Figuring out what makes populations sick:

unraveling disease mysteries

James A. Hanley PhD

Dept. of Epidemiology, Biostatistics & Occupational Health McGill University, Montréal, Québec, Canada

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Outline

- The practice of community vs. clinical medicine
- Epidemiological Research → knowledge for the practice of community medicine (public health)
- Research challenges: people; timescales; safety/scale
- Population-level epidemiological research: examples:
 - 18th&19th century: smallpox; cholera; puerperal fever
 - 20th&21st: birth defects; illnesses of childhood & adulthood
 - hospital-acquired infections (MUHC)
 - The biggest-ever public health experiment

Community vs. clinical medicine

- Clinical doctor's clients are individuals, cared for one at a time
- Community doctor's client is the population of the community (s)he serves
- Task: keeping people in the community from becoming *patients*
- US Public Health Service definition of public health
 - 'the science and art of preventing disease, prolonging life and promoting health through the organized efforts and informed choices of society, organizations, public and private, communities and individuals'

Population-level epidemiological research is not easy

• People



- Timescales: hours days weeks years decades
- Safety: 1 adverse event in 10 100 1,000 100,000



A bright young *chachem* told his grandmother that he was going to be a Doctor of Philosophy.

She smiled proudly: 'Wonderful. But what kind of disease is philosophy?'

Leo Rosten: The Joys of Yiddish (1970), cited in a 2011 mini-dictionary of epidemiology

Disease

THE EXTRAORDINARY STORIES BEHIND HISTORY'S DEADLIEST KILLERS

MARY DOBSON

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Onchocerciasis

Syphilis, painted in 1910 by the artist Richard Cooper.

VIRAL DISEASES SMALLPOX 128 MEASLES 140 YELLOW FEVER 146 DENGUE FEVER 152 RABIES 156 Polio 162 INFLUENZA 1^{-2} EBOLA 184

AIDS 192 SARS 202

The birdy louze, carrier of typous.



A depiction of the 1832 cholers epidemic in Paris.

LIFESTYLE DISEASES

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16 days after inoculation with



A dairymaid with cowpox, May 1796



First (Documented) 'Vaccination': May 14, 1796



He was inoculated on the 1st of July with variolous matter, immediately taken from a pustule, but no disease followed.

Repeated several months later, and again no disease.

Edward Jenner vaccinating his 11 month old son



16 days after inoculation with



Montreal 1885



Bangladesh 1973



http://phil.cdc.gov/phil/details.asp?pid=3265

CHOLERA

c1831: Venetian, aged 23, depicted before and after contracting CHOLERA



Theories as to how the cholera 'poison' is spread

- Direct person-to-person contact
- Miasma:
 - a vaporous exhalation
 - a heavy vaporous emanation or atmosphere
 - an unpleasant or unhealthy smell or vapour
 - Miasma Theories

attribute diseases to an infection from an invisible and possibly otherwise undetectable, emanation from rotting organic matter - swamps, sewers or filthy cities. [Hamlin]

Daily Numbers of Deaths from Cholera in England in 1849



JOHN SNOW

Anaesthetist to a Queen and Epidemiologist to a Nation

Biography David A.E. Shephard

1849 pamphlet:

• FAECAL-ORAL ; WATERBORNE

 'When no other water can be obtained, so much of it as is used for drinking and culinary purposes should be filtered and well-boiled'









Meanwhile, starting night of Thursday Aug. 31, in Soho district



Situation of deaths in and around Broad Street

Local curate identified 'Index Case'



Rev. Henry Whitehead, 20 years later

- Infant died on day 3 of epidemic, but diarrhea 4 days previous to death
- Soiled diapers steeped in pail; water from pail poured into cesspool
- Cesspool blocked; brickwork defective; leaked contents into drain. Drain less than 3 feet from well that fed pump
- defective brickwork of drain let fluid matter seep into well.

12 years on: Cholera returns; worst in East London



1st August, 1866

(Wellcome Images)



DEATH'S DISPENSARY OPEN TO THE POOR, GRATIS BY THE PERMISSION OF THE PARISH

George J. Pinwell, August 18, 1866

20th CENTURY

Birth Defects

Defect	Agent	Counter-measure
Eyes, ears, heart ['41]	1st trimester rubella	Vaccination ['69 \rightarrow]
Limbs ['61]	Thalidomide	Withdrawn from market
Central nervous system ['65]	Folate deficiency	Supplements, fortification †

 † White flour & bread ['98 $\!\!\rightarrow$]

Infancy / youth / ...

Sickness	Agent	Counter-measures
Poliomyelitis	Virus	Vaccination
Dental Caries	$Fluoride^\dagger$	Paste/supplements/drinking water
Vaginal Cancer	In utero DES	Avoidance

[†] Preventive

Adulthood

Sickness

Agents/ Preventives

Heart Disease Cancer Pulmonary Disease Bone Fracture Diabetes Pulmonary Embolus Ruptured Abdominal Aortic Aneurysm Dementia

...

