**CONTINUᴇᴅ**

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- Use a hardwired Internet connection
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- Call 800-753-2160 (M-F, 8 AM-8 PM ET)
- Email customerservice@AudiologyOnline.com

**continued**

CONTINU**ED**

# Understanding the Hearing Loss- Dementia Relationship: What Epidemiologic Studies Can and Cannot Tell Us

## Jennifer A. Deal, PhD

Assistant Professor | Epidemiology | Otolaryngology-Head and Neck Surgery

Associate Director of Academic Training | Cochlear Center for Hearing and Public Health

Johns Hopkins University

1

CONTINU**ED**

# Course Description

This presentation will review and evaluate recent public health research that demonstrates the implications of hearing loss for the health and functioning of older adults, particularly with respect to cognitive functioning, brain aging, and dementia. It will focus on the strengths and limitations of epidemiologic research in order to provide practicing audiologists with some basic tools needed to interpret and apply epidemiologic research in the clinical setting, as well as to define priorities for future research.

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**conTINUED**

- **Presenter Disclosure:** Financial: Jennifer A. Deal is an Assistant Professor of Epidemiology and Otolaryngology-Head & Neck Surgery at the Johns Hopkins University and Core Faculty and Associate Director for Academic Training with the Johns Hopkins Cochlear Center for Hearing and Public Health. She received an honorarium for this presentation. Non-financial: Jennifer A. Deal has no relevant non-financial relationships to disclose.

- **Content Disclosure:** This learning event does not focus exclusively on any specific product or service.

- **Sponsor Disclosure:** This course is presented by SpeechTherapy.com.

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**conTINUED**

# Learning Outcomes

After this course, participants will be able to:

- Summarize and interpret current epidemiologic evidence for an association between hearing loss and dementia and cognitive decline in older adults.

- Evaluate potential explanations for epidemiologic associations between hearing loss and dementia and cognitive decline in older adults.

- Identify key epidemiologic and public health questions pertaining to hearing loss and gerontology/geriatrics that remain unanswered.

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# Agenda

| 0-5 Minutes | Introduction |
|---|---|
| 5-15 Minutes | 1. Brief overview of epidemiology and its role in public health |
| 15-25 Minutes | 2. Review of current evidence supporting a relationship between hearing loss and dementia |
| 25-45 Minutes | 3. Evaluation of the evidence |
| 45-55 Minutes | 4. Implication for clinical practice and future research |
| 55-60 Minutes | 5. Summary, Q & A |

5

**continuED**

# Motivation

For Better Brain Health, Preserve Your Hearing

Hearing loss is the largest modifiable risk factor for developing dementia, exceeding that of smoking, high blood pressure, lack of exercise and social isolation.

https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

Brody, J. E. (2019, December 30). For Better Brain Health, Preserve Your Hearing. Retrieved July 07, 2020, from https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

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**continuED**

## Slide 7

CONTINUED

# Motivation

> For Better Brain Health, Preserve Your Hearing
>
> Hearing loss is the largest modifiable risk factor for developing dementia, exceeding that of smoking, high blood pressure, lack of exercise and social isolation.

https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

- *Is this true?*

Brody, J. E. (2019, December 30). For Better Brain Health, Preserve Your Hearing. Retrieved July 07, 2020, from
https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

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## Slide 8

CONTINUED

# Motivation

> For Better Brain Health, Preserve Your Hearing
>
> Hearing loss is the largest modifiable risk factor for developing dementia, exceeding that of smoking, high blood pressure, lack of exercise and social isolation.

https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

- *Is this true?*
- *What is/how do we interpret the evidence?*

Brody, J. E. (2019, December 30). For Better Brain Health, Preserve Your Hearing. Retrieved July 07, 2020, from
https://www.nytimes.com/2019/12/30/well/live/brain-health-hearing-dementia-alzheimers.html

8

CONTINUED

# 1. Epidemiology & Its Role in Public Health

9

## What is Epidemiology?

The study of how disease is distributed in populations & what factors influence or determine this distribution

Porta, Miquel S. *A Dictionary of Epidemiology.* 5th ed. Oxford: Oxford University Press, 2008

10

**CONTINU ED**

What is Epidemiology?

The study of how [disease] is distributed in populations & what factors influence or determine this distribution

& other health states

Porta, Miquel S. *A Dictionary of Epidemiology.* 5th ed. Oxford: Oxford University Press, 2008

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What is Epidemiology?

The study of how [disease] is distributed in ☆populations & what factors influence or determine this distribution

Porta, Miquel S. *A Dictionary of Epidemiology.* 5th ed. Oxford: Oxford University Press, 2008

12

**continued**

# Why Epidemiology?

- Assess burden of disease
- Determine causes of disease
- Study natural history & prognosis of disease
- Evaluate interventions
- Inform policy
- Inform the public

Celentano DD, Szklo M, Gordis L. *Gordis Epidemiology.* Sixth edition. Philadelphia, PA: Elsevier, 2019.

