

# Introduction to Epidemiology

Lecture prepared by Dr. Hailey Banack, PhD

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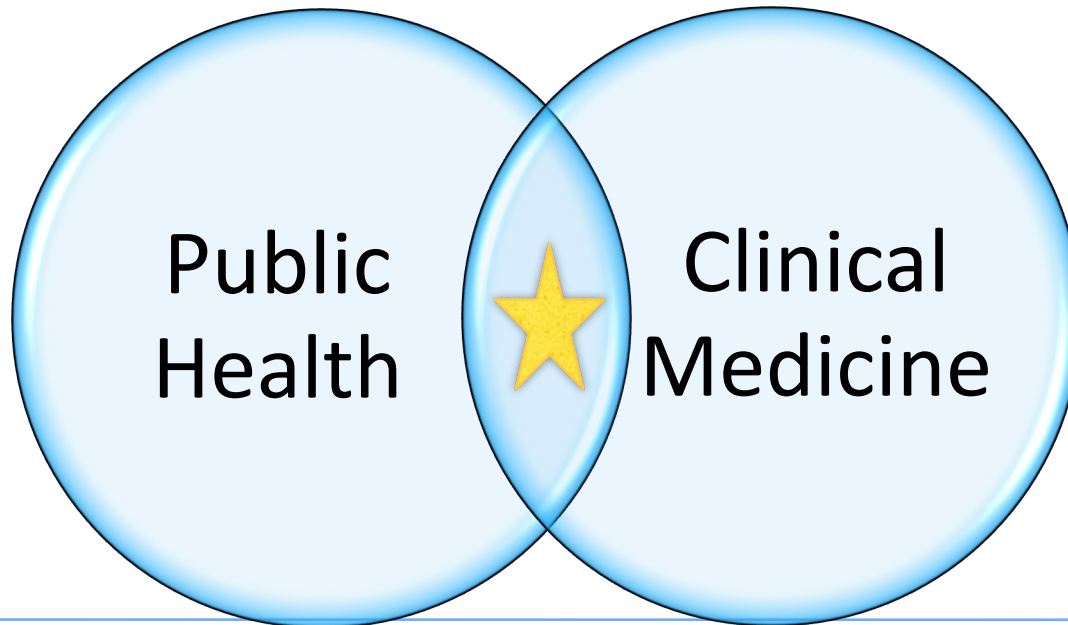
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What is Epidemiology?

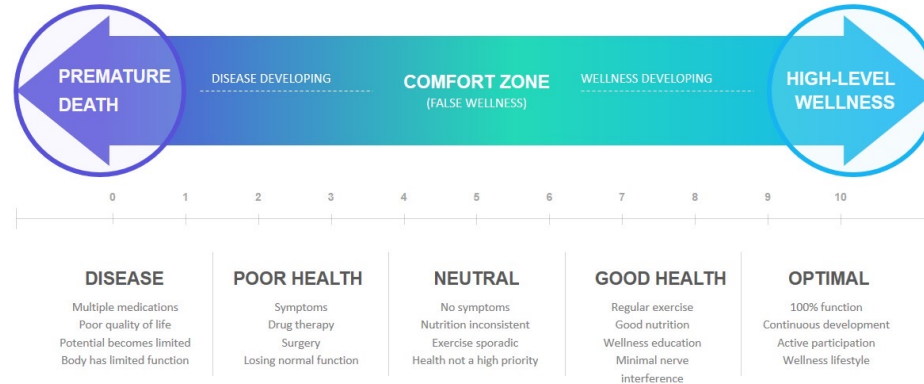
# Definition

- The study of the distribution and determinants of health-related states or events in specified populations and the application of this study to control of health problems



# “Study of distributions and determinants”

- Disease, illness, poor health, excellent health status are not randomly distributed in our population



- Each individual has certain characteristics that predispose (or protect) them against disease
  - Genetic factors or family history
  - Environmental exposures
  - Health behaviours
  - Socioeconomic factors

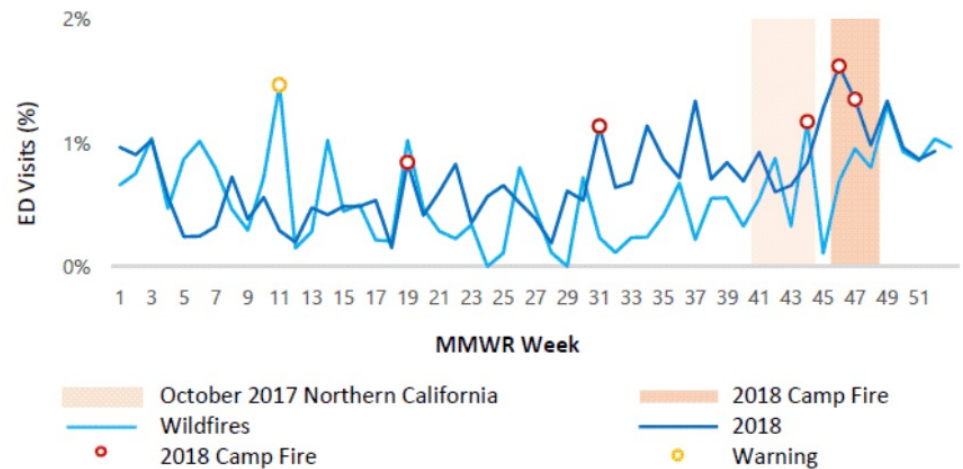
# Example: Wildfires and asthma

-Individuals with asthma are susceptible to exacerbations when air quality is low (i.e., wildfire smoke)



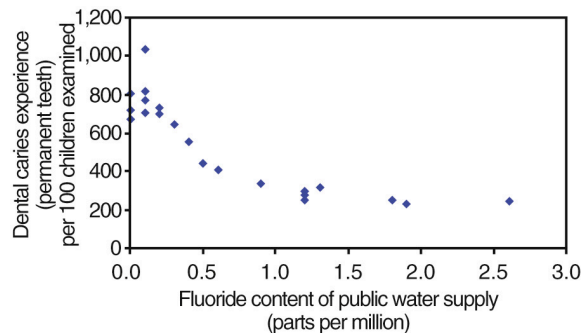
The Camp Fire (11/8/18) was the deadliest wildfire in California history and sixth-deadliest U.S. wildfire to date

## D. Asthma-related ED Visits, San Mateo County

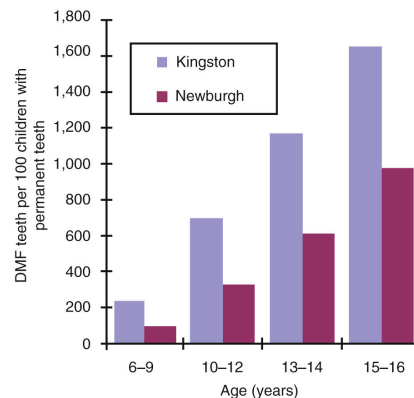


# Application to control health problems

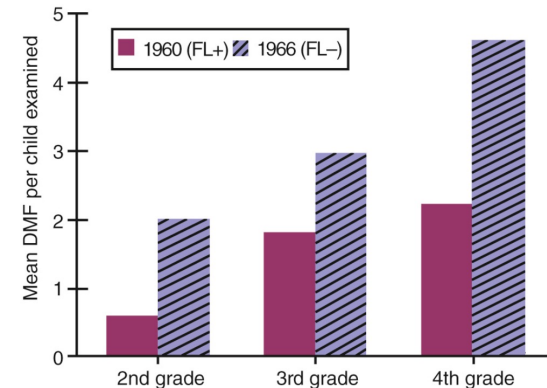
- Epidemiologists use the insights gathered in their research to determine how disease within a population affects our society and health systems



Increased fluoride, decreased caries



DMF indices after 10 years of fluoridation, 1954–1955.



Removal of fluoride in Antigo, Wisconsin

# Objectives of Epidemiology

- Identifies causes of disease & risk factors for disease (etiology)
- Determines the extent or burden of disease in a population
- Studies the natural history and prognosis of disease
- Evaluates the effect of preventive and therapeutic measures and approaches to health care on disease
- Provides scientific evidence to inform public health and environmental policies

# 1. Etiology of Illness

What many people want to know:

Does an exposure of interest CAUSE the outcome of interest?



Stated differently: if I manipulate an exposure (+) does it cause the outcome? Or if I manipulate an exposure (-) does it remove outcome risk?



# What is a cause?

“Cause of a disease event is an event, condition or characteristic that preceded the disease event and without which the disease event either would not have occurred at all or would not have occurred until some other time.”