...

TOOLS

1941

CONGENITAL CATARACT FOLLOWING GERMAN MEASLES IN THE MOTHER.

By N. McAlister Gregg, Sydney.

In the first half of the year, 1941, an unusual number of cases of congenital cataract made their appearance in Sydney.

The total

number of cases included in this review is seventy-eight.

In all but ten cases in this series the history of "German measles" infection is present.

Transactions of the Ophthalmological Society of Australia 3 (1941): 35-46

THALIDOMIDE AND CONGENITAL ABNORMALITIES

SIR,—Congenital abnormalities are present in approximately 1.5% of babies. In recent months I have observed that the incidence of multiple severe abnormalities in babies delivered of women who were given the drug thalidomide ('Distaval') during pregnancy, as an antiemetic or as a sedative, to be almost 20%.

These abnormalities are present in structures developed from mesenchyme—i.e., the bones and musculature of the gut. Bony development seems to be affected in a very striking manner, resulting in polydactyly, syndactyly, and failure of development of long bones (abnormally short femora and radii).

Have any of your readers seen similar abnormalities in babies delivered of women who have taken this drug during pregnancy?

Hurstville, New South Wales.

W. G. MCBRIDE.

FOLIC ACID METABOLISM AND HUMAN EMBRYOPATHY

RESULTS OF FIGLU EXCRETION TESTS IN 98 MOTHERS OF MALFORMED INFANTS

Hathan	FIGLU ex	cretion test	Tetal	% Figlu- positive	
Mothers	Positive	Negative	Total		
Of all malformed infants.	61	37	98	62	
malformations	48	25	73	66	
Matched pairs:			1	1	
Mothers of malformed infants	35	19	54	65	
Mothers of normal in- fants	8	46	54	17	
Mothers of infants with C.N.S. malformation	24	11	35	69	
fants	6	29	35	17	

THE NEW ENGLAND JOURNAL OF MEDICINE

ADENOCARCINOMA OF THE VAGINA*

Association of Maternal Stilbestrol Therapy with Tumor Appearance in Young Women

ARTHUR L. HERBST, M.D., HOWARD ULFELDER, M.D., AND DAVID C. POSKANZER, M.D.

Abstract Adenocarcinoma of the vagina in young women had been recorded rarely before the report of several cases treated at the Vincent Memorial Hospital between 1966 and 1969. The unusual occurrence of this tumor in eight patients born in New England hospitals between 1946 and 1951 led us to conduct a retrospective investigation in search of factors that might be associated with tumor appearance. Four matched controls were established for each patient; data were obtained by personal interview. Results show maternal bleeding during the current pregnancy and previous pregnancy loss were more common in the study group. Most significantly, seven of the eight mothers of patients with carcinoma had been treated with diethylstilbestrol started during the first trimester. None in the control group were so treated (p less than 0.00001). Maternal ingestion of stilbestrol during early pregnancy appears to have enhanced the risk of vaginal adenocarcinoma developing years later in the offspring exposed.

Summary of Data Comparing Patients with Matched Controls.

CASE No.	MATERNAL Age (Yr)		MATERNAL Smoking		BLEEDING IN This Pregnancy		ANY PRIOR PREGNANCY LOSS	
	CASE	MEAN OF 4 CONTROLS	CASE	CONTROL	CASE	CONTROL	CASE	CONTROL
1	25	32	Yes	2/4	No	0/4	Yes	1/4
2	30	30	Yes	3/4	No	0/4	Yes	1/4
3	22	31	Yes	1/4	Yes	0/4	No	1/4
4	33	30	Yes	3/4	Yes	0/4	Yes	0/4
5	22	27	Yes	3/4	No	1/4	No	1/4
6	21	29	Yes	3/4	Yes	0/4	Yes	0/4
7	30	27	No	3/4	No	0/4	Yes	1/4
8	26	28	Yes	3/4	No	0/4	Yes	0/4
otal	-	100	7/8	21/32	3/8	1/32	6/8	5/32
Mean	26.1	29.3	_					
Chi square (1 df)*		0.53		4.52		7.16		
value	(1	I.S.)†	0 (N	.50 I.S.)	<	0.05	<	0.01

* Matched control chi-square test used as described by Pike & Morrow.9

*Standard error of difference 1.7 yr (paired t-test); N.S. = not statistically significant,

Summary of Data Comparing Patients with Matched Controls.

