UNDERSTANDING GLOBAL SEASONAL SYNCHRONIZATION OF INFECTIOUS DISEASES USING REMOTE SENSING

Elena N. Naumova

Tufts University School of Engineering, Medford MA USA

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Tufts UNIVERSITY

Now let us consider the seasons and the way we can predict whether it is going to be a healthy or an unhealthy year.

Hippocrates. *Air, Waters, Places,* 10

Objective

To provide an overview for

rationale,

methods,

caveats,

applications

of **seasonality synchronization** in environmental epidemiology with the emphasis on **waterborne infection.**

Why waterborne diseases?

Diarrheal and waterborne diseases including dysentery and hepatitis are causing

4 billion cases of diarrhea annually,

2.2 million deaths:

80% of them in the first 2 years of their life

18% of deaths in children under 5 years of age

42,000 a week

6,000 a day

4 every minute

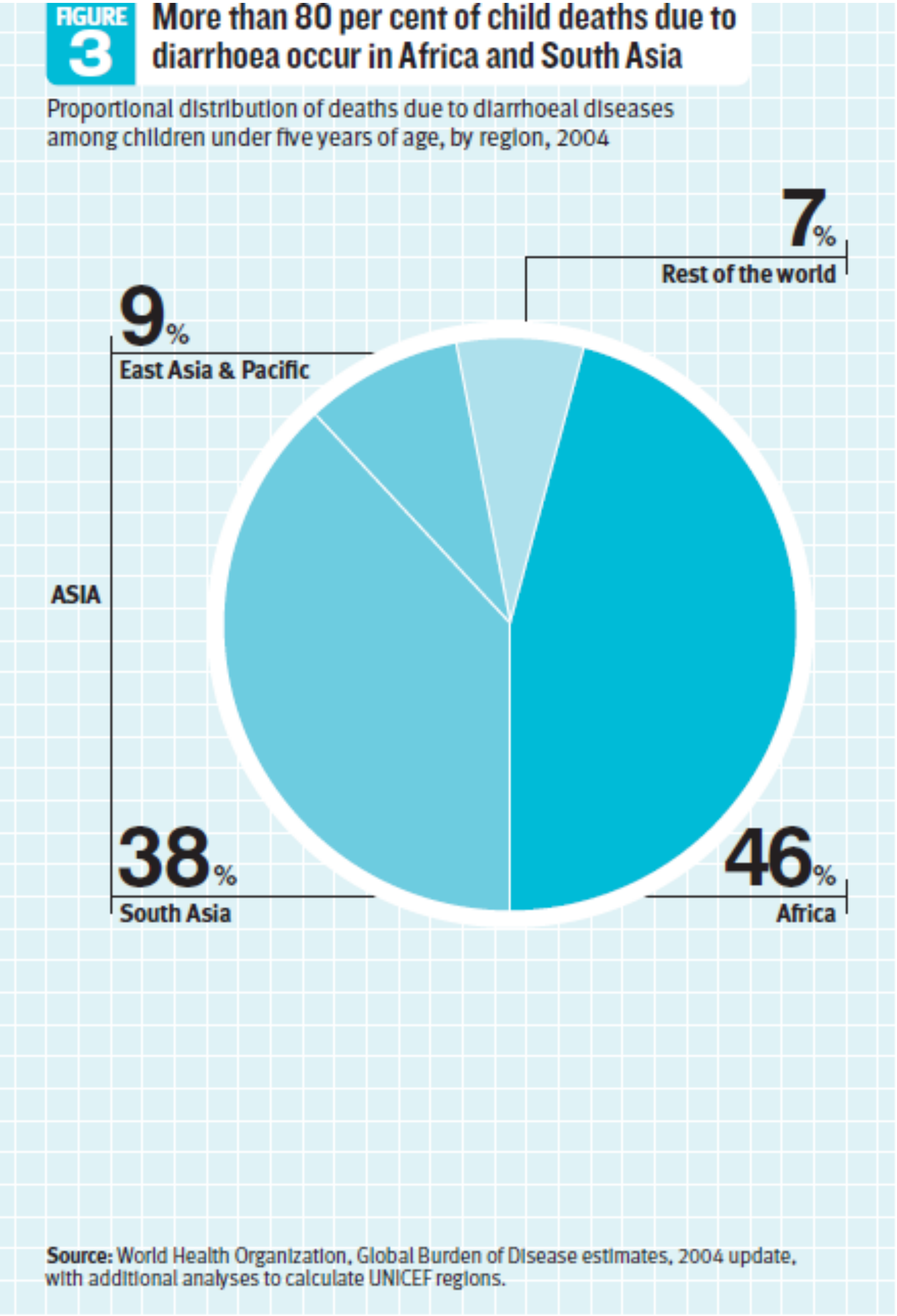
1 every fourteen seconds

Fewtrell L, Pruss-Ustun A, Bos R, Gore F, Bartram J. *Water, sanitation and hygiene. Quantifying the health impact at national and local levels in countries with incomplete water supply and sanitation coverage. WHO Environmental Burden of Disease Series No. 15*. Geneva: WHO; 2007.

Boschi-Pinto C, Velebit L, Shibuya K. Estimating child mortality due to diarrhoea in developing countries. *Bulletin of the WHO*. 2008. 86: 710-7.

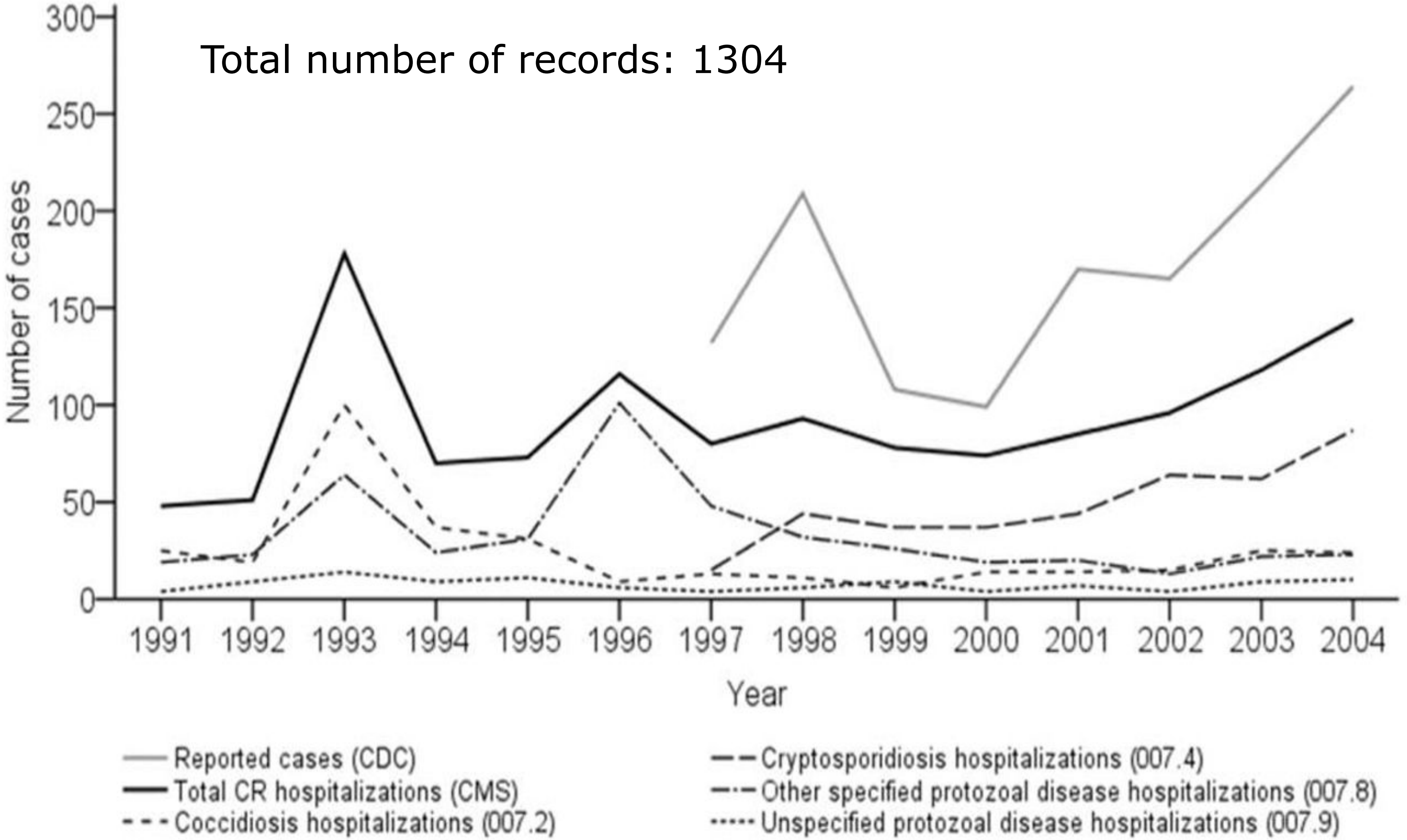
In resource-poor settings

88% of diarrhea cases thought to be due to unsafe water, inadequate sanitation, and poor hygiene



WHO 2004

Cryptosporidiosis in the US elderly



Mor S, DeMaria A, Griffiths JK, Naumova EN. Cryptosporidiosis in the US elderly. *ClD.* 2009; 48(6):698-705

Why Seasonality?

Practically all waterborne diseases exhibit strong seasonal patterns distinct for a specific pathogen in a given population and locality.

Notion of seasonality

Definition

Seasonality is a systematic (or repetitive) periodic fluctuation in a parameter of interest (e.g. the disease incidence) that occurs within a course of a year.

Seasonality can be described by peak timing, amplitude and duration.

Person, time and space concept

A seasonal pattern of a disease may differ:

- in different subpopulations and by age
- from year to year and geographically

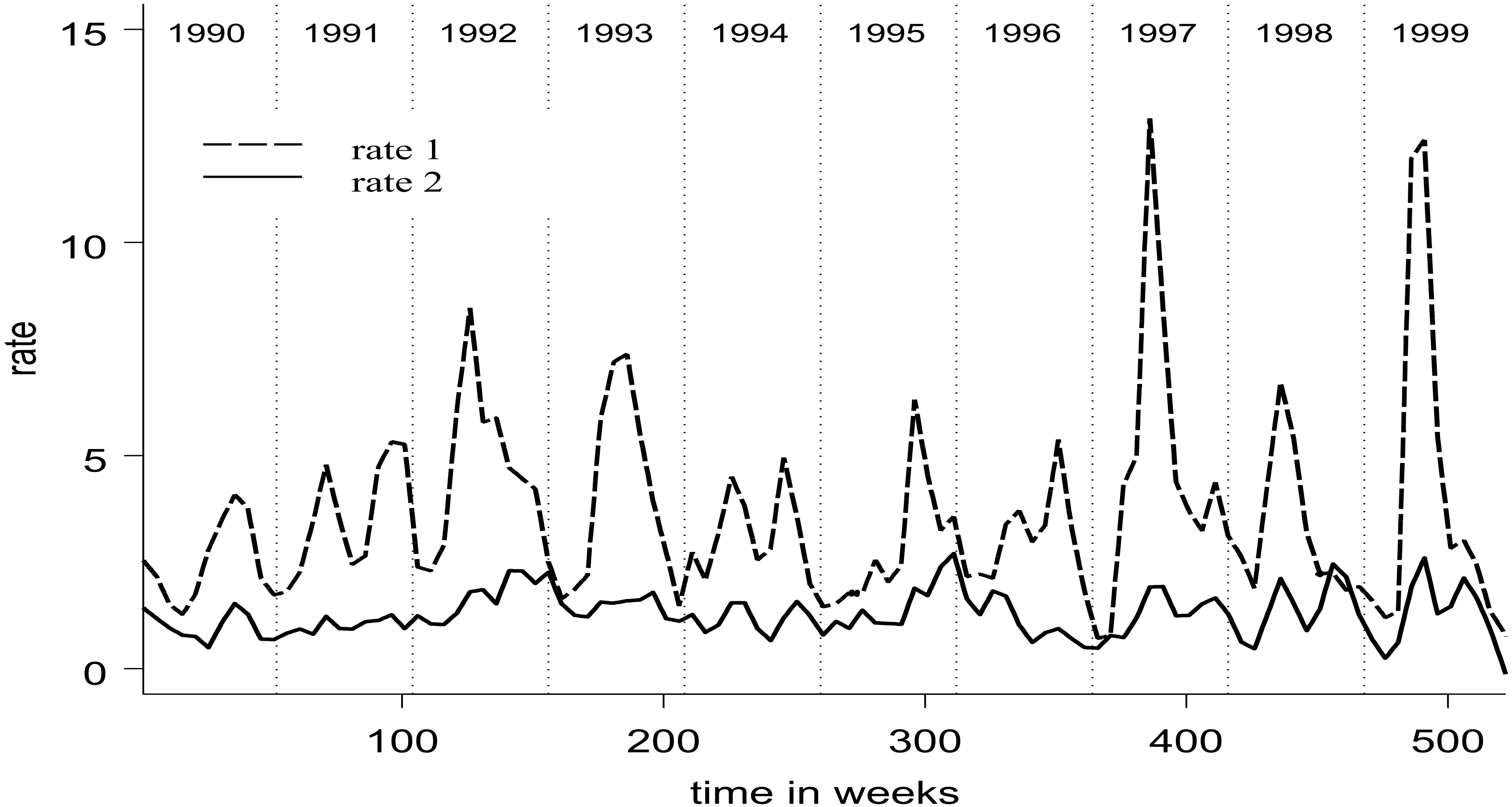
Model Interpretability

Variability in the seasonal characteristics can provide clues on important factors influencing a disease occurrence, exposure, spread, and manifestations.

