3 Epidemic Data and Time Series Tools

McMaster University

Mathematics and Statistics

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

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

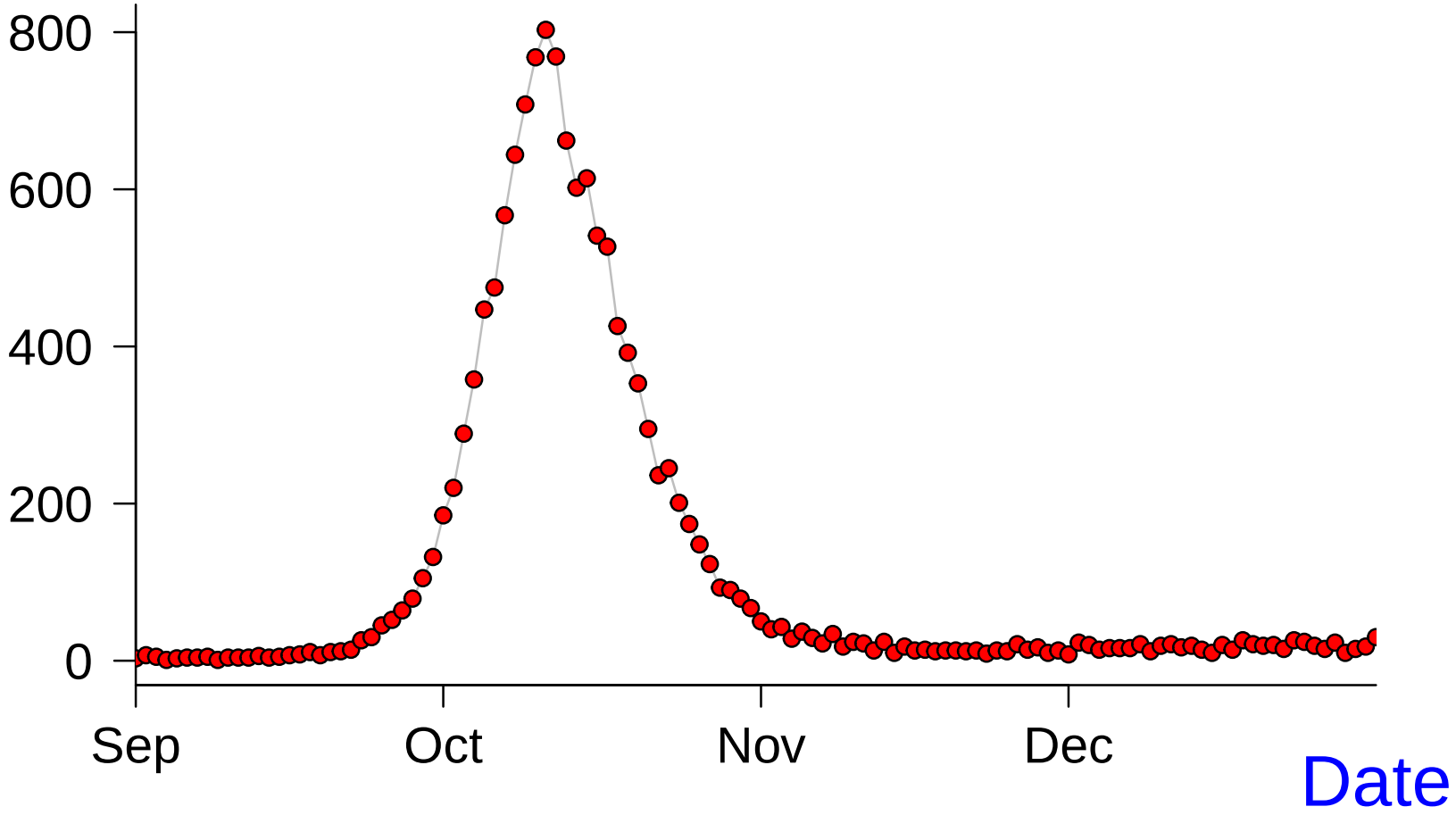
Lecture 3
Epidemic Data and Time Series Tools
Tuesday 17 September 2024

Announcements

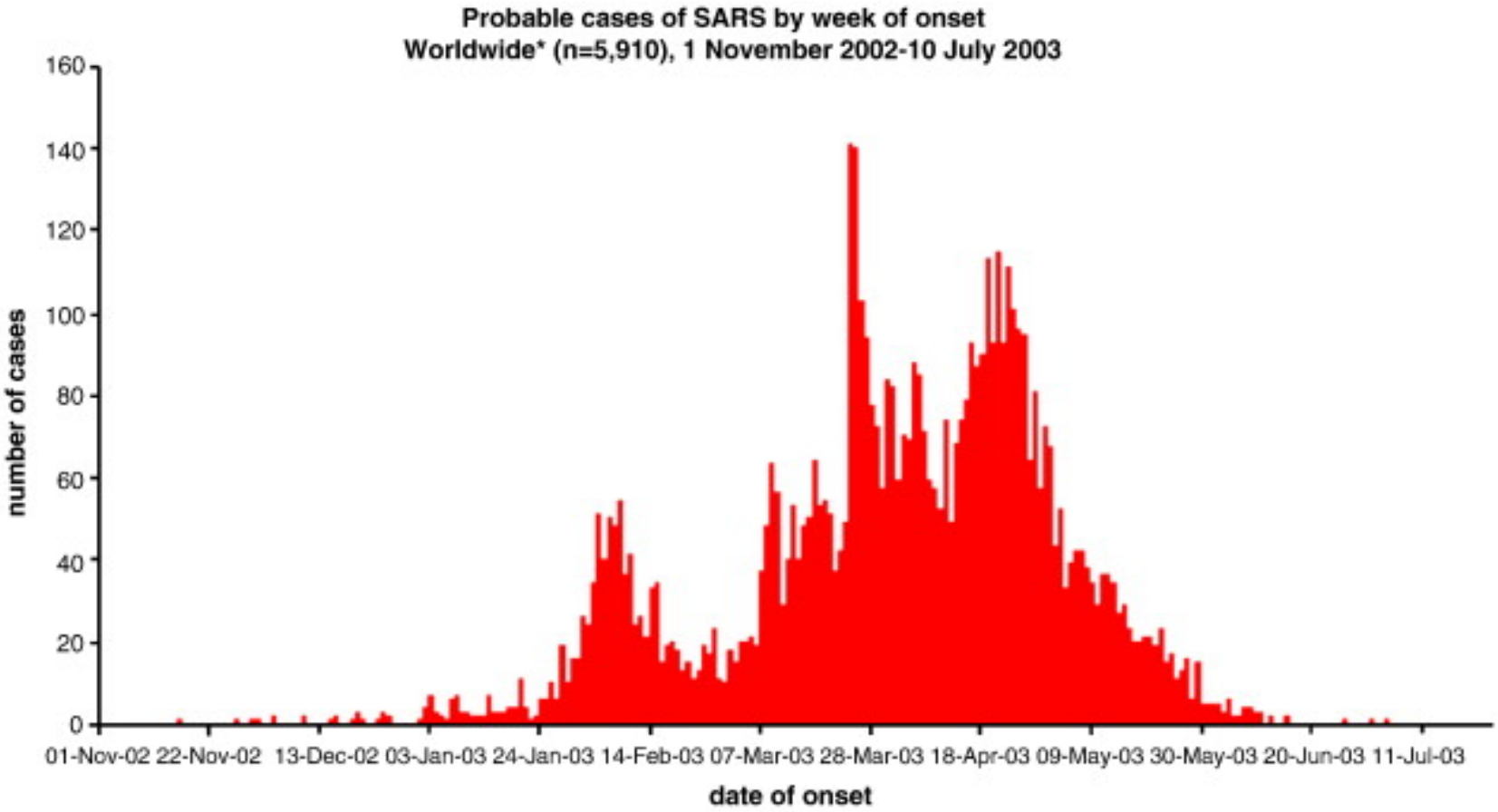
- Next week's lecture will be recorded in advance and posted on the Echo 360 page for this course.
  - Live Q&A, either in last hour of scheduled class or at a mutually convenient time.
- Assignments:
  - Assignment 1 due 23 Sep 2024 (next Monday)
  - Assignment 2 due 7 Oct 2024
    (good to work on before class on 1 Oct 2024)
- Class on 1 Oct 2024 will be given by Mikael Jagan
  (install `epigrowthfit` before that class)
- Lecture on 8 Oct 2024 will pre-recorded and posted

P&I Mortality, Philadelphia, 1918

P&I Deaths

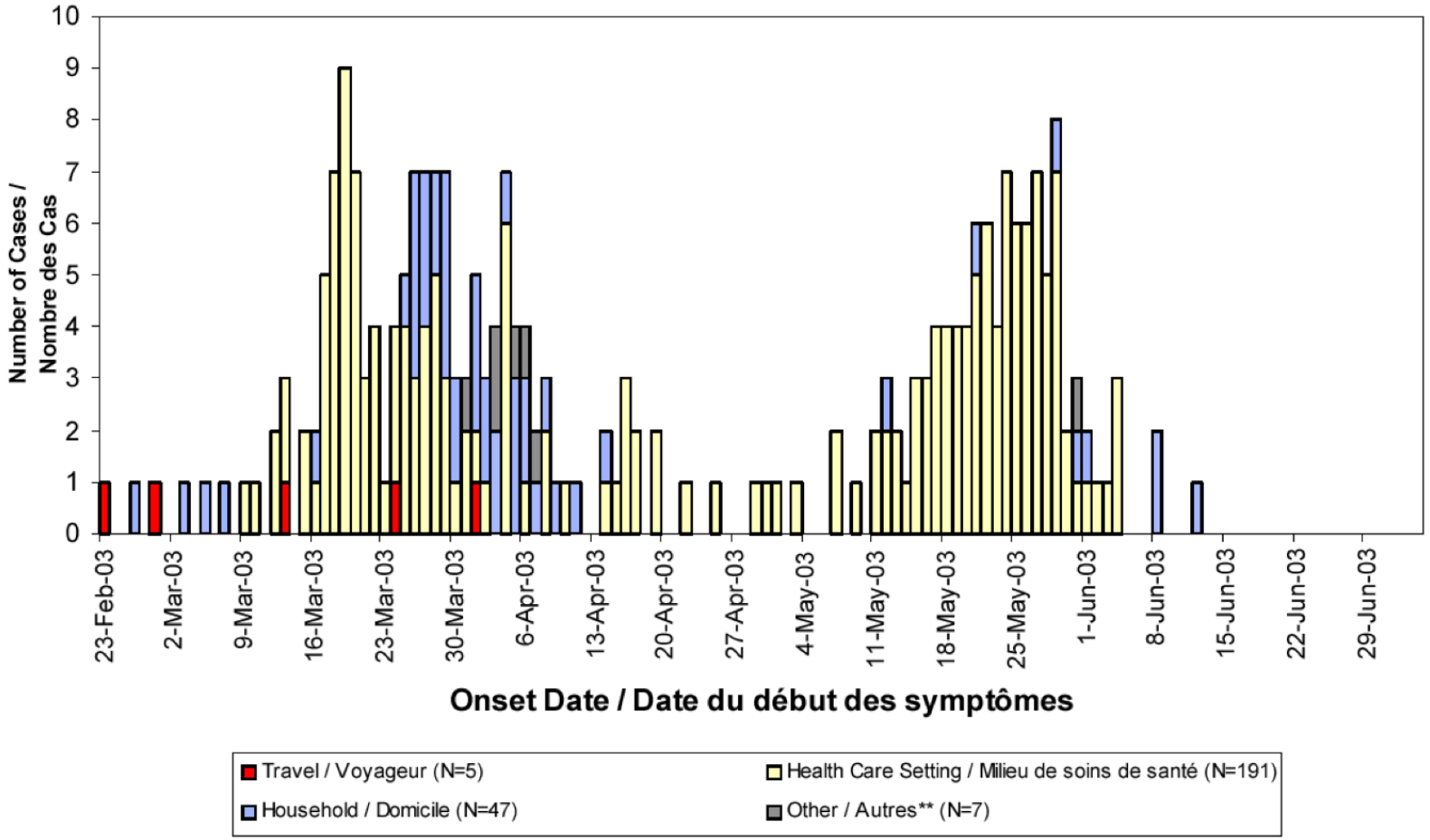


SARS in 2003 (Worldwide)



*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?

COVID (ancestral) hospitalization and survival in Ontario

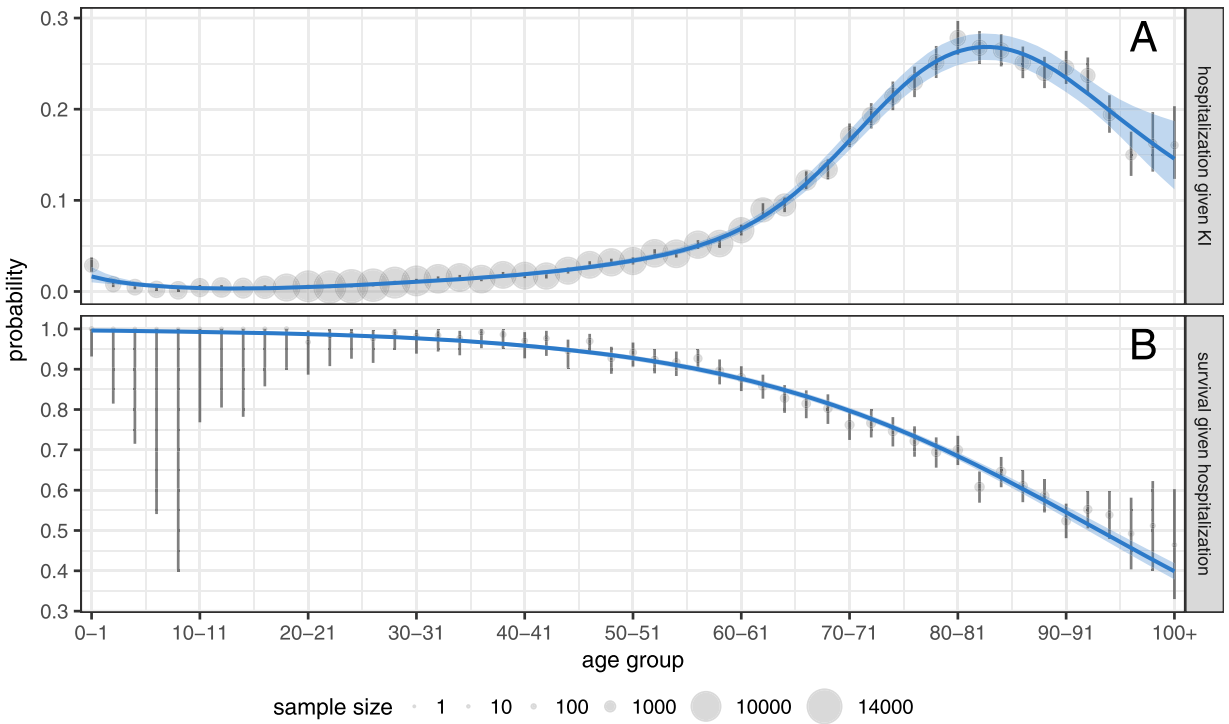
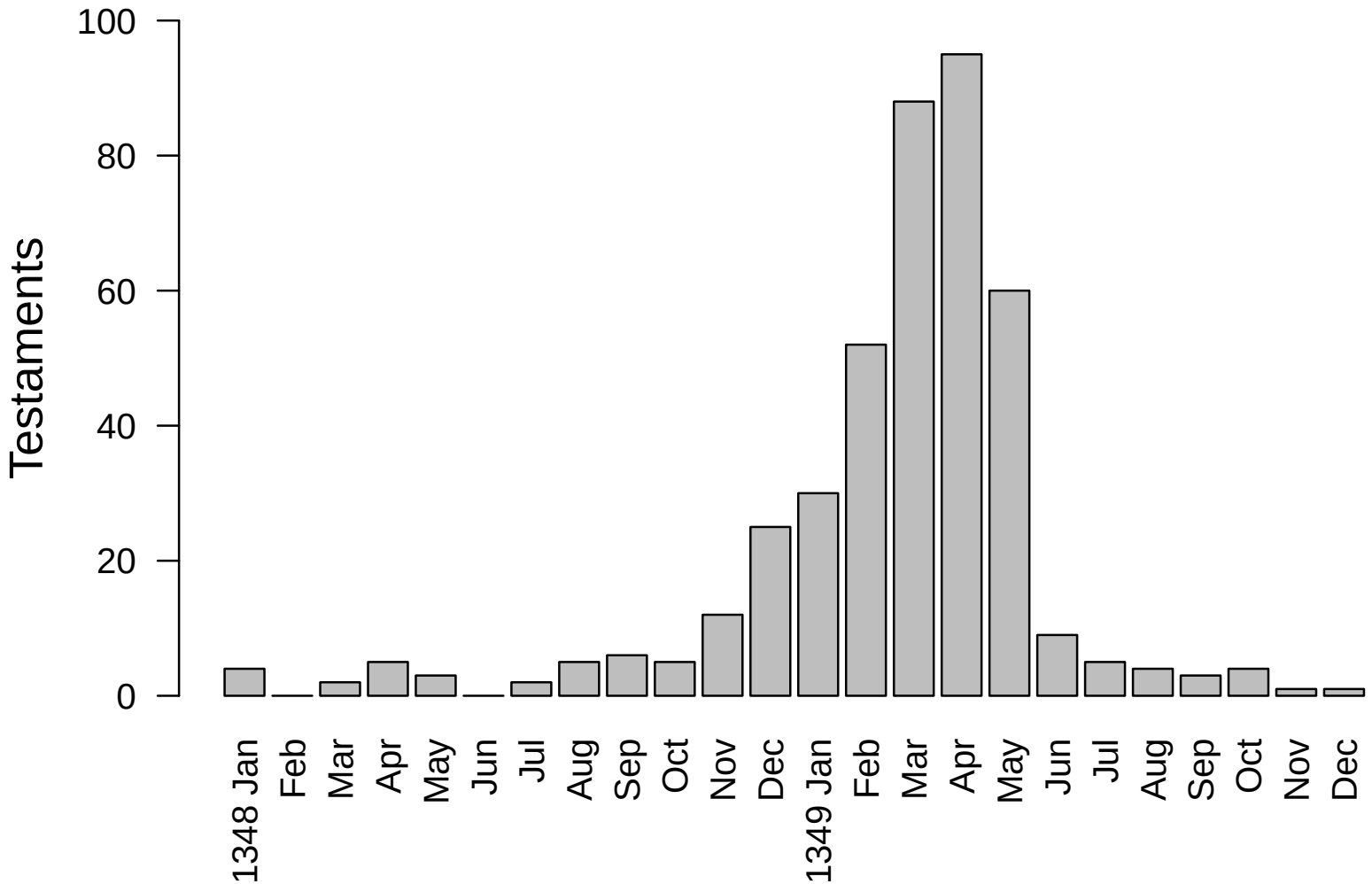


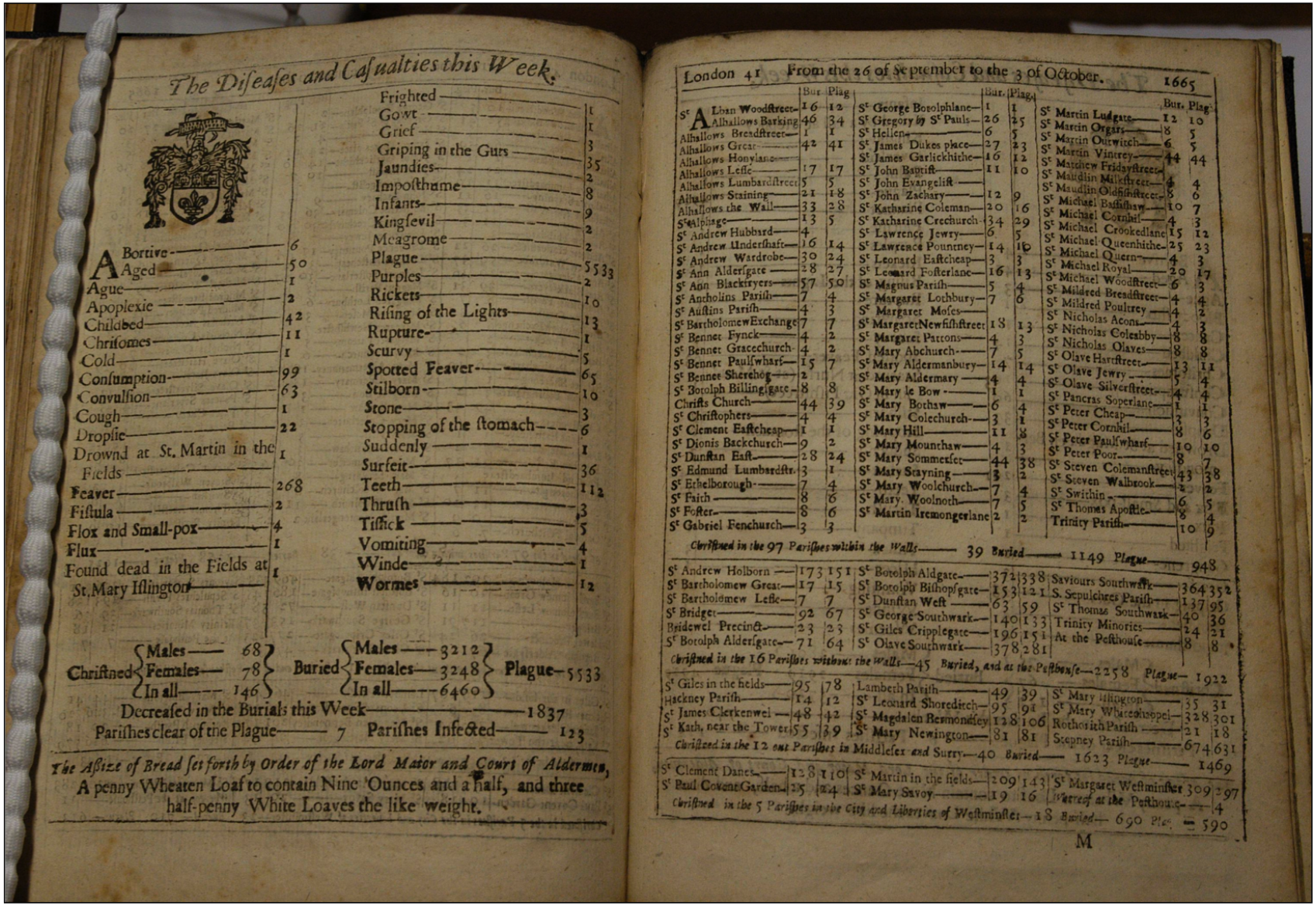
Fig. 4 Age-dependent COVID-19 hospitalization probability for known SARS-CoV-2 infection (panel **a**) and survival probability for hospitalized patients (panel **b**) in Ontario. We give age-by-age estimates of each probability (points; 95% exact binomial confidence intervals given by vertical lines), where point area is proportional to age-specific sample size. We additionally provide more precise estimates of these probabilities under stricter assumptions, modelling the hospitalization probability using a generalized additive model and the survival probability using a generalized linear model (curves; 95% confidence bands given by shaded regions). See "Methods" section for details

Papst et al (2021), BMC Public Health

The Black Death in London, England, 1348–1349



London Bill of Mortality, 26 Sept to 3 Oct 1665



The Diseases and Casualties this Week.

Abortive	6	Frighted	1
Aged	50	Gowt	1
Ague	1	Grief	3
Apoplexie	2	Griping in the Guts	35
Childbed	42	Jaundies	2
Chrisomes	11	Impostume	8
Cold	1	Infants	9
Consumption	99	Kingsevil	2
Convulsion	63	Meagrome	2
Cough	1	Plague	5533
Dropsie	22	Purples	2
Drownd at St. Martin in the Fields	1	Rickets	10
Feaver	268	Rising of the Lights	13
Fistula	2	Rupture	1
Flox and Small-pox	4	Scurvy	5
Flux	1	Spotted Feaver	65
Found dead in the Fields at St. Mary Islington	1	Stilborn	10
		Stone	3
		Stopping of the stomach	6
		Suddenly	1
		Surfeit	36
		Teeth	112
		Thrush	3
		Tissick	5
		Vomiting	4
		Winde	1
		Wormes	12

Christned { Males 68, Females 78, In all 146 } Buried { Males 3212, Females 3248, In all 6460 } Plague 5533

Decreased in the Burials this Week 1837

Parishes clear of the Plague 7 Parishes Infected 123

The Assize of Bread set forth by Order of the Lord Maior and Court of Aldermen,
A penny Wheaten Loaf to contain Nine Ounces and a half, and three half-penny White Loaves the like weight.