13

**continued**

# An Epidemiologist's Toolbox

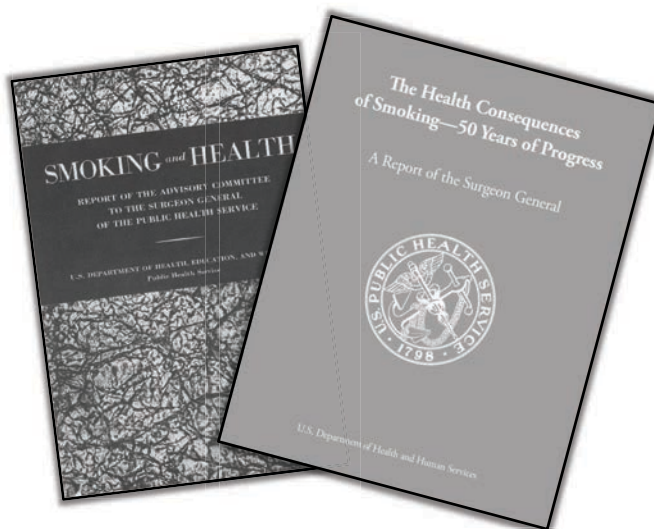- Experimental studies
- Observational studies

14

**continued**

# An Epidemiologist's Toolbox

- Experimental studies ← Randomized Trials
- Observational studies ← Our focus today

15

# Sometimes We're Successful…



SMOKING and HEALTH

REPORT OF THE ADVISORY COMMITTEE
TO THE SURGEON GENERAL
OF THE PUBLIC HEALTH SERVICE

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

The Health Consequences
of Smoking—50 Years of Progress

A Report of the Surgeon General

U.S. Department of Health and Human Services

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**continuED**

**continuED**

# Sometimes We Fail…

## Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women
Principal Results From the Women's Health Initiative Randomized Controlled Trial

Writing Group for the Women's Health Initiative Investigators. *JAMA.* 2002;288(3):321–333.

17

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**continuED**

# And Sometimes … ?

## Foods That Are Surprisingly Bad for Your Cholesterol
Your morning cup of joe just might give your cholesterol level an unwanted jolt. French press or Turkish coffee lets through cafestol, which raises levels of LDL, or "bad," cholesterol. Espresso does too, but serving sizes are small, so there's less to worry about.  If you drink drip coffee, you're in the clear. The filter catches cafestol, so stick to drip.

webmd.com/cholesterol-management/ss/slideshow-surprising-cholesterol-foods

Foods That Are Surprisingly Bad for Cholesterol. (n.d.). Retrieved July 07, 2020, from
https://www.webmd.com/cholesterol-management/ss/slideshow-surprising-cholesterol-foods

18

**continuED**

## And Sometimes … ?

**Foods That Are Surprisingly Bad for Your Cholesterol**

Your morning cu... your cholesterol level an unwanted jolt. French pres... ...stol, which raises levels of LDL, or "bad... ...are small, so there's less... The filter catches cate...

webmd.com/cholesterol-management...

**Three cups of coffee a day 'may have health benefits'**

bbc.com/news/health-42081278

Foods That Are Surprisingly Bad for Cholesterol. (n.d.). Retrieved July 07, 2020, from
https://www.webmd.com/cholesterol-management/ss/slideshow-surprising-cholesterol-foods

19

## And Sometimes … ?

**Foods That Are Surprisingly Bad for Your Cholesterol**

Your morning cup of joe just might give your cholesterol ... ...nted jolt. French press or Turkish ... ...vels of LD... ...all,

...erol-foods

**California judge rules that coffee requires cancer warning**

- A California judge said coffee sellers in the state should have to post cancer warnings.
- The culprit is a chemical produced in the bean roasting process that is a known carcinogen and has been at the heart of an eight-year legal struggle between a tiny nonprofit group and Big Coffee.

cnbc.com/2018/03/30/california-judge-rules-that-coffee-requires-cancer-warning.html

...efits'
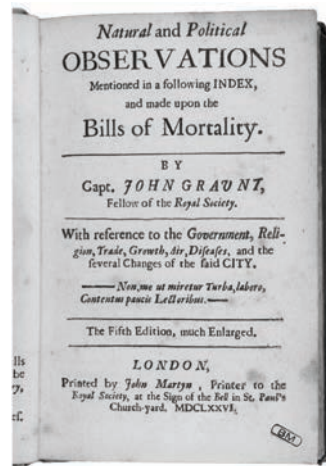
...offee a day 'may have

bbc.com/news/health-42081278

Foods That Are Surprisingly Bad for Cholesterol. (n.d.). Retrieved July 07, 2020, from
https://www.webmd.com/cholesterol-management/ss/slideshow-surprising-cholesterol-foods

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**continuED**

## continuED

# Why is Epidemiology Useful?

Natural and Political
OBSERVATIONS
Mentioned in a following INDEX,
and made upon the
Bills of Mortality.

