Causation in infectious disease epidemiology

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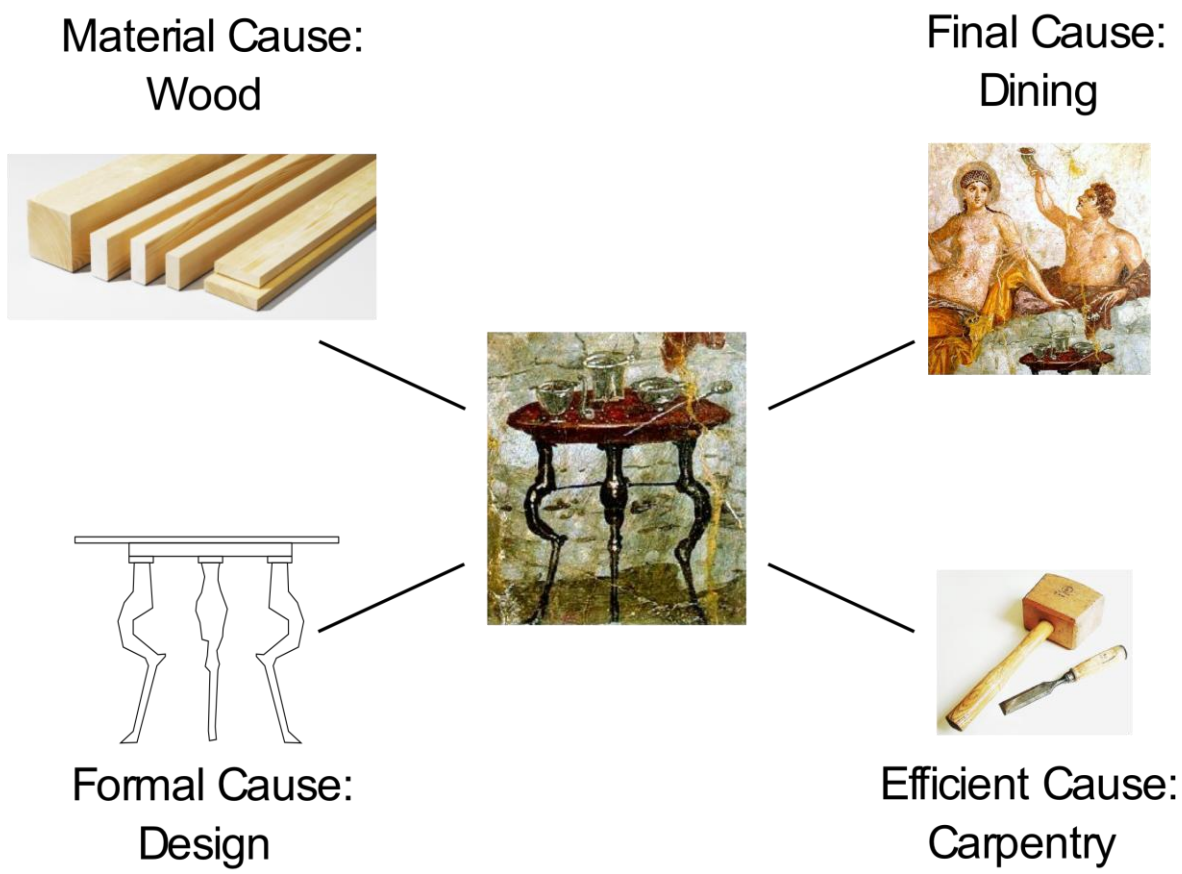
Aristotle's four kinds of cause

Material cause: the wood (tree) that the table is made from.

Formal cause: the design, shape or appearance of the table.

Efficient cause: an agency that changes or moves to create the table (a carpenter).

Final cause: a change or movement that is the reason a table is made (i.e. for dining).

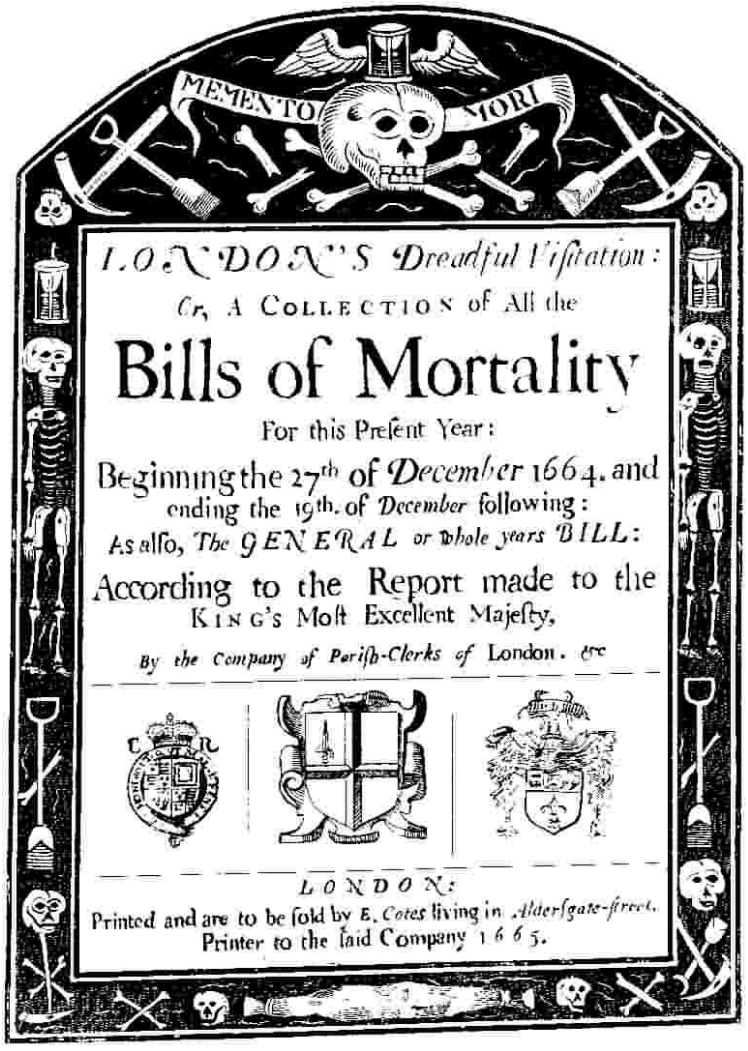


Source: Wikipedia

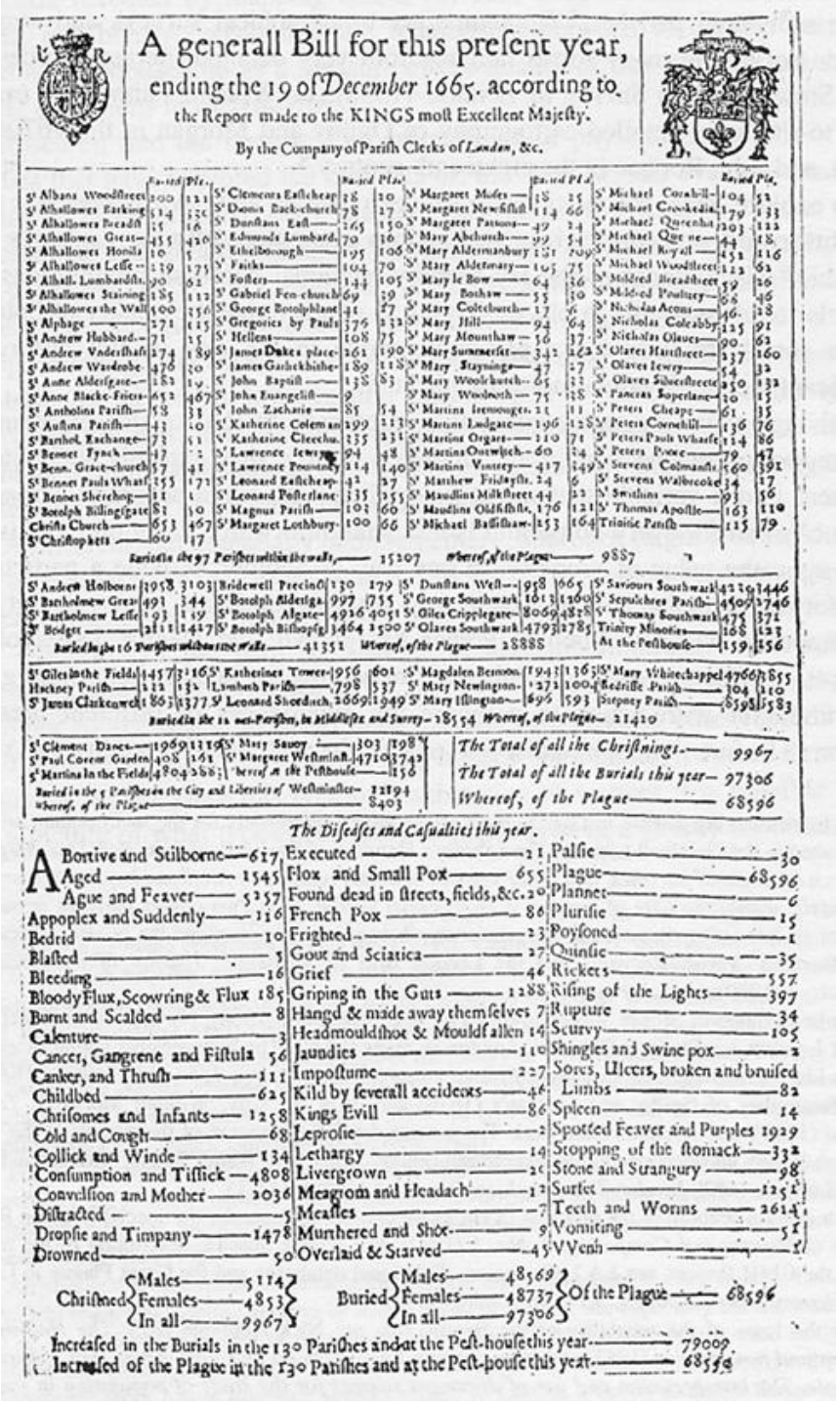
Epidemiology

- **Study of patterns, causes, and effects of disease conditions in defined populations.**
  - Cornerstone of public health
  - Informs policy, evidence-based medicine & prevention
  - Documents disease characteristics
  - Examines disease aetiology, distribution & transmission
  - Outbreak detection, investigation & control
  - Treatment effectiveness, including in clinical trials.
  - Methodology used in clinical research
  - Design, implement & review interventions

Cause detection - the history of surveillance



Under King Charles II



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.