London 41 From the 26 of September to the 3 of October. 1665

	Bur.	Plag.		Bur.	Plag.		Bur.	Plag.
St Alban Woodstreet	16	12	St George Botolphlane	1	1	St Martin Ludgate	12	10
Allhallows Barking	46	34	St Gregory by St Pauls	26	25	St Martin Organs	8	5
Allhallows Bread-street	1	1	St Hellen	6	5	St Martin Outwitch	6	5
Allhallows Great	42	41	St James Dukes place	27	23	St Martin Vintrey	44	44
Allhallows Honylane			St James Garlickhithe	16	12	St Matthew Fridaystreet		
Allhallows Lesse	17	17	St John Baptist	11	10	St Maudlin Milkstreet	4	4
Allhallows Lumbardstreet	5	5	St John Evangelist			St Maudlin Oldfishstreet	8	6
Allhallows Staining	21	18	St John Zachary	12	9	St Michael Bassishaw	10	7
Allhallows the Wall	33	28	St Katharine Coleman	20	16	St Michael Cornhil	4	3
St Alphage	13	5	St Katharine Crechurch	34	29	St Michael Crookedlane	15	12
St Andrew Hubbard	4		St Lawrence Jewry	6	5	St Michael Queenhithe	25	23
St Andrew Undershaft	16	14	St Lawrence Pountney	14	10	St Michael Quern	4	3
St Andrew Wardrobe	30	24	St Leonard Eastcheap	3	3	St Michael Royal	20	17
St Ann Aldersgate	28	27	St Leonard Fosterlane	16	13	St Michael Woodstreet	6	3
St Ann Blackfryers	57	50	St Magnus Parish	5	4	St Mildred Bread-street	4	4
St Antholins Parish	7	4	St Margaret Lothbury	7	6	St Mildred Poultrey	4	2
St Austins Parish	4	3	St Margaret Moses			St Nicholas Acons	4	3
St Bartholomew Exchange	7	7	St Margaret Newfishstreet	18	13	St Nicholas Colesabby	8	8
St Bennet Fynck	4	2	St Margaret Pattons	4	3	St Nicholas Olaves	8	8
St Bennet Gracechurch	4	2	St Mary Abchurch	7	5	St Olave Hartstreet	13	11
St Bennet Paulswharf	15	7	St Mary Aldermanbury	14	14	St Olave Jewry	5	4
St Bennet Sherehog	2		St Mary Aldermary	4	4	St Olave Silverstreet	4	4
St Botolph Billingsgate	8	8	St Mary le Bow	1	1	St Pancras Soperlane	1	1
Christs Church	44	39	St Mary Bothaw	6	4	St Peter Cheap	3	3
St Christophers	4	4	St Mary Colechurch	3	1	St Peter Cornhil	8	6
St Clement Eastcheap	1	1	St Mary Hill	11	8	St Peter Paulswharf	10	10
St Dionis Backchurch	9	2	St Mary Mounthaw	4	3	St Peter Poor	8	7
St Dunstan East	28	24	St Mary Sommersetstreet	44	38	St Steven Colemanstreet	43	38
St Edmund Lumbardstr.	3	1	St Mary Stayning	3	2	St Steven Walbrook	2	2
St Ethelborough	7	4	St Mary Woolchurch	7	4	St Swithin	6	5
St Faith	8	6	St Mary Woolnoth	7	5	St Thomas Apostle	8	4
St Foster	8	6	St Martin Iremongerlane	2	2	Trinity Parish	10	9

Christned in the 97 Parishes within the Walls 39 *Buried* 1149 *Plague* 948

St Andrew Holborn	173	151	St Botolph Aldgate	372	338	Saviours Southwark	364	352
St Bartholomew Great	17	15	St Botolph Bishopsgate	153	121	S. Sepulchres Parish	137	95
St Bartholomew Lesse	7	7	St Dunstan West	63	59	St Thomas Southwark	40	36
St Bridget	92	67	St George Southwark	140	133	Trinity Minories	24	21
Bridewel Precinct	23	23	St Giles Cripplegate	196	151	At the Pesthouse	8	8
St Botolph Aldersgate	71	64	St Olave Southwark	378	281			

Christned in the 16 Parishes without the Walls 45 *Buried, and at the Pesthouse* 2258 *Plague* 1922

St Giles in the fields	95	78	Lambeth Parish	49	39	St Mary Islington	35	31
Hackney Parish	14	12	St Leonard Shoreditch	95	91	St Mary Whitechappel	328	301
St James Clerkenwel	48	42	St Magdalen Bermondsey	128	106	Rotherith Parish	21	18
St Kath. near the Tower	55	39	St Mary Newington	81	81	Stepney Parish	674	631

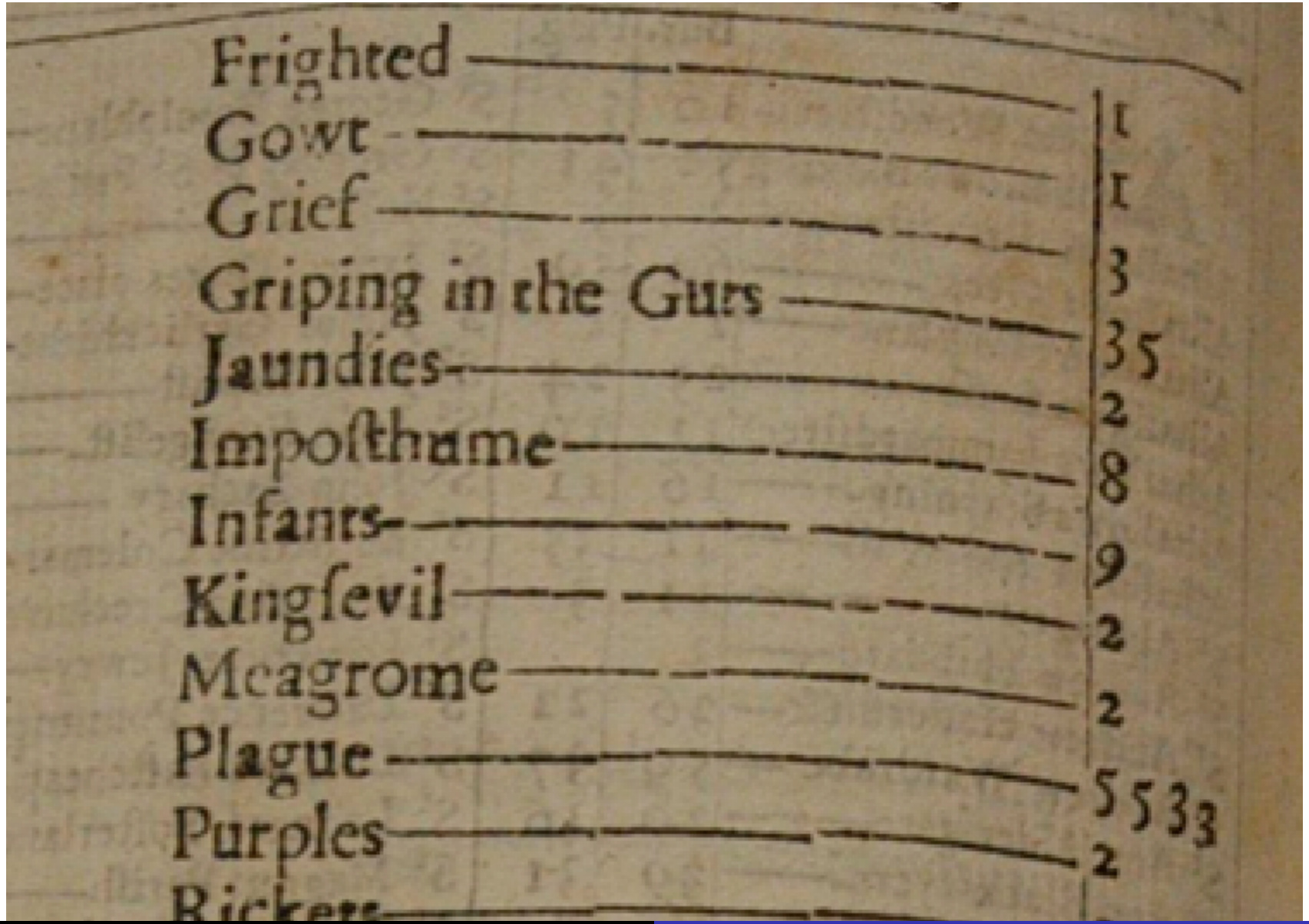
Christned in the 12 out Parishes in Middlesex and Surry 40 *Buried* 1623 *Plague* 1469

St Clement Danes	128	110	St Martin in the fields	209	143	St Margaret Westminster	309	297
St Paul Covent Garden	25	24	St Mary Savoy	19	16	*Buried at the Pesthouse*		4

Christned in the 5 Parishes in the City and Liberties of Westminster 18 *Buried* 690 *Plag.* 590

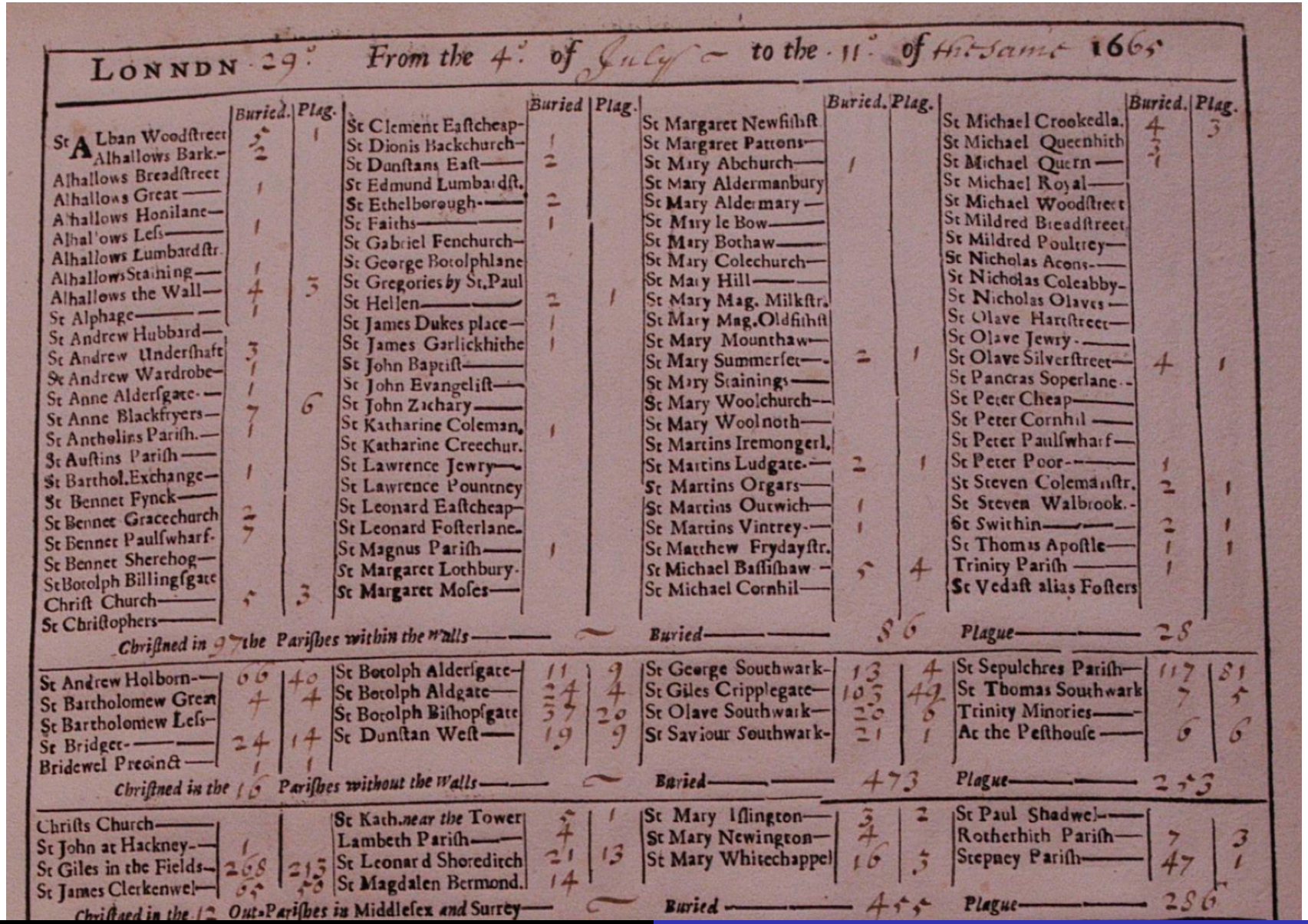
M

London Bill of Mortality, 26 Sept to 3 Oct 1665



Frighted	1
Gowt	1
Grief	3
Griping in the Guts	35
Jaundies	2
Impoſthume	8
Infants	9
Kingſevil	2
Meagrome	2
Plague	5533
Purples	2
Rickets	

Mortality Bills are typically handwritten



LONNDN 29. From the 4. of July to the 11. of Hr. Jame 1665

	Buried.	Plag.
St Alban Woodstreet	2	1
Allhallows Bark.	2	
Allhallows Breadstreet		
Allhallows Great	1	
Allhallows Honilane		
Allhallows Lefs		
Allhallows Lumbardstr.	1	
Allhallows Staining		
Allhallows the Wall	4	3
St Alphage	1	
St Andrew Hubbard		
St Andrew Undershaft	3	
St Andrew Wardrobe	1	
St Anne Aldersgate	1	
St Anne Blackfryers	7	6
St Antholins Parish.	1	
St Auftins Parish		
St Barthol. Exchange	1	
St Bennet Fynck		
St Bennet Gracechurch	2	
St Bennet Paulswharf	3	
St Bennet Sherehog		
St Botolph Billingsgate		
Christ Church	5	3
St Chriftophers		
St Clement Eaftcheap		
St Dionis Backchurch	1	
St Dunftans East	2	
St Edmund Lumbardft.		
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 Baptift		
St John Evangelift		
St John Zachary		
St Katharine Coleman	1	
St Katharine Creechur.		
St Lawrence Jewry		
St Lawrence Pountney		
St Leonard Eaftcheap		
St Leonard Fofterlane		
St Magnus Parifh	1	
St Margaret Lothbury		
St Margaret Mofes		
St Margaret Newfifhft		
St Margaret Pattons		
St Mary Abchurch	1	
St Mary Aldermanbury		
St Mary Aldermary		
St Mary le Bow		
St Mary Bothaw		
St Mary Colechurch		
St Mary Hill		
St Mary Mag. Milkftr.		
St Mary Mag. Oldfifhft		
St Mary Mounthaw		
St Mary Summerfet	2	1
St Mary Stainings		
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 Fridayftr.		
St Michael Baffifhaw	5	4
St Michael Cornhil		
St Michael Crookedla.	4	3
St Michael Queenhith	3	
St Michael Quern	1	
St Michael Royal		
St Michael Woodftreet		
St Mildred Breadftreet		
St Mildred Poultrey		
St Nicholas Acons		
St Nicholas Coleabby		
St Nicholas Olaves		
St Olave Hartftreet		
St Olave Jewry		
St Olave Silverftreet	4	1
St Pancras Soperlane		
St Peter Cheap		
St Peter Cornhil		
St Peter Paulfwharf		
St Peter Poor	1	
St Steven Colemanftr.	2	1
St Steven Walbrook.		
St Swithin	2	1
St Thomas Apoftle	1	1
Trinity Parifh	1	
St Vedaft alias Fofters		

Chriftned in 97 the Parifhes within the Walls — Buried — 86 — Plague — 28

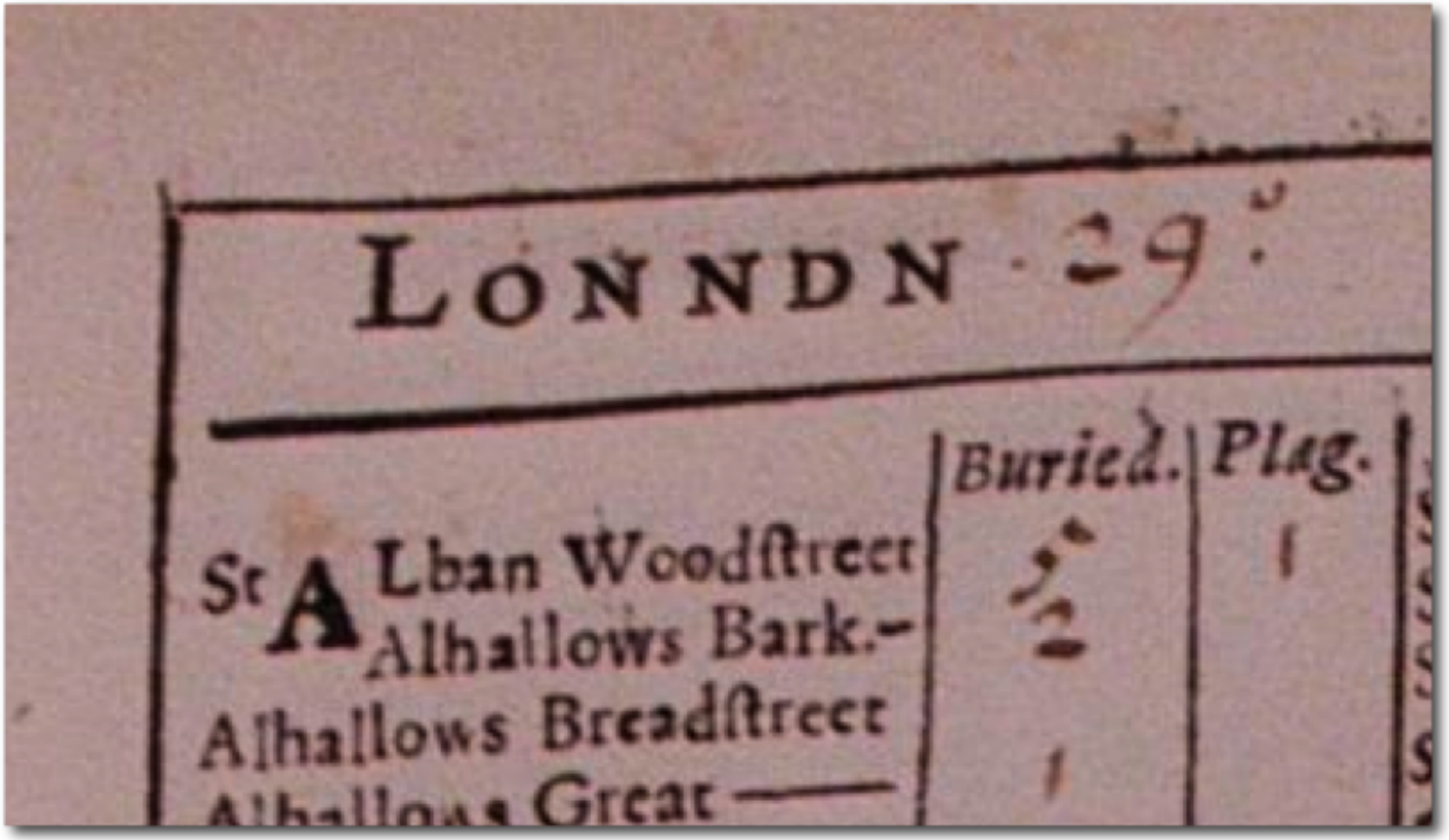
St Andrew Holborn	66	40	St Botolph Aldersgate	11	9	St George Southwark	13	4	St Sepulchres Parifh	117	81
St Bartholomew Great	4	4	St Botolph Aldgate	24	4	St Giles Cripplegate	103	49	St Thomas Southwark	7	5
St Bartholomew Less			St Botolph Bifhopfgate	37	20	St Olave Southwark	20	6	Trinity Minories		
St Bridget	24	14	St Dunftan West	19	9	St Saviour Southwark	21	1	At the Pefthoufe	6	6
Bridewel Precinct	1	1									

Chriftned in the 16 Parifhes without the Walls — Buried — 473 — Plague — 253

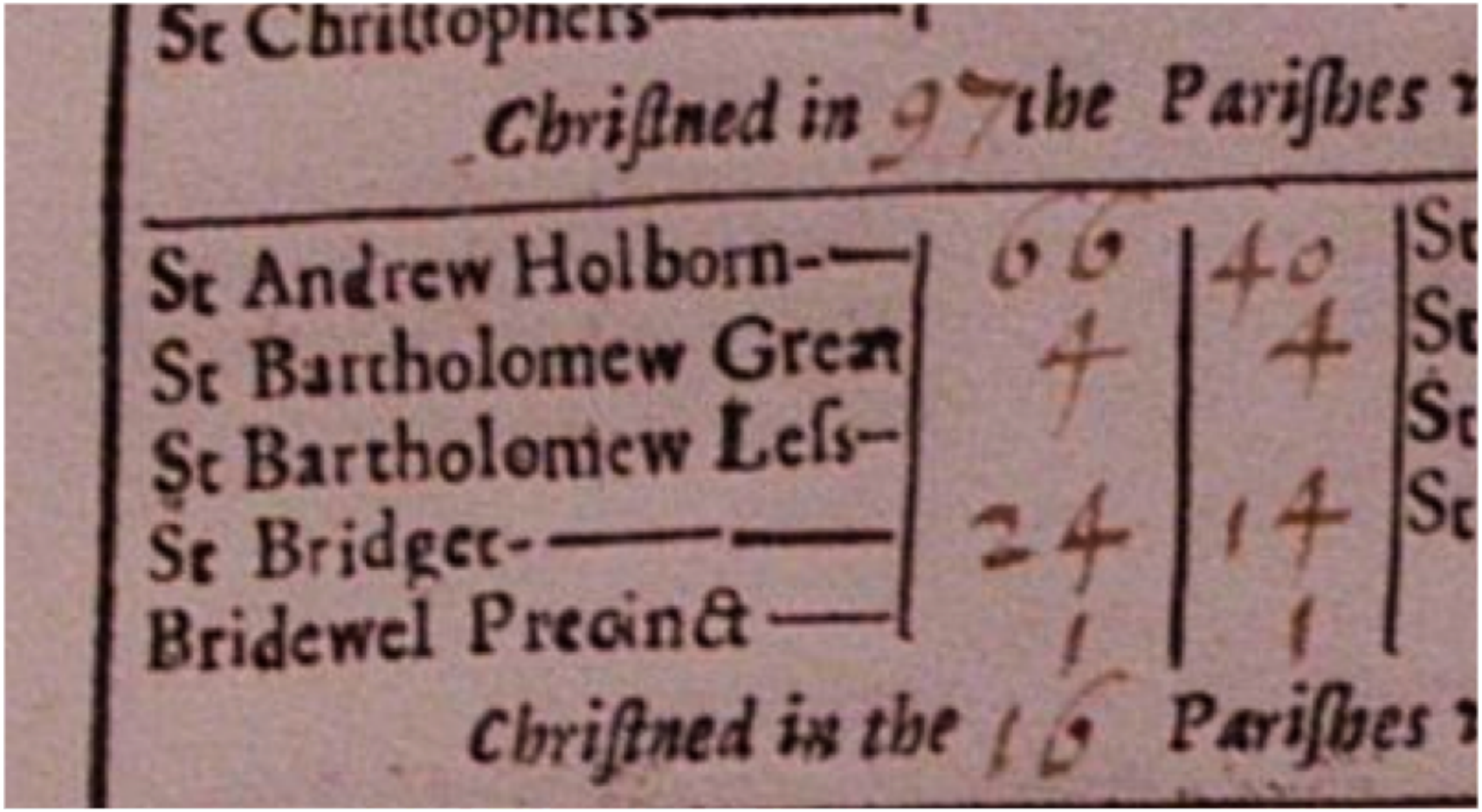
Chrifts Church			St Kath. near the Tower	5	1	St Mary Iflington	3	2	St Paul Shadwel		
St John at Hackney	1		Lambeth Parifh	4		St Mary Newington	4		Rotherhith Parifh	7	3
St Giles in the Fields	268	213	St Leonard Shoreditch	21	13	St Mary Whitechappel	16	3	Stepney Parifh	47	1
St James Clerkenwel	65	50	St Magdalen Bermond.	14							

Chriftned in the 12 Out-Parifhes in Middlefex and Surrey — Buried — 455 — Plague — 256

But handwriting is usually very clear



But handwriting is usually very clear

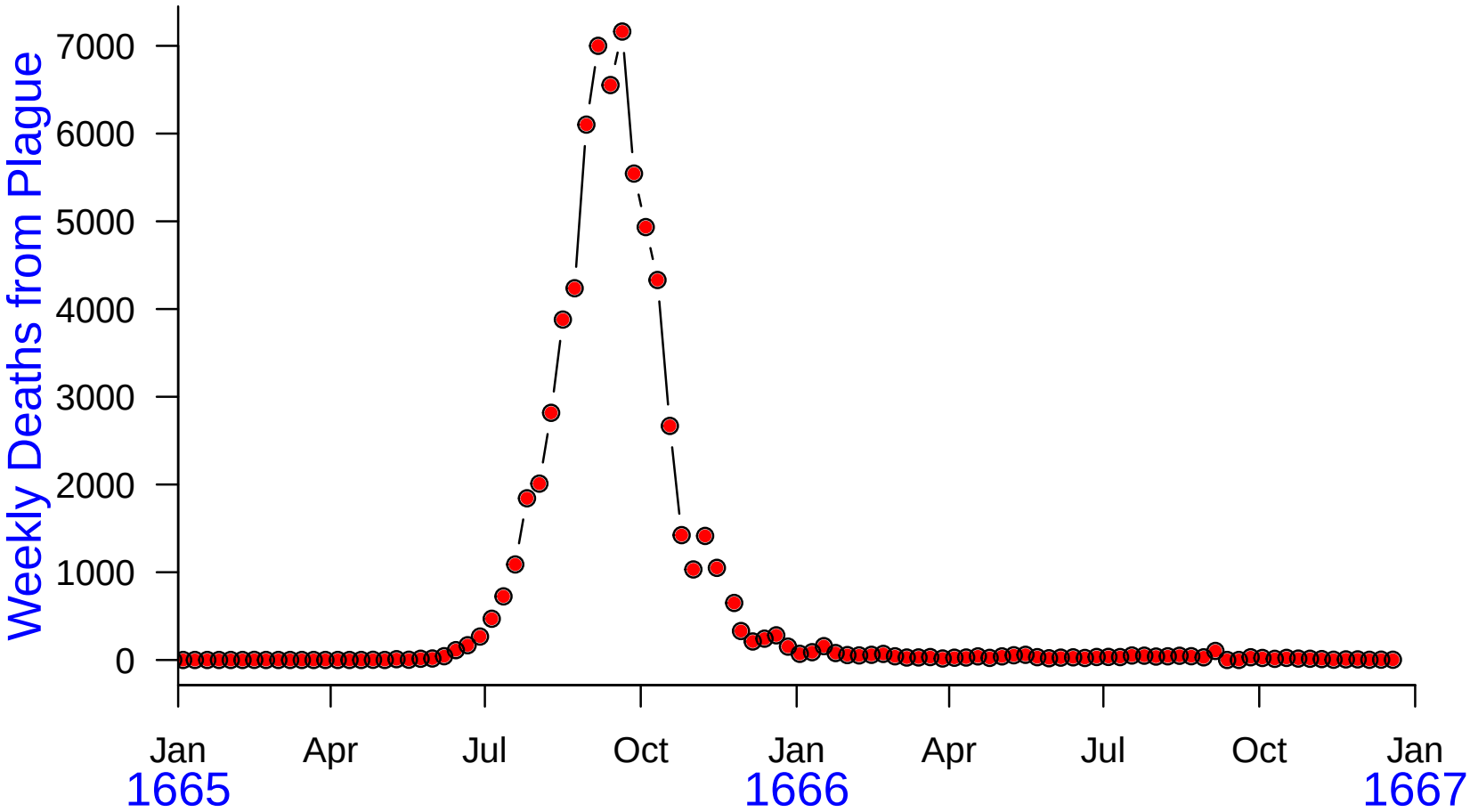

St Christophers ——— 1

Christned in 97 the Parishes

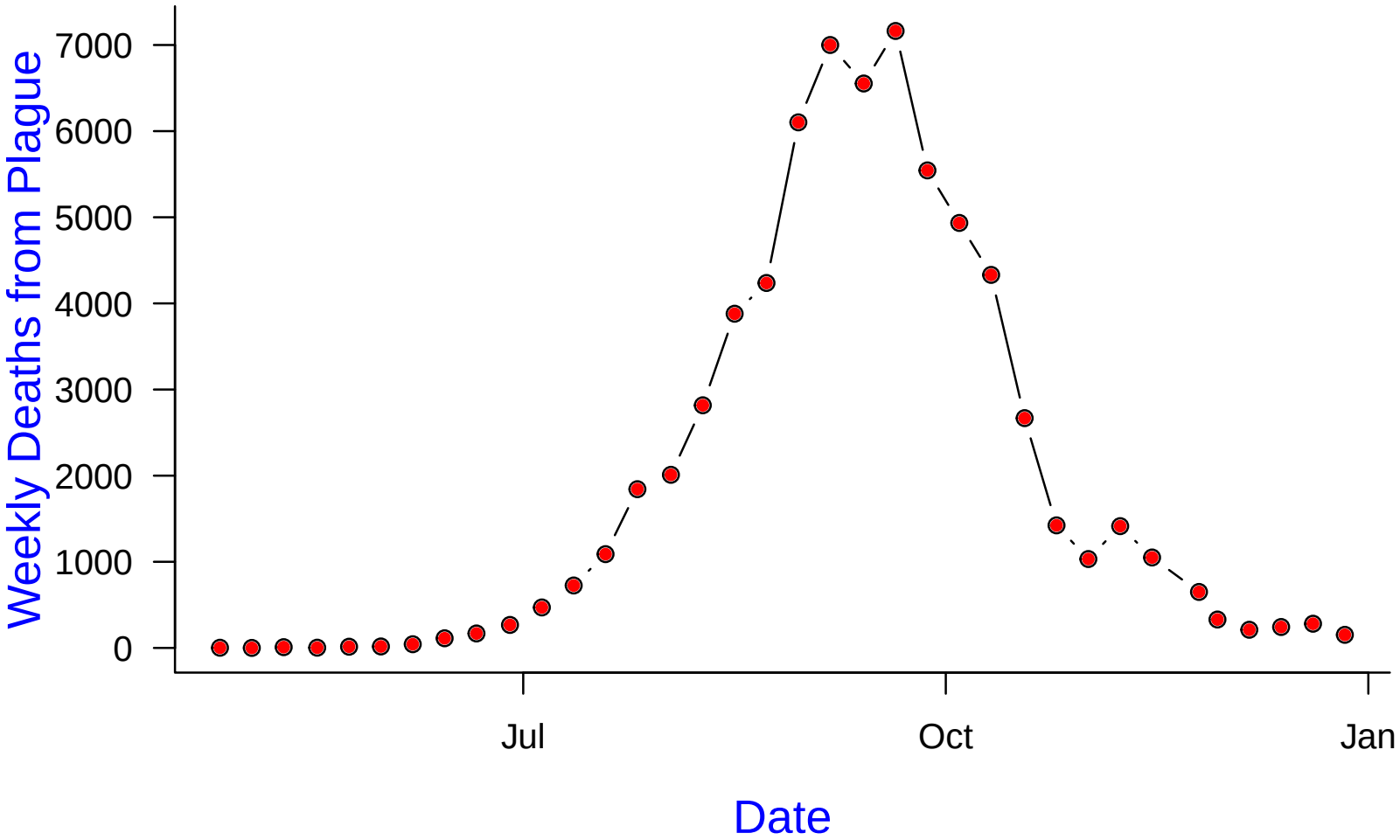
St Andrew Holborn-	66	40	St
St Bartholomew Great	4	4	St
St Bartholomew Less-			St
St Bridget-	24	14	St
Bridewel Precinct	1	1	

