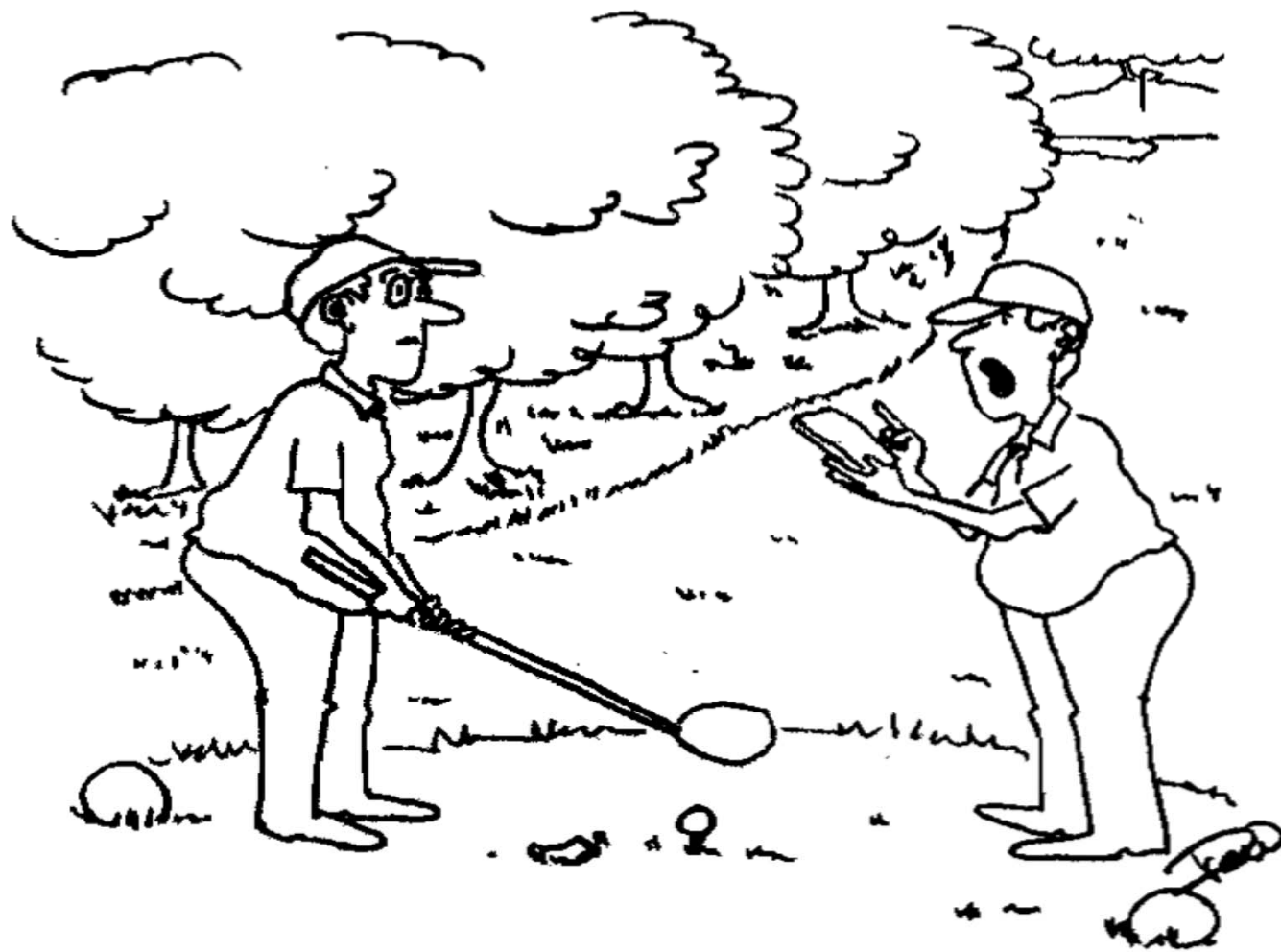




# CAUSATION-AN OVERVIEW

MARK H. HYMAN, MD, FACP, FIAIME



**“With this new app, I can examine patients from here!”**

# DISCLAIMERS

- The information for practitioners notes that decisions to adopt particular courses of actions must be made by trained practitioners and on the basis of the available resources and the particular circumstances presented by the individual patient. Accordingly, the above disclaims responsibility for any injury or damage resulting from actions taken by practitioners after considering these guides.

# DISCLAIMERS

- I DID NOT SAY WHAT YOU THOUGHT I SAID
- YOU DID NOT HEAR WHAT YOU THOUGHT YOU HEARD
- ANY STATEMENT THAT IS AN ERROR IS MY FAULT AND NOT THE FAULT OF MY CO-EDITORS OR CHAPTER AUTHORS
- Hospitality is the art of making guests feel like they're at home when you wish they were



