

**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  
Wednesday 24 January 2018

# 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  $\text{\LaTeX}$  for one assignment.

# More Announcements!

- **Assignment 2:**

Due Monday 5 February 2018 in class (and by e-mail) at 11:30am.

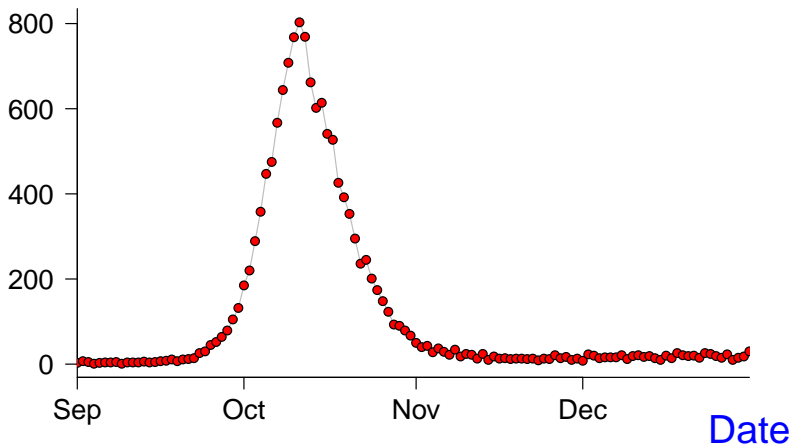
- **Midterm test:**

- *Date:* week of 5–9 March? or 12–16 March?
- *Time:* TBA
- *Location:* TBA

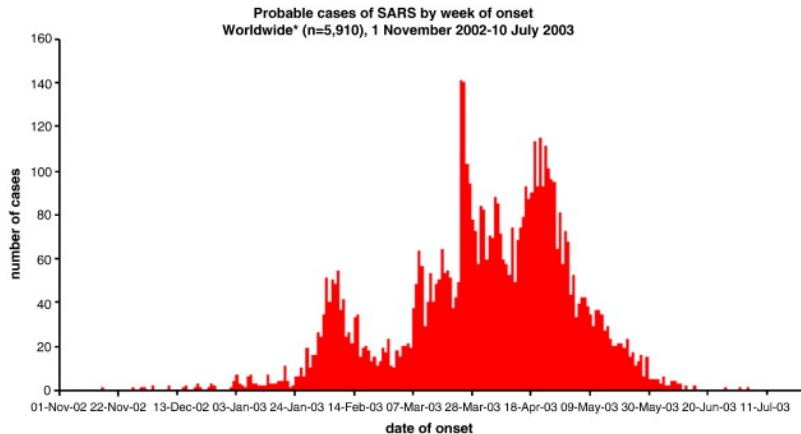


# P&I Mortality, Philadelphia, 1918

## P&I Deaths

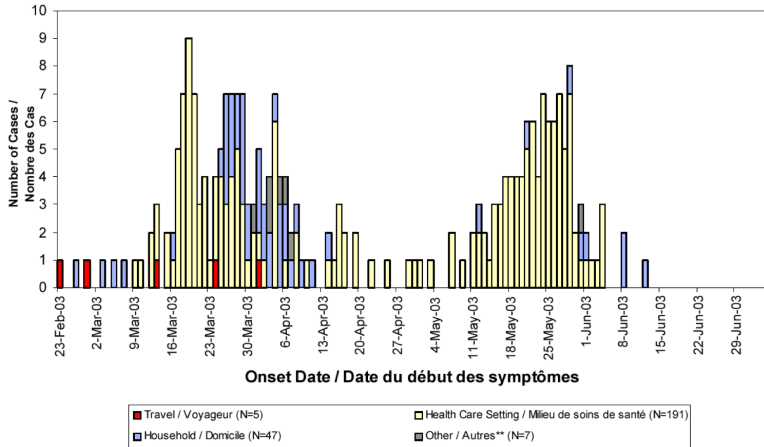


# SARS in 2003 (Worldwide)



\*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)

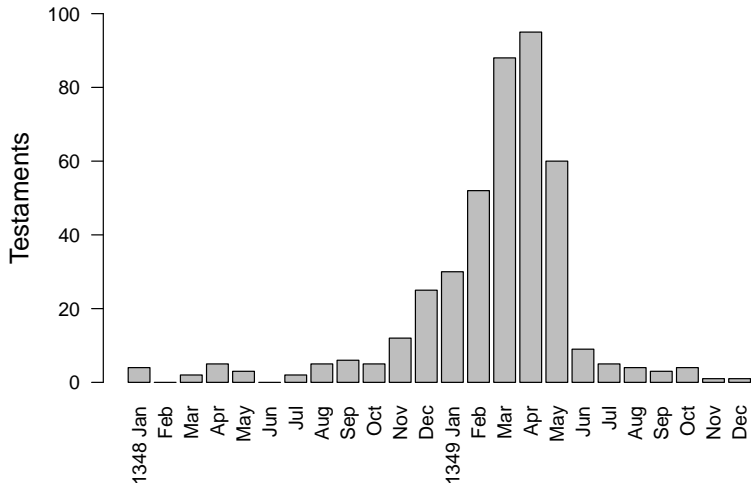


$N = 249$  (of 250 reported)