CASE NO.	MATERNAL Age (Yr)		Estrogen Given in This Pregnancy		BREAST FEEDING		Intra- uterine X-Ray Exposure	
	CASE	MEAN OF 4 CONTROLS	CASE	CONTROL	CASE	CONTROL	CASE	CONTROL
T.	25	32	Yes	0/4	No	0/4	No	1/4
2	30	30	Yes	0/4	No	1/4	No	0/4
3	22	31	Yes	0/4	Yes	0/4	No	0/4
4	33	30	Yes	0/4	Yes	2/4	No	0/4
5	22	27	No	0/4	No	0/4	No	0/4
6	21	29	Yes	0/4	No	0/4	No	1/4
7	30	27	Yes	0/4	Yes	0/4	No	1/4
8	26	28	Yes	0/4	No	0/4	Yes	1/4
Total		The second	7/8	0/32	3/8	3/32	1/8	4/32
Mean	26.1	29.3		1.1	1000			_
Chi square (1 df)*		f)*	23.22		2.35		0	
p value	(N	1.S.)†	< 0.	00001	0 (N	.20 I.S.)	(1	N.S.)

Matched control chi-square test used as described by Pike & Morrow.

*Standard error of difference 1.7 yr (paired t-test); N.S. = not statistically significant.



Framingham Heart Study

A Project of the National Heart, Lung, and Blood Institute and Boston University

About

Participants

ur Investigerer

Pisk Functions

Bibliograph

For Renaments

Update Your Medical History

Original Cohort

Offspring Cohort

Generation Three Cohort

New Offspring Spouse Cohort

Omni Coho

Brain Tis: Program News Men Consent Women

Totals

Age

Original Cohort

The Original Cohort of the Framingham Heart Study consisted of 5,209 respondents of a random sample of 2/3 of the adult population of Framingham, Massachusetts, 30 to 62 years of age by household, in 1948. Exam 28 for the Original Cohort ended in December of 2005. Exam 30 for the Original Cohort began in May of 2008 and ends in February of 2010.

AGE-SEX DISTRIBUTION AT ENTRY (1948)

29-39	40-49	50-62	Totals
835	779	722	2,336
1,042	962	869	2,873
1,877	1.741	1,591	5,209

Nurses' Health Study

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Data Collection Tour

Findings: Some Highlights

Newsletters

Questionnaires

For Participants

FAQ

Forms

NHS1 Login

NHS2 Login



The Nurses' Health Studies are among

the largest and longest running investigations of factors that influence women's health. Started in 1976 and expanded in 1989, the information provided by the 238,000 dedicated nurse-participants has led to many new insights on health and disease. While the prevention of cancer is still a primary focus, the study has also produced landmark data on cardiovascular disease, diabetes and many other conditions. Most importantly, these studies have shown that diet, physical activity and other lifestyle factors can powerfully promote better health.

Please choose from the links across the top of the page or the navigation menu on the left to find out more about the Nurses' Health Studies.

Join NHS3!

The Nurses' Health Study is recruiting 100,000 female RNs, LPNs, and nursing students for NHS3. Become part of the next generation of NHS! Join NHS2!





Do We Really Know What Makes Us Healthy?



Reinhard Hunger

By GARY TAUBES Published: September 16, 2007



Canadian Longitudinal Study on Aging Étude longitudinale canadienne sur le vieillissement

bout Us Participants Privacy Data Collection Sites Enabling Units Parti

Learn more about the CLSA

The Canadian Longitudinal Study on Aging (CLSA) is a large, national, longterm study that will follow approximately 50,000 men and women between the ages of 45 and 85 for at least 20 years.





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Étude OUALITY Study Centre de recherche du CHU Sainte-Justine, local 3732 3175 chemin de la Côte-Ste-Catherine Montréal, Québec, H3T 1C5 famille@recherche-ste-justine.gc.ca

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About Us

Updated June 9 2014





OUebec Adipose and Lifestyle InvesTigation in Youth

About Us

Welcome to the QUALITY website!

QUALITY is short for QUebec Adipose and Lifestyle InvesTigation in Youth. The main purpose of the study is to increase understanding of the natural history of cardiovascular disease risk factors and Type 2 diabetes in children. Our findings will help program planners design effective health promotion and disease prevention interventions.

MUHC hospital, 2015

ORIGINAL INVESTIGATION

Infection Acquisition Following Intensive Care Unit Room Privatization

Dana Y. Teltsch, MSc; James Hanley, PhD; Vivian Loo, MD, MSc, FRCPC; Peter Goldberg, MD, FRCPC; Ash Gursahaney, MD, FRCPC; David L. Buckeridge, MD, PhD, FRCPC

ORIGINAL INVESTIGATION

Infection RATES Following Intensive Care Unit SWITCH TO AN ALL-PRIVATE-ROOMS

Dana Y. Teltsch, MSc; James Hanley, PhD; Vivian Loo, MD, MSc, FRCPC; Peter Goldberg, MD, FRCPC; Ash Gursahaney, MD, FRCPC; David L. Buckeridge, MD, PhD, FRCPC

EACL MG H Methods: We compared the rates of acquisition of infectious organisms in $\frac{1}{2}$ an ICU before and after a change from multibed to single rooms. As a control, we used acquisition rates in the ICU of a nearby university teaching hospital, which contained both multibed and single $\frac{1}{2}$ H rooms, during the study period. We used a statistical model to adjust for background time trends common to both hospitals.