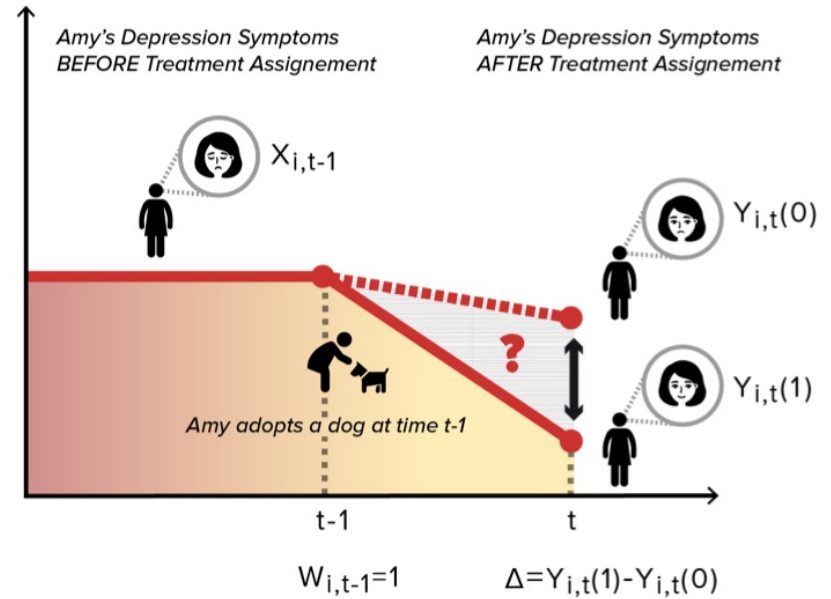
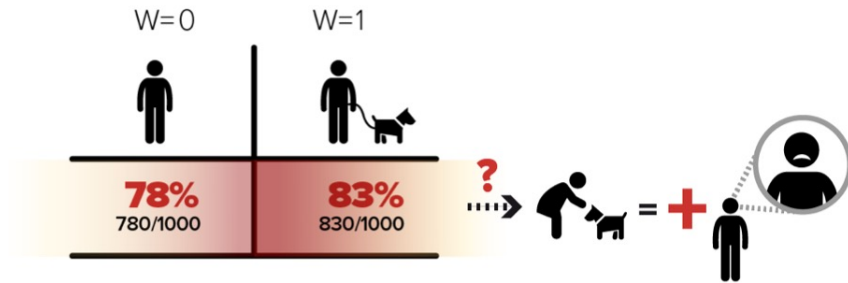
[Rothman & Greenland, 1998]

# Intuition about causation

Even before studying causal inference, we all have experience with causal effects:

- Starting now, if I stop eating ice cream at night, how much weight will I lose in three months?
- If I adopt a puppy, will the severity of my depression symptoms improve in one year?
- If I give my patient new chemotherapy instead of the standard chemotherapy, how many more months will he/she live?
- If my government implement stricter regulatory policies for air pollution, how much longer can I expect to live?
- If my country or state had implemented a mask mandate three months ago to slow down the spread of COVID-19, how many lives would have been saved?

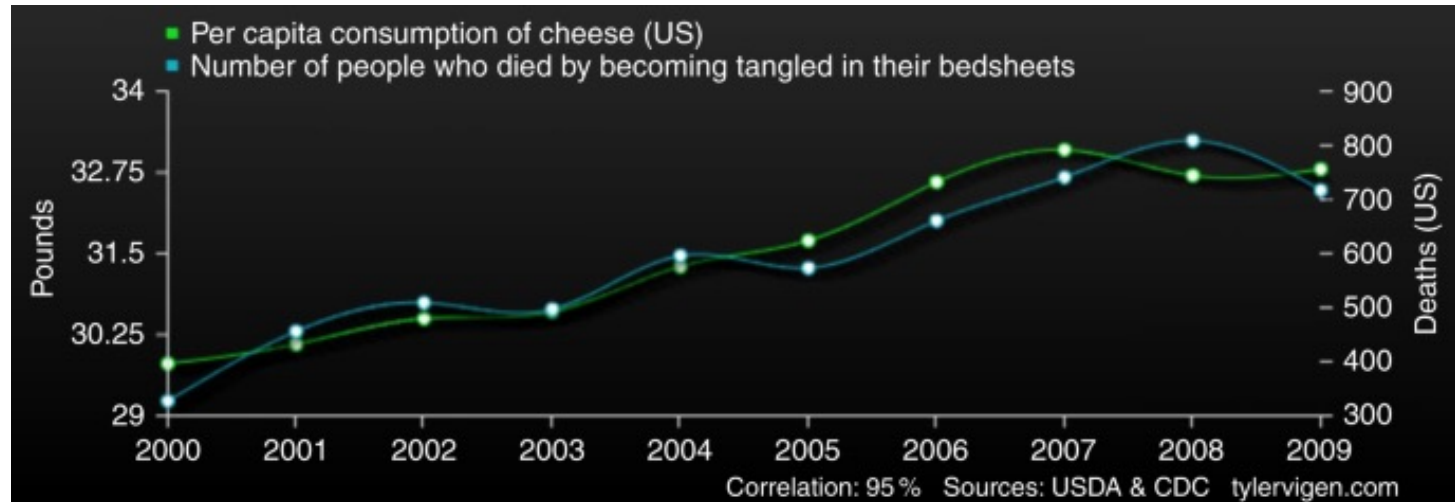
# Causal contrast



# Definition

- Cause
  - **Must precede the effect** (absolute requirement)
  - Can be either
    - positive = the presence of an exposure
    - negative = the absence of exposure (e.g. vaccination)
- Should **always** be set up as a comparison

# Correlation does not equal causation!



- Does consuming cheese cause mortality due to people to getting tangled in their bedsheets?
- Even though there is an apparent correlation, if you were to do an RCT, unlikely randomizing cheese consumption vs. dairy free diet would have an impact on bedsheet-related mortality

## 2. Determining extent & burden of disease in a population

- Vast field of epidemiology called descriptive or surveillance epidemiology
- Monitoring the health of a population group
- Example: National Health and Nutrition Examination Survey (NHANES) is a survey of Americans to better understand health of our population
  1. Interview: directly interviewing the survey participant and those within their household about their health.
  2. Examination: conducting clinical tests, anthropometric , biochemical , and radiological measurements, and physical examinations.

# NHANES is publicly available

*not so*  
**Fun Fact**

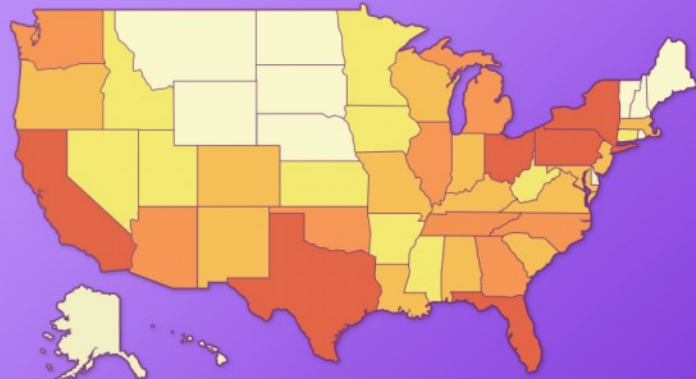
Fewer than  
**9 out of 10**  
people don't get enough  
**FIBER**

Many **Kellogg's**  
cereals are a good or excellent  
source of fiber, including:



<sup>1</sup>What We Eat in America, NHANES 2007-2010, individuals 1 year and over, dietary intake data. Prepared by the Food Surveys Research Group, Beltsville Human Nutrition Research Center. Agricultural Research Services, U.S. Department of Agriculture.

Approximately **2.3 million people** in the U.S. are living with **Hepatitis C**, but, fortunately, there is a cure.



Estimated Number of People Living with Hepatitis C, 2013-2016

0 - 10,000    10,001 - 25,000    25,001 - 50,000    50,001 - 75,000    75,001+

CDC recommends Hepatitis C testing for



**BABY BOOMERS**  
(BORN BETWEEN 1945-1965)

and anyone with a



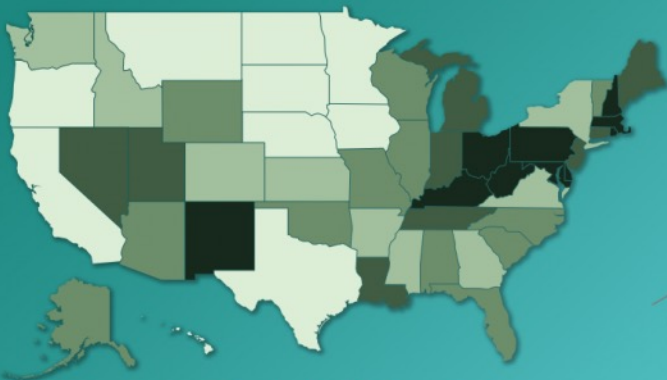
**HISTORY OF  
INJECTION DRUG USE**

Data can be used to guide policies and improve health

Understand the health of the population

Eliminates \$\$\$ of collecting primary data

In 2017, **47,600 people** died from an **opioid-related overdose** – over **5,000 more people** than in 2016.



Narcotic Overdose Mortality Rate, 2013-2016

0 - 11.5    11.6 - 17.0    17.1 - 20.0    20.1 - 25.0    25.1+

Drug overdose deaths **more than doubled** between 2007 and 2017.