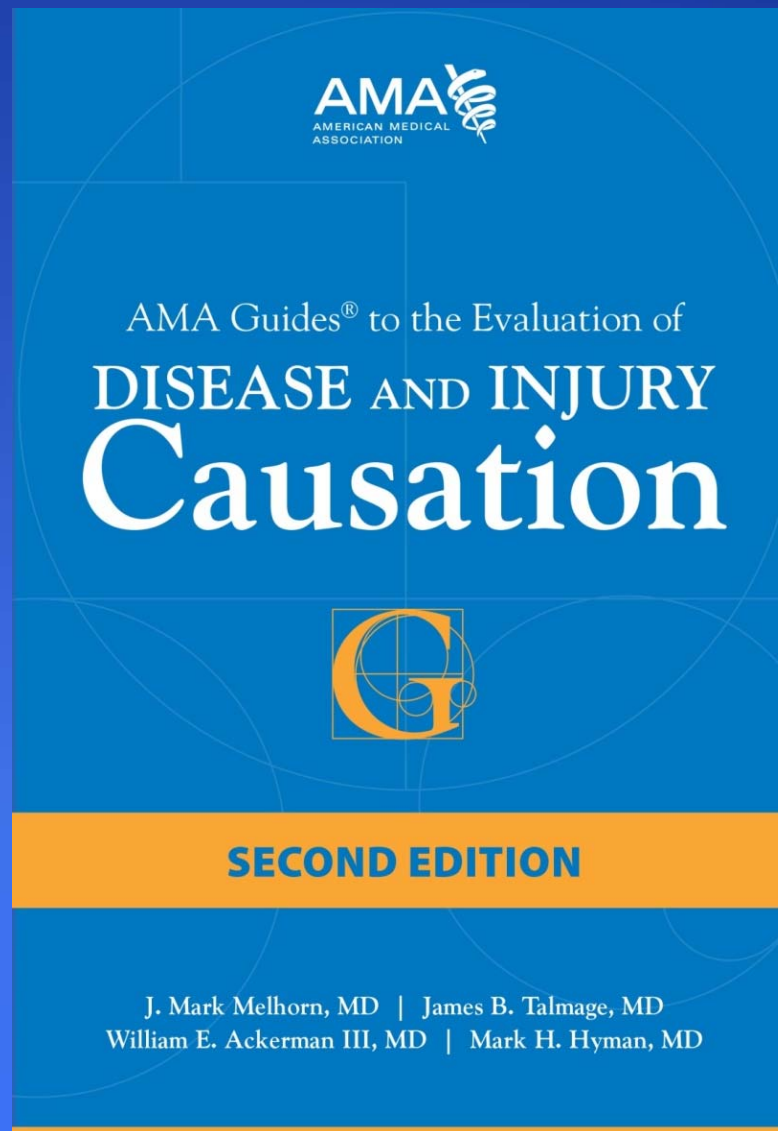
# ACKNOWLEDGMENTS

- J. MARK MELHORN AND JIM TALMAGE
- AMA
- IAIME
- ACOEM
- MD GUIDELINES BY THE REED GROUP
- MY FAMILY
- MY OFFICE STAFF



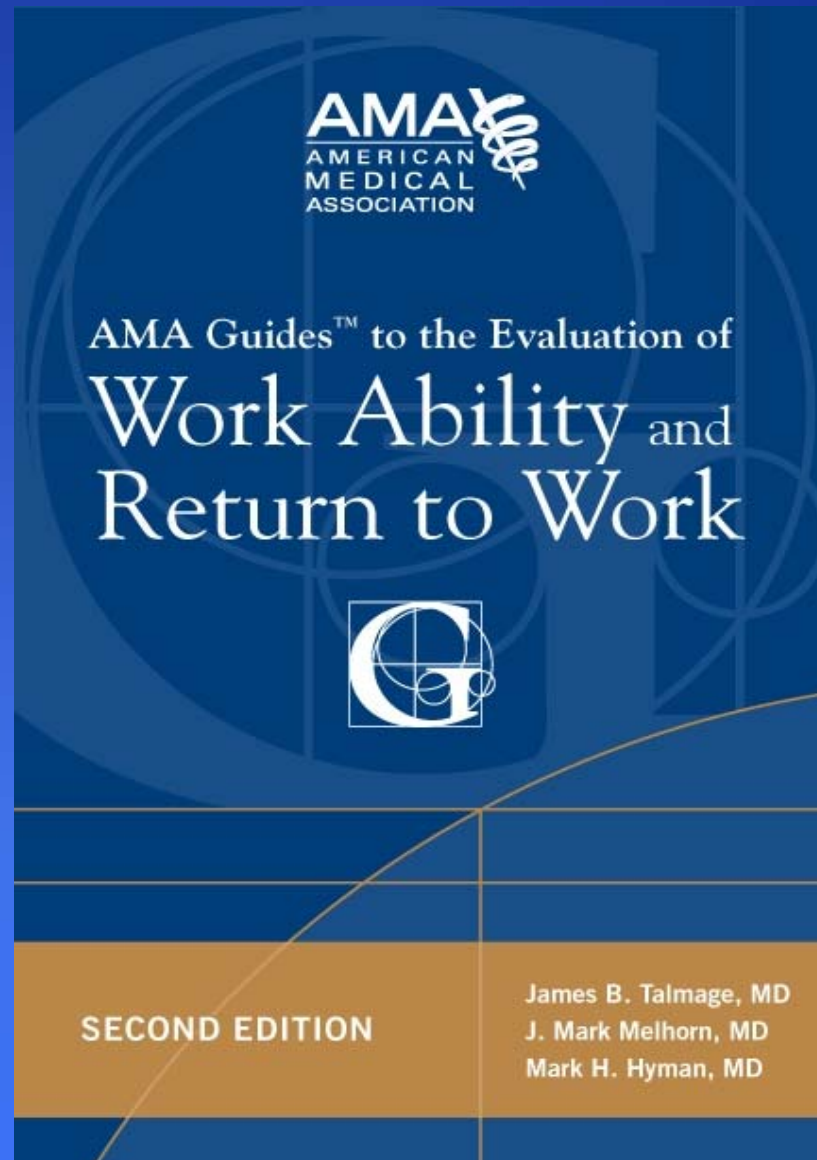
# FINANCIAL CONFLICT OF INTEREST

Editors  
WILL  
RECEIVE  
Royalties



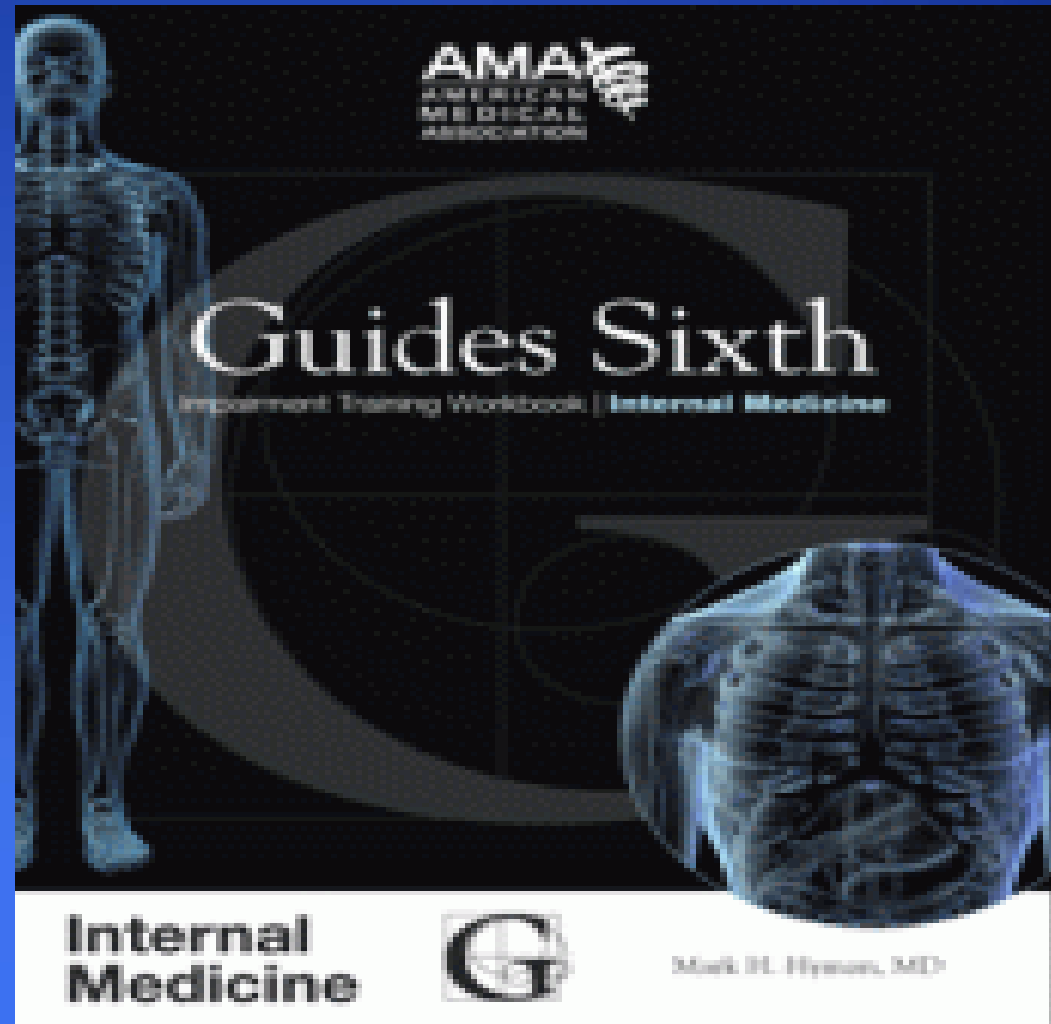
# FINANCIAL CONFLICT OF INTEREST

Editors  
WILL  
RECEIVE  
Royalties



# FINANCIAL CONFLICT OF INTEREST

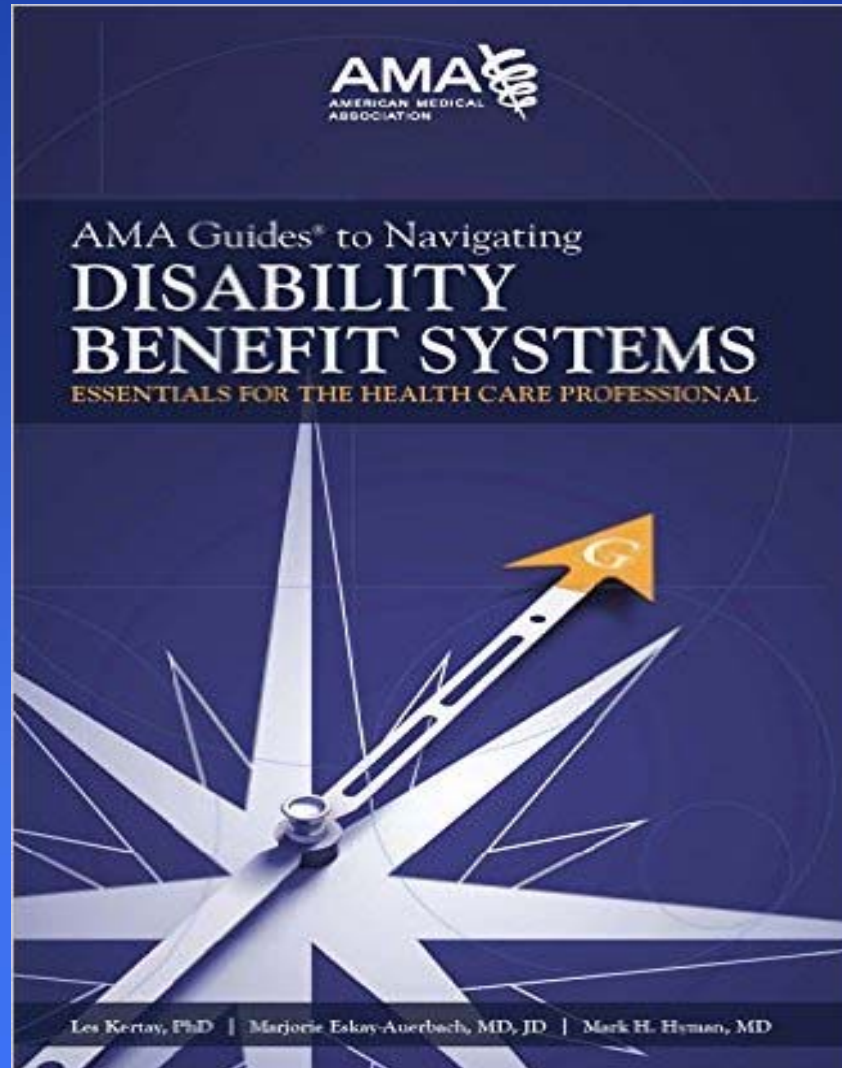
Editor(me)  
WILL  
RECEIVE  
Royalties





# FINANCIAL CONFLICT OF INTEREST

Editors  
WILL  
RECEIVE  
Royalties



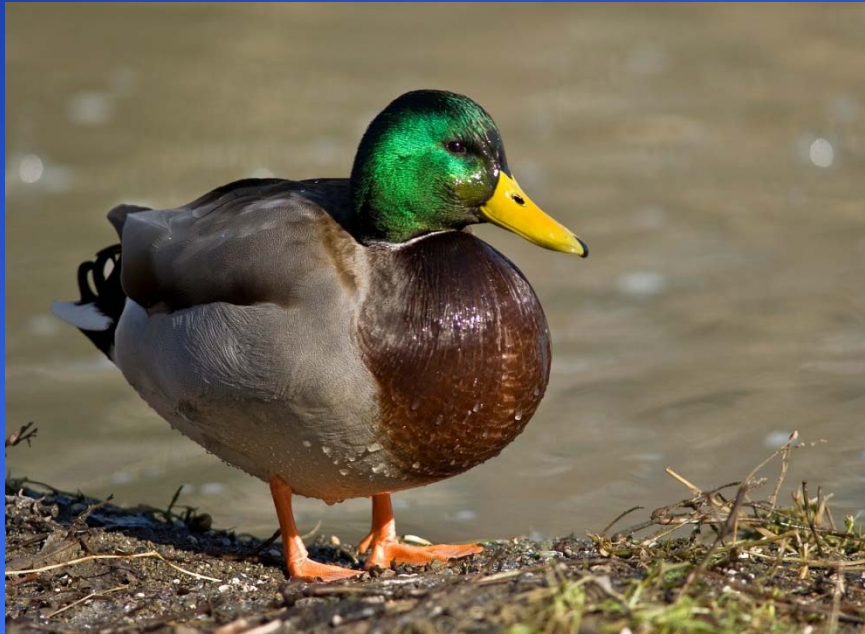
# FINANCIAL CONFLICT OF INTEREST

I AM A PAID CONSULTANT TO MD  
GUIDELINES WHICH MAY COME UP IN  
OUR DISCUSSION

I PRACTICE MEDICINE FULL TIME, I  
SUPPORT MY OFFICE STAFF AND MY  
FAMILY, SO I HAVE A FINANCIAL  
CONFLICT OF INTEREST BEING HERE AS  
OPPOSED TO BEING IN MY OFFICE

# Causation Example

Which Duck is more likely to find a mate?



A



B

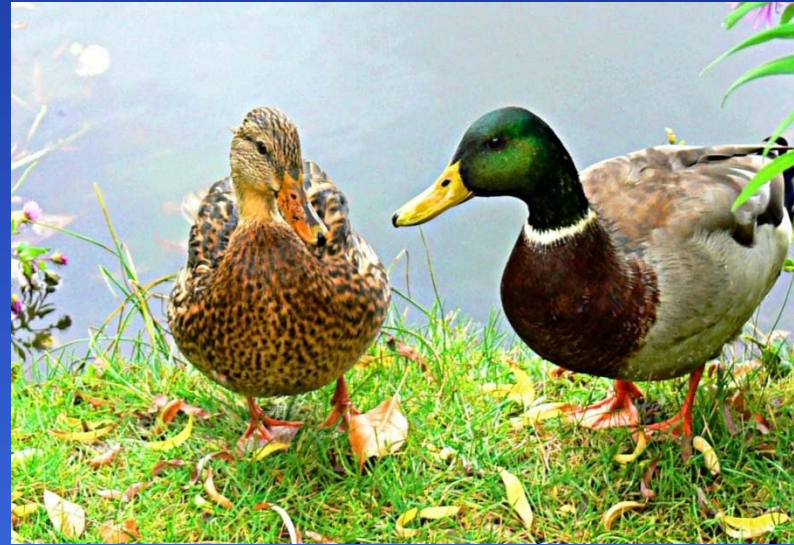
WHY ?



# Causation Example



A



B

Bright Orange Legs =  
Vitamins = beta-carotene  
More Antioxidants  
Better immune system  
Better genes = Better Mate

# Causation Example

What type of tree is hit by lightning more frequently than others?

- Simple question
- Frequency established
- What is the cause?



# Causation Example

What type of tree is hit by lightning more frequently than others?

- Hint
- National Tree
- Why?





# Causation Example

What type of tree is hit by lightning more frequently than others? OAK

1. Generally grows taller
2. Deeper roots
3. High moisture content
4. More conductive



# Causation Example

Who is more likely to have an ACL Strain - Tear from Jumping?

1. Males
2. Females
3. Tall people
4. Increased tibial slope angle

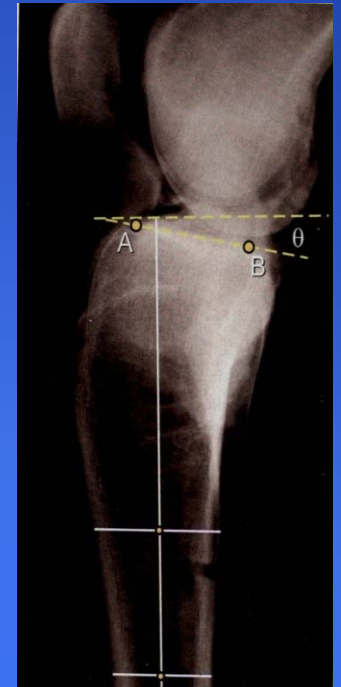


# Causation Example

Who is more likely to have an ACL Strain - Tear from Jumping?



1. ~~Males~~
2. Females
3. ~~Tall people~~
4. Increased tibial slope angle





# Causation Example

Long-term exposure to residential road traffic noise is associated with a higher risk of MI?

Yes

No



# Causation Example

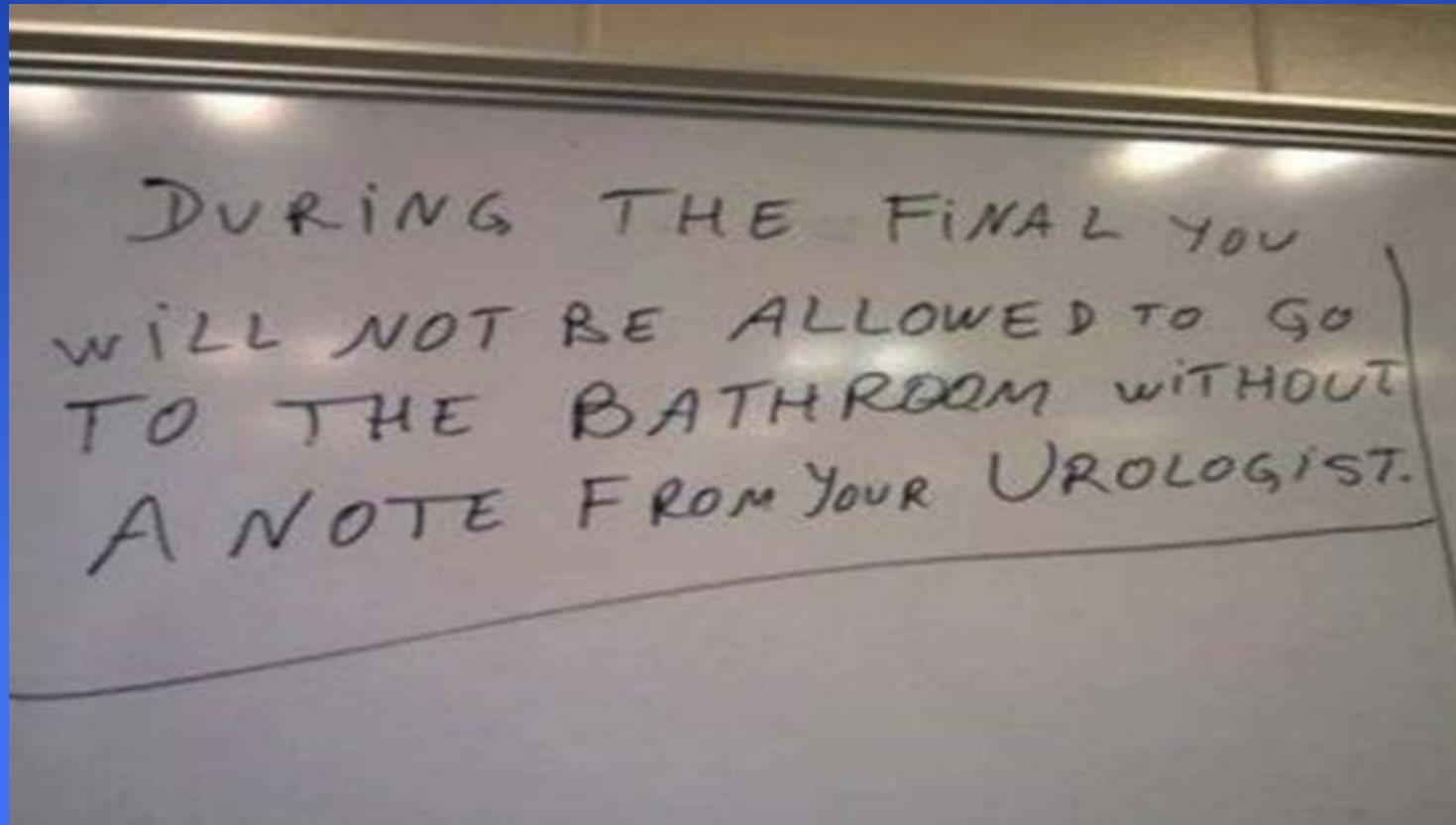
Yes

- Prospective cohort 57,053
- incidence rate ratio 1.12 per 10 dB
- Yearly exposures 95% CI: 1.02-1.22
- 5 years 95% CI: 1.02-1.23
- Linear dose-response relationship
- M. Sorensen, Z. J. Andersen, R. B. Nordsborg, S. S. Jensen, K. G. Lillelund, R. Beelen, E. B. Schmidt, A. Tjønneland, K. Overvad, and O. Raaschou-Nielsen. Road traffic noise and incident myocardial infarction: a prospective cohort study. PLoS One 7 (6):e39283, 2012.



# Causation Example

Coffee-Does it lead to worse health outcomes?



# Causation Example

Coffee-Does it lead to worse health outcomes?

- Largest pooled study ever done
- Looked at 201 Meta-analyses
  - Ref: Poole R, et. al. Coffee Consumption and Health. BMJ 2017;359;j5024



# Causation Example

Coffee-Does it lead to worse health outcomes?