BY
Capt. JOHN GRAUNT,
Fellow of the Royal Society.

With reference to the Government, Religion, Trade, Growth, Air, Diseases, and the several Changes of the said CITY.

—— Non, me ut miretur Turba, labero,
Contentus paucis Lectoribus.——

The Fifth Edition, much Enlarged.

LONDON,
Printed by John Martyn, Printer to the
Royal Society, at the Sign of the Bell in St. Paul's
Church-yard, MDCLXXVI.

### John Graunt
### (1620 - 1674)

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## continuED

# Graunt's Bills of Mortality



THE TABLE OF CASUALTIES

- At a population level, we can see (and predict!) patterns that we cannot discern at the level of the individual

22

## continuED

## Why Epidemiology?

- Assess burden of disease
- Determine causes of disease
- Study natural history & prognosis of disease
- Evaluate interventions
- Inform policy
- Inform the public

Important! But we can also get into trouble…
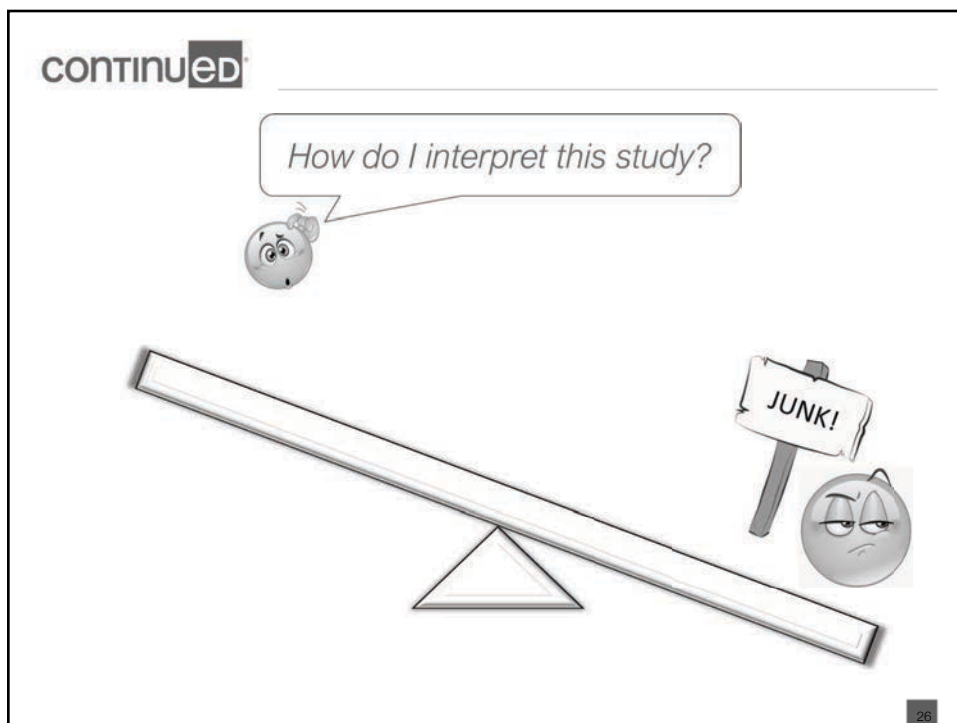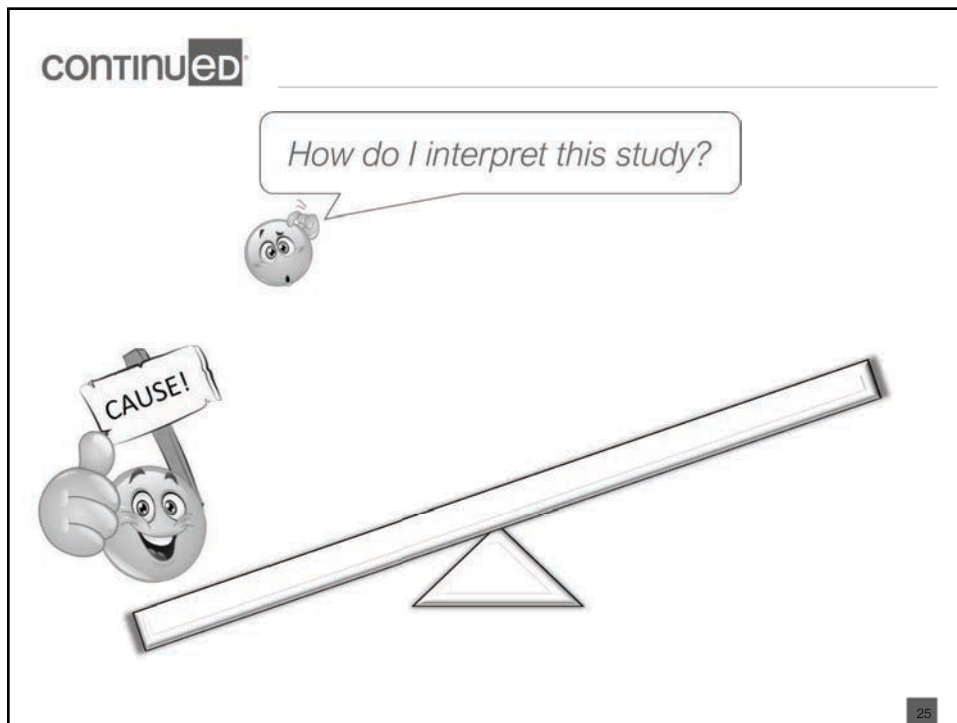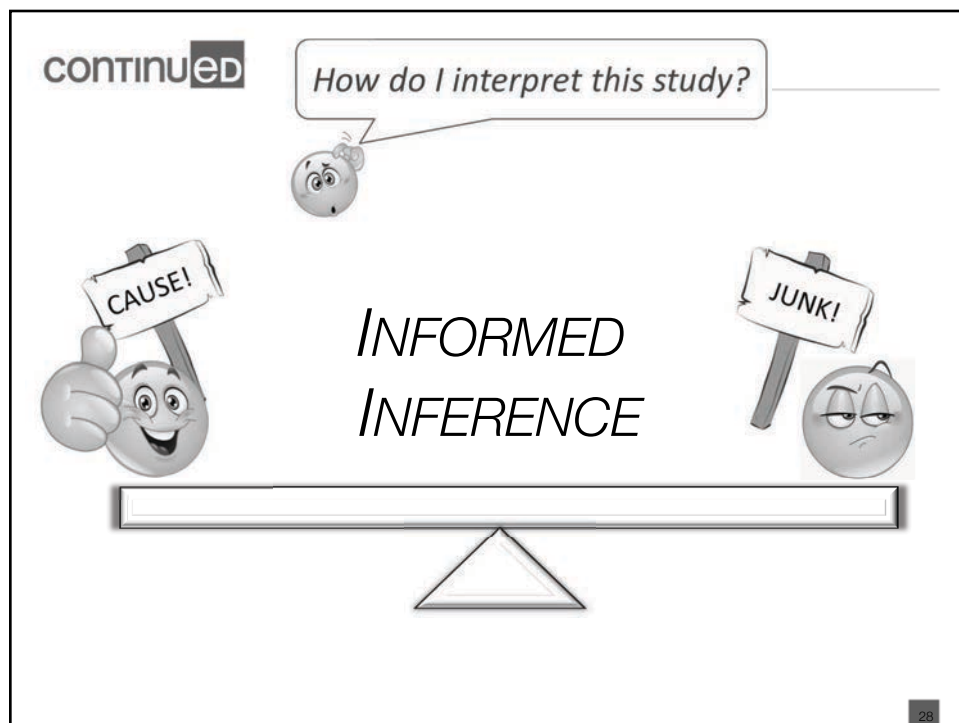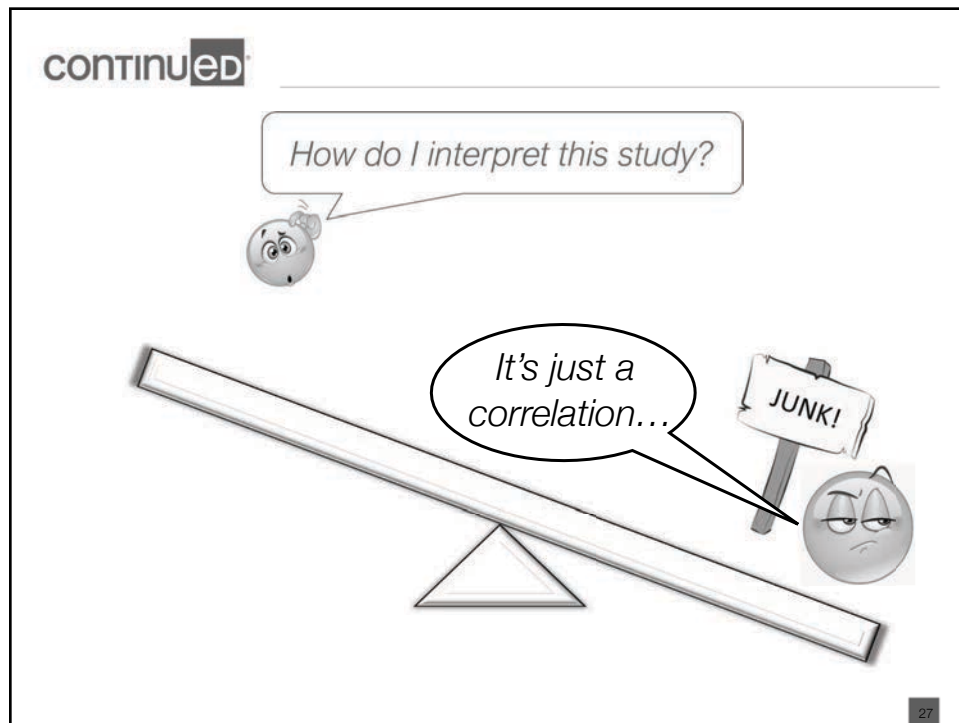
23