	Buried	Plc.		Buried	Plc.		Buried	Plc.		Buried	Plc.
S' Albans Woodstreet	100	121	S' Clements Eastcheap	28	10	S' Margaret Moses	18	25	S' Michael Cornhill	104	52
S' Alhallowes Barking	134	156	S' Dionis Back-church	78	27	S' Margaret Newfishſt	114	66	S' Michael Crookedlā	179	133
S' Alhallowes Bread ſt	15	16	S' Dunſtans East	265	150	S' Margaret Pattens	49	24	S' Michael Quernhit	203	122
S' Alhallowes Great	455	420	S' Edmonds Lombard	70	16	S' Mary Abchurch	99	54	S' Michael Qu ne	44	18
S' Alhallowes Honila	10	5	S' Ethelburough	195	106	S' Mary Aldermanbury	131	109	S' Michael Royall	152	116
S' Alhallowes Leſſe	139	175	S' Faiths	104	70	S' Mary Aldermary	105	75	S' Michael Woodſtreet	123	62
S' Alhall. Lombardſt.	30	62	S' Fosters	144	105	S' Mary le Bow	64	16	S' Mildred Breadſtreet	59	26
S' Alhallowes Staining	185	112	S' Gabriel Fen-church	69	39	S' Mary Botham	55	30	S' Mildred Poultry	86	46
S' Alhallowes the Wall	300	256	S' George Botolphlane	41	47	S' Mary Colechurch	17	6	S' Nicholas Acons	46	28
S' Alphage	271	125	S' Gregories by Pauls	376	232	S' Mary Hill	94	64	S' Nicholas Colesbby	125	91
S' Andrew Hubbard	71	25	S' Hellens	108	75	S' Mary Mounthaw	56	37	S' Nicholas Olaves	90	63
S' Andrew Vnderſhaft	274	189	S' James Dukes place	261	190	S' Mary Summerſet	342	262	S' Olaves Hartſtreet	237	160
S' Andrew Wardrobe	476	20	S' James Garlickhithe	189	118	S' Mary Stayninge	47	17	S' Olaves Iewry	54	32
S' Anne Aldersgate	182	14	S' John Baptiſt	138	83	S' Mary Woolchurch	65	22	S' Olaves Silverſtreete	250	132
S' Anne Blacke-Friers	452	467	S' John Evangeliſt	9		S' Mary Woolnoth	75	28	S' Pancras Superlane	20	15
S' Antholins Pariſh	18	38	S' John Zachariſe	85	54	S' Martins Ironmonger	21	11	S' Peters Cheape	61	35
S' Auſtins Pariſh	42	20	S' Katherine Colemā	199	121	S' Martins Ludgate	196	128	S' Peters Cornehill	136	76
S' Barthol. Exchange	72	61	S' Katherine Cleechu.	135	231	S' Martins Organ	210	71	S' Peters Poul Wharfe	114	86
S' Bennet Fynch	47	2	S' Lawrence Iewry	94	48	S' Martins Outwich	60	24	S' Peters Poore	79	47
S' Benn. Great-church	57	41	S' Lawrence Pountney	114	140	S' Martins Vintry	417	149	S' Stevens Colmanſtr	160	391
S' Bennet Pauls Wharf	155	173	S' Leonard Eaſtcheap	42	27	S' Matthew Fridayſtr.	24	6	S' Stevens Walbrooke	34	17
S' Benitt Sherehog	11	1	S' Leonard Foſterlane	135	255	S' Maudlins Milkſtreet	44	22	S' Swithins	93	56
S' Botolph Billingſgate	81	30	S' Magnus Pariſh	102	60	S' Maudlins Oldfiſhſt.	176	121	S' Thomas Apoſtle	163	110
Chriſts Church	653	467	S' Margaret Lothbury	100	66	S' Michael Baſſiſhaw	153	164	Trinitie Pariſh	115	79
S' Chriſtophers	60	17									

Buried in the 97 Pariſhes within the walls — 15207 Whereof, of the Plague — 9887

S' Andrew Holborne	1058	3103	Bridewell Precinct	130	179	S' Dunſtans Weſt	958	665	S' Saviours Southwark	4276	1446
S' Bartholmew Great	491	344	S' Botolph Aldersga	997	1755	S' George Southwark	1013	1300	S' Sepulchres Pariſh	4509	1746
S' Bartholmew Leſſe	193	149	S' Botolph Algate	4926	4051	S' Giles Cripplegate	8069	4878	S' Thomas Southwark	475	371
S' Bodget	2811	1417	S' Botolph Billingſg	3464	2500	S' Olaves Southwark	4793	2785	Trinity Minories	168	128
Buried in the 16 Pariſhes without the walls — 41351 Whereof, of the Plague — 28888									At the Peſthouſe	159	156

S' Giles in the Fields	1457	3165	S' Katherines Tower	956	601	S' Magdalen Bermon.	1943	1363	S' Mary Whitechappel	4766	1855
Hackney Pariſh	122	134	Lambeth Pariſh	798	537	S' Mary Newingtō	1272	1004	Bedriffe Pariſh	304	210
S' James Clarkenwell	863	1377	S' Leonard Shordich	2669	1949	S' Mary Iſlingtō	696	593	Stepney Pariſh	6598	1583
Buried in the 11 out-Pariſhes, in Middleſex and Surrey — 18554 Whereof, of the Plague — 21410											

S' Clement Danes	1969	1219	S' Mary Savoy	303	198						
S' Paul Covent Garden	408	261	S' Margaret Weſtmiſt.	4710	3742						
S' Martins in the Fields	4804	2681	Whereof in the Peſthouſe	150							
Buried in the 5 Pariſhes in the City and Liberties of Weſtminſter — 12194 Whereof, of the Plague — 8403											

The Total of all the Chriſtnings	9967
The Total of all the Burials this year	97306
Whereof, of the Plague	68596

The Diſeaſes and Caſualties this year.

Abortive and Stilborne	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	Hanged & made away themſelves	7	Rupture	34
Calenture	3	Headmouldſhot & Mouldfallen	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	46	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	26	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	9	Vvenh	5
Drowned	50	Overlaid & Starved	45		

Chriſtned { Males 5114, Females 4853, In all 9967 }

Buried { Males 48569, Females 48737, In all 97306 } Of the Plague 68596

Increaſed in the Burials in the 130 Pariſhes and at the Peſt-houſe this year — 79009

Increaſed of the Plague in the 130 Pariſhes and at the Peſt-houſe this year — 68554

Smallpox

Malaria

Syphilis

Dysentery

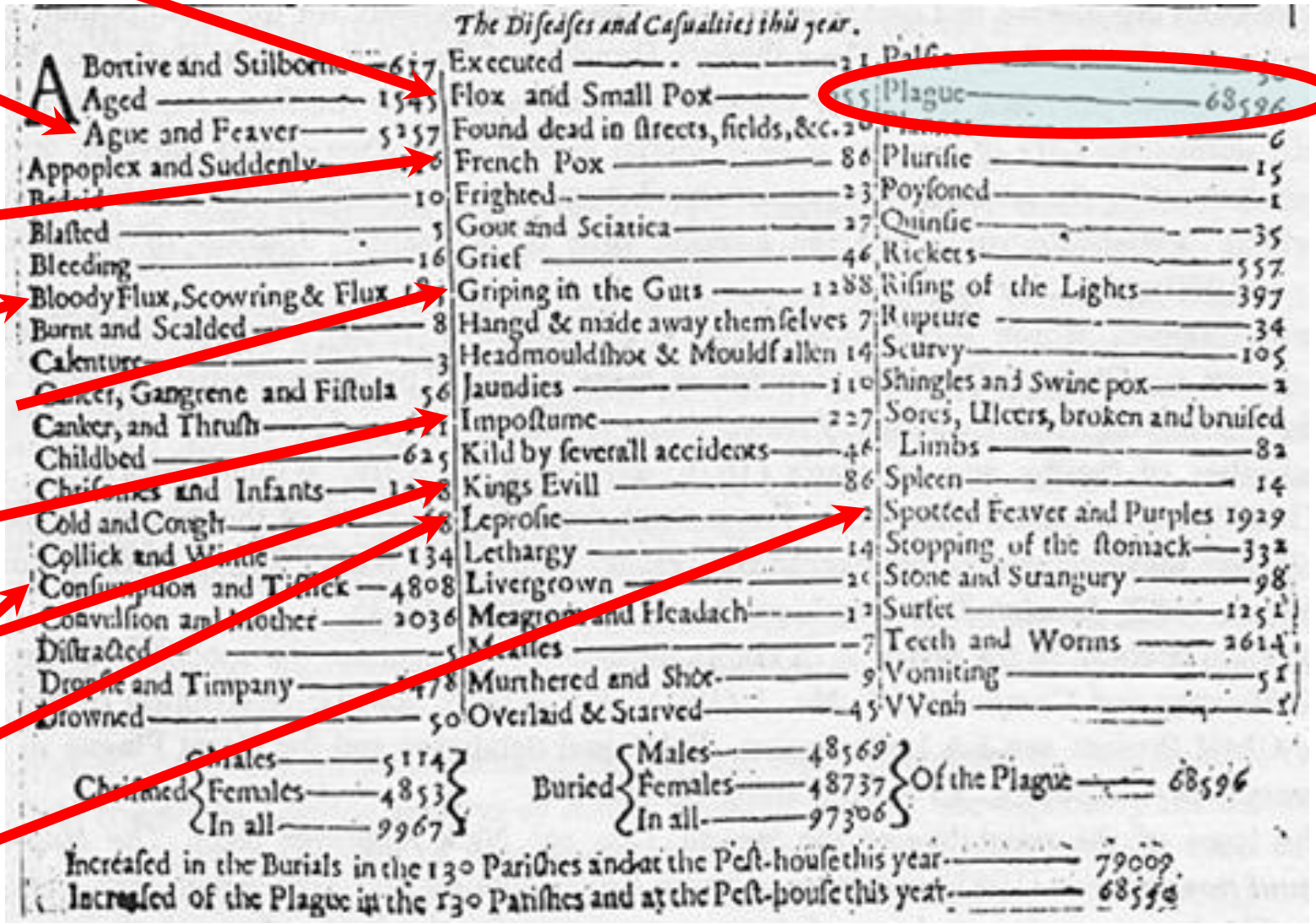
Gastroenteritis

Abscess

Tuberculosis

Leprosy

Typhus



The Diſeaſes and Caſualties this year.

Abortive and Stilborn	617	Executed	21	Palſie	
Aged	1545	Flox and Small Pox	655	Plague	68596
Ague and Feaver	5257	Found dead in ſtreets, fields, &c.	20		6
Appoplex and Suddenly	10	French Pox	86	Pluriſie	15
	10	Frighted	23	Poyſoned	1
Blaſted	5	Gout and Sciatica	27	Quinſie	35
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Chriſoms and Infants	1	Kings Evill	86	Spotted Feaver and Purples	1929
Cold and Cough	78	Leproſie	2	Stopping of the ſtomack	332
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Diſtracted	5	Meaſles	7	Vomiting	51
Dropſie and Timpany	478	Murthered and Shot	9	VVenh	1
Drowned	50	Overlaid & Starved	45		

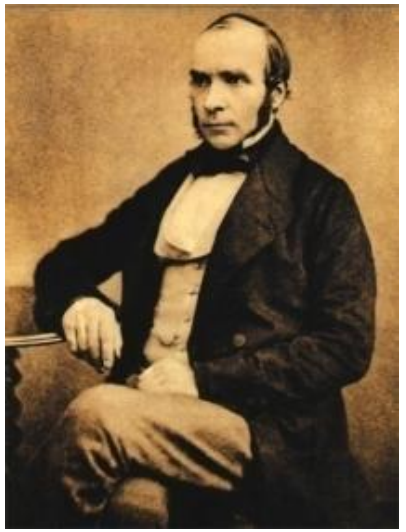
Chriſtned	Males	5114	Buried	Males 48569
	Females	4853		Females 48737
	In all	9967		In all 97306

Of the Plague 68596

Increaſed in the Burials in the 130 Pariſhes and at the Peſt-houſe this year 79009.
Increaſed of the Plague in the 130 Pariſhes and at the Peſt-houſe this year 68590

For year 1665 there were 68,596 reported deaths from plague

The causes of cholera using descriptive epidemiology and public health intervention



- Large outbreak of cholera in Soho, London in 1854
- Used descriptive epidemiology & evidence based public health intervention
- John Snow removed the Broad Street water pump handle
- Spread of cholera dramatically stopped
- Disproved the view that infection was spread by ‘miasma’ in the atmosphere
- Identified the outbreak as caused by drinking water contaminated as a result of poor systems for disposal of sewage
- Attributed the disease to a source (human faeces) and a route of transmission (water from the Broad Street pump)

Cholera pandemics

1st pandemic. 1817-1823 Asiatic Cholera originated near Calcutta and spread to SE Asia, China and Japan but did not reach Europe

2nd pandemic. 1826 -1837, began in Bengal and spread through India. Cholera entered UK in 1831 (31,000 died).