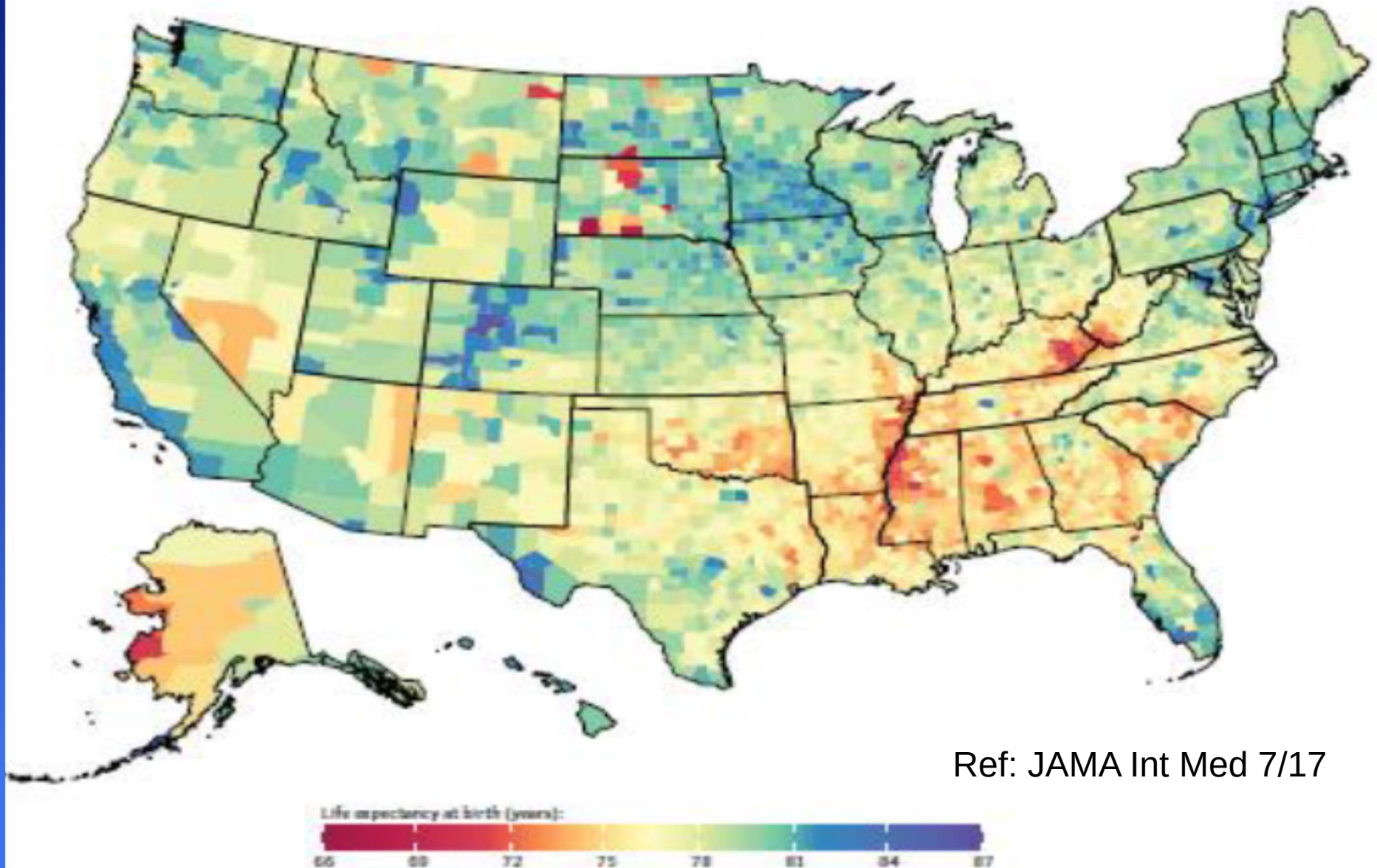
- Largest risk REDUCTION was seen at intakes of 3-4 cups/day:
  - All cause mortality 0.83(0.83-0.88)
  - Cardiovascular mortality 0.81(0.72-0.90)
  - Cardiovascular disease 0.85(0.80-0.90)
  - Incidence of Cancer 0.82(0.74-0.89)
  - Lower risks seen in specific cancers, metabolism, liver conditions

BUT, What is the Cause?



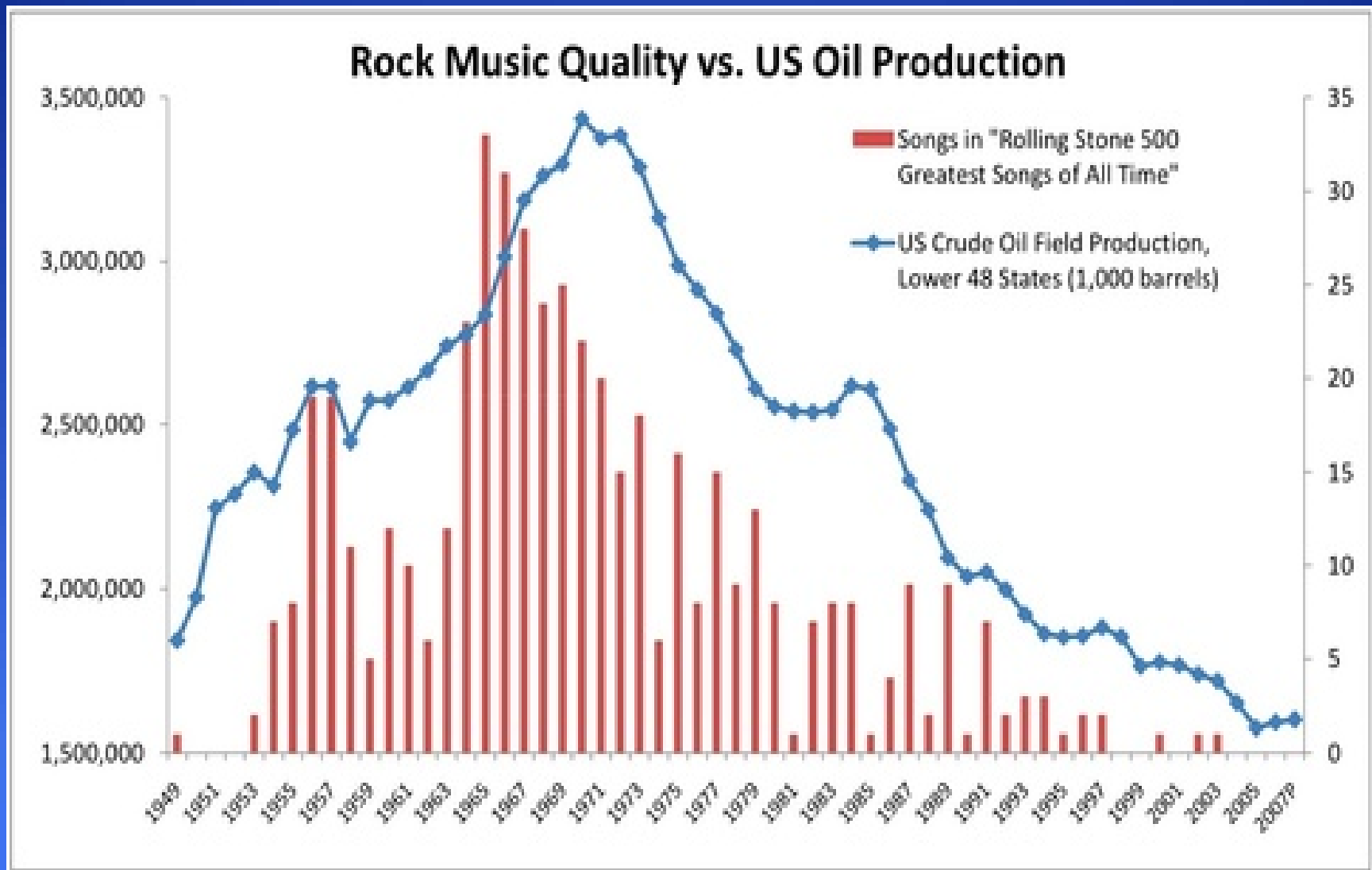
# Causation—maybe depends on where you are born