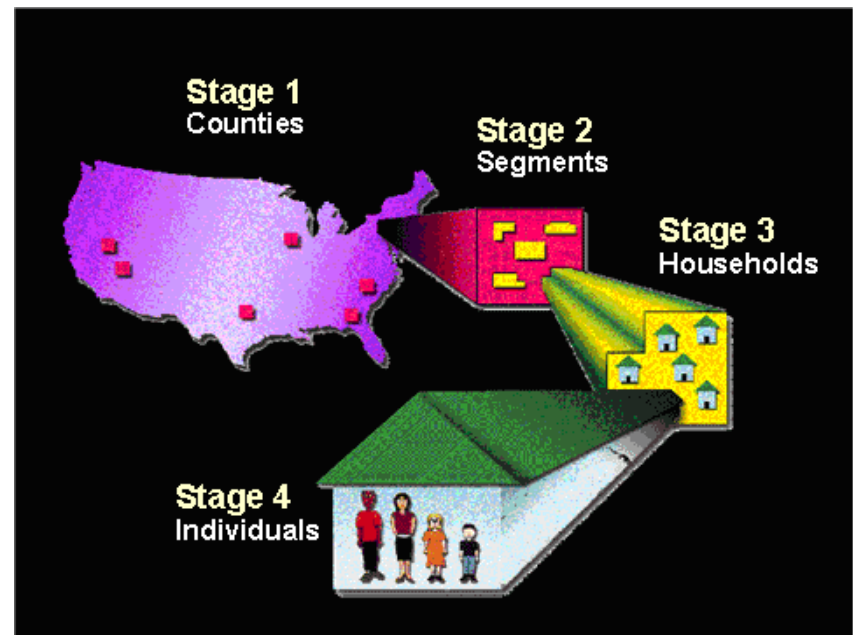




# NHANES is representative

Probability-based complex sampling design:

1. Select 15 primary sampling units (counties or small groups of counties) ~5000 individuals in each PSU
2. Select segments--cluster of neighbourhood blocks (depending on housing density)
3. Select households from segments
4. Select participants from households



# Disproportionate burden of COVID-19

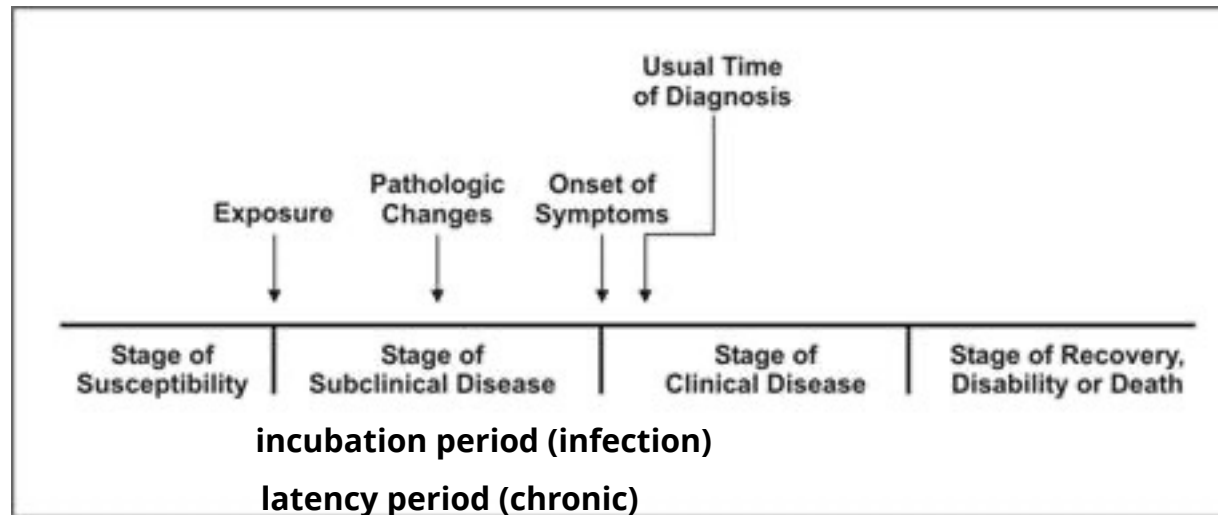
*“Covid is the great equalizer”*

*“Everyone is subject to this virus...I don’t care how smart, how rich, how powerful you think you are.” –Andrew Cuomo*

- Descriptive epidemiology has played a hugely important role in helping us understand that these claims are **untrue**
- Worsening health disparities: hurting low-income communities, individuals of colour, and other marginalized groups
  - Work from home vs. front line workers (hospitals, grocery store)
  - Food security (food bank vs. Instacart)
  - Structural racism and existing health disparities leading to worse outcomes in individuals in black and brown communities

# 3. Natural history and disease prognosis

- Natural history: Progression of disease process in an individual or population group over time in the absence of treatment



# Saxitoxin Poisoning



Southern Puffer Fish



Red Tide

Paralytic shellfish poisoning  
(tingling, numbness around  
lips and fingertips, giddiness,  
incoherent speech,  
respiratory paralysis,  
sometimes death)

Occurs within few minutes  
to 30 minutes

# 4. Assessing preventive measures

Harm reduction is a set of practical strategies and ideas aimed at reducing negative consequences associated with certain behaviours

- Continuing level of drug use in society is inevitable and defines objectives as reducing adverse consequences
- Evidence from that harm reduction approaches greatly reduce morbidity and mortality associated with risky health behaviours
- Needle-exchange programs → mean annual decreases in HIV seroprevalence compared with those areas that have not introduced needle-exchange programs

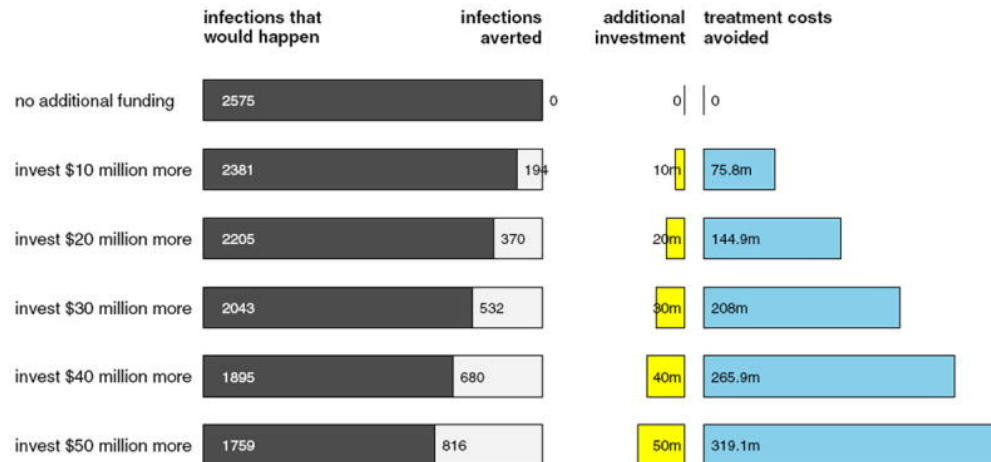
# Needle Exchange Programs

-First introduced in Tacoma, Washington and now >300 across the USA

-Allow individuals to get sterile needles free of charge and safely dispose of dirty needles and syringes used for drug injection

-Opportunity to offer educational and medical services, such as referrals to substance use disorder programs and testing

-For every dollar invested in expanding a needle exchange program, \$6 could be saved in HIV treatment.



# Therapeutic interventions

- 1954 → polio vaccine field trials
- >620,000 schoolchildren were randomly assigned to receive vaccine or placebo (+ more than 1 million observed controls)
- 1955 → evidence showed Salk vaccine was 80-90% effective in preventing paralytic poliomyelitis (polio)



# 5. Evidence to inform public health and environmental policies

**Viceroy**  
**FILTER**  
**the Smoke!**

As your Dentist,  
I would recommend  
**VICEROYS**

VICEROY  
Filter Tip  
CIGARETTES

## BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 26 1954

### THE MORTALITY OF DOCTORS IN RELATION TO THEIR SMOKING HABITS A PRELIMINARY REPORT

BY

**RICHARD DOLL, M.D., M.R.C.P.**

*Member of the Statistical Research Unit of the Medical Research Council*

AND

**A. BRADFORD HILL, C.B.E., F.R.S.**

*Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council*

*According to a recent Nationwide survey:*

## MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

- Like the rest of us, doctors smoke for pleasure. Their taste recognizes and appreciates full flavor and cool mildness just as yours does.
- And when 112,397 doctors were asked to name the cigarette they smoked, more doctors named Camels than any other brand.
- These nationally known independent research organizations conducted the survey. They queried doctors in every branch of medicine.

