

8 Epidemic Data

9 Epidemic Data II

10 Epidemic Data III



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 8
Epidemic Data
Monday 21 January 2019

Announcements

- Thanks everyone for doing the contributions survey for Assignment 1.
- Don't stress about the ratings about each other's contributions. The issue is whether some group members did not pull their weight. If somebody didn't try and others had to pick up the slack, that person should be penalized. I will not penalize somebody because they tried but felt they didn't contribute as much to the final document as they could have. Do try to even out the work across the assignments.
- Make sure everyone in your group gets a chance to be in control of the \LaTeX for one assignment.

More Announcements!

- **Assignment 2:**

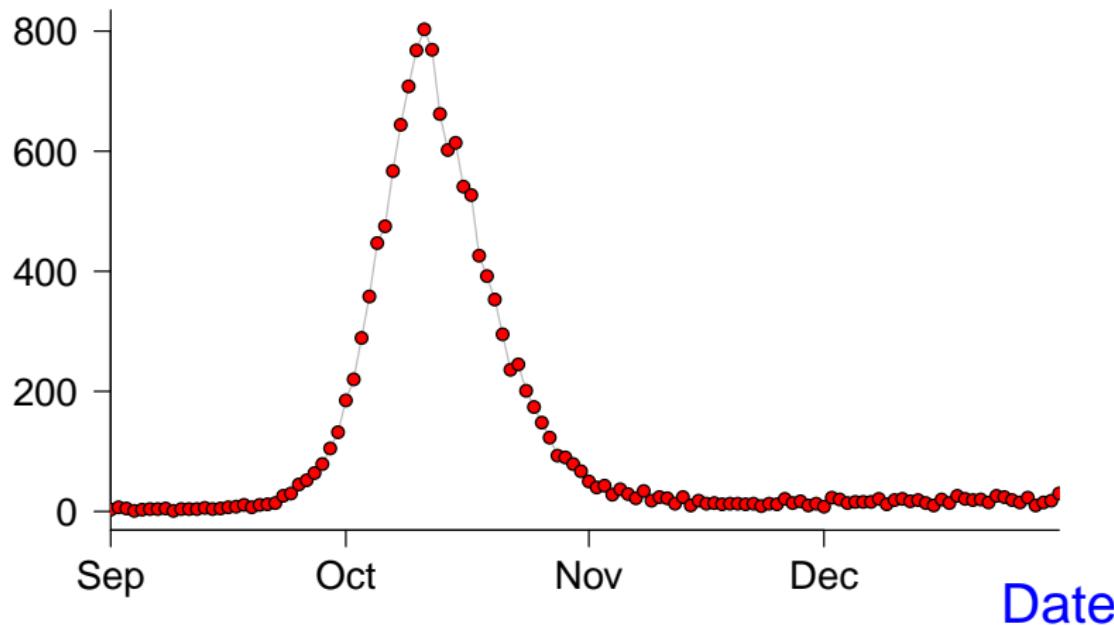
Due Monday 4 February 2019 in class (and by e-mail) at 9:30am.

- **Midterm test:**

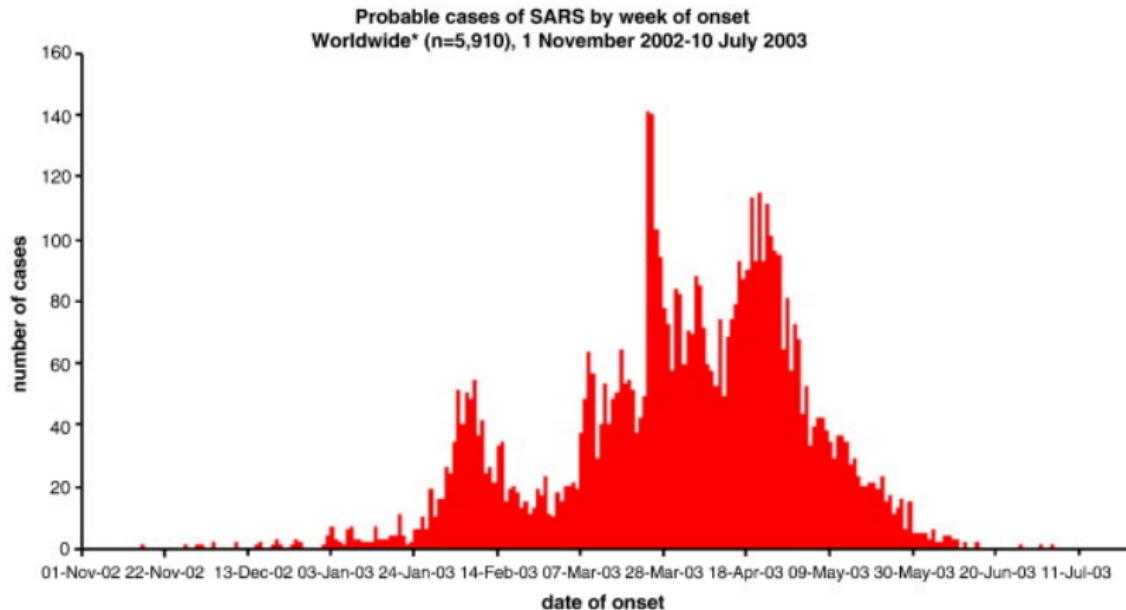
- *Date:* Monday 11 March 2019
- *Time:* 9:30am–11:20am
- *Location:* Hamilton Hall 410

P&I Mortality, Philadelphia, 1918

P&I Deaths

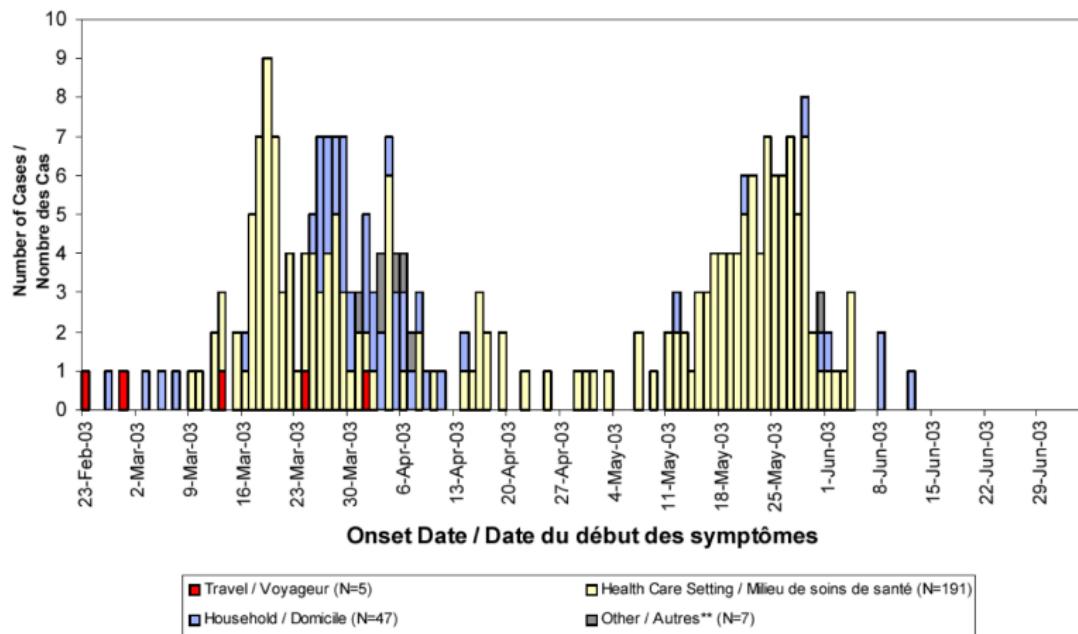


SARS in 2003 (Worldwide)



*This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

SARS in 2003 (Toronto)

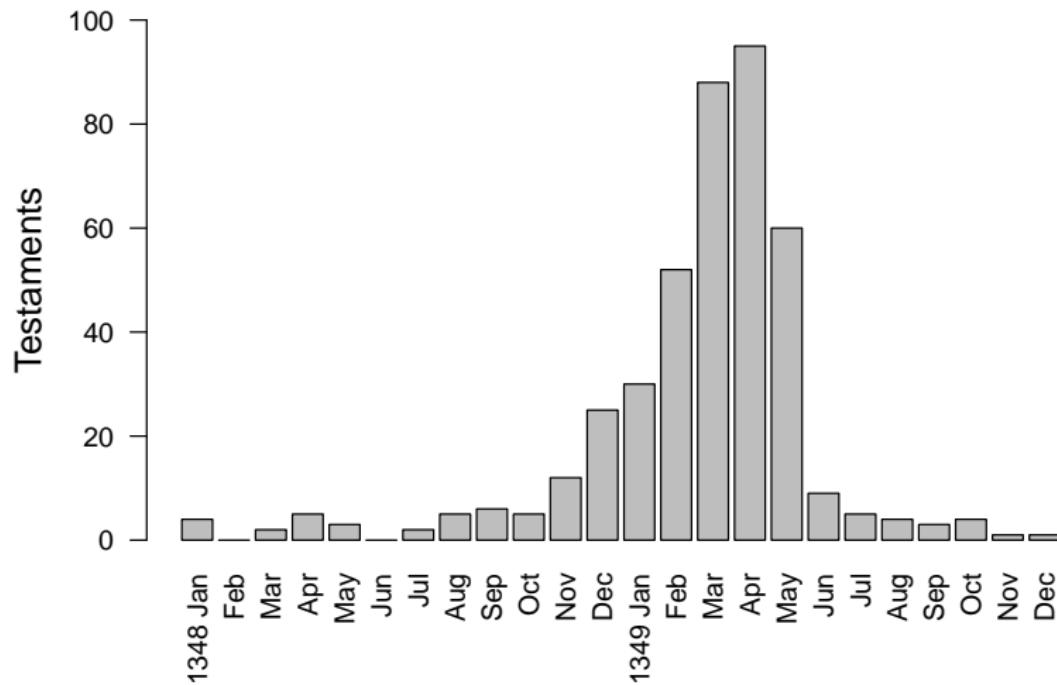


$N = 249$ (of 250 reported)

Some SARS Facts

- High case fatality
 - 1918 flu < 3%
 - SARS > 10%
- Long hospital stays
 - Mean time from admission to discharge or death:
~ 25 days in Hong Kong
- 8098 probable cases, 774 deaths
- How bad would it have been if it had not been controlled?