Life Expectancy at Birth by County, 2014



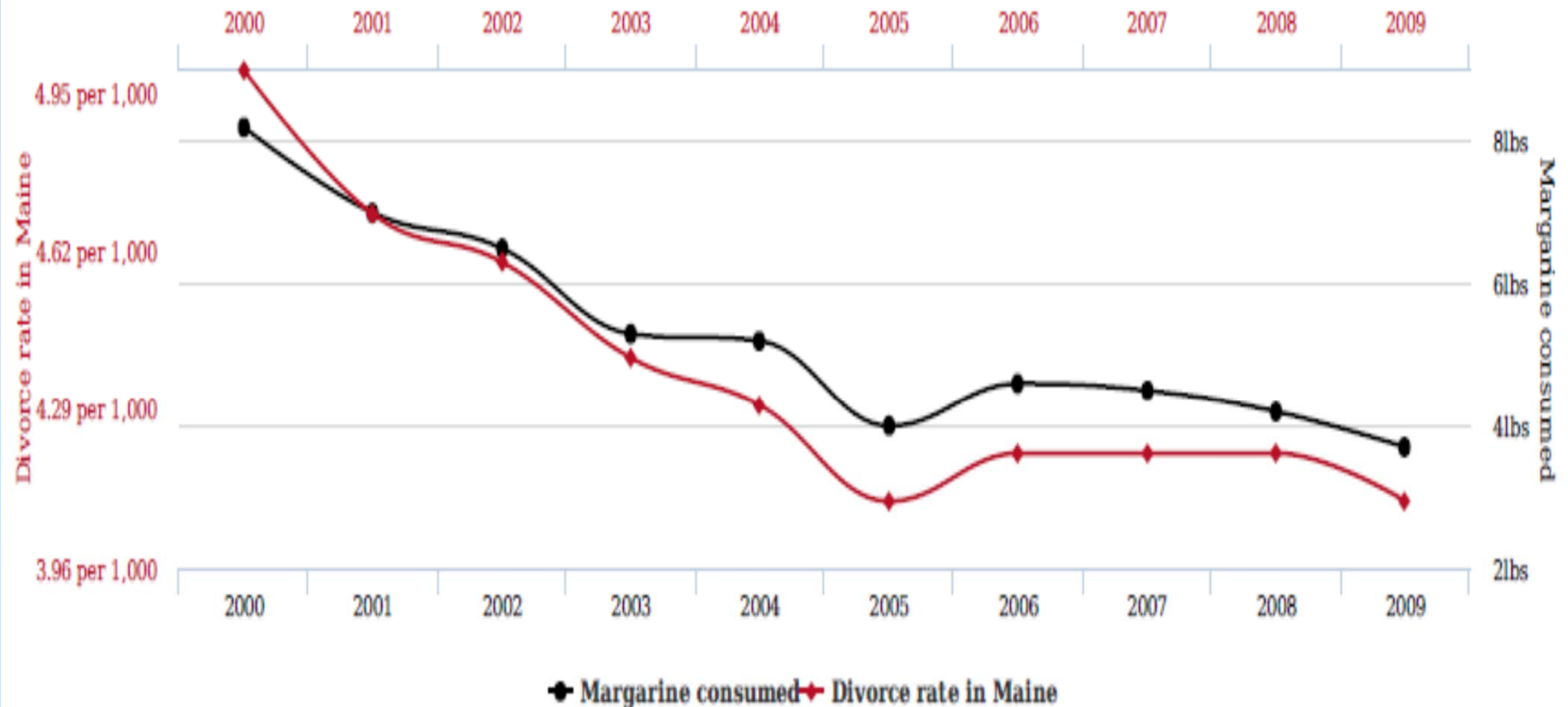
Ref: JAMA Int Med 7/17

# Correlation Does NOT Equal Causation



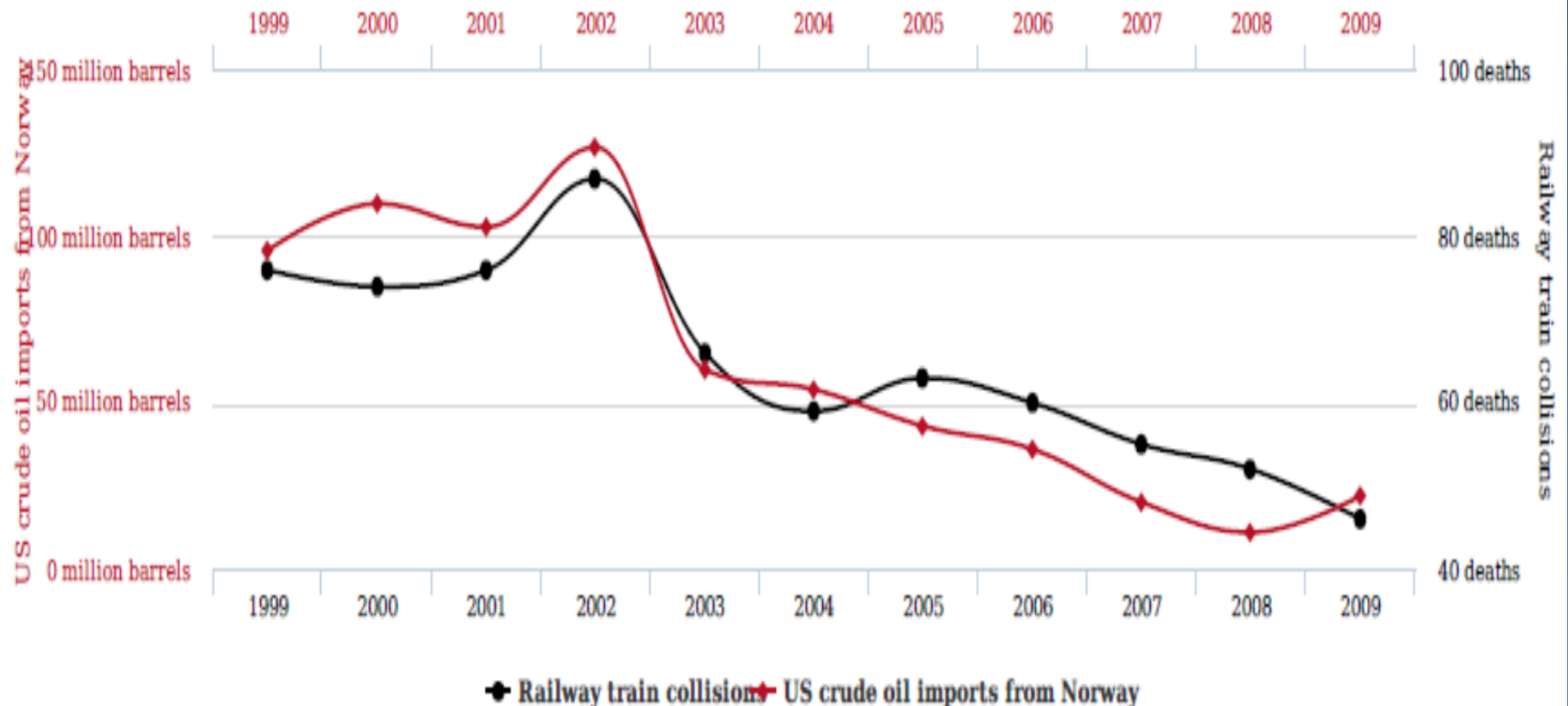
# Correlation Does NOT Equal Causation

**Divorce rate in Maine**  
correlates with  
**Per capita consumption of margarine**



# Correlation Does NOT Equal Causation

## US crude oil imports from Norway correlates with Drivers killed in collision with railway train

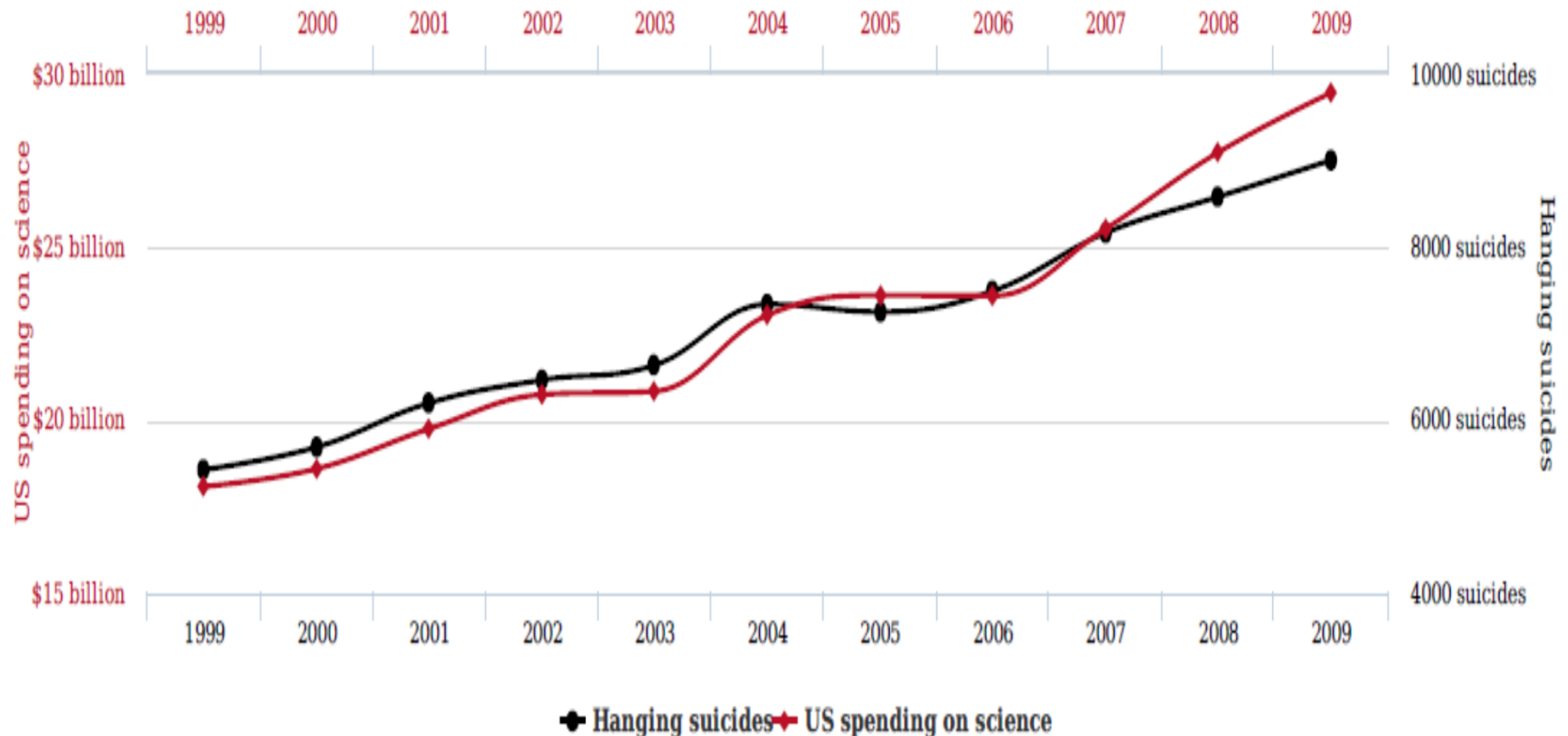


# Correlation Does NOT Equal Causation

**US spending on science, space, and technology**

correlates with

**Suicides by hanging, strangulation and suffocation**





# Causation Example



# Causation Example

Paediatric and  
Perinatal Epidemiology  
Volume 18 Issue 1



**Pages 88 - 92, Published Online: 22 Jan 2004**

Data from Berlin (Germany) show a significant correlation between the increase in the stork population around the city and the increase in deliveries outside city hospitals (out-of-hospital deliveries). However, there is no correlation between deliveries in hospital buildings (clinical deliveries) and the stork population. The decline in the number of pairs of storks in the German state of Lower Saxony between 1970 and 1985 correlated with the decrease of deliveries in that area. The nearly constant number of deliveries from 1985 to 1995 was associated with an unchanged stork population (no statistical significance). However, the relevance of the stork for the birth rate in that part of Germany remains unclear, because the number of out-of-hospital deliveries in this area is not well documented. A lack of statistical information on out-of-hospital deliveries in general is a severe handicap for further proof for the Theory of the Stork.

# Causation Example

Long-term exposure to  
Powerpoint  
presentations results  
in a lower IQ after 60  
minutes?

Yes

No



# Causation Example

Long-term exposure to Powerpoint presentations results in low IQ after 60 minutes. - No current study



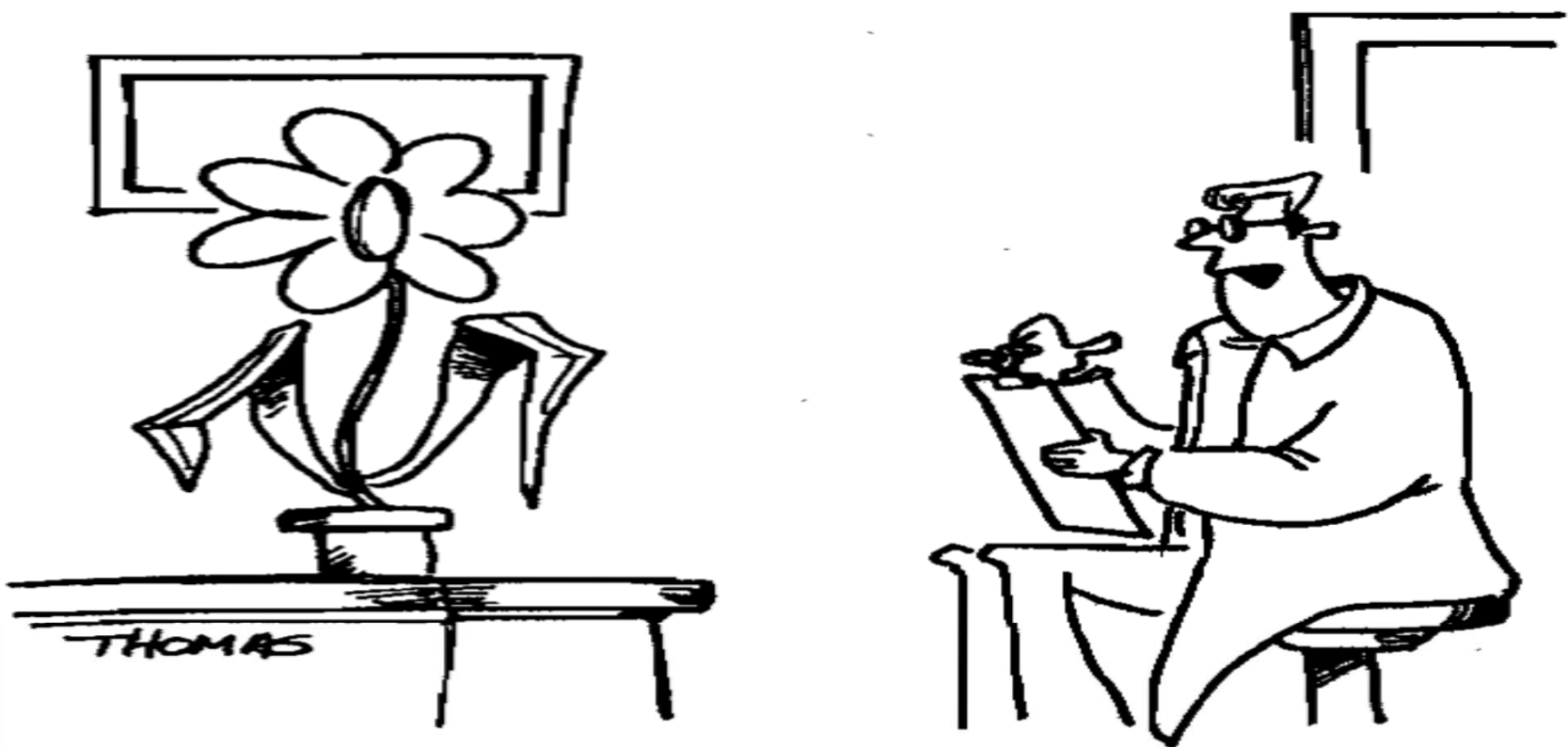


# Causation Example





# REST STOP



**“According to your chart, it looks like you’re gonna need a transplant.”**

# Chapters to Cover

- Chapter 12-Cardiovascular
- Chapter 13-Pulmonary
- Chapter 15-Rheumatologic
- Chapter 17-Genitourinary
- Chapter 18-Gastrointestinal
- Chapter 19-EENT



# Chapter 12-Cardiovascular

- Established CV risk factors probably account for 90% of MI:
  - Lipids
  - Smoking
  - HTN
  - Diabetes
  - Abdominal Obesity
  - Psychosocial Factors
  - Lack of Exercise
  - Diet esp. low consumption fruits, vegetables, alcohol

# Chapter 12-Cardiovascular

- Novel CV risk factors have “some” evidence of impact:
  - Hs-CRP
  - Coffee in slow caffeine metabolizers
  - Psoriasis
  - Testosterone deficiency
  - Migraine headaches
  - HIV treatment
  - HRT
  - NSAID's-? Occupational injury
  - Air Pollution or High CO levels-? Occupational

# Chapter 12-Cardiovascular

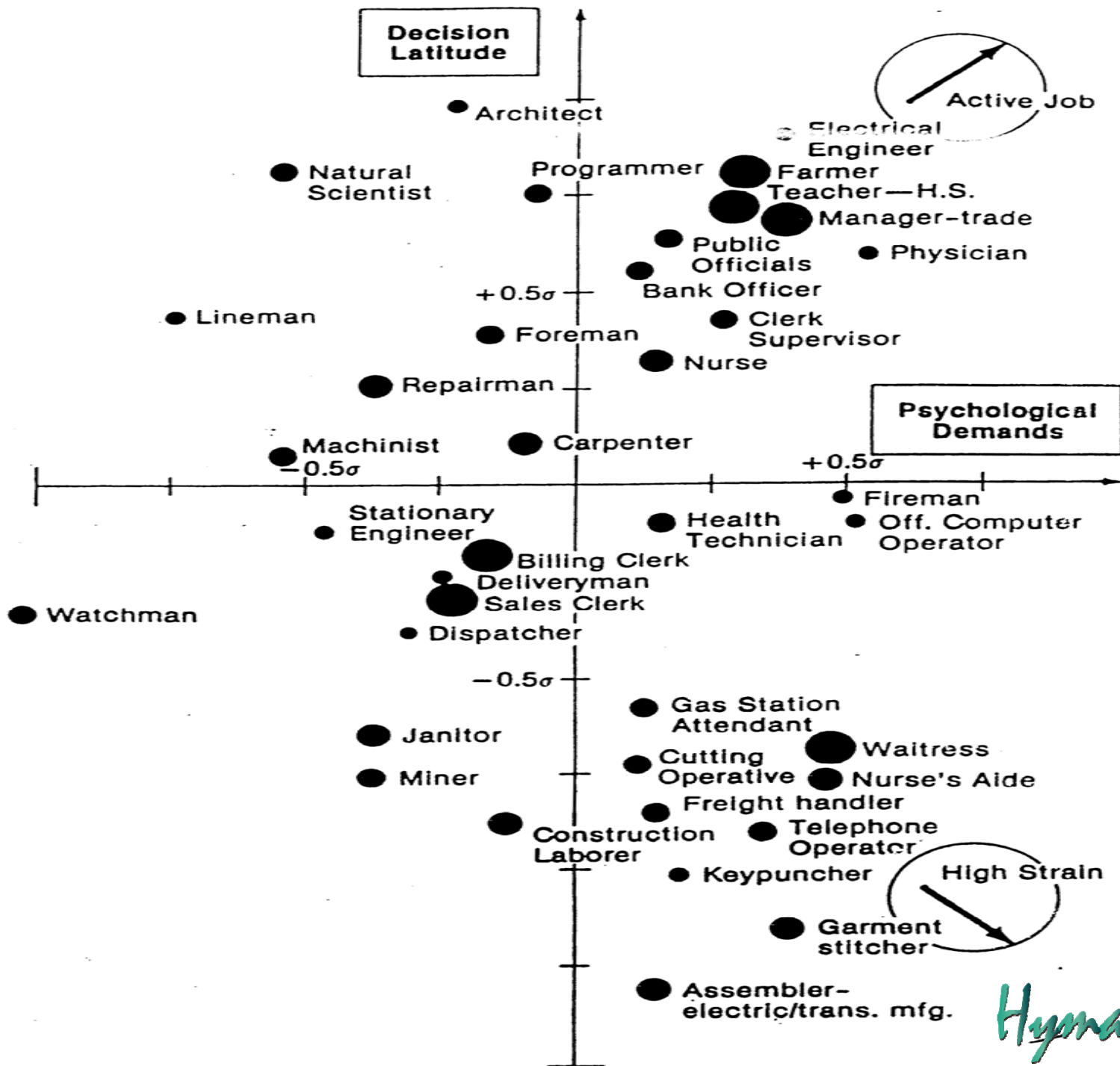
- CV risk factors with “insufficient” evidence:
  - Organic solvents
  - Organophosphates
  - Polycyclic aromatic compounds
  - Noise (ok for HTN but ? For CAD)