Naumova EN. Mystery of seasonality: getting the rhythm of nature. *JPHP.* 2006; 27(1):2-12.

Seasonality of Cryptosporidiosis in UK

up to 80% of temporal variability is explained by semi-annual seasonality

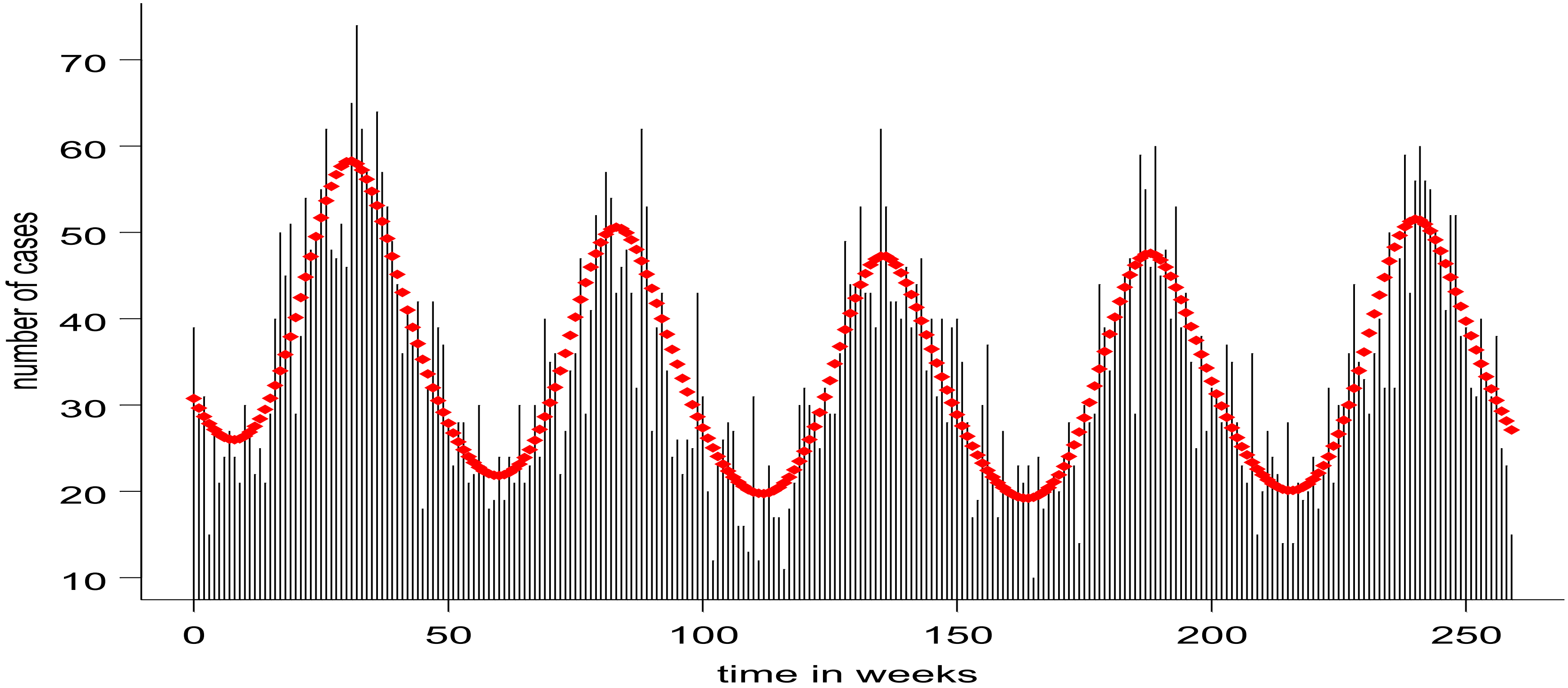


Naumova EN, Christodouleas J, Hunter PR, Sued Q. Temporal and spatial variability in cryptosporidiosis recorded by the surveillance system in North West England in 1990 - 1999. *Water & Health*. 2005; 3(2):185-96.

Hospitalizations due to Salmonellosis, USA

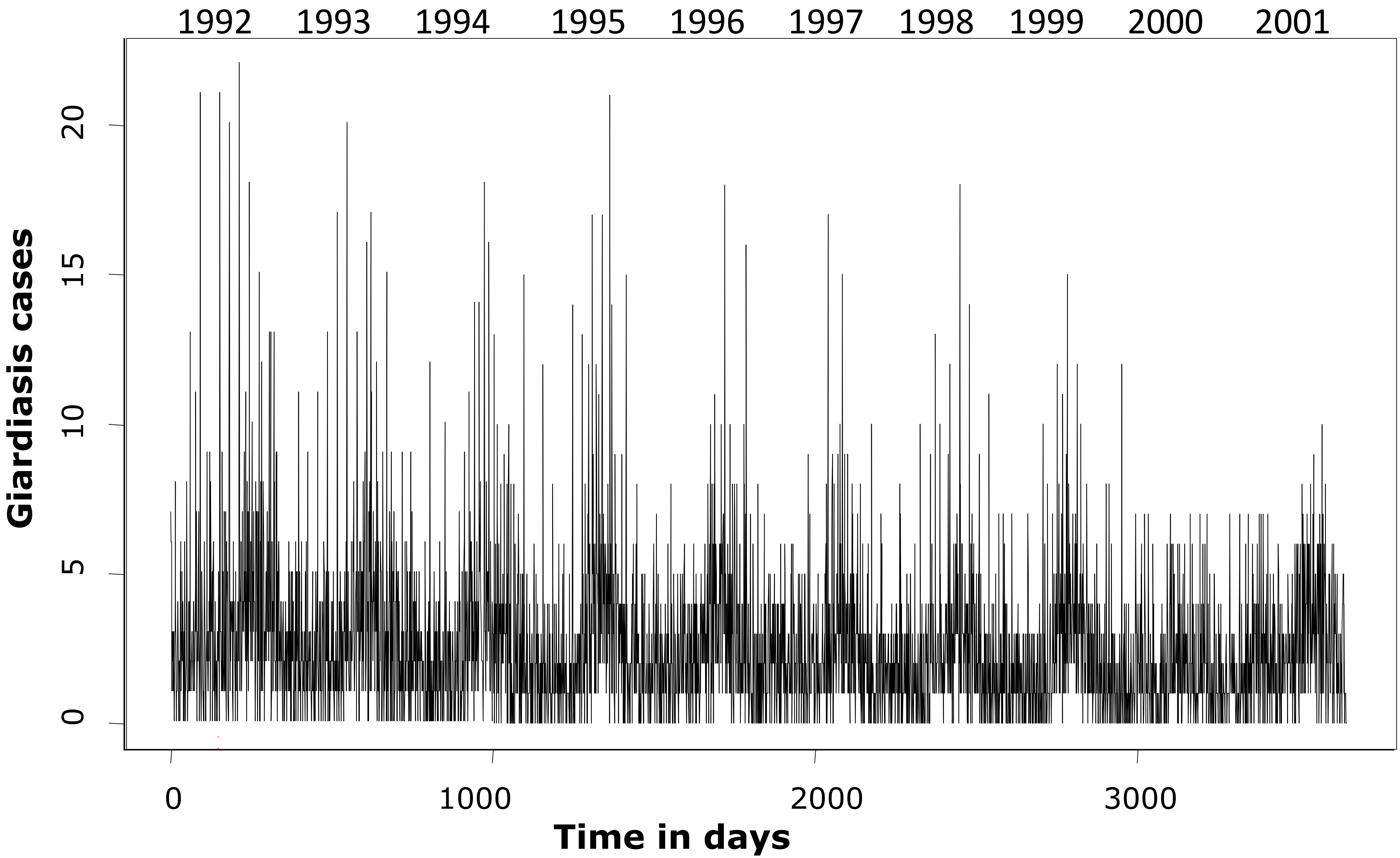
- *Salmonella* Infection: in the USA elderly — 72% variability is explained by seasonal and trend components*

Summer time: 1998 1999 2000 2001 2002



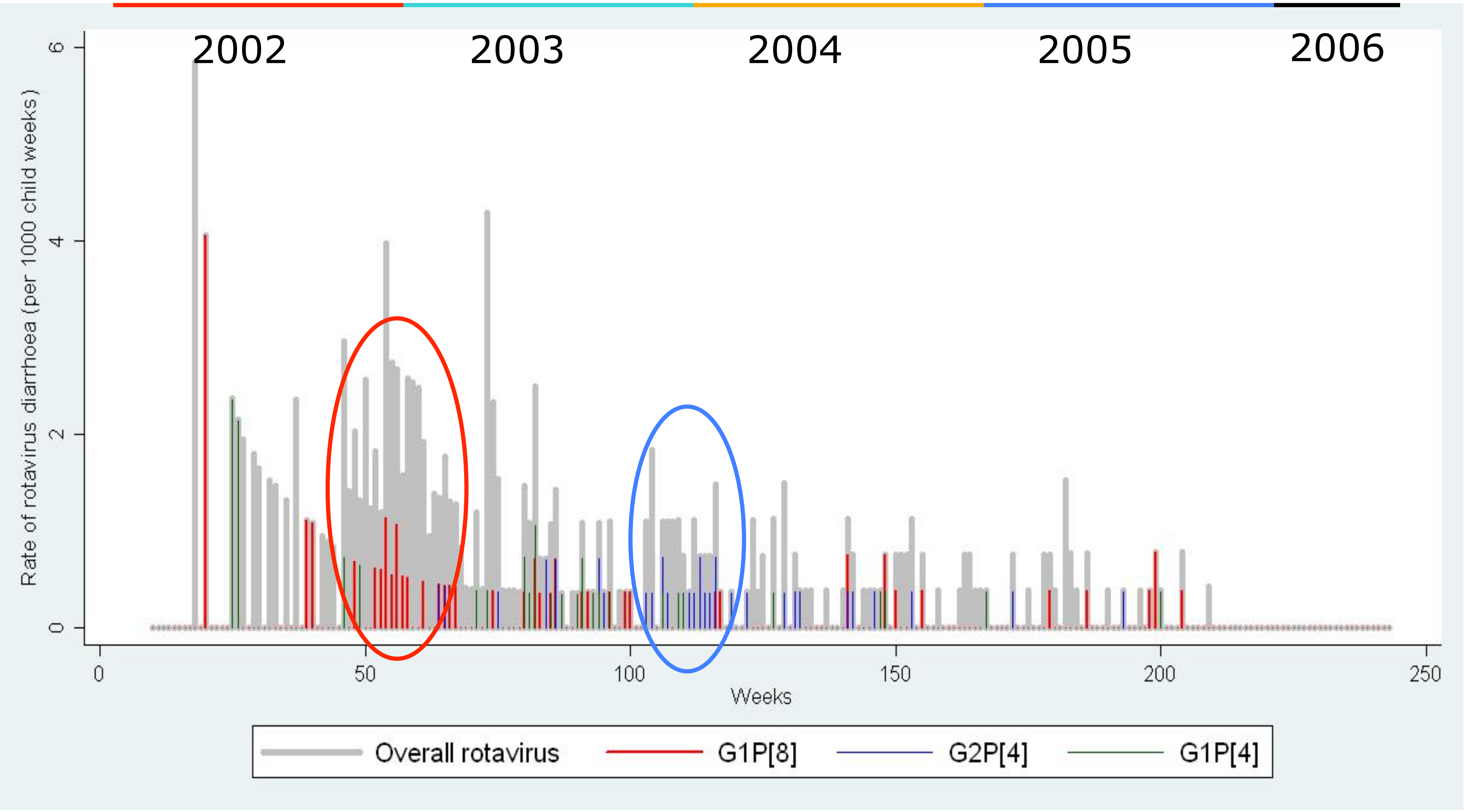
Chui K, Webb P, Russell RM, Naumova EN. Geographic variations and temporal trends of *Salmonella*-associated hospitalization in the US elderly, 1991-2004: A time series analysis of the impact of HACCP regulation. *BMC Public Health*. 2009. 9(1):447

Reported Giardiasis in MA, 1992-2001



Naumova EN, Chen JT, Griffiths JK, Matyas BT, Estes-Smargiassi S, Morris RD. The use of passive surveillance data to study temporal and spatial variation in the incidence of giardiasis and cryptosporidiosis. *Public Health Reports*. 2000; 151: 38-50.