3rd pandemic. 1846-1863, reached Europe and the U.S. in 1848. **John Snow** observed during the 1848 London epidemic that the disease was spread by contaminated water.

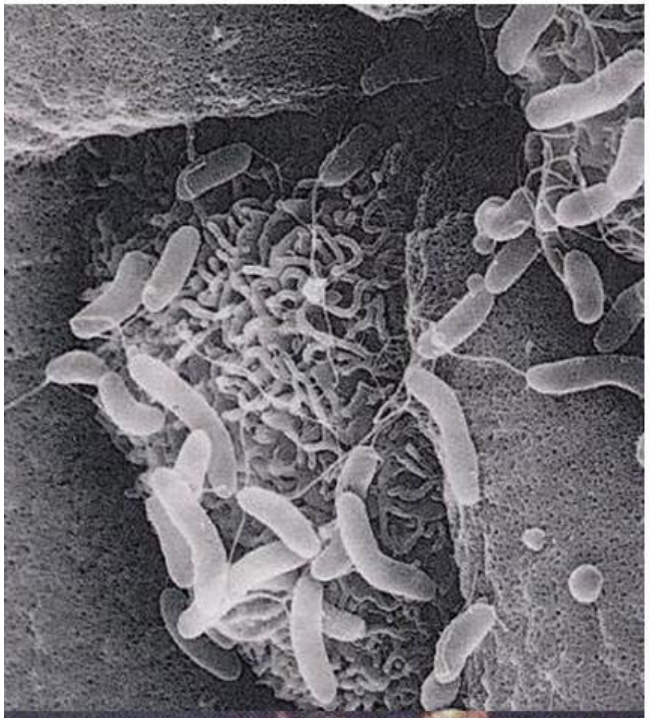
4th pandemic. 1863-1866, spread first to the Middle East, then to the Mediterranean and on to New York. Tens of thousands died, but public health reforms moderated the death toll.

5th pandemic. 1881-1896. Improved sanitation, diagnosis and quarantine kept it from reaching many European cities or the U.S. Robert Koch discovered that *Vibrio cholerae* caused the disease.

6th pandemic. 1899-1923, also affecting Asia but failing to reach western European or the U.S., again due to developments in water treatment and sanitation.

7th pandemic. 1961- present, began in Indonesia and reached Peru and neighboring countries. It continues with periodic outbreaks in many areas of the world. The outbreak in Peru resulted from a halt in water chlorination.

Causes of cholera pandemics

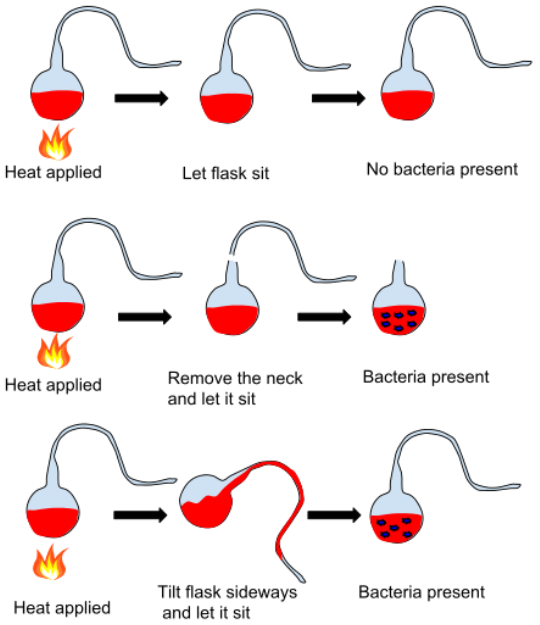


Vibrio cholerae

- Associated with famine, migration, flooding etc.
- High infective dose
- *V.cholerae* can grow in plankton
- Satellite monitoring of water temperature and blooms
- Role of ship's ballast water

Pasteur and germ theory

- Pasteur investigated fermentation
  - Berzelius & von Liebig suggested fermentation resulted from decomposition. Pasteur showed this was wrong – yeast fermented sugar to produce alcohol.
  - Other microorganisms in wine produce lactic acid, making it sour. Less sugar fermented when the yeast was exposed to air than when not Pasteur effect).
  - The skin of grapes was the source of yeasts. Sterilized grapes and grape juice never fermented.
- The cause of silkworm disease (pébrine & flacherie)
  - Pasteur worked for 5 years on the economic losses in silkworm production. Pébrine, a hereditary disease (now known as a microsporidian) was prevented by examining pulped female moths after they had laid their eggs. The eggs of infected moths were destroyed.
  - Hygiene was used to prevent accidental flacherie (now known to be a virus).
- Spontaneous generation disproved
  - There was a belief in spontaneous generation. Redi (17th century) and Spallanzani (18th century) provided evidence against spontaneous generation and Pouchet conducted experiments to prove spontaneous generation (1850s).
  - Pasteur used swan neck flasks to show nothing grew in boiled broths and that the living organisms that grew in such broths came from outside, on dust, rather than spontaneously generating within the liquid or from the action of pure air.
- Vaccination
  - Successful treatment of rabies with a vaccine
  - A weakened anthrax strain was used to produce a vaccine that protected sheep
  - A vaccine for chicken cholera (*Pasteurella multocida*) was protective
  - Evidence of immunity



Causal inference in Microbiology: Koch's & Loeffler's postulates 1883

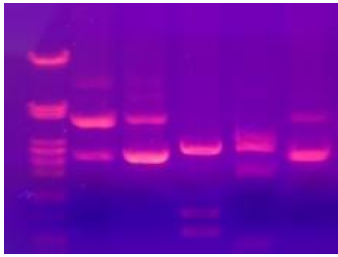
- The microorganism must be found in all people suffering from the disease, but not in healthy people
- The microorganism must be isolated from a diseased person and grown in pure culture.
- The cultured microorganism should cause disease when introduced into a healthy animal model (Ilya Metchnikoff drank a cholera culture).
- The microorganism must be re-isolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.

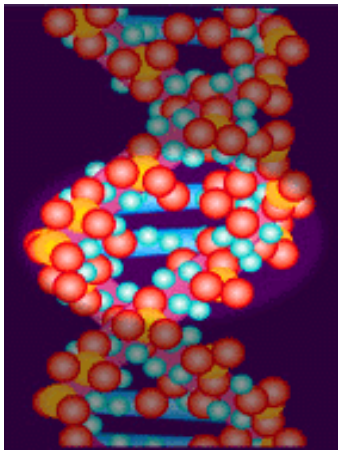
Causal inference in Microbiology: Stanley Falkow's molecular postulates 1988

- The phenotype, property or gene under investigation should be associated with pathogenic members of a genus or pathogenic strains of a species but be absent from non-pathogenic strains.

- Specific inactivation of the gene(s) associated with the suspected virulence trait should lead to a measurable loss in pathogenicity or virulence in an appropriate animal model.

- Reversion or allelic replacement of the mutated gene should lead to restoration of pathogenicity in the animal model.

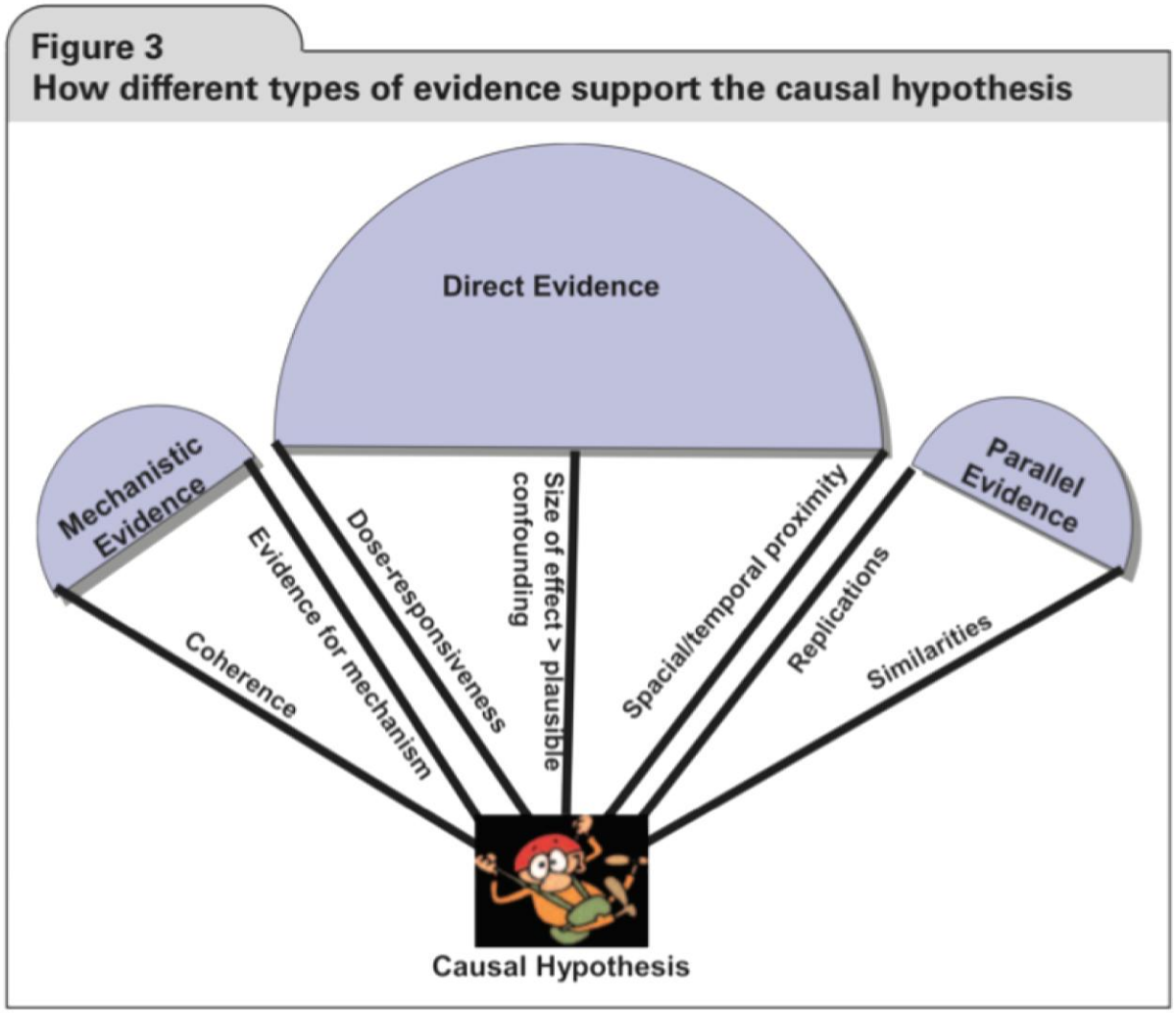




Causation and the nine Bradford Hill Criteria

Criteria	Description
Analogy	Are there other similar illnesses that behave in a similar way?
Biological gradient	Is the disease more common in those people with most exposure to the risk factor?
Coherence	Does the epidemiological data conflict with other biological and clinical data suggesting causality?
Consistency	Do the results from different researchers all suggest an association?
Experiment	Is it possible to design experimental interventions to demonstrate causality?
Plausibility	From what is already known of the biology of the potential pathogen, is it plausible that the exposure causes disease?
Specificity	Is the disease specific to contact with the risk factor or are there other known causes?
Strength of association	Is any epidemiological study association between disease and risk factor, statistically significant?
Temporality	Does the disease follow exposure to the proposed risk factor (rather than precede it)?