Christned in the 16 Parishes

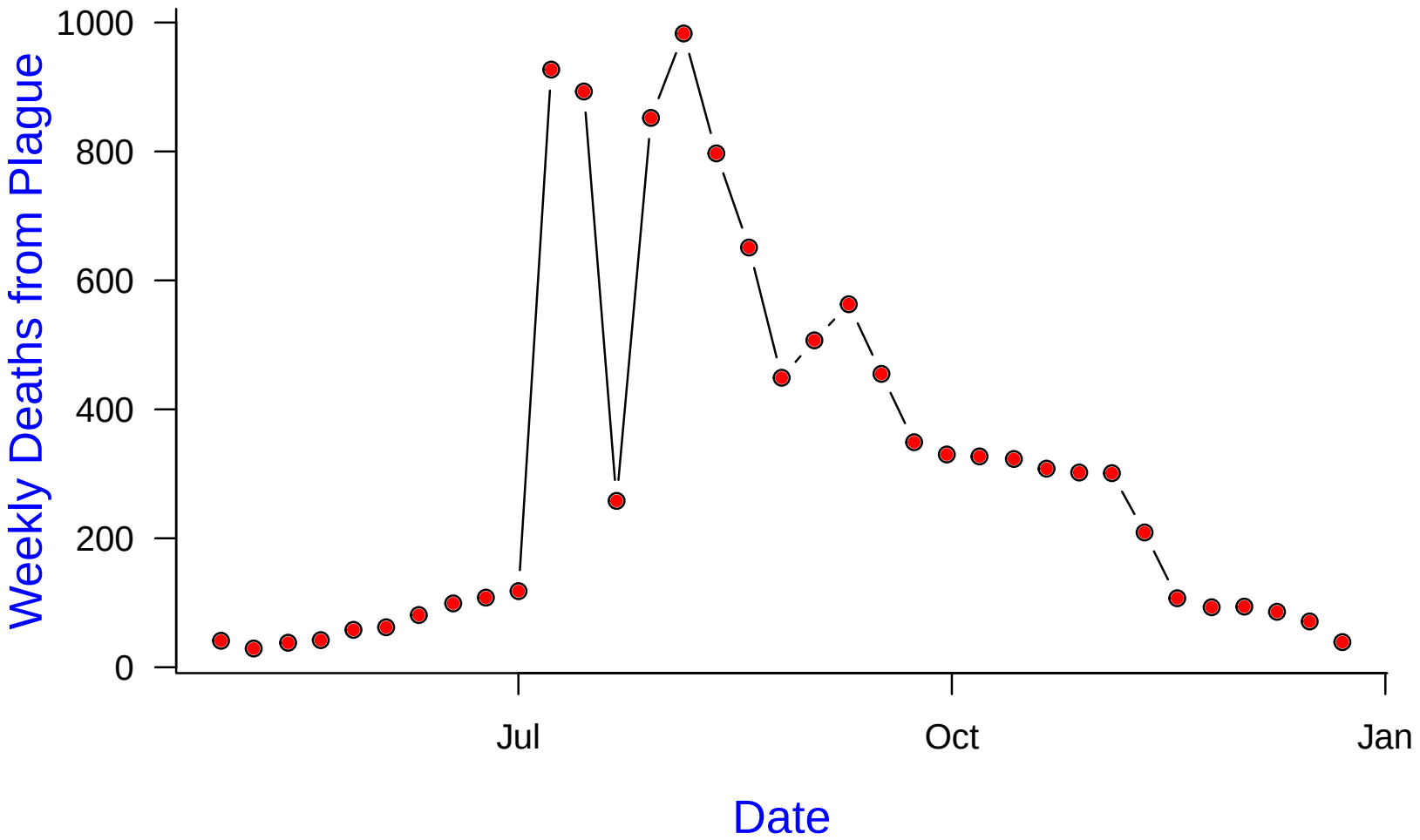
The Great Plague of London, 1665



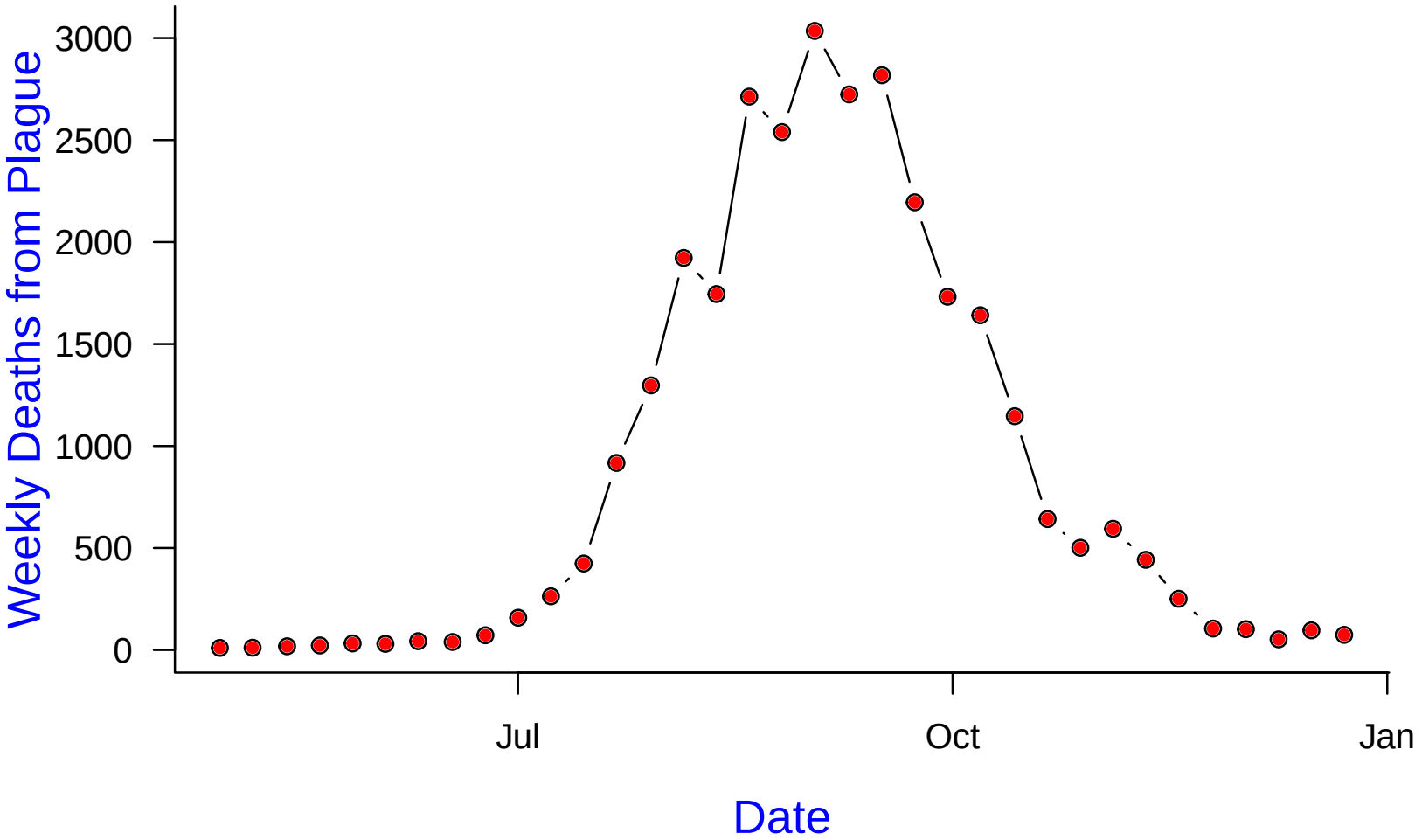
The Great Plague of London, 1665



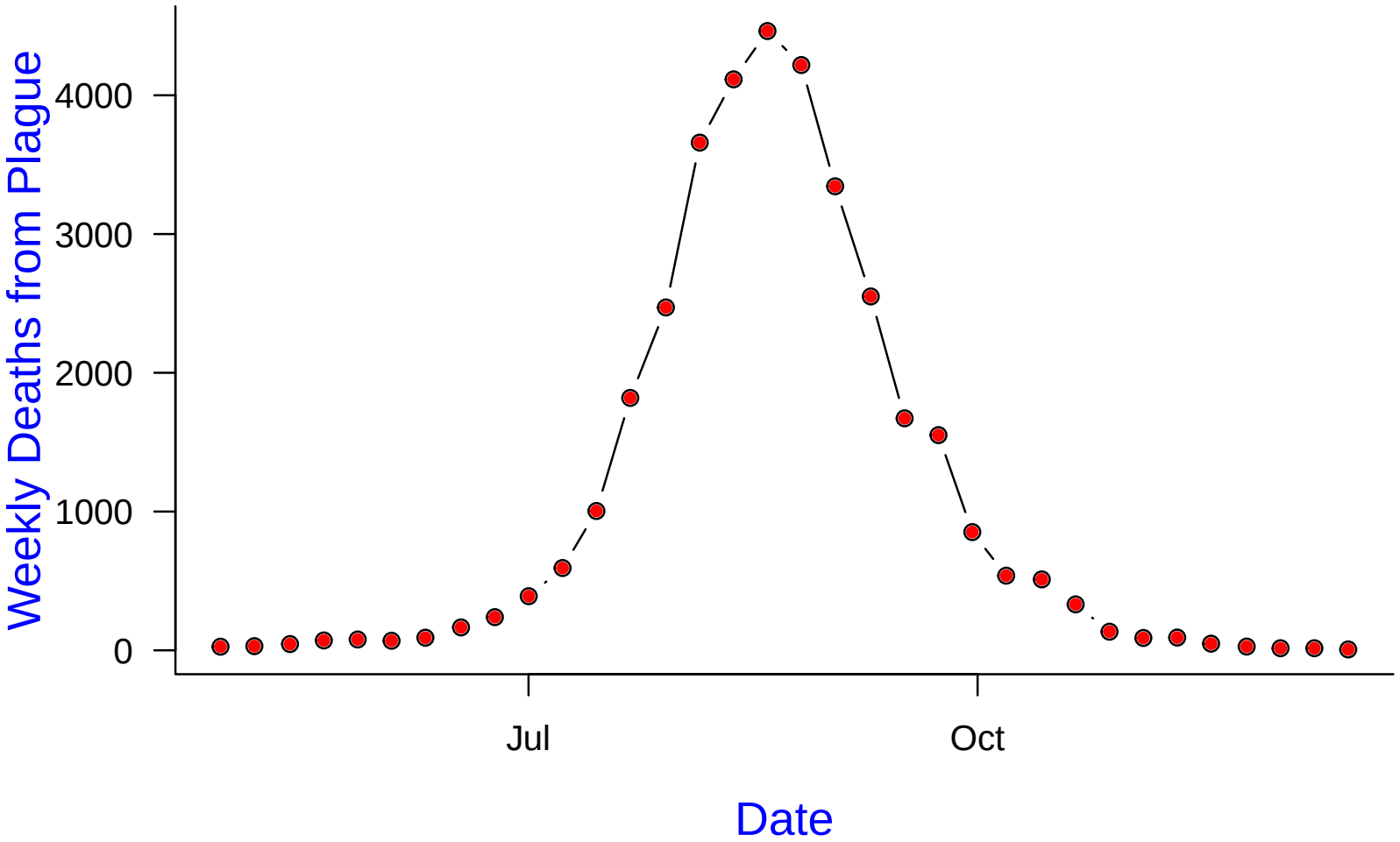
London Plague of 1593



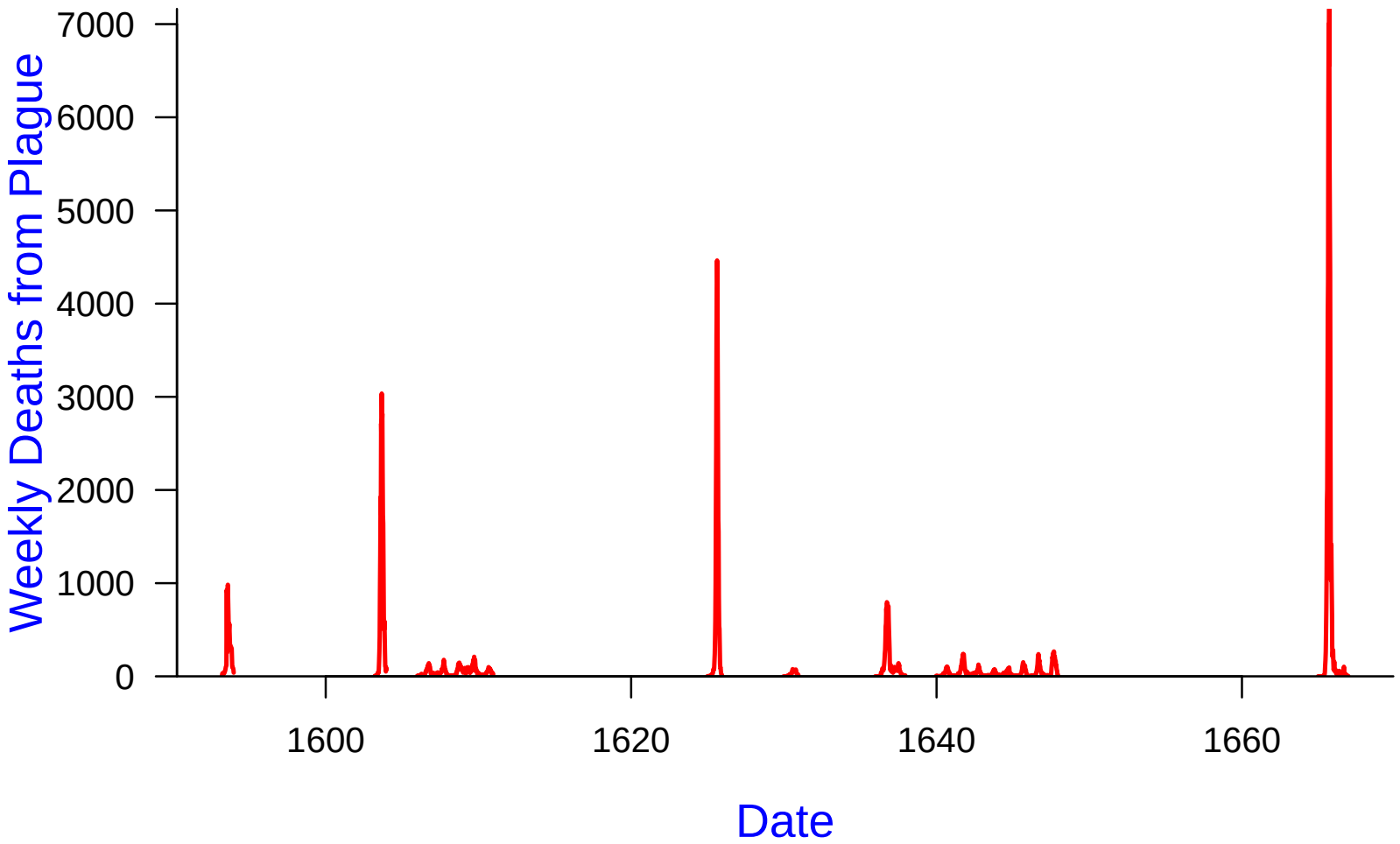
London Plague of 1603



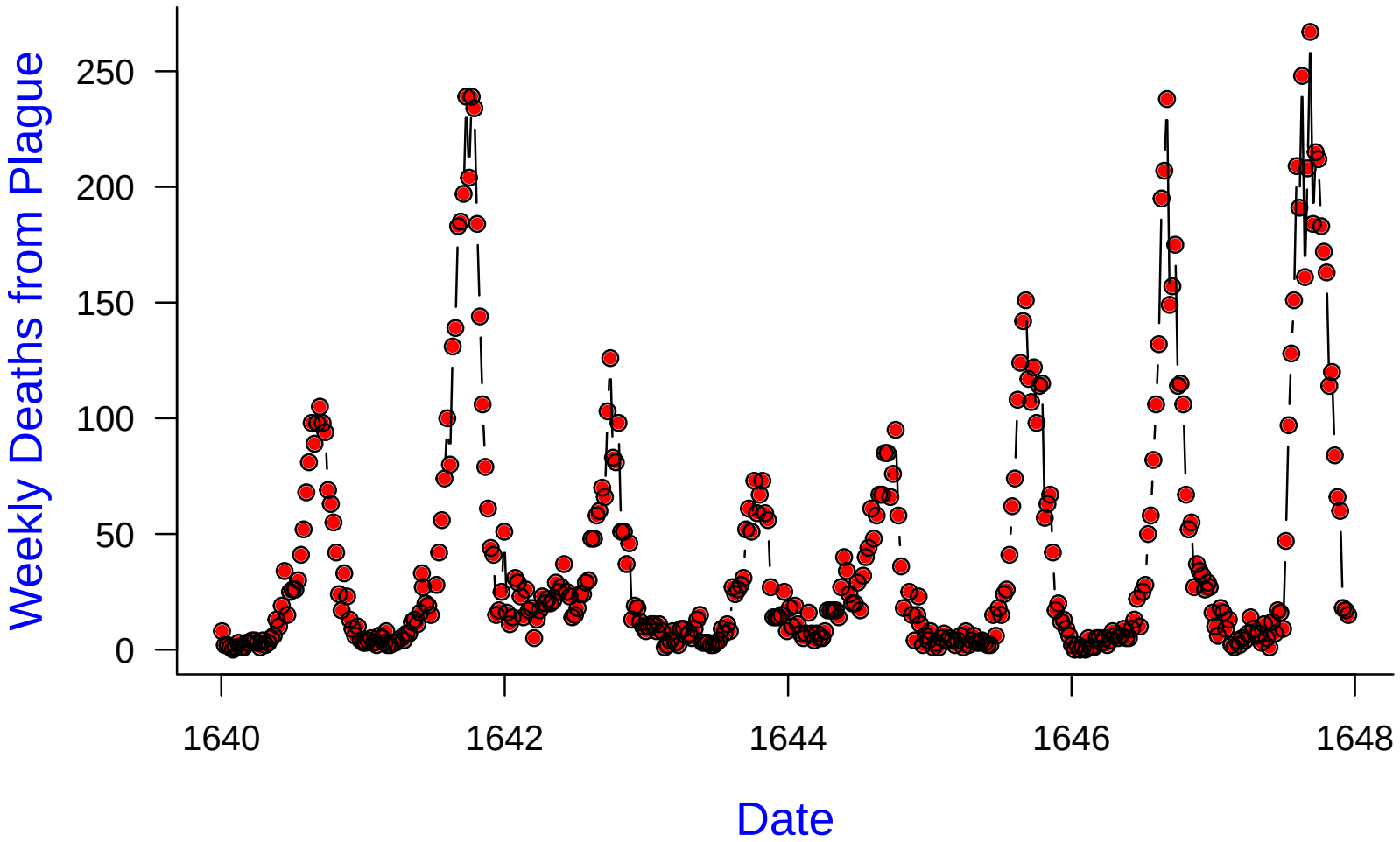
London Plague of 1625



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...

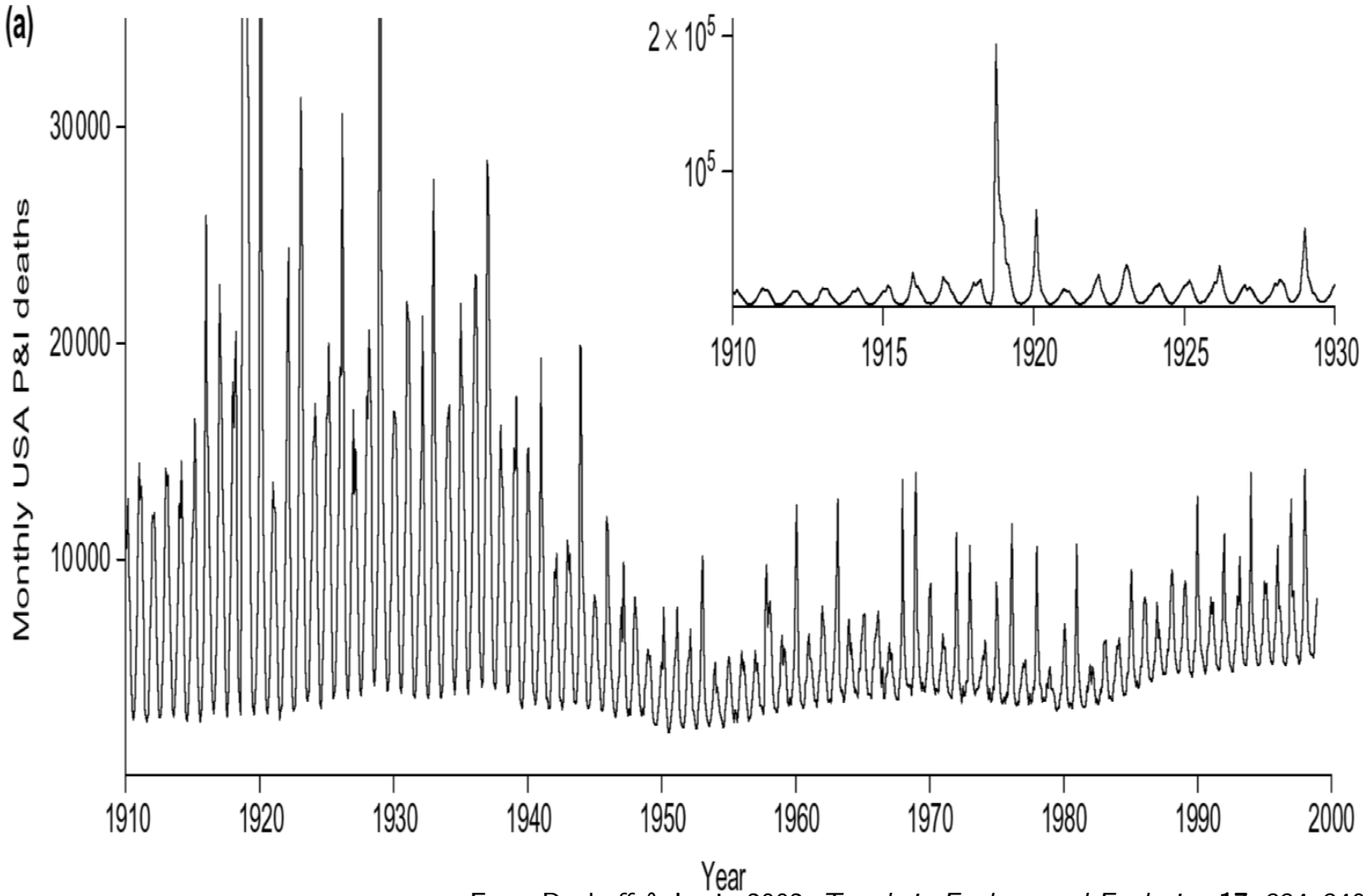
Visualization of spatial structure of Great Plague

- 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

Visualization of entire course of the Great Plague

- What happenned 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.