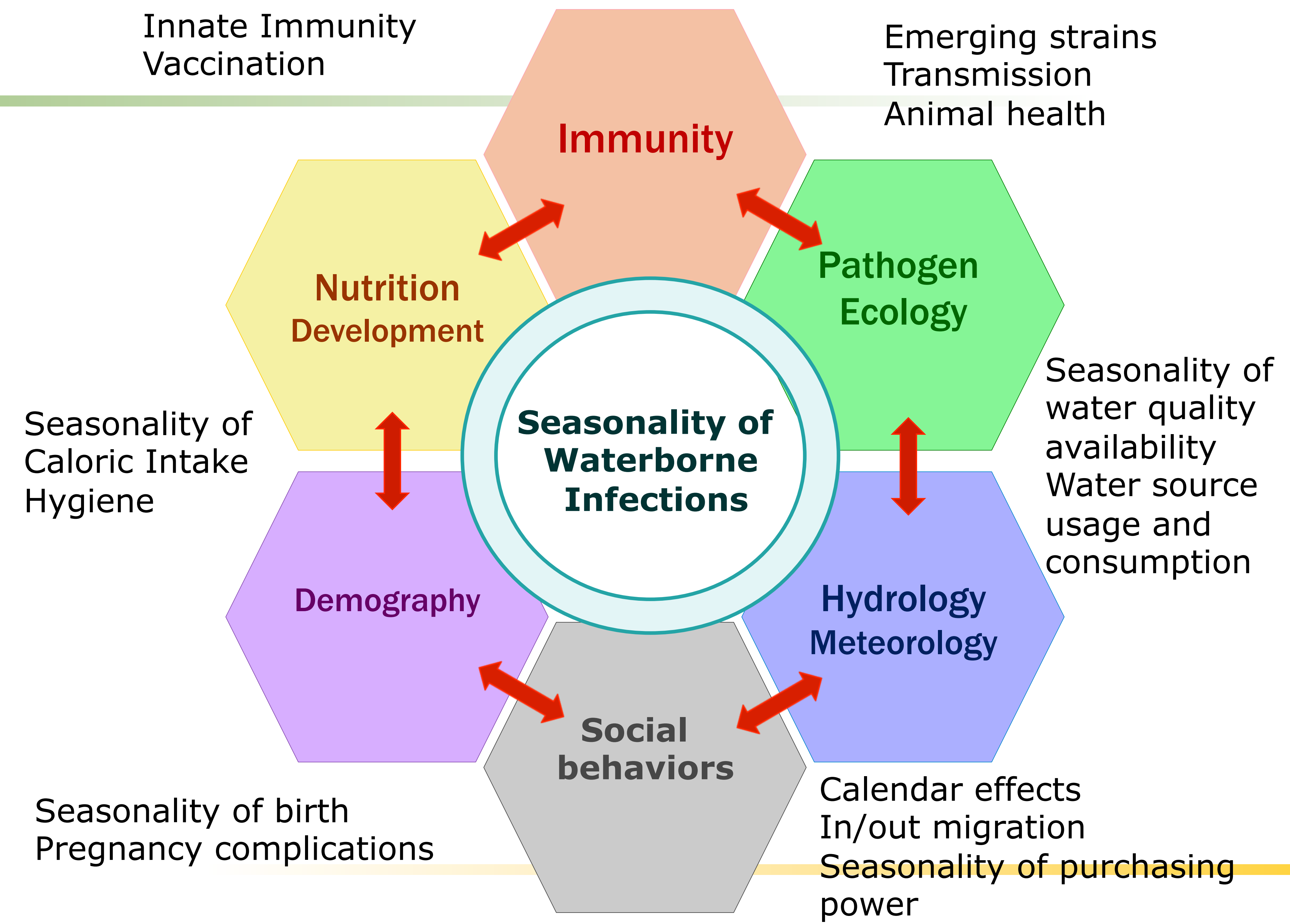
Seasonality of Rotavirus in India



Sarkar R, Gladstone BR, Kang G, Jagai JS, Ward H, Naumova EN. Seasonality of pediatric enteric infections in tropical climates: time-series analysis of data from a birth cohort on diarrheal disease. In the Proc. of the ISEE Symposium. Pasadena, CA. 2008.

What is in Seasonality?

- Explanations for self-sustained oscillations in waterborne infections remain elusive
- Reliance on the ability to establish the link with drinking or recreational water is difficult
- Complexities of governing principles and changing dominant routes of transmission are immense

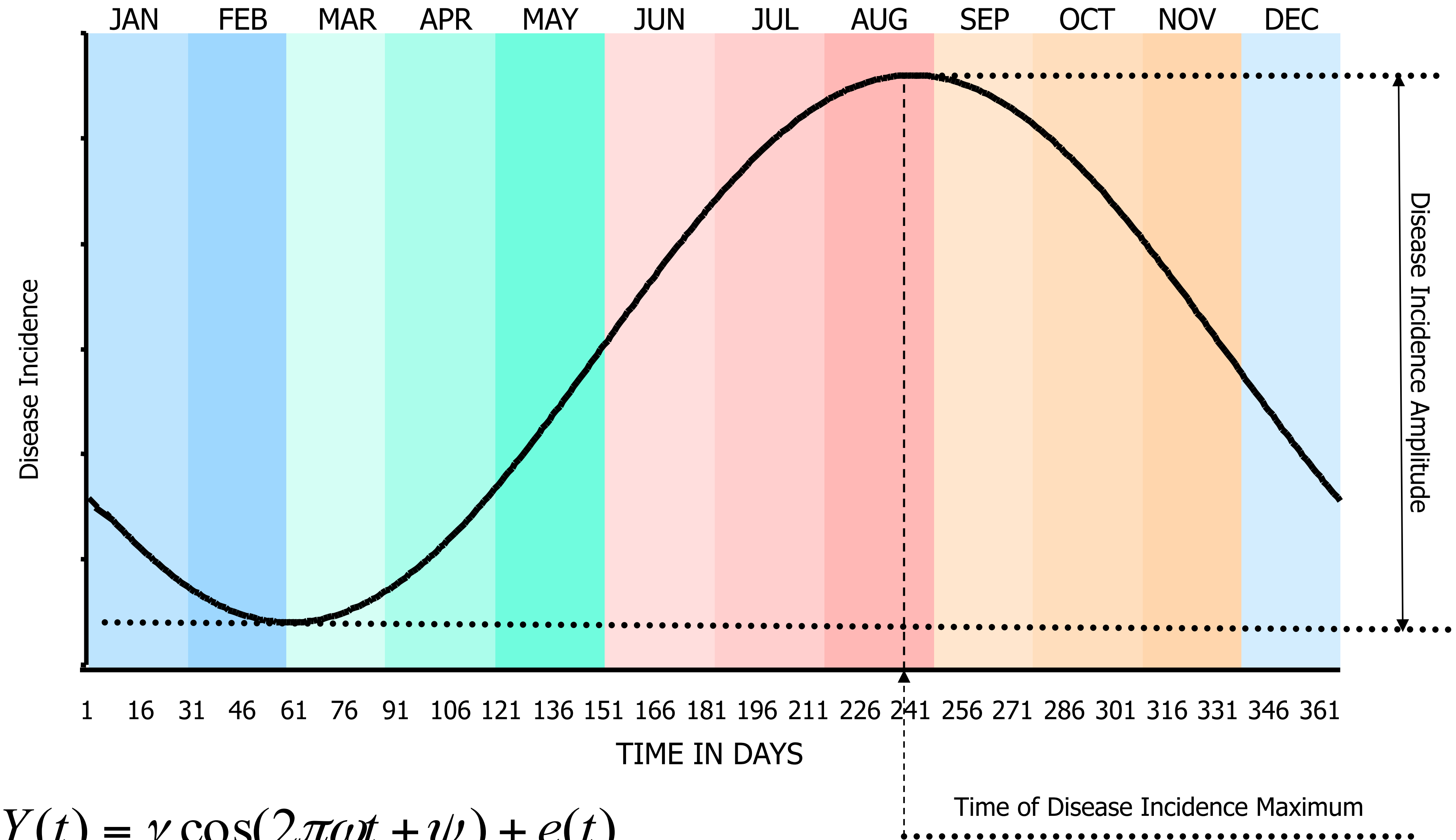

Innate Immunity
Vaccination
Immunity
Emerging strains
Transmission
Animal health
Nutrition
Development
Pathogen
Ecology
Seasonality of
Waterborne
Infections
Seasonality of
Caloric Intake
Hygiene
Seasonality of
water quality
availability
Water source
usage and
consumption
Demography
Hydrology
Meteorology
Social
behaviors
Seasonality of birth
Pregnancy complications
Calendar effects
In/out migration
Seasonality of purchasing
power

Changing Seasonal Patterns

Man-made catastrophic events and natural disasters that cause deaths, population displacement, contamination of source water, infrastructural damages affecting availability of potable water and pathogen ecology, might trigger long-term alterations in seasonal profiles of waterborne diseases.

The timing and intensity of waterborne outbreak can be affected by disturbances in human-environment interactions due to emergence of novel pathogens, viral mutations and drug resistance.

Simple Seasonal Pattern



$$Y(t) = \gamma \cos(2\pi\omega t + \psi) + e(t)$$

Seasonality Model and δ-method

$$Y(t) = \gamma \cos(2\pi\omega t + \psi) + e(t)$$

$$Y(t) = \beta_1 \sin(2\pi\omega t) + \beta_2 \cos(2\pi\omega t) + e(t)$$

For the amplitude, the estimates are:

$$\hat{\gamma} = f(\hat{\beta}_1, \hat{\beta}_2) = (\hat{\beta}_1{}^2 + \hat{\beta}_2{}^2)^{1/2}$$

$$Var(\hat{\gamma}) = (\hat{\sigma}^2_{\beta_1}\hat{\beta}_1^2 + \hat{\sigma}^2_{\beta_2}\hat{\beta}_2^2 + 2\hat{\sigma}_{\beta_1\beta_2}\hat{\beta}_1\hat{\beta}_2)/(\hat{\beta}_1{}^2 + \hat{\beta}_2{}^2)$$

For the phase angle, the estimates are:

$$\hat{\psi} = -\arctan(\hat{\beta}_1 / \hat{\beta}_2)$$

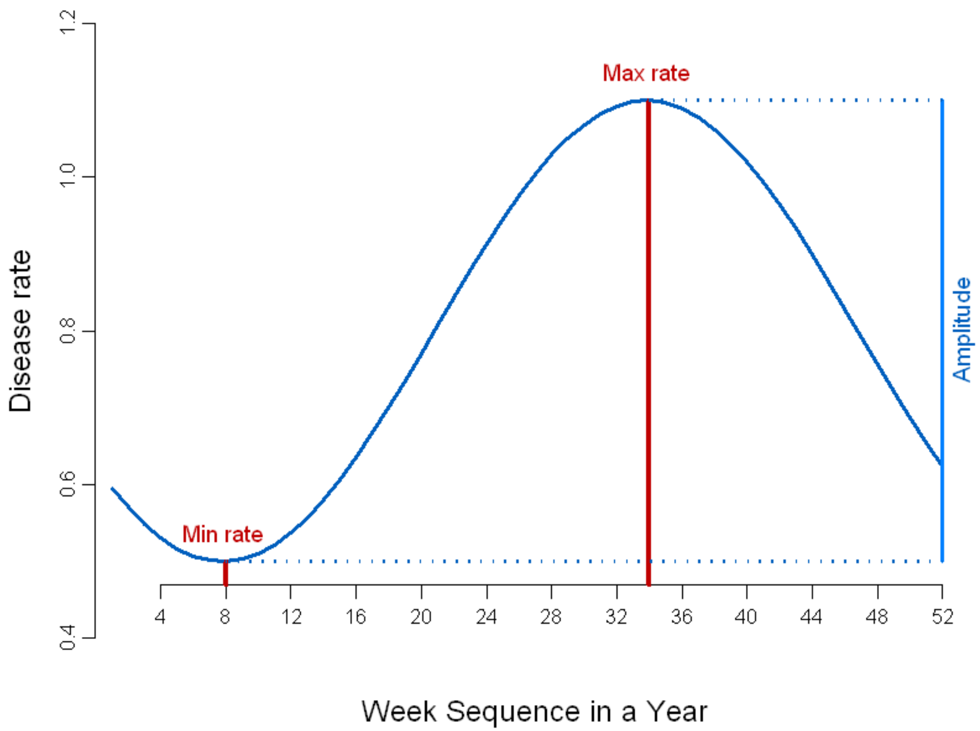
$$Var(\hat{\psi}) = (\hat{\sigma}^2_{\beta_1}\hat{\beta}_2^2 + \hat{\sigma}^2_{\beta_2}\hat{\beta}_1^2 - 2\hat{\sigma}_{\beta_1\beta_2}\hat{\beta}_1\hat{\beta}_2)/(\hat{\beta}_1{}^2 + \hat{\beta}_2{}^2)^2$$

Naumova EN, MacNeill IB. Seasonality assessment for biosurveillance systems. In: *Advances in Statistical Methods for the Health Sciences: Applications to Cancer and AIDS Studies, Genome Sequence Analysis, and Survival Analysis*. Ed. Balakrishnan et al. 2006. Birkhauser, Boston.