Hill, Austin Bradford (1965). "The Environment and Disease: Association or Causation?". Proceedings of the Royal Society of Medicine. 58 (5): 295–300.



Howick J, Glasziou P, Aronson JK. The evolution of evidence hierarchies: what can Bradford Hill's 'guidelines for causation' contribute? Journal of the Royal Society of Medicine. 2009;102(5):186-94.

Causation – seasonality and trend

Campylobacter late spring

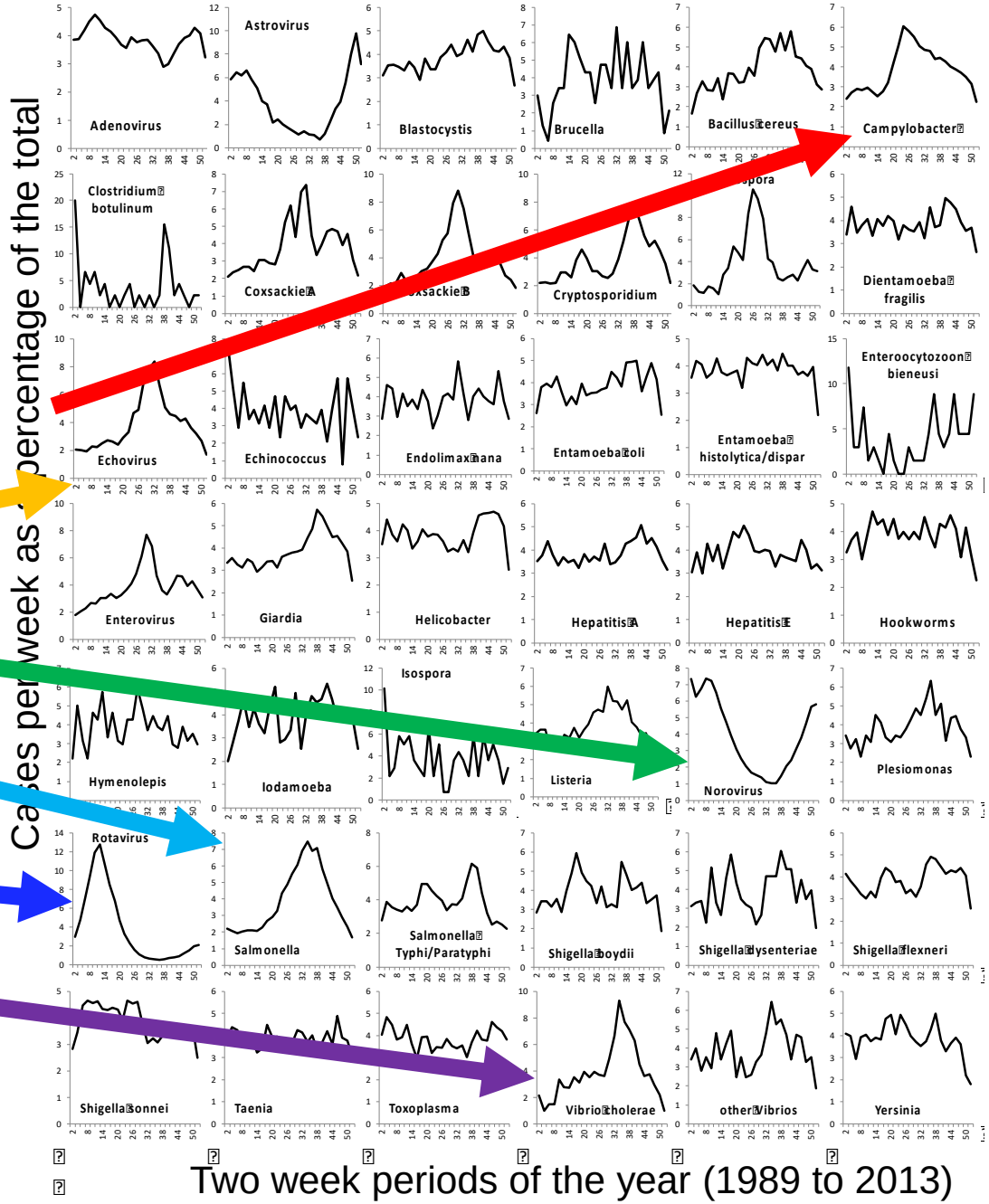
Echovirus summer

Norovirus winter

Salmonella summer

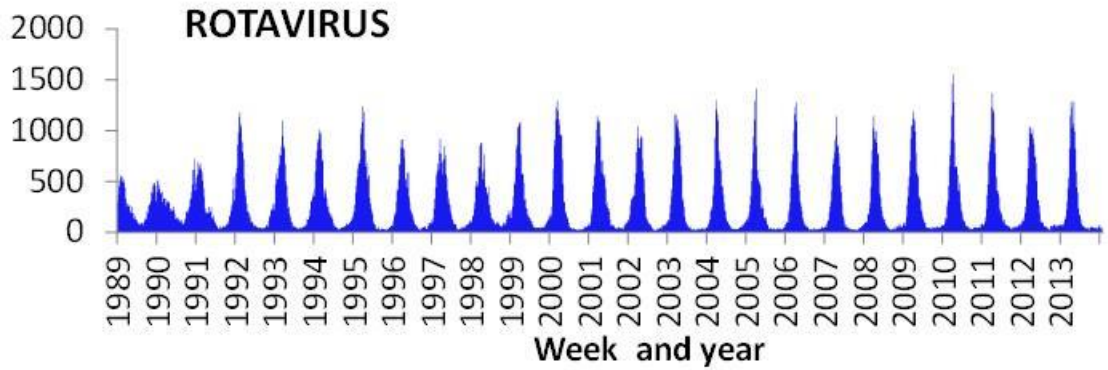
Rotavirus late winter

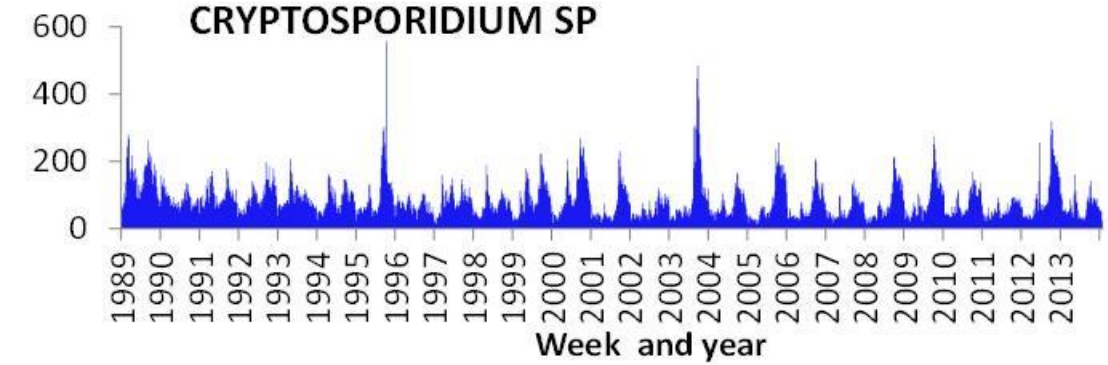
Cholera summer

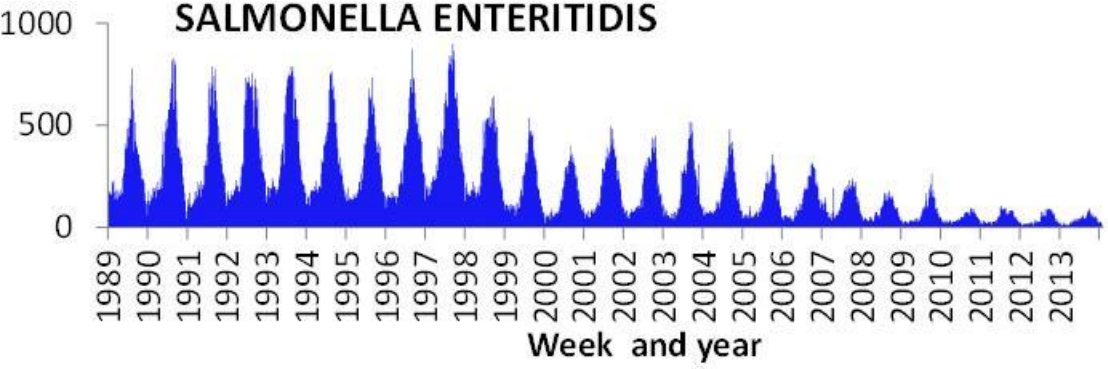


Association is not necessarily evidence of causation

Causes of temporality







Propagated epidemic

- Propagated annual epidemic resulting from person to person transmission and number of susceptible children.
- The cyclic nature of the annual winter increase is presumed to reflect the impact of sunlight and temperature on the survival of the virus

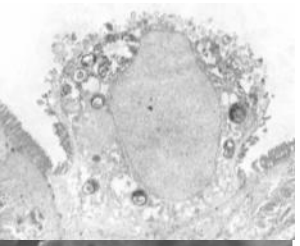
Point source outbreaks

- Regular annual increases in spring and autumn. The spring cases have mostly disappeared since 2001.
- Spring *C. parvum*, autumn *C. hominis*.
- The more erratic seasonality is related to point source outbreaks and sporadic cases caused by drinking water, farm visits, travel and swimming pools.

