MMED
African Institute for the Mathematical Sciences
Muizenberg, South Africa
May-June, 2016

Public Health, Epidemiology, and Models

Travis Porco, Jonathan Dushoff and Jim Scott

John Graunt

- Published analysis of London mortality data in 1662
- Recognized patterns and trends such as male-female disparities and high infant mortality

Captain John Graunt

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Captain John Graunt

Natural and *Political*

OBSERVATIONS

Mentioned in a following Index,

and made upon the

Bills of Mortality.

By *JOHN GRAUNT*,

Citizen of

LONDON.

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

—— *Non, me ut miretur Turba, laboro,*
Contentus paucis Lectoribus ——

LONDON,
Printed by *Tho: Roycroft*, for *John Martin*, *James Allestry*, and *Tho: Dicas*, at the Sign of the *Bell* in St. *Paul's* Church-yard, MDCLXII.

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Captain John Graunt

9. Whereas we have found, that of 100 quick Conceptions about 36 of them die before they be six years old, and that perhaps but one surviveth [or] 76, we, having seven *Decads* between six and 76, we sought six mean proportional numbers between 64, the remainder, living at six years, and the one, which survives 76, and finde, that the numbers following are practically near enough to the truth; for men do not die in exact Proportions, nor in Fractions: from whence arises this Table following.

Viz. of 100 there dies within the first six years	36	The fourth	6
		The next	4
The next ten years, or *Decad*	24	The next	3
		The next	2
The second *Decad*	15	The next	1
The third *Decad*	09		

10. From whence it follows, that of the said 100 conceived there remains alive at six years end 64.

At Sixteen years end	40	At Fifty six	6
At Twenty six	25	At Sixty six	3
At Tirty six	16	At Seventy six	1
At Fourty six	10	At Eighty	0

A generall Bill for this preſent year,

ending the 19 of *December* 1665. according to the Report made to the KINGS moſt Excellent Majeſty.

By the Company of Pariſh Clerks of *London*, &c.

The Diſeaſes and Caſualties this year.

Abortive and Stillborne	617	Executed	21	Palſie	30
Aged	1545	Flox and Small Pox	655	Plague	68596
Ague and Feaver	5257	Found dead in ſtreets, fields, &c.	20	Planet	6
Appoplex and Suddenly	116	French Pox	86	Pluriſie	15
Bedrid	10	Frighted	23	Poyſoned	1
Blaſted	5	Gout and Sciatica	27	Quinſie	35
Bleeding	16	Grief	46	Rickets	557
Bloody Flux, Scowring & Flux	185	Griping in the Guts	1288	Riſing of the Lights	397
Burnt and Scalded	8	Hangd & made away themſelves	7	Rupture	34
Calenture	3	Headmouldſhot & Mouldſallen	14	Scurvy	105
Cancer, Gangrene and Fiſtula	56	Jaundies	110	Shingles and Swine pox	2
Canker, and Thruſh	111	Impoſtume	227	Sores, Ulcers, broken and bruiſed Limbs	82
Childbed	625	Kild by ſeverall accidents	41	Spleen	14
Chriſomes and Infants	1258	Kings Evill	86	Spotted Feaver and Purples	1929
Cold and Cough	68	Leproſie	2	Stopping of the ſtomack	332
Collick and Winde	134	Lethargy	14	Stone and Strangury	98
Conſumption and Tiſſick	4808	Livergrown	2	Surfet	1251
Convulſion and Mother	2036	Meagrom and Headach	12	Teeth and Worms	2614
Diſtracted	5	Meaſles	7	Vomiting	51
Dropſie and Timpany	1478	Murthered and Shot	5	VVem	1
Drowned	50	Overlaid & Starved	45		

Christned	Males	5114	Buried	Males	48569	Of the Plague 68596
	Females	4853		Females	48737	
	In all	9967		In all	97306	

In 1632
Plague: 8

Buried:
9535

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Captain John Graunt

The Conclusion.

IT may be now asked, to what purpoſe tends all this laborious buzzling, and groping? To know,

1. The number of the People?
2. How many *Males*, and *Females*?
3. How many Married, and ſingle?
4. How many *Teeming* Women?
5. How many of every *Septenary*, or *Decad* of years in *age*?
6. How many *Fighting* Men?
7. How much *London* is, and by what ſteps it hath increaſed?
8. In what time the houſing is replenished after a *Plague*?
9. What proportion die of each general and perticular *Casualties*?
10. What years are Fruitfull, and Mortal, and in what Spaces, and Intervals, they follow each other?
11. In what proportion Men neglect the Orders of the *Church*, and *Sects* have increaſed?
12. The diſproportion of Pariſhes?
13. Why the Burials in *London* exceed the Chriſtnings, when the contrary is viſible in the Country?