*Your "T-Zone" will tell you*

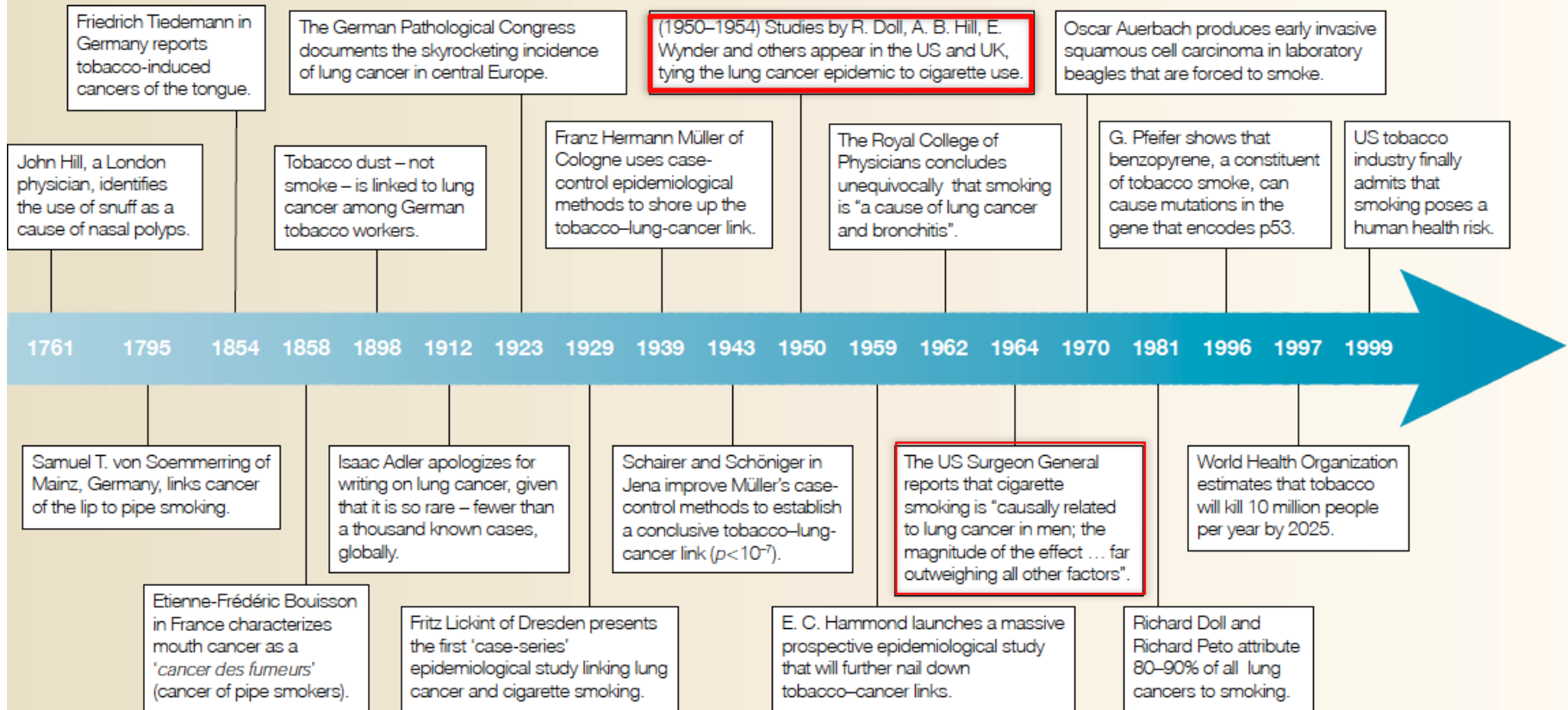
**T for Taste...**  
**T for Throat...**

- Taste and Throat... your "T-Zone"... that's your proving ground for any cigarette.
- See how your own critical sense responds to the rich, full flavor of Camel's choice tobaccos. Tobacco of uncompromising quality... tobaccos blended in the fine, traditional Camel way.
- See how your throat reacts to the cool mildness of Camels.
- See if Camels don't suit your "T-Zone" as a "T."



# Tobacco and Lung Cancer

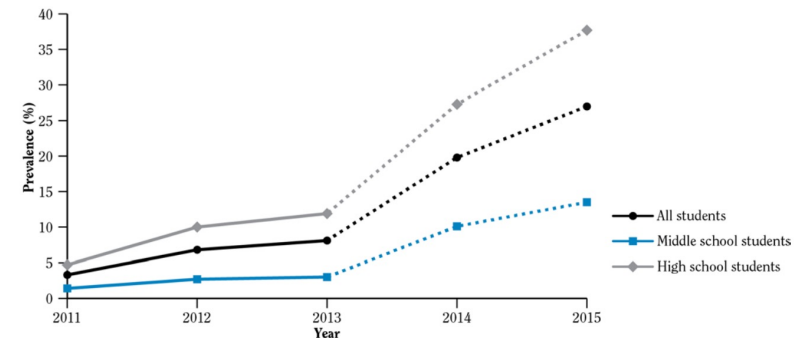
## Timeline | Key events in the discovery of tobacco-cancer causation



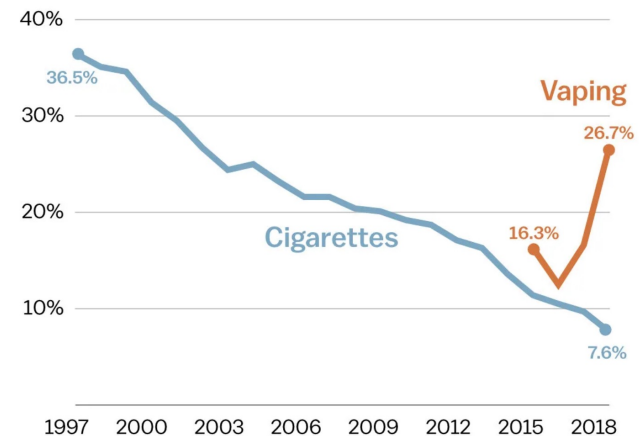
# E-cigarette use in young adults

- In recent years, e-cigarette use by youth and young adults has increased
- E-cigarettes (including vaping devices) are now the most commonly used tobacco product among youth
  - E-cigarettes are tobacco products that deliver nicotine
- E-cigarettes can expose users to several chemicals, including nicotine, carbonyl compounds, and volatile organic compounds
- The health effects and potentially harmful doses of heated and aerosolized constituents of e-cigarette liquids, including solvents, flavorants, and toxicants, are not completely understood.

Figure 1 Trends in ever e-cigarette use<sup>a</sup> among U.S. middle and high school students; National Youth Tobacco Survey (NYTS) 2011–2015



Trends in use of cigarettes and vape devices in the past 30 days among 12th-graders



# The Juul controversy



- Is Juul a harm reduction tool intended to provide a safer alternative to cigarettes?
- Or is Juul a new era of cigarette intended to get teens and young adults hooked on a highly addictive chemical?