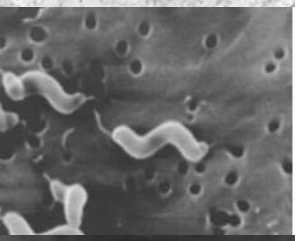
Seasonal distribution

- Annual series of point source outbreaks and individual cases resulting from the contamination of food with raw eggs
- Summer increase reflects the ability of the organism to grow in contaminated raw eggs and in ready to eat foods with the contaminated egg
- Intervention (vaccination of chickens & biosecurity) has reduced disease

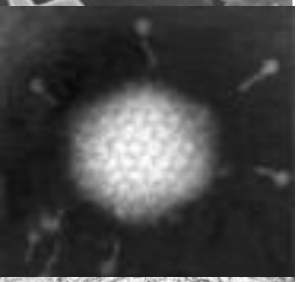
Published waterborne outbreaks indicating a microbial cause



Microsporidiosis outbreak linked to drinking water supply in Lyon, France



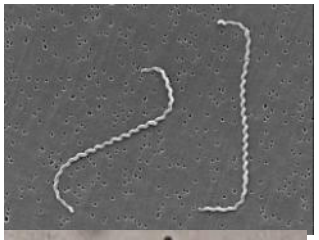
Campylobacter outbreak linked to unchlorinated drinking water supply in Alsvåg Norway



Mixed adenovirus, rotavirus and norovirus outbreak linked to untreated drinking water supply contaminated by sewage in Noormarkku Finland

Toxoplasmosis associated with unfiltered water in Panama, Vancouver and Brazil

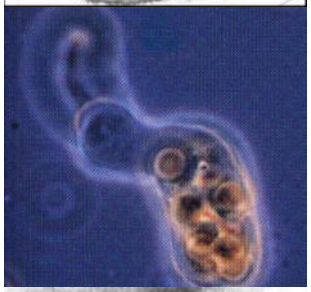
Cyclospora associated with unfiltered water contamination of soft fruit in Guatemala



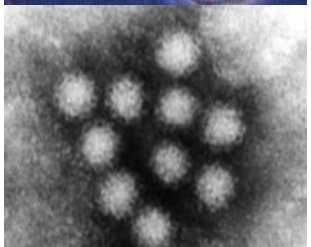
Leptospirosis outbreak linked to drinking fountain water in Pictracuta, Italy

Liver failure and death associated with cyanobacterial toxins in dialysed patients in Portugal and Brazil

Cryptosporidium outbreak linked to treated mains water in Devon, England

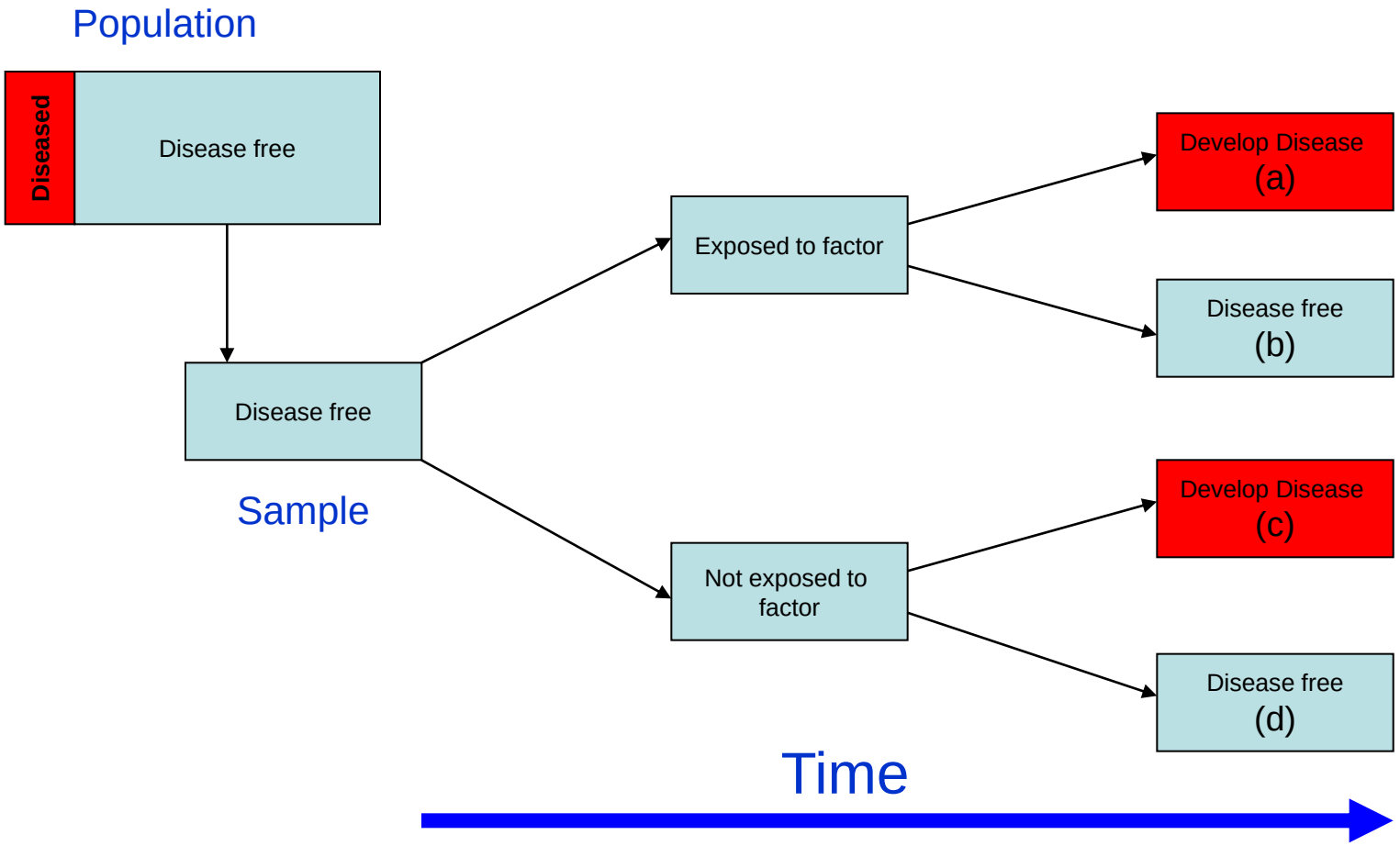


G. lamblia and *E. histolytica* outbreak linked to sewage backing up into treated drinking water in Sälen, Sweden



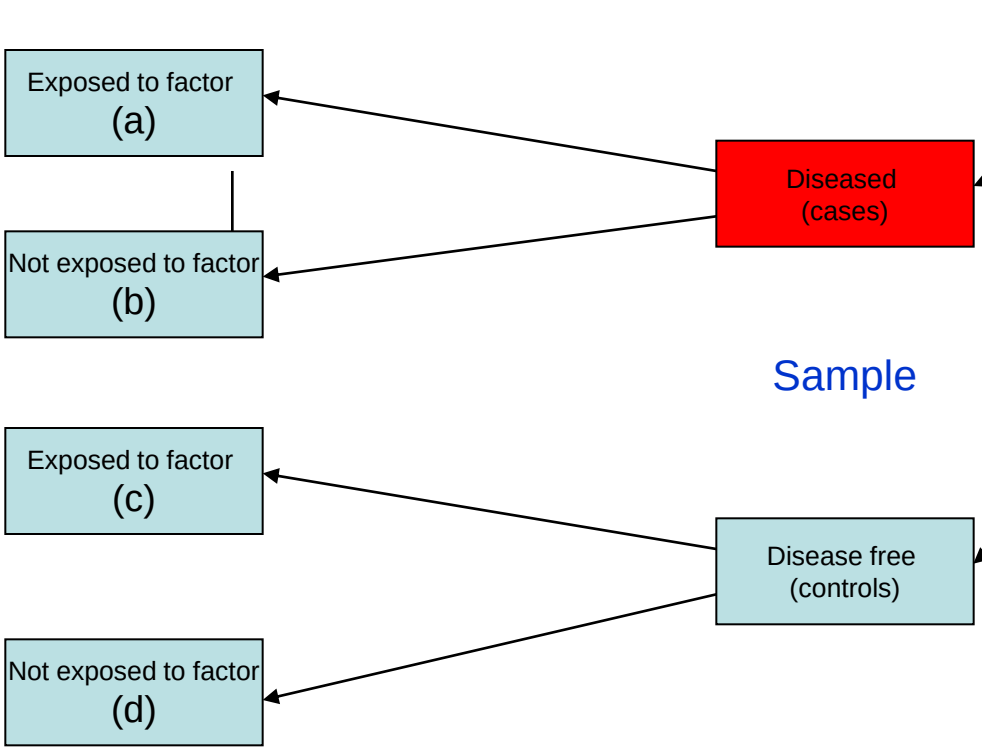
Norovirus outbreak associated with faecally contaminated untreated water in Bermuda

Cause determination using cohort study



The relative risk = risk in exposed (a/a+c)
risk in unexposed (b/b+d)

Cause determination using case-control study



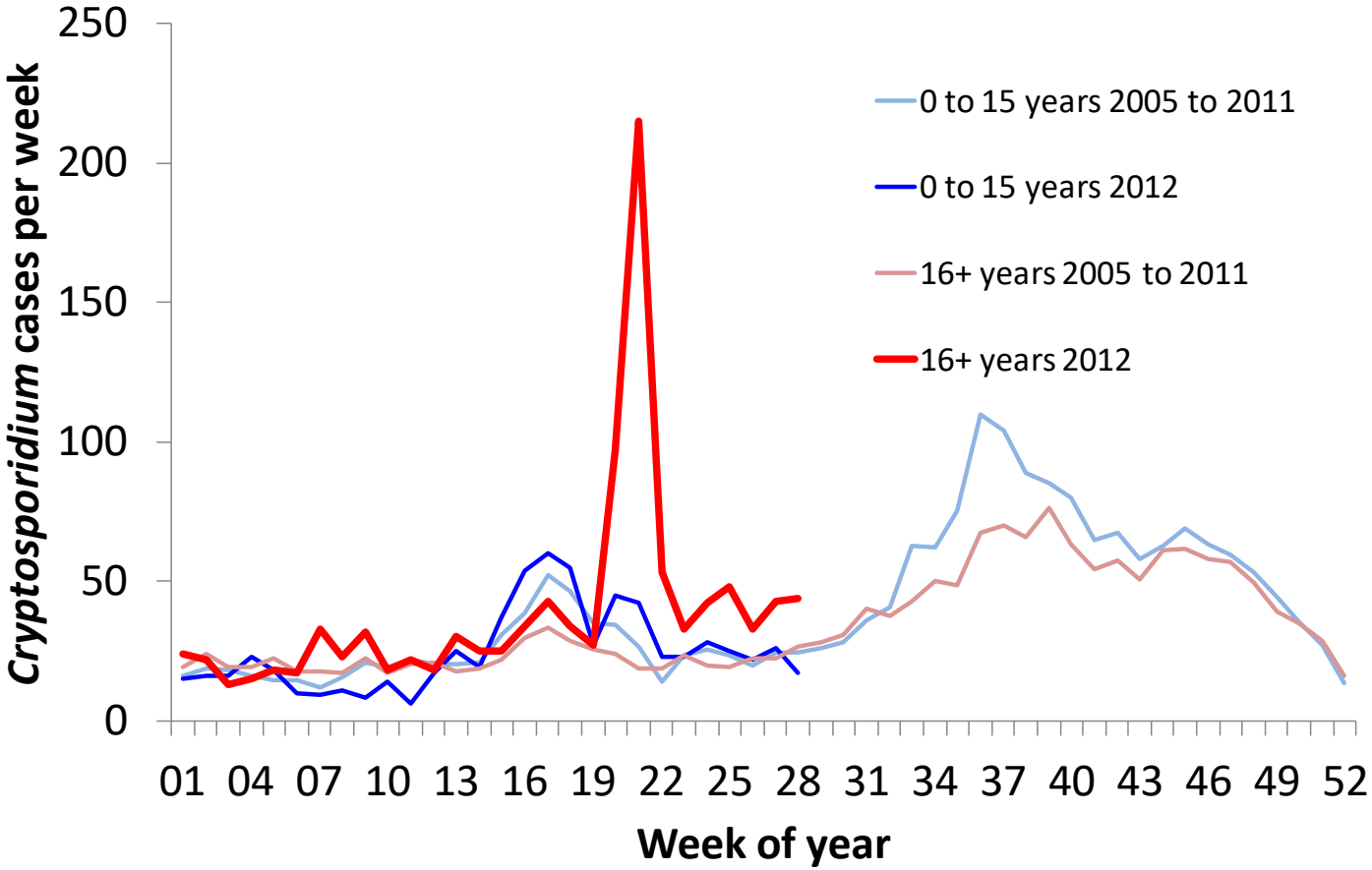
	Observed (diseased group)	Expected (no disease group)
exposed to risk	25	37
not exposed to risk	67	72