To this I might anſwer in general by ſaying, that thoſe, who cannot apprehend the reaſon of theſe Enquiries, are unfit to trouble themſelves to aſk them.[72]

What is publichealth ?

Public Health

- "The science of *preventing* disease, *prolonging* life, and *promoting* physical health and efficiency through organized community efforts… " - Winslow
  - Prevention is job #1
  - Works at the population level

Public Health
Prevent. Promote. Protect.

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History

"I believe the history of public health might be written as a record of successive redefinings of the unacceptable."
- Sir Geoffrey Vickers

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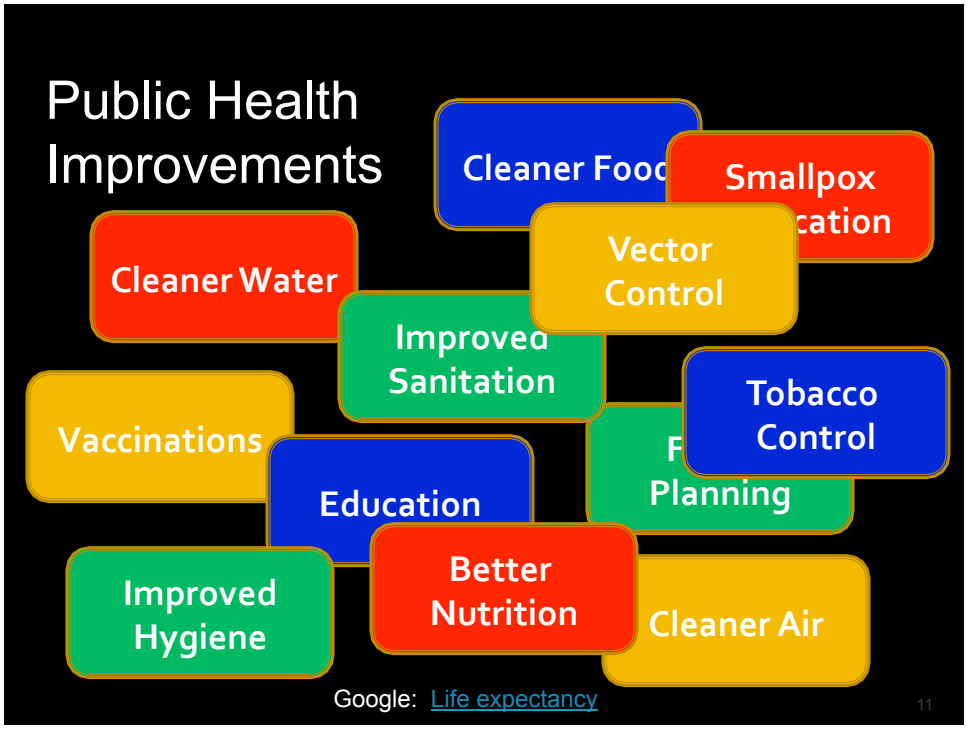
History

A Summarized History of International Public Health (Merson, Black, Mills, 2nd ed.)

400 BCE	Hippocrates presents causal relation between environment and disease
1st Century	Romans introduce public sanitation and organized water supply system
14th Century	Black Death leads to quarantine
Middle Ages	Colonial expansion spreads infectious disease aroung the world
1750-1850	Industrial Revolution results in health and social improvements
1850-1910	Expansion of knowledge about infectious disease agents and transmission
1910-1945	Reductions in child mortality; Development of schools of public health; International foundations
1945-1990	Creation of World Bank; WHO; Eradication of smallpox; Beginning of HIV pandemic
1990-Present	Priority given to health sector reform, equity, health and development



Public Health vs. Medicine

Public Health

- Assess health of populations (surveillance)
- Policy development
- Assure that services are available
- Prevent disease

THIS IS PUBLIC HEALTH.
thisispublichealth.org

Medicine

- Assess health of individuals (diagnosis)
- Develop treatment plan (regimen)
- Administer treatment
- Cure the patient

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How Does Public Health Work?