*How do I interpret this study?*

Perspectives:
- Patient & Family
- Healthcare provider
- Journalist
- Epidemiologist
- Statistician
- Policymaker

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**CONTINUED**

# 1. Epidemiology - Summary

- Epidemiology = the science of public health
- Identify associations between and exposure & outcome at the *population-level*
- More than a correlation, but not always a cause
- Need for care in interpreting results
  - Balancing uncertainty & needs of different stakeholders

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**CONTINUED**

# 2. Hearing Loss & Dementia: A Review of the Evidence

30

**CONTINUED**

**CONTINU ED**

> *"Dementia is the greatest global challenge for health and social care in the 21st century"*

Livingston et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734

31

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**CONTINU ED**

## The Cost of Dementia

### FRAYING AT THE EDGES

By N.R. Kleinfeld

A withered person with a scrambled mind, memories sealed away: This is the familiar face of Alzheimer's. But there is also the waiting period….

https://www.nytimes.com/interactive/2016/05/01/nyregion/living-with-alzheimers.html

Kleinfeld, N. (2016, April 30). Fraying at the Edges: Her Fight to Live With Alzheimer's. Retrieved July 07, 2020, from
https://www.nytimes.com/interactive/2016/05/01/nyregion/living-with-alzheimers.html

32

**CONTINU ED**

**CONTINU㉫D**

# Dementia: What Can We Do?

- No treatments alter the natural history of dementia
- *Prevention!*

33

**CONTINU㉫D**

# State of Dementia Prevention

- The Lancet Commission on Dementia Prevention, Intervention and Care determined the global risk of dementia associated with a number of modifiable risk factors:

- **Hearing loss – 9%**
- Less education – 8%
- *APOE* e4 – 7%
- Smoking – 5%
- Depression – 4%
- Physical inactivity – 3%
- Hypertension – 2%
- Social isolation – 2%
- Obesity – 1%
- Diabetes – 1%

Livingston et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734

34

**CONTINU㉫D**

**CONTINU€D**

# Interpretation

**9%** of dementia in the world is
due to hearing loss &
could have been prevented
if no one in the world
had hearing loss*

*Assumes no bias, no confounding, and
that hearing loss causes dementia

Livingston et al. Lancet Commission 2017

Livingston et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734

35

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**CONTINU€D**

# Why is Potential Impact of Hearing Loss So Great?

1. Hearing loss impacts a large proportion of older adults
2. The association between hearing loss and dementia is stronger than for other risk factors

Livingston et al. Lancet Commission 2017

**Q6** 36

**CONTINU€D**

**continu**ed

## Hearing Loss & Dementia – Strength of the Association

| Study | Relative Risk (95% Confidence Interval) |
|---|---|
| Lin et al. 2011 | 2.32 (1.32 – 4.07) |
| Gallacher et al. 2012 | 2.67 (1.38 – 5.17) |
| Deal et al. 2016 | 1.55 (1.10 – 2.19) |
| Overall | 1.94 (1.38 – 2.73) |

Livingston et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734

37

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**continu**ed

## 2. Reviewing the Evidence - Summary

- Individual epidemiologic studies consistently show an association between hearing loss & dementia

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**continu**ed

**CONTINUED**

## 2. Reviewing the Evidence - Summary

- Individual epidemiologic studies consistently show an association between hearing loss & dementia

*How do I interpret these studies?*

39

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**CONTINUED**

# 3. Hearing Loss & Dementia: Evaluating the Evidence

40

**CONTINUED**

**continu⊡D**

## Possible Reasons for Associations

- Bias
  - Selection bias
  - Information bias
  - Confounding
- Chance

41

**continu⊡D**

## Possible Reasons for Associations

- Bias
  - Selection bias
  - Information bias
  - Confounding
- Chance

Bias can occur at the phase of the study design, conduct, analysis or interpretation

**Q7** 42

**continu⊡D**

Evaluating Non-Causal Reasons
for an Association

- Bias
  - Selection bias          Epidemiology
  - Information bias
  - Confounding             Clinical Knowledge
- Chance                     Statistics

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Possible Reasons for Associations

- Bias
  - Selection bias
  - Information bias
  - Confounding
- Chance
- **Cause**

44

## What is a cause?

A DICTIONARY OF
**EPIDEMIOLOGY**
EDITED BY
MIQUEL PORTA

**ETIOLOGY**

Literally, the science of causes, causality; in common usage, cause.

- A ➞ B
- If A changes, does B change?

Porta, Miquel S., et al. *A Dictionary of Epidemiology.* Sixth edition / Oxford: Oxford University Press, 2014.