Harmonic Poisson Regression

Adapted for count data, suitable for health outcomes:

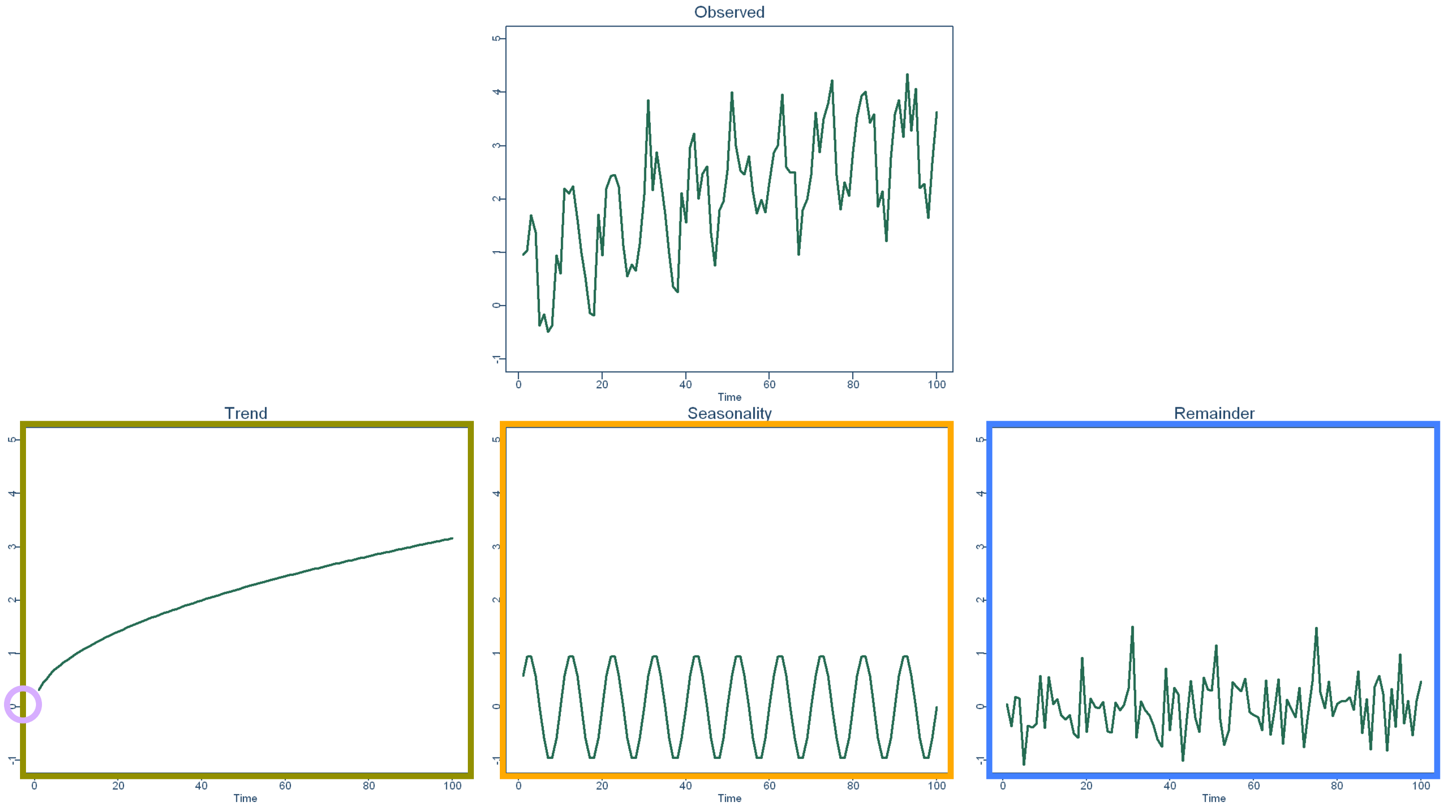
$$log[E(Y_t)] = \beta_0 + \beta_1 sin(2\pi\omega t) + \beta_2 cos(2\pi\omega t) + \epsilon_t$$



Gamma (γ)	$\sqrt{(\beta_1^2 + \beta_2^2)}$
Seasonal Peak	$e^{\beta_0 + \gamma}$
Seasonal Nadir	$e^{\beta_0 - \gamma}$
Intensity	$e^{2\gamma}$
Peak timing	$Mf(.)$

Wenger JB, Naumova EN. Seasonal synchronization of influenza in the United States older adult population. *PLoS ONE*. 2010 ; 15;5(4):e10187.

Time Series Decomposition



$$log[E(Y)] = \beta_0 + \beta_1(t) + \beta_2(t^2) + \beta_3(t^3) + \beta_4 sin(2\pi\omega t) + \beta_5 cos(2\pi\omega t) + \beta_6(u_t) + \epsilon$$

Decomposition of Time Series

$$Y_t = \beta_0 + \beta_1(T_t) + \beta_2(S_t) + \beta_3(C_t) + \beta_4(H_t) + \beta_5(I_t) + \beta_6(X_t) + \varepsilon$$

T: Trend component

S: Seasonal component

C: Day-of-the-week effect

H: Holiday effect

I: Irregular component

X: Exposure

Te: Trend component

Se: Seasonal component

Ce: Day-of-the-week effect

He: Holiday effect

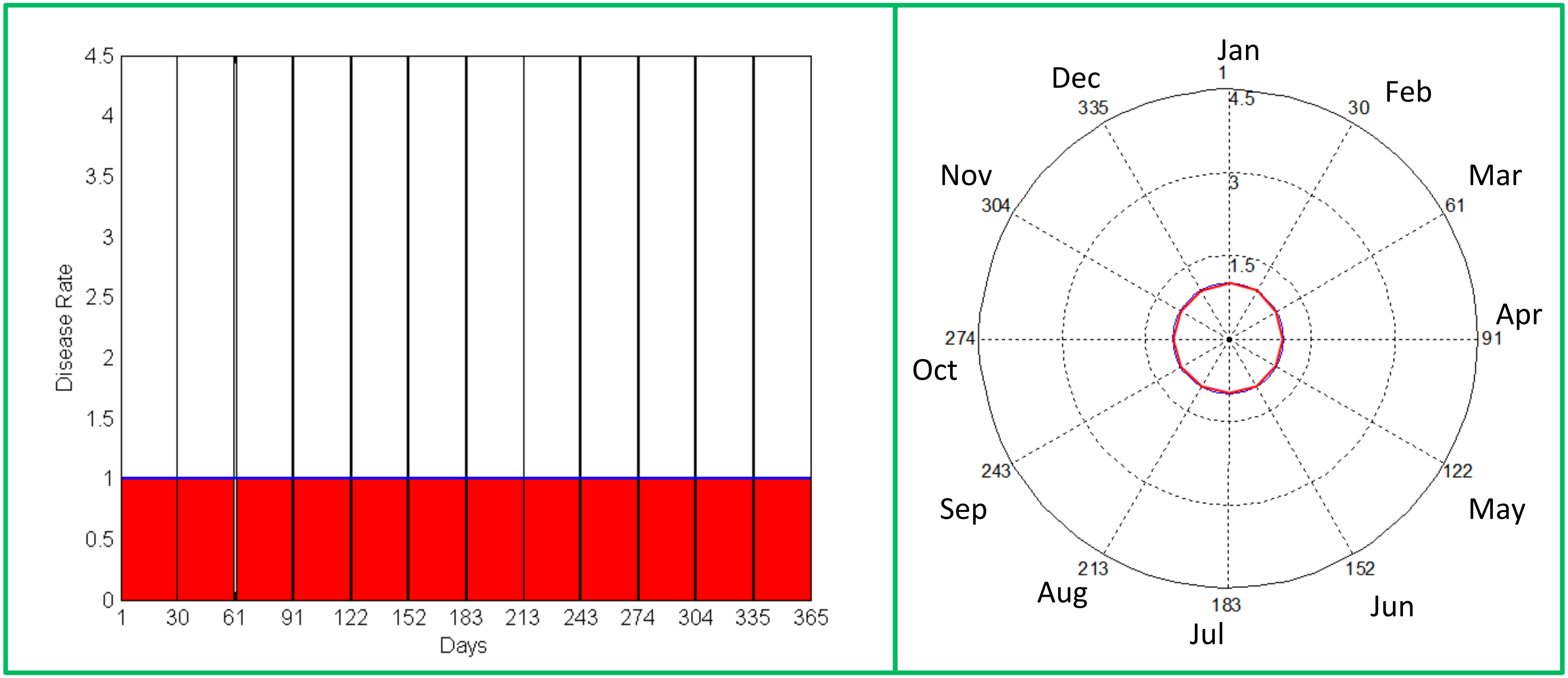
Ie: Irregular component

SINGLE ANNUAL PEAK

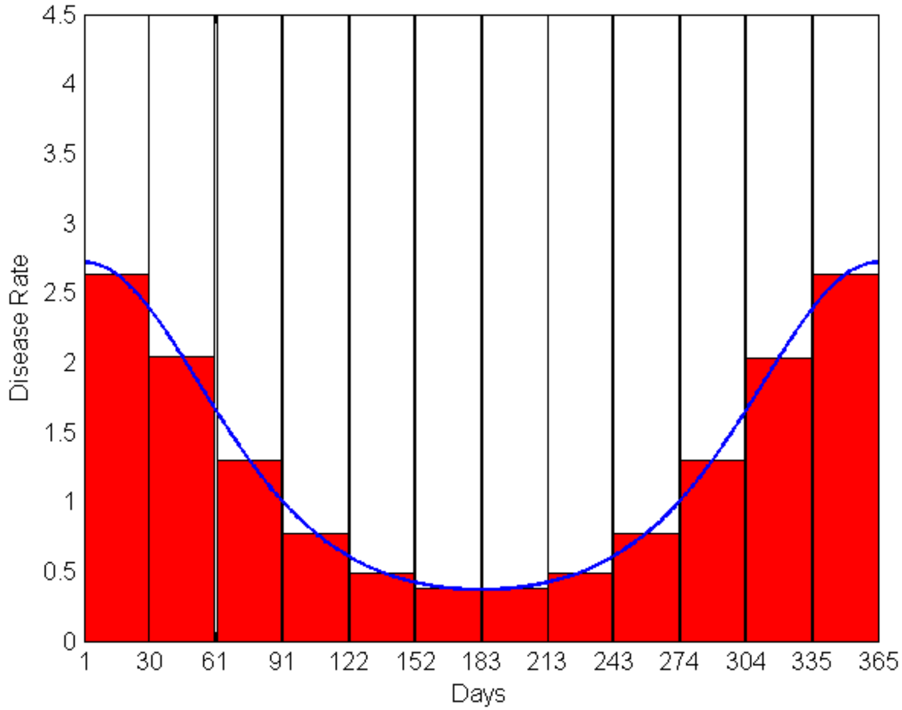
The progression of peaks throughout the year

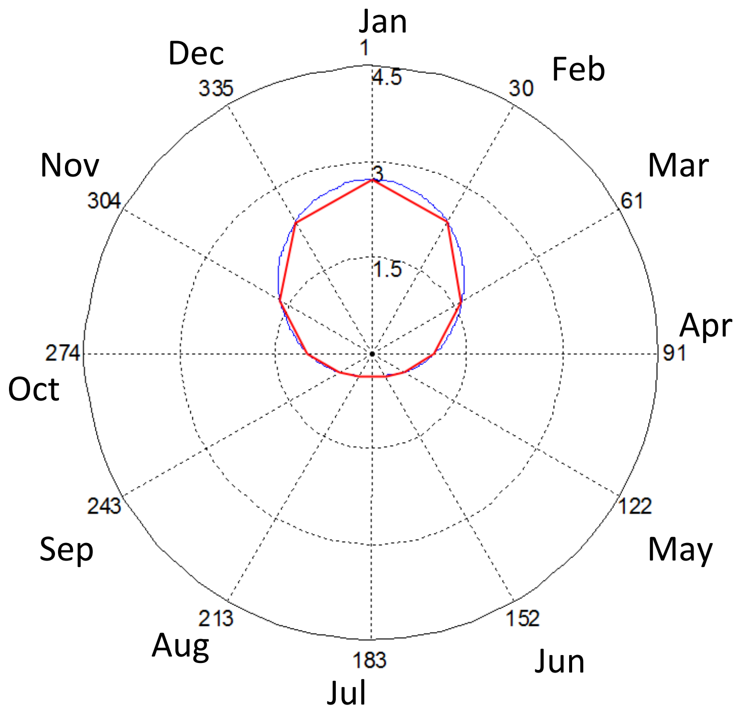
in Cartesian and Polar coordinates plots