The Black Death in London, England, 1348–1349



London Bill of Mortality, 26 Sept to 3 Oct 1665

Mortality Bills are typically handwritten

But handwriting is usually very clear

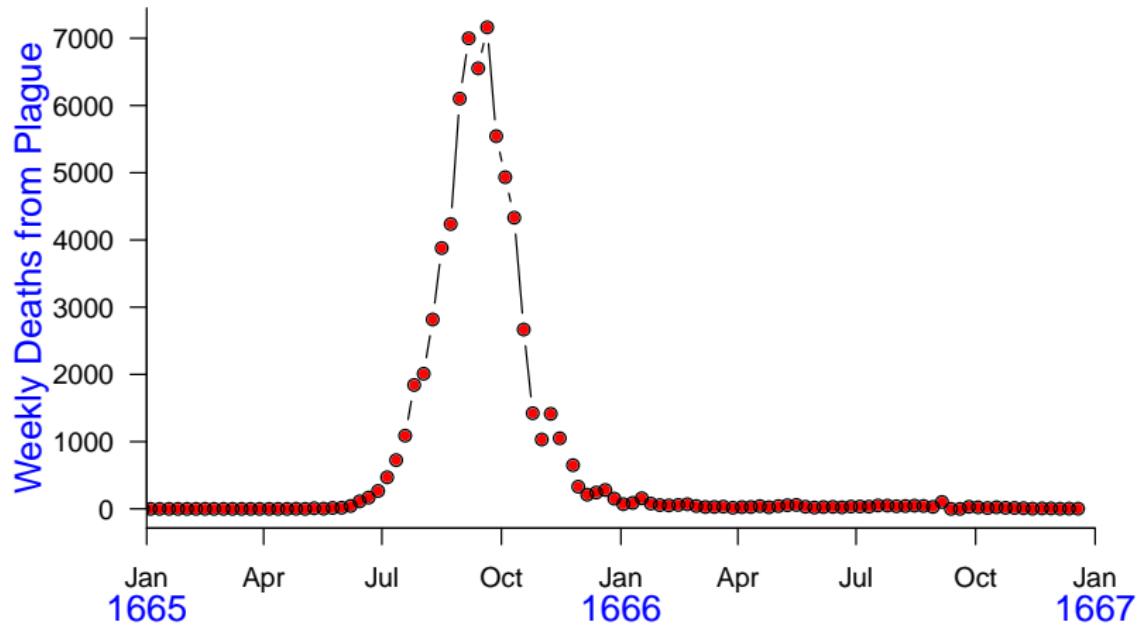
A historical ledger page from London, dated 29th [unclear]. The page is divided into columns for location, burials, and plague cases.

Location	Buried	Plag.
St Alban Woodstreet	2	1
Alhallows Bark-	2	
Alhallows Breadstreet	1	
Alhallows Great	1	

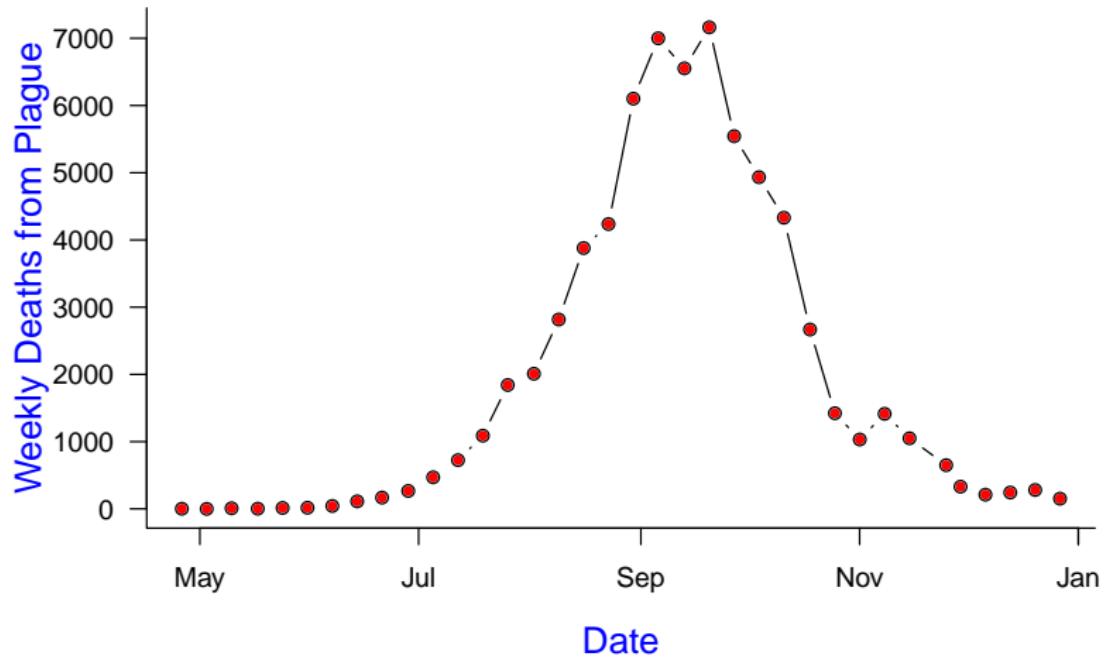
But handwriting is usually very clear

St Christopher's ———			Christened in 971 the Parishes :		
St Andrew Holborn —	66	40	S		
St Bartholomew Great	+	+	S		
St Bartholomew Less —			S		
St Bridget ——— —	24	14	S		
Bridewell Precept —	1	1	S		
Christened in the 16 Parishes :					

