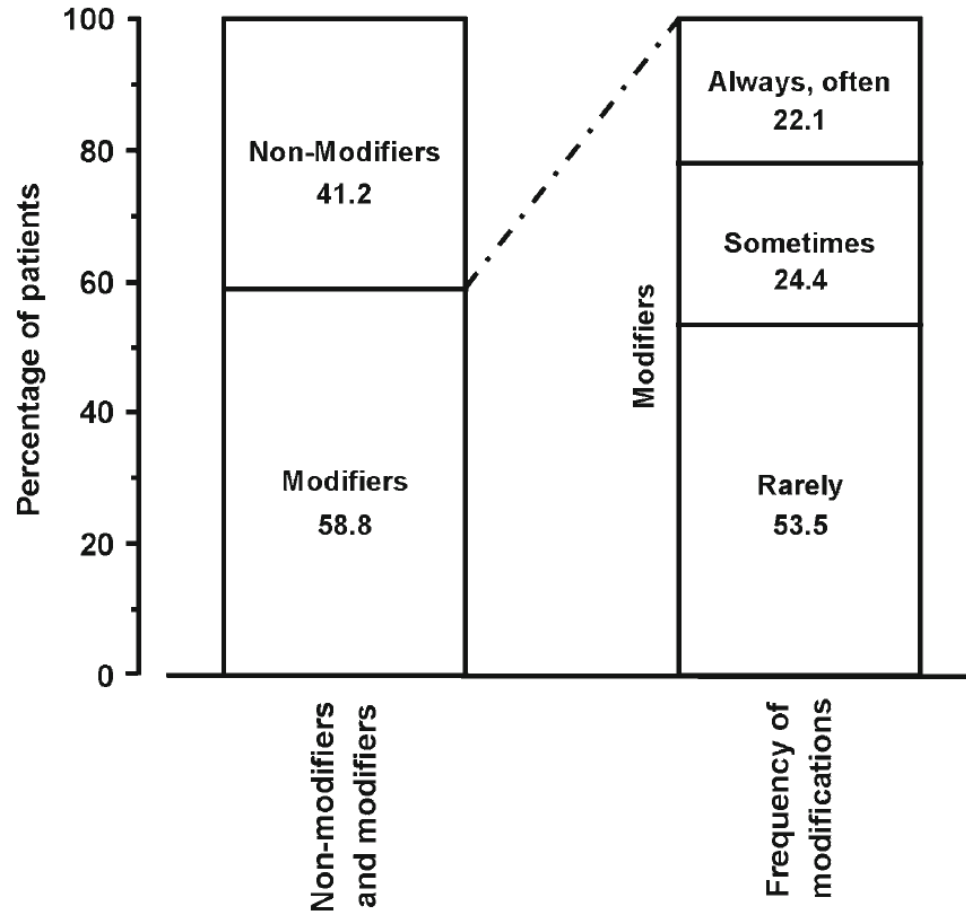
Schiele, J. T., et al. (2013). "Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms." European journal of clinical pharmacology **69**(4): 937-948.

Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.