# Chapter 12-Cardiovascular

- Table 12-1 (partial list)

| Risk Factor         | Level of Risk   |
|---------------------|-----------------|
| Age                 | 1.05(1.0-1.06)  |
| HTN Stage 1         | 1.73(1.32-2.26) |
| LDL Chol $\geq$ 160 | 1.74(1.36-2.24) |
| Cigarette Use       | 1.71(1.39-2.10) |
| Diabetes            | 1.47(1.04-2.08) |
| BMI $\geq$ 30       | 1.45(1.04-2.01) |
| Sibling with CAD    | 1.45(1.10-1.91) |
| Air Pollution       | 1.26(1.08-1.47) |
| Job Strain          | 1.63(1.08-2.46) |
| COX-2               | 1.42(1.13-1.78) |



# Chapter 12 Cardiovascular

## Obesity by Occupation

A sampling of U.S. jobs and the prevalence of obesity in that occupational group

### Sample Jobs

### Obesity Rate for Group

#### HIGHEST



Police officers, firefighters, security guards

40.7%



Social workers, clergy, counselors

35.6



Home health aides, massage therapists

34.8



Architects, engineers

34.1



Bus drivers, truckers, crane operators, garbage collectors

32.8

#### LOWEST



Janitors, maids, landscapers

23.5%



Cooks, bartenders, food servers

23.1



Physicians, dentists, EMTs, nurses

22.0



Artists, actors, athletes, reporters

20.1



Economists, scientists, psychologists

14.2

Average U.S. worker: 27.7%

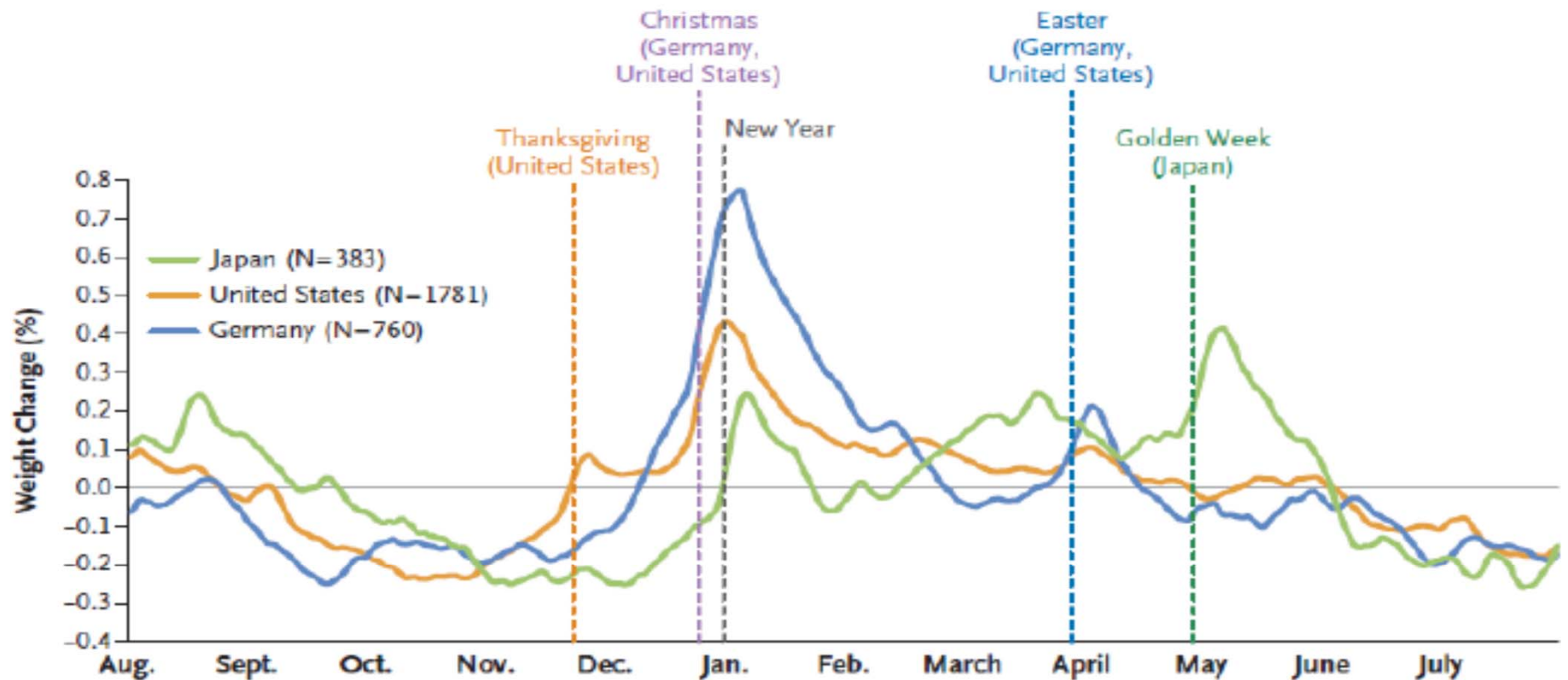
Note: Obesity defined as body mass index of 30 or above

Source: American Journal of Preventive Medicine's 2014 report based on 2010 data

The Wall Street Journal



# Chapter 12 Cardiovascular

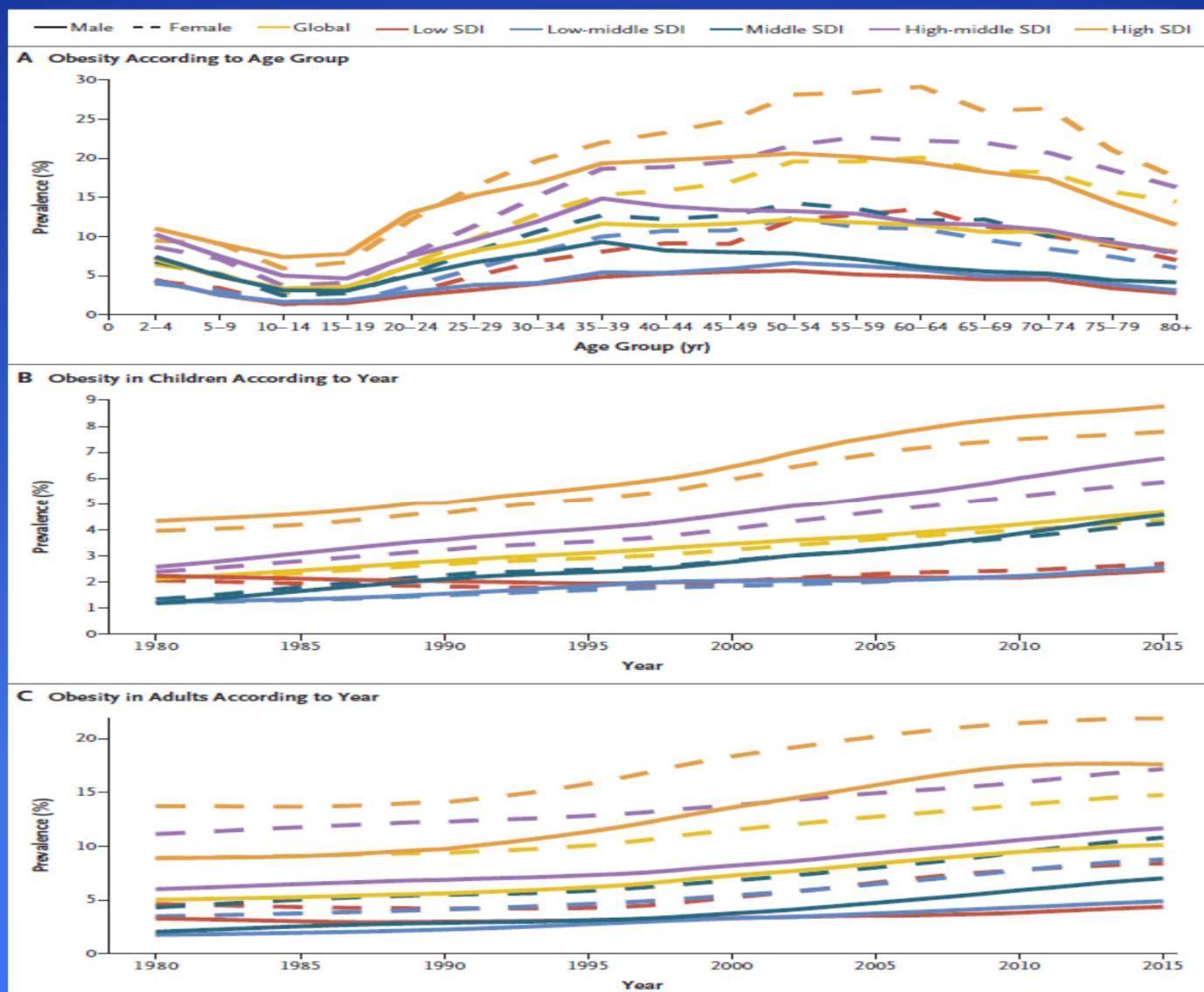


**Figure 1. Yearly Holiday Weight Gain.**

Owing to the subtraction of the annual linear trend for each participant, the starting-weight values are not at the zero mark.