# 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





# Mortality Bills are typically handwritten

LONDON 29 <sup>th</sup> From the 4 <sup>th</sup> of July to the 11 <sup>th</sup> of August 1665			
Buried.	Plag.	Buried.	Plag.
St Alban Woodstreet	2	1	
Alhallows Bark-			
Alhallows Breadstreet			
Alhallows Great	1		
Alhallows Honilane			
Alhallows Lumbardstr.	1		
Alhallows Staining			
Alhallows the Wall	4	3	
St Alphage	1		
St Andrew Hubbard			
St Andrew Underthafe	3		
St Andrew Wardrobe			
St Anne Aldersgate	1		
St Anne Blackfyers	7	6	
St Antholiers Parish.	7		
St Austins Parish			
St Barthol. Exchange	1		
St Bennet Fynck			
St Bennet Gracechurch			
St Bennet Paulwharf	7		
St Bennet Sherchog			
St Borolgh Billingsgate			
Christ Church	5	3	
St Christophers			
Buried. Plag.		Buried. Plag.	
St Clement Eastcheap		1	
St Dionis Backchurch		1	
St Dunstons East		2	
St Edmund Lumbardstr.			
St Ethelborough		2	
St Faiths		1	
St Gabriel Fenchurch			
St George Botolphlane			
St Gregories by St. Paul			
St Hellen		2	1
St James Dukes place		1	
St James Garlickhithe		1	
St John Baptist			
St John Evangelist			
St John Zichary			
St Katharine Coleman		1	
St Katharine Creechur.			
St Lawrence Jewry			
St Lawrence Pountney			
St Leonard Eastcheap			
St Leonard Fosterlane.			
St Magnus Parish		1	
St Margaret Lothbury.			
St Margaret Mofes			
St Margaret Newfishst			
St Margaret Pattons			
St Mary Abchurch		1	
St Mary Aldermanbury			
St Mary Alde mary			
St Mary le Bow			
St Mary Bothaw			
St Mary Colechurch			
St Mary Hill			
St Mary Mag. Milkstr.			
St Mary Mag. Oldfishst			
St Mary Mounthaw			
St Mary Summerset		2	1
St Mary Staining			
St Mary Woolchurch			
St Mary Woolnoth			
St Martins Iremongerl.			
St Martins Ludgate		2	1
St Martins Orgars			
St Martins Outwich		1	
St Martins Vintrey		1	
St Matthew Frydaystr.			
St Michael Bassishaw		5	4
St Michael Cornhil			
St Michael Crookedla.			
St Michael Queenhit		4	3
St Michael Quern		7	
St Michael Royal			
St Michael Woodstreet			
St Mildred Breadstreet			
St Mildred Poultry			
St Nicholas Acons			
St Nicholas Coleabby-			
St Nicholas Olaves			
St Olave Hartstreet			
St Olave Jewry			
St Olave Silverstreet			
St Pancras Soperlane			
St Peter Cheap		4	1
St Peter Cornhil			
St Peter Paulwharf			
St Peter Poor			
St Steven Colemanstr.		1	
St Steven Walbrook		2	1
St Swithin		2	1
St Thomas Apottle		1	1
Trinity Parish		1	
St Vedast alias Fosters			
Buried. Plag.		Buried. Plag.	
86		28	
Christened in the Parishes within the walls			
Buried		Plague	
111		4	
St Andrew Holborn	10	40	
St Bartholomew Great	7	4	
St Bartholomew Leli-			
St Bridget	24	17	
Bridewell Precinct	1		
St Borolgh Aldergate	11	9	
St Borolgh Aldgate	24	4	
St Borolgh Bishopgate	37	20	
St Dunstan West	19	9	
St Giles Southwark	13	4	
St Giles Cripplegate	105	49	
St Olave Southwark	20	6	
St Saviour Southwark	21	1	
St Sepulchres Parish			117
St Thomas Southwark			7
Trinity Minorities			6
At the Pesthouse			6
Christened in the 15 Parishes without the walls			
Buried		Plague	
473		273	
Christ's Church			
St John at Hackney	1		
St Giles in the Fields	208	215	
St James Clerkenwel	8	43	
St Kath. near the Tower	7	1	
Lambeth Parish	7		
St Leonar d Shoreditch	21	13	
St Magdalen Bermond.	14		
St Mary Islington	3	2	
St Mary Newington	7		
St Mary Whitechappel	16	3	
St Paul Shadwel			7
Rotherhich Parish			3
Stepney Parish			47
Buried		Plague	
473		280	

But handwriting is usually very clear



LONDON 29<sup>th</sup>

	Buried.	Plag.
St Albans Woodstreet	2	1
Alhallows Bark.	2	
Alhallows Breadstreet	1	
Alhallows Great		



But handwriting is usually very clear

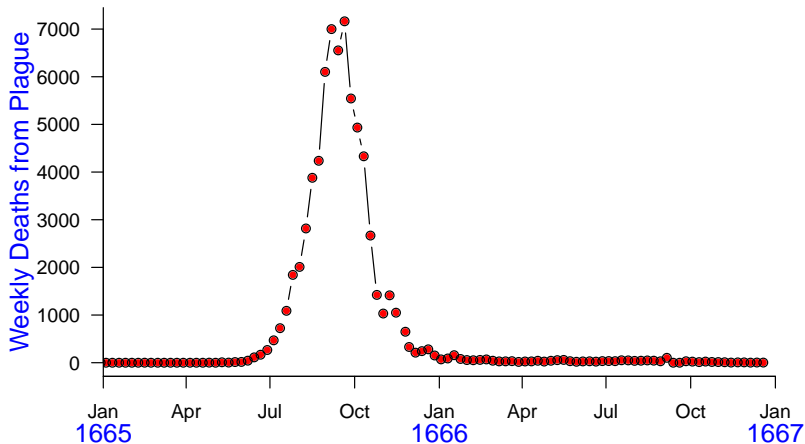
St Chrittophers

Christned in 97 the Parishes

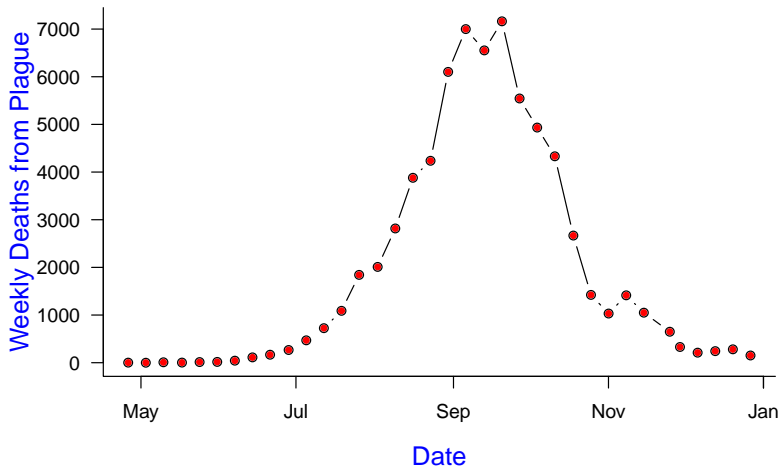
St Andrew Holborn	66	40	St
St Bartholomew Great	7	4	St
St Bartholomew Less			St
St Bridget	24	17	St
Bridewel Precinct	1	1	