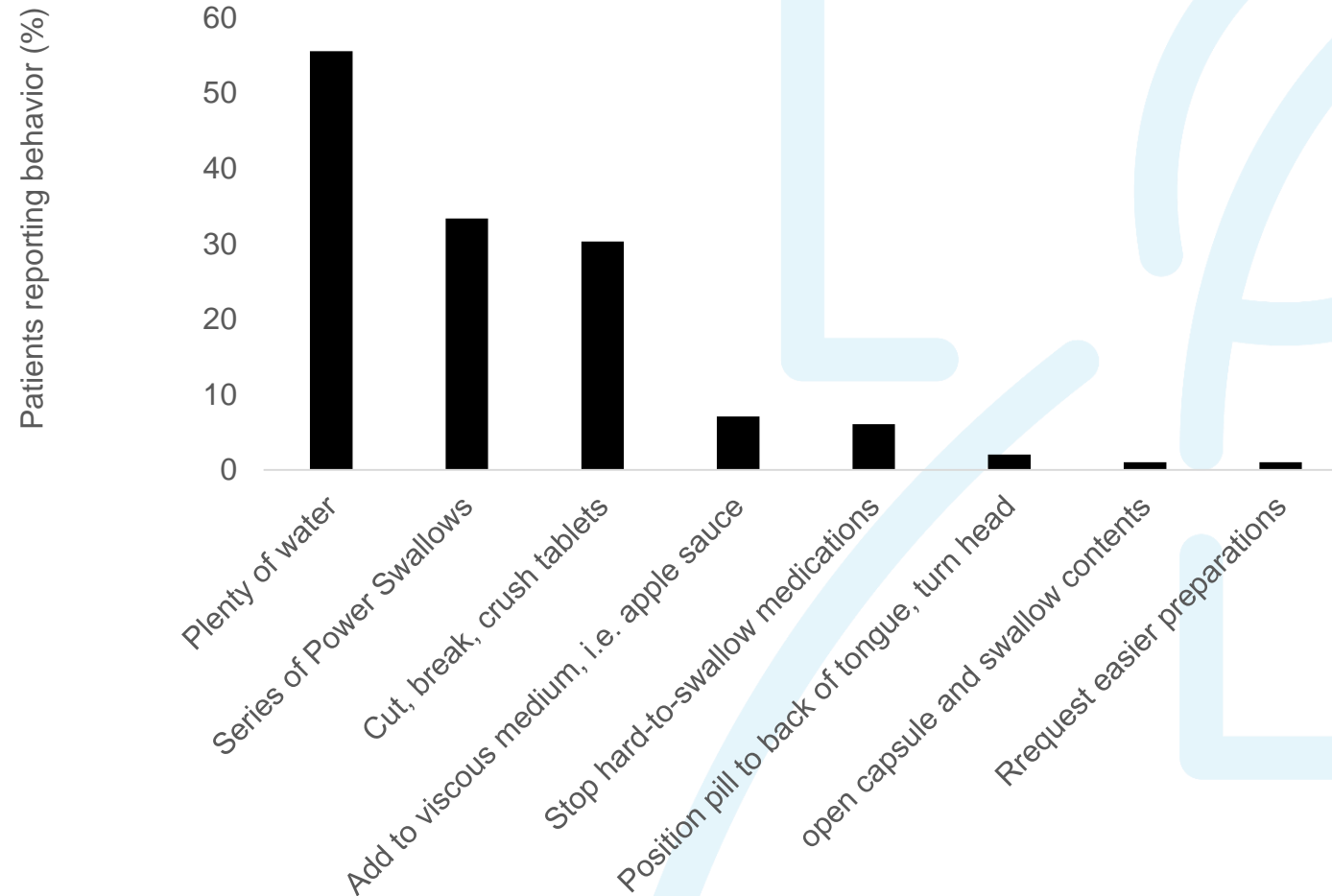
# What do pill users think and do?

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.

Measured Compound and Formulation	AUC <sub>0-24</sub> (ng·hr/mL)	t <sub>max</sub> (hr)	C <sub>max</sub> (ng/mL)
Pentoxifylline			
400 mg intact	921 ± 367	2.55 ± 1.12 <sup>b</sup>	111 ± 40.0 <sup>b</sup>
400 mg crushed	1,447 ± 523	0.70 ± 0.35 <sup>b</sup>	1,316 ± 752 <sup>b</sup>
600 mg intact	1,614 ± 1080	2.25 ± 1.65 <sup>c</sup>	184 ± 86.0 <sup>c</sup>
600 mg crushed	2,201 ± 867	0.60 ± 0.32 <sup>c</sup>	1,789 ± 851 <sup>c</sup>

- Dosage form effects for nutritional supplements seem less clear

Clery, J. D., et al. (1999). "Administration of crushed extended-release pentoxifylline tablets: bioavailability and adverse effects." *American Journal of Health-System Pharmacy* **56**(15): 1529-1534.

Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." *Patient preference and adherence* **12**: 1337.

# 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)
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- Older individuals have a harder time swallowing large round tablets compared to any size oval tablet or capsule
  - Hey, H., et al. (1982). "Oesophageal transit of six commonly used tablets and capsules." Br Med J (Clin Res Ed) **285**(6356): 1717-1719.
- 6 mm oval tablet near perfect swallow score
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.
- Almond was equivalent to elongated; both were easier to swallow than round
  - Bar-Shalom, D., et al. "swallowability."
- Round was perceived as easier to swallow than oval or diamond
  - Wan, X., et al. (2015). "Assessing the expectations associated with pharmaceutical pill colour and shape." Food quality and preference **45**: 171-182.
- Round is best for SMALL tablets, while oval/oblong is best for medium to large tablets
  - Overgaard, A., et al. (2001). "Patients' evaluation of shape, size and colour of solid dosage forms." Pharmacy World and Science **23**(5): 185-188.