Ref: NEJM 9/22/16

# Additional Points Cardiovascular-Risk Factors

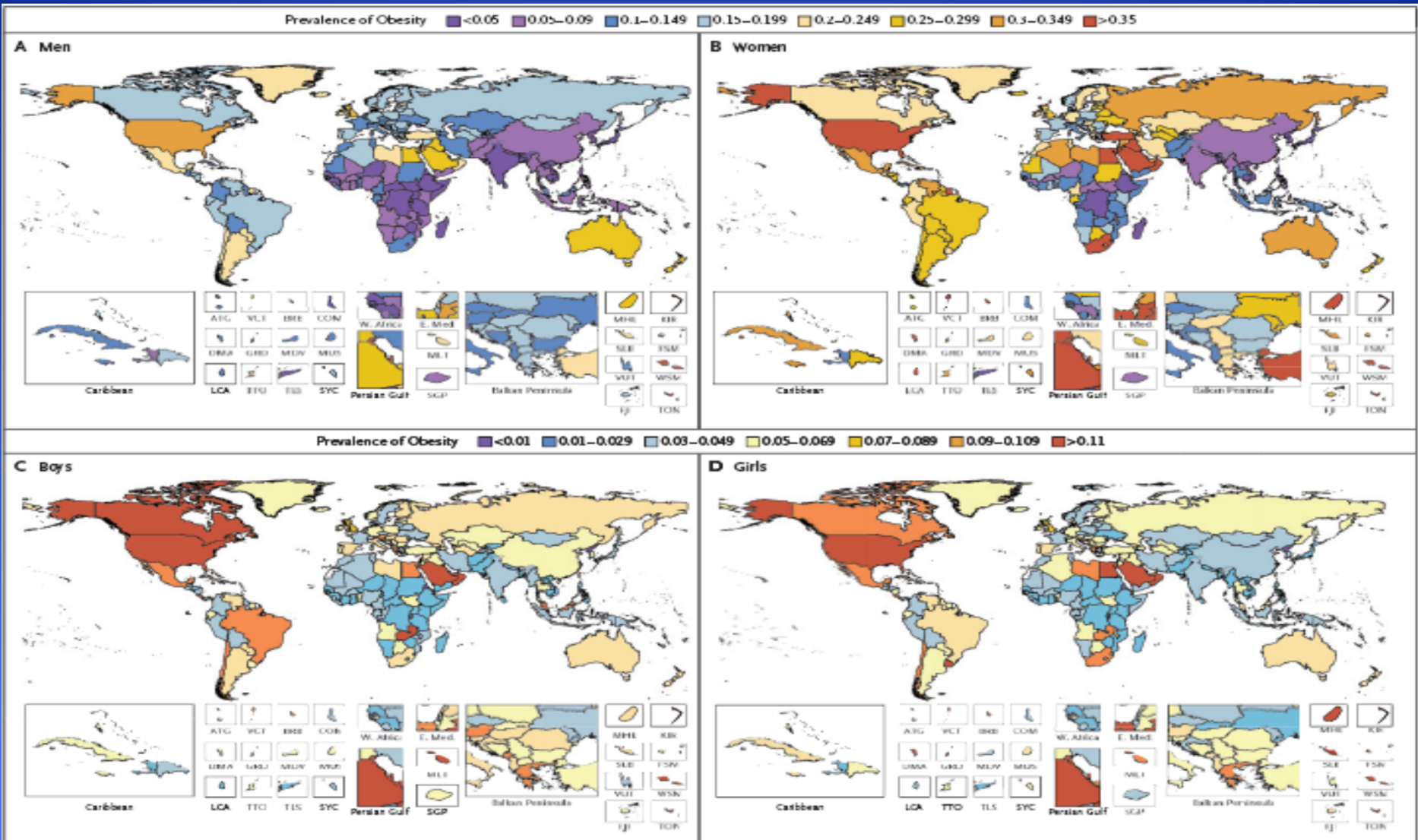


Ref:  
NEJM  
7/6/17

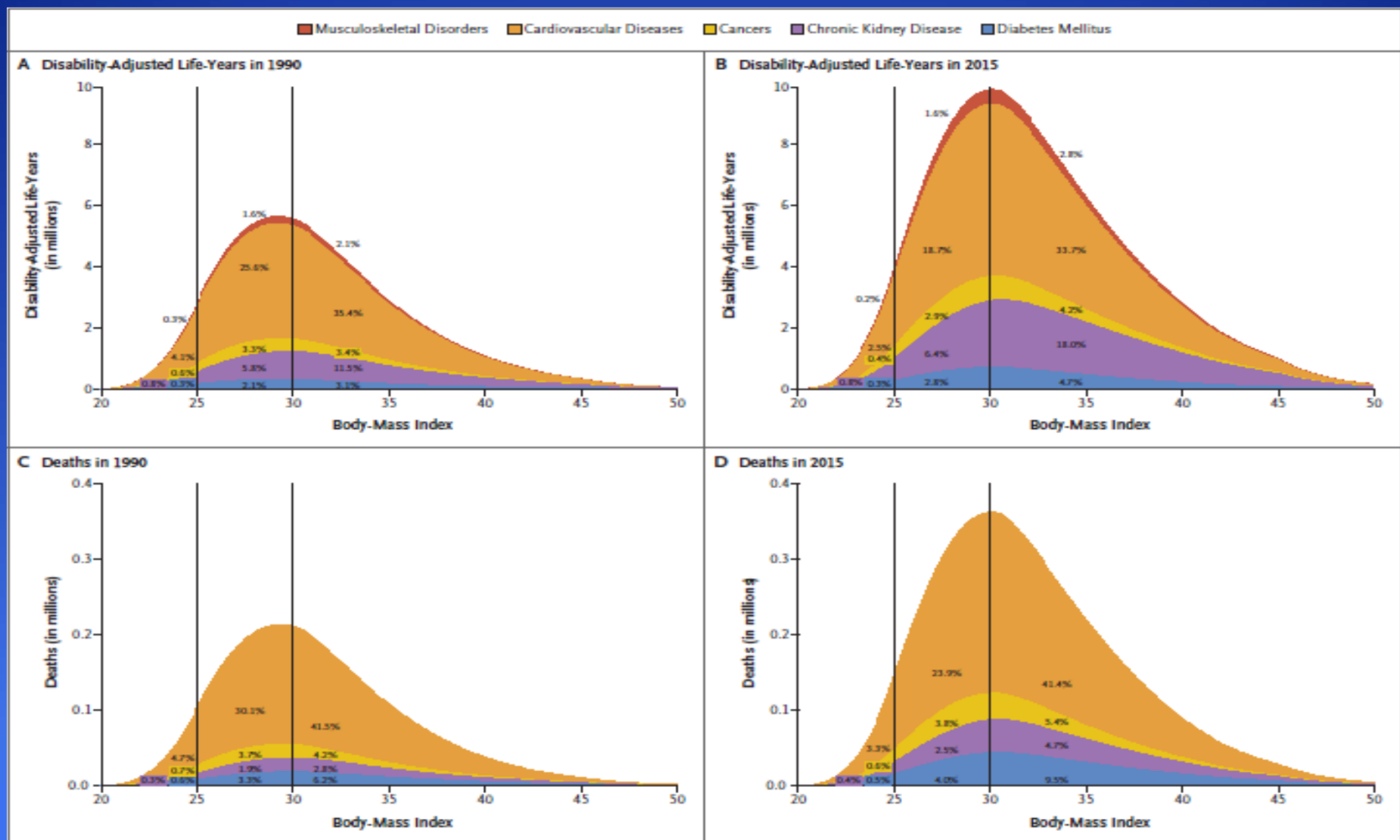


# Additional Points

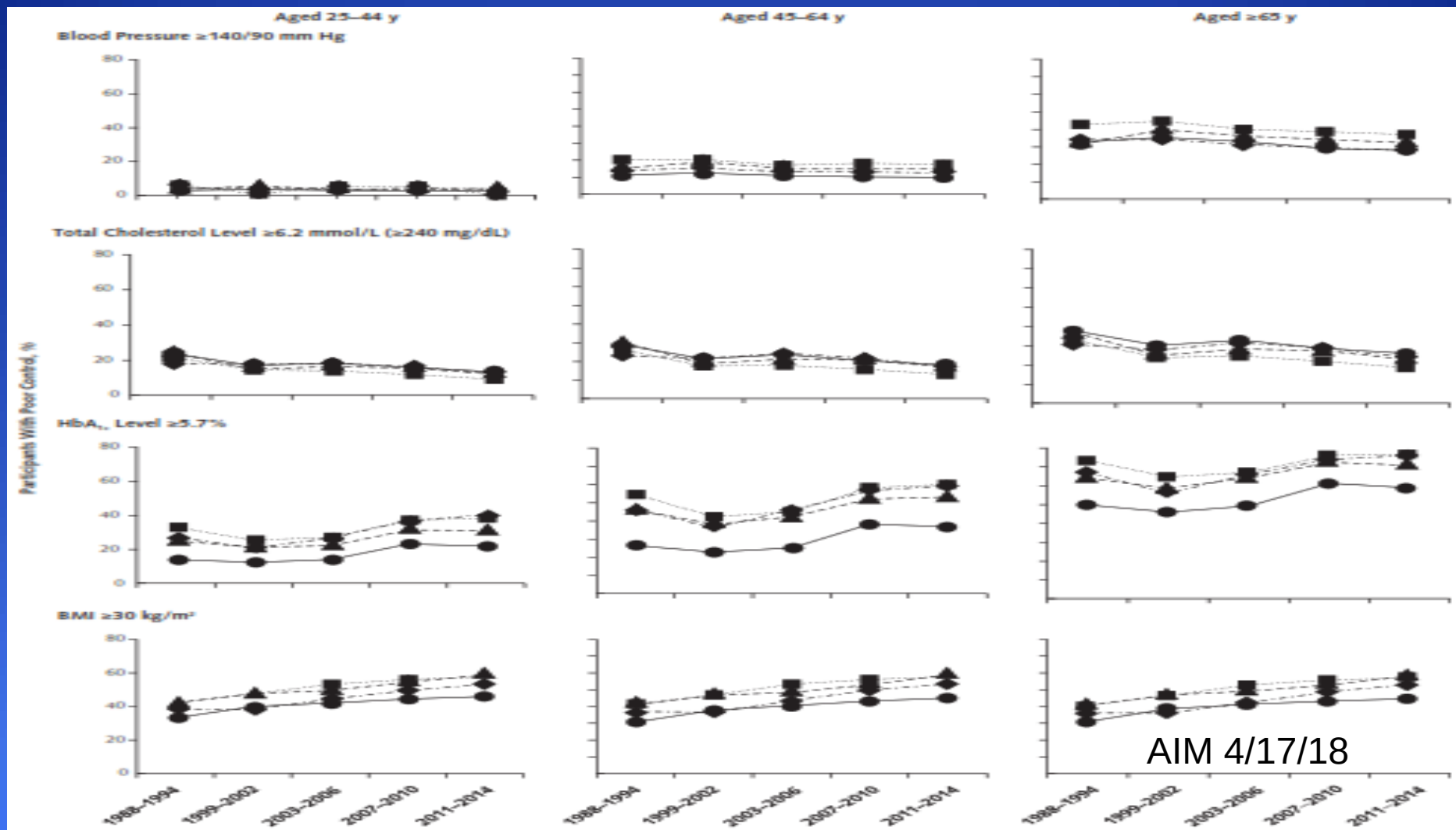
## Cardiovascular-Risk Factors



# Additional Points Cardiovascular-Risk Factors



# Additional Points Cardiovascular-Risk Factors



# Chapter 12-Cardiovascular

- Risk Factors for Heart Disease
  - The Zutphen Elderly Study in Arch Int Med, 2 reports, 2/27/06
  - Cocoa (Chocolate) lowers risk, probably due to flavan-3-ols, part of the flavanoids family
  - "Mood Food"-Rose in Arch IM 4/10 noted chocolate usage increases with worsening depression
  - Does chocolate help or is it a marker of depression? (Of course, I think it helps)

# Chapter 12-Cardiovascular

- Risk Factors for Heart Disease
  - Also, Taubert in JAMA 7/4/07
  - Cocoa , as dark chocolate, lowers BP and raises nitric oxide levels
  - Therefore, Hyman says, (not simon says), yes to chocolate!



# Chapter 12-Cardiovascular

- Risk Factors for Heart Disease
  - Also, Taubert in JAMA 7/4/07 Cocoa , as dark chocolate, lowers BP and raises nitric oxide levels





Havana, Cuba





**MUZEUM  
ČOKOLÁDY**

**Chocolate is the answer.**  
(The question is pretty much irrelevant.)





# The Jewish Love Affair With Chocolate

By Wendy Alt

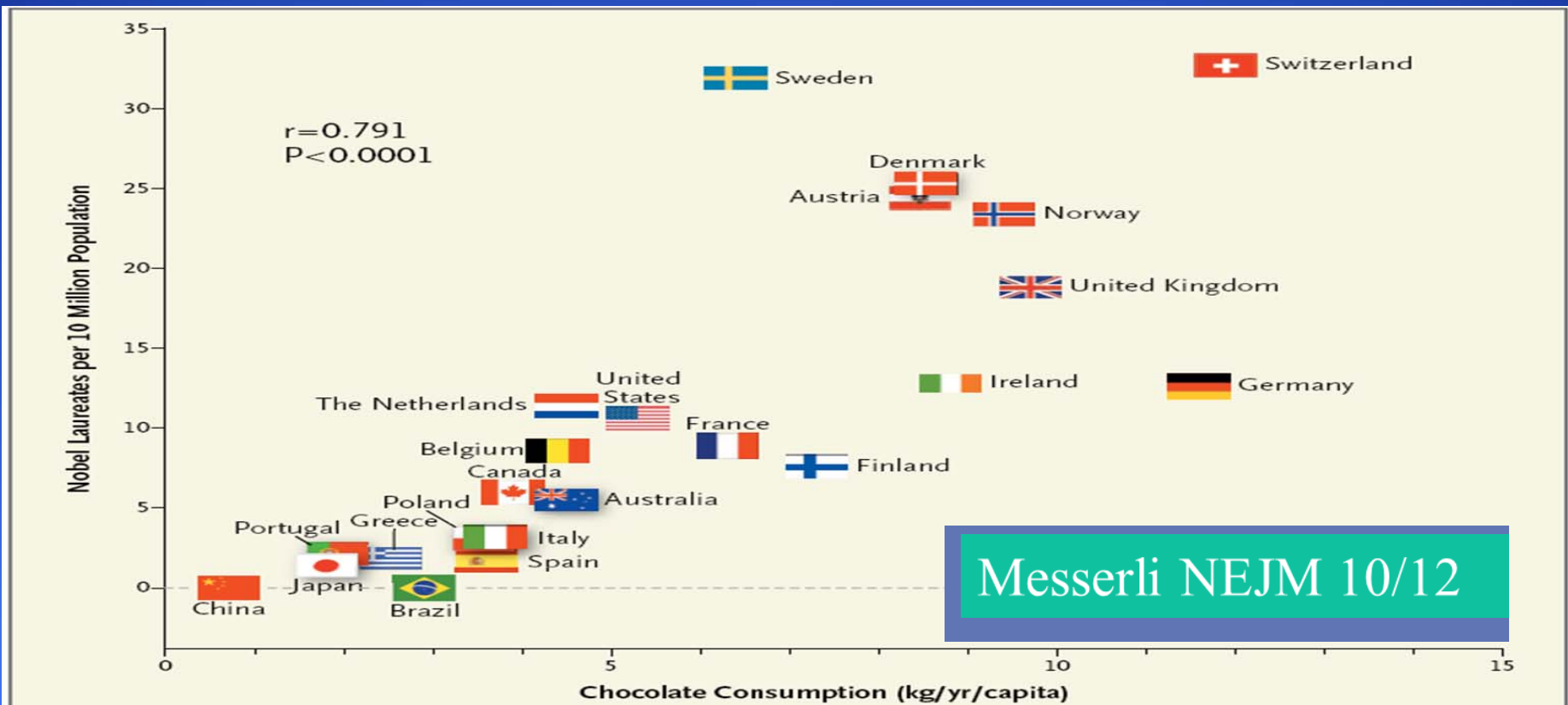
"Yes, separate milk from meat...But do not separate Jews from chocolate."