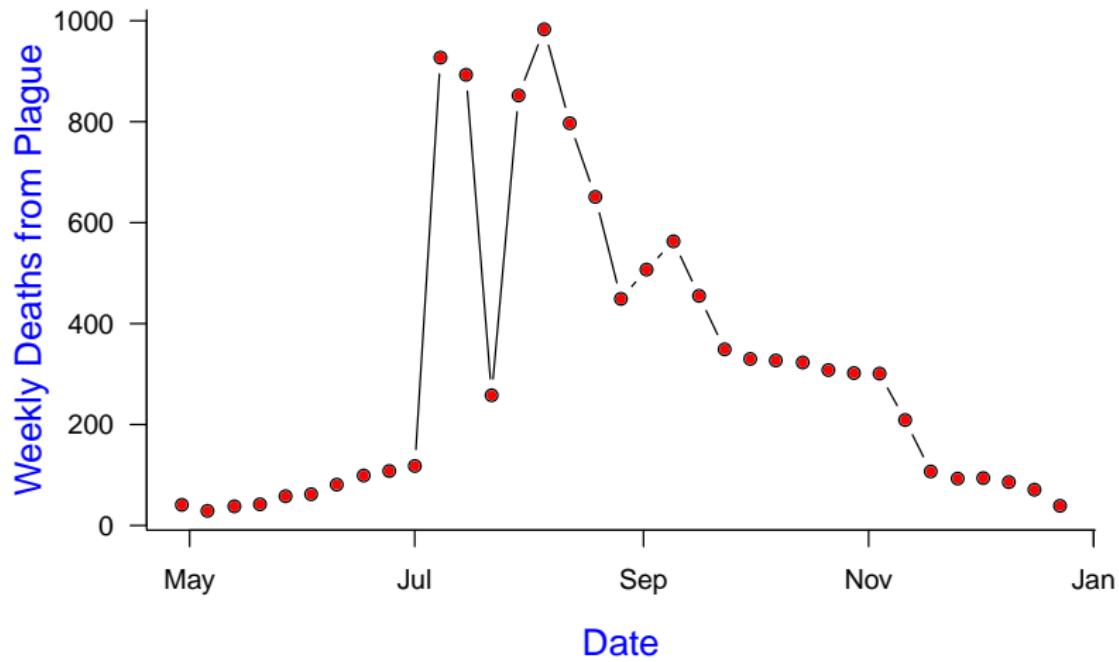
The Great Plague of London, 1665



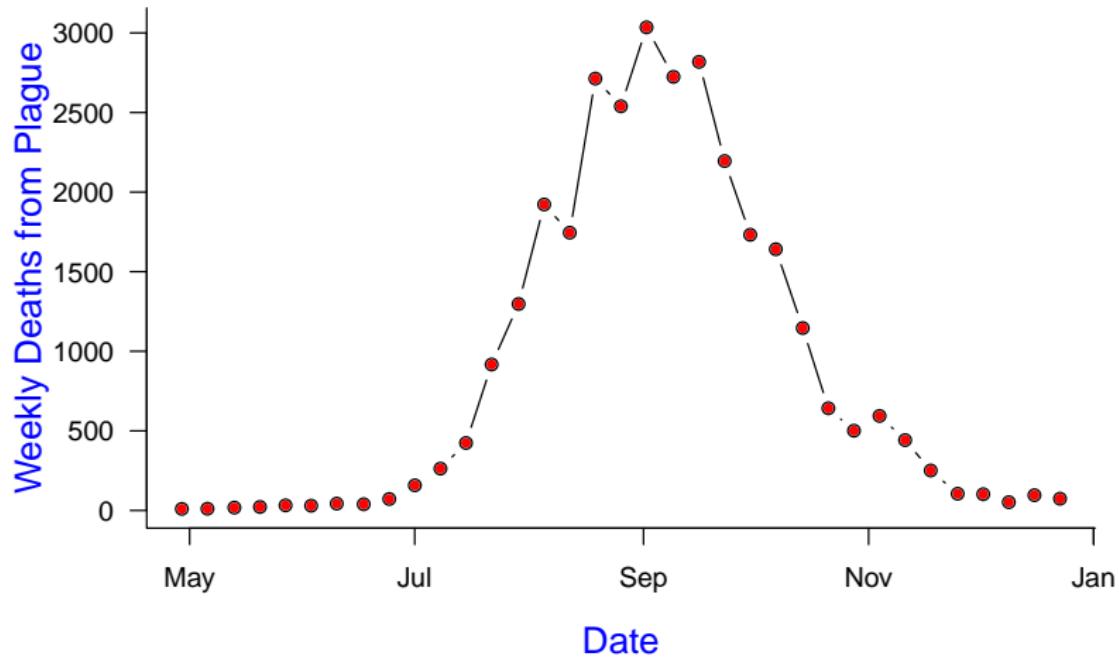
The Great Plague of London, 1665



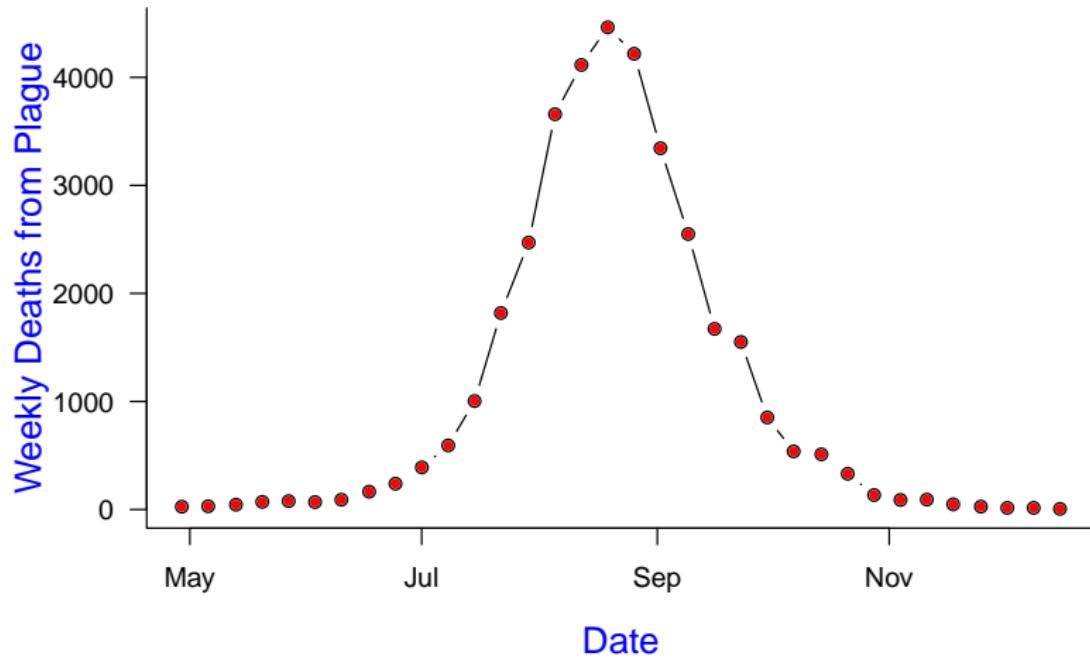
London Plague of 1593



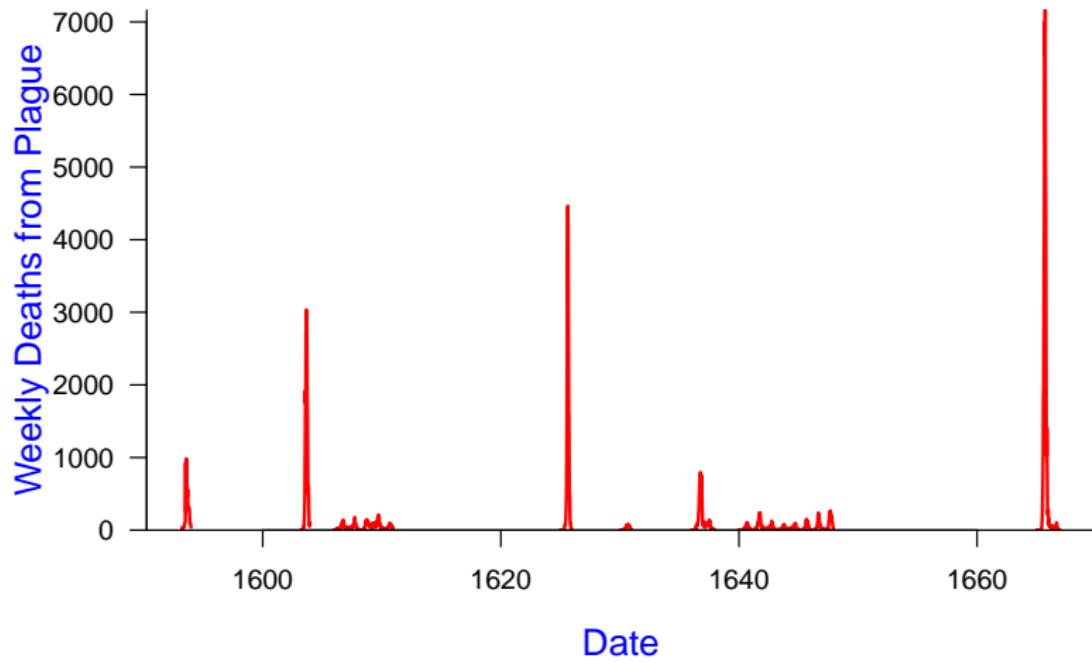
London Plague of 1603



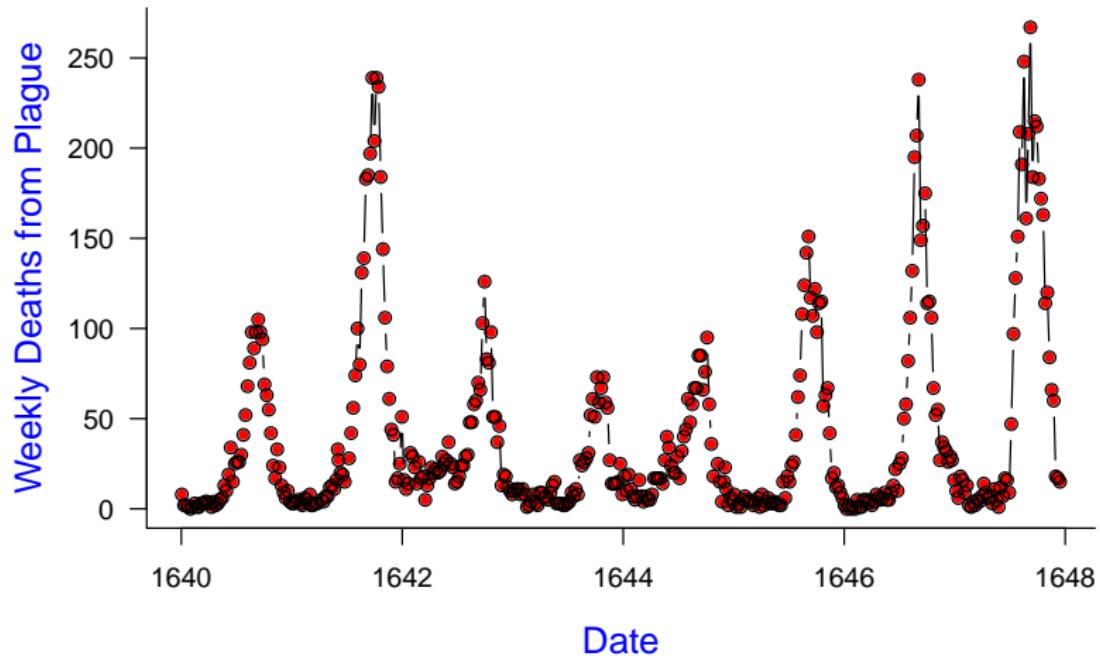
London Plague of 1625



Weekly Deaths from Plague in London, 1592–1666



Weekly Plague in London, 1640–1648



Some Plague Facts

- Plague epidemics recorded from Roman times to early 1900s.
- $\gtrsim 1/3$ Europe's population died in "Black Death" of 1348
 - ~ 300 years for the population to reach the same level.
- Recently (2011) established (at McMaster!) that the pathogen that caused The Black Death was *Yersinia pestis*

[Bos et al. 2011, *Nature* 478, 506–510]

- More recently (2014) established (again at McMaster!) that the pathogen that caused The Plague of Justinian (541–543 AD) was *Yersinia pestis*

[Wagner et al. 2014, *Lancet Infectious Diseases* 14, 319–326]

- *Y. pestis* still a concern?
Yes: Rodent reservoir, antibiotic-resistant strains, bioterrorism
- **Spatial data** for any plagues? Yes, for London in 1665...

Visualization of spatial structure of Great Plague

- GIS encoding of parish boundaries
- Overlay parish boundaries on more modern map for reference
- Colour parishes as they become infected
- Is there evidence for spatial spread or was the spatial pattern random?
- DE low-tech animation...
- CBC high-tech animation...
 - *The Nature of Things*, 21 August 2014.
[http://www.cbc.ca/natureofthings/episodes/
secrets-in-the-bones-the-hunt-for-the-black-death-killer](http://www.cbc.ca/natureofthings/episodes/secrets-in-the-bones-the-hunt-for-the-black-death-killer)



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 9
Epidemic Data II
Monday 28 Jan 2019

Announcements

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■ Midterm test:

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Please consider...

5 minute Student Respiratory Illness Survey:

<https://surveys.mcmaster.ca/limesurvey2/index.php/893454>

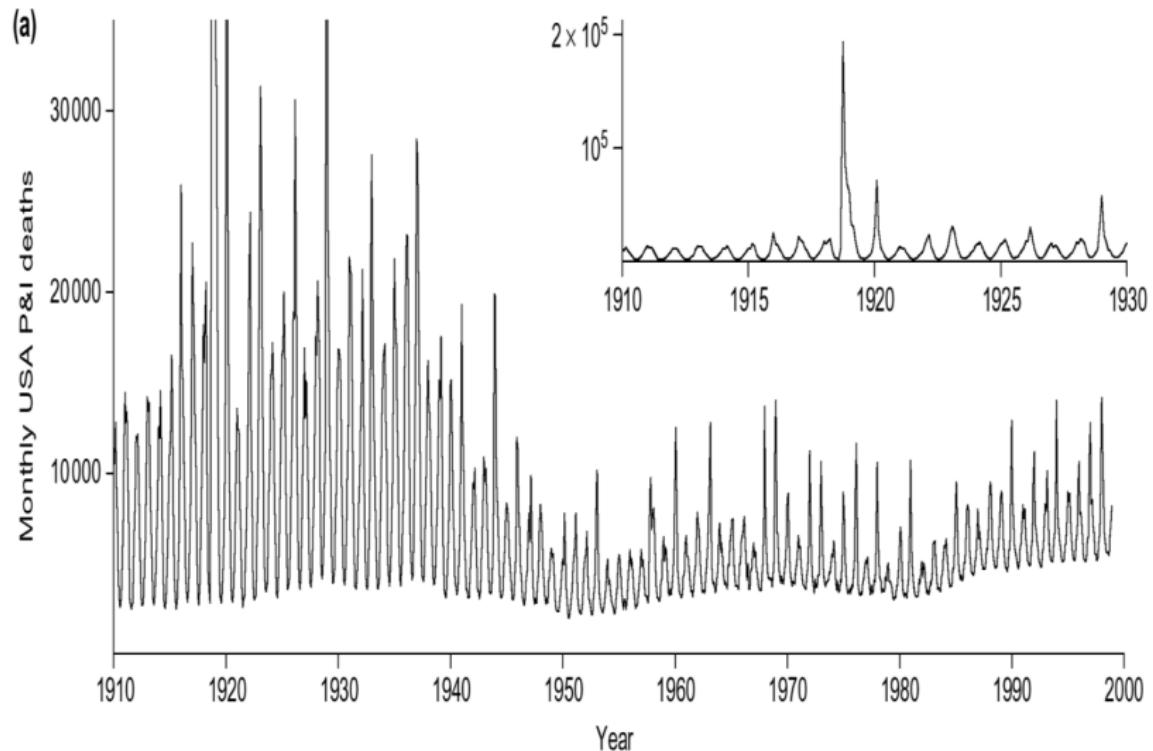
Please complete this anonymous survey to help us monitor the patterns of respiratory illness, over-the-counter drug use, and social contact within the McMaster community. There are no risks to filling out this survey, and your participation is voluntary. You do not need to answer any questions that make you uncomfortable, and all information provided will be kept strictly confidential. Thanks for participating.