**EMPIRICAL SUMMARY (Worst to best):** diamond < round < oval < oblong < irregular < almond

# Known tablet and pill parameters affecting deglutition

## Size

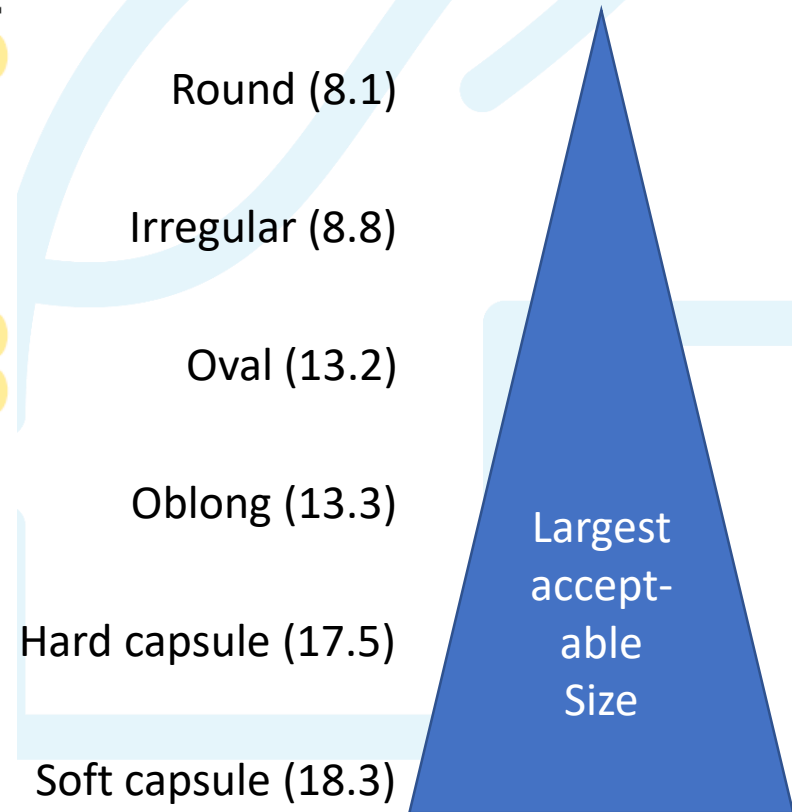
- Transit times for round tablets were shorter with smaller diameters: 5.5 mm < 8 mm < 11 mm
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- 4% of 5mm round tablets vs 20% of 11mm round tablets arrested
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- 6 mm oval tablet near perfect swallow score
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.
- 4/5 consumers prefer 3 medium sized (6 mm) than 1 large (13+ mm)
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.
- 4-5 mm may be too small
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.

# Known tablet and pill parameters affecting deglutition

## Size+Shape

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

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



# Known tablet and pill parameters affecting deglutition

## Weight

- Heavier capsules have faster transit times than lighter capsules (less important than size/shape)
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- Coated tablets had lower transit times than similarly-coated capsules (same size/shape, density tablet > capsule)
  - Perkins, A., et al. (1994). "Impaired oesophageal transit of capsule versus tablet formulations in the elderly." Gut **35**(10): 1363-1367.
  - Perkins, A., et al. (1999). "Esophageal transit of risedronate cellulose-coated tablet and gelatin capsule formulations." International journal of pharmaceutics **186**(2): 169-175.