— A.J. Jacobs



# Chapter 12-Cardiovascular

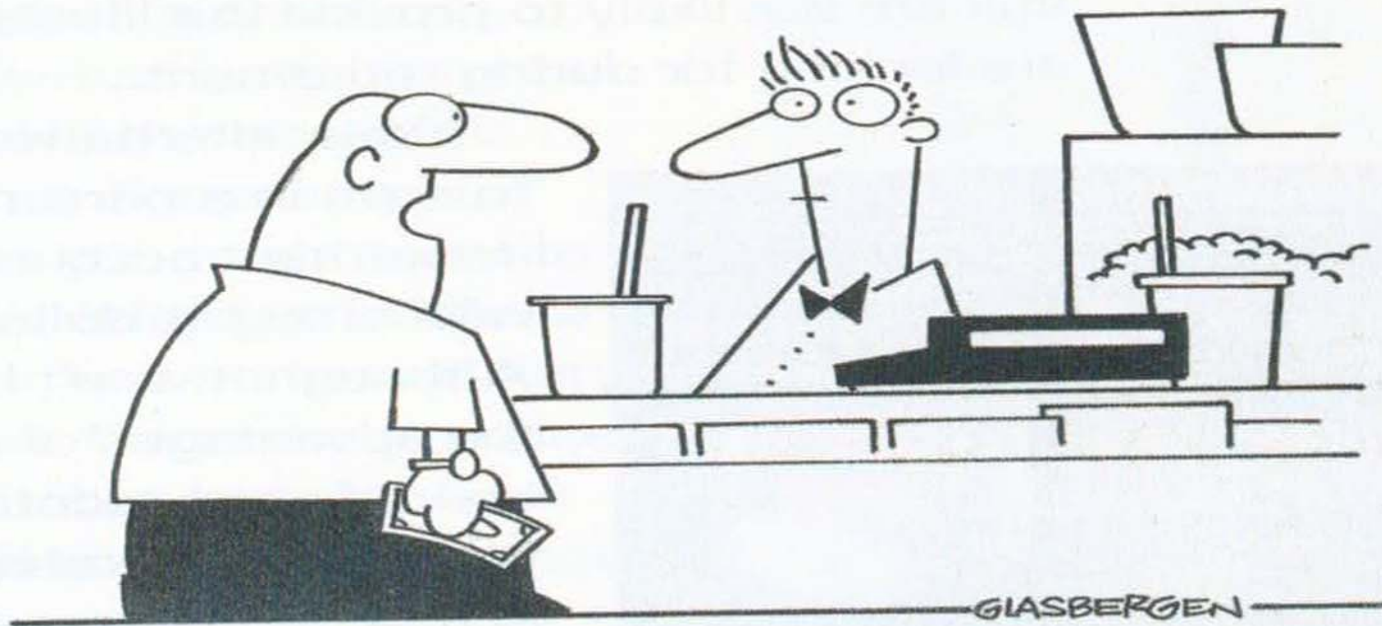
- Risk Factors for Heart Disease



**Figure 1.** Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

# Chapter 12-Cardiovascular

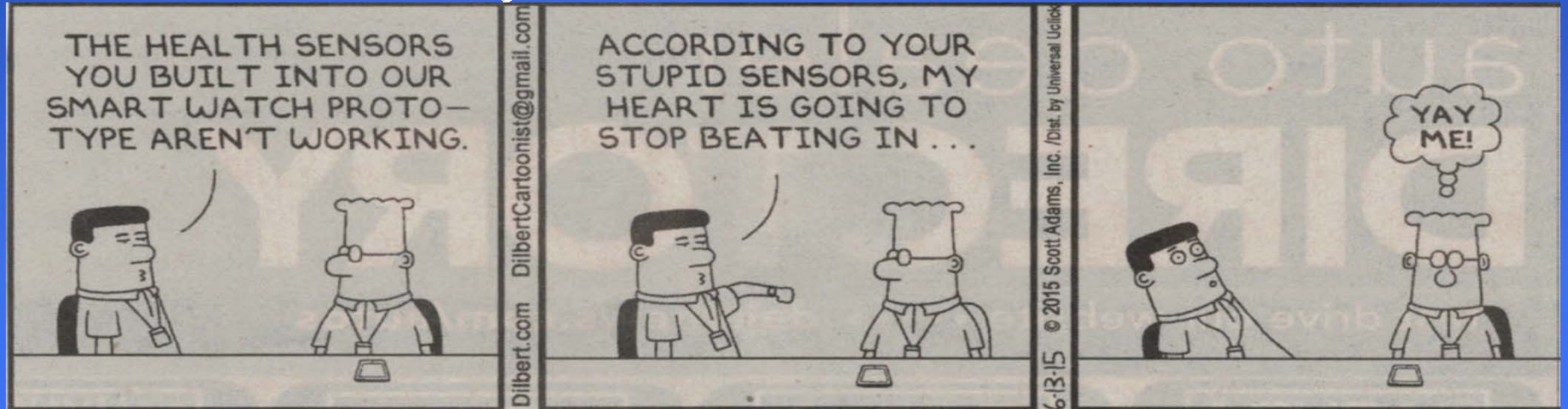
POPCORN-DRINKS-CANDY  
ENJOY THE MOVIE!



**“My doctor is sitting two rows behind me! Do you sell chocolate-covered fish oil capsules?”**

# Chapter 12-Cardiovascular

- Arrhythmias:
  - Cardiovascular Risk Factors
  - OSA
  - Illicit Drugs
  - Cold Preparations
  - Weight Loss Products
  - Herbal Products
  - Familial History



# Chapter 12-Cardiovascular

- Peripheral Arterial Disease:
  - Cardiovascular Risk Factors
  - Heavy metals and materials:
    - Cadmium, lead, barium, cobalt, cesium, molybdenum, antimony, thallium, tungsten
- DVT:
  - Virchow's Triad-injury, stasis, hypercoaguable states



# REST STOP





# Chapter 13-Pulmonary

- Make sure non-airway causes are considered:
  - Heart Failure
  - Pulmonary Emboli
  - Rhinitis with post-nasal drip
  - GERD
- Cigarettes-if present, dominate the clinical picture

# Chapter 13-Pulmonary

- Sources of all known inhaled risk factors is beyond this talk.
- Evaluation of worksite can be very helpful when carried out by standards of ACGIH-American Council of Governmental Industrial Hygienists



# Resources

- **PubMed** a service of the National Library of Medicine (NLM) includes more than 26 million citations from MEDLINE dating back to the 1950 and provides links to research tools [www.pubmed.gov](http://www.pubmed.gov)
- TEHIP-Toxicology and Environmental Health Information Program <https://sis.nlm.nih.gov/enviro.html> Has multiple subdivisions including:
  - Toxnet <http://toxnet.nlm.nih.gov/> which includes:
    - HSDB-Hazardous Substances Data Bank
    - Toxline-effects of drugs
    - ChemIDplus-names
    - LactMed-drugs and lactation
    - DART-Developmental and Reproductive Toxicology
    - TOXMAP-environmental health maps
    - TRI-Toxic Release Inventory
    - Household Products Database
    - Haz-Map-links jobs/tasks with occupational disease/symptoms
    - IRIS-Integrated Risk Information System-hazards with chemicals

# Resources

- **IARC** (*International Agency for Research on Cancer*) publishes a list of known carcinogens. [www.iarc.fr](http://www.iarc.fr)
- **DIR** *California Dept of Industrial Relations* [www.dir.ca.gov](http://www.dir.ca.gov) publishes a list of carcinogens recognized by the Department.
- **EPA** (*U.S. Dept. of Environmental Protection*) [www.epa.gov/](http://www.epa.gov/)
- **CDC** (*Centers for Disease Control and Prevention*) [www.cdc.gov/](http://www.cdc.gov/)
- **FDA** (*U.S. Food and Drug Administration*) [www.fda.gov/](http://www.fda.gov/)
- **Textbooks** e.g. Zenz *Occupational Medicine*

# Resources

- How many chemicals are we talking about?
- When the Toxic Substances Control Act was passed in 1976, 60,000 chemicals were grandfathered in
- Since 1976, 85,000 chemicals have been approved
- About 600 chemicals get EPA approval each year



# Chapter 13-Pulmonary

- Work-related asthma 2 types:
  - Occupational Asthma
  - Work-exacerbated Asthma
- Causes:
  - Sensitizers
    - High molecular weight-animal dander, grain dust, enzymes, mold
    - Low molecular weight-chemicals-anhydrides, diisocyanates, metals
  - Irritants
    - A single high level exposure to a highly irritating gas, fume, mist or vapor Aka RADS-Reactive Airway Dysfunction Syndrome

# Chapter 13-Pulmonary

- Hypersensitivity Pneumonitis
  - The “I” disease-Immunologic inflammation that is infiltrative and interstitial
- Causes(partial Table 13-3):
  - Organic fungi-Thermoactinomyces, Penicillium, Aspergillus, Cryptostroma
  - Bird Proteins-Alternaria, Graphium, Aureobasidium, Merulius, Trichosporon
  - Beryllium

# Chapter 13-Pulmonary

- Fibrotic Lung Disorders(Pneumoconiosis)
  - Causes are inhalation of inorganic mineral dusts:
    - Silica
    - Coal Dust
    - Asbestos-serpentine(chrysotile which is 95% of world production) or amphiboles(includes crocidolite, tremolite, amosite)
    - Libby(Montana) amphiboles cause abnormalities in 87% of miners
      - Ref: Miller JOEM 2/18
- Weaker causative data exists for aluminum, cadmium, cobalt, mercury, emery, graphite, gypsum, marble, mica, perlite, plaster of paris, manufactured vitreous fibers(glass wool), continuous filament mineral wool(slag and rock) and ceramic fiber

# Chapter 13-Pulmonary

- COPD
  - Cigarettes
  - Alpha 1-antitrypsin deficiency (5% of cases)
  - Occupations:
    - Coal miners
    - Hard rock miners
    - Tunnel workers
    - Concrete manufacturing
    - Firefighters

# Chapter 13-Pulmonary

- Lung cancer and Mesothelioma
  - Cigarettes
  - Ionizing radiation
  - Silica possible-quartz, cristobalite, tridymite, tripoli
  - Asbestos-both types



# Chapter 13-Pulmonary

- Bronchiolitis Obliterans-fibrosis and obstruction
  - Most well known recent case was popcorn worker lung due to the butter flavoring fumes
  - Also seen with mineral dusts, infections( viral, mycoplasma, legionella), transplant patients, collagen vascular disease

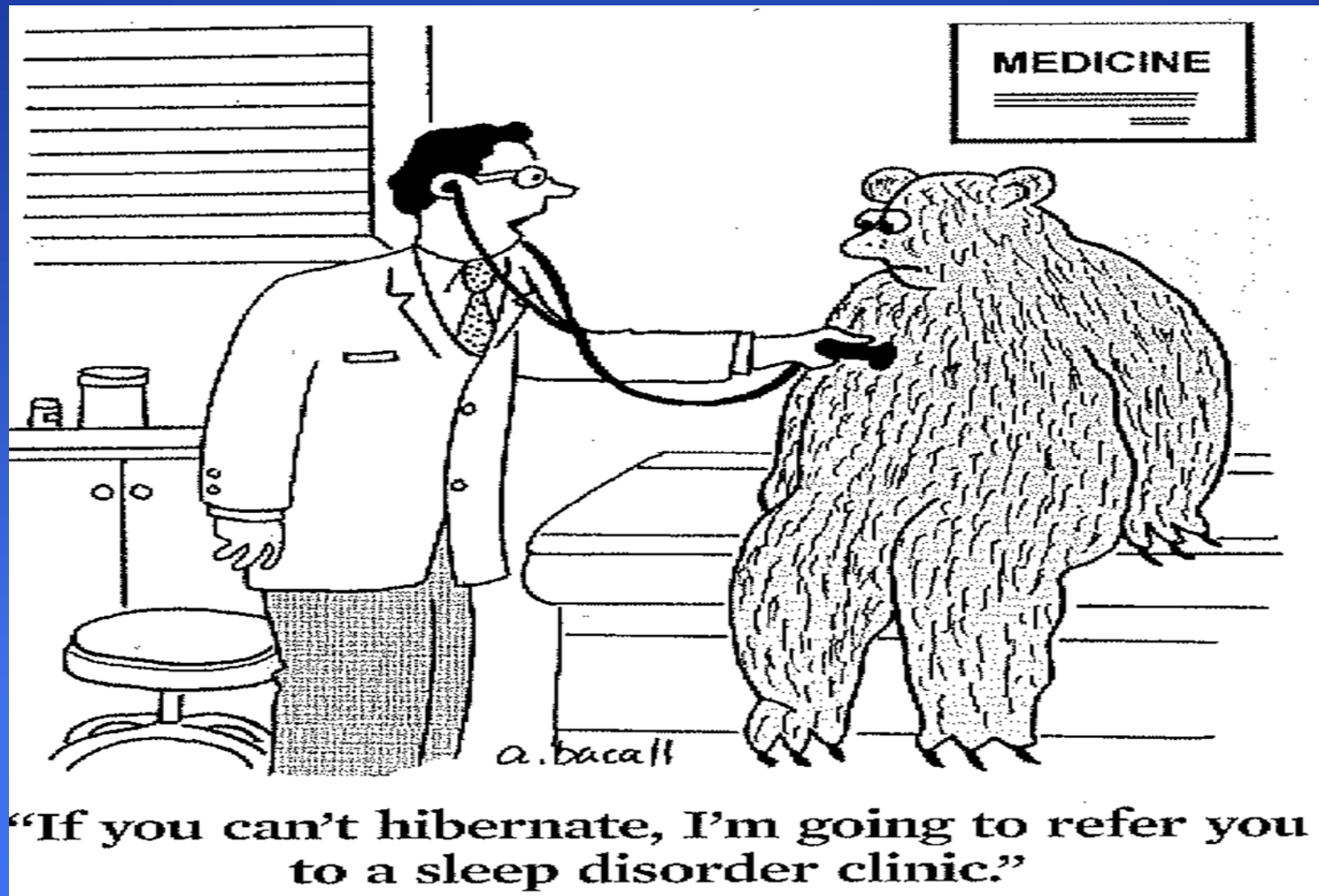
# Chapter 13-Pulmonary

- OSA-Obstructive Sleep Apnea
  - Due to obesity
  - A diagnosis of OSA is especially prudent given the association not only with daytime sleepiness, but also with accidents, hypertension, age, strokes, DVT, diabetes and the metabolic syndrome
  - Can also be seen with deconditioning, as with post-injury, and exercise helps even with no weight loss
  - Some evidence as more common in drivers, seamen and cooks independent of weight

# Chapter 13-Pulmonary



# Chapter 13-Pulmonary





# REST STOP





# Chapter 15-Rheumatology

- Osteoarthritis
  - Genetics
  - Increasing age
  - Women
  - Obesity
  - Sensory neuropathy
  - Muscular deconditioning
  - Hypermobility
  - Repetitive impact sports