Christned in the 16 Parishes

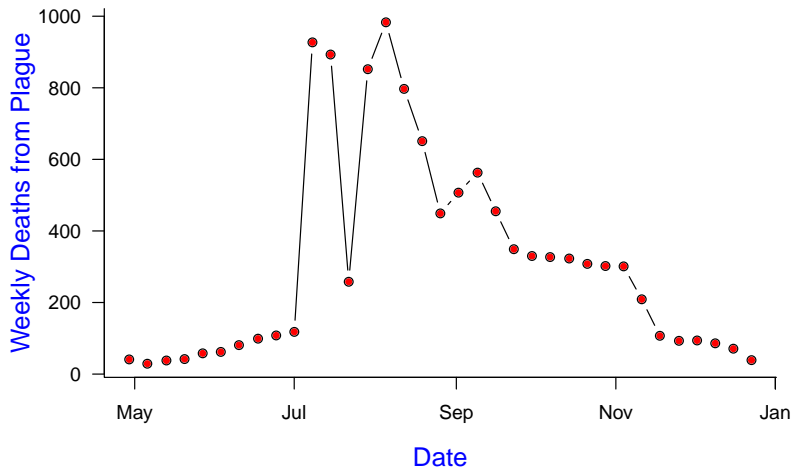
# The Great Plague of London, 1665



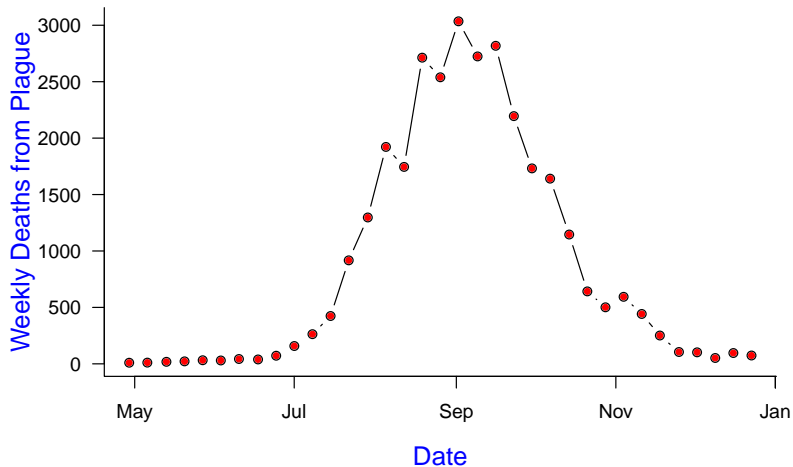
# The Great Plague of London, 1665



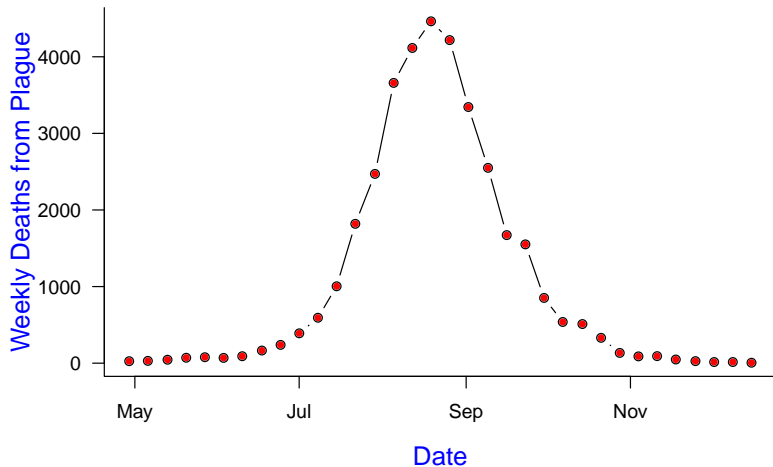
# London Plague of 1593



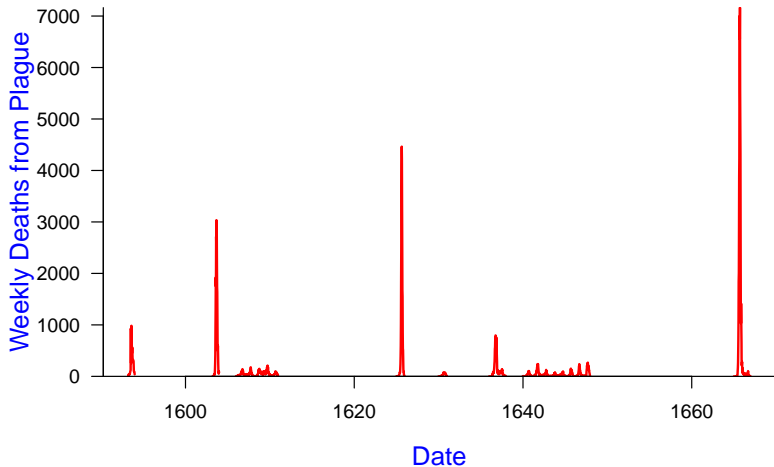
# London Plague of 1603



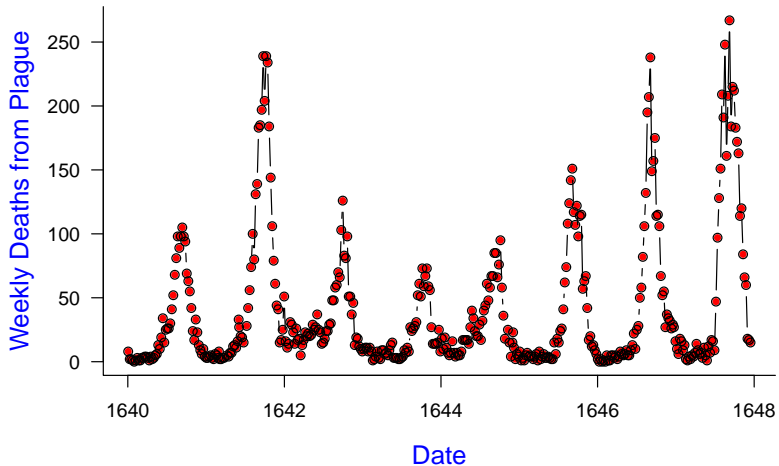
# London Plague of 1625



# 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
  - $\sim 300$  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>



Mathematics  
and Statistics

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

# Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 9  
Epidemic Data II  
Friday 26 Jan 2018

# Announcements

- **Assignment 2:**

Due Monday 5 February 2018 in class (and by e-mail) at 11:30am.