**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
  - Hey, H., et al. (1982). "Oesophageal transit of six commonly used tablets and capsules." Br Med J (Clin Res Ed) **285**(6356): 1717-1719.
- HPMC coating improved transit time in human subjects from 3.2 sec to 2.3 sec on a round tablet
  - McCargar, L., et al. (2001). "The in-vitro porcine adhesion model is not predictive of the esophageal transit of risedronate tablets in humans." International journal of pharmaceutics **222**(2): 191-197.
- Eudragit L100-55 coated tablets had lower transit times than similarly-coated capsules (same size/shape, density tablet > capsule)
  - Perkins, A., et al. (1994). "Impaired oesophageal transit of capsule versus tablet formulations in the elderly." Gut **35**(10): 1363-1367.
- Coatings universally improve ease of swallowing
  - Hofmanová, J., et al. (2019). "Developing methodology to evaluate the oral sensory features of pharmaceutical tablet coatings." International journal of pharmaceutics **562**: 212-217.
- 50% prefer capsules to tablets (smooth, easy gliding), 50% prefer tablets to capsules (capsules too sticky, dissolve)
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.
- Softgels perceived as easier to swallow
  - Bhosle, M., et al. (2009). "Difficult to swallow: patient preferences for alternative valproate pharmaceutical formulations." Patient preference and adherence **3**: 161.
- Gelatin capsule was preferred over a coated tablet, which was preferred over an uncoated tablet
  - Overgaard, A., et al. (2001). "Patients' evaluation of shape, size and colour of solid dosage forms." Pharmacy World and Science **23**(5): 185-188.

**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
  - Wan, X., et al. (2015). "Assessing the expectations associated with pharmaceutical pill colour and shape." Food quality and preference **45**: 171-182.
- For tablets, color preferences for swallowable tablets in Denmark were white > Gold > tan > orange > bright green > dark orange > grey > olive green > orange > turquoise > purple
  - Overgaard, A., et al. (2001). "Patients' evaluation of shape, size and colour of solid dosage forms." Pharmacy World and Science **23**(5): 185-188.

**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
  - Marquis, J., et al. (2013). "Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies." International journal of clinical pharmacy **35**(6): 1130-1136.

**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
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- Delayed transit in supine position is so common that size and shape does not impact transit
  - Channer, K. S. and J. P. Virjee (1986). "The effect of size and shape of tablets on their esophageal transit." The Journal of Clinical Pharmacology **26**(2): 141-146.
- Large tablets should be taken standing, and should stay standing for at least 90 seconds
  - Hey, H., et al. (1982). "Oesophageal transit of six commonly used tablets and capsules." Br Med J (Clin Res Ed) **285**(6356): 1717-1719.