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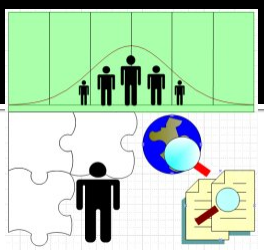
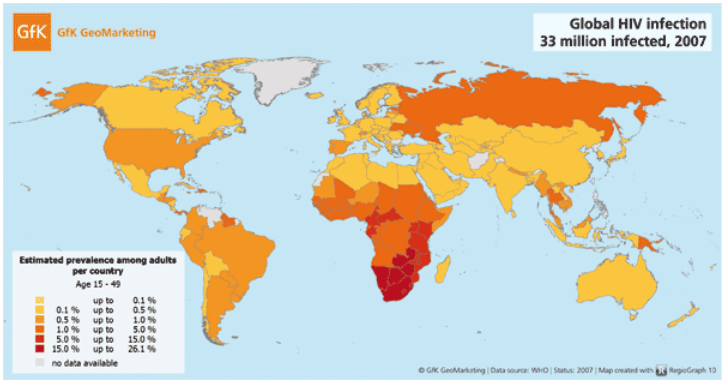
Primary Functions



- Assessment :
  - Epidemiology and Statistics



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Primary Functions

- Policy Development
  - Government and International Organizations

  - e.g. The World Health Organzation

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Primary Functions

- Assurance
  - Implementation and maintenance
  - Governments and Public Health Infrastructure

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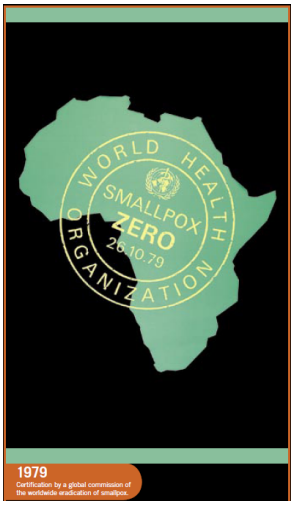
Prevention and Intervention

- Five Steps
  - Define the problem
  - Determine risk factors
  - Develop interventions
  - Implementation
  - Maintenance



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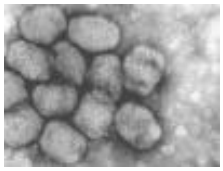
Example: smallpox

- The problem:
  - 1966: 10 – 15 million cases of smallpox in 50+ countries
  - 1-2 million deaths annually
  - ~ 30% case-fatality ratio
  - Higher in children
  - Survivors scarred for life



Source: Millions Saved: Proven Successes in Global Health, Center for Global Development, 2004

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Example: smallpox

- Natural History/Risk Factors
  - Variola virus
  - Airborne / contact with an infected person
  - Non-infectious for up to 17 days
  - Flu-like symptoms – high fever
  - Rash

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Example: smallpox

- Intervention: vaccination
  - In existence since 18th century – Edward Jenner
  - Improved vaccine in 1920s
  - 1959: Global eradication program endorsed by the WHO

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Example: smallpox

- Implementation
  - 1959: 1 fulltime WHO medical officer, 1 assistant
  - National vaccination campaigns
  - 1965: World Health Assembly – "eradication of smallpox is a main objective of the WHO"
  - 1967: Smallpox Eradication Program
  - 1970's: focused 'containment' teams
  - 1973: 5 countries remaining
  - 1977: last endemic case

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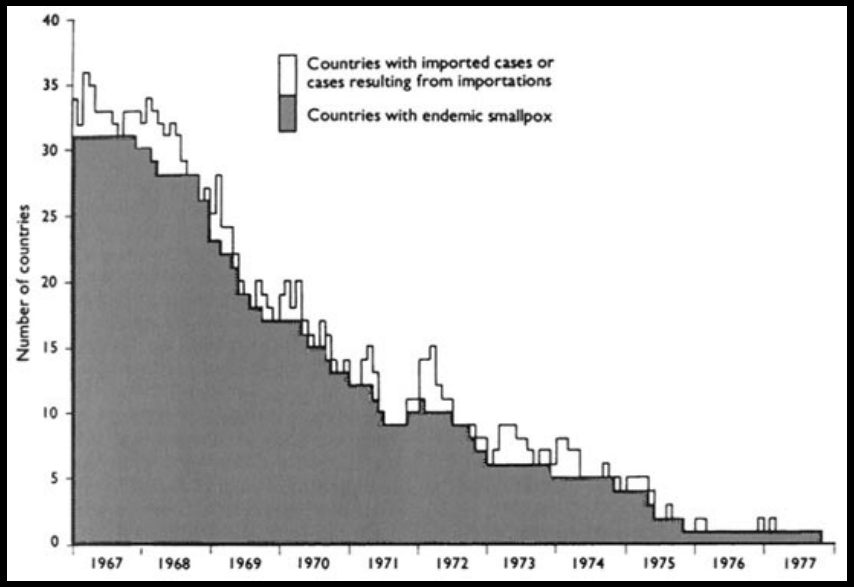
The Decline of Smallpox