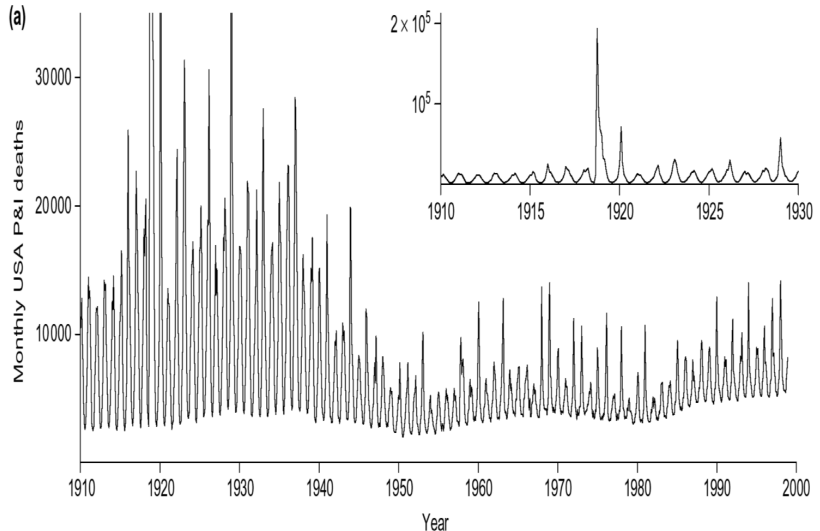
- **Midterm test:** We agreed on:

- *Date:* Thursday 8 March 2018
- *Time:* 7:00pm to 9:00pm
- *Location:* TBA

# Visualization of entire course of the Great Plague

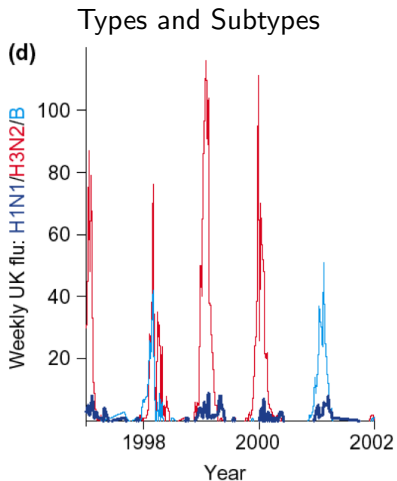
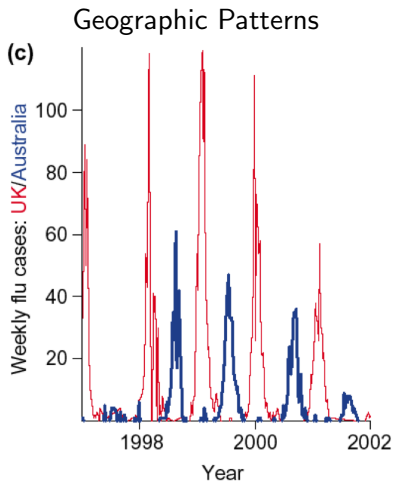
- What happened after initial spatial spread?
- Visualize full spatial epidemic structure
- Show magnitude of epidemic in each parish with cylinder.
- [Epidemic Visualization](#) (EpiVis) software by Junling Ma.

# P&I mortality in U.S.A., 1910–1998



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

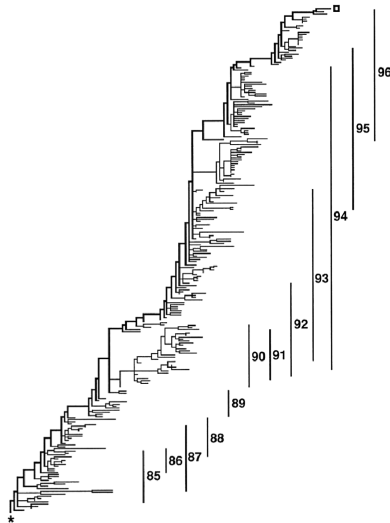
# Influenza Incidence Patterns (lab confirmed)



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

# Influenza Evolution

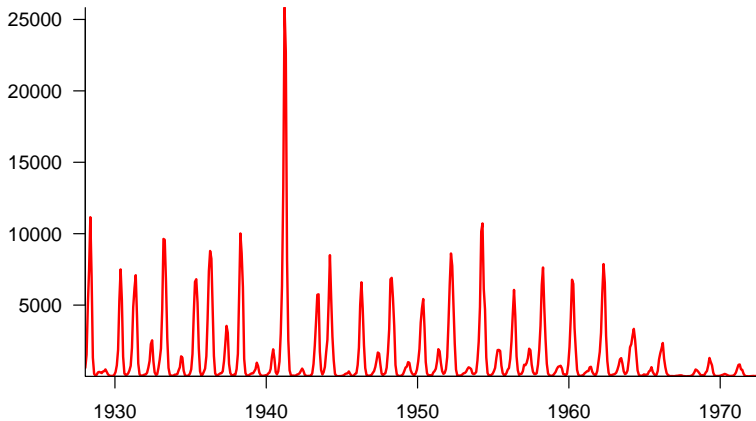
Molecular  
phylogenetic  
reconstruction of  
influenza A/H3N2  
evolution,  
1985–1996  
(Fitch *et al.* 1997)