**Empirical summary: always take pills while upright**

# Known consumer behaviors affecting deglutition

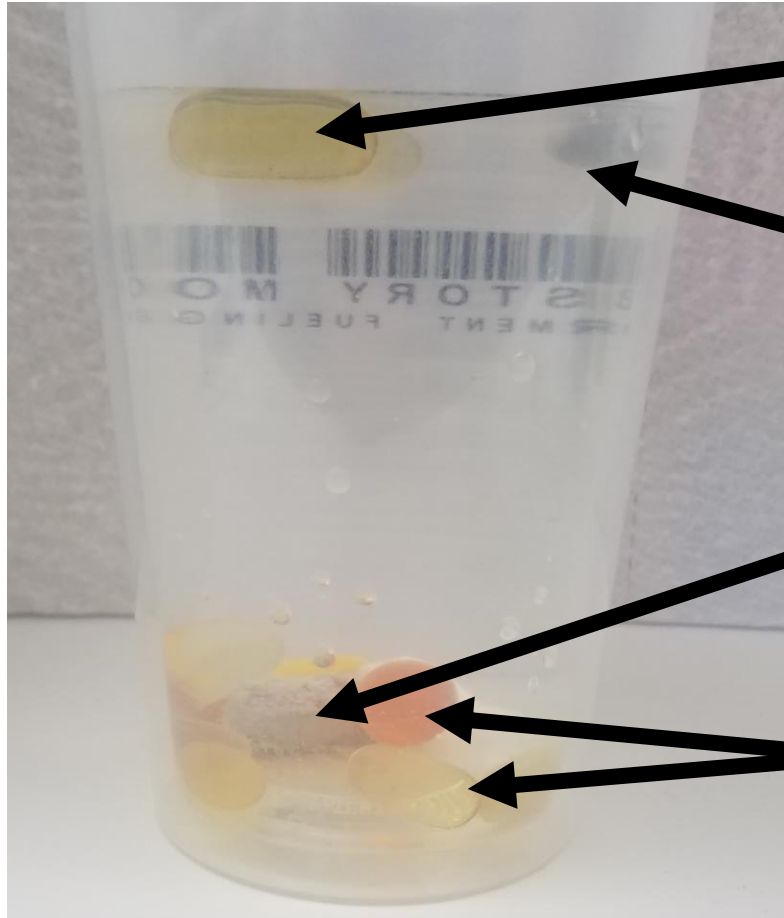
## Head position

- 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
  - Schiele, J. T., et al. (2013). "Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms." European journal of clinical pharmacology **69**(4): 937-948.
- Head down or head straight are preferred to head back as head back opens airway more readily
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.
- Chin tuck is supported by literature to prevent aspiration in dysphagia
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.

**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

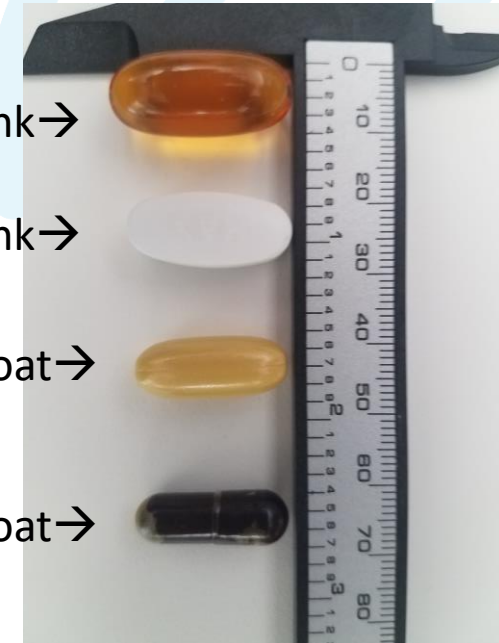


Evening  
primrose oil,  
starflower oil

Capsule

Multivit tablet

Fish oil capsules,  
large and small



Sink →

Sink →

Float →

Float →

**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.**

# 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
  - Bailey Jr, R. T., et al. (1987). "Factors influencing the transit of a gelatin capsule in the esophagus." Drug intelligence & clinical pharmacy **21**(3): 282-285.
- 100mL fluid preferable to 25mL fluid in all cases, **but elderly had some problems swallowing 100 mL**
  - Hey, H., et al. (1982). "Oesophageal transit of six commonly used tablets and capsules." Br Med J (Clin Res Ed) **285**(6356): 1717-1719.
- 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
  - Schiele, J. T., et al. (2013). "Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms." European journal of clinical pharmacology **69**(4): 937-948.
- 10-20mL fluid is necessary for peristalsis
  - Hey, H., et al. (1982). "Oesophageal transit of six commonly used tablets and capsules." Br Med J (Clin Res Ed) **285**(6356): 1717-1719.
- Subjects using 50mL water had faster, less variable, and less adherent swallowing activities than subjects using 30mL water (uncoated tablets)
  - McCargar, L., et al. (2001). "The in-vitro porcine adhesion model is not predictive of the esophageal transit of risedronate tablets in humans." International journal of pharmaceutics **222**(2): 191-197.
- 40 mL was deemed to be the cutoff for acceptable amount of fluid for swallowing
  - Hofmanová, J., et al. (2019). "Developing methodology to evaluate the oral sensory features of pharmaceutical tablet coatings." International journal of pharmaceutics **562**: 212-217.

**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
  - Robertson, C. S. and J. G. Hardy (1988). "Oesophageal transit of small tablets." Journal of pharmacy and pharmacology **40**(8): 595-596.
- 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
  - Fields, J., et al. (2015). "Pill properties that cause dysphagia and treatment failure." Current Therapeutic Research **77**: 79-82.
- 82.8% of patients preferred taking a small soft gel capsule 2x per day rather than 1 tablet once/day
  - Bhosle, M., et al. (2009). "Difficult to swallow: patient preferences for alternative valproate pharmaceutical formulations." Patient preference and adherence **3**: 161.
- At least 2% of patients think swallowing too many tablets at once causes swallowing difficulties
  - Marquis, J., et al. (2013). "Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies." International journal of clinical pharmacy **35**(6): 1130-1136.