$\beta_1 = 0, \beta_2 = 0$

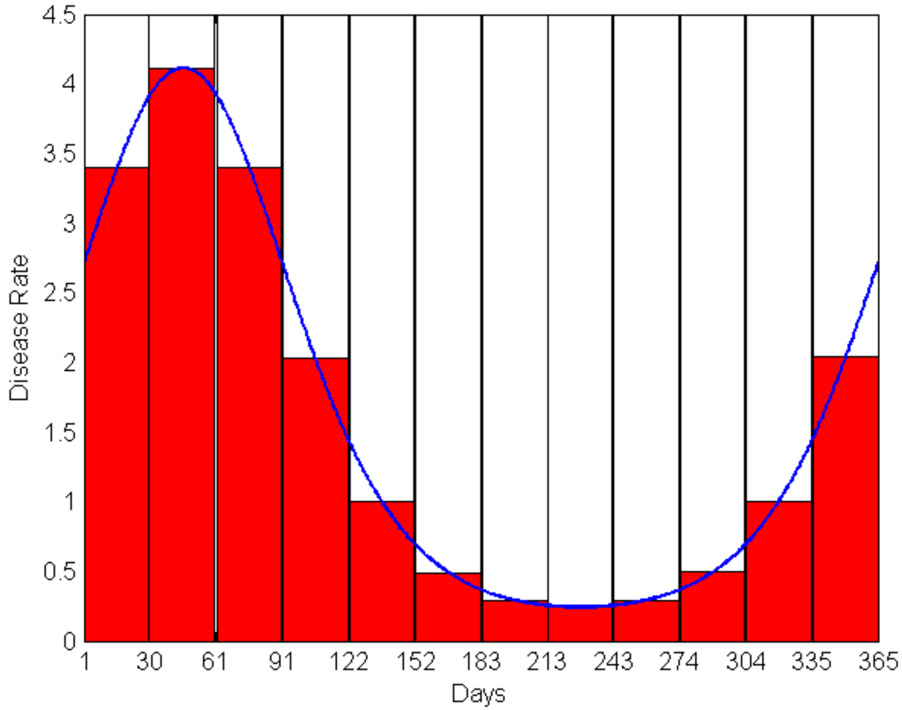


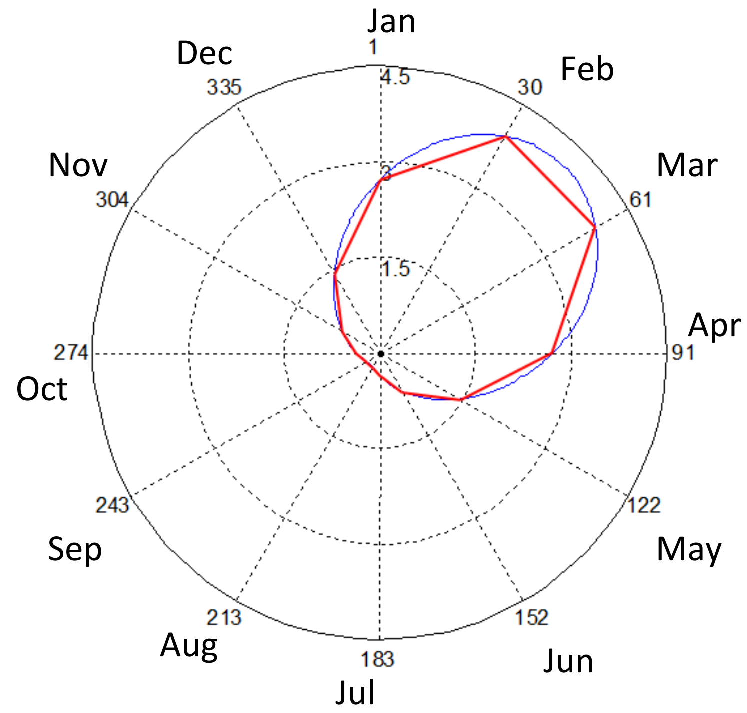
$\beta_1 = 0, \beta_2 = 1$



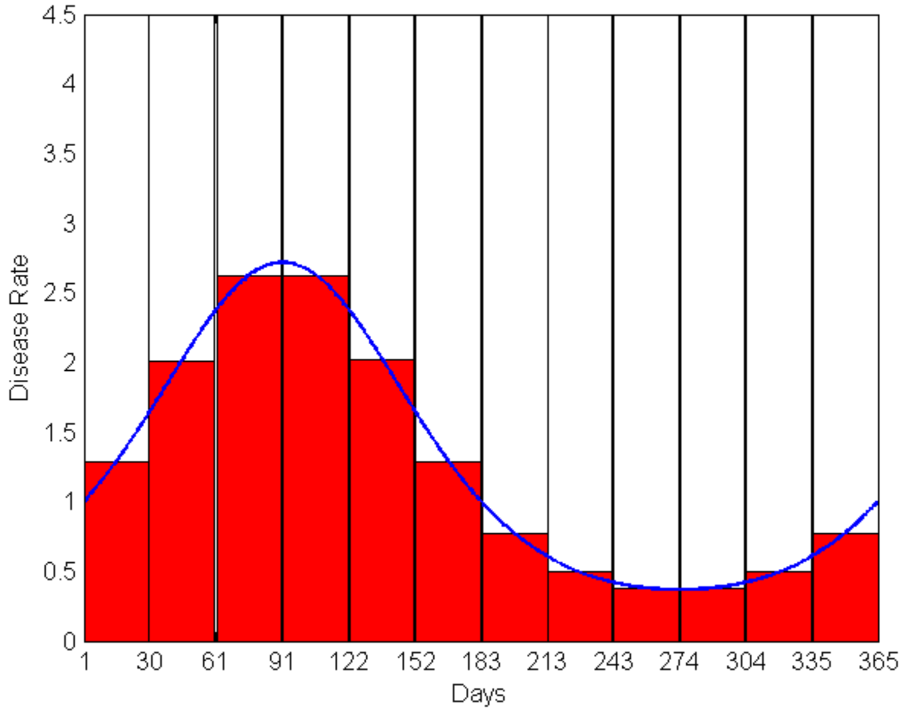


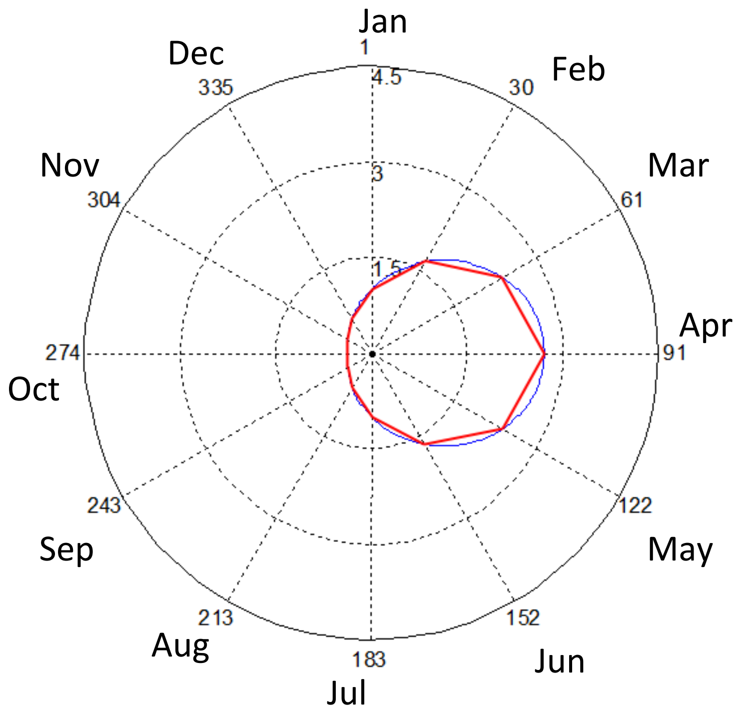
$\beta_1 = 1, \beta_2 = 1$



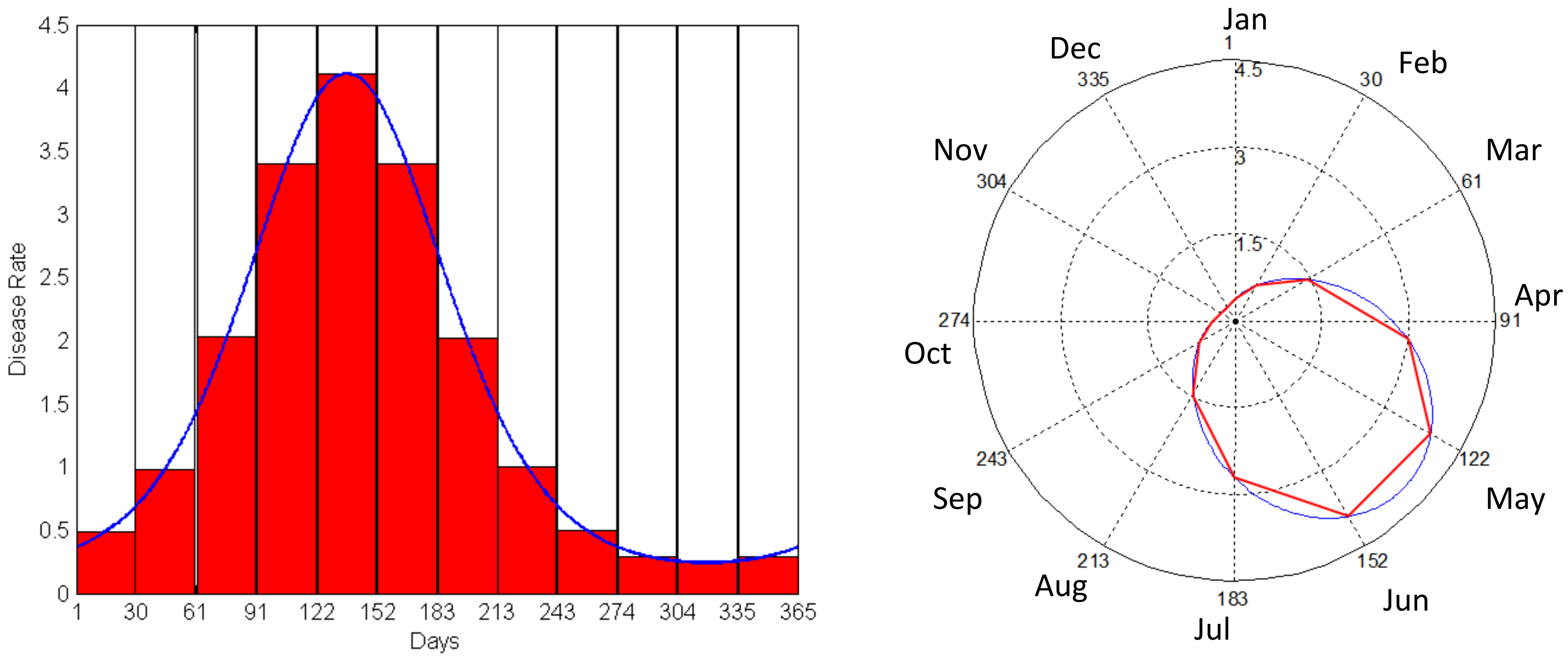


$\beta_1 = 1, \beta_2 = 0$

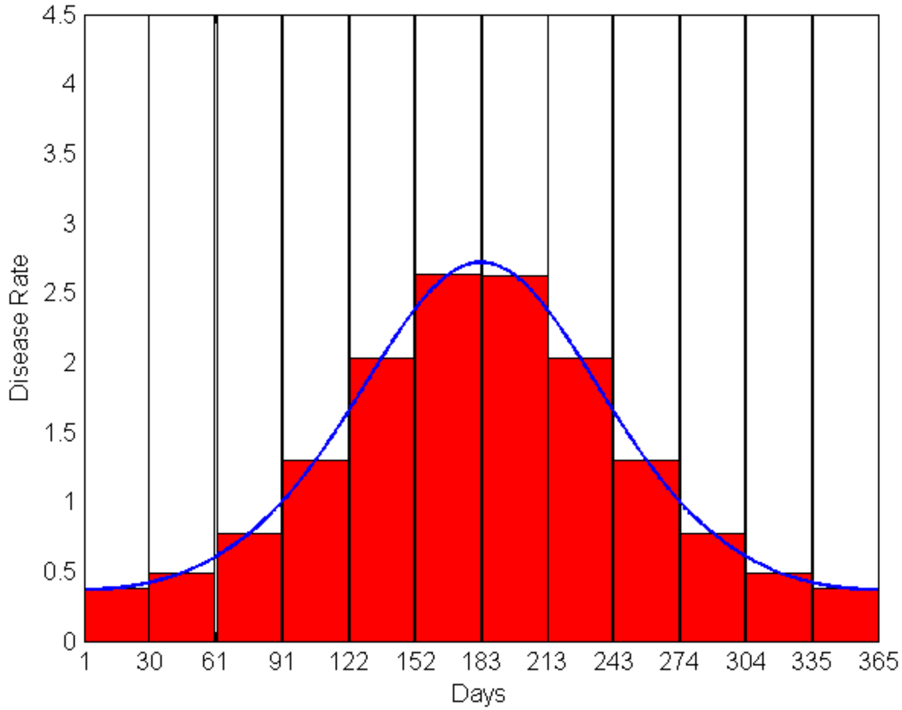


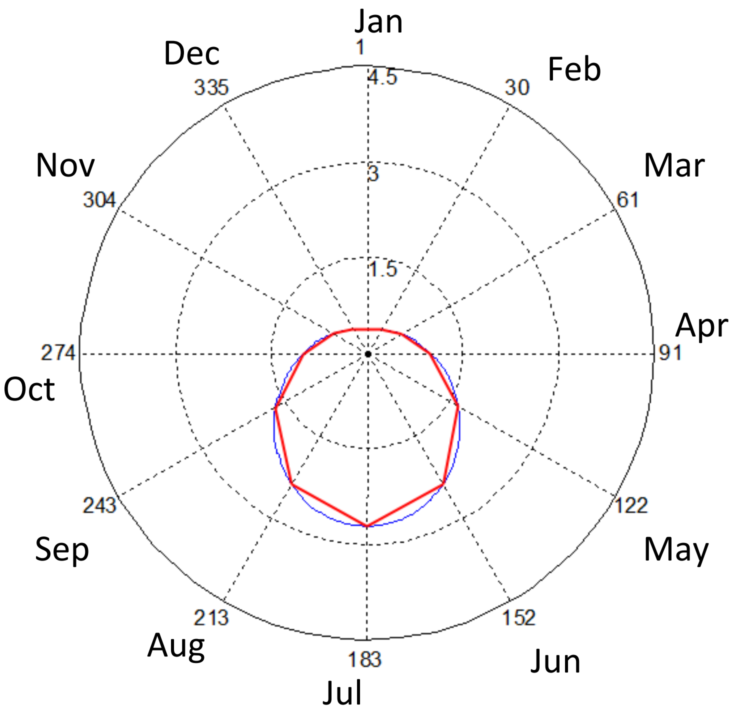


$\beta_1 = 1, \beta_2 = -1$

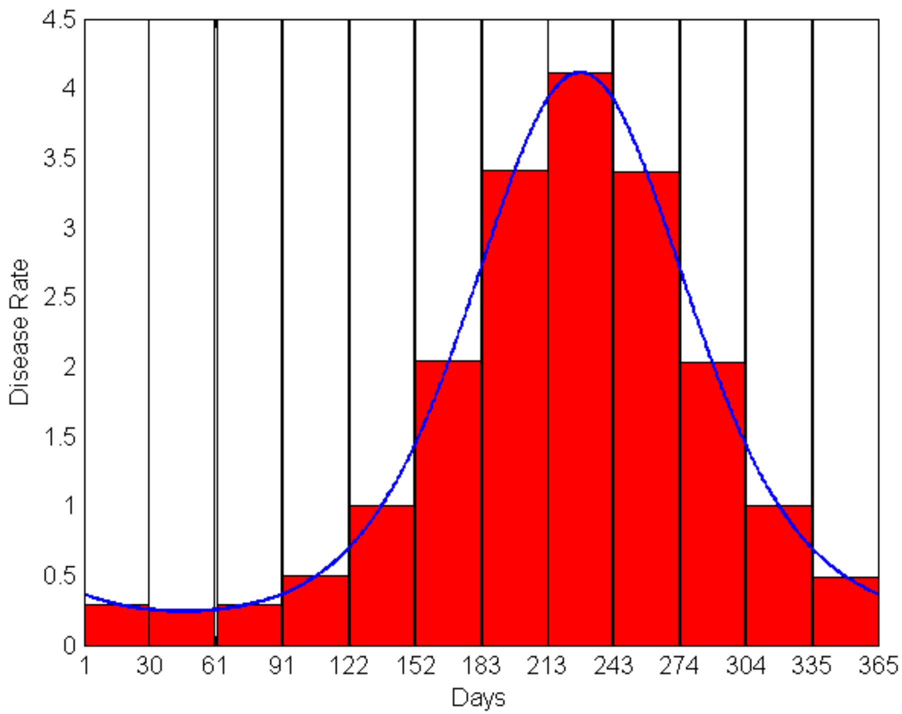