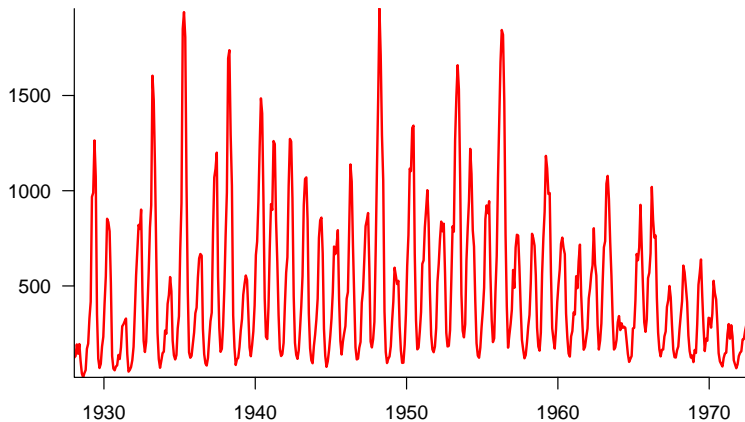
# Measles in New York City, 1928–1972

## Monthly Cases



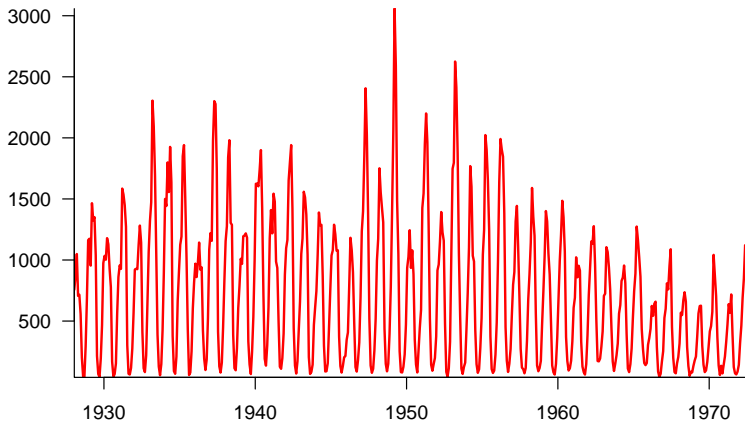
# Mumps in New York City, 1928–1972

## Monthly Cases

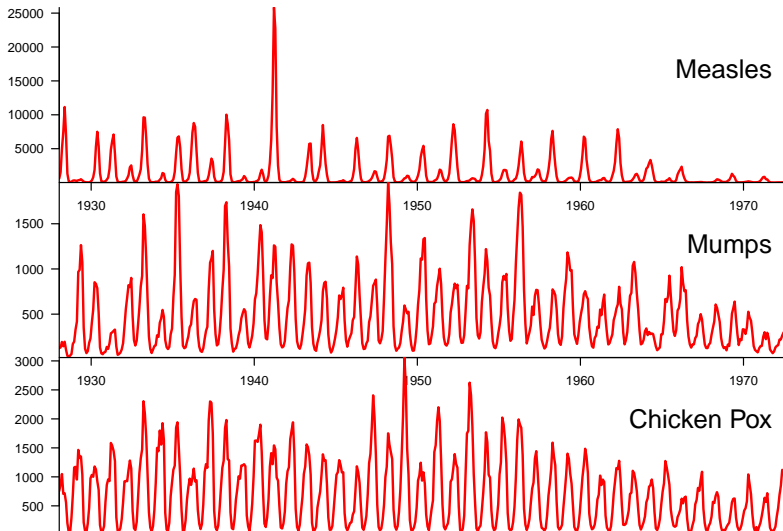


# Chicken Pox in New York City, 1928–1972

## Monthly Cases

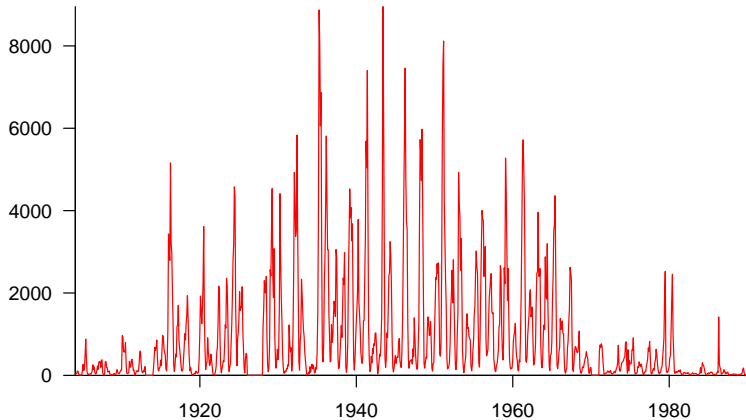


# Childhood diseases in New York City, 1928–1972



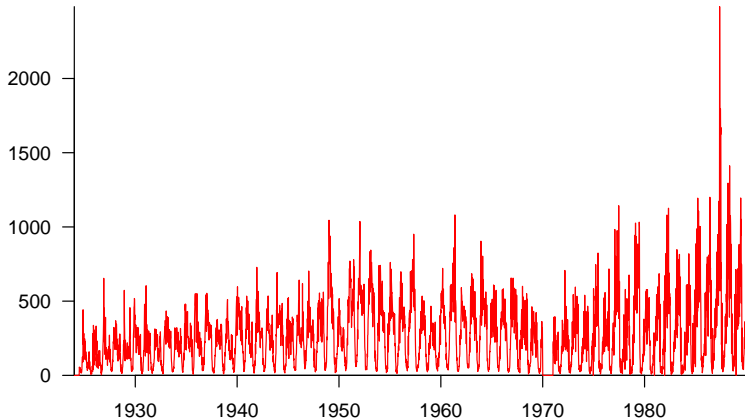
# Measles in Ontario, 1904–1989

## Monthly Cases



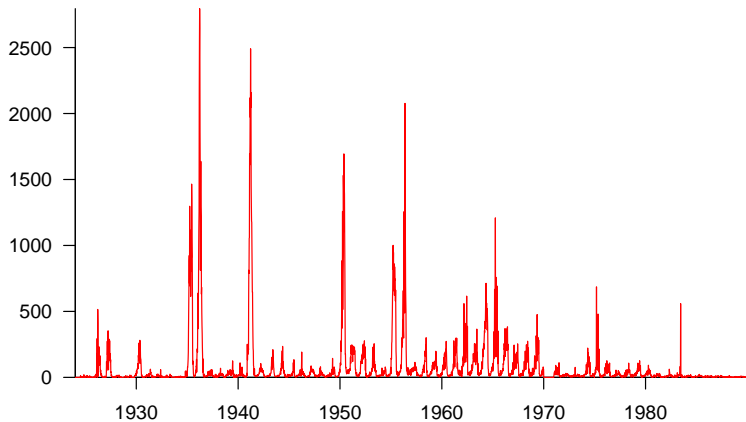
# Chicken Pox in Ontario, 1924–1989

## Monthly Cases



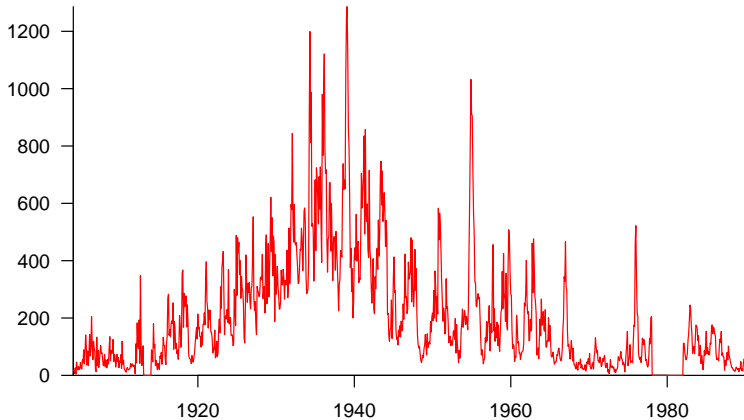
# Rubella in Ontario, 1924–1989

## Weekly Cases



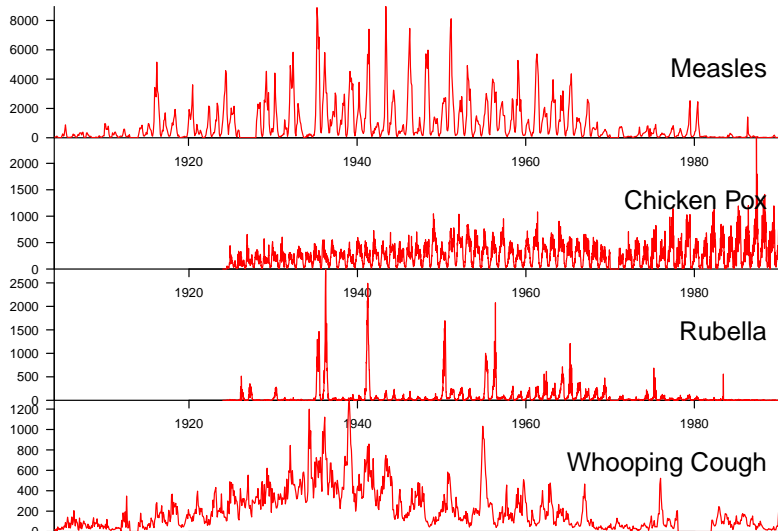
# Whooping Cough in Ontario, 1904–1989

## Monthly Cases





# Childhood diseases in Ontario, 1904–1989



## Ontario Disease Notification Data

Province of O

YEAR: 1939 \* COUNTY..... MUNICIPALITY.....

*Callow*  
*Windsor*  
*Windsor*

Month	Week End.	CSM		C.P.		DIP.		DYS. A/B		EN. LETH.		ERY.S.		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	1490	0	8	0					5	0	82	0	21	1	18	0	18	0	850	0	92	0	1	0	
	21	3	2	1511	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	1931	1	22	3	1	0	0	1	17	1	343	0	208	4	71	0	85	0	3385	2	210	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	1363	0	1	0	1	0			7	0	82	0	27	1	47	1	29	0	1033	0	91	0	1	0	
	18	7	2	1354	1	2	0					4	1	68	0	103	1	35	0	44	0	1161	0	59	0			