Source: Vaccines, 3rd ed. ,W.B. Saunders Co. 1999

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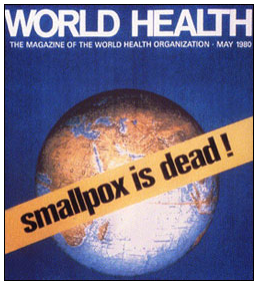
Example: smallpox

- Assessment
  - 2 years of surveillance and searching
  - May 1980: Smallpox declared "eradicated"



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Barriers to Public Health

- Barriers to public health
  - Economic
  - Moral/religious
  - Individual freedom
  - Political

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Summary

- Public Health
  - Prevention
  - Populations
  - Challenging

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Epidemiology: where does it fit in?

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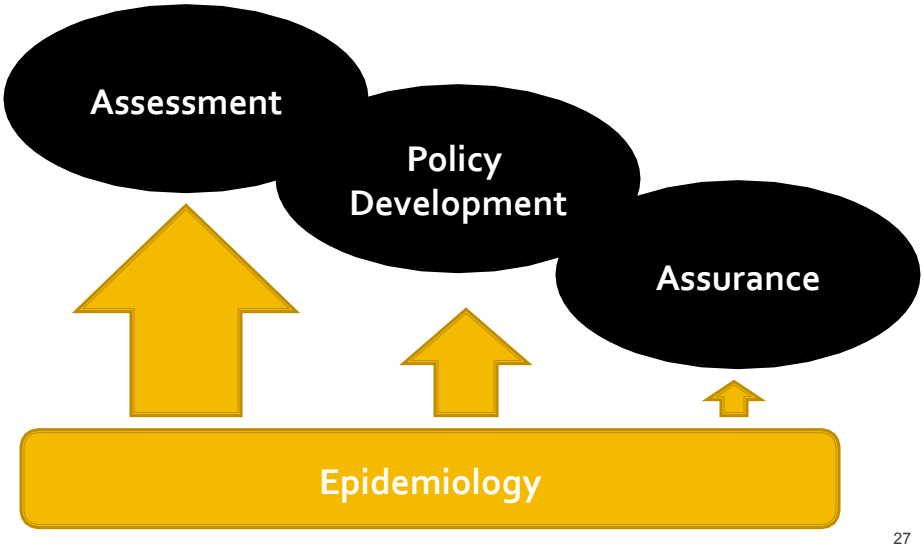
Epidemiology: where does it fit in?



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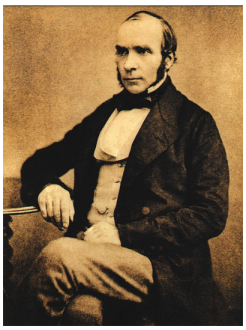
Definition of Epidemiology

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



- J. Last, *Dictionary of Epidemiology*

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OR....

- The...
  - Who
  - What
  - When
  - Where
  - Why
  - and How

Descriptive Epidemiology

Analytic Epidemiology

.....of Disease

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Hippocrates, 5th century B.C.E.

On Airs, Waters, and Places

Whoever wishes to investigate medicine properly, should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces. Then the winds, the hot and the cold, especially such as are common to all countries, and then such as are peculiar to each locality. One must also consider the qualities of the waters, for as they differ from one another in taste and weight, so also do they differ much in their effects.....and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labor....From these things he must proceed to investigate everything else. For if he knows all these things well,....he cannot miss knowing , when he comes to a strange city, either the diseases peculiar to the place, or the particular nature of common diseases....

Slide courtesy of Warren Winkelstein 30

Five Goals of Epidemiology

- Describe Disease in the Population
  - Surveillance, observation, research, experiments
  - Person, place, and time
- Determinants
  - Physical, biological, social and behavioral factors that influence health
- Natural History of Disease
  - Symptoms, pathogenisis, incubation
- Design/Implement interventions
  - Control disease
- Inform Policy
  - Use findings to promote, protect, and restore health – "Big Picture"

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Examples

- Describe Disease in the Population

  - Surveillance

  - Distribution of disease

- Interventions

- Mathematical modeling

- Determinants of Disease

  - Outbreak investigations

  - Observational studies

  - Experimental studies (RCTs)

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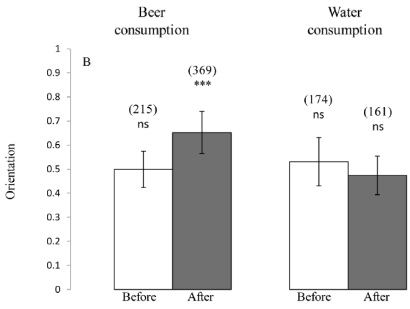
Determinants