# Chapter 15-Rheumatology

- Rheumatoid Arthritis
  - Genetics
  - Smoking
  - Silica
  - “Some” evidence for jobs with heavy hand use, excessive typing, heavy lifting, improper ergonomics, stress, solvents, pesticide, farmers

# Chapter 15-Rheumatology

- SLE-Systemic Lupus Erythematosus
  - UV-B light exposure-jobs with heavy sun exposure
  - Chemicals-aromatic amines, hydrazines, plastic, anticorrosives, rubber, herbicides, pesticides, preservatives, textiles, dyes, pharmaceuticals
  - Drug-induced include hydralazine, procainamide, quinidine
  - Alfalfa sprouts
  - Unclear if affected by trauma or stress

# Chapter 15-Rheumatology

- Fibromyalgia
  - Female
  - Increasing age
  - Genetics
  - Abuse-physical or sexual
  - Autoimmune disease
  - “Some” evidence of diabetes

# Chapter 15-Rheumatology

- Osteoporosis

- Immobilization
- Increasing age
- Meds:
  - Aluminum-containing antacids
  - Antiseizure medicines (only some) such as Dilantin® or Phenobarbital
  - Aromatase inhibitors such as Arimidex®, Aromasin® and Femara®
  - Cancer chemotherapeutic drugs
  - Cyclosporine A and FK506 (Tacrolimus)
  - Gonadotropin releasing hormone (GnRH) such as Lupron® and Zoladex®
  - Heparin
  - Lithium
  - Medroxyprogesterone acetate for contraception (Depo-Provera®)
  - Methotrexate
  - Proton pump inhibitors (PPIs) such as Nexium®, Prevacid® and Prilosec®
  - Selective serotonin reuptake inhibitors (SSRIs) Lexapro®, Prozac® and Zoloft®
  - Steroids (glucocorticoids) such as cortisone and prednisone
  - Tamoxifen® (premenopausal use)
  - Thiazolidinediones such as Actos® and Avandia®
  - Thyroid hormones in excess



# REST STOP



# Chapter 17-Genitourinary

- Cancers:
  - Kidney-smoking, obesity, HTN
  - Bladder-cigarettes, aromatic amines from rubber and dye industries, though insufficient data on the workers
  - Prostate-genetics, increasing age, african-american
  - Testicular-genetics, undescended testicle
- Stones:
  - Dehydration, with “Some” evidence in lifeguards, factory workers in high ambient temperature

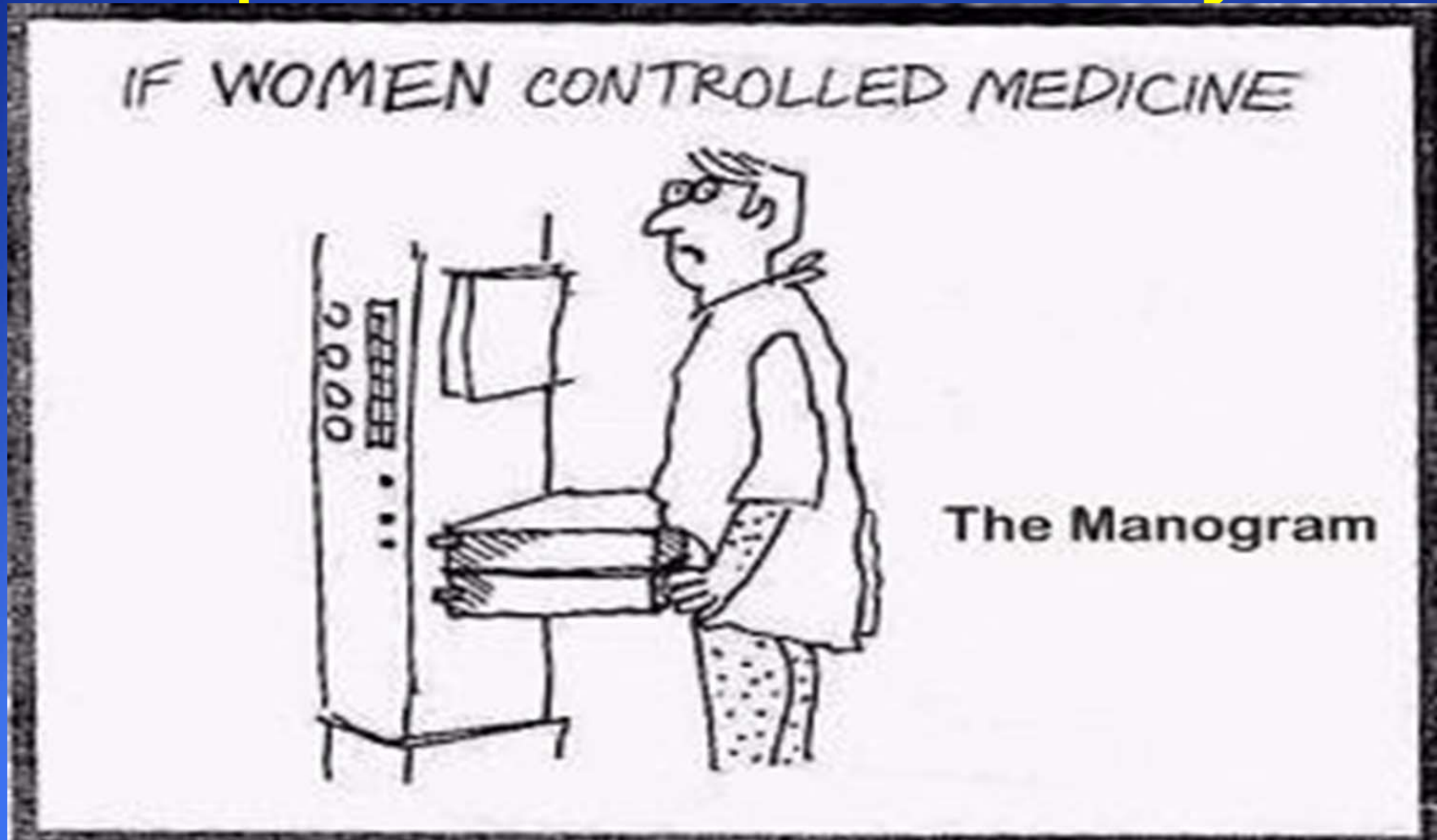
# Chapter 17-Genitourinary

- Acute Kidney Injury(AKI):
  - Apart from hospitalization and medications, ethylene glycol(used in anti-freeze, plastics), herbicide paraquat
  - “Some” evidence Chinese adulterated products with melamine
- Chronic Kidney Injury:
  - HTN, DM, Obesity, GN, recurrent AKI (prob gets you 90%) with risk due to lead and cadmium
- Voiding dysfunction
  - Occupational usually only seen in spinal cord injury

# Chapter 17-Genitourinary

- Male Infertility:
  - 15% of couples, with equal male:female causes
  - Smoking, obesity, alcohol, genetics, ionizing radiation
  - “Insufficient” for endocrine disruptors(chemicals) that seem to affect prenatal development but not certain for adults-PCB, DDT
- Sexual Dysfunction:
  - HTN, DM, Psychologic
  - Long term Opiate therapy
  - How do we measure Sexual Dysfunction in men?

# Chapter 17-Genitourinary





# REST STOP



# Chapter 18-Gastrointestinal

| Condition | Risk Factor                                                      | Level of Evidence                                      |
|-----------|------------------------------------------------------------------|--------------------------------------------------------|
| Dyspepsia | Occupation<br>Stress                                             | No risk<br>Some                                        |
| PUD       | Occupation<br>NSAID's                                            | No risk<br>Strong                                      |
| H.pylori  | Occupation                                                       | No risk                                                |
| GERD      | Occupation<br>Stress<br>Obesity<br>Opera, Wind, or Glass Blowers | Insufficient<br>Insufficient<br>Strong<br>Insufficient |
| IBS       | Occupation<br>Stress<br>Shift Work                               | No risk<br>Strong<br>Insufficient                      |
| IBD       | Occupation<br>NSAID's                                            | Insufficient<br>Insufficient                           |
| Hernia    | Occupation                                                       | Insufficient                                           |

# REST STOP



# Chapter 19-Ear Eye Nose Throat(EENT)

- Hearing Loss
  - 3 types-conductive, sensorineural or both
  - Can consult ACOEM, National Institute of Hearing Loss Guides or OSHA
  - Occupational noise-induced hearing loss(chronic) vs. occupational acoustic trauma(acute)
  - High-frequency is usually lost first
  - Typical non-occupational causes include infection, noise, increasing age, meds (aminoglycoside, salicylates, loop diuretic, chemo), acoustic neuroma, carbon monoxide

# Chapter 19-Ear Eye Nose Throat(EENT)

- Hearing Loss

- Typical occupational causes include airline ground maintenance, large machinery, farming, construction, railroad, probably firefighters, weapons
- Styrene(in plastics), toluene, hydrogen cyanide, mercury, lead, arsenic, manganese
- OSHA guidelines for HCP(hearing conservation program):
  - 85 dB begins entry into program for observation and protection, no more than 8 hours per day
  - 115 dB continuous exposure limit(anything > 1 second)
  - 140 dB limit for sudden noise(anything < 1 second)



# Chapter 19-Ear Eye Nose Throat(EENT)

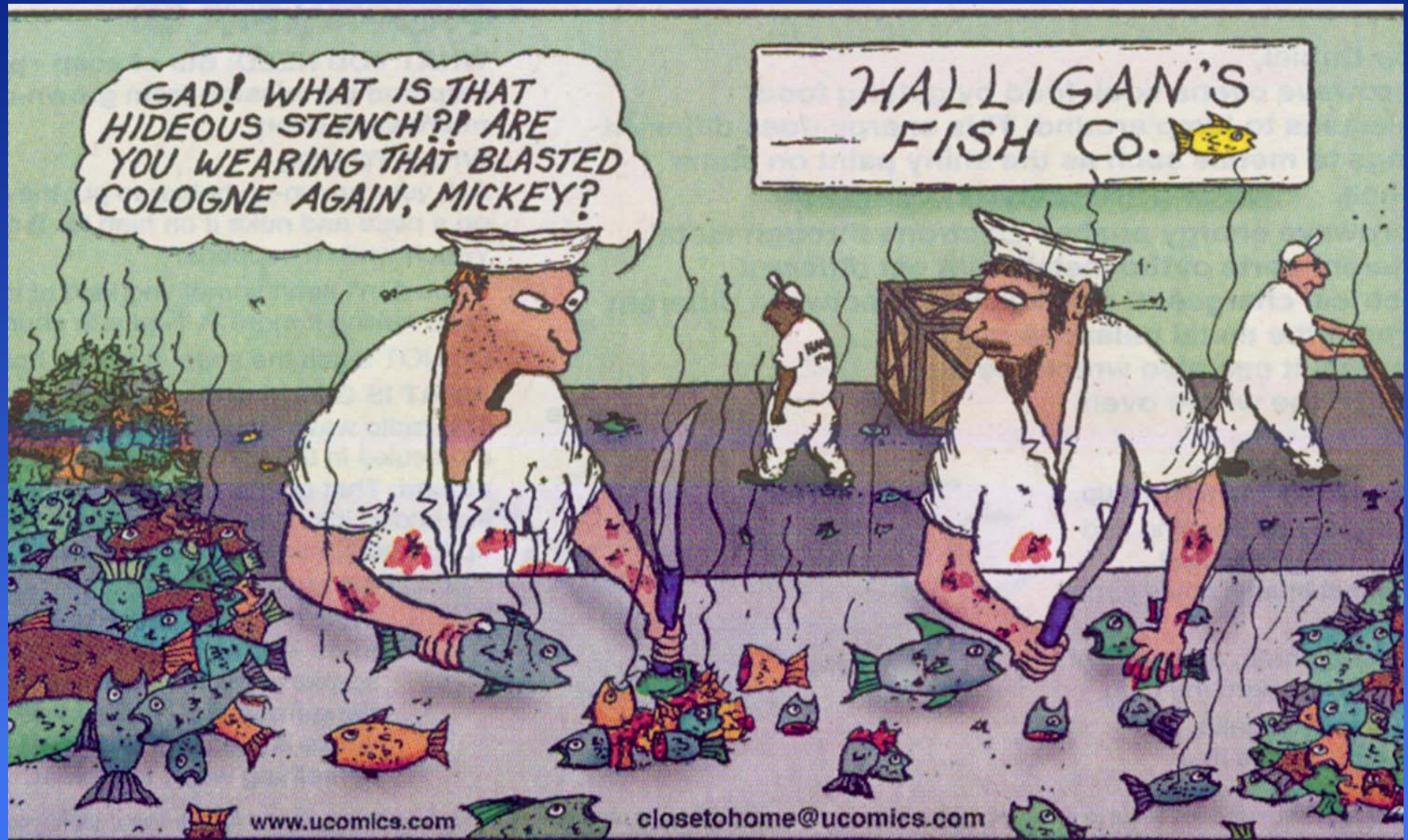
- Cataracts
  - Increasing age, smoking, HTN, DM, UV light exposure, rare genetic conditions, steroids, ionizing radiation
  - Occupational risk due to radiation seen in airline pilots, astronauts, physicians (in particular radiologist, invasive cardiologist, anesthesiologist, radiation oncologist), electrical injury

# Chapter 19-Ear Eye Nose Throat(EENT)

- Nose and Throat

- Many symptoms are vague, non-specific. The more specific allergic rhinitis would have causes similar to asthma discussed previously
- Sick Building Syndrome or Building Related Illness is usually due to temperature, humidity, and/or poor ventilation and not chemicals
- Indoor environments can have one of up to 1000 volatile organic compounds-formaldehyde, acetaldehyde, toluene, xylene and others
- The home environment must always be considered
- Occupations to consider include chromium electroplating, leather industry who use chromium salts and tannins, glassblowers, volunteers at natural disasters

# Chapter 19-Ear Eye Nose Throat(EENT)





# THANK YOU!!