	25	8	1	1308	0	2	0					9	0	56	0	177	0	19	0	28	0	999	0	73	0			
	Total	5	3	1388	1	12	1	2	0			23	1	289	0	367	3	19	1	126	0	4788	1	338	0	2	0	
Mar.	4	9	1	271	0	7	1	3	1			7	0	93	0	114	19	21	0	40	0	1131	2	109	0	1	0	
	11	10		239	0	7	0	2	0			8	1	61	0	137	8	31	0	32	0	845	0	91	0	2	0	
	18	11		166	0							6	0	66	0	122	6	5	0	59	0	969	2	69	0	1	0	
	25	12	1	236	0	1	0	1	0			7	0	63	0	306	16	9	0	20	0	879	0	170	0	2	0	
	Total	2	3	912	0	15	1	6	1			28	1	283	0	623	49	66	0	151	0	3824	4	383	0	34	0	
Apr.	1	13	2	0	139	0	3	0	1	0			8	0	95	0	66	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	73	22			14	0	790	0	65	0	1	0
	15	15	2	0	108	0	1	0			0	1	11	0	41	0	52	16	2	0	16	0	745	0	56	0		
	22	16	5	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	1	1	167	0	4	0	2	0	2	1	3	0	55	0	124	9	2	1	13	0	746	1	120	0		
		Total	13	2	710	0	11	0	5	0	3	3	33	0	372	0	634	61	7	1	99	0	4016	1	384	0	4	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 *H. Hooping cough* Reported by Provincial Health Departments, Year *1924*

WEEK ENDING	P.E.I.		N.S.		N.B.		QUE.		ONT.		MAN.		SASK.		ALTA.		B.C.		CANADA	
	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT	WHS	NOT
1 JAN 5			11										1							12
2 12			29										18							49
3 19			37										32							69
4 26			75	52			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				7797
9 MAR 1			2										21							23
10 8													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	37	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 29 Jan 2018