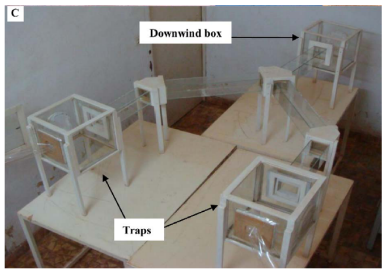
OPEN ACCESS Freely available online

PLoS one

Beer Consumption Increases Human Attractiveness to Malaria Mosquitoes

Thierry Lefèvre[1]*, Louis-Clément Gouagna[2,3], Kounbobr Roch Dabiré[3,4], Eric Elguero[1], Didier Fontenille[2], François Renaud[1], Carlo Costantini[2,5], Frédéric Thomas[1,6]





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Determinants

Sexual Practices and Risk of Infection by the Human Immunodeficiency Virus

The San Francisco Men's Health Study

JAMA, Jan 16, 1987—Vol 257, No. 3

Warren Winkelstein, Jr, MD, MPH; David M. Lyman, MD, MPH; Nancy Padian, MS, MPH; Robert Grant, MPH; Michael Samuel; James A. Wiley, PhD; Robert E. Anderson, MD; William Lang, MD; John Riggs, PhD; Jay A. Levy, MD

Table 1.—Association of Number of Male Sexual Partners in Previous Two Years and Human Immunodeficiency Virus (HIV) Serologic Status*

	Study Sample		Population	
No. of Male Partners	No. Examined	% HIV Antibody Positive	% HIV Antibody Positive†	95% Confidence Interval
None	17	17.6	19.2	5.2-41.5
1	66	18.2	17.9	9.5-29.0
2-9	206	31.6	31.9	25.2-39.0
10-49	312	53.8	53.7	47.4-59.6
≥50	195	70.8	70.5	62.7-76.8
Total	796	48.5	48.2	44.3-52.0

*Subjects with missing data (n=13) were excluded. The χ^2 for trend of the association of number of partners and HIV antibody seropositivity in the sample is 86.7, $P<.0001$.
†Weighted for sampling fraction and difference in participation rates between census tracts.

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Intervention Design

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial

Bertran Auvert[1,2,3,4*], Dirk Taljaard[5], Emmanuel Lagarde[2,4], Joëlle Sobngwi-Tambekou[2], Rémi Sitta[2,4], Adrian Puren[6]

PLoS Medicine | www.plosmedicine.org November 2005 | Volume 2 | Issue 11 | e298

Table 4. Multivariate RRs of HIV Incidence

Categories of Factors	Factors	Values of Factors	HIV Cases	Follow-Up (py)	HIV Incidence Rates (95% CI; per 100 py)[a]	Incidence RRs (95% CI) of Intervention versus Control (95% CI)[a,b]
	Randomization group	Intervention	20	2,354	0.85 (0.55–1.32)	0.39 (0.23–0.66) $p = 0.00049$
		Control	49	2,339	2.11 (1.60–2.80)	1

0.85 vs 2.11, a reduction in HIV incidence of approximately 60%

Informing Policy

Comparison of the date of discovery of a measure to prevent a disease with the date of identification of its true causative or preventive agent

Disease	Discoverer of preventive measure	Year of discovery preventive measure	Year of discovery of agent	Discoverer of agent
Scurvy	J. Lind	1753	1928	A. Szent-Gyorgi
Pellagra	J. Goldberger	1755	1924	G. Casal et al.
Scrotal cancer	P. Pott	1775	1933	J.W. Cook et al.
Smallpox	E. Jenner	1798	1958	F. Fenner
Puerperal fever	I. Semmelweis	1847	1879	L. Pasteur
Cholera	J. Snow	1849	1893	R. Koch
Bladder cancer[a]	L. Rehn	1895	1938	W.C. Hueper et al.
Yellow fever	W. Reed et al.	1901	1928	A. Stokes et al.
Oral cancer[b]	R. Abbe	1915	1974	D. Hoffmann et al.

rev. 10/23/1999, 1/17/2000, 3/23/2001

Informing Policy

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

Results "We were unable to identify any randomised controlled trials of parachute intervention."

Conclusion "We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomized, placebo controlled, crossover trial of the parachute."