–Dr. Marek Smieja (Infectious Diseases)

Visualization of entire course of the Great Plague

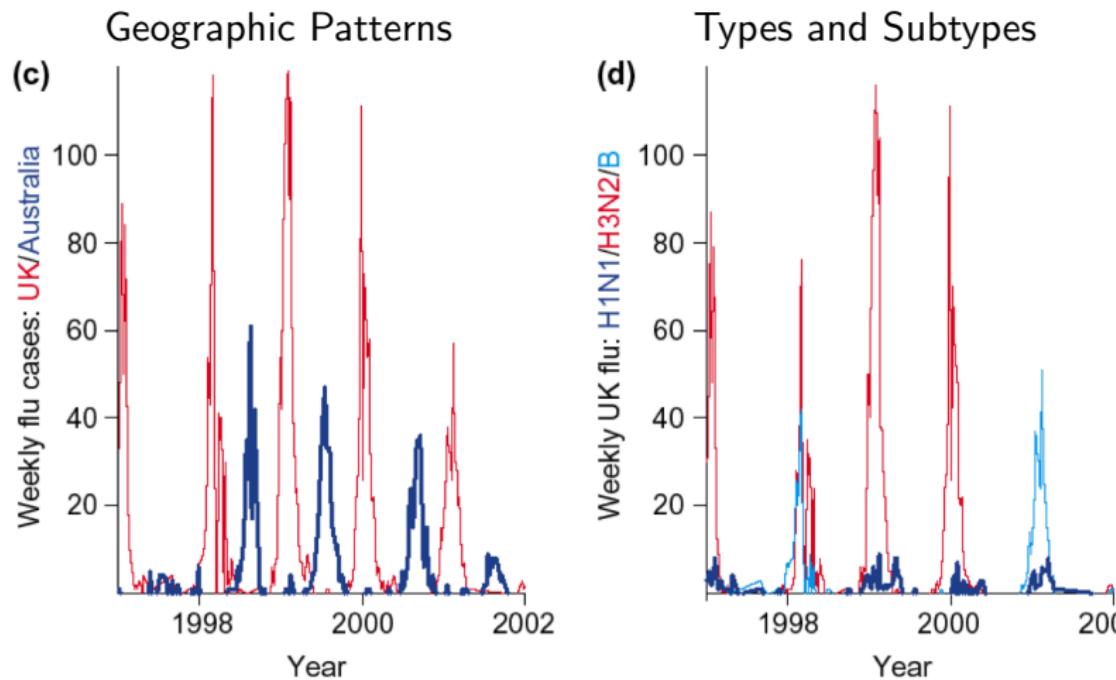
- What happened after initial spatial spread?
- Visualize full spatial epidemic structure
- Show magnitude of epidemic in each parish with cylinder.
- **Epidemic Visualization** (EpiVis) software by Junling Ma.

P&I mortality in U.S.A., 1910–1998



Earn, Dushoff & Levin 2002, *Trends in Ecology and Evolution* 17, 334–340

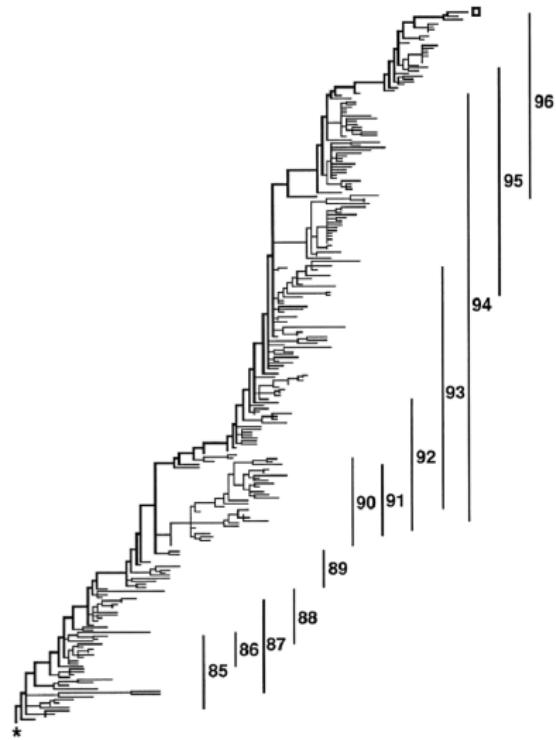
Influenza Incidence Patterns (lab confirmed)



Earn, Dushoff & Levin 2002, *Trends in Ecology and Evolution* 17, 334–340

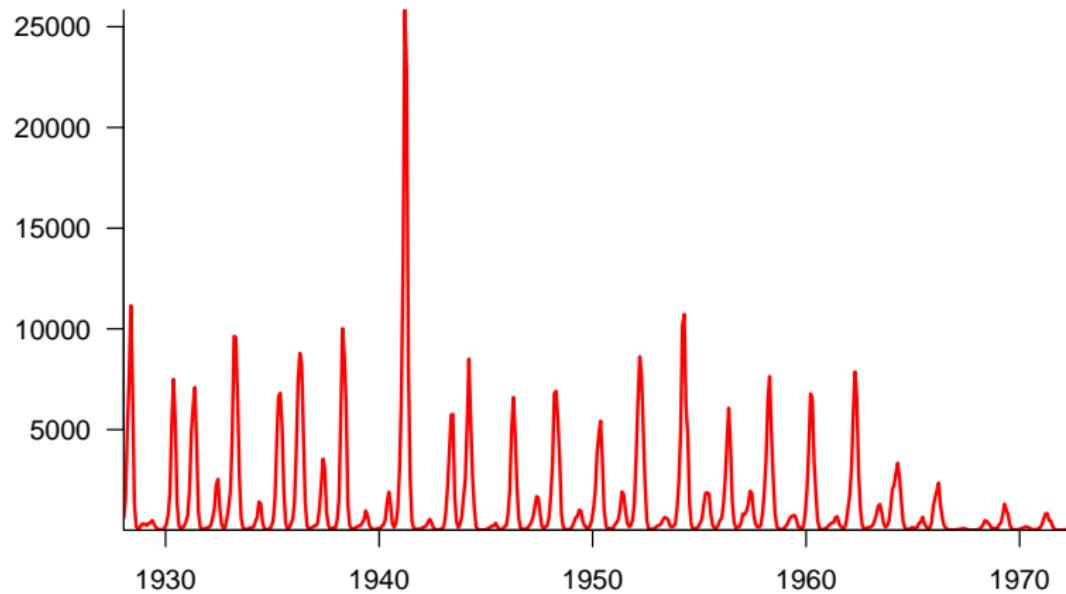
Influenza Evolution

Molecular phylogenetic reconstruction of influenza A/H3N2 evolution, 1985–1996 (Fitch *et al.* 1997)