The estimated odds ratio =

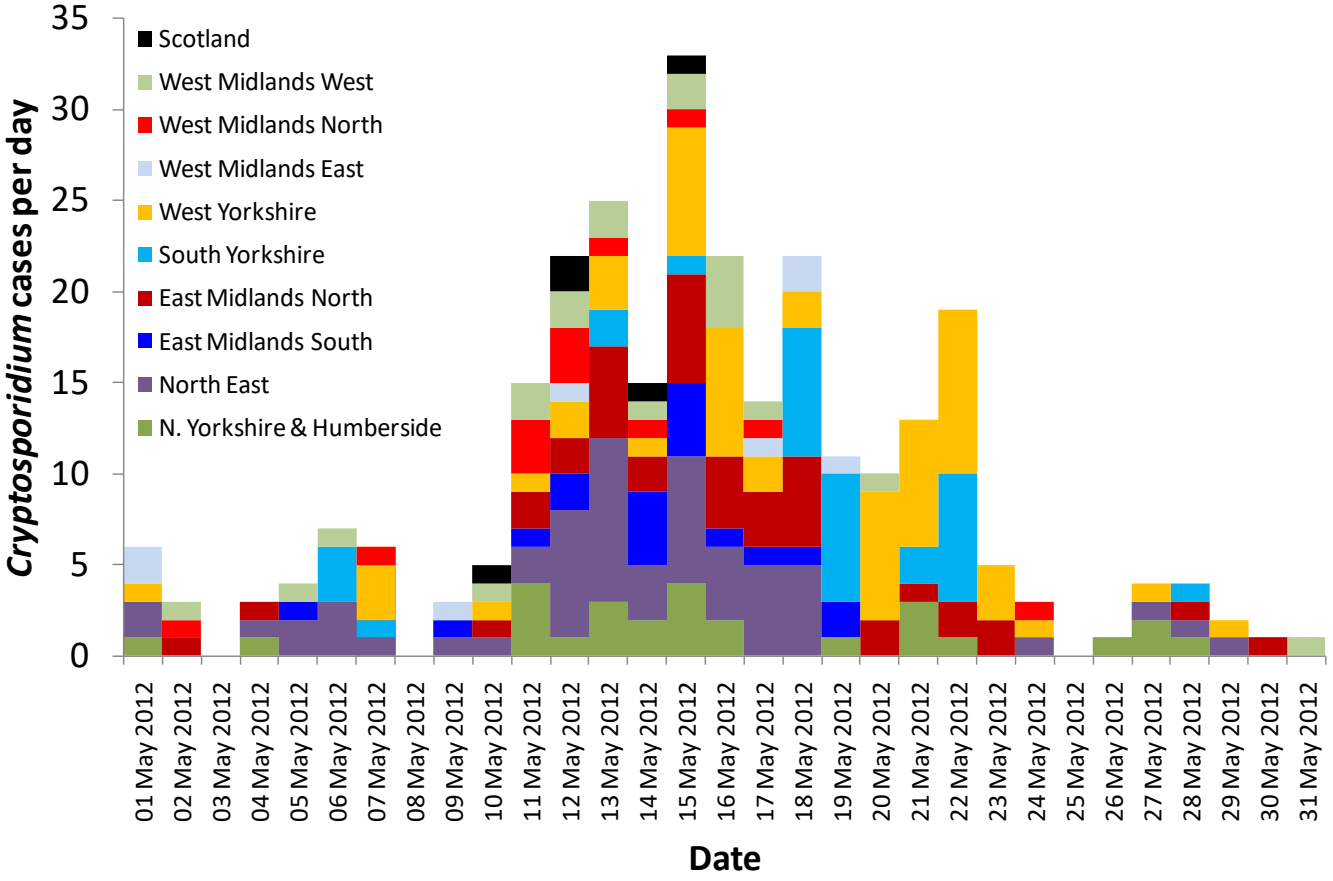
probability of being a case in the exposed group (a/a+c)

probability of being a case in the unexposed group (b/b+d)

Cause of change between years Cryptosporidium 2012



Cause of an outbreak - epidemic curve of *Cryptosporidium* cases by onset date May 2012 (n=285)



Cases onset dates between 11th and 22nd May 2012. The single peak was consistent with a common source outbreak with an exposure period in early May.

McKerr C ., Adak G.K., **Nichols G**., Gorton, R., Chalmers R.M., Kafatos G., Cosford P., Charlett A., Reacher M, Pollock K.G., Alexander C.L., Morton S. An outbreak of Cryptosporidium parvum across England & Scotland associated with consumption of fresh pre-cut salad leaves, May 2012. PLOSOne 2015,10(5):e0125955.

Cause from multivariable analysis

Table 4. Multivariable logistic regression analysis adjusting for gender and age.

Exposure	Level†	No (%) cases' exposure	OR	95% CI	p-value
Pre-cut mixed leaves from Supermarket A	no	32 (48.5)	baseline		
	yes	34 (51.5)	7.71	(2.40, 24.78)	<0.001
Plum tomatoes bought from Supermarket B	no	68 (91.9)	baseline		
	yes	6 (0.08)	10.71	(1.27,.)	0.017
Pre-cut spinach bought from Supermarket C	no	65 (89.0)	baseline		
	yes	8 (11.0)	11.27	(1.40,.)	0.028
Milk bought from Supermarket A	no	58 (79.5)	baseline		
	yes	15 (20.5)	4.33	(0.69, 27.05)	0.096

† The level refers to whether the patient responded with a yes or no to the exposure question.

The Grocer

"We very strongly dispute we were anything to with this," a spokesman for Morrisons said. "We didn't see any complaints from any customers on this issue. Morrisons shares the same supply chain used for its bagged salads with several other retailers, meaning they would also have been affected by this outbreak.

Analysis included:

1. Descriptive study – Outbreak over 2 weeks in May 2012
2. Case-case between year study – Link to R4 & Salad
3. Trawling Questionnaire – R4 & salad main hypotheses
4. Geographic study – link to R4 stores
5. E & W comparison with previous years – many regions including Scotland
6. Case-control study single variable analysis – R4 & Salad
7. Multivariable analysis – R4 & Salad
8. Outbreak strain multivariable analysis – R4 & Salad
9. Food chain analysis – No evidence
10. Consultant analysis of HPA statistical studies – Not R4
11. Legal challenge of findings by R4
12. Publication in peer review
13. Clear overall evidence of link to R4 and bagged salad

Cause through coincidence

RAPID COMMUNICATIONS

Simultaneous increase of *Cryptosporidium* infections in the Netherlands, the United Kingdom and Germany in late summer season, 2012

N Fournet[1,2,3], M P Deege[3,4,5], A T Urbanus[3], G Nichols[6], B M Rosner[7], R M Chalmers[8], R Gorton[9], K G Pollock[8,9], J W B van der Giessen[1], P C Wever[10], J W Dorigo-Zetsma[11,12], B Mulder[13], T G Mank[14], I Overdevest[15], J G Kusters[5], W van Pelt[1], L M Kortbeek (Titia.Kortbeek@rivm.nl)[1]

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14. Regional Laboratory for Medical Microbiology and Public Health, Haarlem, the Netherlands
15. Laboratory for Medical Microbiology and Immunology, St Elisabeth Hospital, Tilburg, the Netherlands

Citation style for this article:
Fournet N, Deege MP, Urbanus AT, Nichols G, Rosner BM, Chalmers RM, Gorton R, Pollock KG, van der Giessen JW, Wever PC, Dorigo-Zetsma JW, Mulder B, Mank TG, Overdevest I, Kusters JG, van Pelt W, Kortbeek LM. Simultaneous increase of Cryptosporidium infections in the Netherlands, the United Kingdom and Germany in late summer season, 2012. Euro Surveill. 2013;18(2):pii=20348. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20348

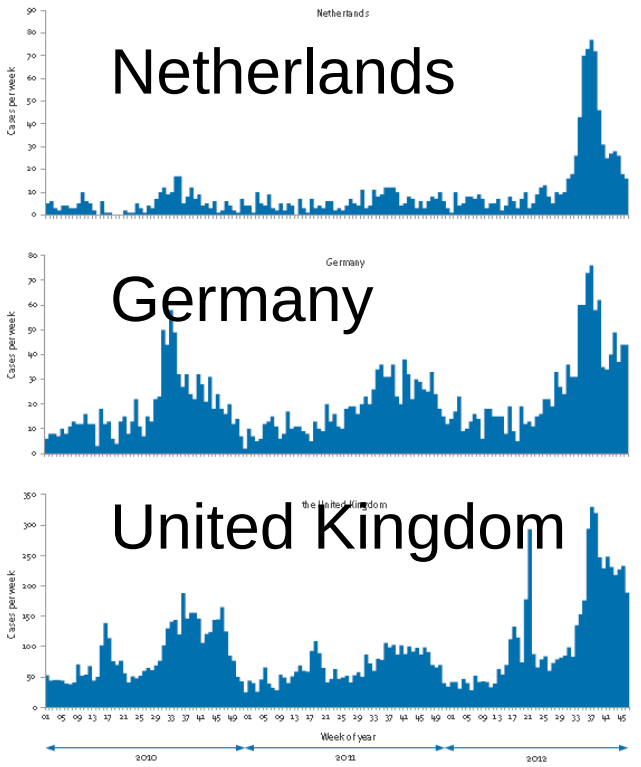
Article submitted on 12 December 2012 / published on 10 January 2013

Starting August 2012, an increase in *Cryptosporidium* infections was reported in the Netherlands, the United Kingdom and Germany. It represented a 1.8 to 4.9-fold increase compared to previous years. Most samples were *C. hominis* IbA10G2. A case–control study was performed in the Netherlands but did not identify an endemic source. A case–case study in the north of England found travel abroad to be the most common risk factor.