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## Guidelines for Judging if an Association is Causal

1. Temporal relationship
   - The only guideline that <u>must</u> be met
2. Strength of the association
3. Dose-response relationship
4. Replication of the findings
5. Cessation of exposure
6. Biologic plausibility
7. Consider alternate explanations
8. Consistency with other knowledge
9. Specificity of the association

If met, it is less likely that an observed association is due to bias

Hill AB. Proc R Soc Med 1965;58:295-300
https://en.wikipedia.org/wiki/Austin_Bradford_Hill#/media/File:Austin_Bradford_Hill.jpg

**Q4** 46

## Slide 47

**CONTINUED**

# Guidelines for Judging if an Association is Causal

1. Temporal relationship
   - The only guideline that <u>must</u> be met
2. Strength of the association
3. Dose-response relationship
4. Replication of the findings
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Hill AB. Proc R Soc Med 1965;58:295-300
https://en.wikipedia.org/wiki/Austin_Bradford_Hill#/media/File:Austin_Bradford_Hill.jpg
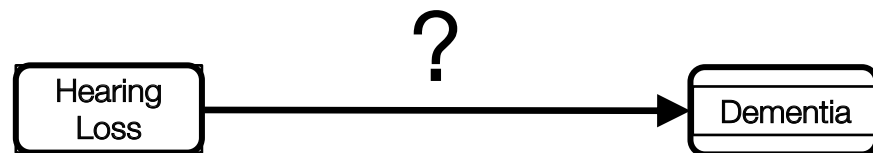
47

## Slide 48

**CONTINUED**

We *don't* know
if hearing loss causes dementia &
cognitive decline,
but there are some pathways through
which we think it might.

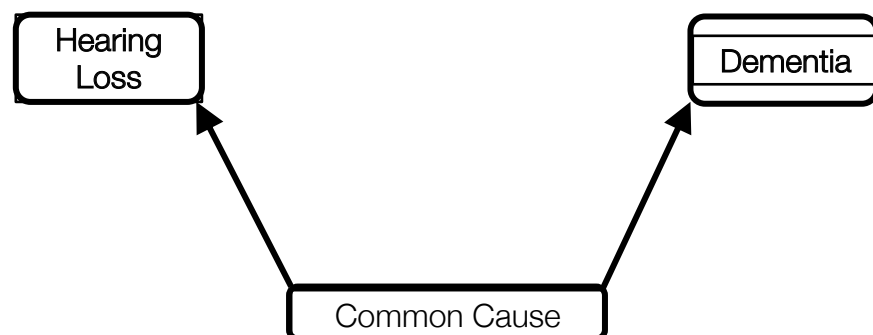**Q5** 48

**CONTINUED**

Pathways Linking Hearing & Dementia

Lin and Albert. 2014 Aug;18(6):671-673

49



Pathways Linking Hearing & Dementia

Lin and Albert. 2014 Aug;18(6):671-673

**Q1** 50

**continued**

# Pathways Linking Hearing & Dementia



```
           Cognitive Load
          /              \
  Hearing                 Dementia
   Loss                  /
      \                 /
        Common Cause
```
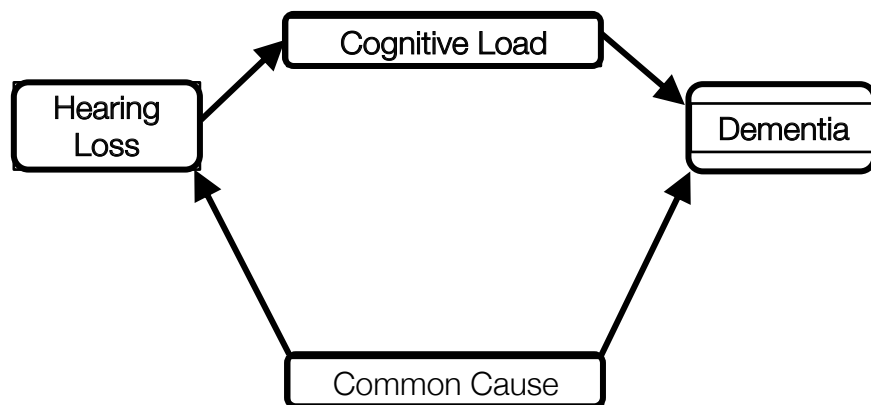
Lin and Albert. Aging Ment Health. 2014 Aug;18(6):671-673

51

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**continued**

# Increased Cognitive Load

Cognitive Load

- Hearing
  - Peripheral transduction of sound in cochlea, followed by
  - Central processing in brain