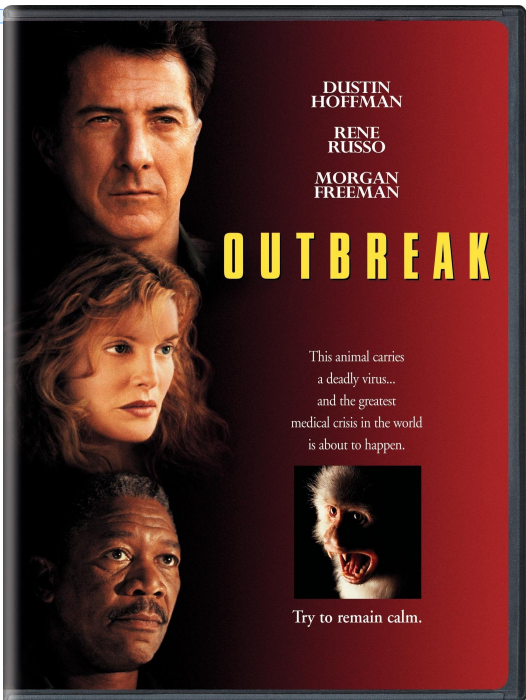
# Marketing to a young audience



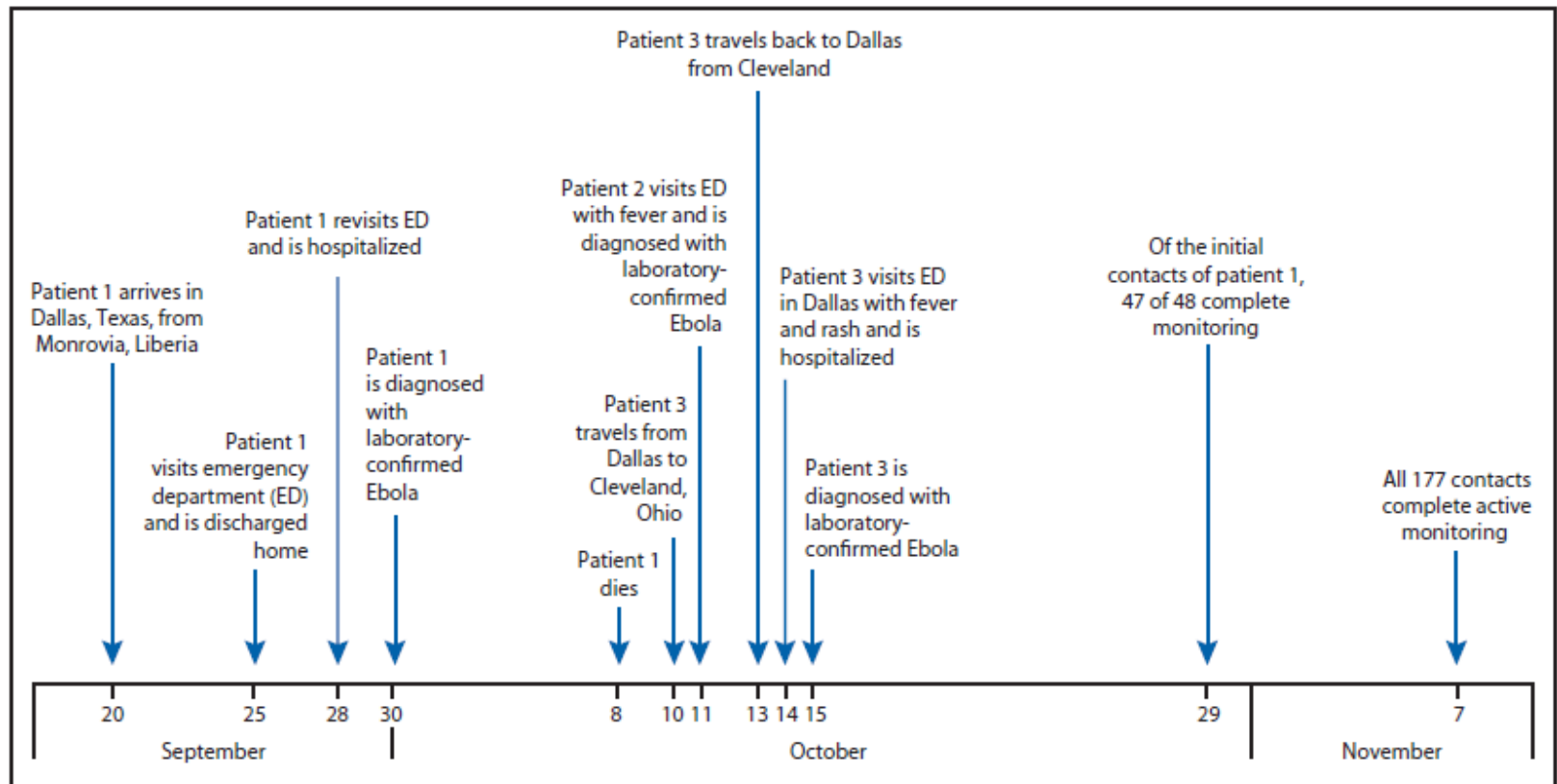
“Maybe more important than the content of the ads was the media Juul used to reach people. “What Juul did that’s different is it exploited social media, where American middle and high school kids live...that was their innovation.”

– Dr. Robert Jackler

# Epidemiology = more than epidemics



# 2014 Ebola Virus Cluster in Dallas, Texas



## Trial by Ebola



Dallas County chief epidemiologist Dr. Wendy Chung, far right, and members of her team—from left, Sonya Hughes, Emily Hall, and Sibeso Joyner. Chung suspected Thomas Eric Duncan had Ebola and urged that he be tested, despite doubts from the Centers for Disease Control and Prevention. Photograph by Dan Winters.

When Ebola reached America, arriving in Dallas on September 20, the city had no real plan to handle the outbreak. Nor, it appeared, did the federal government. As epidemiologist Wendy Chung, county judge Clay Jenkins, and other local officials quickly realized, they were largely on their own. Bryan Burroughs has the untold story of their heroic response.

<http://www.vanityfair.com/news/2015/02/ebola-us-dallas-epidemic>

“Behind the scenes, much of the work that week had fallen to teams of county and C.D.C. epidemiologists, who tracked down and interviewed the dozens of people who had come into contact with Duncan after his arrival in America.

Eventually 177 people in the Dallas area would fall under some type of quarantine. Monitoring these people became a monumental job. The epi had to visit each person twice a day to take his or her temperature, every visit limited by strict medical guidelines. The epi couldn't approach within three feet of the person; the person took his or her own temperature, then held the thermometer aloft for the epi to read. But tending to the quarantined quickly became more than just medical visits. Once people were restricted to their homes, they had to be brought groceries and medicine. Children who couldn't go to school still needed their homework.”

# Field Epidemiology

1. identify patients with Ebola at presentation to minimize potential exposures
2. rapidly identify contacts of Ebola patients and evaluate their level of exposure risk
3. monitor potentially large numbers of community and health care contacts
4. assess infection control practices and conduct large-scale training sessions
5. develop protocols to safely transport suspected Ebola patients to hospitals and safely evaluate these patients within a hospital
6. designate facilities to care for patients with confirmed Ebola.



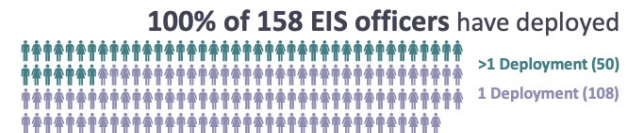
# Epidemic Intelligence Service (EIS)

## What EIS Officers Do

EIS officers serve on the front lines of public health, protecting Americans and the global community, while training under the guidance of seasoned mentors. When disease outbreaks or other public health threats emerge, EIS officers investigate, identify the cause, rapidly implement control measures, and collect evidence to recommend preventive actions.

### **EIS officers have responded to a multitude of major health threats since 1951, including:**

- Investigating biological warfare during the Korean war
- Providing disaster relief following Hurricanes Harvey, Irma, Maria, and Katrina, and 9/11
- Providing on-the-ground response to Ebola and Zika virus outbreaks.

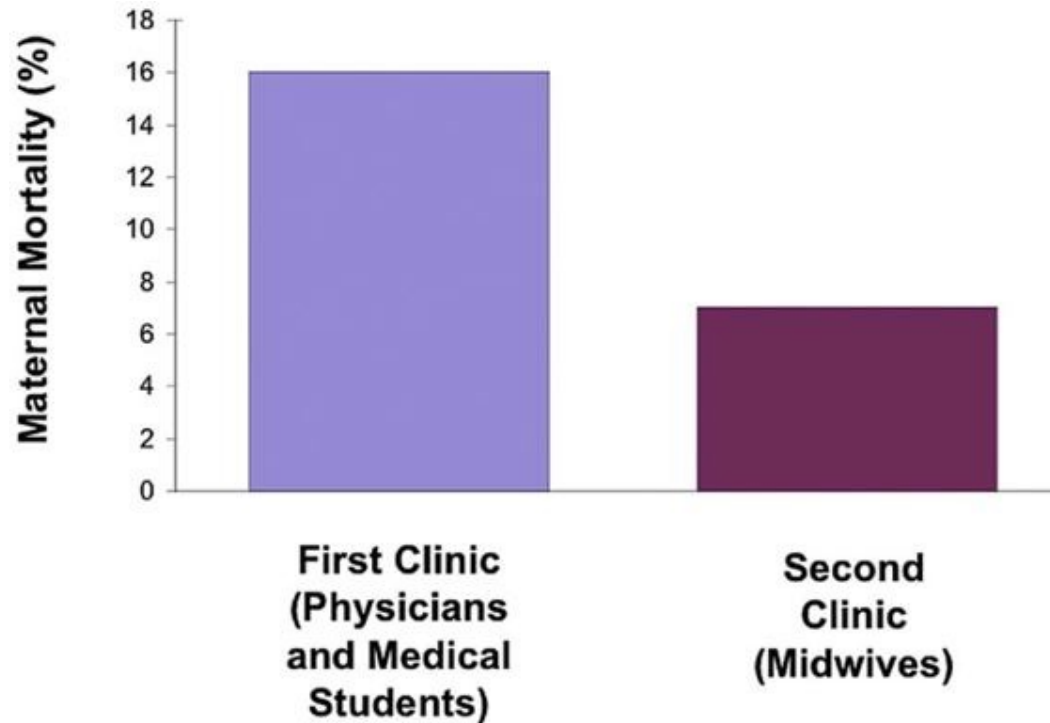


# History of Epidemiology

- Before population-representative datasets and analyses of millions of observations were even conceivable, epidemiologists used **observations** from the natural world to create interventions to improve population health
- **Historic examples:**
  - 1. Childbed fever (maternal fever post-delivery)
  - 2. Smallpox
  - 3. Cholera