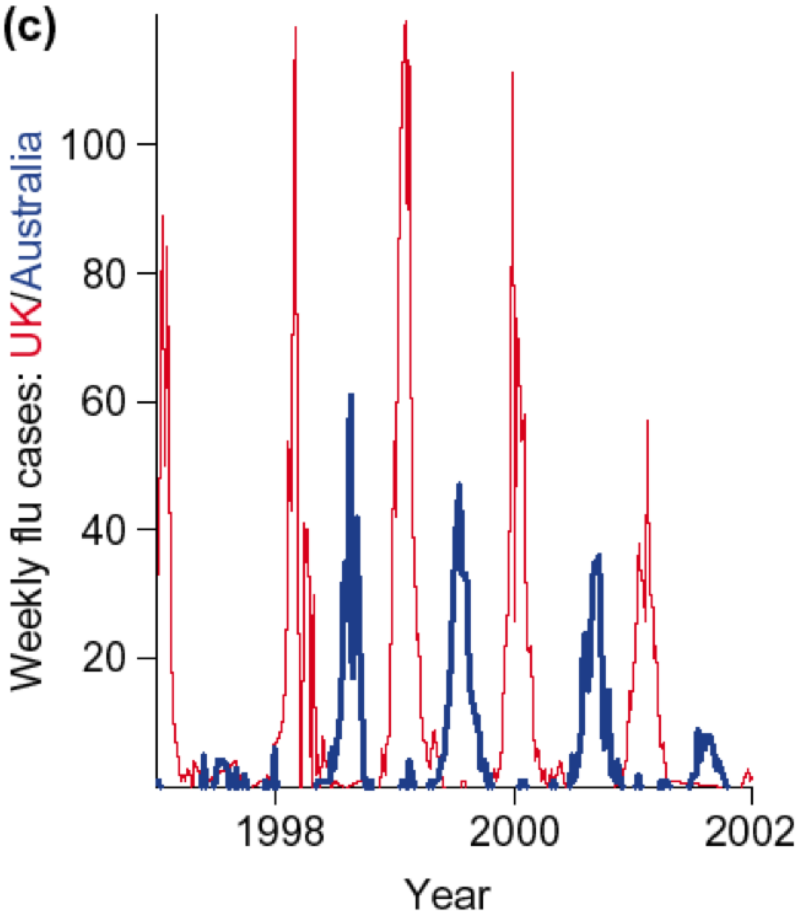
P&I mortality in U.S.A., 1910–1998



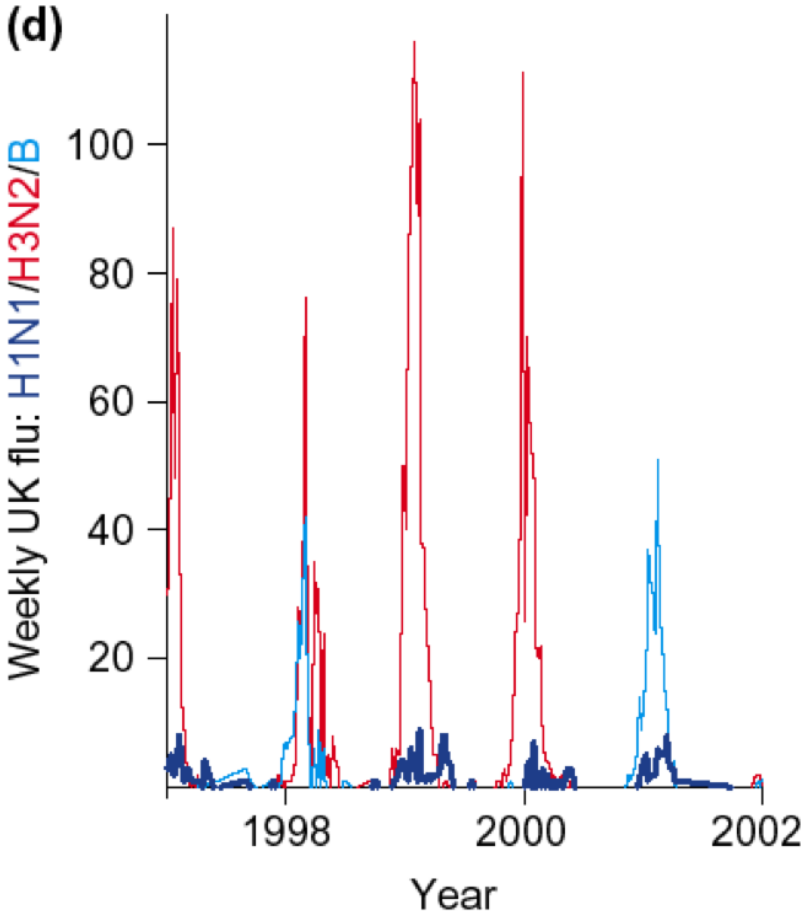
Earn, Dushoff & Levin 2002, *Trends in Ecology and Evolution* **17**, 334–340

Influenza Incidence Patterns (lab confirmed)