BMJ 2003;327:1459-1461
doi:10.1136/bmj.327.7429.1459

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

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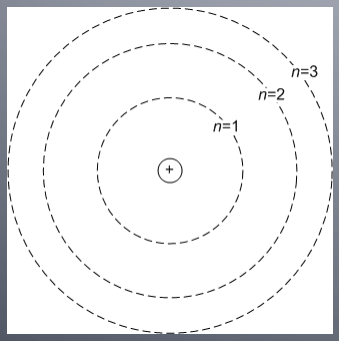
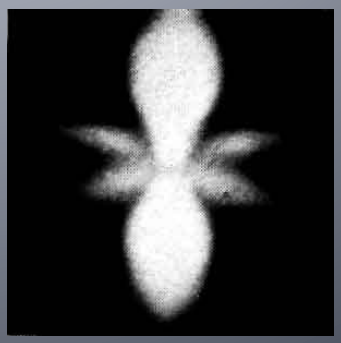
Where does modeling fit in?





Source: Google Images

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A *Natural Fit* for Public Health

- Models allow us to gain insight into *public health* questions (e.g. Universal testing)
  - Differences between:
    - What factors increase the risk of HIV transmission? (Analytic Epidemiology)
    - In what populations is HIV incidence/prevalence the highest? (Descriptive Epidemiology)
    - By how much could we expect the incidence of HIV to decrease in South Africa if 80% of all sexually active people used condoms 80% of the time? (Public Health Impact)

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Models should be *useful*

- 1) Simple as possible
  - Avoid unnecessary complexity
  - Only add complexity when the *research question* demands it
- 2) Based on what is known
  - Biological systems
  - DATA

Implies we must know relevant:
- biology
- statistics (how to make sense of data)

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Informing Policy

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

Lancet 2009; 373

	Deaths (thousands)	Deaths averted (thousands)
Neither strategy		
2015	269	..
2030	263	..
2050	263	..
2008–50	11078	..
ART started when CD4+ count <350 cells per μL		
2015	193	76
2030	202	61
2050	210	53
2008–50	8658	2419
ART started when CD4+ count <350 cells per μL and universal voluntary HIV testing/immediate ART		
2015	165	104
2030	76	187
2050	17	246
2008–50	3879	7199
ART started when CD4+ count <350 cells per μL, universal voluntary HIV testing/immediate ART, and other adult prevention strategies		
2015	164	105
2030	72	191
2050	12	251
2008–50	3727	7350

ART=antiretroviral therapy.

Table: Estimated number of AIDS-related deaths for the years 2015, 2030, 2050, and 2008–50 with different strategies

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Modeling is not new

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Modeling is not new

- This process has been in practice since at least 1760
  - What do I mean by "process"

'I simply wish that, in a matter which so closely concerns the wellbeing of the human race, no decision shall be made without all the knowledge which a little analysis and calculation can provide'
Daniel Bernoulli 1760.

Daniel Bernoulli

Commons.wikipedia.org

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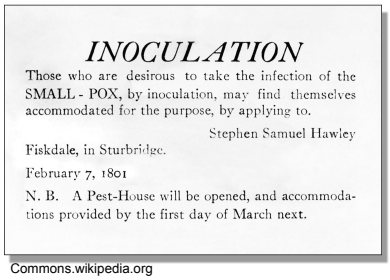
Bernoulli and Smallpox

- Inoculation as prevention
- Not without costs
- Is it worth the risk?



INOCULATION

Those who are desirous to take the infection of the SMALL-POX, by inoculation, may find themselves accommodated for the purpose, by applying to.

Stephen Samuel Hawley

Fiskdale, in Sturbridge.

February 7, 1801

N. B. A Pest-House will be opened, and accommodations provided by the first day of March next.

Commons.wikipedia.org

en.wikipedia.org

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The first counterfactual?

- Bernoulli worked out solutions for a system of differential equations (impressive at the time!)
- Determined:
  - Life expectancy with inoculation
  - Life expectancy without inoculation

Age x	Alive $P(x)$	Susceptible $S(x)$	Immune $R(x)$	Smallpox deaths	No smallpox $P^*(x)$
0	1300	1300	0	17.2	1300
1	1000	896	104	12.3	1015
2	855	685	170	9.8	879
3	798	571	227	8.2	830
4	760	485	275	7.0	799
5	732	416	316	6.1	777
6	710	359	351	5.2	760
7	692	311	381	4.6	746
8	680	272	408	4.0	738
9	670	238	432	3.5	732
10	661	208	453	3.0	726
11	653	182	471	2.7	720
12	646	160	486	2.3	715
13	640	140	500	2.1	711
14	634	123	511	1.8	707
15	628	108	520	1.6	702
16	622	94	528	1.4	697
17	616	83	533	1.2	692
18	610	72	538	1.1	687
19	604	63	541	0.9	681
20	598	55	543	0.8	676
21	592	49	543	0.7	670
22	586	42	544	0.6	664
23	579	37	542	0.5	656
24	572	32	540		649
⋮	⋮	⋮	⋮	⋮	⋮