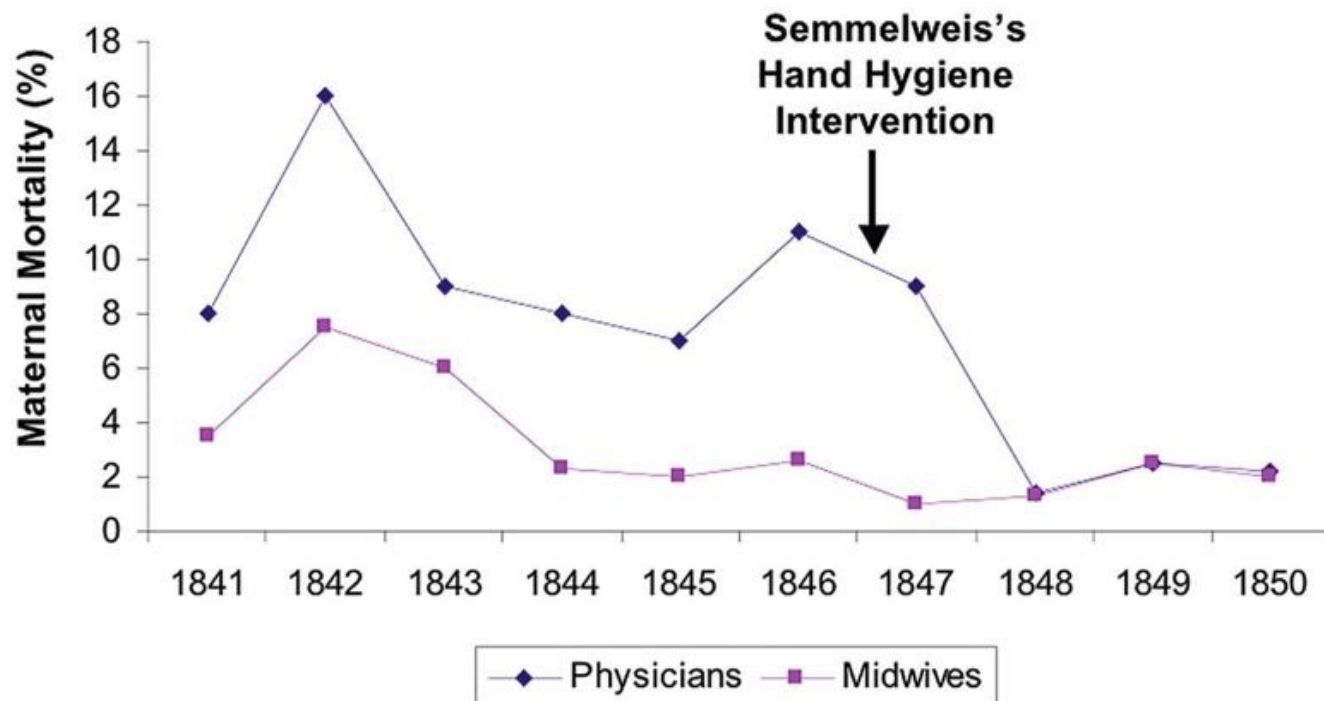
# Historic Examples of Epidemiology

## Semmelweis and childbed fever



# Historic Example 1

What could be the cause of the differing mortality rates?



# Historic Example 2

## Jenner and Smallpox

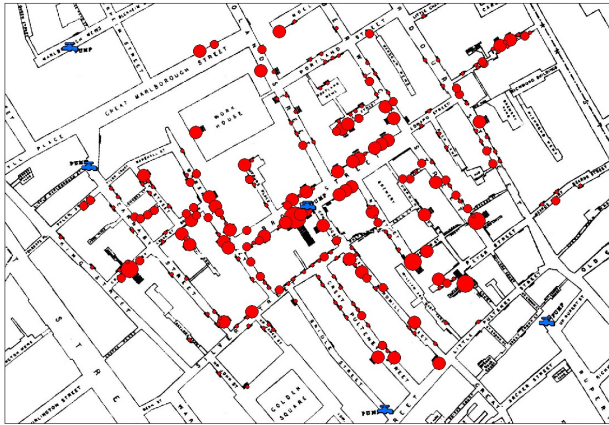
- In the 1800s, ~400,000 people died each yr
- Survivors were immune
- “Variolation” procedure (less than ideal!)
- Cowpox survivors also immune
- Tested his theory and observed the results
  
- WHO reports smallpox eradicated in 1980

Interesting fact: The term “vaccination” is derived from *vacca*, the Latin word for “cow.”

# Historic Example 3

## John Snow and Cholera

- 600 deaths all around the Broad Street Pump in 1854
- Is Cholera transmitted through water? Or via miasma (Farr)?



Water Supply	No. of Houses	Deaths from Cholera	Deaths per 10,000 Houses
Southwark and Vauxhall Co.	40,046	1,263	315
Lambeth Co.	26,107	98	38

# The Breadth of Epidemiology

- There's an area of epidemiology for almost every interest, a few include:
  - Pharmacoepidemiology
  - Social epidemiology
  - Environmental epidemiology
  - Clinical epidemiology
  - Genetic epidemiology
  - Health services research
  - Health policy research
  - Psychiatric epidemiology
  - Nutritional epidemiology
  - Reproductive and perinatal epidemiology

# Cardiovascular Disease

- In 1950s, 1 in 3 men would develop CVD before age 60
  - Public health efforts around WWII resulted in improvements in infectious diseases (e.g., sanitation, penicillin)

*As part of the longitudinal study on the development of cardiovascular disease which is being conducted at Framingham, Mass., attention is being given to a variety of specific factors. This report presents evidence on national origin, educational status, and smoking and drinking habits.*

## **SOME FACTORS ASSOCIATED WITH THE DEVELOPMENT OF CORONARY HEART DISEASE**

### **SIX YEARS' FOLLOW-UP EXPERIENCE IN THE FRAMINGHAM STUDY**

*Thomas R. Dawber, M.D.; William B. Kannel, M.D.; Nicholas Resotshie, M.D.; Joseph Stokes, III, M.D.; Abraham Kagan, M.D.; and Tavia Gordon*

Nearly 800,000 Americans die each year from heart disease and stroke. Most of the major risk factors can be managed or prevented.

#### **Risk factors and solutions for managing them**



**High blood pressure** – Make control your goal.



**High cholesterol** – Work with your doctor on a treatment plan to manage your cholesterol.



**Diabetes** – Work with your doctor on a treatment plan to manage your diabetes.



**Tobacco use** – If you don't smoke, don't start. If you do smoke get help to quit.



**Unhealthy diet** – Eat a healthy diet, low in sodium and trans fats and high in fresh fruits and vegetables.



**Physical inactivity** – The Surgeon General recommends adults engage in moderate-intensity exercise for 2 hours and 30 minutes every week.



**Obesity** – Work to maintain a healthy weight.



# Occupational Epidemiology



All EHP content is accessible to individuals with disabilities. A fully accessible (Section 508-compliant) HTML version of this article is available at <http://dx.doi.org/10.1289/ehp.1205894>.

Research

## Cancer Incidence in World Trade Center Rescue and Recovery Workers, 2001–2008

Samara Solan,<sup>1</sup> Sylvan Wallenstein,<sup>1</sup> Moshe Shapiro,<sup>1</sup> Susan L. Teitelbaum,<sup>1</sup> Lori Stevenson,<sup>1</sup> Anne Kochman,<sup>1</sup> Julia Kaplan,<sup>1</sup> Cornelia Dellenbaugh,<sup>1,\*</sup> Amy Kahn,<sup>2</sup> F. Noah Biro,<sup>1</sup> Michael Crane,<sup>1</sup> Laura Crowley,<sup>1</sup> Janice Gabrilove,<sup>2</sup> Lou Gonsalves,<sup>4</sup> Denise Harrison,<sup>5</sup> Robin Herbert,<sup>1</sup> Benjamin Luft,<sup>6</sup> Steven B. Markowitz,<sup>7</sup> Jacqueline Moline,<sup>8</sup> Xiaoling Niu,<sup>9</sup> Henry Sacks,<sup>1</sup> Gauri Shukla,<sup>1</sup> Iris Udasin,<sup>10</sup> Roberto G. Lucchini,<sup>1,11</sup> Paolo Boffetta,<sup>12</sup> and Philip J. Landrigan<sup>1</sup>

**BACKGROUND:** World Trade Center (WTC) rescue and recovery workers were exposed to a complex mix of pollutants and carcinogens.

**OBJECTIVE:** The purpose of this investigation was to evaluate cancer incidence in responders during the first 7 years after 11 September 2001.

**METHODS:** Cancers among 20,984 consented participants in the WTC Health Program were identified through linkage to state tumor registries in New York, New Jersey, Connecticut, and Pennsylvania. Standardized incidence ratios (SIRs) were calculated to compare cancers diagnosed in responders to predicted numbers for the general population. Multivariate regression models were used to estimate associations with degree of exposure.

**RESULTS:** A total of 575 cancers were diagnosed in 552 individuals. Increases above registry-based expectations were noted for all cancer sites combined (SIR = 1.15; 95% CI: 1.06, 1.25), thyroid cancer (SIR = 2.39; 95% CI: 1.70, 3.27), prostate cancer (SIR = 1.21; 95% CI: 1.01, 1.44), combined hematopoietic and lymphoid cancers (SIR = 1.36; 95% CI: 1.07, 1.71), and soft tissue cancers (SIR = 2.26; 95% CI: 1.13, 4.05). When restricted to 302 cancers diagnosed  $\geq$  6 months after enrollment, the SIR for all cancers decreased to 1.06 (95% CI: 0.94, 1.18), but thyroid and prostate cancer diagnoses remained greater than expected. All cancers combined were increased in very highly exposed responders and among those exposed to significant amounts of dust, compared with responders who reported lower levels of exposure.