Geographic Patterns



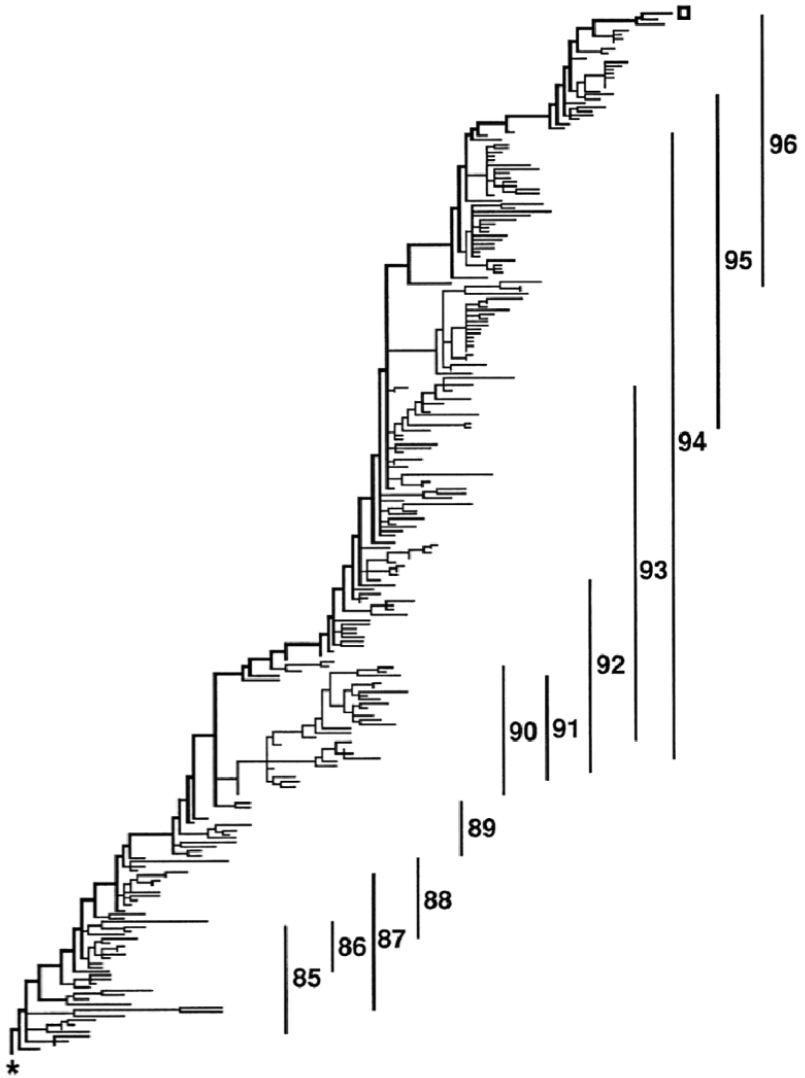
Types and Subtypes



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

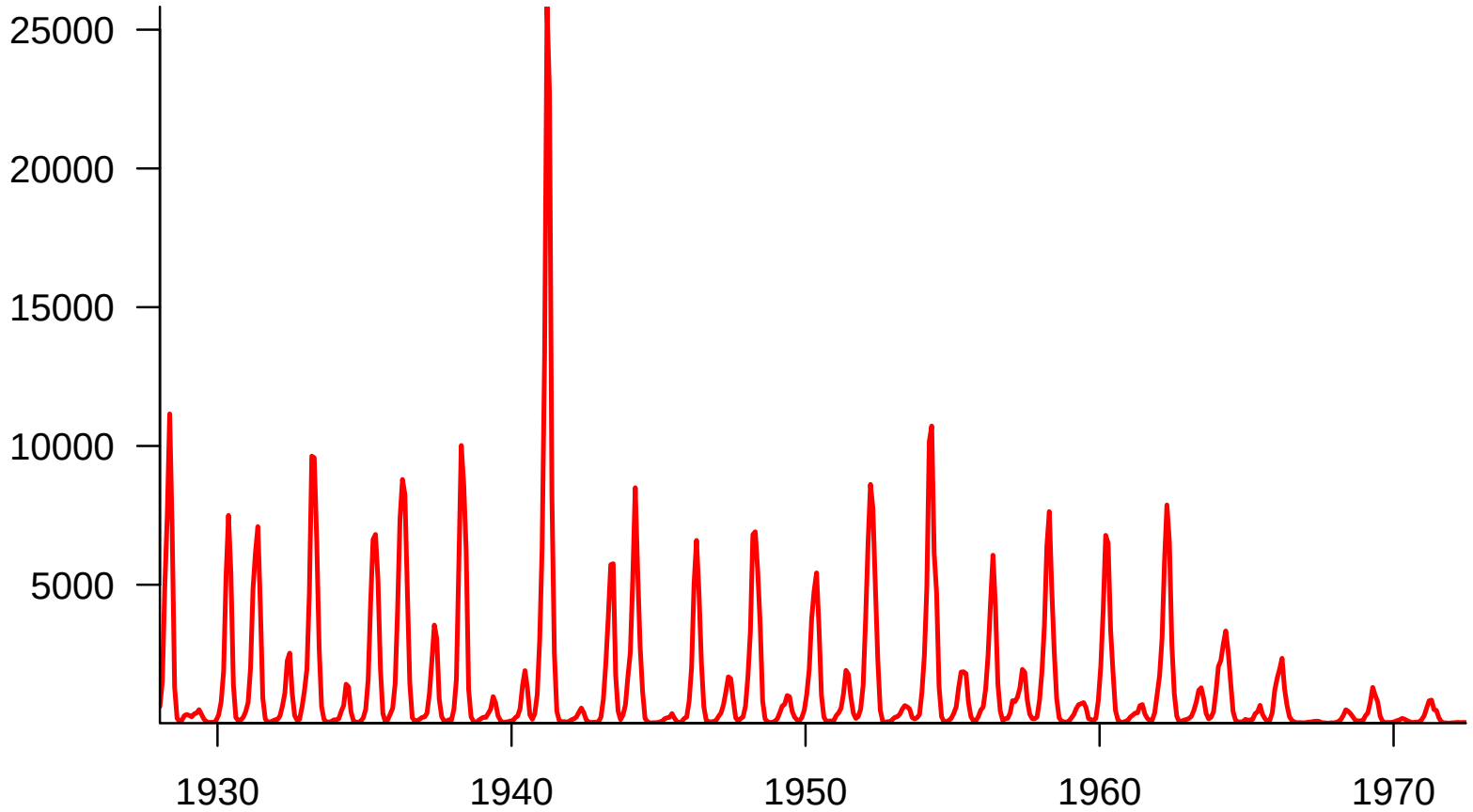
Influenza Evolution

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



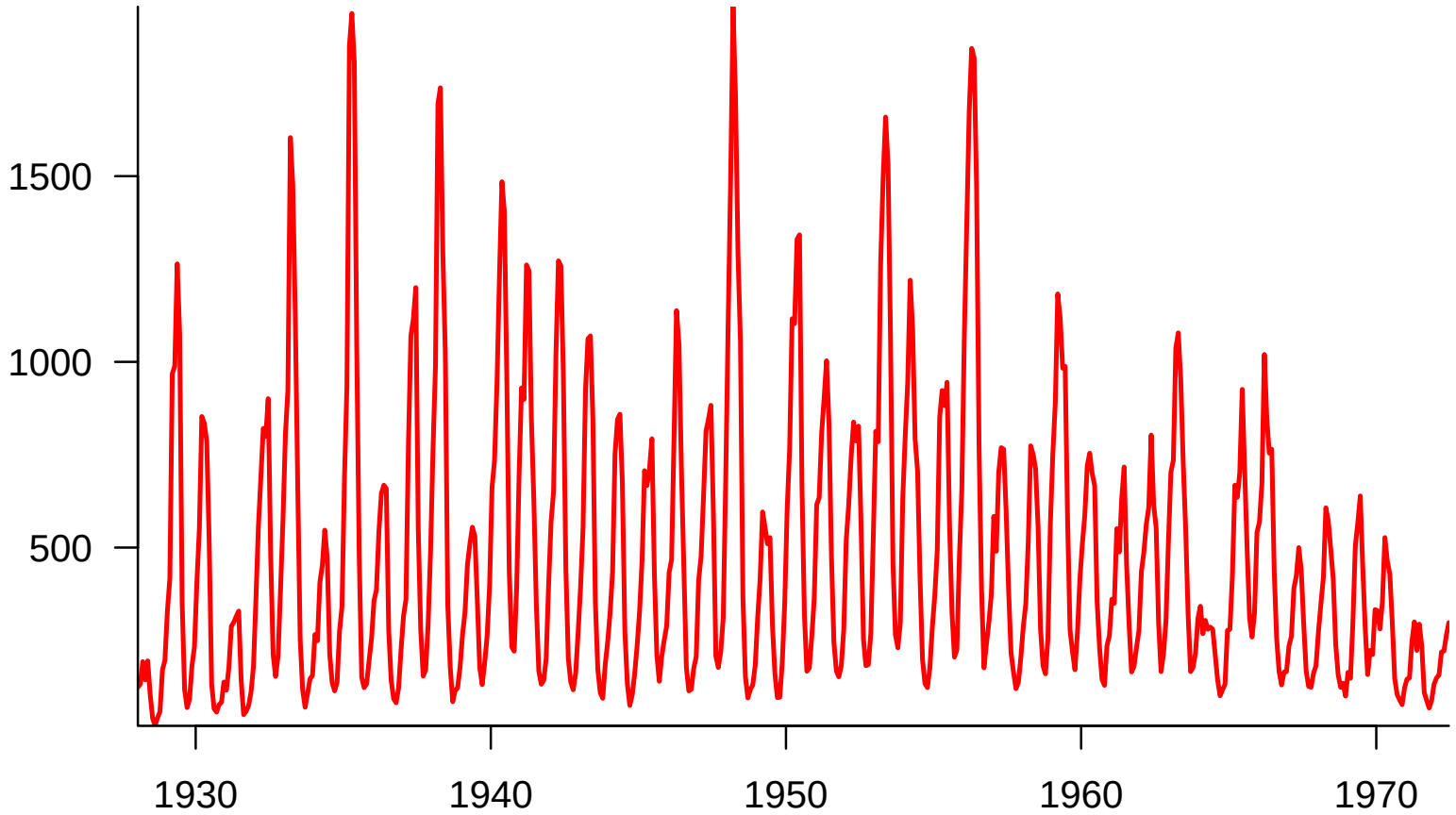
Measles in New York City, 1928–1972

Monthly Cases



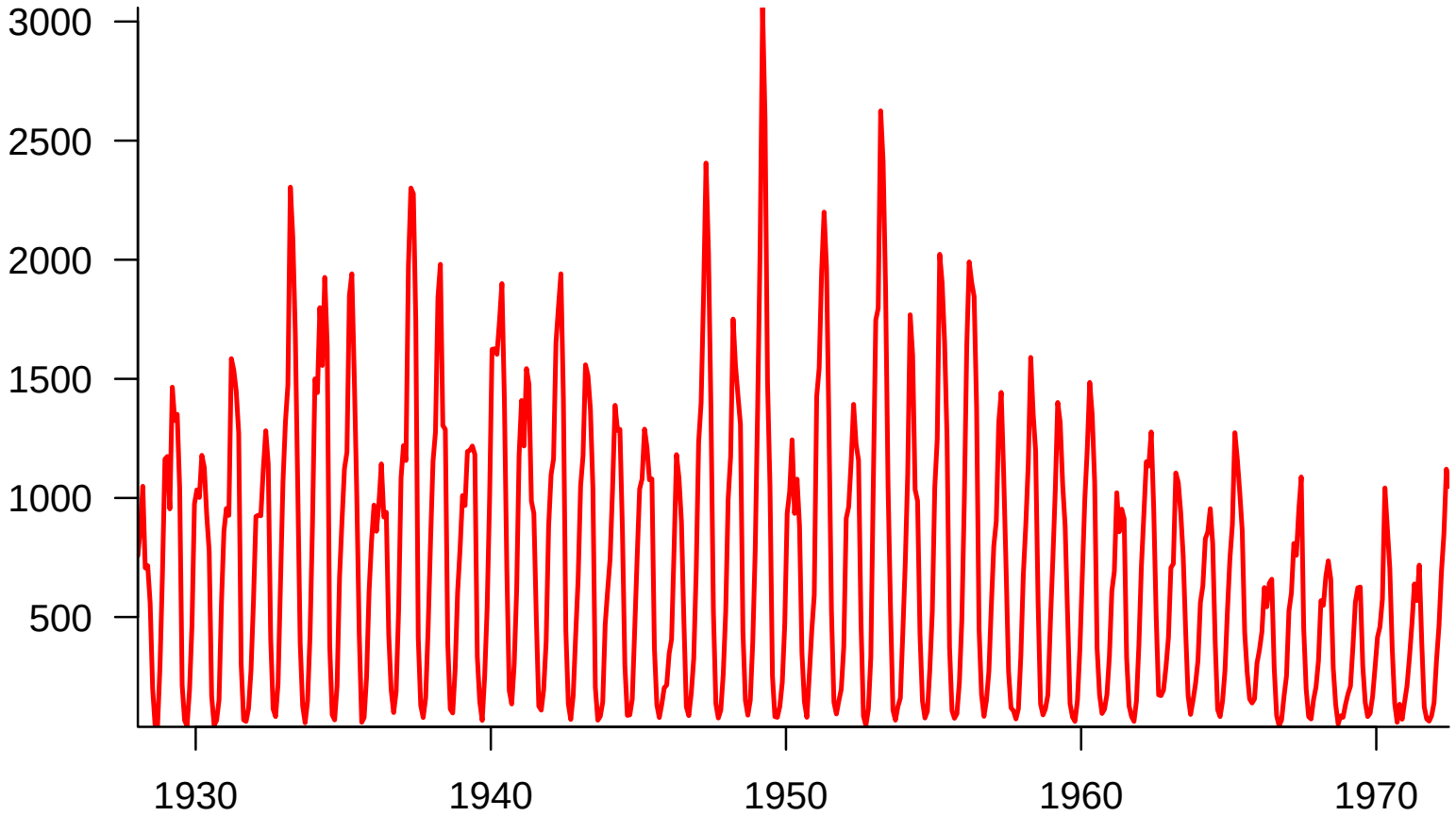
Mumps in New York City, 1928–1972

Monthly Cases

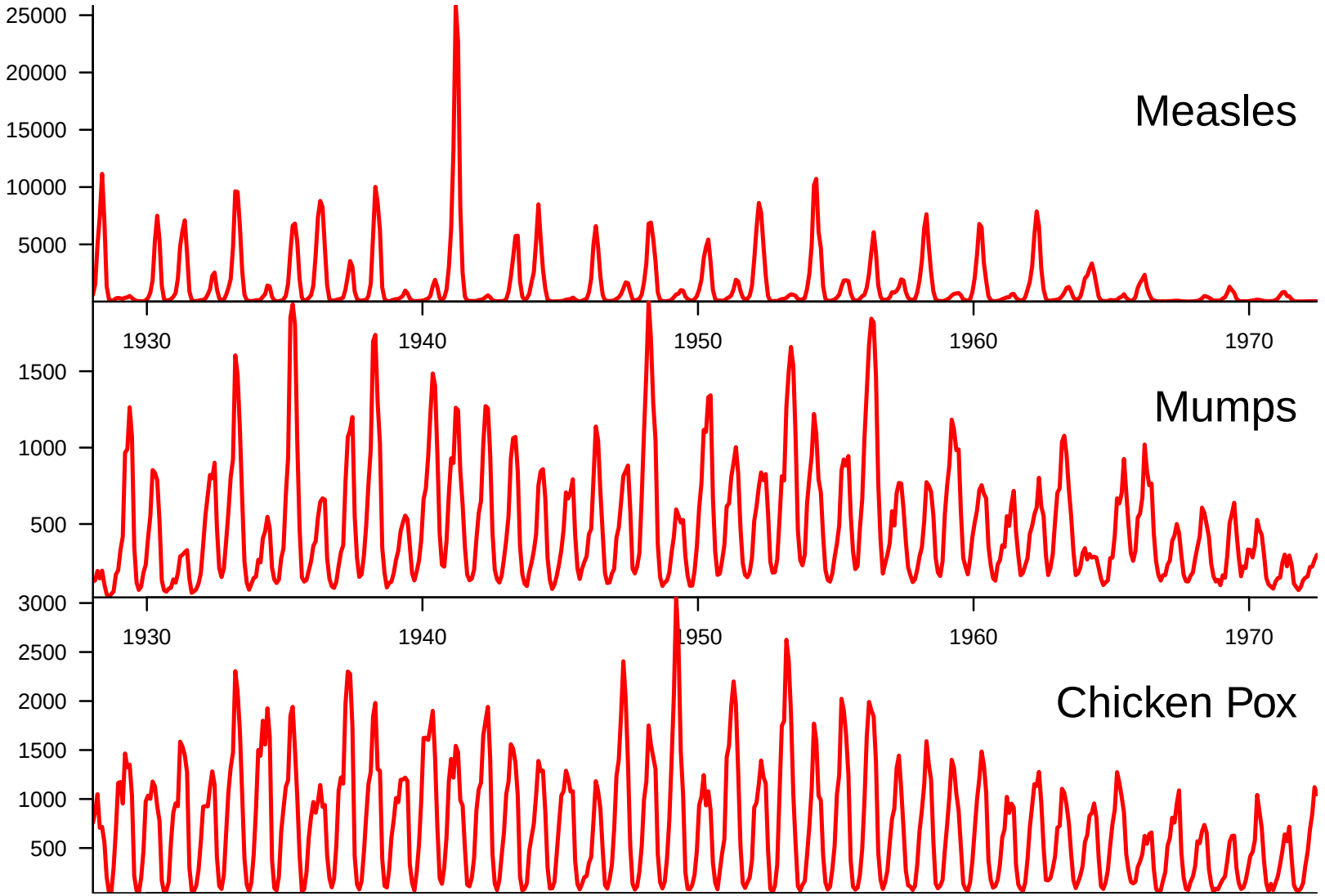


Chicken Pox in New York City, 1928–1972

Monthly Cases

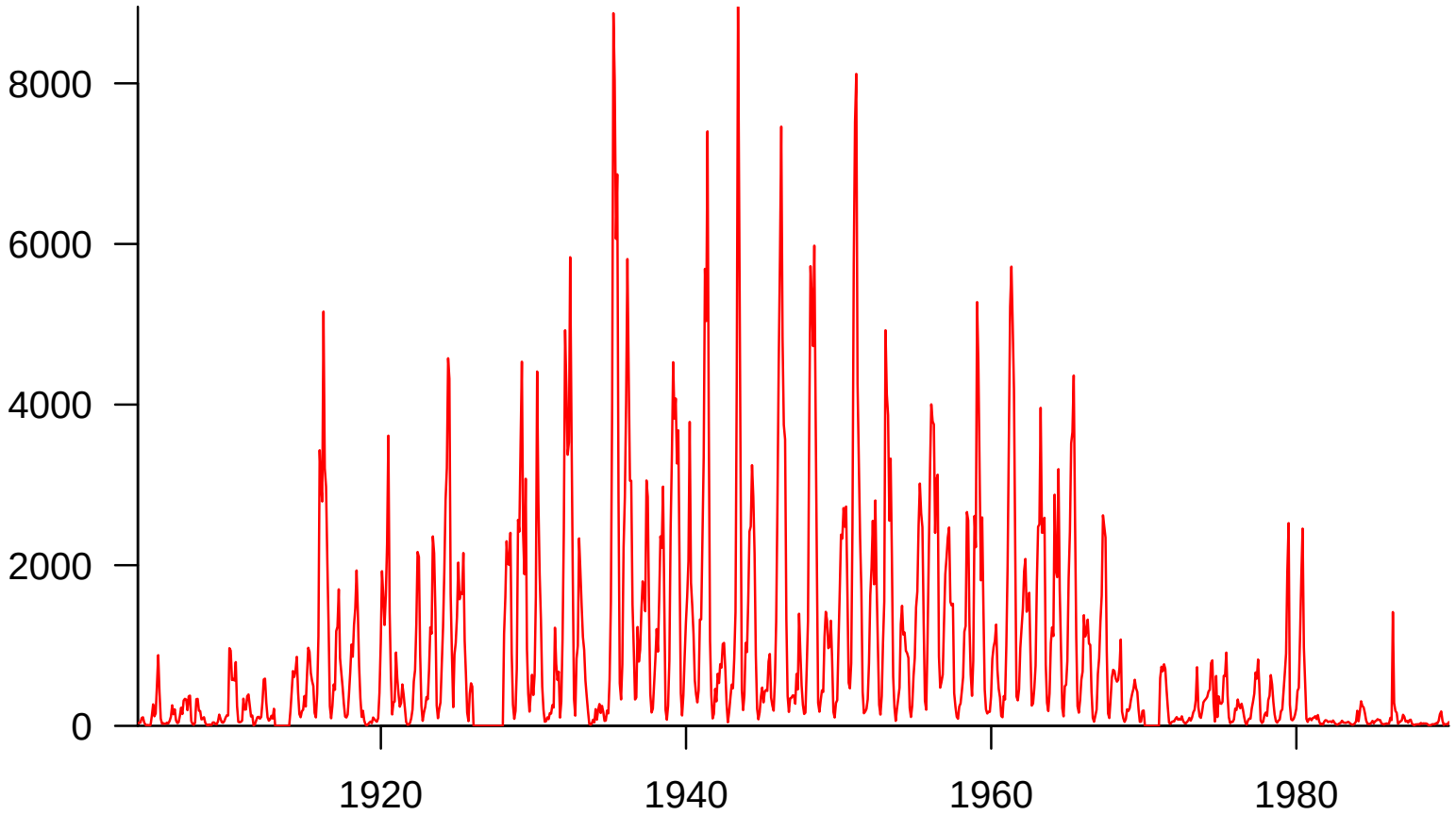


Childhood diseases in New York City, 1928–1972



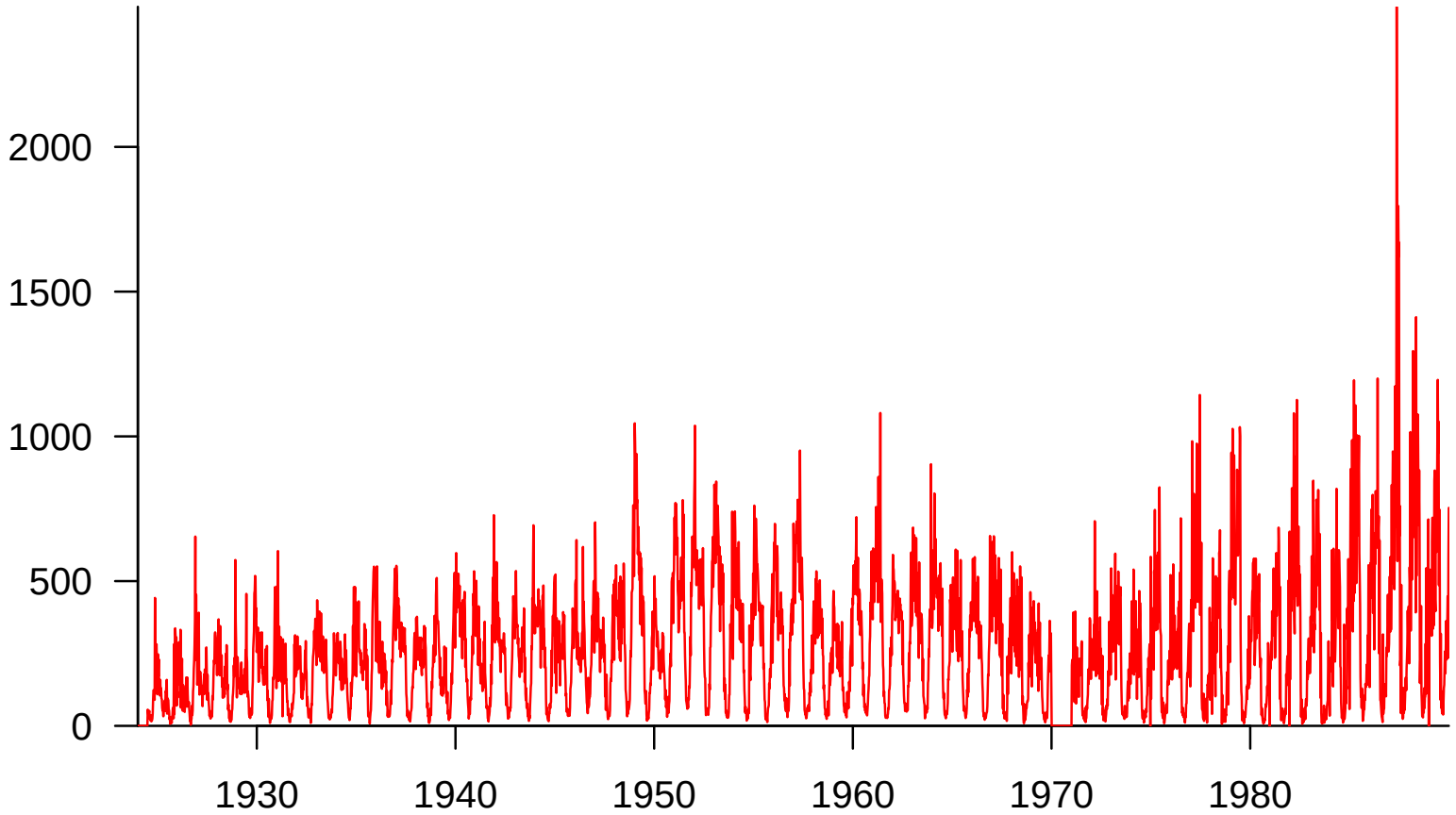
Measles in Ontario, 1904–1989

Monthly Cases



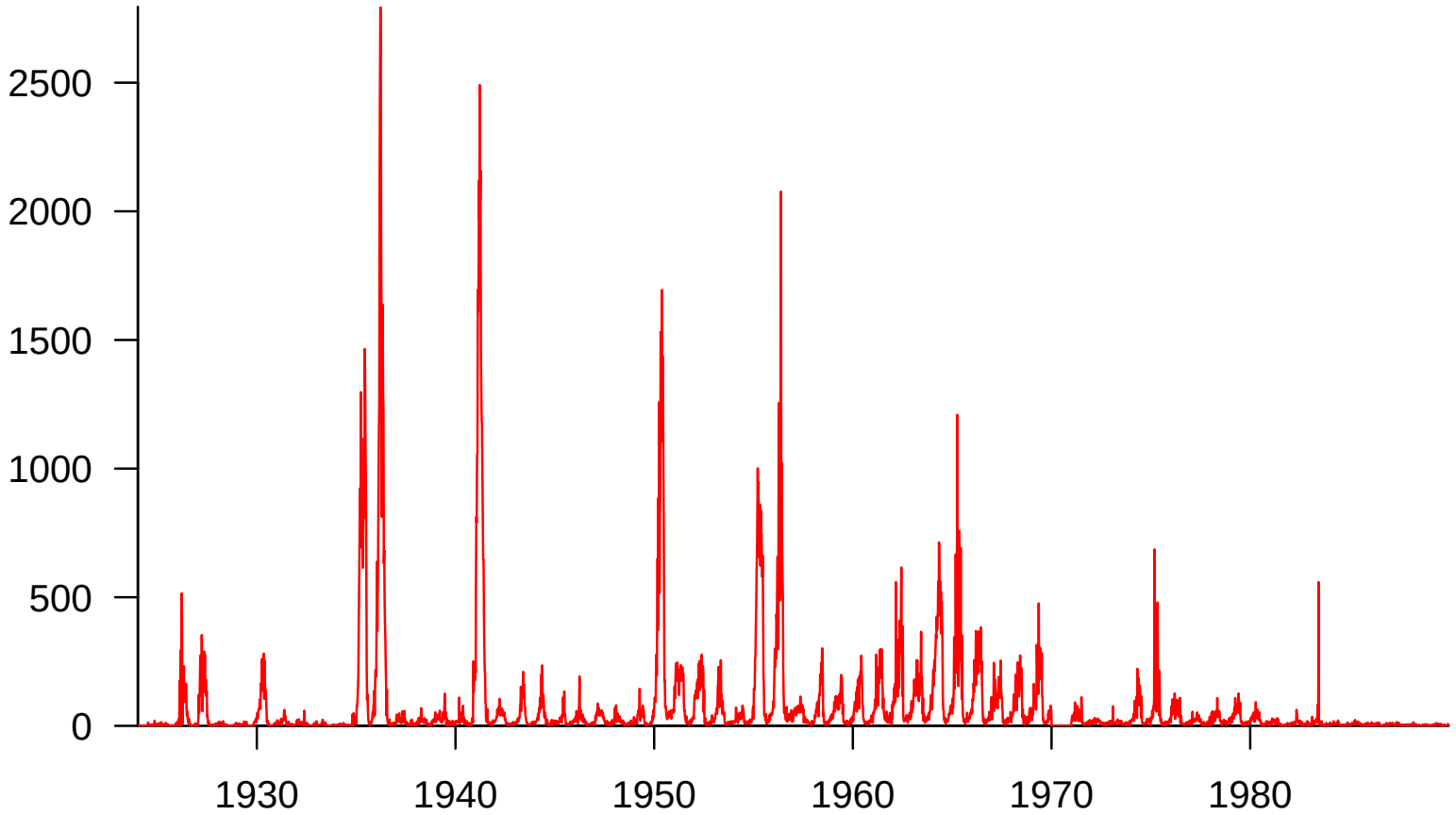
Chicken Pox in Ontario, 1924–1989

Monthly Cases



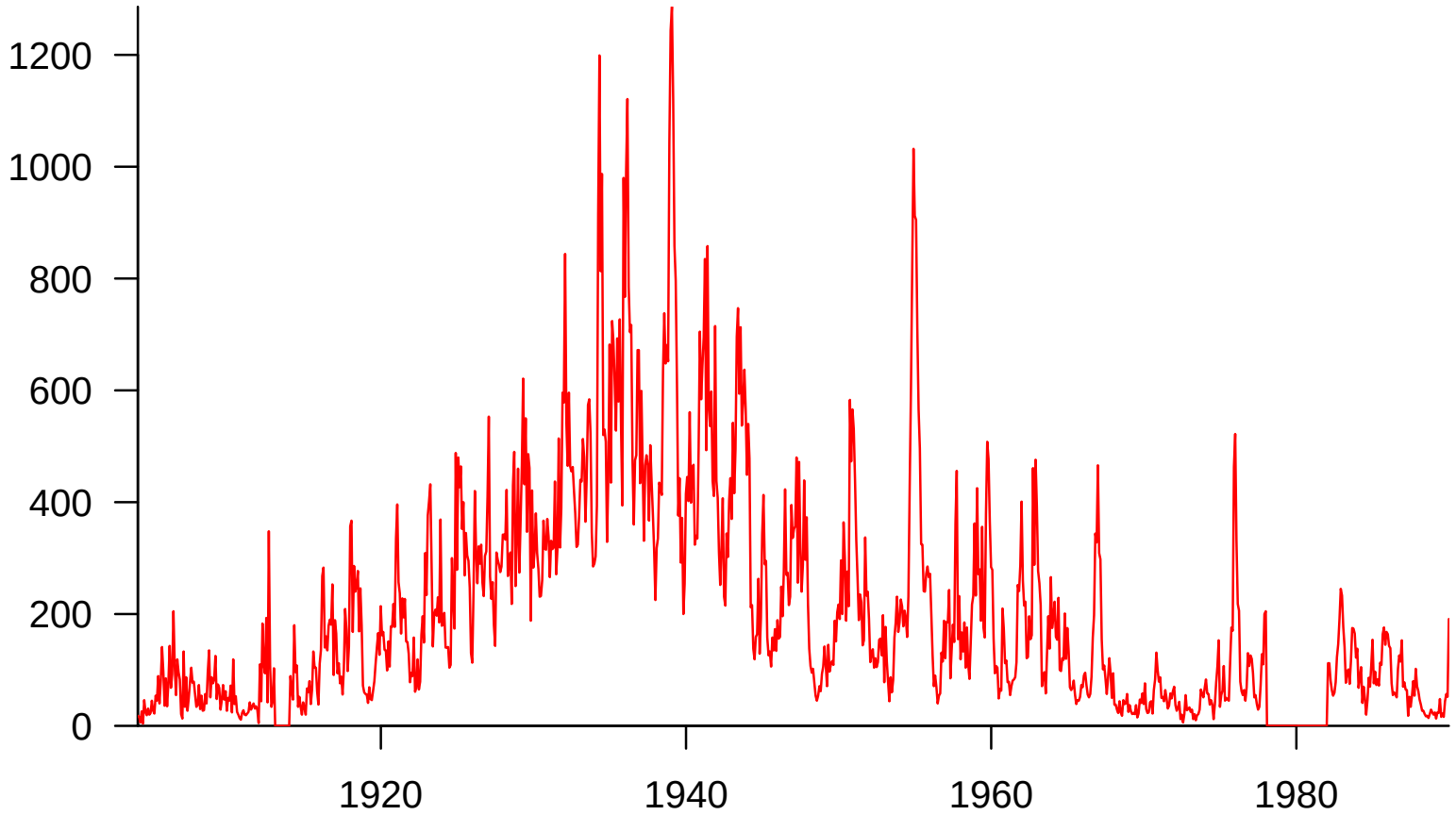
Rubella in Ontario, 1924–1989

Weekly Cases

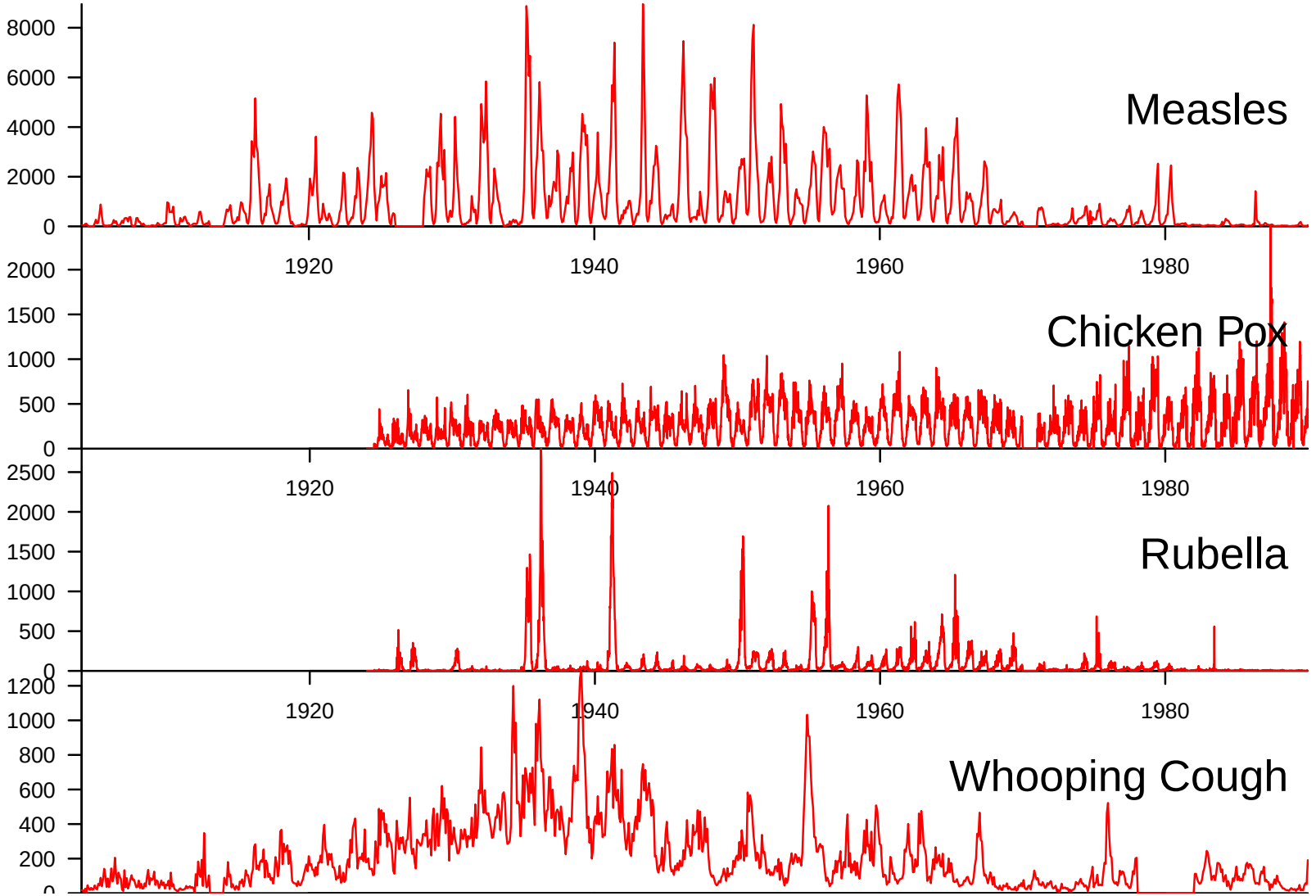


Whooping Cough in Ontario, 1904–1989

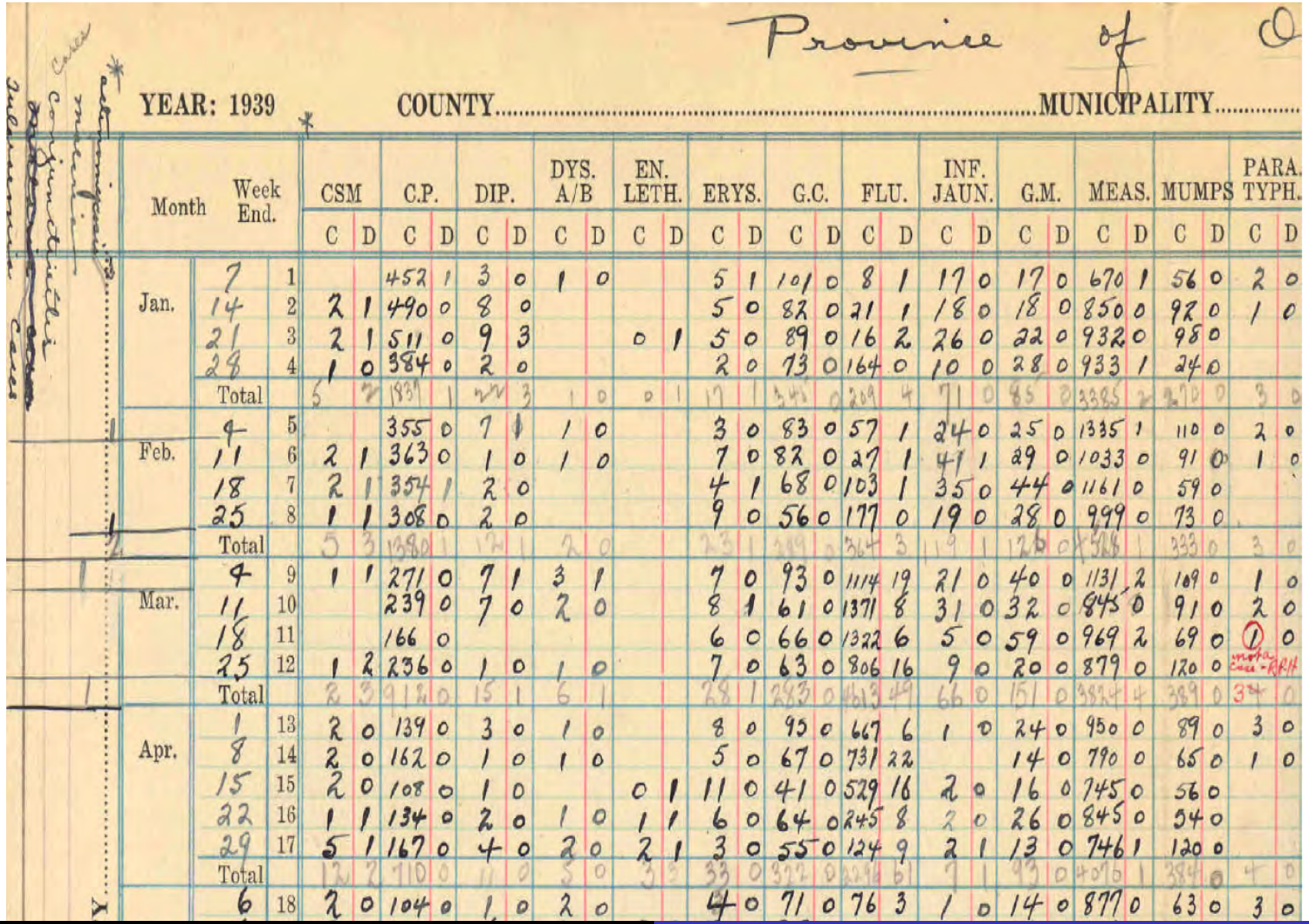
Monthly Cases



Childhood diseases in Ontario, 1904–1989



Ontario Disease Notification Data



Province of O

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

Month	Week End.		CSM C	CSM D	C.P. C	C.P. D	DIP. C	DIP. D	DYS. A/B C	DYS. A/B D	EN. LETH. C	EN. LETH. D	ERYS. C	ERYS. D	G.C. C	G.C. D	FLU. C	FLU. D	INF. JAUN. C	INF. JAUN. D	G.M. C	G.M. D	MEAS. C	MEAS. D	MUMPS C	MUMPS D	PARA. TYPH. C	PARA. TYPH. D
	7	1			452	1	3	0	1	0			5	1	101	0	8	1	17	0	17	0	670	1	56	0	2	0
Jan.	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	1839	1	22	3	1	0	0	1	17	1	345	0	209	4	71	0	85	2	3385	2	270	0	3	0
	4	5			355	0	7	1	1	0			3	0	83	0	57	1	24	0	25	0	1335	1	110	0	2	0
Feb.	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	56	0	177	0	19	0	28	0	999	0	73	0		
	Total		5	3	1380	1	12	1	2	0			23	1	289	0	364	3	119	1	126	0	4528	1	333	0	3	0
	4	9	1	1	271	0	7	1	3	1			7	0	93	0	1114	19	21	0	40	0	1131	2	109	0	1	0
Mar.	11	10			239	0	7	0	2	0			8	1	61	0	1371	8	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		
	Total		2	3	912	0	15	1	6	1			28	1	283	0	4613	49	66	0	151	0	3824	4	389	0	34	0
	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
Apr.	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	710	0	11	0	5	0	3	2	33	0	322	0	2294	61	7	1	93	0	4076	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 Whooping 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	
	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT	WK	MT
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 8													9						9	
11 15			3										11						14	
12 22			60										34						94	
13 29			2	67				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	

All Historical Canadian Infectious Disease Data

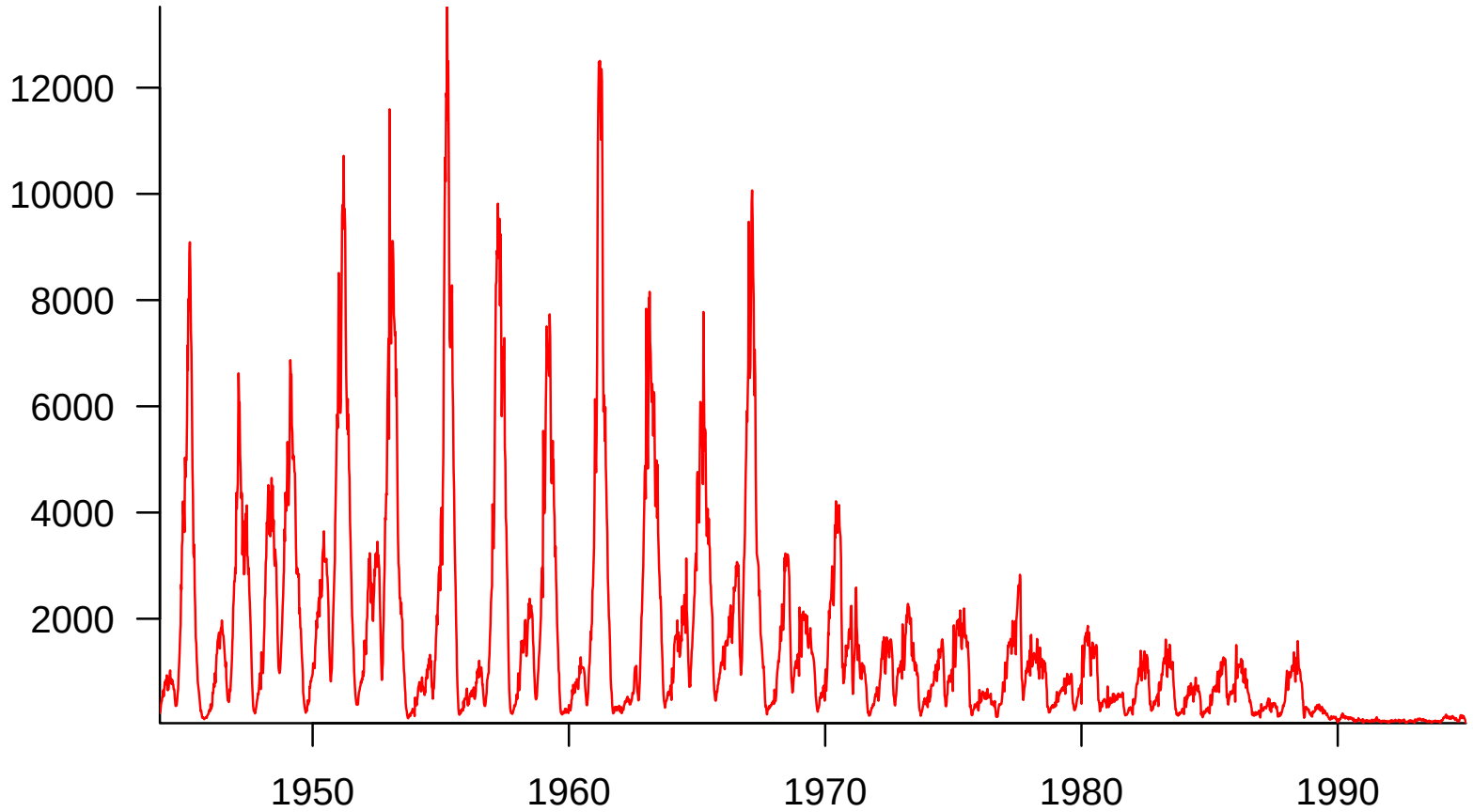
https://canmod.net/digitization/

Recurrent epidemics of childhood infections

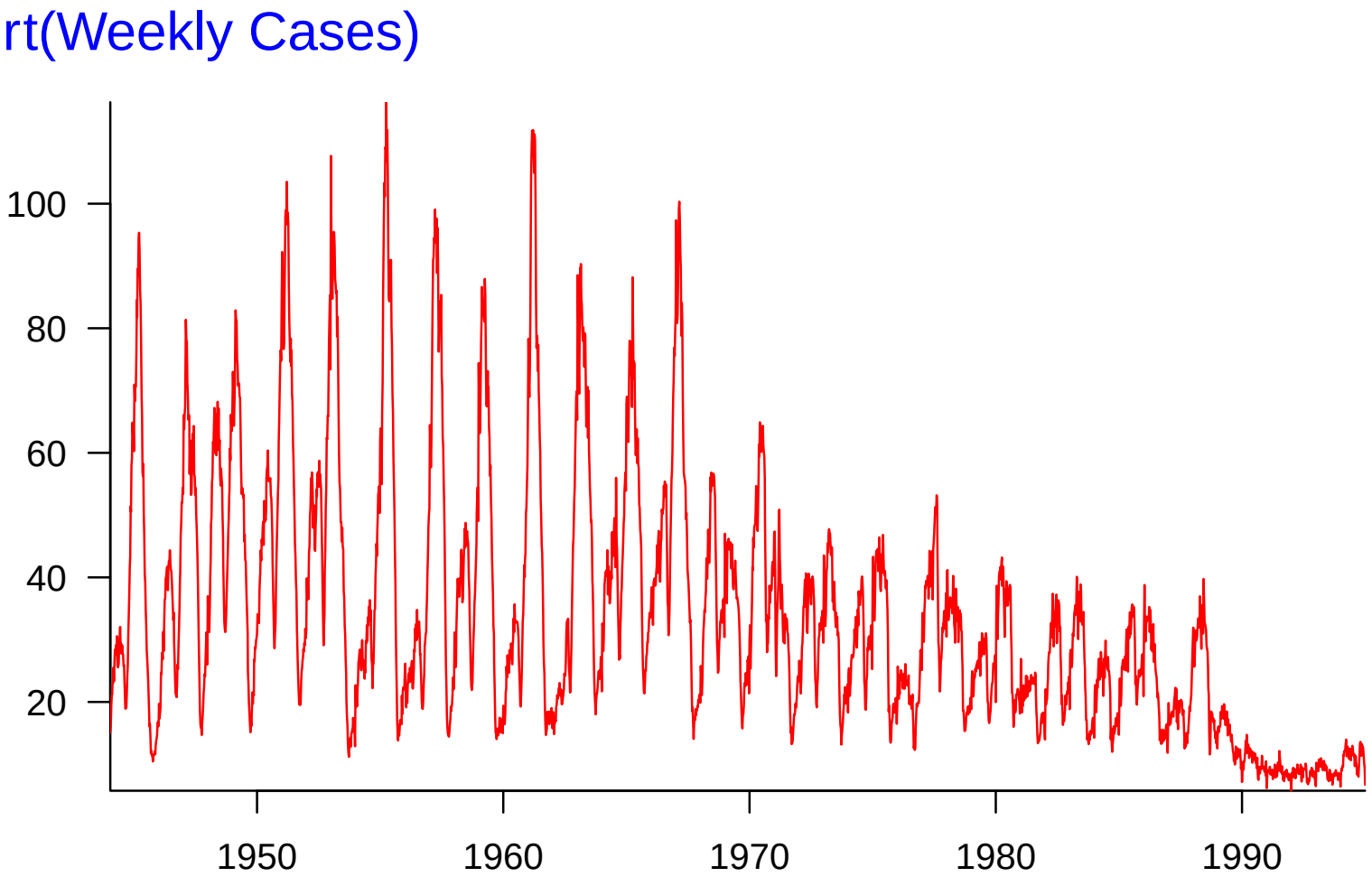
- Childhood diseases in New York City, 1928–1972
- Childhood diseases in Ontario, 1904–1989

Measles incidence in England and Wales, 1944–1995

Weekly Cases



Measles incidence in England and Wales, 1944–1995



Why study measles epidemics?

- $\sim 140,000$ annual 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!