# Announcements

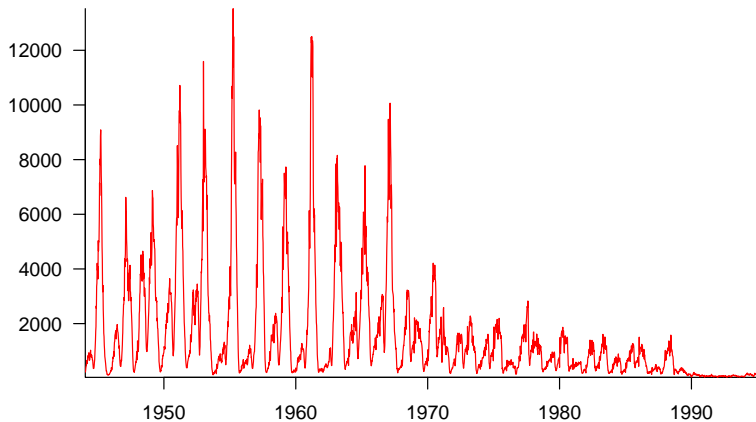
- Comment from TA on Assignment 1:  
“For a few of the groups, I would recommend that they look over the work that their group members have done. Question 2c and 2d in particular were closely related and there were a few obvious cases where the students had not communicated with each other.”
- **Assignment 2:**  
Due Monday 5 February 2018 in class (and by e-mail) at 11:30am.
- **Midterm test:** We agreed on:
  - *Date:* Thursday 8 March 2018
  - *Time:* 7:00pm to 9:00pm
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# Recurrent epidemics of childhood infections

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

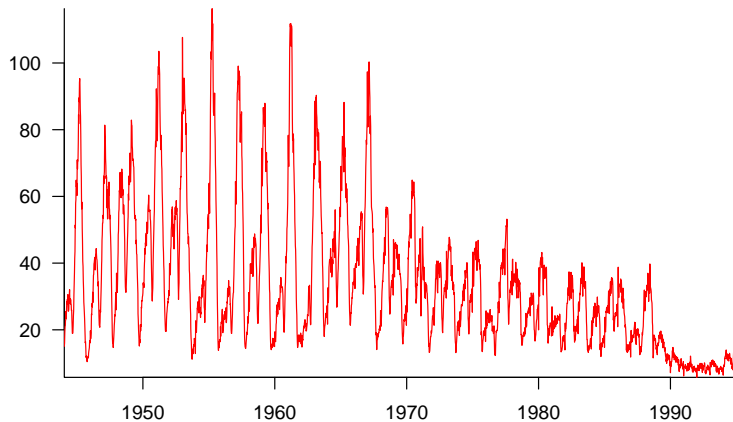
# Measles incidence in England and Wales, 1944–1995

## Weekly Cases



# Measles incidence in England and Wales, 1944–1995

Sqrt(Weekly Cases)





# Why study measles epidemics?

- $\sim 90,000$  children died from measles in 2016.
- 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...

**BRING  
MEASLES  
TO ITS  
KNEEZLES!**



# 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!

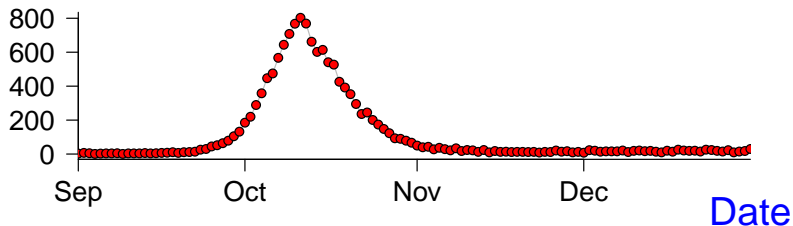
# Modelling population dynamics childhood infections

- The basic SIR model cannot explain recurrent epidemics.
- What should we do? . . .
  - 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.

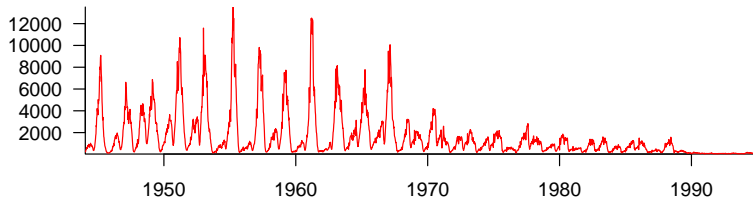
# Epidemic Data Analysis

# Time Plots of Temporal Epidemic Patterns

## 1918 P&I

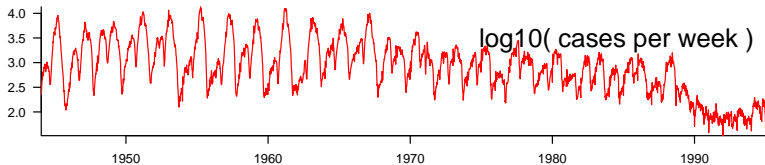
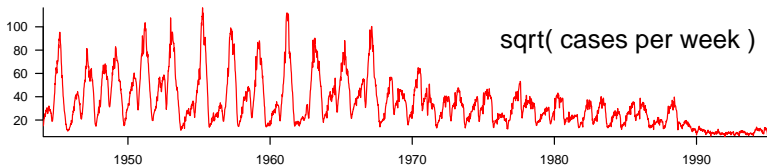
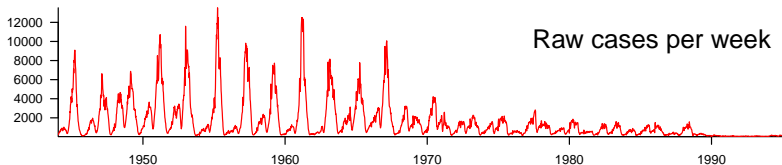


## Weekly Measles in England and Wales



# 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:*

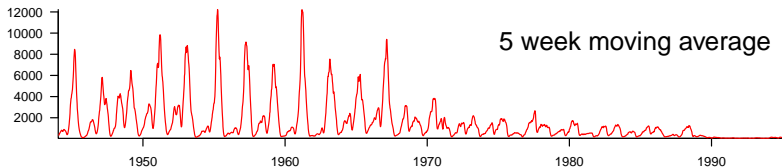
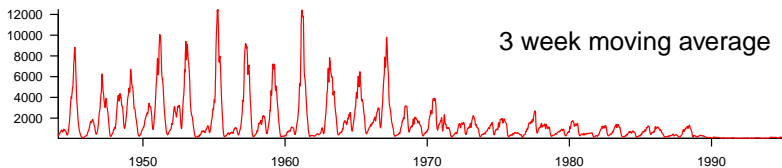
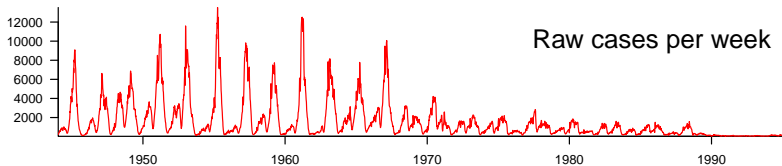
$$x_t \rightarrow \frac{1}{2a+1} \sum_{i=-a}^a x_{t+i}$$