**CONCLUSION:** Estimates should be interpreted with caution given the short follow-up and long latency period for most cancers, the intensive medical surveillance of this cohort, and the small numbers of cancers at specific sites. However, our findings highlight the need for continued follow-up and surveillance of WTC responders.

**KEY WORDS:** cancer, cancer incidence, cancer registry, epidemiology, September 11th, World Trade Center, WTC Health Program. *Environ Health Perspect* 121:699–704 (2013). <http://dx.doi.org/10.1289/ehp.1205894> [Online 23 April 2013]

# Infectious Disease Epidemiology

Articles

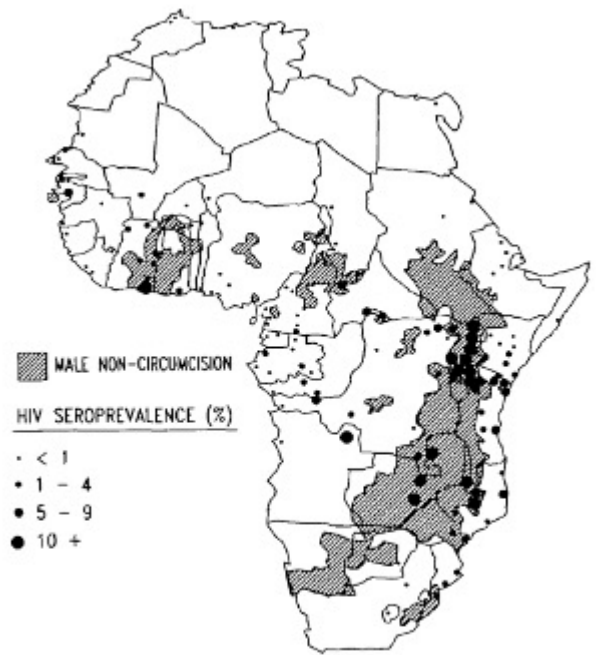


FIGURE 1. Map of Africa showing political boundaries and usual male circumcision practice, with point estimates of general adult population HIV seroprevalence superimposed

## Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial

Richard Ochiyo, Daphne Mwaheki, Cornelius P. Obura, Aggrey O. Ombaka, Joseph A. Ayumu, Geoffrey A. H. Njoroge, Richard T. Condon, John A. O. Njoroge et al.

**Summary**  
Background: Male circumcision can provide substantial protection against acquisition of HIV infection. Our aim was to determine whether male circumcision had a protective effect against HIV infection, and to assess safety and changes in sexual behaviour related to the intervention.

**Methods:** We did a randomised controlled trial of 2700 men aged 16–29 years in Kisumu, Kenya. We were randomly allocated to an intervention group (circumcision; n = 1351) or a control group (delayed circumcision; 1349) and assessed by HIV testing, medical examinations, and behavioural interviews during follow-up at 0, 3, 6, 12, 18, and 24 months. HIV seroprevalence was estimated in an intention-to-treat analysis. The trial is registered with ClinicalTrials.gov with the number NCT00593377.

**Findings:** The trial was stopped early on December 12, 2008, after a final interim analysis revealed by the data and safety monitoring board. The median length of follow-up was 21 months. Follow-up for HIV seroprevalence included 2303 (85%) participants, 1222 in the intervention group and 1081 in the control group had used patches for HIV when the study was stopped. The 2-year HIV incidence was 2.1% (95% CI 1.5–2.8) in the circumcision group and 4.2% (3.3–5.2) in the control group (p<0.001); the relative risk of HIV infection in circumcised men was 0.57 (95% CI 0.39–0.83), which corresponds to a reduction in the risk of acquiring an HIV infection of 43% (33–57). Adherence to instructions to abstain and avoiding sex with men found to be seropositive to syphilis, the protective effect of circumcision was 65% (32–87). Serious adverse events related to the intervention (21 events in 1.5% of those circumcised) resolved quickly. No additional risk complications after circumcision was observed.

**Interpretation:** Male circumcision significantly reduces the risk of HIV acquisition in young men in Africa. Where appropriate, voluntary, safe, and affordable circumcision services should be provided with other HIV prevention strategies.

**Introduction**  
HIV infection is a leading cause of morbidity and mortality worldwide. In sub-Saharan Africa, HIV infection is a major cause of death and disability. The World Health Organization (WHO) estimates that 25 million people are living with HIV infection, and 2 million die each year from AIDS-related complications.<sup>1</sup> In sub-Saharan Africa, the prevalence of HIV infection is high, and the risk of acquiring an HIV infection is high. In Kenya, the prevalence of HIV infection is 12.5% among men aged 15–49 years.<sup>2</sup> In Kisumu, Kenya, the prevalence of HIV infection is 12.5% among men aged 15–49 years.<sup>3</sup> In Kisumu, Kenya, the prevalence of HIV infection is 12.5% among men aged 15–49 years.<sup>3</sup>

Study name	Statistics for each study				Risk ratio and 95% CI
	Risk ratio	Lower limit	Upper limit	p-Value	
Auvert, RSA	0.42	0.25	0.70	0.001	
Bailey, Kenya	0.41	0.24	0.70	0.001	
Gray, Uganda	0.50	0.30	0.83	0.007	
Combined	0.44	0.33	0.60	<0.0001	

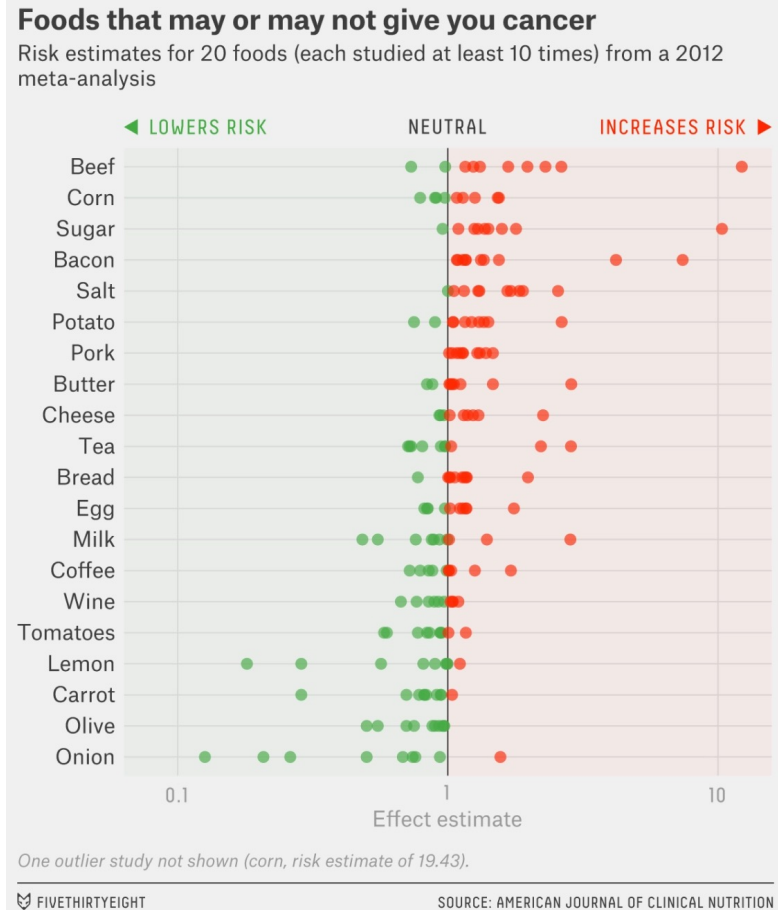
0.01 0.1 1 10 100  
Favours Circumcision Favours Control

(Moses et al., 1990; Mills et al., 2008)

# You Can't Trust What You Read About Nutrition

We found a link between cabbage and innie bellybuttons, but that doesn't mean it's real.

- Nearly all nutrition studies rely on measures of food consumption that require people to remember and report what they ate
- Generate huge datasets --> easy to find spurious associations, associations that won't be replicated



# Do We Really Know What Makes Us Healthy?



→ Not really. So much confusion!



**BBC NEWS** **WATCH One-Minute World News**

Last Updated: Friday, 8 August, 2003, 11:21 GMT 12:21 UK  
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## HRT 'doubles breast cancer risk'

Taking certain types of hormone replacement therapy (HRT) can double the risk of developing breast cancer, says a study of more than a million women.



Breast cancer could be more deadly after HRT

The largest ever study into the link between HRT and breast cancer was conducted by scientists at Cancer Research UK's Epidemiology Unit in Oxford.

The research suggests the single pill moderately increases the risk of breast cancer, but the combined pill doubles the risk.

It estimates HRT, taken by women to relieve the unpleasant symptoms of menopause, may have been responsible for an extra 20,000 cases of the disease in Britain in the last decade.

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A Fuller Spectrum of News

## Combo HRT linked to lower-risk breast cancers

### Tumors tend have better prognosis than after estrogen-only therapy

**REUTERS**  
Updated: 8:42 p.m. ET June 5, 2007

The types of breast tumors that occur after [combination hormone replacement therapy](#) in women going through menopause and in post-menopausal women tend to have a better prognosis than those that occur after estrogen-only replacement therapy, Swedish researchers report.