N. Bacaër, *A Short History of Mathematical Population Dynamics*, DOI 10.1007/978-0-85729-115-8_4, © Springer-Verlag London Limited 2011

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Results

- Inoculating everyone at birth increased overall life expectancy by about 3 years
- Effective as long as the probability of dying from smallpox right after inoculation is less than ~ 11%
- Bernoulli estimated this risk to be ~1%

- Despite these results, inoculations were never performed on a large scale (in France)

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Much of modeling is "new"

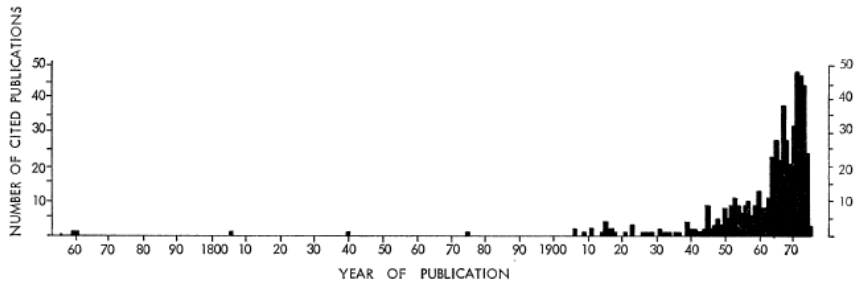

FIG. 1. The mathematical epidemiology literature, as reflected in the bibliography of Bailey's (1975) review. Though not a complete catalogue of all publications on this subject, this represents the most comprehensive available bibliography, and gives a valid impression of the growth of the literature.

Source: Fine, PEM. John Brownlee and the Measurement of Infectiousness. J.R. Stastist. Soc. A, Vol. 142, No. 3 (1979)

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Some historical figures and ideas

- William Farr (1840): Fitting curves to mortality data
- Predicted smallpox deaths
- Descriptive technique

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Some historical figures and ideas

- P.D. En'ko (1889)
- Formulated discrete time models and fit them to observed measles epidemics

3. En'ko's Epidemic Model

If one expresses En'ko's assumptions and notation in current notation his model satisfies the following system of iterative equations:

$$C_{t+1} = S_t\left\{1 - \left(1 - \frac{C_t}{N_t - 1}\right)^{kN_t}\right\},$$

$$S_{t+1} = S_t\left(1 - \frac{C_t}{N_t - 1}\right)^{kN_t},$$

$$N_{t+1} = N_t - C_t.$$

Source: Dietz K. The first epidemic model: A historical note on P.D. En'ko. Austral J. of Statist., 30A, 1988.

Table 1a. Observed and expected epidemics — St. Petersburg Alexander Institute

	1865			1875			1879	
	Obs.	Exp.(1)	Exp.(2)	Obs.	Exp.(1)	Exp.(2)	Obs.	Exp.
S_0		61	67		100	100		50
k		0.2	0.1		0.5	0.25		0.5
C_0	1	1	1	3	3	3	2	2
C_1	13	11	6	52	76	51	28	30
C_2	25	45	27	28	21	46	14	18
C_3	12	4	31	1	0	0	1	0
C_4	4	0	2	0	0	0	0	0

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Some historical figures and ideas

- William Hamer (1906): Recurrence of measles
- Discrete time model
- Incidence is related to the product of prevalence times susceptibles
- "Mass Action"

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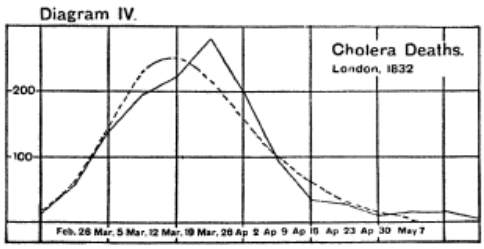
Some historical figures and ideas

- John Brownlee (1907)
- Sought to quantify "infectivity"
- Suggested infectivity changes over time



Source: Fine, PEM. John Brownlee and the Measurement of Infectiousness. J.R. Stastist. Soc. A, Vol. 142, No. 3 (1979)

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Some historical figures and ideas

- Ronald Ross (1911): Suggested malaria could be eradicated by reducing mosquitoes
- Used models to explore this claim
- Not necessary to eliminate all mosquitoes
- First to explore "mass action" in continuous time (e.g. $dy/dt = ky(1 - y)$, y = *prevalence)*

"As a matter of fact all epidemiology, concerned as it is with the variation of disease from time to time or place to place, must be considered mathematically, however many variables are implicated if it is to be considered scientifically at all." R. Ross.