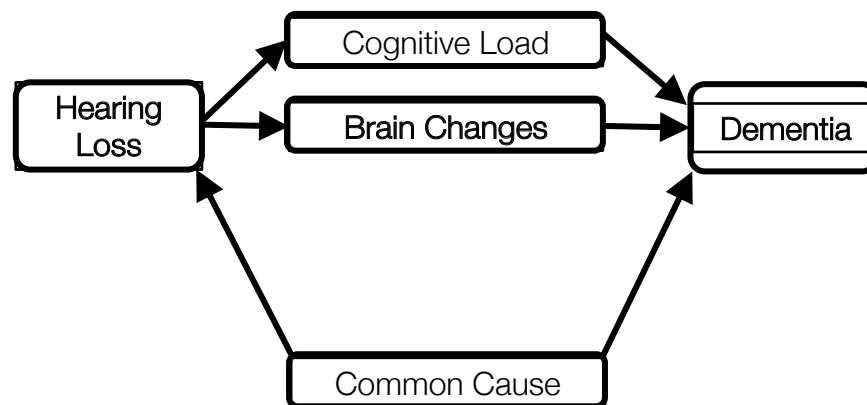- With cochlear impairment, decreased sensitivity & distortion in sound encoding

- Effortful listening"

52

**continued**

Pathways Linking Hearing & Dementia

Lin and Albert. Aging Ment Health. 2014 Aug;18(6):671-673

53



Changes in Brain Structure/Function

Brain Changes

- Hearing loss → lower grey matter volume in primary auditory cortex

- Recruitment of executive networks (*outside* of primary auditory cortex) with hearing loss

- Hearing loss → faster rates of brain atrophy in temporal lobe & whole brain

Peelle JE et al. *J Neurosci*. 2011;31(35):12638-12643.
Lin FR et al. *Neuroimage*. 2014;90:84-92.

**Q9** 54
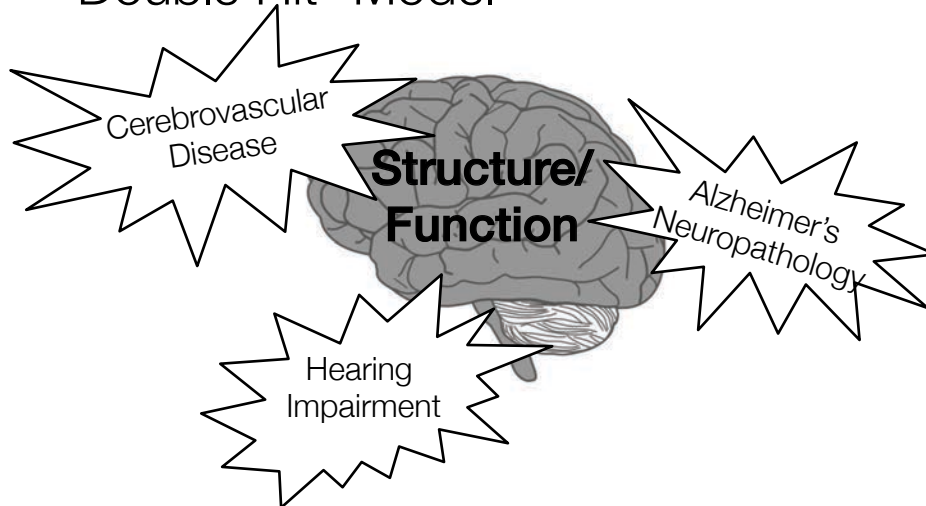
## "Double Hit" Model

Cerebrovascular Disease

**Structure/ Function**

Alzheimer's Neuropathology

Hearing Impairment

Lin and Albert. Aging Ment Health. 2014 Aug;18(6):671-673

55

## Pathways Linking Hearing & Dementia

Hearing Loss

Cognitive Load

Brain Changes

Social Isolation

Common Cause

Dementia
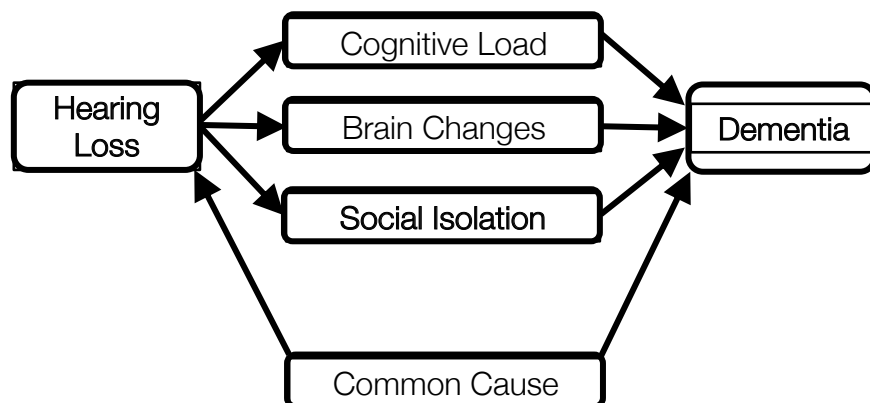
Lin and Albert. Aging Ment Health. 2014 Aug;18(6):671-673

56

## Hill on the Causal Guidelines

> Here then are nine different viewpoints from all of which we should study association before we cry causation. What I do not believe – and this has been suggested – is that we can usefully lay down some hard-and-fast rules of evidence that *must* be obeyed before we accept cause and effect. None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental question – is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?