0.5

0.5



Figure. Monthly contrasts of event rates and length of stay (LOS) in the intervention (Int) vs comparison (FeI) hospitals preintervention (Pei) and positintervention (Pos). Black circles represent ratios within each monthic highter (red) circles represent high left is the axis of the ratios; on the right, the magnitude of the change in the average (Ave) ratios pre-posi intervention. A. Monthly ratios of acquisition rates of likely exogenous organisms. B. Monthly ratios of acquisition rates of likely endogenous organisms.

Infection Acquisition Following Intensive Care Unit Room Privatization

Dana Y. Teltsch, MSc; James Hanley, PhD; Vivian Loo, MD, MSc, FRCPC; Peter Goldberg, MD, FRCPC; Ash Gursahaney, MD, FRCPC; David L. Buckeridge, MD, PhD, FRCPC

Background: Patients in intensive care units (ICUs) often acquire infections, which impose a heavy human and financial burden. The use of private rooms may reduce the acquisition of certain pathogens, but the limited evidence on this topic is inconsistent.

Methods: We compared the rates of acquisition of infectious organisms in an ICU before and after a change from multibed to single rooms. As a control, we used acquisition rates in the ICU of a nearby university teaching hospital, which contained both multibed and single rooms, during the study period. We used a statistical model to adjust for background time trends common to both hospitals.

Results: The adjusted rate of acquisition of *Clostridium difficile*, vancomycin-resistant *Enterococcus* species, and methicillin-resistant *Staphylococcus aureus* combined decreased by 54% (95% confidence interval [CI], 29%-70%) following the intervention. The methicillin-

resistant *S aureus* acquisition rate fell by 47% (95% CI,1%-71%), the *C difficile* acquisition rate fell by 43% (95% CI, 7%-65%), and the yeast acquisition rate fell by 51% (95% CI, 34%-64%). Twelve common and likely exogenous organisms and exogenous/endogenous organisms had a reduction in acquisition rates after the intervention; for 6 of them, this reduction was statistically significant. No effect was observed on the acquisition rate of coagulasenegative *Staphylococcus* species, the most common endogenous organism, for which no change would be expected. The adjusted rate ratio of the average length of stay in the ICU was 10% (95% CI, 0%-19%) lower after the intervention.

Conclusion: Conversion to single rooms can substantially reduce the rate at which patients acquire infectious organisms while in the ICU.

Arch Intern Med. 2011;171(1):32-38

The biggest-ever public health experiment



FIGURE 1 Poliomyelitis in the U.S., 1930– 56. Source: Meier (1957)

STUDY GROUP	STUDY POPULATION
All areas: Total	1,829,916
Placebo control areas: Total	749,236
Vaccinated	200,745
Placebo	201,229
Not inoculated*	338,778
Observed control areas: Total	1,080,680
Vaccinated	221,998
Controls**	725,173
Grade 2 not inoculated	123,605

Source: Adapted from Francis (1955), Tables 2 and 3.

* Includes 8,577 children who received one or two injections of placebo. ** First- and third-grade total population.

POLIOMYELITIS CASES

		Para	ılytic	
STUDY GROUP	STUDY POPULATION	No.	Rate	
All areas: Total	1,829,916	685	37	
Placebo control areas: Total	749,236	270	36	
Vaccinated	200,745	33	16	
Placebo	201,229	115	57	
Not inoculated*	338,778	121	36	
Observed control areas: Total	1,080,680	415	38	
Vaccinated	221,998	38	17	
Controls**	725,173	330	46	
Grade 2 not inoculated	123,605	43	35	

Source: Adapted from Francis (1955), Tables 2 and 3.

* Includes 8,577 children who received one or two injections of placebo. ** First- and third-grade total population.

(Rates per 100,000)

Take-away messages

- The knowledge behind public health practice: it's a major contributor to improved longevity & health
- Evidence that advances this knowledge is not easily obtained
- It takes smarts, big (and small) data, time, ...
- It takes time for evidence to be translated into correct knowledge

FUNDING, CO-ORDINATES, DOWNLOADS

Natural Sciences and Engineering Research Council of Canada

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.....

James.Hanley@McGill.CA

http://www.med.mcgill.ca/epidemiology/hanley/minimed