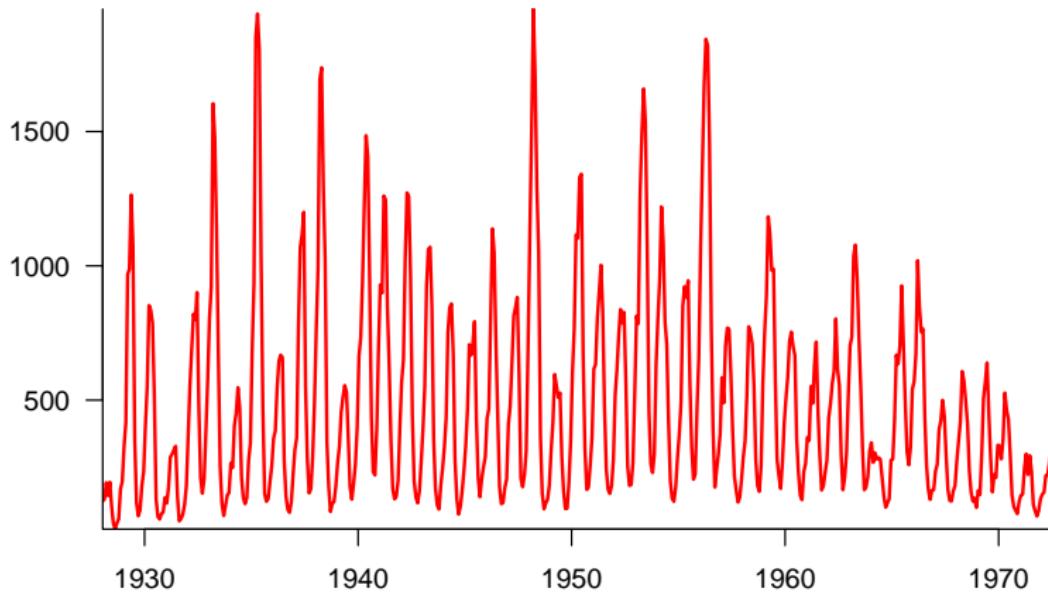
Measles in New York City, 1928–1972

Monthly Cases



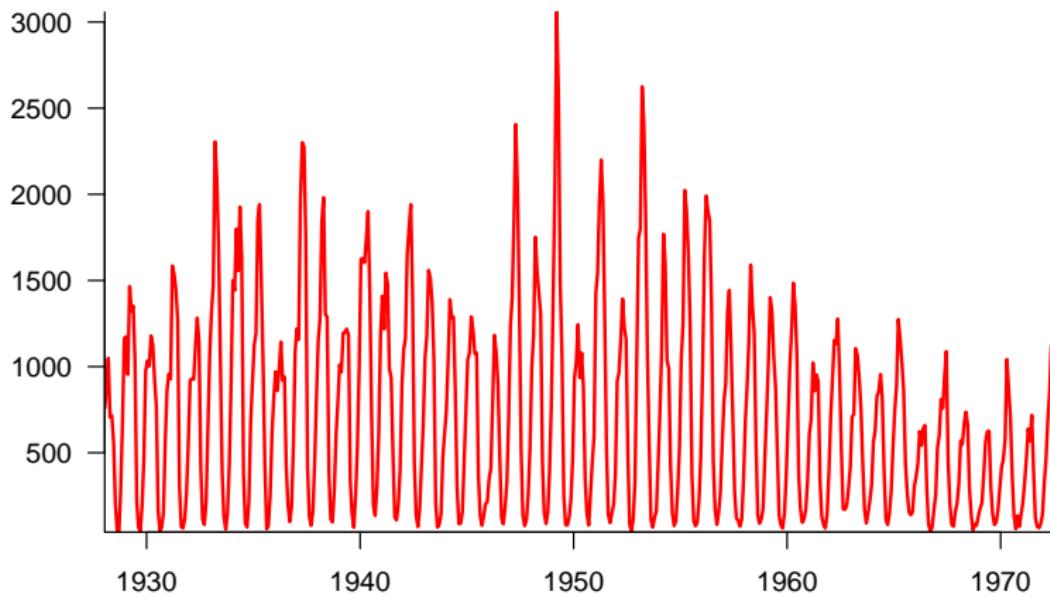
Mumps in New York City, 1928–1972

Monthly Cases

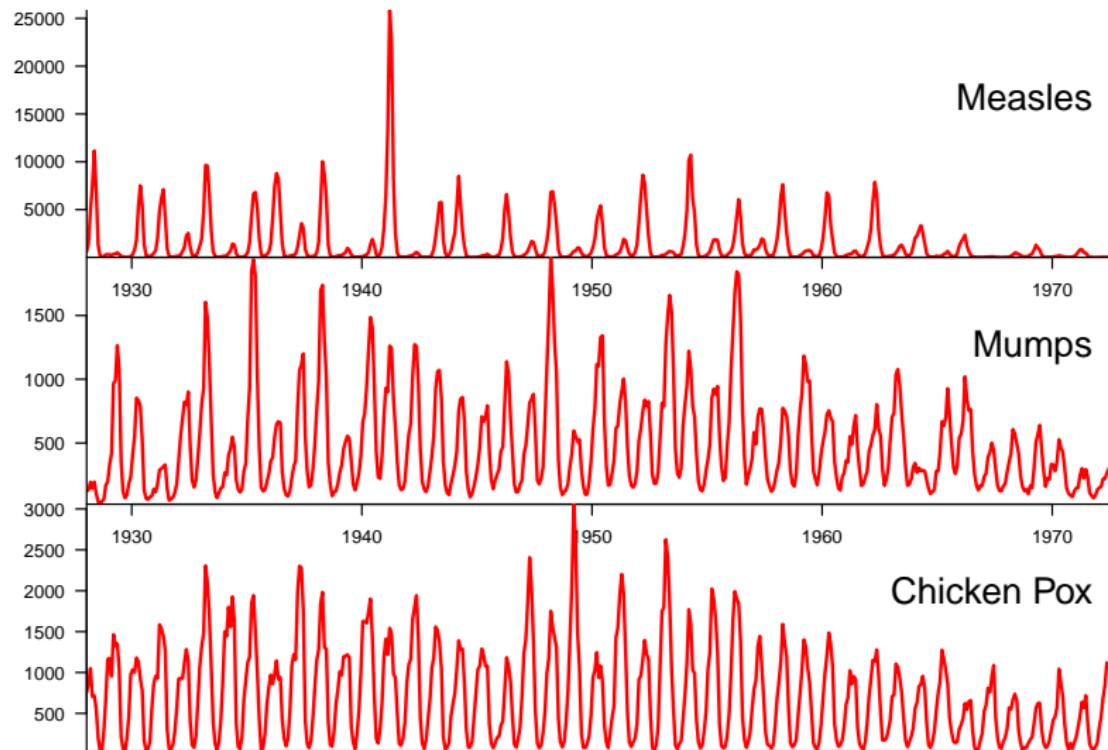


Chicken Pox in New York City, 1928–1972

Monthly Cases

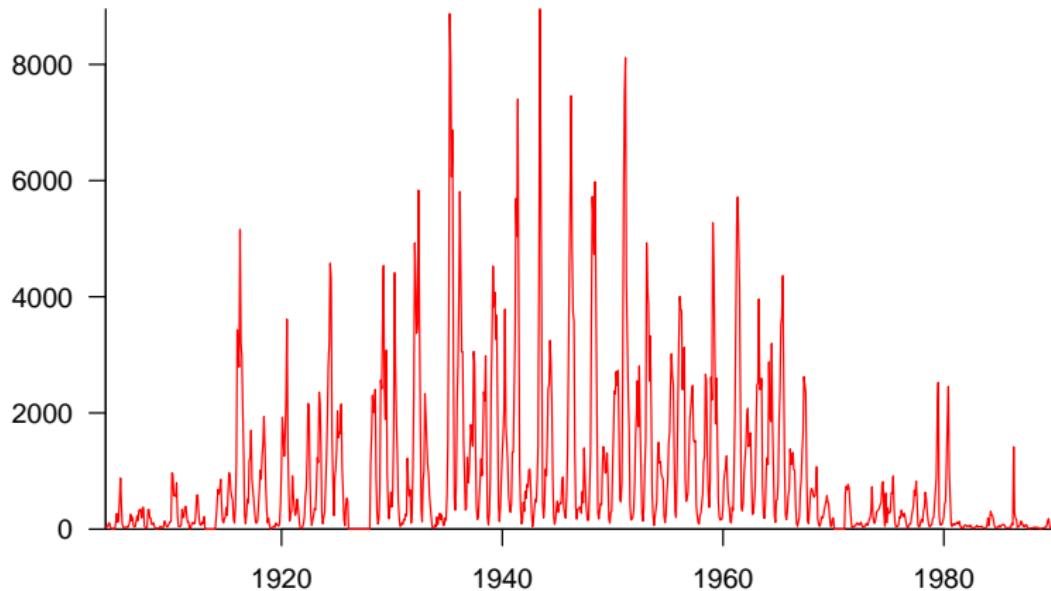


Childhood diseases in New York City, 1928–1972



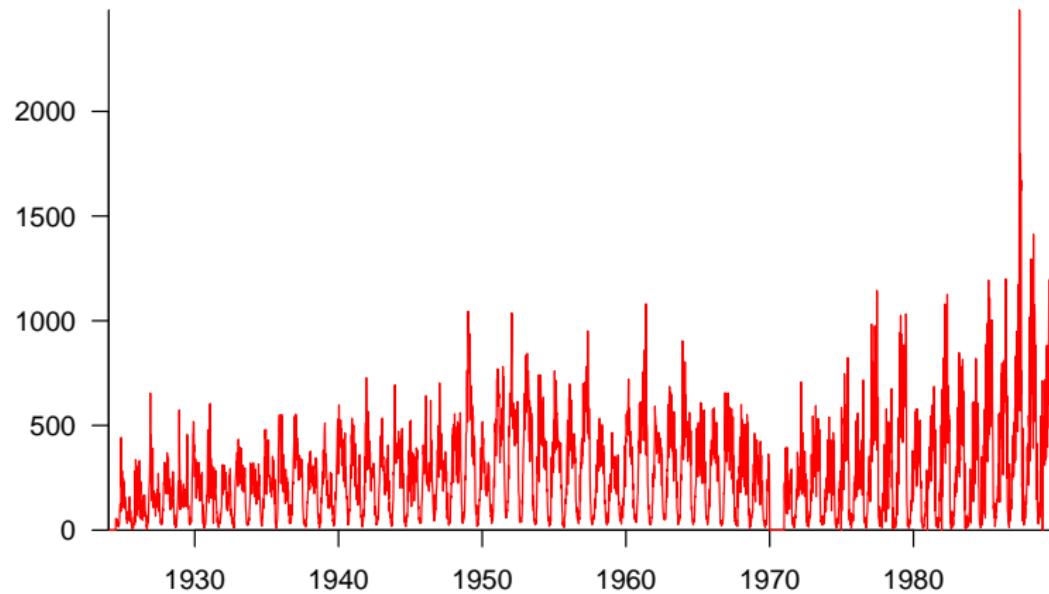
Measles in Ontario, 1904–1989

Monthly Cases



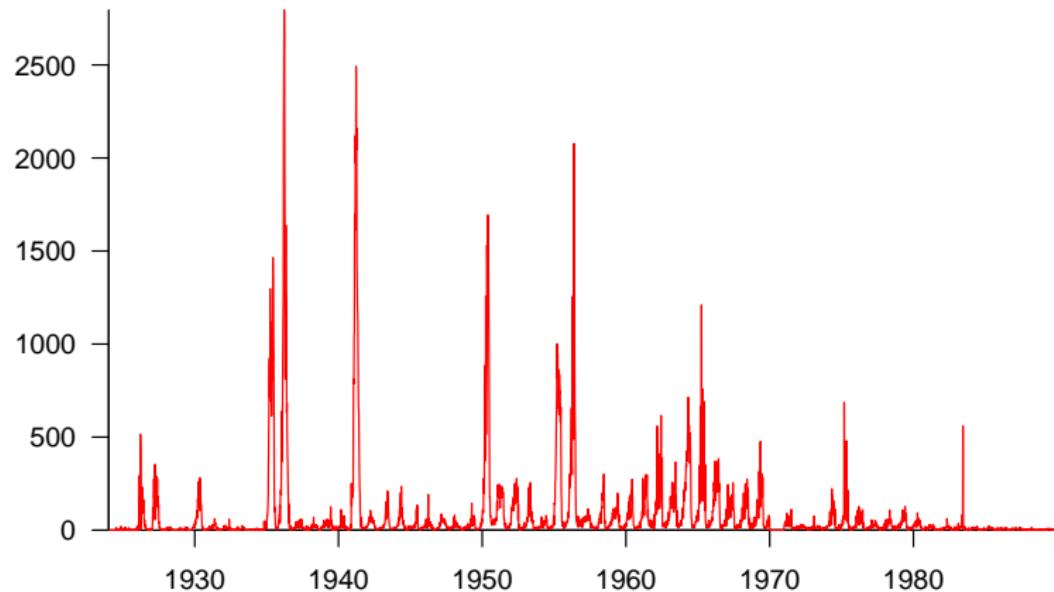
Chicken Pox in Ontario, 1924–1989

Monthly Cases



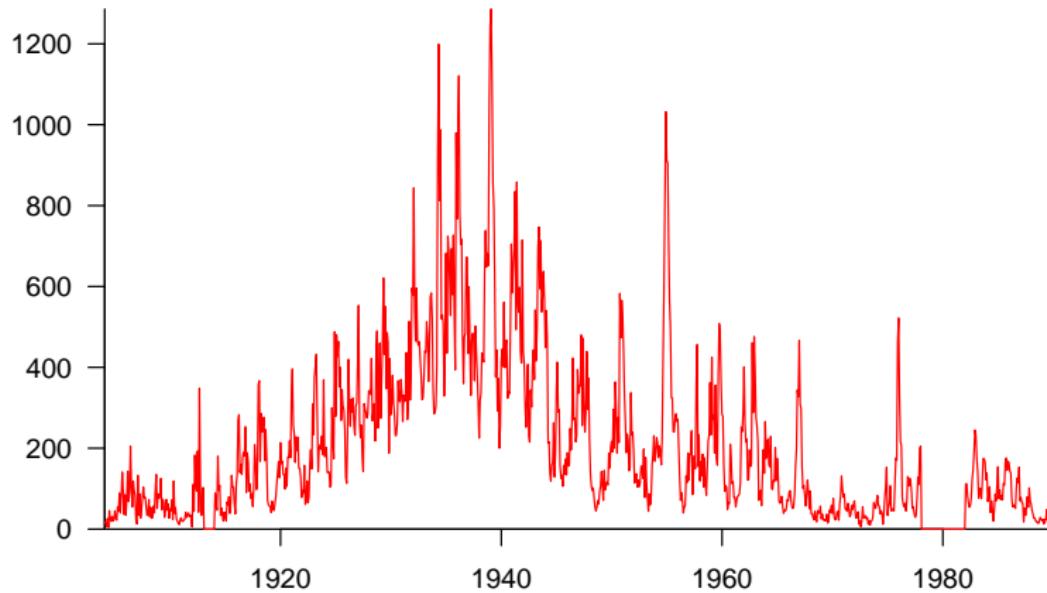
Rubella in Ontario, 1924–1989

Weekly Cases

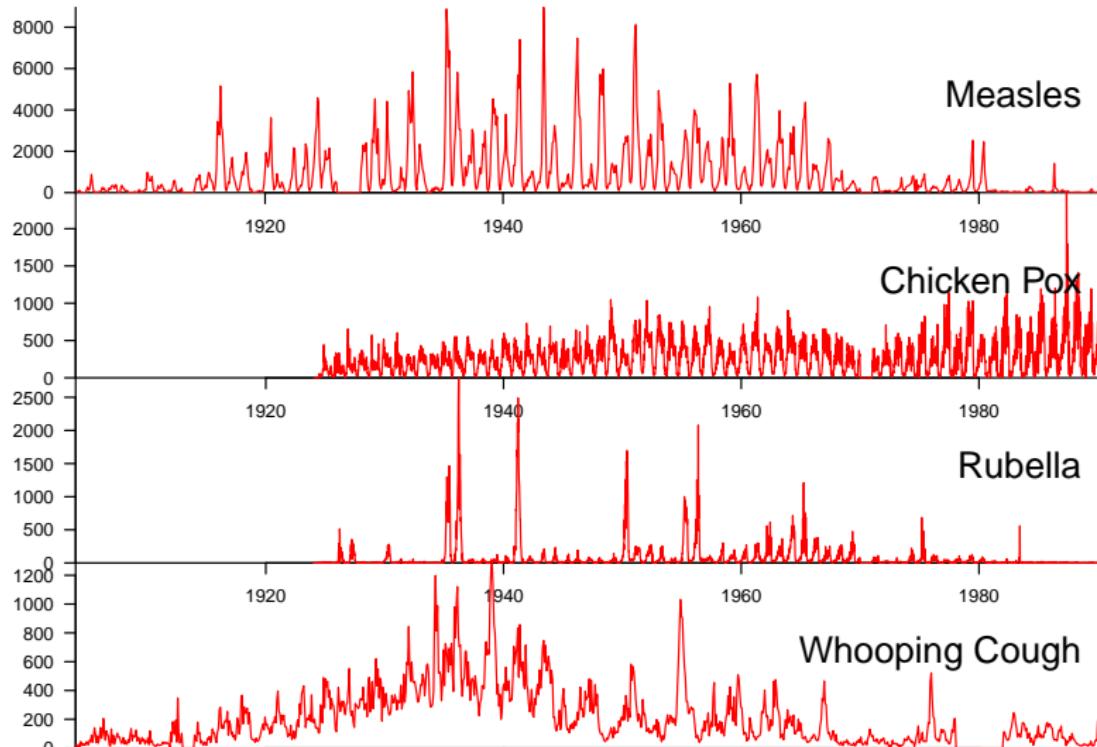


Whooping Cough in Ontario, 1904–1989

Monthly Cases



Childhood diseases in Ontario, 1904–1989



Ontario Disease Notification Data

Province of O

YEAR: 1939 COUNTY..... MUNICIPALITY.....

Month	Week End.	COUNTY.....												MUNICIPALITY.....													
		CSM		C.P.		DIP.		DYS. A/B		EN. LETH.		ERYS.		G.C.		FLU.		INF. JAUN.		G.M.		MEAS.		MUMPS		PARA. TYPH.	
		C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D
Jan.	7 1			452	1	3	0	1	0			5	1	101	0	8	1	17	0	17	0	670	1	56	0	2	0
	14 2	2	1	490	0	8	0					5	0	82	0	21	1	18	0	18	0	850	0	92	0	1	0
	21 3	2	1	511	0	9	3			0	1	5	0	89	0	16	2	26	0	22	0	932	0	98	0		
	28 4	1	0	384	0	2	0					2	0	73	0	164	0	10	0	28	0	933	1	24	0		
	Total	5	2	193	1	21	3	1	0	0	1	7	0	218	4	71	0	65	2	338	5	240	0	3	0		
Feb.	4 5			355	0	7	1	1	0			3	0	83	0	57	1	24	0	25	0	1335	1	110	0	2	0
	11 6	2	1	363	0	1	0	1	0			7	0	82	0	27	1	41	1	29	0	1033	0	91	0	1	0
	18 7	2	1	354	1	2	0					4	1	68	0	103	1	35	0	44	0	1161	0	59	0		
	25 8	1	1	308	0	2	0					9	0	560	177	0	19	0	28	0	999	0	73	0			
	Total	5	3	1980	1	19	2	0				34	3	19	1	126	0	158	1	338	0	240	0	3	0		
Mar.	4 9	1	1	271	0	7	1	3	1			7	0	93	0	114	19	21	0	40	0	131	2	109	0	1	0
	11 10			239	0	7	0	2	0			8	1	61	0	137	18	31	0	32	0	845	0	91	0	2	0
	18 11			166	0							6	0	66	0	1322	6	5	0	59	0	969	2	69	0	1	0
	25 12	1	2	236	0	1	0	1	0			7	0	63	0	806	16	9	0	20	0	879	0	120	0	case	PAH
	Total	8	3	118	0	15	1	6	1			28	1	283	0	613	4	66	0	151	0	353	1	389	0	34	0
Apr.	1 13	2	0	139	0	3	0	1	0			8	0	95	0	667	6	1	0	24	0	950	0	89	0	3	0
	8 14	2	0	162	0	1	0	1	0			5	0	67	0	731	22			14	0	790	0	65	0	1	0
	15 15	2	0	108	0	1	0			0	1	11	0	41	0	529	16	2	0	16	0	745	0	56	0		
	22 16	1	1	134	0	2	0	1	0	1	1	6	0	64	0	245	8	2	0	26	0	845	0	54	0		