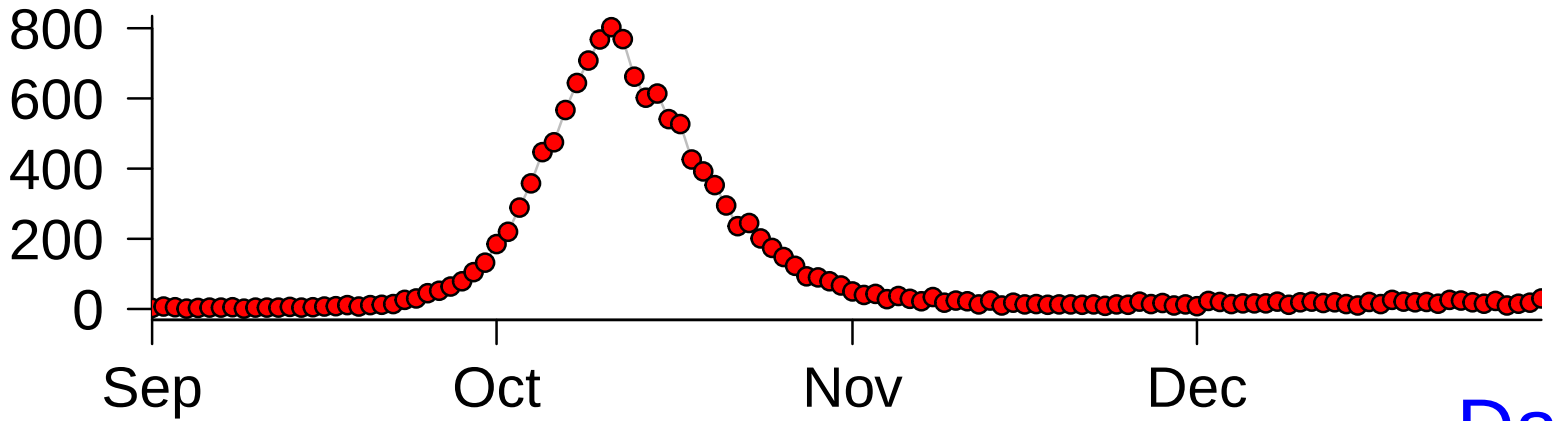
Modelling population dynamics of childhood infections

- 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.

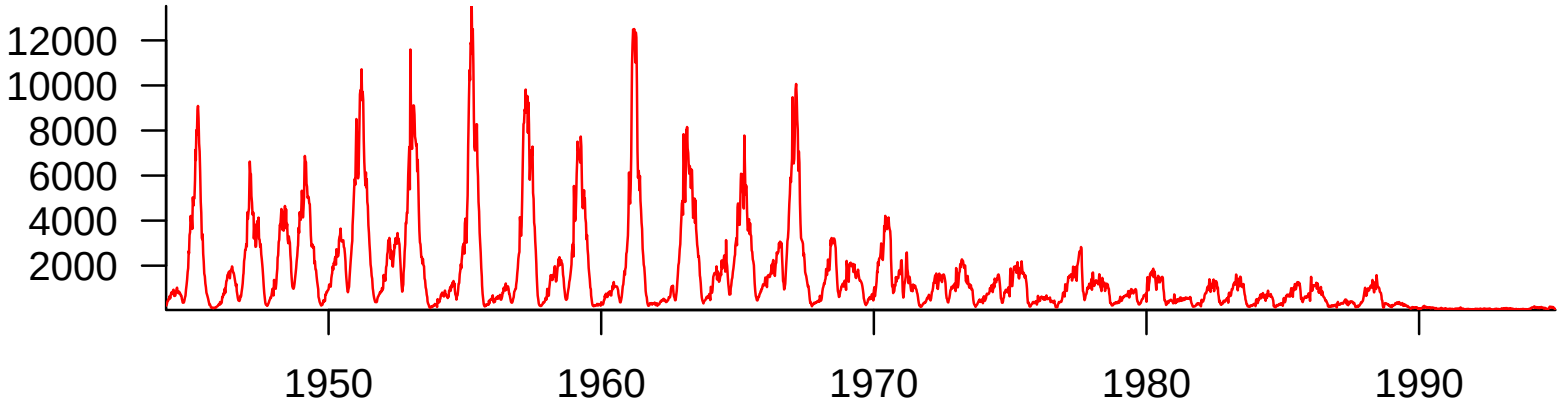
Epidemic Data Analysis

Time Plots of Temporal Epidemic Patterns

1918 P&I

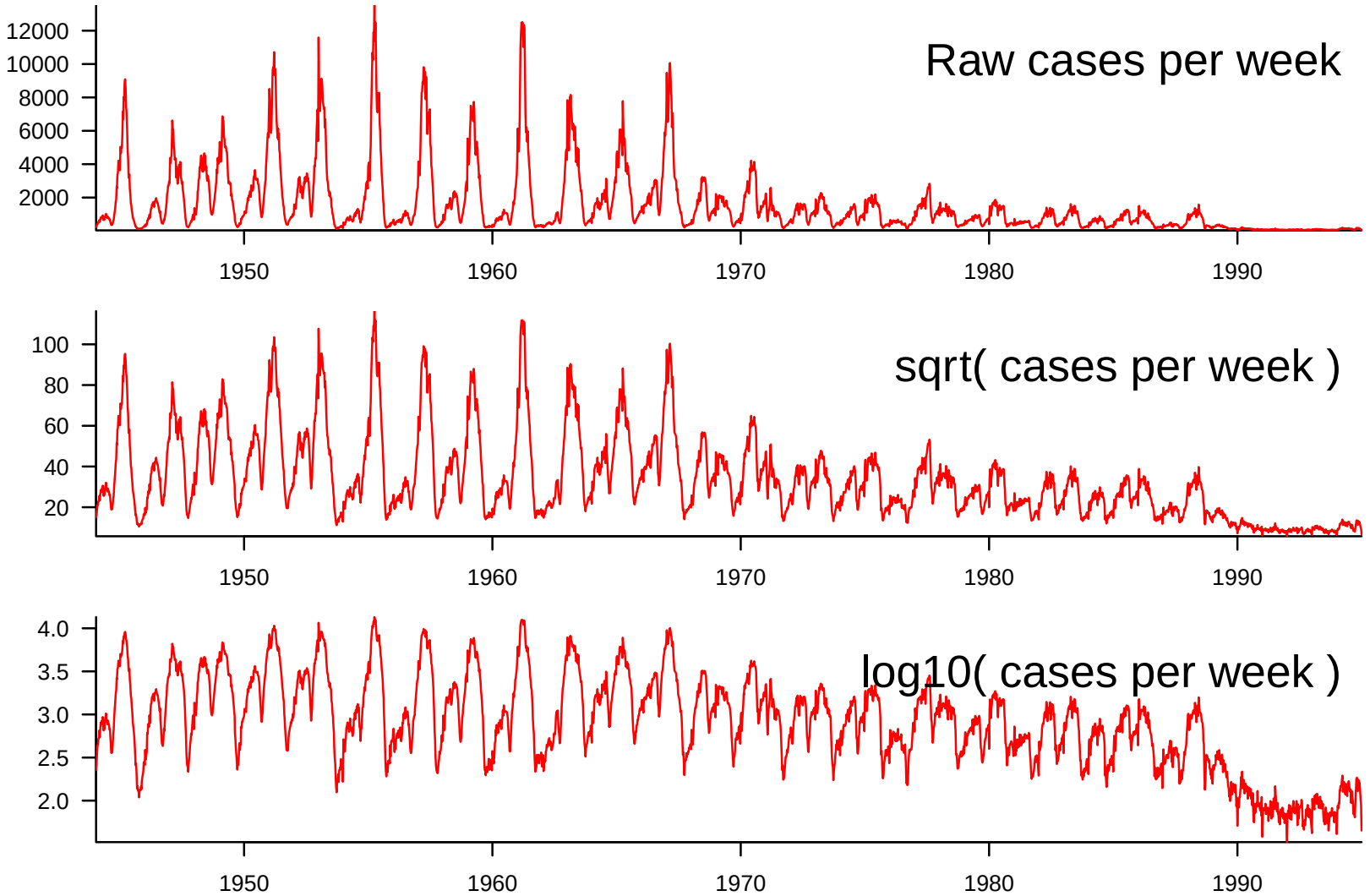


Weekly Measles in England and Wales



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:*

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

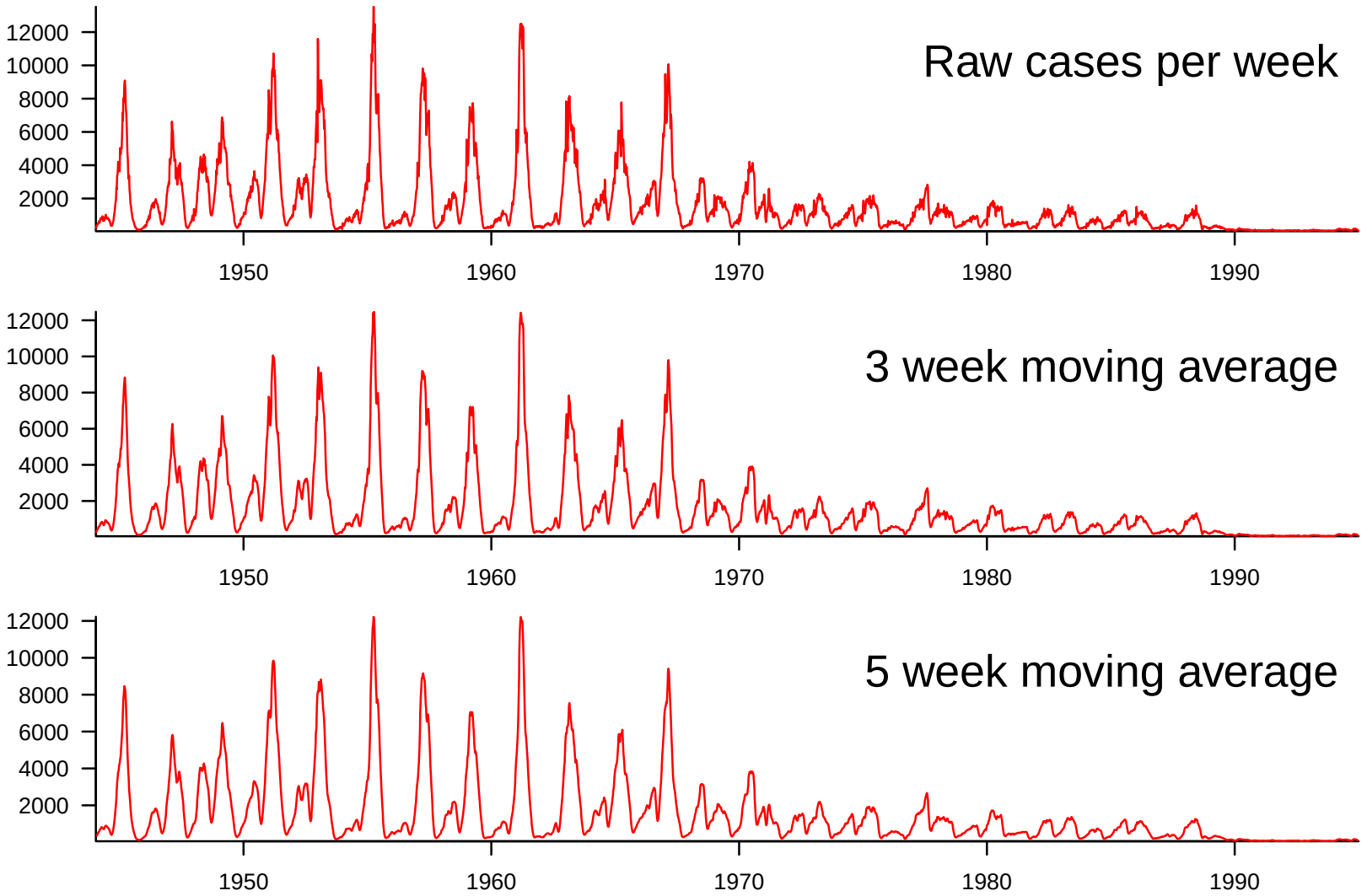
  - Replace original data points x_t with averages of nearby points.

- *Linear filter:*

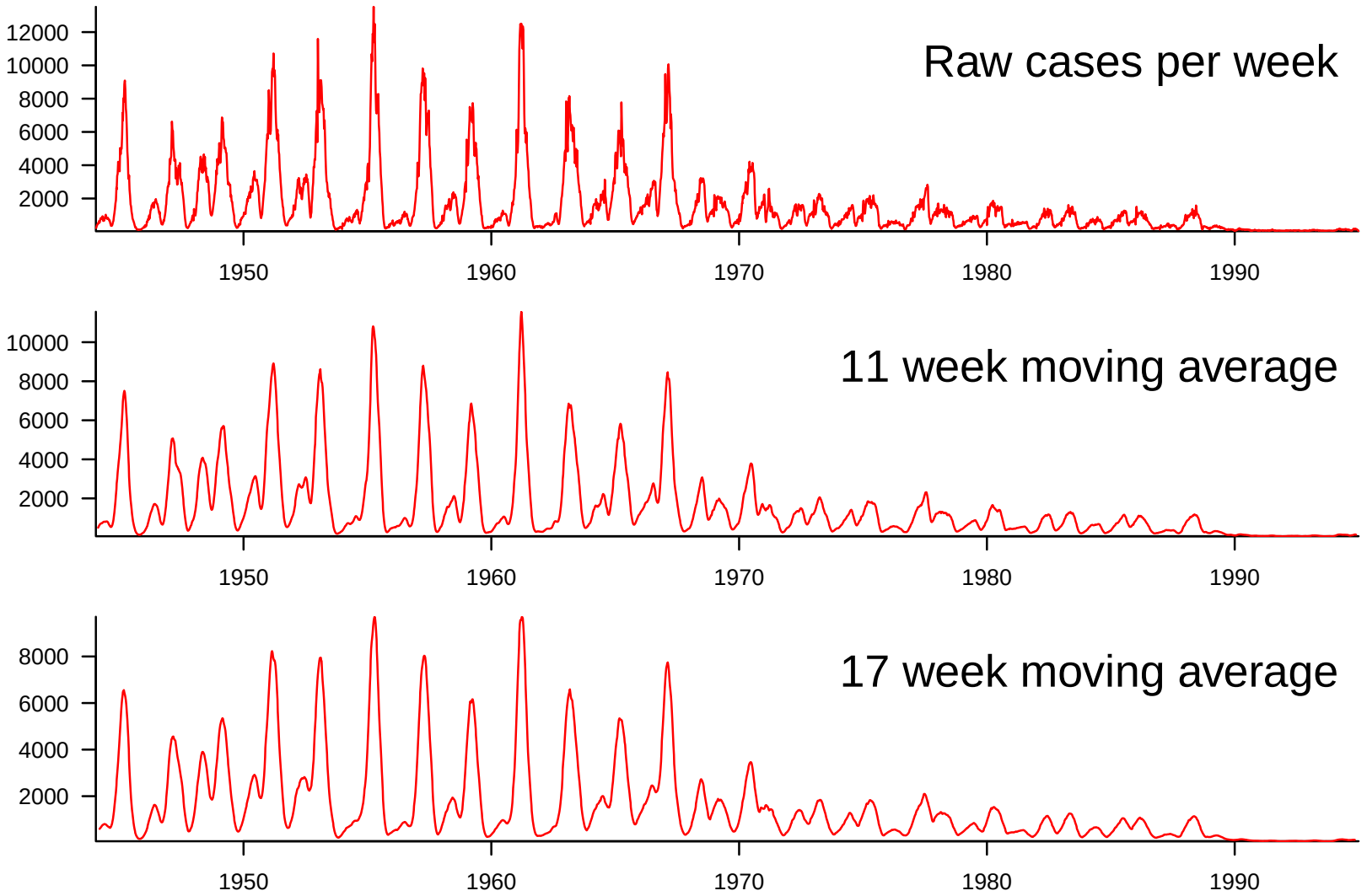
$$x_t \to \sum_{i=-\infty}^{\infty} \lambda_i x_{t+i}$$

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

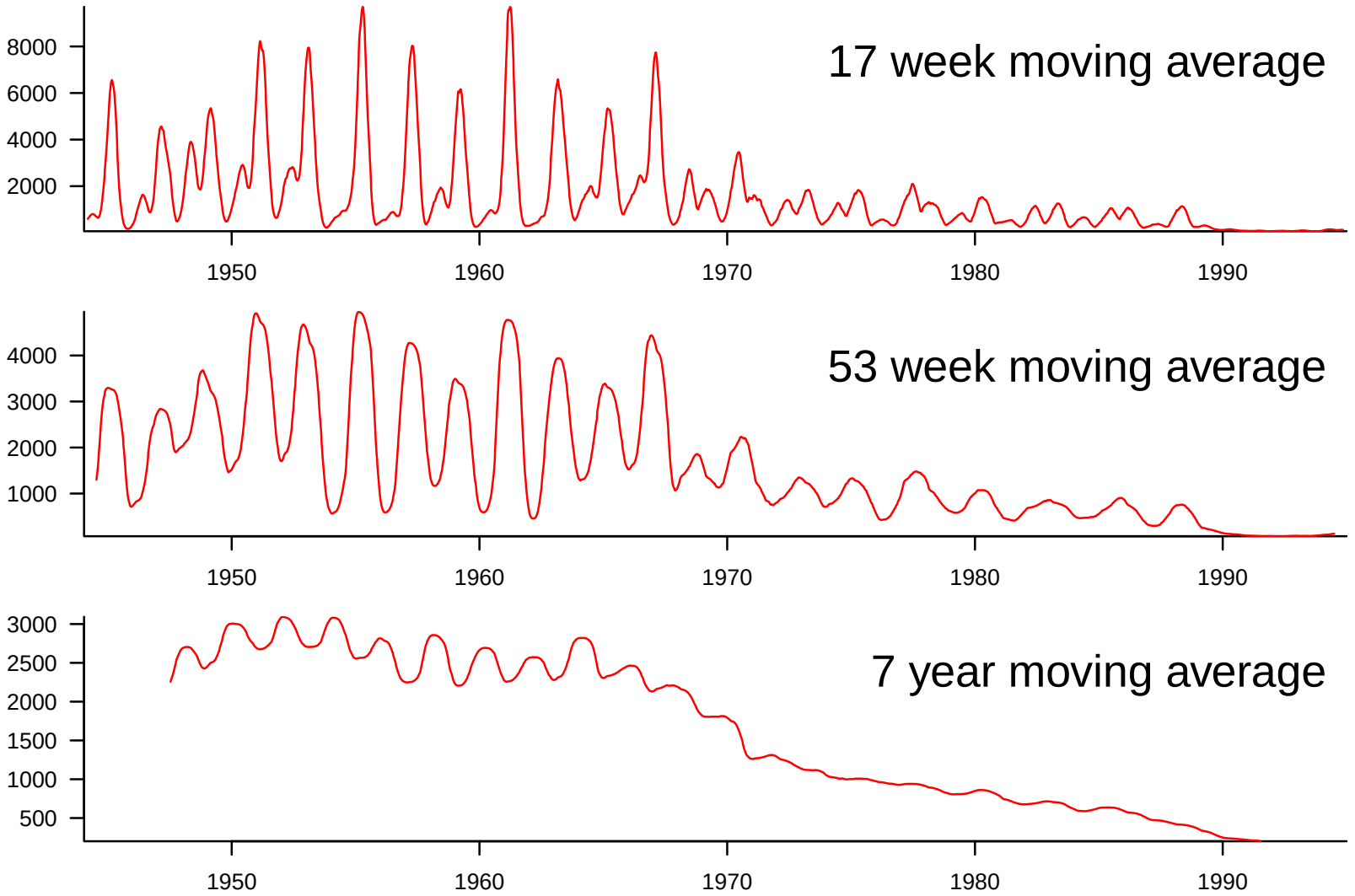
Times Plots of Smoothed Data



Times Plots of Smoothed Data



Times Plots of Smoothed Data



Correlation

- Recurrent epidemics $\Longrightarrow$ number of cases now is correlated with number of cases in the past and the future.
- Given N pairs of observations of different quantities, $\{(x_i, y_i) : i = 1, \ldots, N\}$, 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 $\{x_t : t = 1, \ldots, N\}$, we can compute the correlation of each observation with the observation k time steps in the future.

- Thus, we consider the pairs of observations $\{(x_t, x_{k+t}) : t = 1, \ldots, N-k\}$ 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.

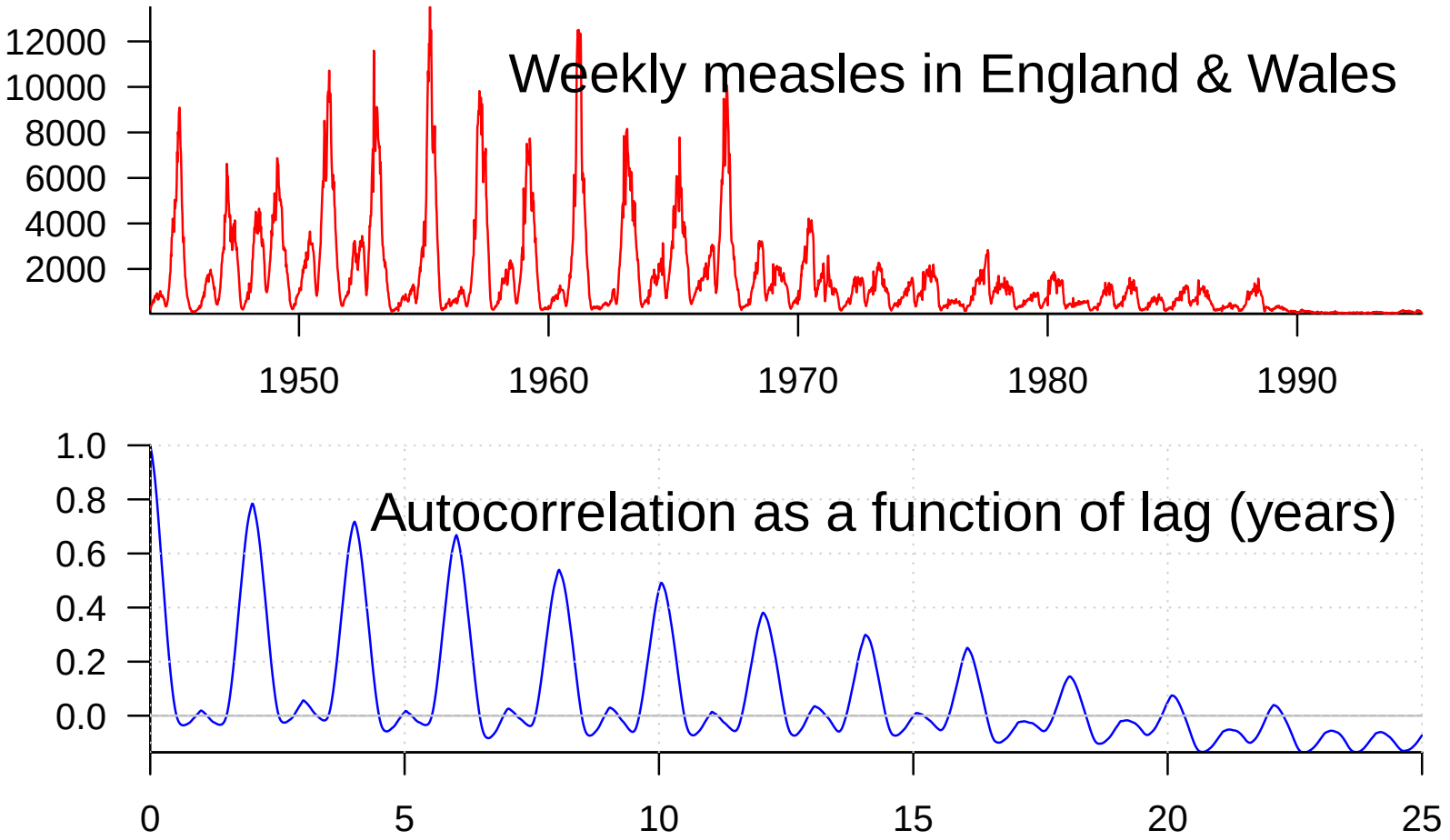
Autocorrelation

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

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

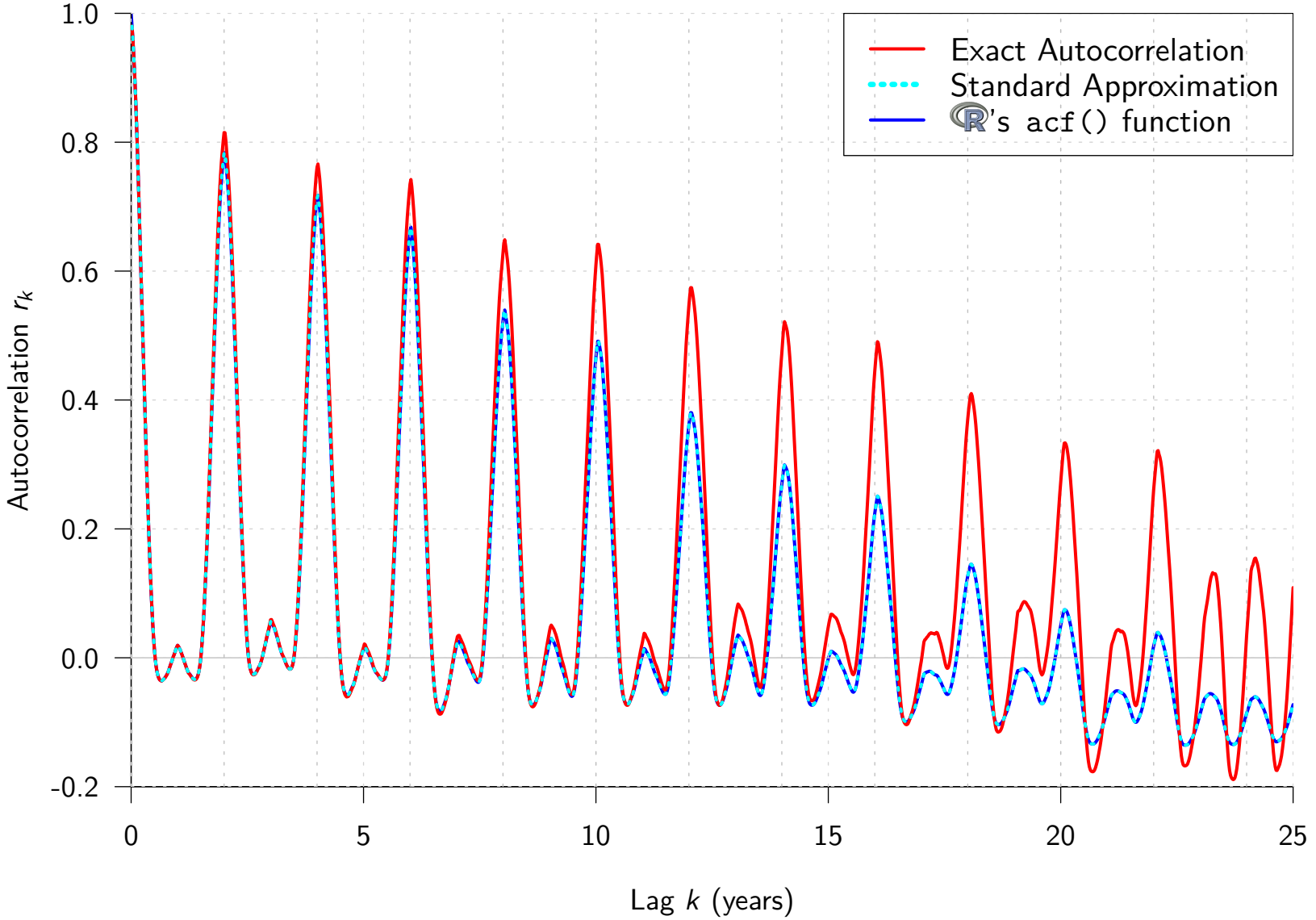
- Approximation of r_k is worse for larger lags k
- Plot of autocorrelation r_k as a function of lag k is called the *correlogram*.