A team at Malmo University Hospital conducted a study involving 12,583 peri- or post-menopausal women whose medical records were linked to national cancer registries. Of the group, 513 had a [history of breast cancer](#) prior to

**Q & A library**  
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Breast cancer	Ovarian cancer
Colon cancer	Prostate cancer
Melanoma	

**Related Stories**    What's this?

- Is it safe to get pregnant after breast cancer?
- Older women shouldn't take hormones
- Group therapy doesn't extend life in cancer
- Early Ovarian Surgery Linked to Dementia

# Contradictions

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**The New York Times**

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## Gene Is Linked to Susceptibility to Depression

By MARY DUENWALD  
Published: Friday, July 18, 2003

Scientists have identified a gene that may help explain why some people become depressed in response to the stresses of life and others skate by relatively unscathed.

The gene, which comes in two forms, or alleles, can either protect people from depression or make them more vulnerable, researchers report today in the journal *Science*.

In the study, people who experienced job loss, death in the family, abuse or other traumas were much more likely to develop depression if they possessed two copies of the short allele. Those with two copies of the long allele (pronounced uh-LEEL) were able to withstand such events without becoming depressed.

"No matter how many stressful events they had in a five-year period, they were no more likely to become depressed than people who had

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## Science

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## Report on Gene for Depression Is Now Faulted

By BENEDICT CAREY  
Published: June 16, 2009

One of the most celebrated findings in modern [psychiatry](#) — that a single gene helps determine one's risk of depression in response to a divorce, a lost job or another serious reversal — has not held up to scientific scrutiny, researchers reported Tuesday.

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Readers shared their thoughts on this article.  
[Read All Comments \(48\) »](#)

[The original finding](#), published in 2003, created a sensation among scientists and the public because it offered the first specific, plausible explanation of why some people bounce back after a stressful life event while others plunge into lasting despair.

The new report, by several of the most prominent researchers in the field,

does not imply that interactions between genes and life experiences are trivial; they are

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# Retractions

## Vaccination and Autism

### Early report

#### Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, SH Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

#### Summary

**Background** We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

**Methods** 12 children (mean age 6 years [range 3-10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Haecoscintigraphy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

**Findings** Onset of behavioural symptoms was associated with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had ileal/lymphoid-nodular hyperplasia (range from lymphoid nodular hyperplasia to pseudo-tuberculosis). Histology showed patchy chronic inflammation. In 11 children and reactive lymphoid hyperplasia in seven, but no granulomas. Biopsy findings included autism (nine), disintegrative psychosis (one), and possible postviral or vacuolar encephalopathy (two). There were no focal neurological abnormalities and EEG tests were normal. Abnormal laboratory results were significantly raised urinary homovanillic acid compared with age-matched controls (mean 10.5, low haemoglobin in four children, mean low hemoglobin in 10 children).

**Interpretation** An idiopathic associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

Lancet 1998; **351**: 637-41  
See Commentary page 642

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield), A Anthony, S Linnell, M A Thomson, S E Davies, S K Davies, M Berelowitz and the University Departments of Paediatric Gastroenterology (S H Murch), D M Casson, M Malik, M Thomson, J A Walker-Smith, J A Walker-Smith, Child and Adolescent Psychiatry (M Berelowitz), Neurology (P Harvey), and Radiology (A Valentine), Royal Free Hospital and School of Medicine, London NW3 2QG, UK  
Correspondence to: Dr A J Wakefield

THE LANCET • Vol 351 • February 28, 1998

#### EARLY REPORT

#### Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and vomiting and, in some cases, food intolerance. We describe the clinical course, and gastrointestinal features of these children.

#### Patients and methods

12 children, consecutively referred to a department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of skills and associated symptoms (autism, abdominal pain, bloating and food intolerance), were included. All children were admitted to the ward for work-up, accepted by their parents.

#### Clinical investigations

We took histories including details of immunisations and exposure to infectious disease, and assessed the children. In 11 cases, the histories obtained by the senior clinician (W.S.). Neurological and psychiatric assessments were done by consultant staff (P.H., M.B.) with HMS-4 criteria. Developmental histories included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessments in hospital; all had had assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, haecoscintigraphy was performed by SHM or MAT under sedation with midazolam and pethidine. Peril from and formalin-fixed mucosal biopsy samples were taken from the terminal ileum, ascending, caecum, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain wave auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

#### Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.<sup>1</sup> Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antimicrobial antibodies and boys were screened for fragile-X if this had not been done

#### ARTICLES

### Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association

Brent Taylor, Elizabeth Miller, C Paddy Farrington, Maria-Christina Petropoulos, Isabelle Favot-Mayaud, Jun Li, Pauline A Waight

#### Summary

**Background** We undertook an epidemiological study to investigate whether measles, mumps, and rubella (MMR) vaccine may be causally associated with autism.

**Methods** Children with autism born since 1979 were identified from special needs/disability registers and special schools in eight North Thames health districts, UK. Information from clinical records was linked to immunisation data held on the child health computing system. We looked for evidence of a change in trend in incidence or age at diagnosis associated with the introduction of MMR vaccination to the UK in 1988. Clustering of onsets within defined postvaccination periods was investigated by the case-series method.

**Findings** We identified 498 cases of autism (261 of core autism, 166 of atypical autism, and 71 of Asperger's syndrome). In 293 cases the diagnosis could be confirmed by the criteria of the International Classification of Diseases, tenth revision (ICD10): 214 [82%] core autism, 52 [31%] atypical autism, 27 [38%] Asperger's syndrome. There was a steady increase in cases by year of birth with no sudden "step-up" or change in the trend line after the introduction of MMR vaccination. There was no difference in age at diagnosis between the cases vaccinated before or after 18 months of age and those never vaccinated. There was no temporal association between onset of autism within 1 or 2 years after vaccination with MMR (relative incidence compared with control period 0-94 [95% CI 0-60-1-47] and 1-09 [0-79-1-52]). Developmental regression was not clustered in the months after vaccination (relative incidence within 2 months and 4 months after MMR vaccination 0-92 [0-38-2-21] and 1-00 [0-52-1-95]). No significant temporal clustering for age at onset of parental concern was seen for cases of core autism or atypical autism with the exception of a single interval within 6 months of MMR vaccination. This appeared to be an artifact related to the difficulty of defining precisely the onset of symptoms in this disorder.

**Interpretation** Our analyses do not support a causal association between MMR vaccine and autism. If such an association occurs, it is so rare that it could not be identified in this large regional sample.

#### Introduction

Wakefield and colleagues<sup>1</sup> postulated that measles, mumps, and rubella (MMR) vaccination might be causally linked with autism. Although there is no scientific evidence to support this claim,<sup>2-4</sup> neither are there robust data on the prevalence of autism in children born before and after the introduction of MMR vaccine to the UK in 1988. The postulated causal link between MMR vaccination and autism was based on a reported close temporal association between these two events.<sup>1</sup> Since MMR vaccine is given at around 12-15 months of age and the mean age at which parents of children with autism first report concern about their child's development is 18-19 months,<sup>5</sup> a close temporal association in some autistic children would be expected by chance.<sup>6</sup>

We undertook a population-based study in the North East Thames region to investigate trends in the incidence of autistic disorders before and after the introduction of MMR vaccine in October, 1988, and the immunisation histories of children with these disorders. We used case-series analysis methods to test for clustering of onsets within defined postvaccination periods.

#### Patients and methods

Children with autistic disorders born since 1979 were identified in eight health districts in mid-1998 from computerised special needs/disability registers at child development centres and from records in special schools. Information on children with such disorders who were younger than 16 years of age was extracted from clinical records by one of three experienced paediatric registrars. The information extracted included the age at which the autistic disorder was diagnosed, the recorded age at which the parents first became concerned about the child's developmental state, and the age at which the regression became obvious, if that was a feature.

By use of criteria of the International Classification of Diseases, tenth revision (ICD10), the diagnosis of autism was checked against information in the available records on the child's present condition and his or her condition between the ages of 18 months and 3 years. Study investigators worked in pairs with opportunity for discussion to reach consensus when there was ambiguity. Inter-rater reliability was tested on 20 case records (independent completion of the data-collection form); the concordance was above 95%. Immunisation data, which were recorded independently of the clinical record, with exact

# Today's Random Medical News

from the New England  
Journal of  
Panic-Inducing  
Gobbledygook

JIM BORGMAN



**Figure 3:** New England Journal of Panic-Inducing Gobbledygook.

Source: Jim Borgman, The Cincinnati Enquirer (27 April 1997, E4).

# Be skeptical!

- Don't always believe what you read
- Form your own opinions
- **Be an informed reader of the medical literature**
- Critical appraisal



# Readings for this Week

<http://fivethirtyeight.com/features/you-cant-trust-what-you-read-about-nutrition/>

[http://www.nytimes.com/2007/09/16/magazine/16epidemiology-t.html?\\_r=0](http://www.nytimes.com/2007/09/16/magazine/16epidemiology-t.html?_r=0)

<https://www.vox.com/2020/4/10/21207520/coronavirus-deaths-economy-layoffs-inequality-covid-pandemic>