	29 17	5	1	167	0	4	0	2	0	2	1	3	0	55	0	124	9	2	1	13	0	746	1	120	0		
	Total	12	2	110	0	10	0	3	0			33	0	312	0	616	1	1	0	24	0	450	0	384	0	47	0
	6 18	2	0	104	0	1	0	2	0			4	0	71	0	76	3	1	0	14	0	877	0	63	0	3	0

Dominion Bureau of Statistics Disease Notification Data

VITAL STATISTICS BRANCH - COMMUNICABLE DISEASE SECTION

Cases of ~~Influenza~~ Reported by Provincial Health Departments, Year 1924

WEEK ENDING	P.E.I.	N.S.	N.B.	QUE.	ONT.	MAN.	SASK.	ALTA.	B.C.	CANADA
	W15-22	W15-22								
1 Jan 5		11						1		12
2	12	29						18		47
3	19	37						32		69
4	26	75 152		68	181	36	13 64	97	4 88 602	
5 FEB 2	12	1					53			66
6	9	5					40			45
7	16	31					14			45
8	23	- 2 50	1 2	267	202	48	4 111	116	1 7 797	
9 MAR 1		2					21			23
10	1						9			9
11	15	3					11			14
12	22	60					34			94
13	29	2 61		144	140	52	15 90	15	7 17 515	
14 APR 5		9					11			20
15	12	1					12			13
16	19	26	1				8			35
17	26	14 50	3 4	42	140	39	16 47	67	5 33 394	
18 MAY 3		26					2			28



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 10
Epidemic Data III
Monday 28 Jan 2019

Announcements

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■ Midterm test:

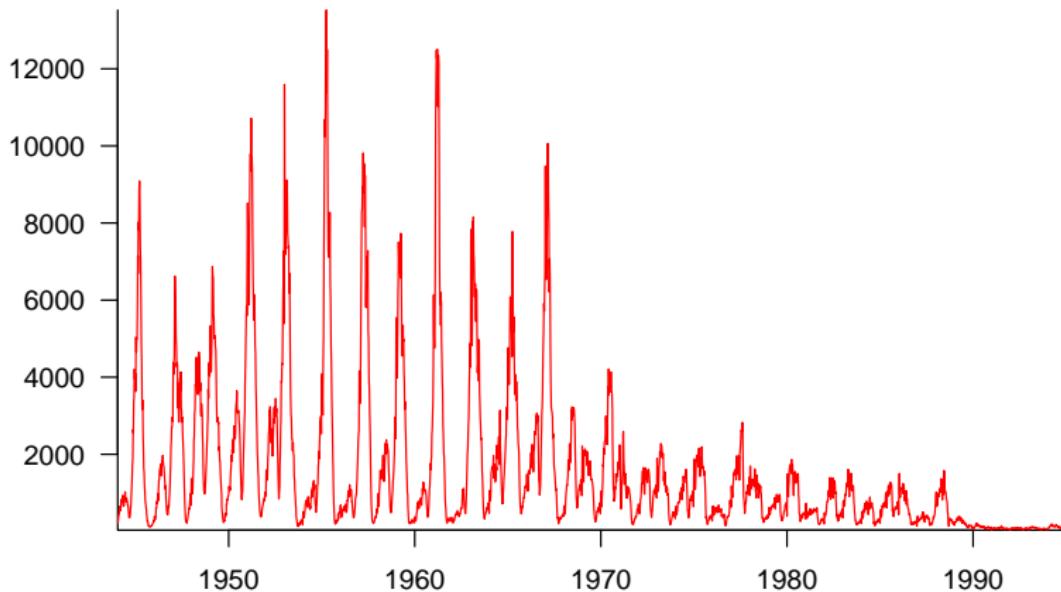
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Recurrent epidemics of childhood infections

- Childhood diseases in New York City, 1928–1972
- Childhood diseases in Ontario, 1904–1989

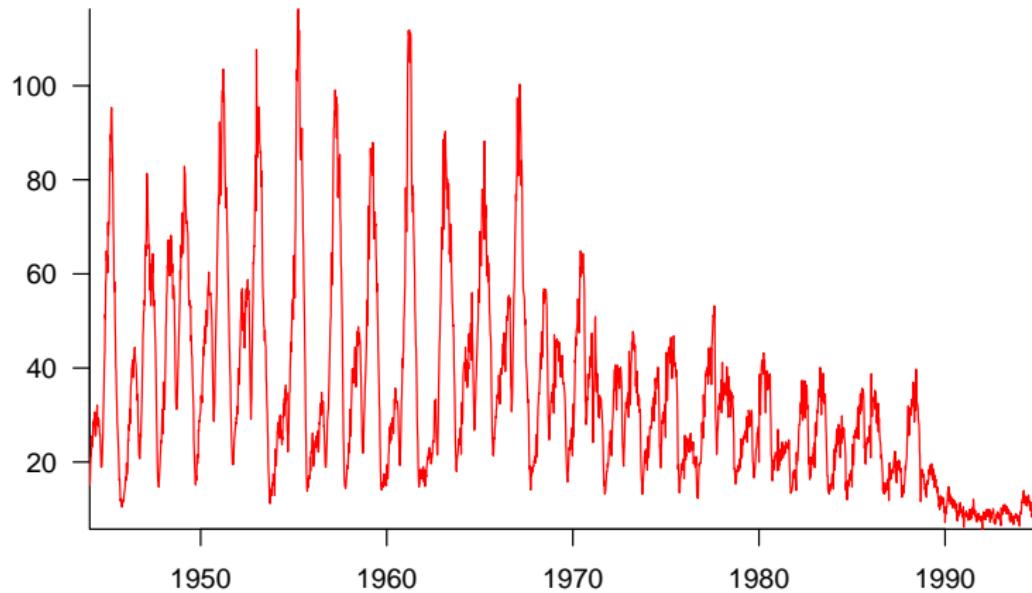
Measles incidence in England and Wales, 1944–1995

Weekly Cases



Measles incidence in England and Wales, 1944–1995

Sqrt(Weekly Cases)



Why study measles epidemics?

- In 2017, $\sim 110,000$ deaths from measles
- A major cause of *vaccine-preventable* deaths.
- Potential impact in developed countries during vaccine scares (e.g., MMR scare in UK in 1990s).

- Understand past patterns
- Predict future patterns
- Manipulate future patterns
- Develop vaccination strategy that can...



Other reasons to model infectious disease epidemics

- Mathematical models make hypotheses and inferences precise
 - Give better advice to policymakers
 - Make better predictions
- Host-pathogen dynamics are important aspects of ecosystem dynamics
 - Infectious disease models more likely to be successful than predator-prey models
- Excellent data for human infectious diseases
 - Models can be tested!