Correlogram



- Peaks in correlogram $\Longrightarrow$ 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:

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

  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:

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

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

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

  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.

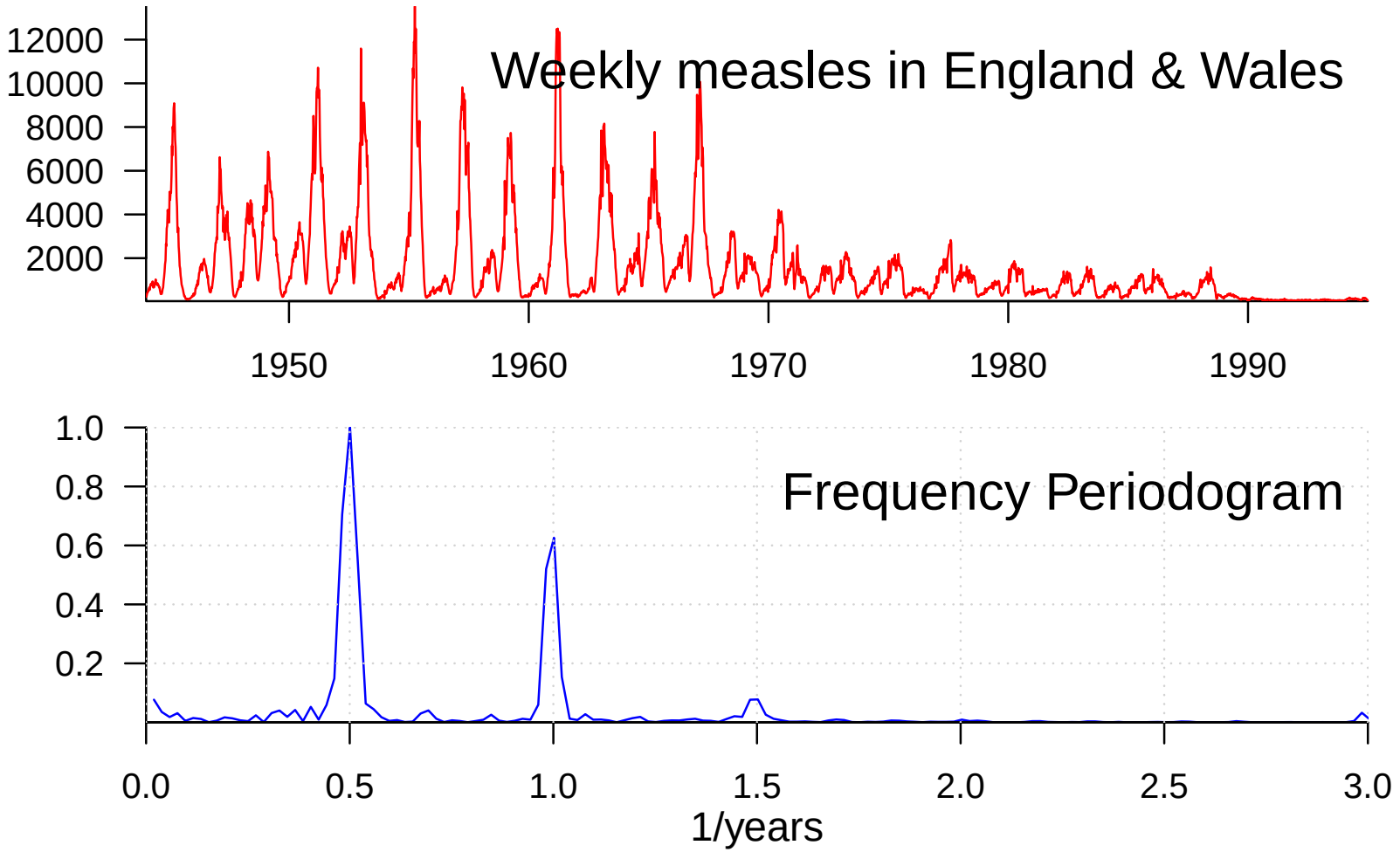
Spectral Density

- There are many different ways to express the power spectral density (aka *power spectrum*).
- Most common/useful equivalence is that the power spectrum is the discrete Fourier transform of the correlogram:

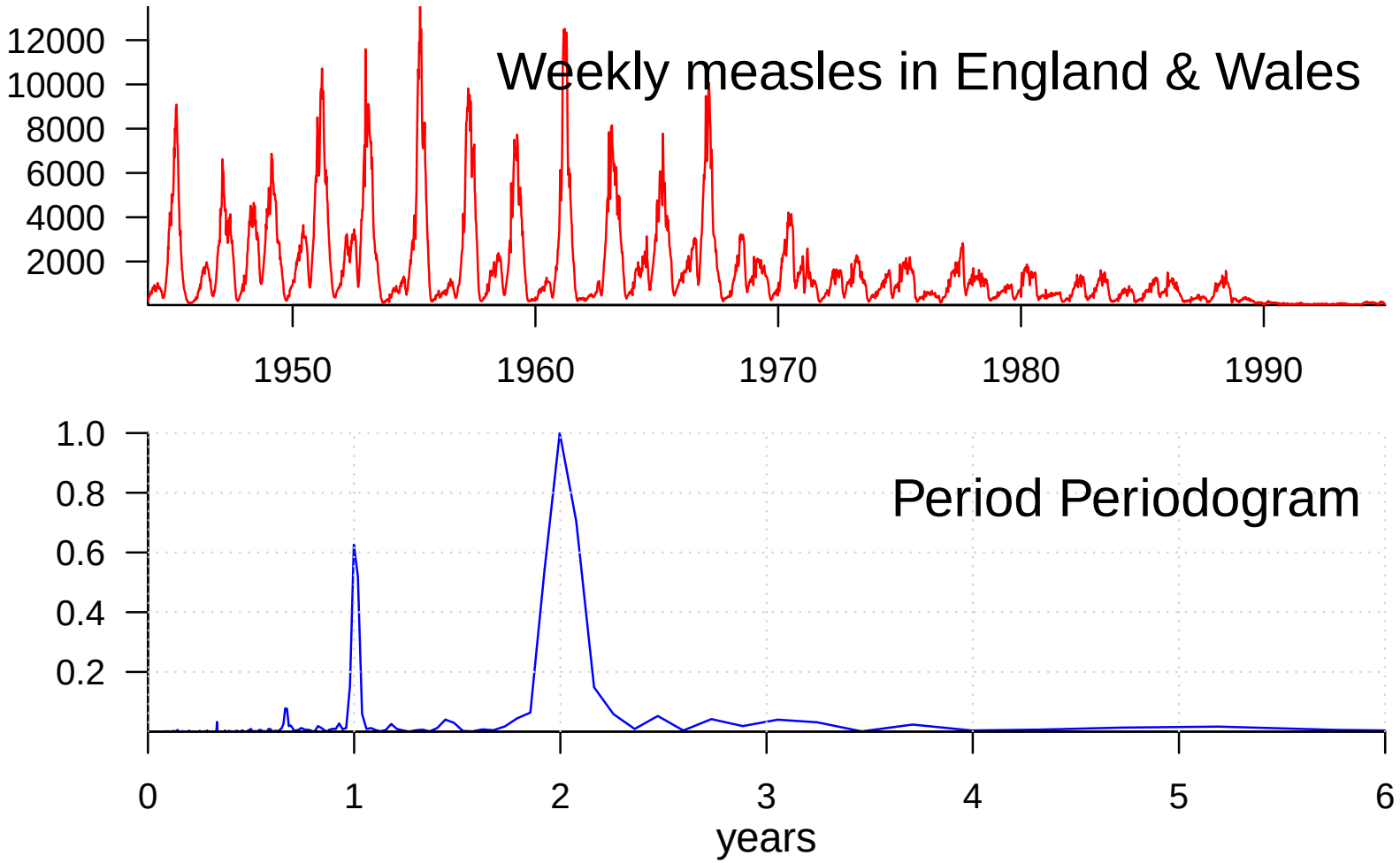
$$I(\omega_p) = \frac{1}{\pi}\left(r_0 + 2\sum_{k=1}^{N-1} r_k \cos \omega_p k\right)$$

- Plot of estimated power spectrum as a function of frequency ω_p is called the *frequency periodogram* or just the *periodogram*.

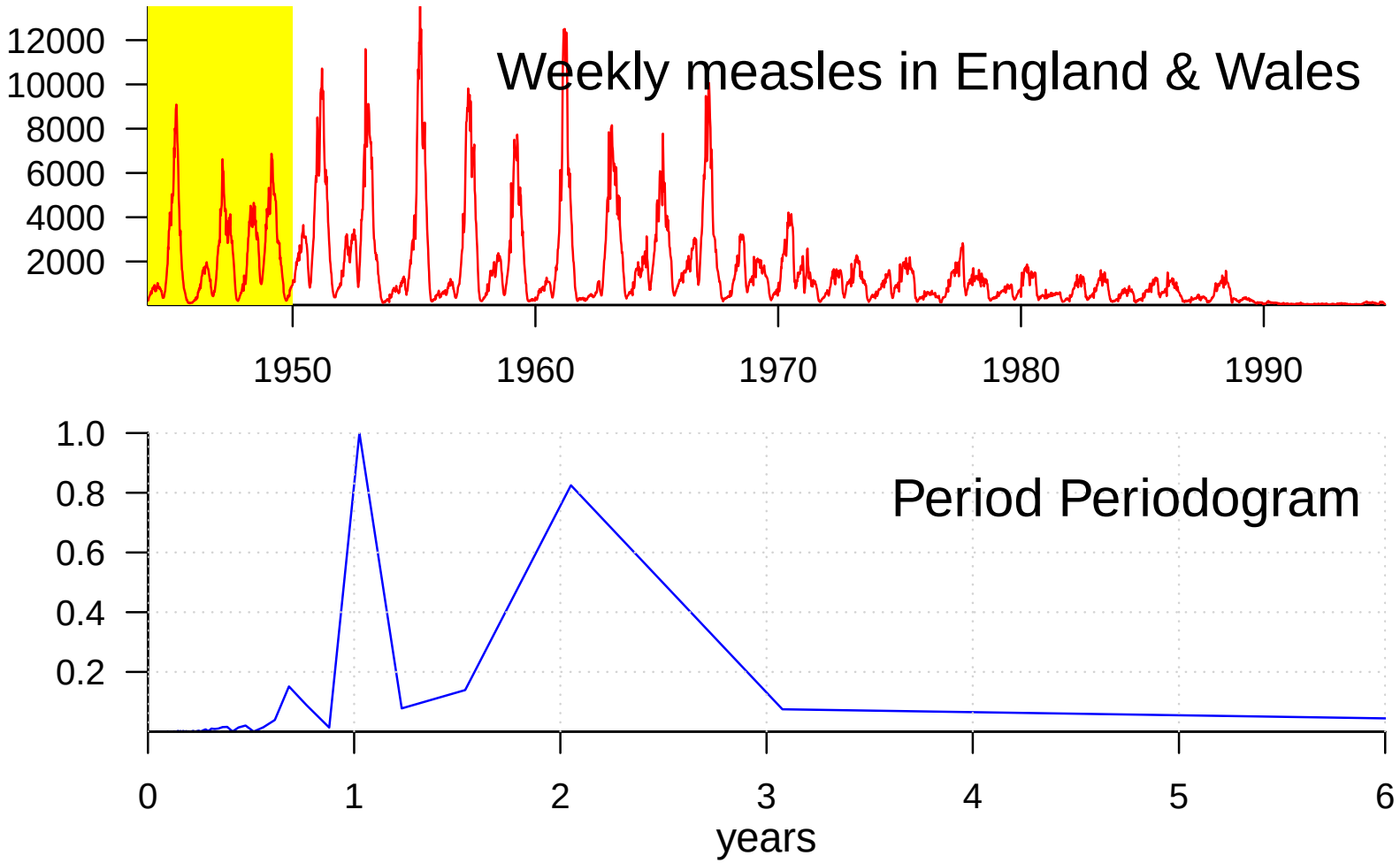
Spectral Density



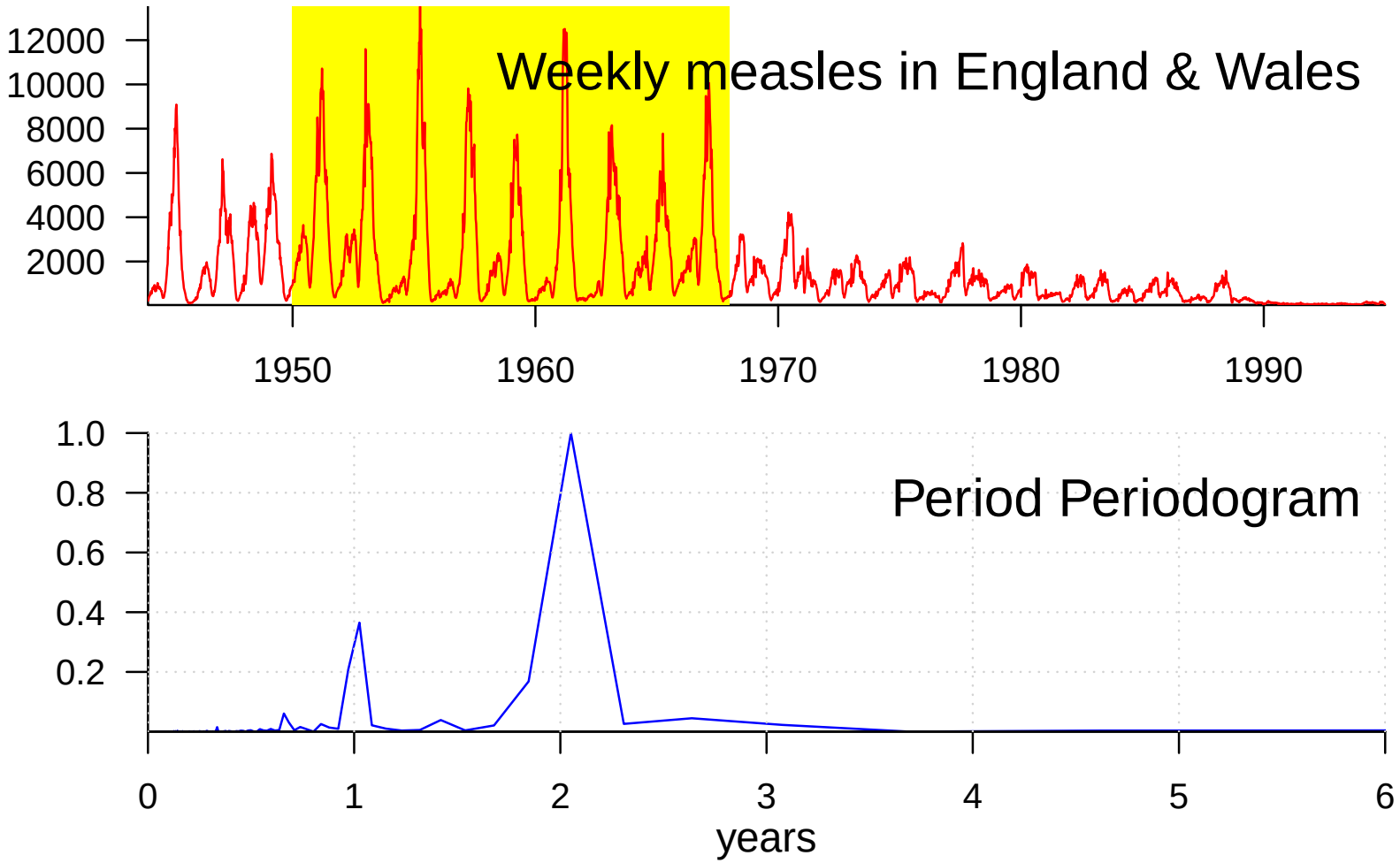
Spectral Density



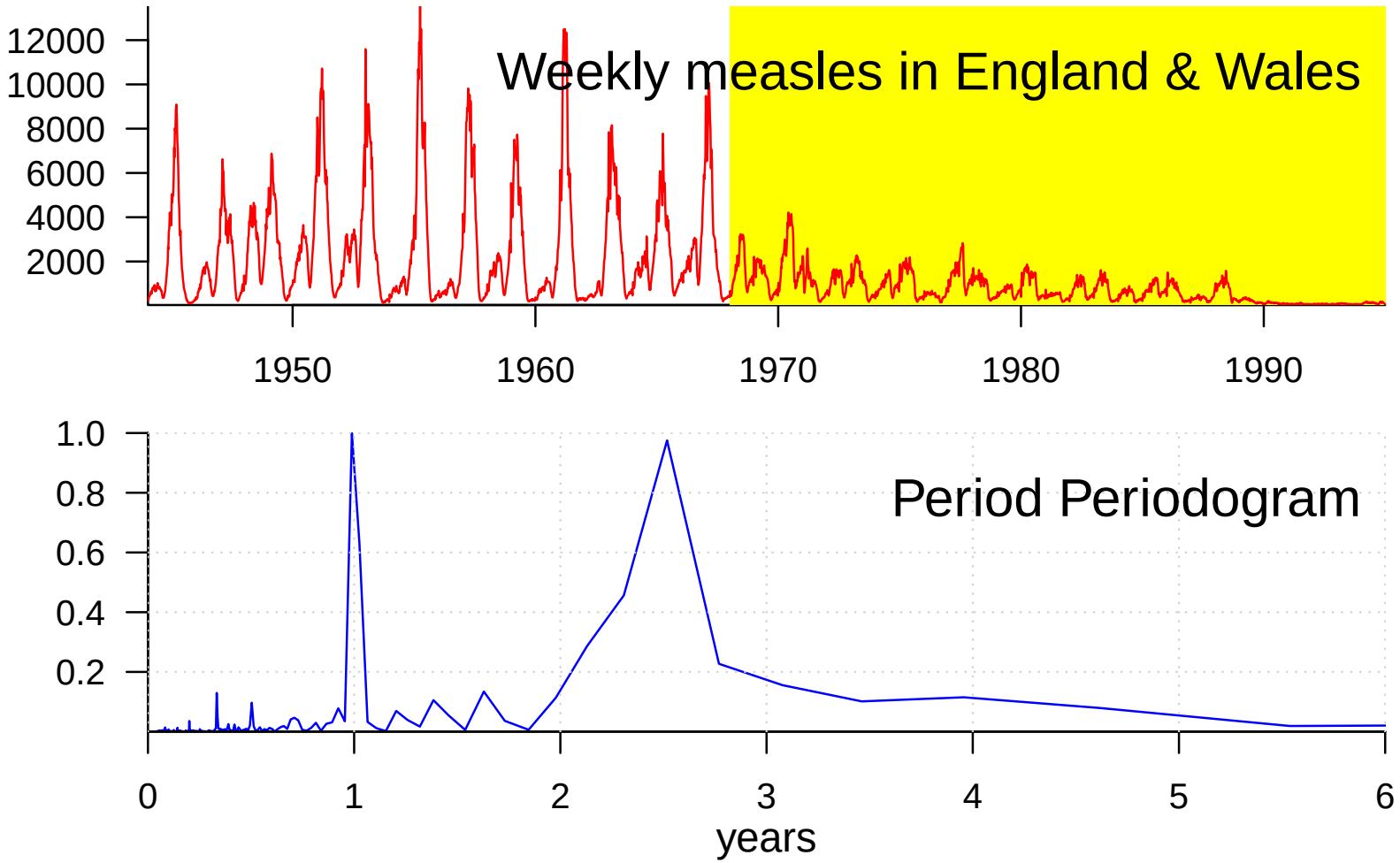
Spectral Density of Temporal Segments



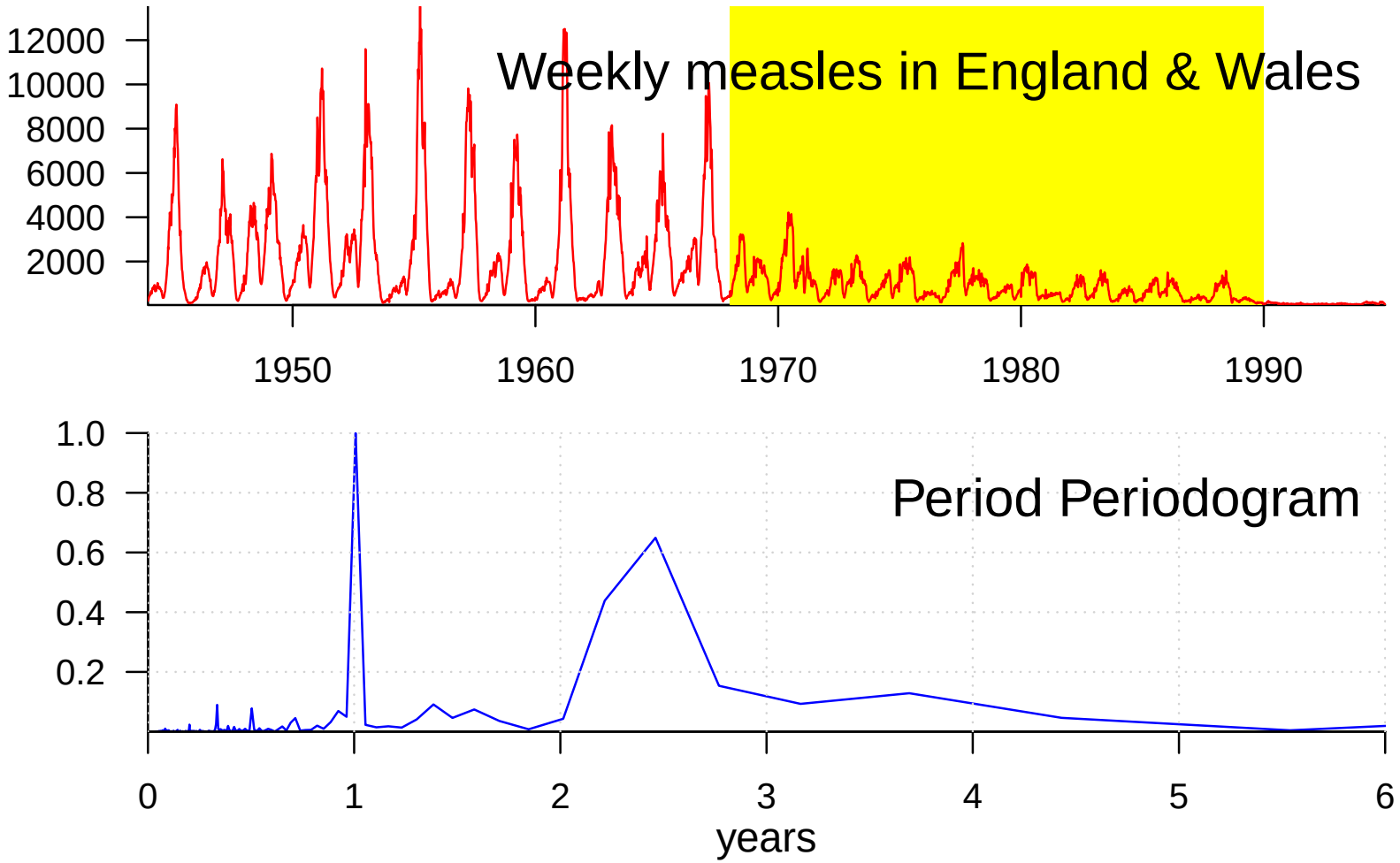
Spectral Density of Temporal Segments



Spectral Density of Temporal Segments



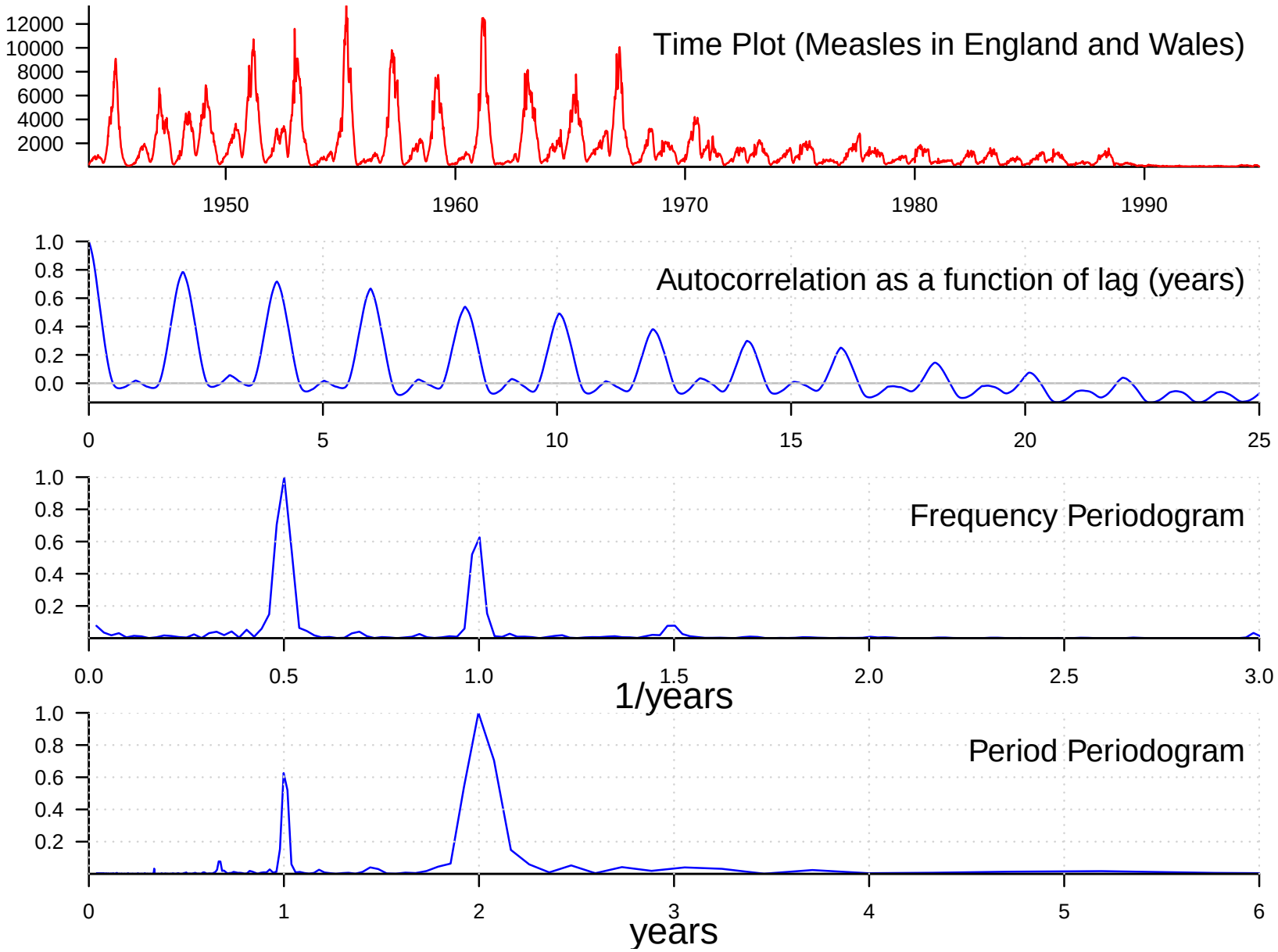
Spectral Density of Temporal Segments



Spectral Density Properties

- Periodogram is discrete Fourier transform of correlogram
- Same information in correlogram and periodogram
- Periodogram usually easier to interpret
- In  , calculate power spectrum with `spectrum()`
- The power spectrum $I(\omega_p)$ partitions the variance in the time series with respect to frequency ω_p.
  - Parseval's theorem implies $\frac{1}{N}\sum_t (x_t - \bar{x})^2 = \frac{1}{2\pi N}\sum_{p>0} I(\omega_p)$. But $\frac{1}{N}\sum_t (x_t - \bar{x})^2 = \mathrm{Var}\{x_t\}$, hence $I(\omega_p)/(2\pi N)$ is the proportion of the variance in the time series associated with period $2\pi/\omega_p$. [For details, see Chatfield (2004).]