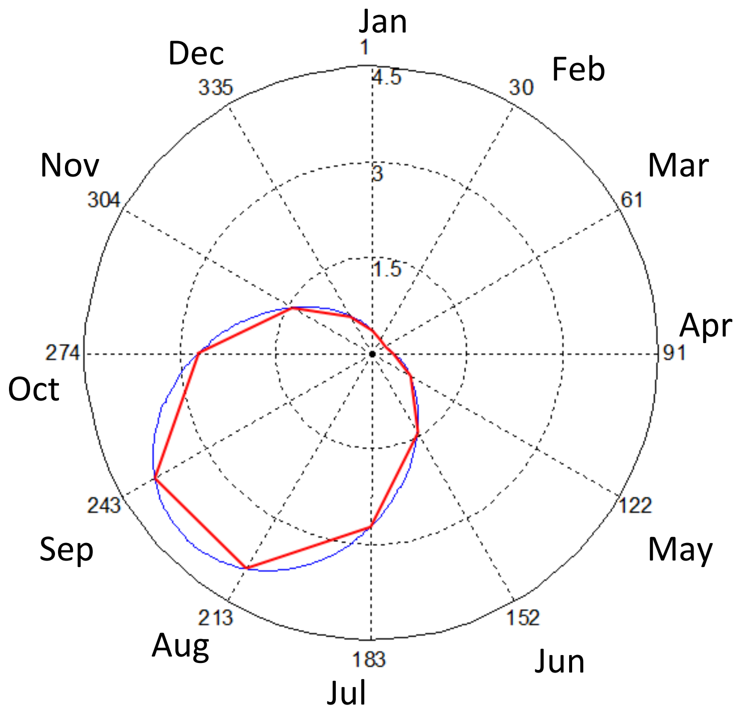
$\beta_1 = 0, \beta_2 = -1$



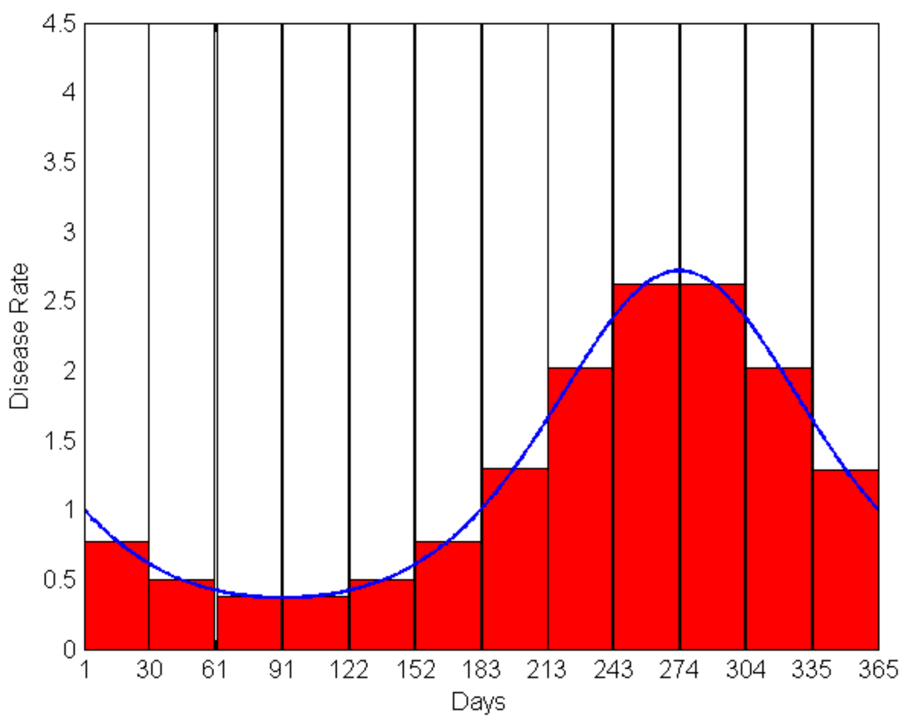


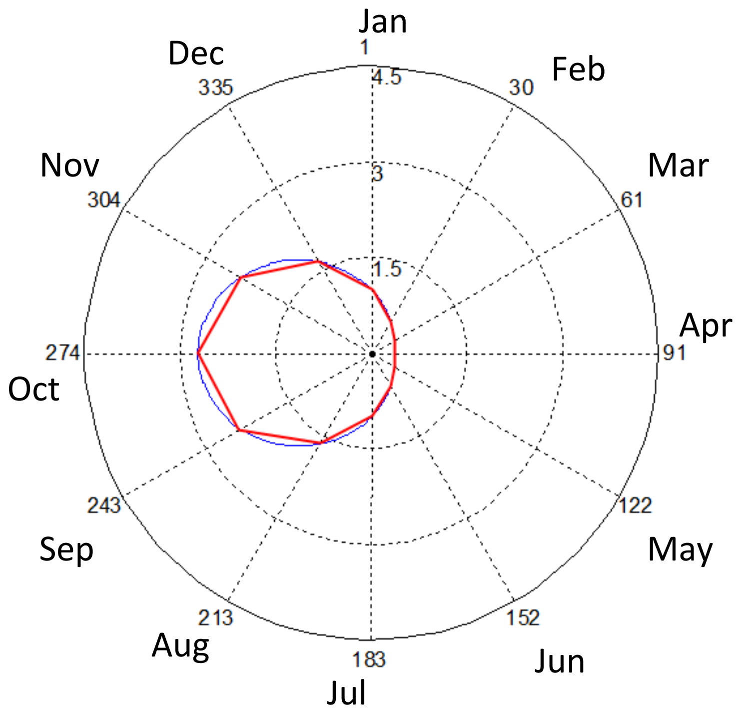
β_1= -1, β_2= -1



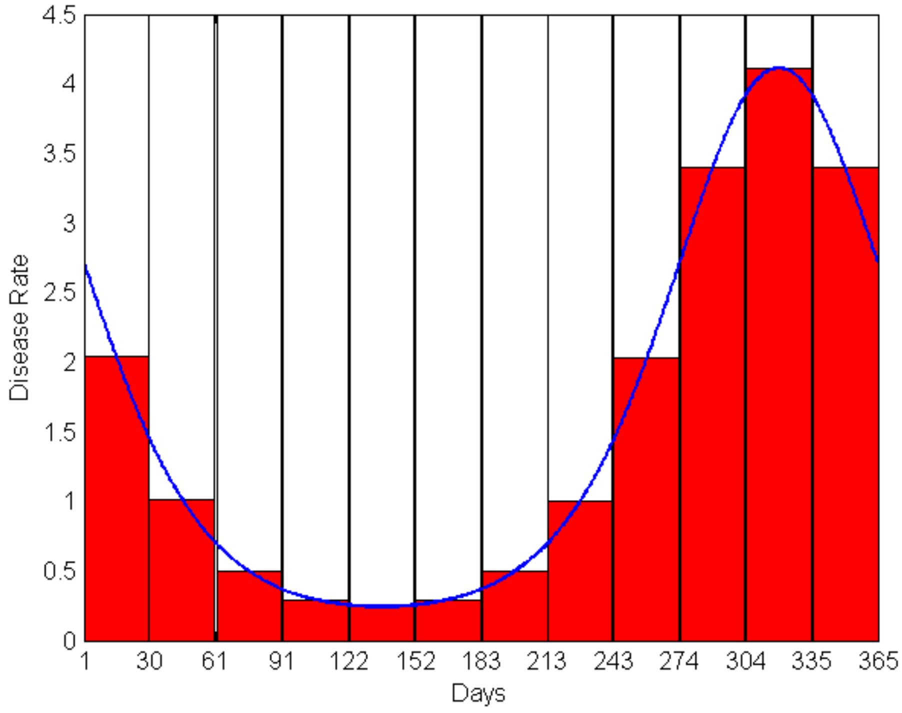


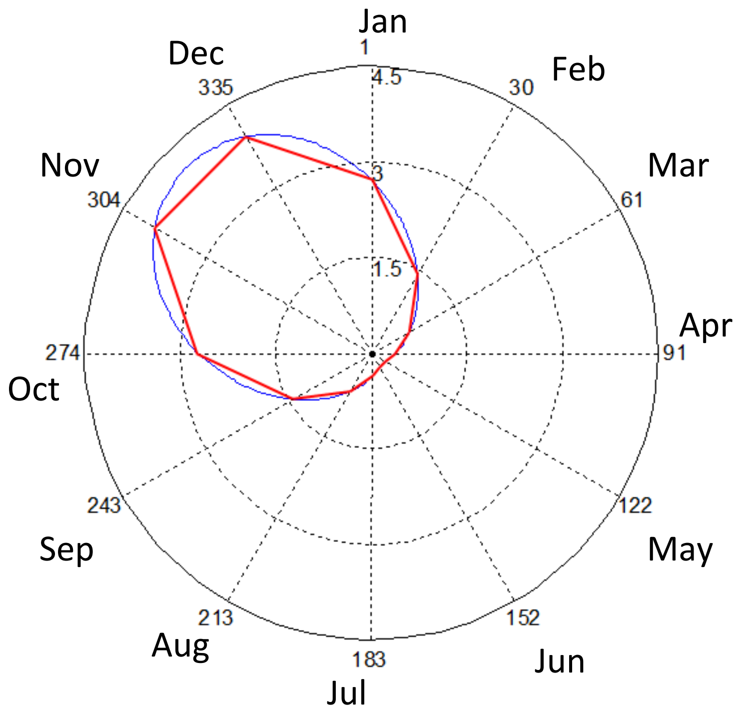
$\beta_1 = -1, \beta_2 = 0$





$\beta_1 = -1, \beta_2 = 1$

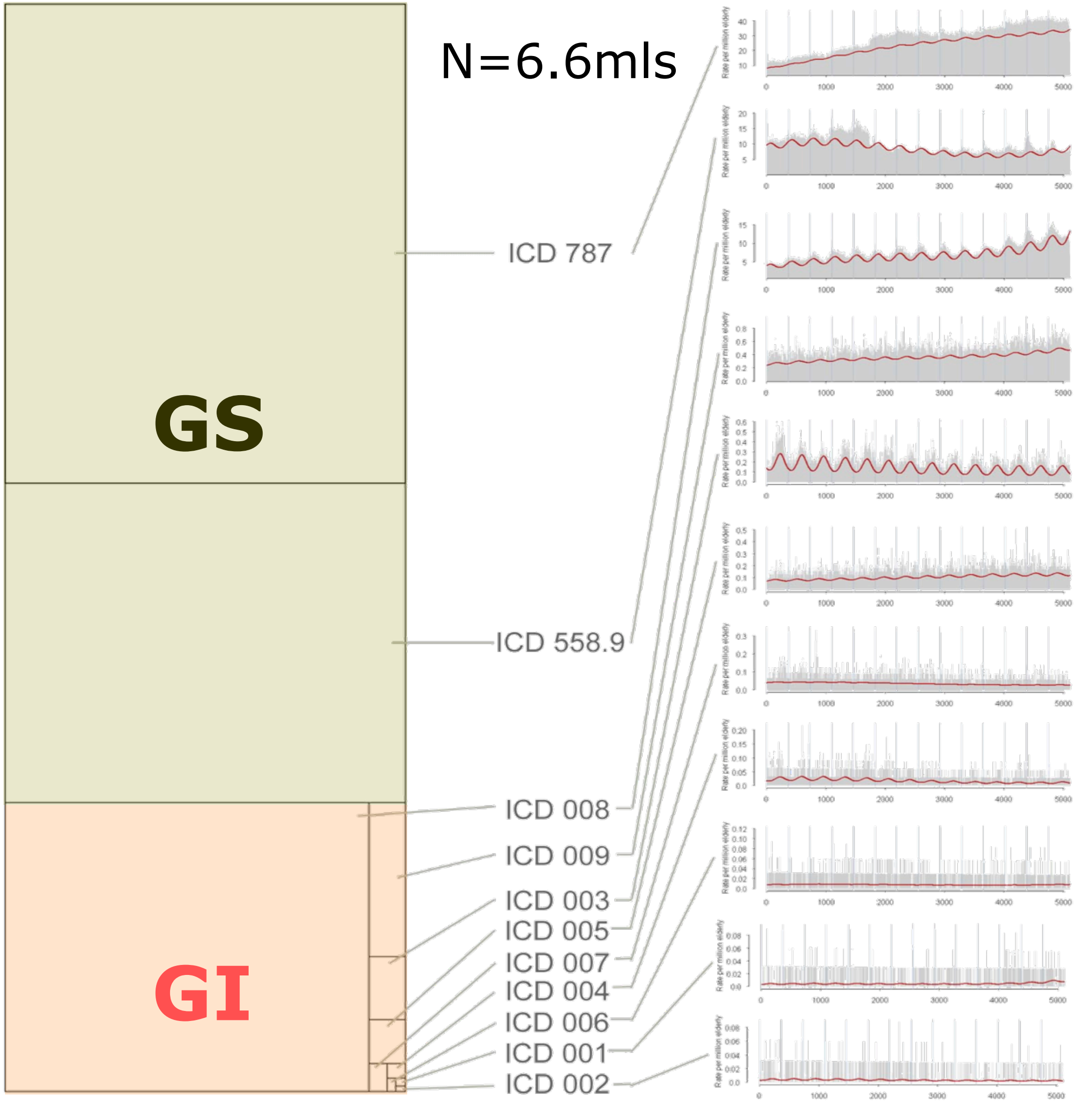




EXAMPLE 1

A search for etiological clues in seasonality of hospitalizations due to non-specific gastrointestinal diseases