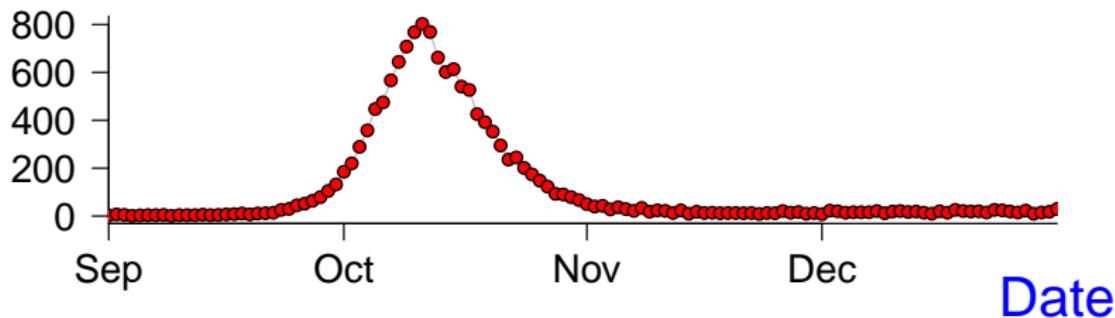
Modelling population dynamics of childhood infections

- The basic SIR model cannot explain recurrent epidemics.
- What should we do?... The usual options:
 - 1 Get depressed, drop the course.
 - 2 Keep developing models until we can explain recurrent epidemics.
- First, let's talk about tools that allow us to make our questions about time series data more precise.

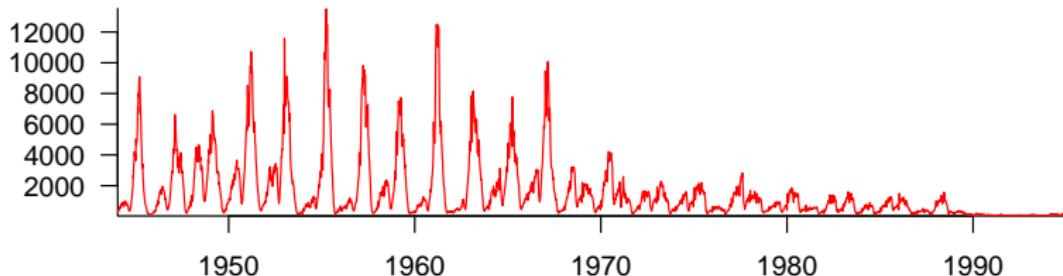
Epidemic Data Analysis

Time Plots of Temporal Epidemic Patterns

1918 P&I

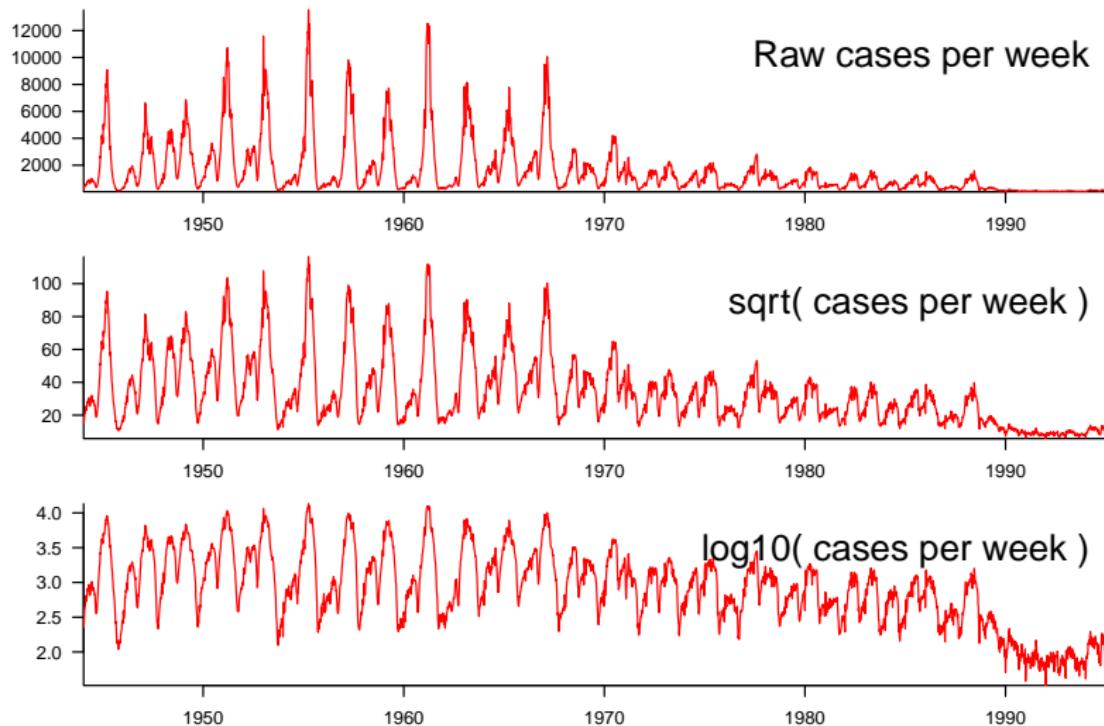


Weekly Measles in England and Wales



Time Plots of Transformed Data

- Reveal unobvious aspects of time series



Times Plots of Smoothed Data

- Reveal trends clouded by noise or seasonality
- *Moving Average:*

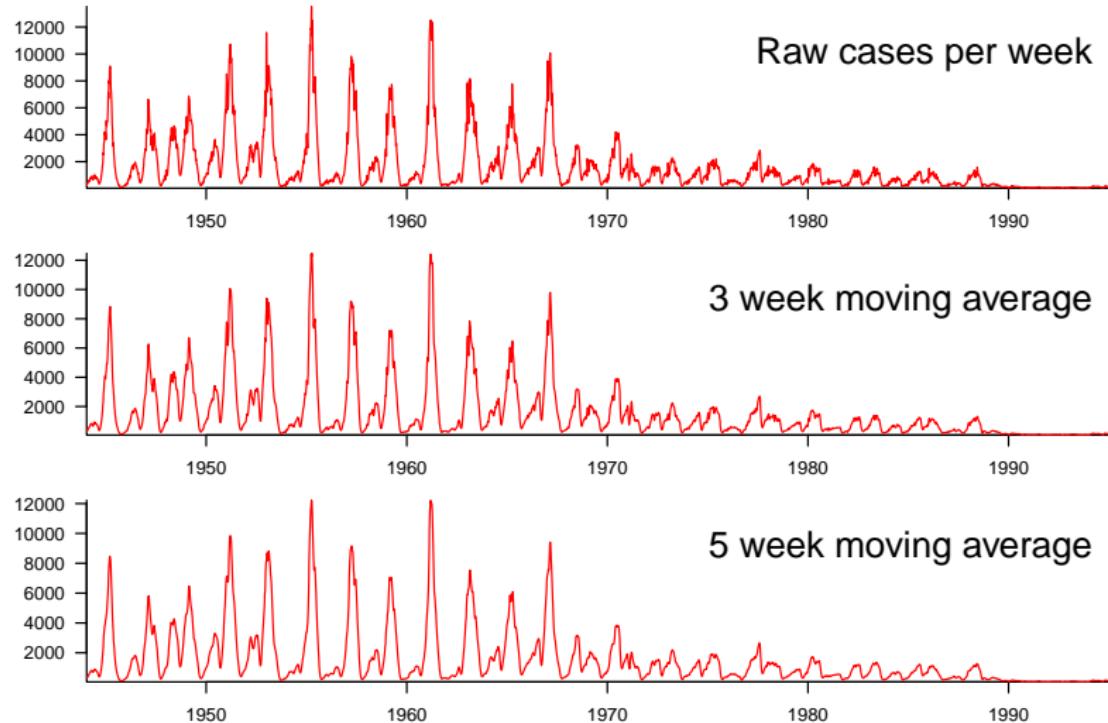
$$x_t \rightarrow \frac{1}{2a+1} \sum_{i=-a}^a x_{t+i}$$

- Replace original data points x_t with averages of nearby points.
- *Linear filter:*

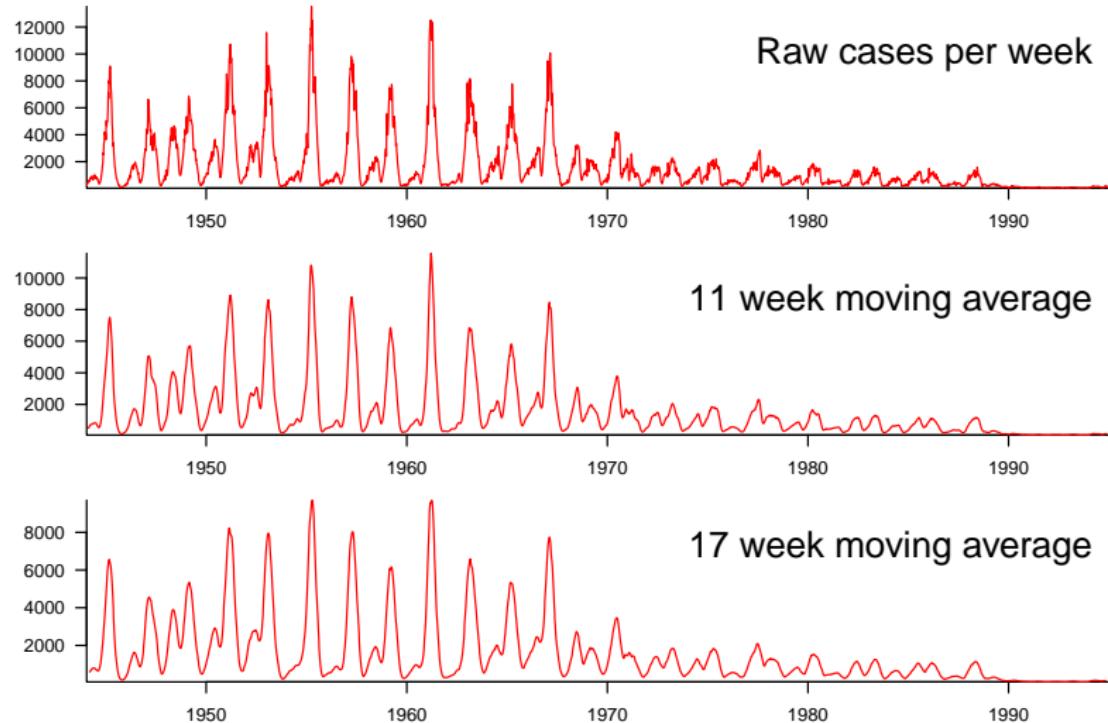
$$x_t \rightarrow \sum_{i=-\infty}^{\infty} \lambda_i x_{t+i}$$

- Generalization of moving average.
- Weights λ_i can be nonlinear functions of i .