N. Bacaër, *A Short History of Mathematical Population Dynamics*, DOI 10.1007/978-0-85729-115-8_4, © Springer-Verlag London Limited 2011

Fine, PEM. John Brownlee and the Measurement of Infectiousness. J.R. Stastist. Soc. A, Vol. 142, No. 3 (1979)

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Some historical figures and ideas

- A. McKendrick (1927) & W. Kermack (1927)
- Deterministic epidemic models
- Epidemic threshold

  dI/dt = I(t) (aS(t) – b)

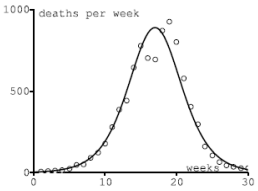
  If S(o) < b/a then dI/dt < o

  - infection dies out

  If S(o) > b/a then dI/dt >o

  - Infection spreads
- Ro = Basic reproductive ratio

$$\frac{dS}{dt} = -aSI,$$
$$\frac{dI}{dt} = aSI - bI,$$
$$\frac{dR}{dt} = bI.$$



N. Bacaër, *A Short History of Mathematical Population Dynamics*,
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Some historical figures and ideas

- William Farr (1840) Curve fitting
- P.D. En'ko (1889) Discrete time model
- W. H. Hamer (1906)
- J. Brownlee (1906)
- R.A. Ross (1911)
- A. McKendrick (1927)
- W. Kermack (1927)
- Many others

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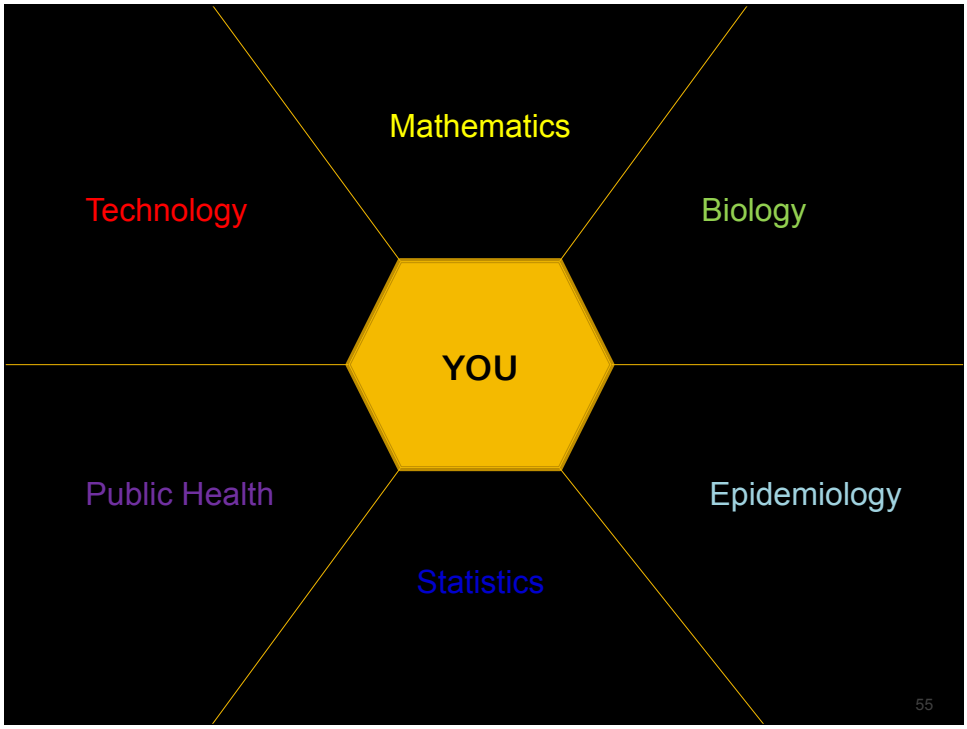

Hippocrates

Aphorisms

I.1. Life is short and the art long; the occasion fleeting, experience fallacious, and judgement difficult.

II.39. Old people, on the whole, have fewer complaints than young; but those chronic diseases which befall them generally never leave them.

II.44. Persons who are very fat are apt to die earlier than those who are slender

From: The Genuine Works of Hippocrates, translated from the Greek by Francis Adams, New York, William Wood & Co., 1891.

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