Hill AB. Proc R Soc Med 1965;58:295-300

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## Hill on the Causal Guidelines: Take-Home Messages

- There is no checklist for understanding how to interpret the results of a study

- Each study will have strengths and limitations that must be considered
  - Role of bias? Chance?

- No study is ever perfect but they can be informative

58

*So where does that leave us?*

59

## From Evidence to Action

**Develop evidence**

Observations of people
 - individuals
 - groups

Human experiments

Other research

→

**Synthesize**

Systematic reviews

Meta-analysis

Other evidence

→

**Evaluate**

Expert judgment

Causal guidelines

↓

| ACTION | ← | DECISION | ← | INFERENCE |
|---|---|---|---|---|
| Medical, Public Health Implementation | | Authoritative Bodies | | |

60

# Where Does Epidemiology Fit?

**Develop evidence**

Observations of people
 - individuals
 - groups

Human experiments

Other research

**Synthesize**

Systematic reviews

Meta-analysis

Other evidence

**Evaluate**

Expert judgment

Causal guidelines

ACTION
Medical,
Public Health
Implementation

DECISION
Authoritative
Bodies

INFERENCE

---

Except in the rare case of some definitive clinical trials, cause can <u>never</u> be determined from one study

**CONTINUED**

## 3. Evaluating the Evidence - Summary

- We don't know if hearing loss causes dementia
- But*:
  - Results of multiple studies in multiple populations are consistent
  - Overall, estimated association is strong
  - Association is stronger as hearing loss increases
  - There are some pathways by which hearing loss might cause dementia
  - Studies have adjusted for confounders (age, comorbidity, etc.)
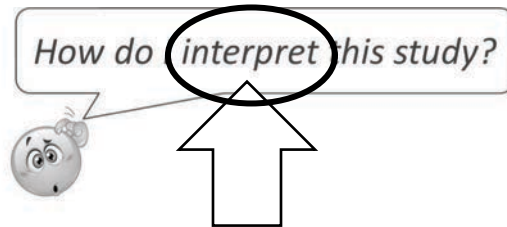- *Hill's Guidelines!*

63

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**CONTINUED**

# 4. Implications for Clinical Practice & Future Research

64

**CONTINUED**

- Suppose an epidemiologic study gives the TRUE relative risk for an exposure-disease association
- No bias, no confounding, there is a causal relationship
- How do we interpret the relative risk for a patient?

65

## Poll: Assume the True RR for Hearing Loss & Dementia in Older Adults is 1.9

*How do we interpret this finding?*

A. If an older adult has hearing loss, they have a 90% increased risk of developing dementia

B. Older adults with hearing loss have, on average, a 90% increased risk of developing dementia compared to older adults without hearing loss

**Q3** 66

**continu**ED

## Assume the True RR for Hearing Loss & Dementia in Older Adults is 1.9

- We cannot determine individual risk from epidemiologic studies, which are, by nature, an average across the population (Graunt!)



**Q3** 67

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**continu**ED

## Interpreting a Population-Level Association for an Individual

- An individual's risk of developing dementia is 0 or 1. They will get it or not.

- Hearing loss may increase the risk, but that does not mean that everyone with hearing loss will get dementia

- The converse is also true, even if hearing loss is treated, the patient may still develop dementia

**Q3; Q10** 68

**continu**ED

## Future Research Needs

- Even if all of Hill's Guidelines are met, we can still get it wrong

- Recall…

  Sometimes We Fail…

  **Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women**
  Principal Results From the Women's Health Initiative Randomized Controlled Trial

  Writing Group for the Women's Health Initiative Investigators. *JAMA.* 2002;288(3):321–333.

- Why?

69

## Future Research Needs

- We can't always account for all bias

- For example, *do hearing aids prevent dementia*?
  - We don't know!

**Q5** 70

35

## Example: Hearing Aids & Dementia Prevention

- Studies are consistent, and suggest that hearing aids may delay dementia

- But hearing aid users are fundamentally different from non-users
  - Higher education
  - Higher SES
  - Greater utilization/access to healthcare

- These factors protect against dementia!

**Q8** 71

## Example: Hearing Aids & Dementia Prevention

- It is incredibly difficult to disentangle the effects of hearing aids from the effects of these other factors

- Randomized trials may help
  - Randomization & masking can help protect against bias

**Q2;Q8** 72

**continued**

## Final Consideration

- Even if a study is free of bias, the population studied may differ from the other groups (for example, the general US population)

- This may mean the study results are valid, but do not apply (are not *'generalizable'*) to the US population

- Just like we cannot directly apply results of a study to an individual, we also have to be careful, they may also <u>not</u> apply to other groups!

73

**continued**

## 4. Implications - Summary

- Results from population studies cannot generally be applied directly to an individual

- And they may also not (always) apply to other populations

- We do not know if hearing aids will prevent dementia – more studies (randomized trials) are needed

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**continued**

Thank you!
Questions?

jdeal1@jhu.edu
@JenniferADeal