Hospitalizations due to GI Infections



787: Symptoms of digestive system

558.9: Unspecified/noninfectious

008: GI due to other organisms

009: Ill-defined intestinal infections

003: *Salmonella* infections

005: Other food poisoning

007: Protozoal intestinal diseases

004: Shigellosis

006: Amebiasis

001: Cholera

002: Typhoid & paratyphoid fevers

Chui KKH, Jagai J, Griffiths JK, Naumova EN. Hospitalization of the Elderly in the United States for Nonspecific Gastrointestinal Diseases: A Search for Etiological Clues. Am J Public Health. 2011: e1-e5. doi:10.2105/AJPH.2010.300096

EXAMPLE 2

An evidence for potential synchronization by a common environmental factor in a given location

Seasonality of Waterborne Diseases

Giardia and *Cryptosporidium spp.*

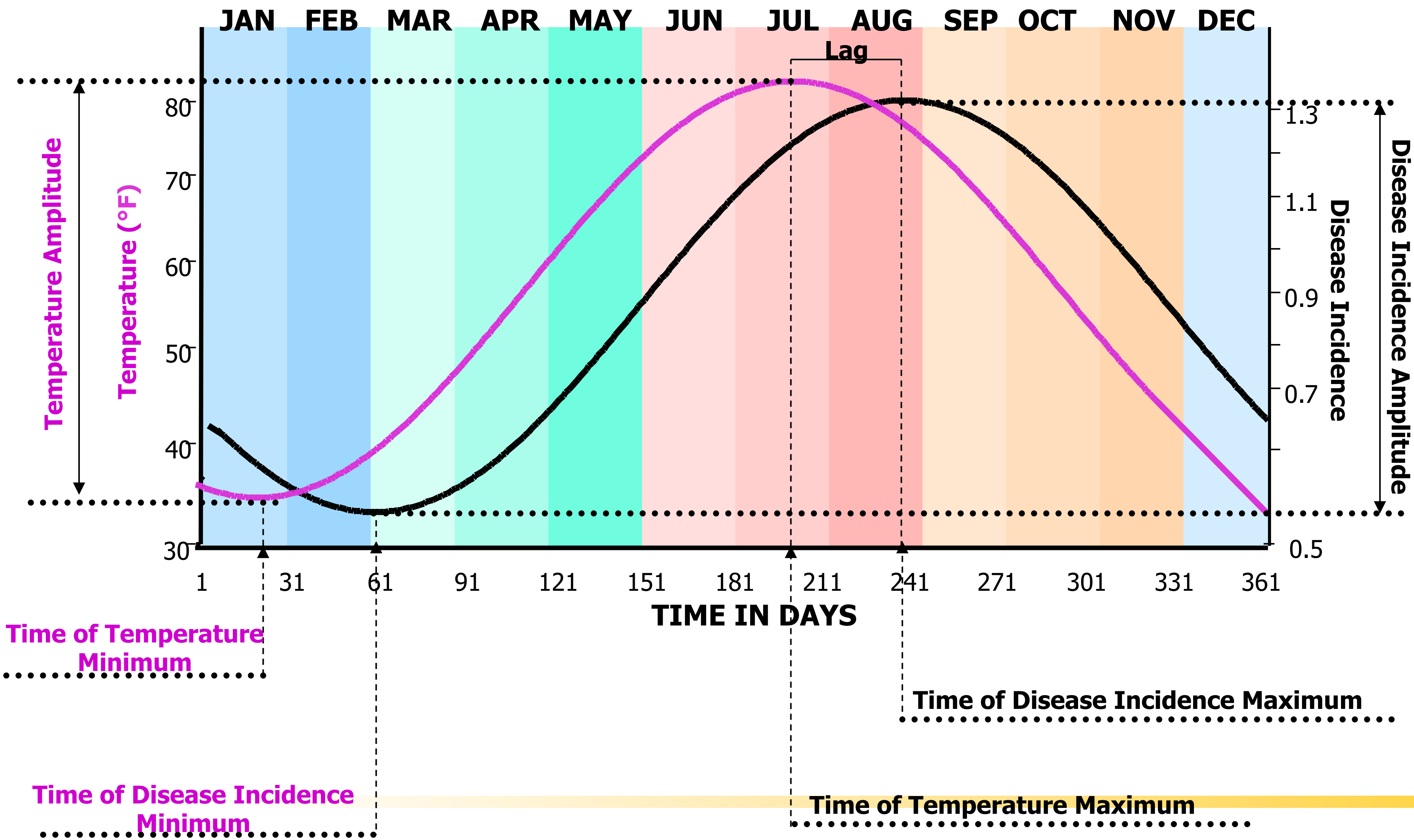
- Demonstrate seasonal patterns in environment[1]
- Present in drinking water supplies and surface waters[2,3]
- Increase concentrations associated with increased precipitation[4]

Giardiasis and cryptosporidiosis

- Outbreaks associated with increased precipitation[5]
- Increased rates associated with water quality parameters
  - Increased turbidity[6]
  - Changes in riverflow[7]

1. Robertson, L. J. and B. Gjerde Scandinavian Journal of Public Health 29(3): 200-7.
2. LeChevallier, M. W., W. D. Norton, et al. Applied & Environmental Microbiology 57(9): 2617-21.
3. LeChevallier, M. W., W. D. Norton, et al. Applied & Environmental Microbiology 57(9): 2610-6.
4. Atherholt, T. B., M. W. LeChevallier, et al. Journal AWWA 90(9): 66-80.
5. Curriero, F. C., J. A. Patz, et al. American Journal of Public Health 91(8): 1194-9.
6. Egorov, A., E. N. Naumova, et al. The International Journal of Environmental Health Research 13: 81-94.
7. Lake, I. R., G. Bentham, et al. Journal of Water & Health 3(4): 469-74.

Seasonal Oscillations: Synchronization



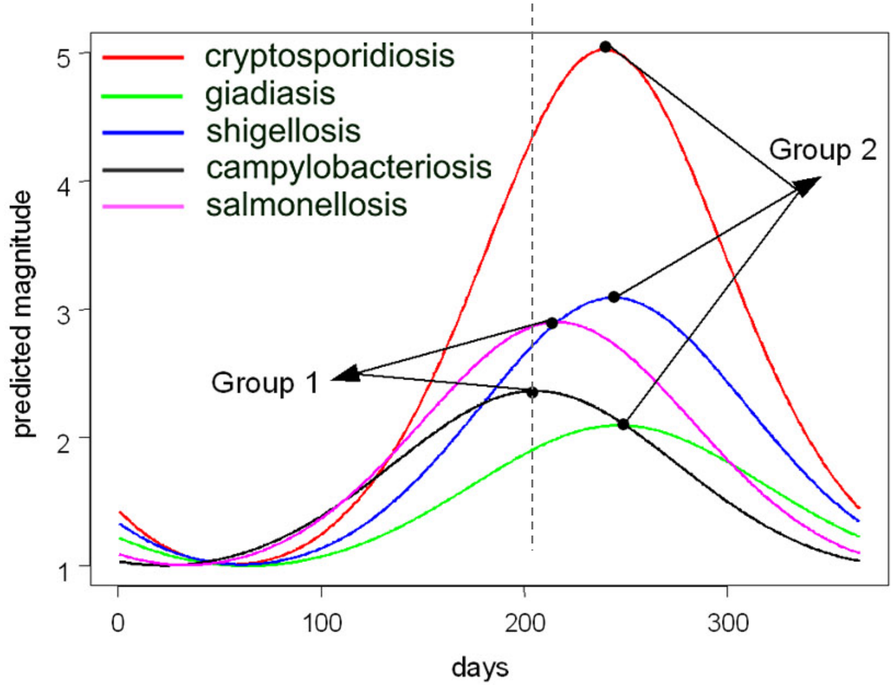
Synchronization of Peak Timing in WBIs in MA

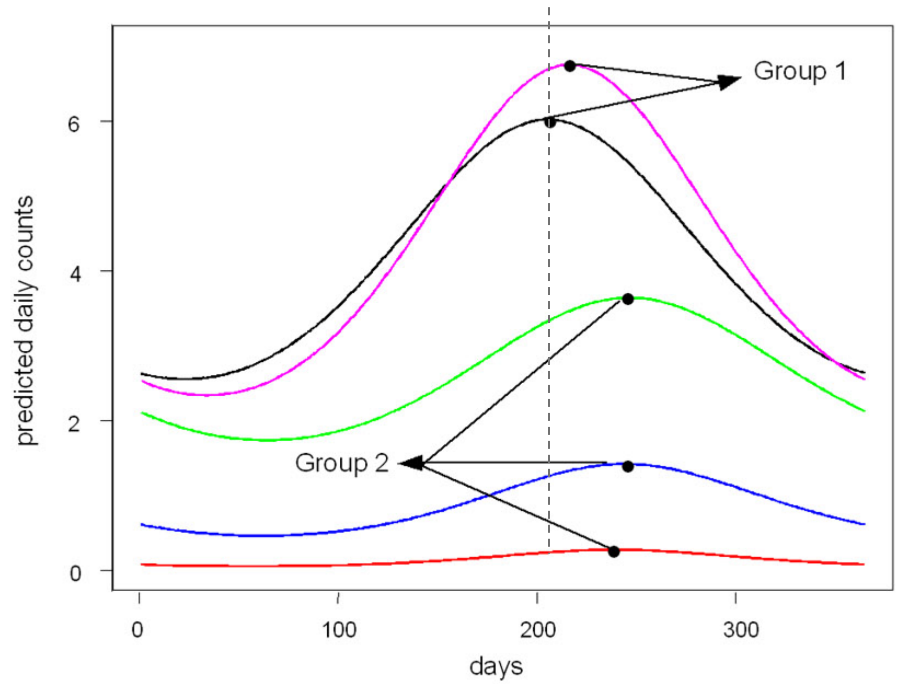
Seasonal peak of six enteric infections with respect to peak in temperature (1992-2001)

Temperature peak – 206th (±0.2) day of the year (typically 24 or 25 July, week 29)

Group 1 – *Campylobacter & Salmonella* infections peaked near temperature peak

Group 2 – Cryptosporidiosis, Shigellosis and Giardiasis peaked ~40 days after temperature





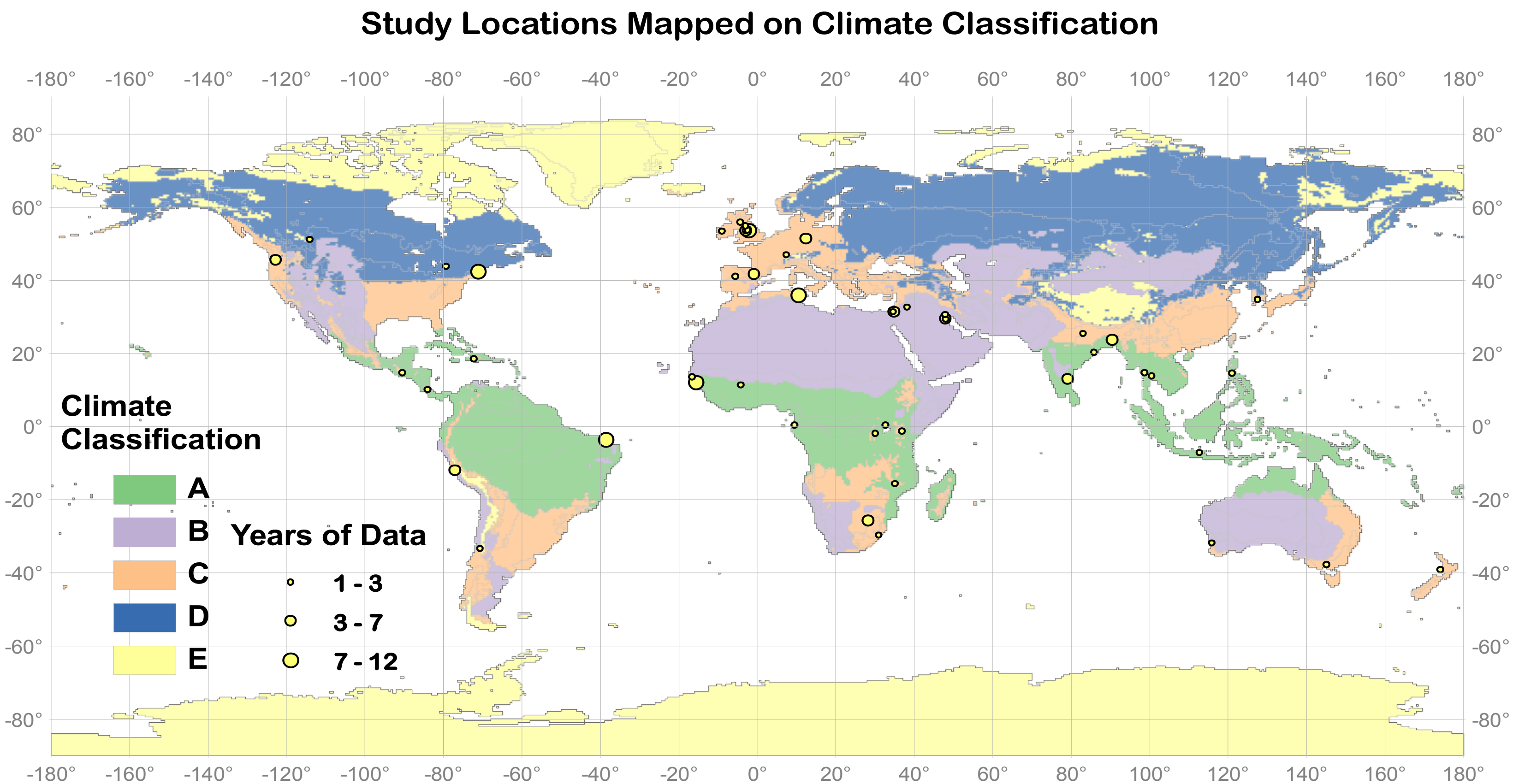
Naumova EN, Jagai J, Matyas B, DeMaria A, MacNeill IB, Griffiths JK. Seasonality in six enterically transmitted diseases and ambient temperature. *Epidemiol Infect. 2007, 135:281-292.*