Basic Time Series Analysis of Epidemic Data



Announcements

Spectral Density of Temporal Segments

- Pre-war measles
- Post-war pre-vaccination measles
- Vaccination era measles
- Vaccination era measles until 1990

Time series analysis functions

 has built-in tools for time series analysis:

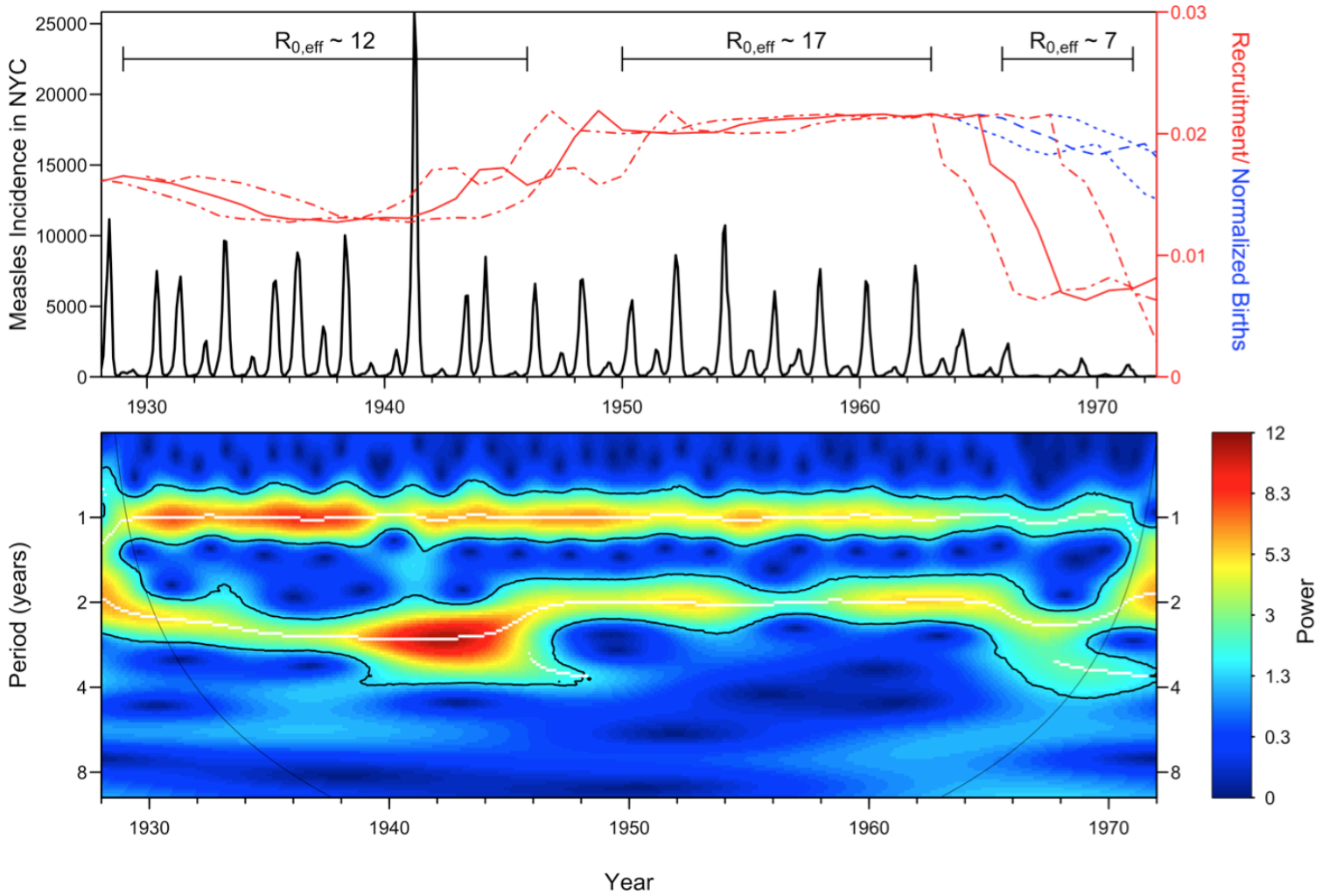
- Time plot: `plot()` *etc.*
- Linear filter (*e.g.*, moving average): `filter()`
- Correlogram (auto-correlation function): `acf()`
- Periodogram (power spectrum): `spectrum()`

You will use all of these functions in **Assignment 4.**

More sophisticated spectral method

- Traditional power spectrum measures frequency content of entire time series.
- Wavelet decomposition is local in time.
  - Reveals changes in the spectrum over time without having to identify distinct temporal segments yourself.
  - Nice intro to wavelet analysis of time series:
    Torrence and Compo (1998) "A Practical Guide to Wavelet Analysis" *Bulletin of the American Meteorological Society* **79**, 61–78
  - $\exists$  packages for wavelet analysis of time series (*e.g.*, WaveletComp, wavelets), and at least one book on wavelet methods in 

Wavelet Spectrum of Monthly Measles in New York City



Krylova & Earn 2013, *J. R. Soc. Interface* **10**, 20130098

Wavelet Spectrum of Weekly Measles in New York City

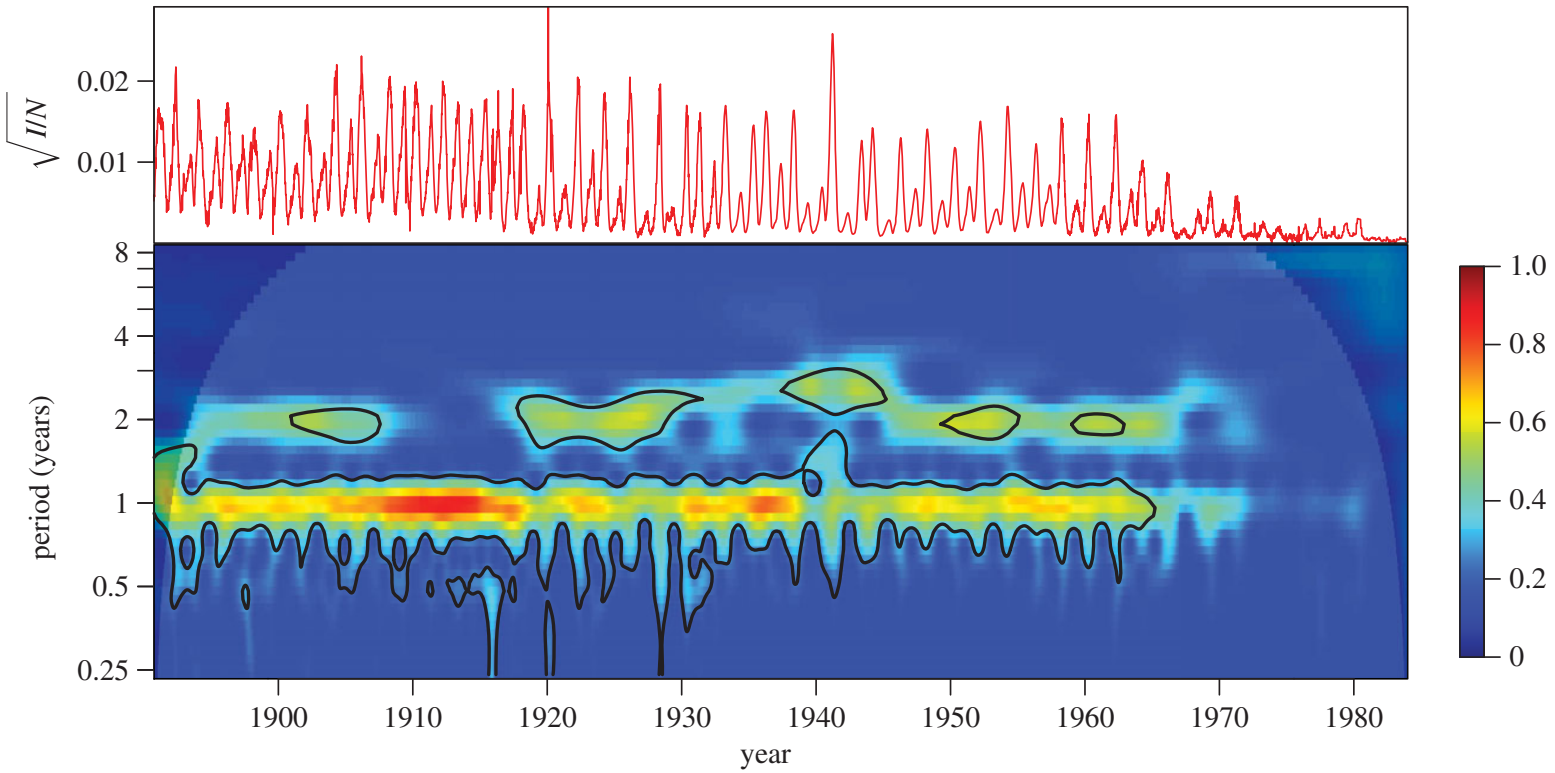
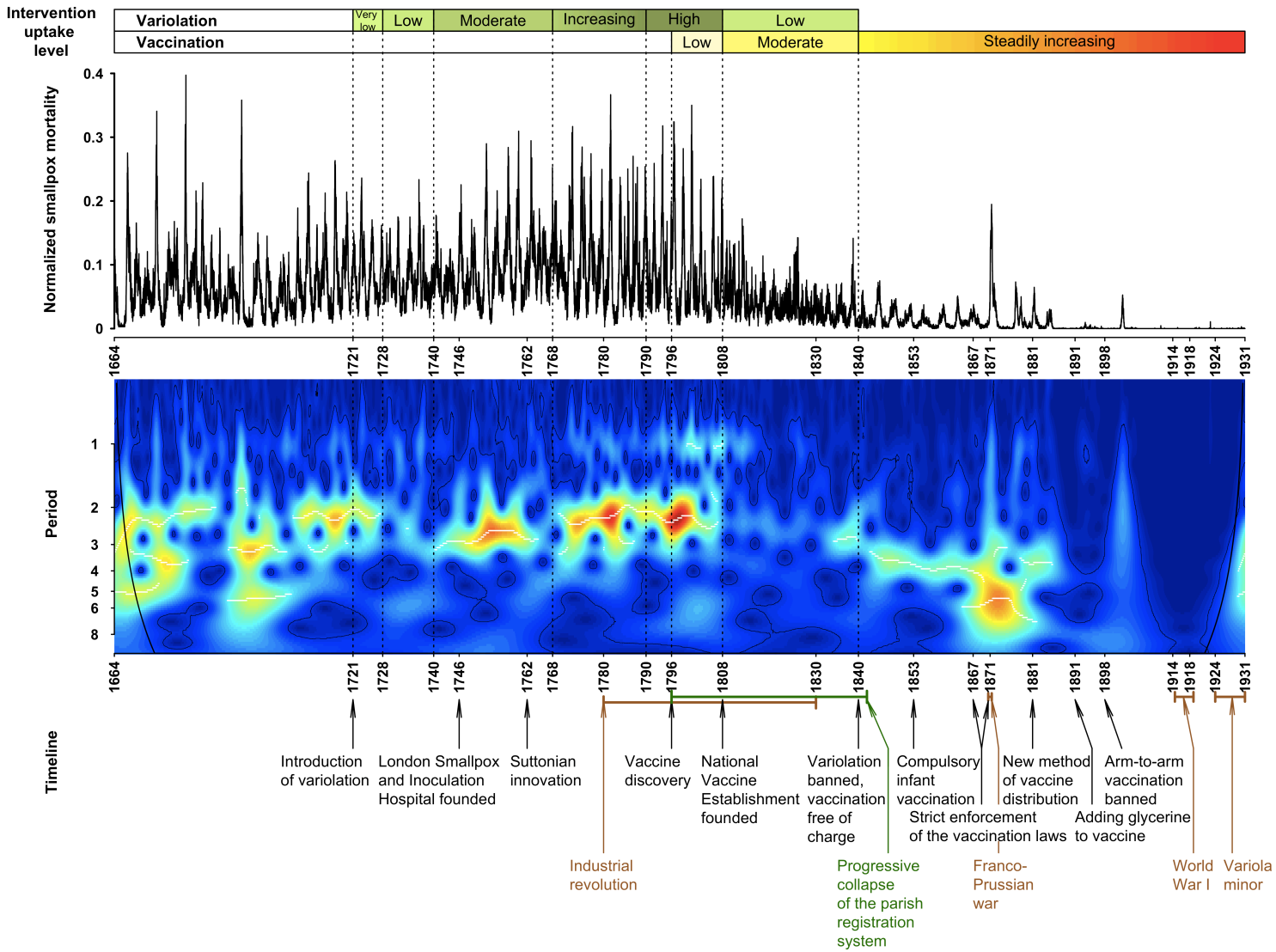


Figure 5. Observed measles dynamics in NYC from 1891 to 1984. (*a*) Square root of measles case reports, normalized by total concurrent population. (*b*) Colour depth plot of a continuous wavelet transform of the square root of normalized observed NYC measles cases (colour warmth scales with spectral power and 95% significance contours are shown in black). Shaded regions in the upper left and right indicate the cone of influence.

Hempel & Earn 2015, *J. R. Soc. Interface* **12**, 20150024

Wavelet Spectrum of Weekly Smallpox in London



Krylova & Earn 2019, *bioRxiv* **doi:** https://doi.org/10.1101/771220

Statistical Modelling of Time Series

Statistical Modelling of Time Series

- Imagine time series $\{X_t\}$ is generated by random processes.
- Simplest case: X_t (number of cases at time t) is simply a random variable with a known distribution,

$$X_t = \mu + Z_t \qquad (*)$$

where μ = time average number of cases
and $\{Z_t\}$ = sequence of random variables with zero mean.

- Might be a reasonable model for importation of new, infectious individuals into a focal community.
- Bad model for epidemics: ignores transmission from one individual to another.
  - There must be a correlation between the number of individuals in the focal community who are infected now and the number who will be infected in the near future.

Statistical Modelling of Time Series: AR and MA

- So, imagine that that successive data points in $\{X_t\}$ are correlated.
- For example, perhaps the data are generated by an *autoregressive (AR) process*:

$$X_t - \mu = \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) + Z_t\,,$$

where the α_i are constants that determine the degree of correlation along the time series.

- Alternatively, the data might be generated by a *moving average (MA) process*:

$$X_t - \mu = \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q}\,,$$

where the β_i are constants that define a weighted average.

Statistical Modelling of Time Series: ARMA

- More generally, the data might be generated by an *autoregressive moving average "ARMA(p, q)" process*:

$$X_t - \mu = \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) + \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q} \,.$$

Statistical Modelling of Time Series: ARIMA

- Finally, an *autoregressive integrated moving average "ARIMA(p, d, q)" model* includes weighted differences of the time series:

$$\begin{aligned} X_t - \mu = {} & \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) \\ & + \gamma_1(X_{t-1} - X_{t-2}) + \gamma_2(X_{t-2} - X_{t-3}) + \cdots \\ & + \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q} \,. \end{aligned}$$

  - The "I" in ARIMA refers to the original time series X_t, which is an "integrated" version of the differenced time series.
  - Technically, an ARIMA model is just an ARMA model with differently labelled coefficients, but explicit differences are often helpful conceptually (*e.g.*, they can "stationarize" a time series).

What kind of process generated our data?

- *How can we tell if our data were generated by such a process? Can we identify an AR(p), MA(q) or ARMA(p, q) process?*

- Compare time plots of these processes with time plot of our data? (Comparison by eye often challenging/unreliable.)
- Compare autocorrelation functions (correlograms) of these processes with correlogram of our data? (Better.)
- Compare power spectra (periodograms) of these processes with periodogram of our data? (Even better.)
- Compare wavelet spectra of these processes with wavelet spectrum of our data? (Better yet.)

Statistical Modelling of Time Series: ARMA fitting

- Looking at the power spectra of ARMA models would be instructive.
- But is there a better approach to discovering if an ARMA model could explain our data?
- Find the *best fit* ARMA parameters by minimizing the residual sum of squares. *e.g.*, for an AR model, minimize:

$$S = \sum_{t=p+1}^{N} \left[(x_t - \mu) - \alpha_1 (x_{t-1} - \mu) - \cdots - \alpha_p (x_{t-p} - \mu) \right]^2 .$$

- More generally, we can find the best fit parameters of an ARIMA(p, d, q) model
  - Non-trivial, but there are standard methods
- Compare models with Akaike Information Criterion (AIC), which penalizes models that have more parameters
  - See Earn (2009) review article for more discussion of this.

Time series tools discussed so far...

- Statistical description of time series:
  time plot, moving average, correlation coefficient, autocorrelation, correlogram, power spectral density (PSD), periodogram, wavelet spectrum
- Time series models:
  AR, MA, ARMA, ARIMA

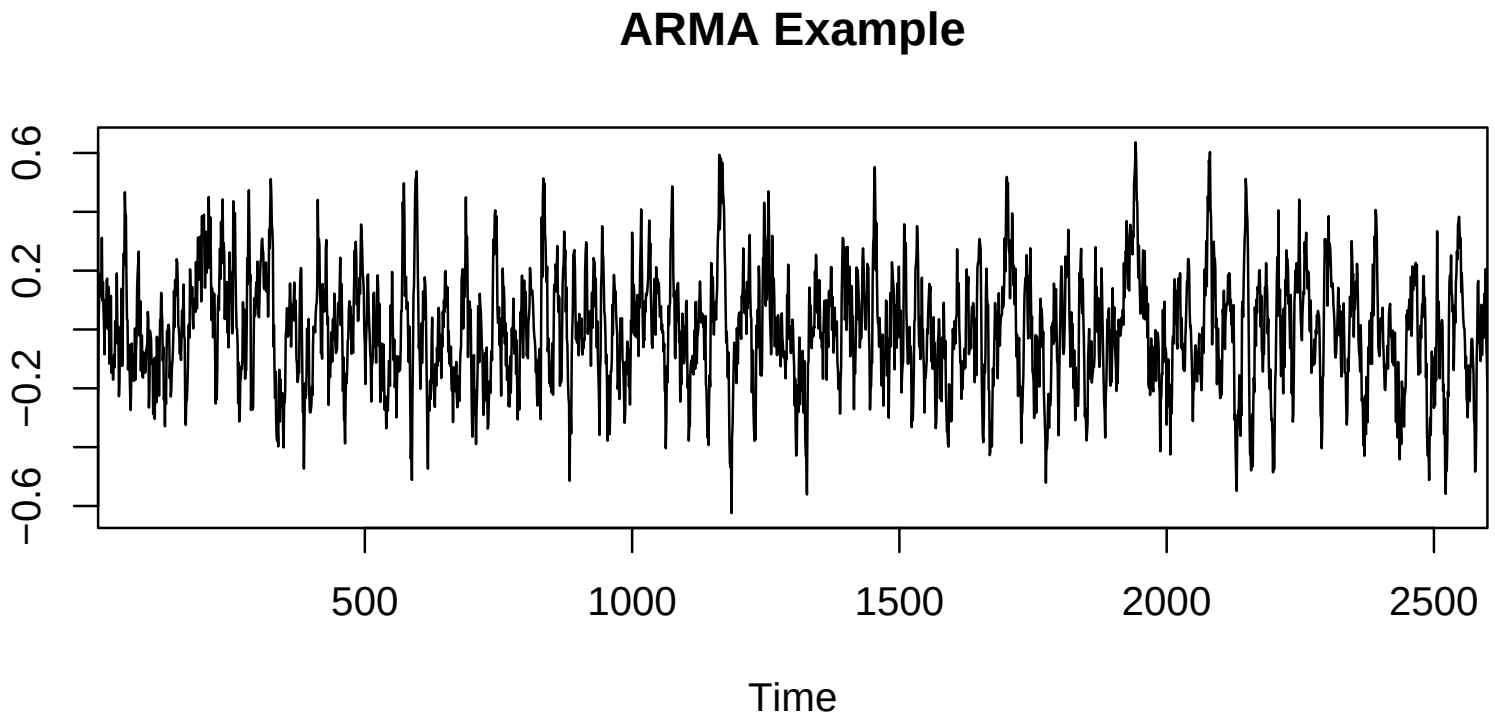
Statistical Modelling of Time Series

How to do it in  ...

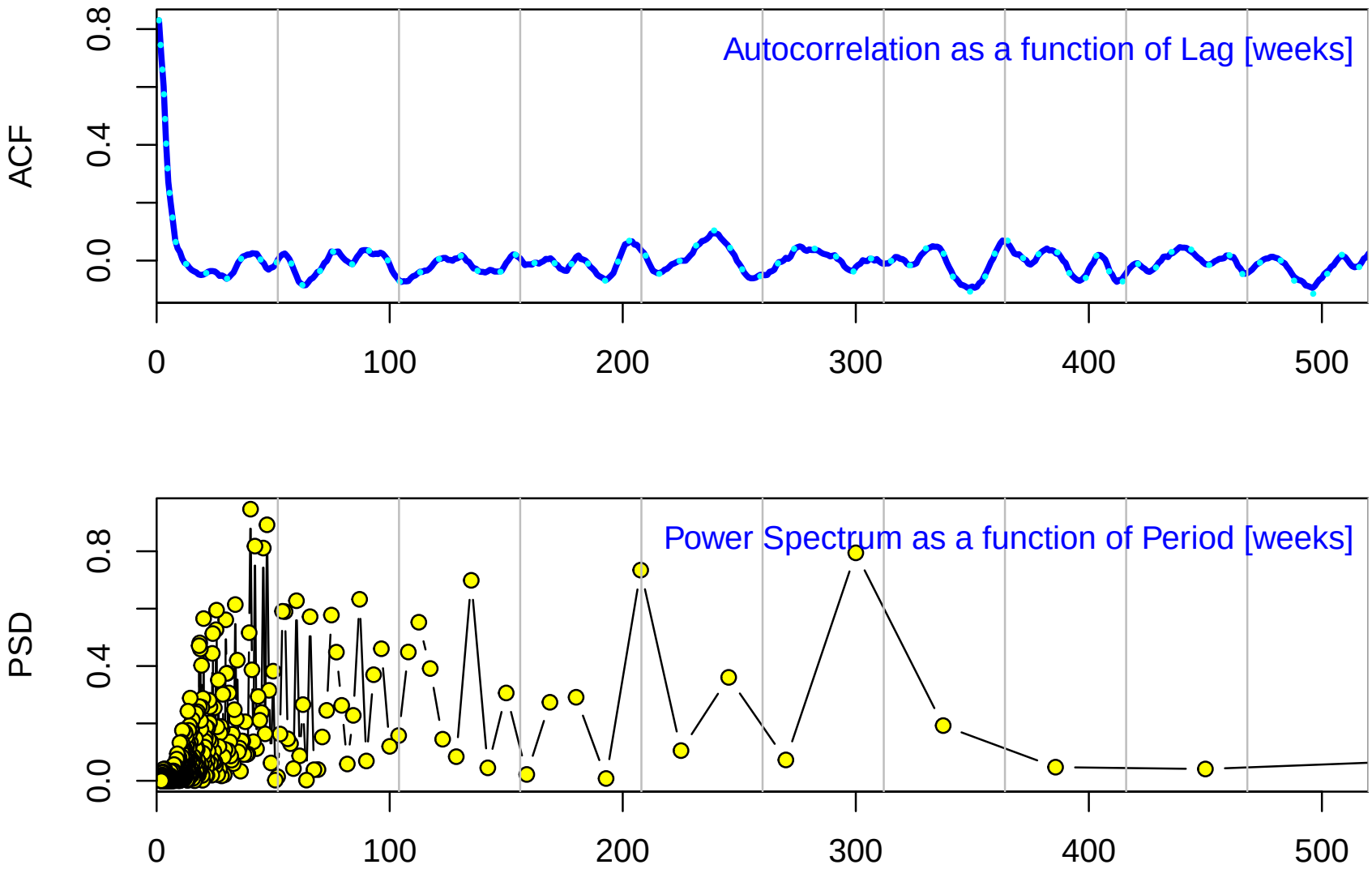
- Simulate any ARIMA(p, d, q) model with `arima.sim()`
- Fit an AR model to a time series with `ar()`
- Fit an ARIMA model to a time series with `arima()`
- Alternatively, there are specialized time series modelling packages.

ARMA Example (50 years of weekly data)

```
my.model <- list(ar=c(1,-0.5,0.5,-0.25),ma=c(-0.25,0.5))
my.sim <- arima.sim(n=52*50,model=my.model,sd=0.1)
plot(my.sim,main="ARMA Example",ylab="",xaxs="i")
```



ARMA Example (ACF and PSD up to 10 year lag)



Statistical Modelling of Time Series: Forecasting

- Once we have a fitted model, we can then use it to *forecast* future observations
- *Validate* this procedure by using part of the data to fit the model and then forecast the remainder of the data (*cf.* cross-validation)

- How successful is this likely to be for an infectious disease time series?
  - Conceivably good for chicken pox in NYC.
  - Less likely to be good for measles. . . at least for the main patterns. . .
  - One of the project options is to look at this more carefully.

Statistical Modelling of Time Series: Limitations

- It might be best to remove mean, trend and seasonality before fitting an ARMA model
  - But this means we will remove the aspects of the data about which we care most!
- The fitted parameters of an ARMA model have no obvious biological meaning
  - The model completely ignores any understanding we have of infectious disease transmission
- Statistical models use the time series itself to parameterize an ARMA (or more general) process
  - It would be better to have a model that we can parameterize from independently collected data and then see if that model can explain the observed time series

Mechanistic Mathematical Modelling

- SIR and all that...
- Takes into account transmission process...

- So why did we just spend time talking about statistical modelling?
  - Important to be familiar with time series models that are in common use.
  - Helps us appreciate the value of mechanistic modelling.
  - Some processes that affect disease dynamics might be better modelled as ARMA or similar processes.
    - Weather (*e.g.*, perhaps model $\beta = \beta(t)$ as an ARMA process)
    - Immigration
  - Ruling out an ARMA model (or at least one with a modest number of parameters) is a step towards finding a good model.
  - A combination of mechanistic and time series models could be useful.