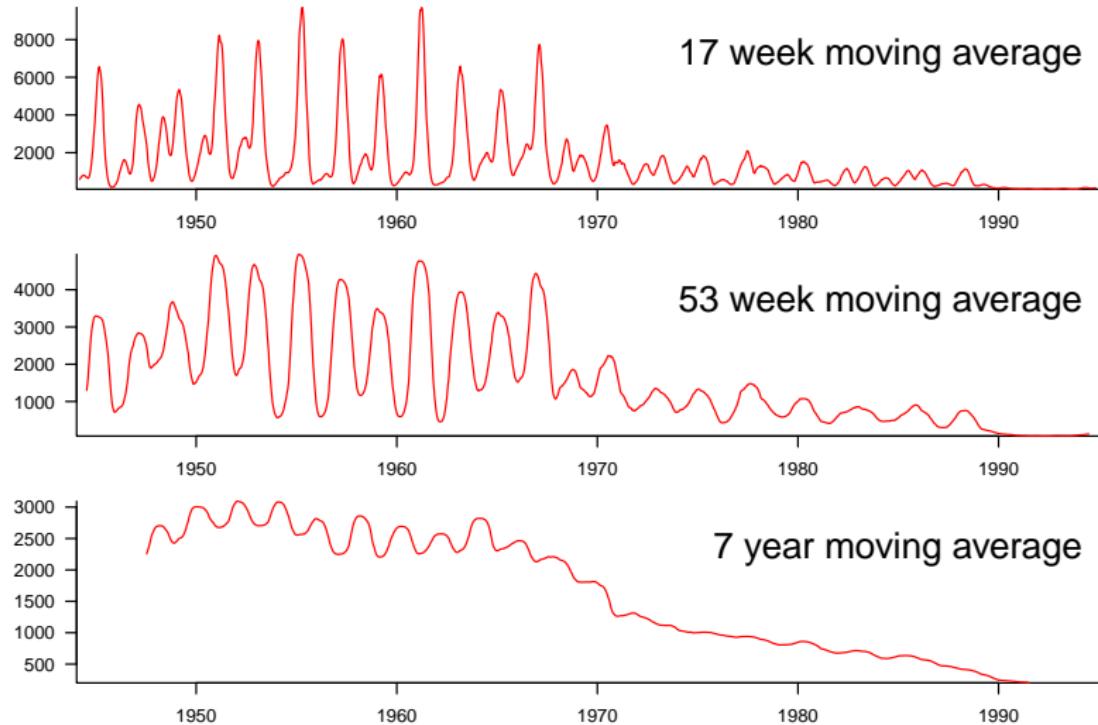
Times Plots of Smoothed Data



Times Plots of Smoothed Data



Times Plots of Smoothed Data



Correlation

- Recurrent epidemics \implies number of cases now is correlated with number of cases in the past and the future.
- Given N pairs of observations of different quantities, $\{(x_i, y_i) : i = 1, \dots, N\}$, the *correlation coefficient* is defined to be

$$r = \frac{\sum_{i=1}^N (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^N (x_i - \bar{x})^2 \sum_{i=1}^N (y_i - \bar{y})^2}}$$

where \bar{x} and \bar{y} are the means of $\{x_i\}$ and $\{y_i\}$, respectively.

Correlation

Properties of the correlation coefficient:

- $-1 \leq r \leq 1$ (Proof? Cauchy-Schwarz inequality)
- $r = 1 \iff$ all points lie on a line with positive slope ("complete positive correlation")
- $r = -1 \iff$ all points lie on a line with negative slope ("complete negative correlation")
- $r \simeq 0 \implies$ "uncorrelated"
- *Interpretation:* r^2 is the proportion of the variance in y explained by a linear function of x .

Derivations and discussions:

- [MathWorld on \$r^2\$](#) , [Wikipedia on \$r^2\$](#)
- [Wikipedia on general coefficient of determination](#)

Autocorrelation

- Given a single sequence of observations $\{x_t : t = 1, \dots, N\}$, we can compute the correlation of each observation with the observation k time steps in the future.
- Thus, we consider the pairs of observations $\{(x_t, x_{k+t}) : t = 1, \dots, N - k\}$ and define the *autocorrelation coefficient at lag k* to be

$$r_k = \frac{\sum_{t=1}^{N-k} (x_t - \bar{x}_{1,N-k})(x_{k+t} - \bar{x}_{k+1,N})}{\sqrt{\sum_{t=1}^{N-k} (x_t - \bar{x}_{1,N-k})^2 \sum_{t=1}^{N-k} (x_{k+t} - \bar{x}_{k+1,N})^2}}$$

where $\bar{x}_{1,N-k}$ and $\bar{x}_{k+1,N}$ are the means of first and last $N - k$ observations, respectively.

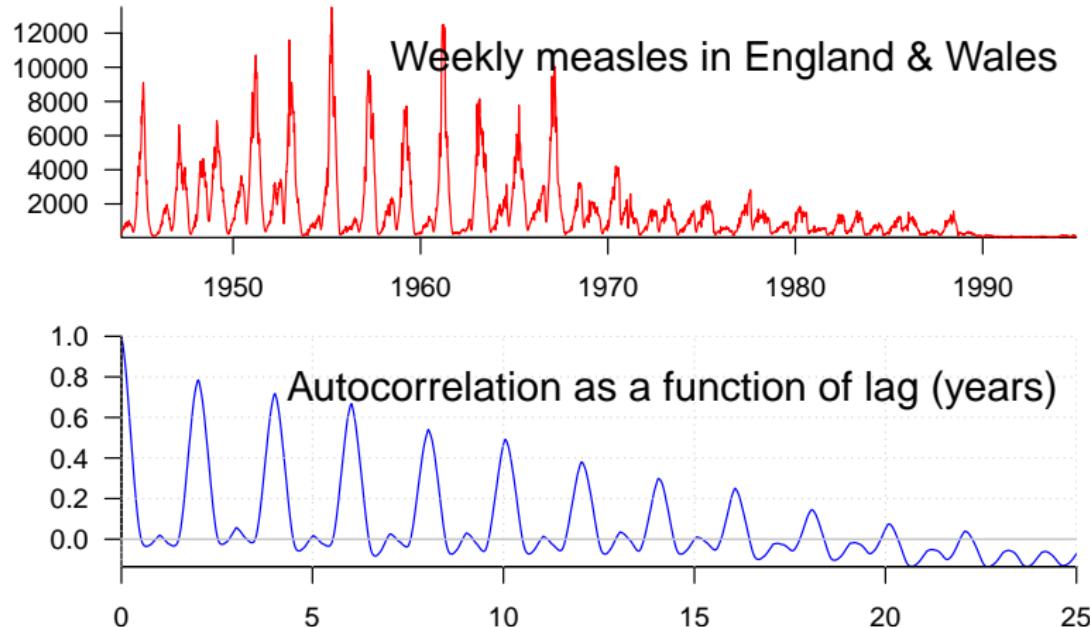
Autocorrelation

- If number of observations N is large and lag $k \ll N$ then

$$r_k \simeq \frac{\sum_{t=1}^{N-k} (x_t - \bar{x})(x_{k+t} - \bar{x})}{\sum_{t=1}^N (x_t - \bar{x})^2}$$

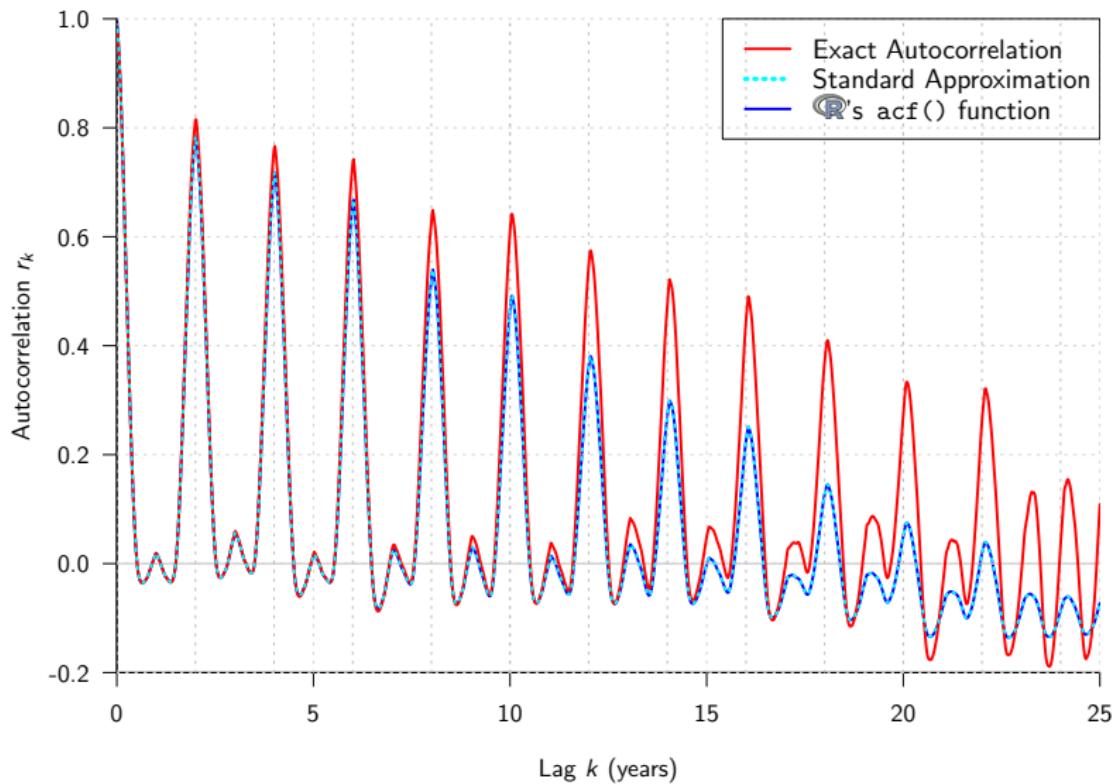
- Approximation of r_k is worse for larger lags k
- Plot of autocorrelation r_k as a function of lag k is called the *correlogram*.

Correlogram



- Peaks in correlogram \implies periodicities in original time series.
- Correlograms of temporal segments are often informative.

Correlogram: exact vs. approximate r_k



Spectral Density

- Can we compute the dominant periods in the time series?
(Rather than estimating them by eye from the [correlogram](#).)
- Express the time series as a [Fourier series](#):

$$x_t = a_0 + \left(\sum_{p=1}^{(N/2)-1} (a_p \cos \omega_p t + b_p \sin \omega_p t) \right) + a_{N/2} \cos \pi t,$$

where $\omega_p = 2\pi p/N$.

- Compute the [Fourier coefficients](#) $\{a_p\}$, $\{b_p\}$ by taking inner products with $\cos \omega_p t$ and $\sin \omega_p t$.

Spectral Density

- Fourier coefficients of x_t are:

$$a_0 = \bar{x} = \frac{1}{N} \sum_t x_t ,$$

$$a_p = \frac{2}{N} \sum_t x_t \cos \omega_p t , \quad b_p = \frac{2}{N} \sum_t x_t \sin \omega_p t ,$$

$$a_{N/2} = \frac{1}{N} \sum_t (-1)^t x_t ,$$

where sum is over observation times.

- Estimated power spectral density (PSD) at frequency ω_p is^{*}:

$$I(\omega_p) = \frac{N}{4\pi} (a_p^2 + b_p^2)$$

*The normalization by $N/4\pi$ is the convention chosen by Chatfield (2004, "Analysis of Time Series: An Introduction"). Other normalization conventions are also in common use.