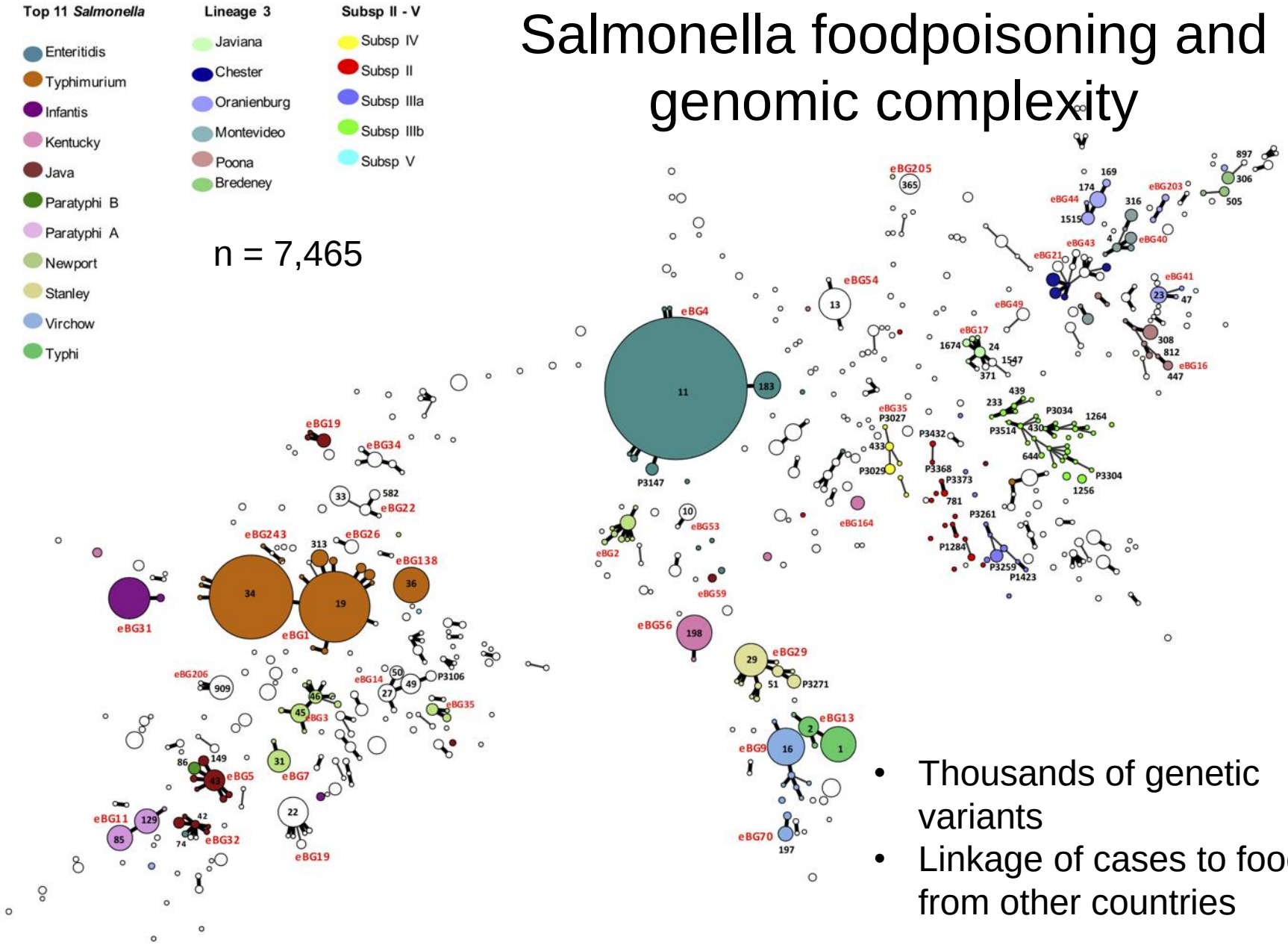
In the Netherlands, *Cryptosporidium* infection is not a notifiable disease, therefore there are no solid data on the incidence of human infections. In the UK, surveillance of *Cryptosporidium* was implemented in the 1990s. Positive results from laboratory testing are now notifiable. In Germany, *C. parvum* infection has been notifiable since 2001, but is mostly reported without species determination.

FIGURE

Cryptosporidium cases reported from eight laboratories in the Netherlands and cases notified in Germany and the United Kingdom, January 2010–November 2012



Salmonella foodpoisoning and genomic complexity



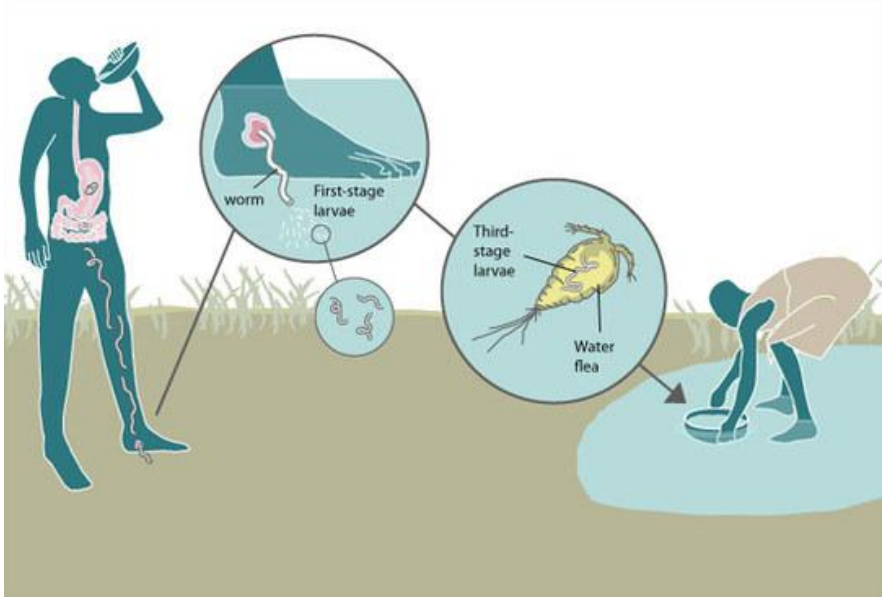
- Thousands of genetic variants
- Linkage of cases to foods from other countries

Figure 1 Population structure of all *Salmonella enterica* isolates submitted to PHE from local and regional hospital laboratories in England and Wales between April 2014 and March 2015 (see Table S1 for details).

Cause of new disease – Serious illness and death in injecting drug users (IDU) – *Clostridium novyi*

- Serious illness and death in injecting drug users
  - Scotland, Ireland and England.
  - IDU presenting to hospital (or found dead) with abscess / significant inflammation at an injection site since within outbreak period
  - Severe inflammatory process at or around injection site
  - Severe systemic reaction with evidence of multi-organ failure and a high white cell count
  - Case fatality was 50% (13=26).
- Standardised active case-finding, data collection and microbiological investigation.
  - A ‘toolkit’ for the surveillance, investigation and management.
  - 26 definite/probable cases in England between 1 April and 31 Aug 2000 (17 in the North).
  - Microbiological testing of heroin through Manchester police
- Risk factor
  - intramuscular or subcutaneous injection (skin popping)
  - use of citric acid mixed with heroin
  - outbreak duration suggested a particular supply of heroin
  - *Clostridium novyi* was isolated from two English cases.

Causes of Guinea worm (*Dracunculus medinensis*)



- *Dracunculus medinensis* occurs in poor communities in remote parts of Africa.
- The disease makes people temporarily unable to work, causing crop losses, social and financial problems.
- Infection confers little protective immunity – people in affected villages suffer regularly.
- The worm infects copepods (water fleas) that are swallowed in drinking water (the only way the infection can be transmitted).
- The worm grows in the leg and larvae are released into the water where they infect copepods
- Diagnosis is easy (presence of an emerging worm).

Eradication of Guinea worm (*Dracunculus medinensis*)

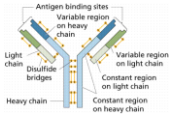
- Interventions are effective, low cost, and simple to implement
- Interruption of transmission with
  - case-containment measures (stopping people with a Guinea worm ulcer from entering ponds and wells used for drinking water)
  - improved water supplies
  - filtering water fleas from drinking water
  - treating water sources with a chemical that kills water fleas (e.g. Abate)
- Eradication campaign through Carter foundation, WHO, CDC, UNICEF established in 1981
  - integrated community-based surveillance, immediate case reporting, zero case reporting, global and national databases
  - health education, certification, advocacy
- Around 3.5 million cases; 21 countries in **1986**.
- 25 cases in **2017**: Chad; Ethiopia; South Sudan.
- Remaining cases in civil war areas.

Summary of causes - *Campylobacter*

Campylobacter strains

Strain diversity
Antibiotic resistance
Strain survival
Virulence differences
Attribution to source

Personal differences



Body flora
Body chemistry
Previous infections
Antibodies
Family history of disease
Susceptibility to disease
Resistance to disease
Maternal antibodies
Age and sex
Stomach acidity

Weather / climate / season

Temperature
Rainfall
Flooding
Latitude & longitude
Seasonal cycles

Environment

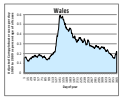
Access to countryside
Recreational water

Water /waste

Drinking water treatment
Private supplies
Rivers & lakes
Groundwater
Sewage
Irrigation
Animal waste
Garbage

Epidemiology

Surveillance systems
Epidemiological knowledge
Outbreak evidence
Surveillance outputs
Assessing interventions

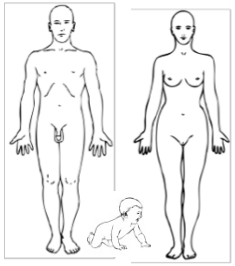


Laboratory

Isolation
Diagnosis
Typing
Antibiotic resistance

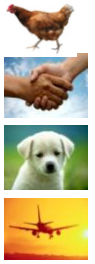
Healthcare

General physicians
Hospital services
Community care
Access to health care
Social model
Healthcare quality



Human disease

Transmission risks



Eating chicken
Preparing chicken
Family outbreaks
Young dogs
Transmission from children
Cross contaminated salads
Food consumption
Drinking water
Contact with food
Countryside exposure
Fomites
Vectors (Cockroach, rat, fly)
Contaminated hands
Foreign travel
Poor food hygiene
Barbecues
Bird pecked milk

Sources

Chicken / poultry
Cattle & sheep
Pets
Wild birds & mammals
Humans

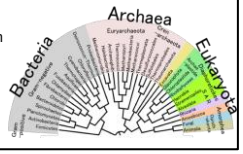
Reservoirs

Animal and bird faeces
Sewage
Wild birds & mammals
Rivers
Coastal waters
Food waste

Behavioral risks

Food hygiene practices
Cleanliness
Risk behavior
Access to countryside
Exposure to recreational waters
Workplace exposure (farming/chickens)
Eating out

Co-evolution



Evolutionary origin of organism
Evolutionary response of host
Types behaving differently
Similarities to other pathogens
Odd typing structure

Food retail / catering

Contaminated packaging
Cross contamination
Sourcing
High risk products
Contamination on display
Food technology changes

Food industry

Transport
Slaughter & scald
Eviceration
Decontamination
Wrapping
Industry good practice

Agriculture

Animal husbandry
Biosecurity
Transmission from wildlife
Breeding flocks & thinning
Vegetable irrigation
Animal watering

Public Environment

Housing
Sewage & drinking water
Waste management
Governance
Legislation
Public health authorities

Social-political environment

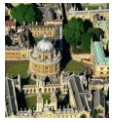
Economic climate
Socioeconomic status/class
Crowding
Warfare
Immigration
Degree of development

Institutional environment

HPA
DEFRA
FSA
DH
NFU
Parliament

Health Protection Agency

Research environment



Universities
Research funders
Epidemiological evidence
Case-control studies
Attribution studies
Intervention approaches

Public health environment

Good primary diagnosis
Environmental health action
Surveillance and response
Historical interventions

Technological environment

MLST / sequence typing
Vaccines
Applied research

Intervention environment

NZ evidence for intervention
Iceland project

Public concern environment

Outbreaks
News stories

Can we modify Bradford Hill Criteria for general use?