**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
  - Ellin, A. (2015). "Can't Swallow a Pill? There's Help for That." 2020, from <https://well.blogs.nytimes.com/2015/09/21/cant-swallow-a-pill-theres-help-for-that/>.
- Some individuals have never been taught pill swallowing, so do not have proper knowledge
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.
- Verbal praise, relaxation techniques, imitation, and repetition can improve pill-swallowing difficulties
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.

**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
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.
- Pill coating devices potentially very efficacious
  - Forough, A. S., et al. (2018). "A spoonful of sugar helps the medicine go down? A review of strategies for making pills easier to swallow." Patient preference and adherence **12**: 1337.
  - 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
  - Smart, J. D., et al. (2013). "An in vitro model for the evaluation of the adhesion of solid oral dosage forms to the oesophagus." International journal of pharmaceuticals **447**(1-2): 199-203.
- Pig oesophagus not representative in 1 case: select model carefully
  - McCargar, L., et al. (2001). "The in-vitro porcine adhesion model is not predictive of the esophageal transit of risedronate tablets in humans." International journal of pharmaceuticals **222**(2): 191-197.
- Advanced in vitro model
  - Marconati, M., et al. (2018). "An in vitro experiment to simulate how easy tablets are to swallow." International journal of pharmaceuticals **535**(1-2): 27-37.

**Empirical summary: physical swallowing models exist but will require substantial investment and validation to be predictive**

# Methods of pill evaluation

## Mathematical modeling

- Bloomfield, J., et al. (2010). "Mathematical modelling of the normal swallow."
- Studies are available on several parameters of different swallowing-related processes that could be incorporated into models, such as
  - **Pharyngeal pressures:** Rosen, S. P., et al. (2017). "Pharyngeal swallowing pressures in the base-of-tongue and hypopharynx regions identified with three-dimensional manometry." The Laryngoscope **127**(9): 1989-1995.
  - **Pharyngeal timings:** Walczak, C. C., et al. (2017). "Pharyngeal pressure and timing during bolus transit." Dysphagia **32**(1): 104-114.

**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
  - Kelly, J., et al. (2010). "Patients with dysphagia: experiences of taking medication." Journal of advanced nursing **66**(1): 82-91.
- Review on several items that supports everything discussed so far: size, shape, coating, density
  - Liu, F., et al. (2014). "Patient-centered pharmaceutical design to improve acceptability of medicines: similarities and differences in paediatric and geriatric populations." Drugs **74**(16): 1871-1889.
- Modification in a care setting
  - Mc Gillicuddy, A., et al. (2017). "Oral medicine modification for older adults: a qualitative study of nurses." BMJ open **7**(12): e018151.
- General problems with pill-taking experience from start to finish (focus on medications but applicable everywhere)
  - Notenboom, K., et al. (2014). "Practical problems with medication use that older people experience: a qualitative study." Journal of the American Geriatrics Society **62**(12): 2339-2344.
- Difficulties swallowing pills is still prevalent in people *without* dysphagia
  - Souza, L. F., et al. (2019). "Medication swallowing difficulties in people without dysphagia." Revista CEFAC **21**(4).

# 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\*\*\***

Bülow, M., Olsson, R., & Ekberg, O. (1999). Videomanometric analysis of supraglottic swallow, effortful swallow, and chin tuck in healthy volunteers. *Dysphagia*, 14(2), 67-72.

Ekberg, O. (Ed.). (2012). *Dysphagia: diagnosis and treatment*. Springer Science & Business Media.



# 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:

**Directions** Swallow 1 capsule at a time and take in an upright position. Bulk-forming fibers like psyllium husk may affect how well medicines work. Take this product at least 2 hours before or after medicines. **New Users:** Start with 1 serving per day; gradually increase to desired daily intake. You may initially experience changes in bowel habits or minor bloating, as your body adjusts to increased fiber intake.

**NOTICE:** Take this product with at least 8 oz (a full glass) of liquid. Taking without enough liquid may cause choking. Do not take if you have difficulty swallowing. **Allergy alert:** This product may cause allergic reaction in people sensitive to inhaled or ingested psyllium.

Contact your doctor **BEFORE USING** this dietary supplement if you have recently experienced a sudden change in bowel habits persisting for 2 weeks, abdominal pain, nausea or vomiting.

# 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?