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

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

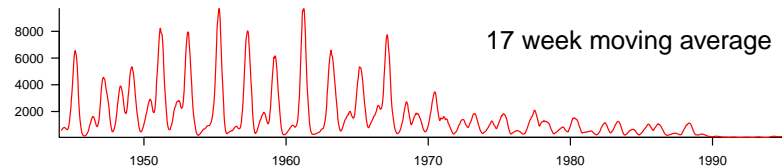
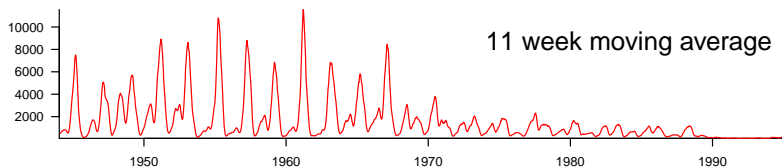
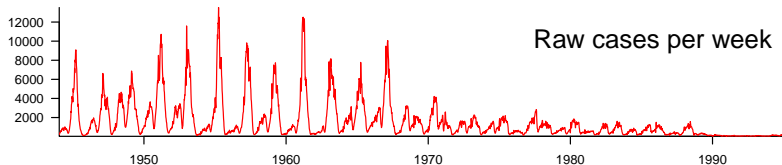
- Generalization of moving average.
- *Weights*  $\lambda_i$  can be nonlinear functions of  $i$ .

# Times Plots of Smoothed Data

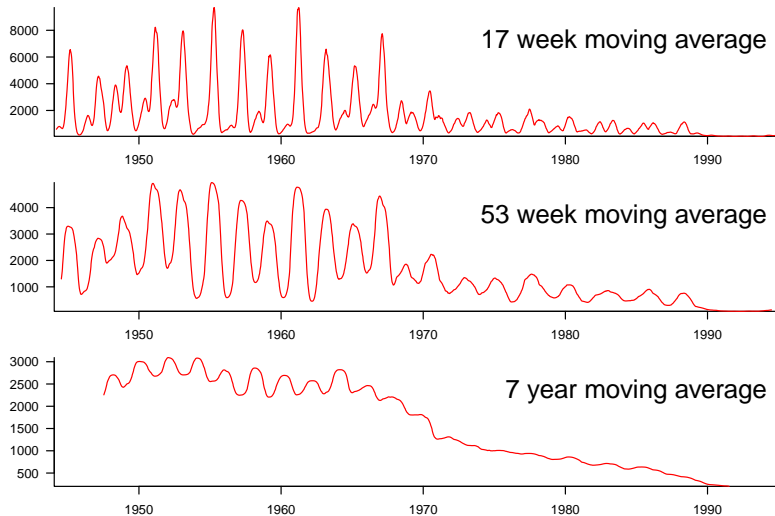




# Times Plots of Smoothed Data



# 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.

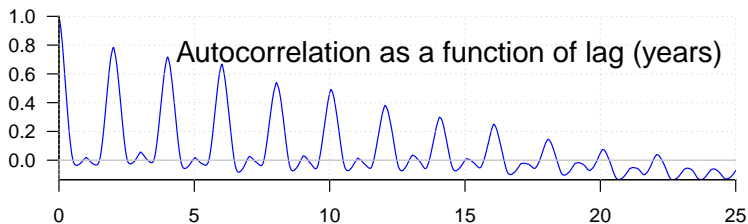
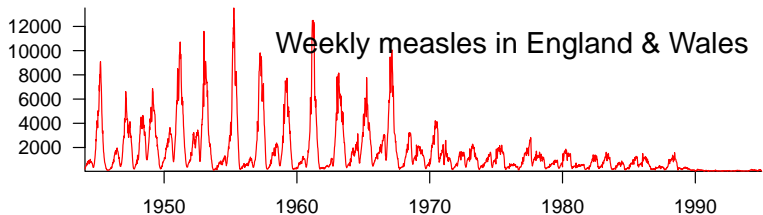
# Autocorrelation

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

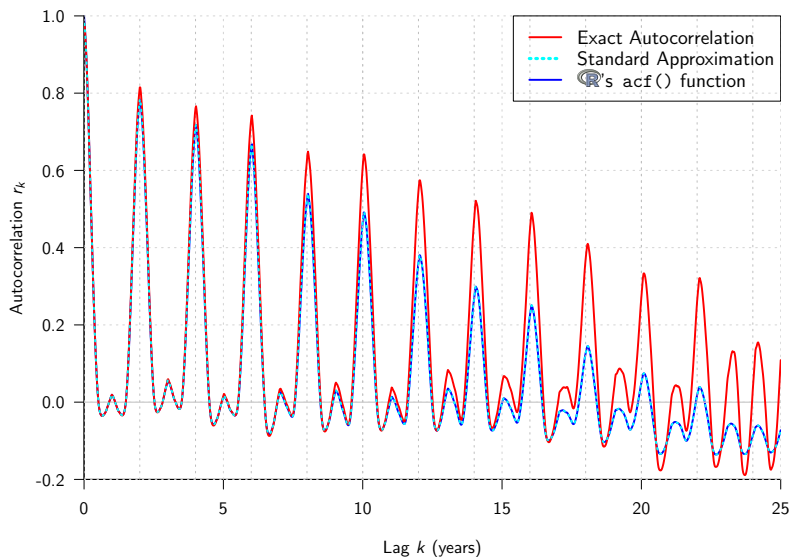
$$r_k \simeq \frac{\sum_{t=1}^{N-k} (x_t - \bar{x})(x_{k+t} - \bar{x})}{\sum_{t=1}^N (x_t - \bar{x})^2}$$

- 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  $\omega_p$  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.