Criteria	Description
Analogy	Are there other similar events that behave in a similar way?
Gradient	Is the event more common where most exposed to the instigating factor?
Coherence	Does the data conflict with other data or evidence suggesting causality?
Consistency	Do the results from different researchers all suggest an association?
Experiment	Is it possible to design experiments to demonstrate causality?
Plausibility	From what is already known, is it plausible that the exposure causes the outcome?
Specificity	Is the event specific to contact with the factor or are there other known causes?
Statistical link	Is any association between event and the factor statistically significant?
Temporality	Does the event follow exposure to the proposed factor (rather than precede it)?
Multiplicity	Are there many different ways in which the events can be triggered?
Evolution	Does the event have an evolutionary explanation?
Surveillance	Is the data for examination of causation collected systematically?

Can we extend Aristotle's kinds of cause?

Evolutionary cause: cosmological and genetic origins of the tree.

Material cause: the wood (tree) that the table is made from.

Formal cause: the design, shape or appearance of the table.

Efficient cause: an agency that changes or moves to create the table (a carpenter).

Final cause: a change or movement that is the reason a table is made (i.e. for dining).

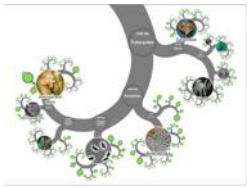
Financial cause: who paid for this table.

Business cause: the company making a living producing these.

Ownership cause: the person who currently owns the table.

Lifecycle cause: how long the table will exist for and where discarded ones go.

Philosophical cause: a tool for discussions about reality.

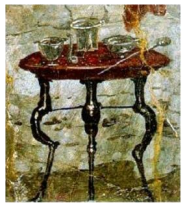


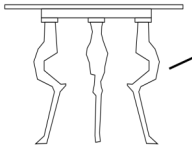
Evolutionary cause: genetics

Ownership cause: who's table

Material Cause: Wood

Final Cause: Dining





Formal Cause: Design

Efficient Cause: Carpentry

Philosophy cause: A rhetorical tool

Lifecycle cause: Stages of existence

Financial cause: who paid

Business cause: the company

Cause in Public Health Action

- Empedocles (490-440BC), according to Diodorus, managed to make Selinunte (S.W. Sicily) a healthy town through irrigation.
- The area suffered from malaria and contaminated water.
- By opening up two rivers to the sea, he channelled ‘slack’ water and drained the swamps making the water drinkable.
- Sanitary works minimised the epidemic of fever which afflicted the people of Selinunta.
- This is thought to be the first known Public Health Project
- It implies attribution of a disease (malaria) to a source (swamp water), although the vector took more than 2000 more years to be identified.

N.P. Stathakou,MD, G.P. Stathakou,MD, S.G. Damianaki,MD, E. Toumbis Ioannou,MD and N.G. Stavrianeas,MD **Empedocles’ bio-medical comments: A precursor of modern science**

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Causation in infectious diseases is predominantly a practical business that involves a reliable surveillance dataset, simple descriptive methods, statistically sophisticated analysis, modern genetic typing and a clear understanding of how to intervene to limit outbreaks and reduce the burden of disease in the future.

Thanks for listening

Definition: *Epidemiologists – A group of people broken down by age and sex*

Summary of disease causation

- What do we already know?
- Does an organism cause disease?
- Where does the source of infection derive from?
- What is the vehicle of transmission?
- What is the transmission pathway?
- How do we examine causes?
- What are the social causes?
- How do we intervene successfully?
- How has the disease evolved?

Attribution and infection

- Attributing disease to a physical cause
  - Historical evidence, descriptive epidemiology, link to activity
- Attributing disease to an organism
  - Koch's Postulates, Falkow's molecular postulates, Bradford Hill criteria, parasite life cycles
- Attributing disease to a source
  - Mapping and descriptive epidemiology
  - Expert elicitation
  - Outbreak investigation, outbreak surveillance
  - Food source attribution
  - Microbial subtyping
  - Comparative Exposure Assessment
- Attributing disease to a transmission pathway
  - Ecological studies
  - Outbreak case-control, sporadic case-control, geographic case-control, cohort and case-case studies
  - Active outbreak response
  - Intervention studies (natural, deliberate, community)
  - Public Health Investigation using microbiology
  - Quantitative Microbiological Risk Assessment
- Attributing disease to other causal factors
  - Consumer questionnaires, syndromic surveillance
  - Climate, weather, seasonality, travel, water disinfection, country comparison
  - Disease burden, eradication
  - New organism, new disease, new transmission route, by-pass, false attribution

Environmental change and health

1.1	Epidemiology of heat and cold
1.2	Evaluation of climate data
1.3	Flooding and health
1.4	Modelling extremes
1.5	Evaluation of heat related mortality
1.6	Climate change risk assessment
2.1	Housing model
2.2	Heat and housing
2.3	Urban atmosphere modelling
2.4	Air pollution
2.5	Co-benefits assessment
3.1	Climate and infectious disease
3.2	Vector-borne disease
3.3	Pollen and health
3.4	Land use mapping
3.5	Green Space / Blue Space
3.6	Harmful Algal Blooms

UNIVERSITY OF EXETER

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

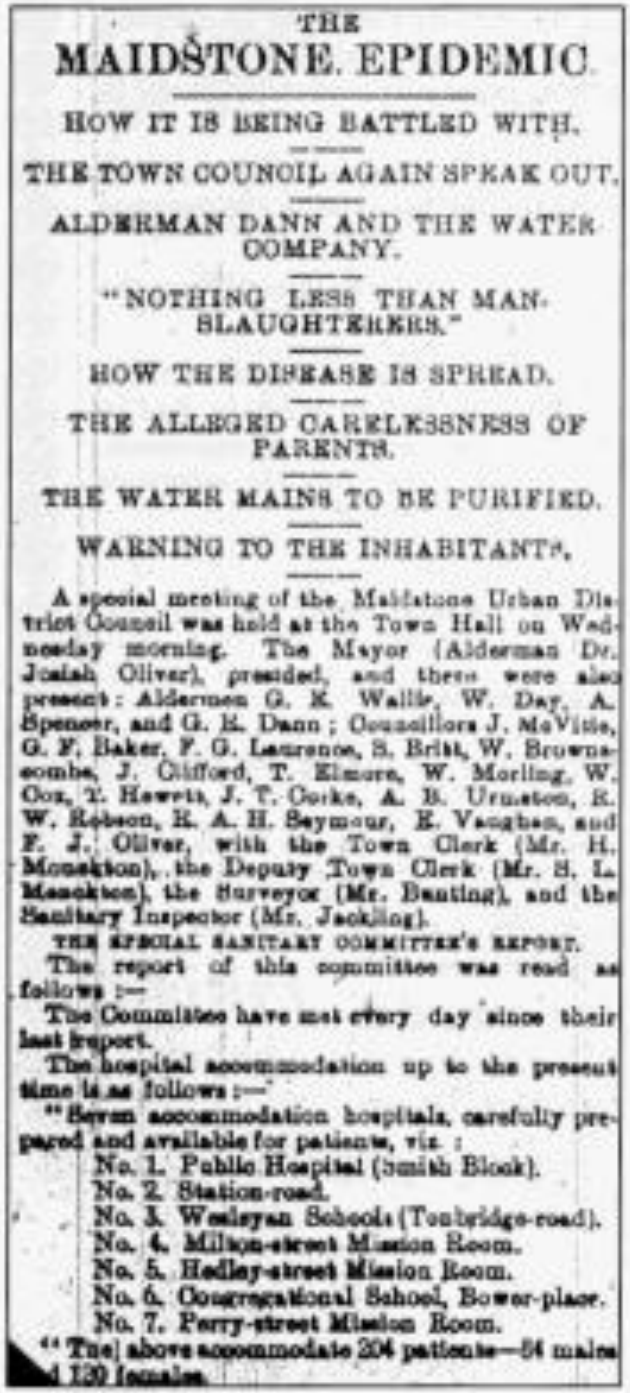
MEDMI

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Public Health England

Met Office

NHS National Institute for Health Research



THE
MAIDSTONE EPIDEMIC.

HOW IT IS BEING BATTLED WITH.

THE TOWN COUNCIL AGAIN SPEAK OUT.

ALDERMAN DANN AND THE WATER COMPANY.

"NOTHING LESS THAN MAN-SLAUGHTERERS."

HOW THE DISEASE IS SPREAD.

THE ALLEGED CARELESSNESS OF PARENTS.

THE WATER MAINS TO BE PURIFIED.

WARNING TO THE INHABITANTS.

A special meeting of the Maidstone Urban District Council was held at the Town Hall on Wednesday morning. The Mayor (Alderman Dr. Josiah Oliver), presided, and there were also present: Aldermen G. K. Wallis, W. Day, A. Spencer, and G. E. Dann; Councillors J. McVittie, G. F. Baker, F. G. Lawrence, S. Britt, W. Brownscombe, J. Clifford, T. Elmore, W. Morling, W. Cox, T. Hewett, J. T. Corke, A. B. Urmston, R. W. Robson, R. A. H. Seymour, E. Vaughan, and F. J. Oliver, with the Town Clerk (Mr. H. Monekton), the Deputy Town Clerk (Mr. S. L. Monekton), the Surveyor (Mr. Bunting), and the Sanitary Inspector (Mr. Jackling).

THE SPECIAL SANITARY COMMITTEE'S REPORT.

The report of this committee was read as follows:—

The Committee have met every day since their last report.

The hospital accommodation up to the present time is as follows:—

"Seven accommodation hospitals, carefully prepared and available for patients, viz.:

No. 1. Public Hospital (Smith Block).
No. 2. Station-road.
No. 3. Wesleyan Schools (Tonbridge-road).
No. 4. Milton-street Mission Room.
No. 5. Hedley-street Mission Room.
No. 6. Congregational School, Bower-place.
No. 7. Perry-street Mission Room.

"The] above accommodate 204 patients—84 males d 120 females.

Evidence from outbreaks

- Maidstone typhoid outbreak 1897-8 involved nearly 2000 typhoid cases, 143 of whom died.
- The cause was traced to contaminated mains water supplied from the Farleigh source by Maidstone Company.
- First recorded trial of immunisation against typhoid
- First trial of the disinfection of a mains water supply, using chloride of lime which laid the foundations for continuous water treatment.
- First use of telephones in outbreak control.
- Unprecedented press attention.
- Typhoid carrier amongst itinerant hop pickers was the suspected source.
- No water sampling had been undertaken for three months before the outbreak to save money.