EXAMPLE 3

An evidence for potential synchronization of cryptosporidiosis by common environmental factors across multiple locations

Meta-analysis approach

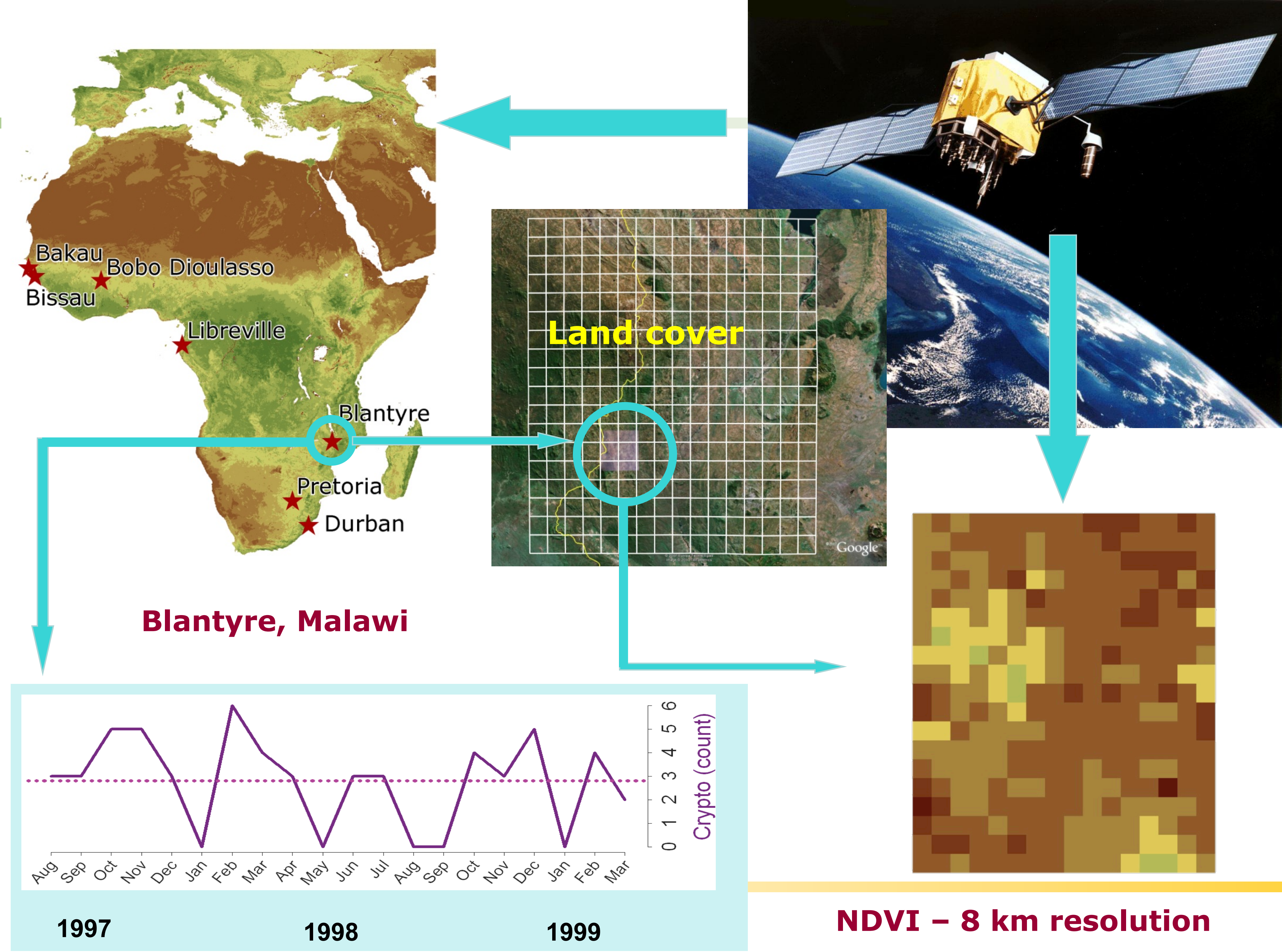
Seasonality on Global Scale



Link published cryptosporidiosis outcome data with temperature and precipitation and normalized vegetation index

61 studies with for 1-12 years of data analyzed (22 studies had NDVI)

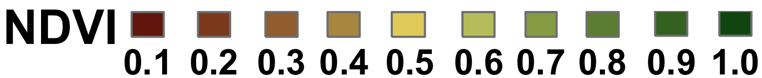
Jagai JS, Castronovo DA, Monchak J, Naumova EN. Seasonality of cryptosporidiosis: a meta-analysis approach. *Environmental Research*. 2009 May: 109(4):465-78.



Bakau
Bobo Dioulasso
Bissau
Libreville
Blantyre
Pretoria
Durban
Land cover
Google
Blantyre, Malawi
NDVI – 8 km resolution
Crypto (count)
0 1 2 3 4 5 6
Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar
1997
1998
1999

Blantyre, Malawi

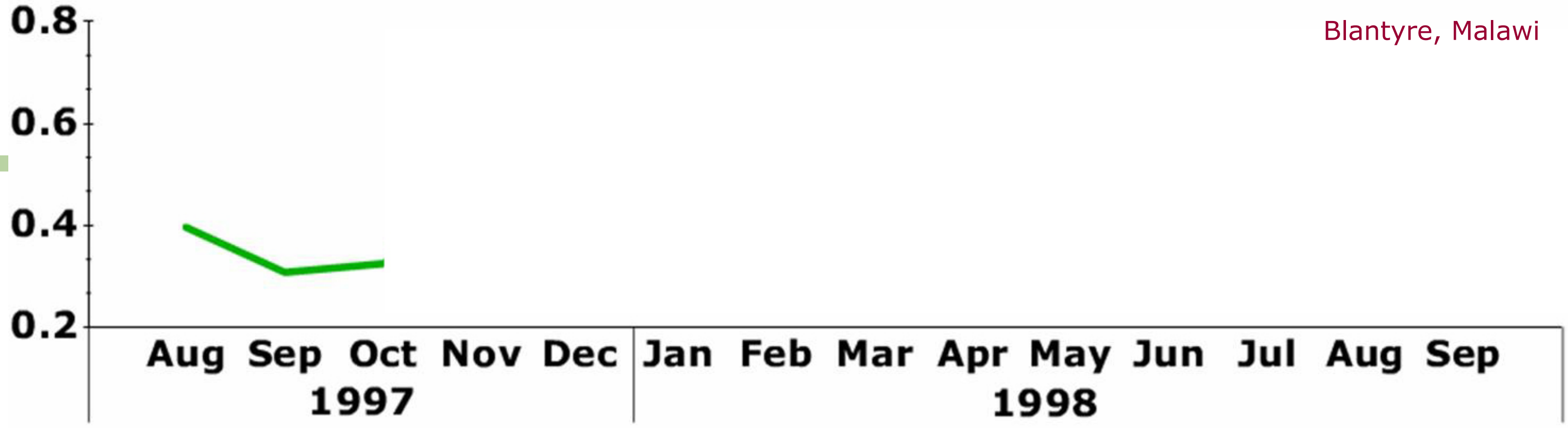
NDVI

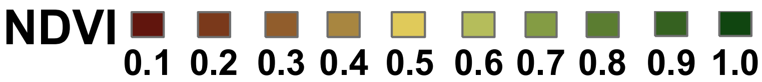


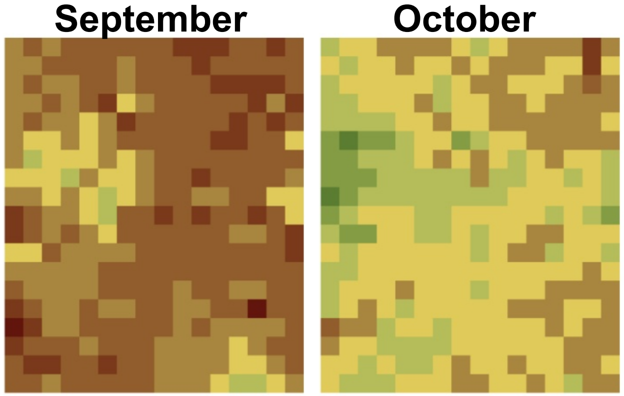
September

Blantyre, Malawi

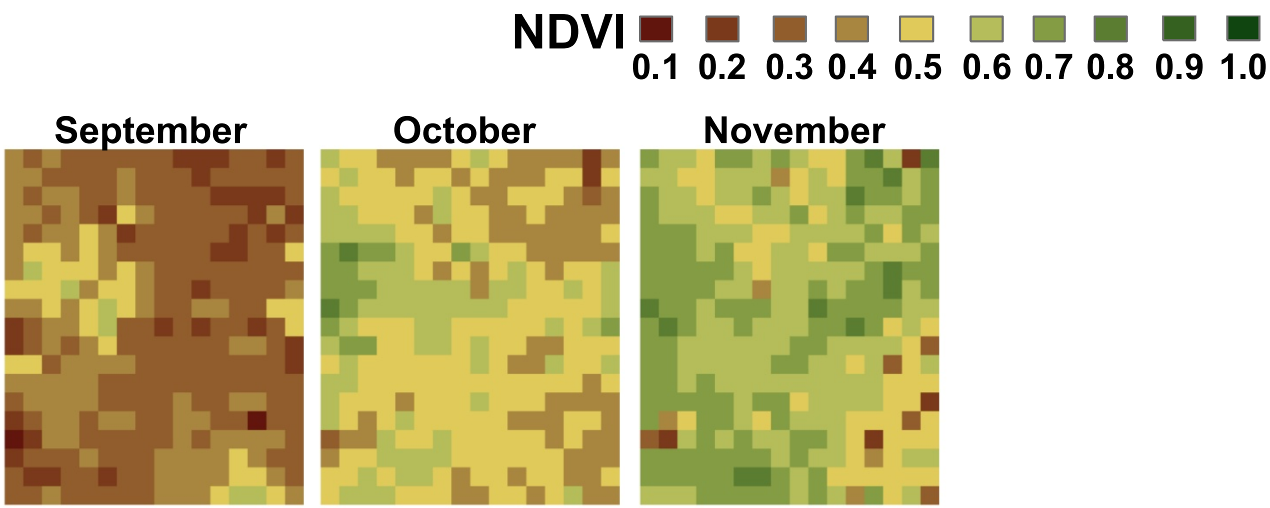
NDVI



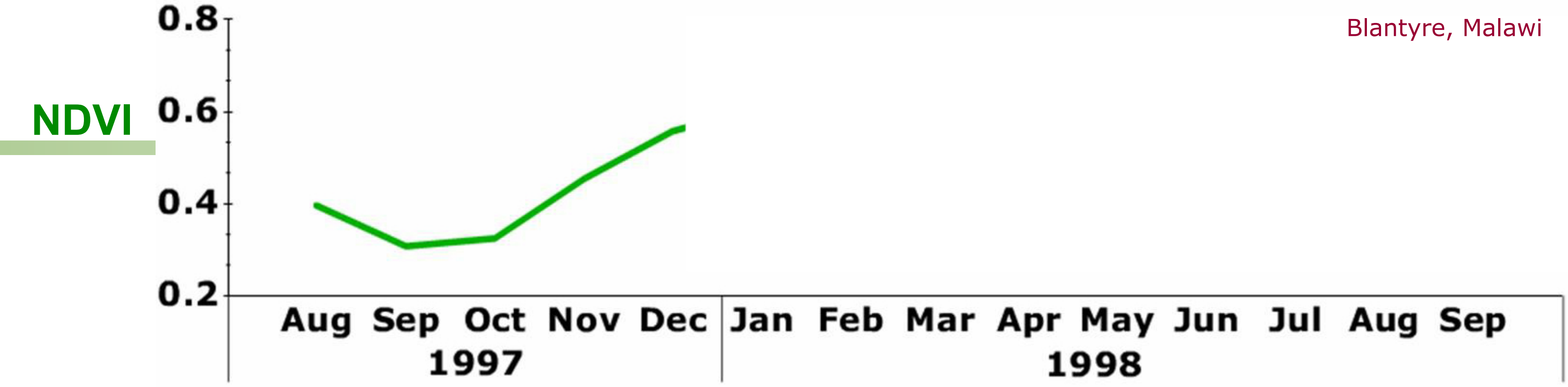


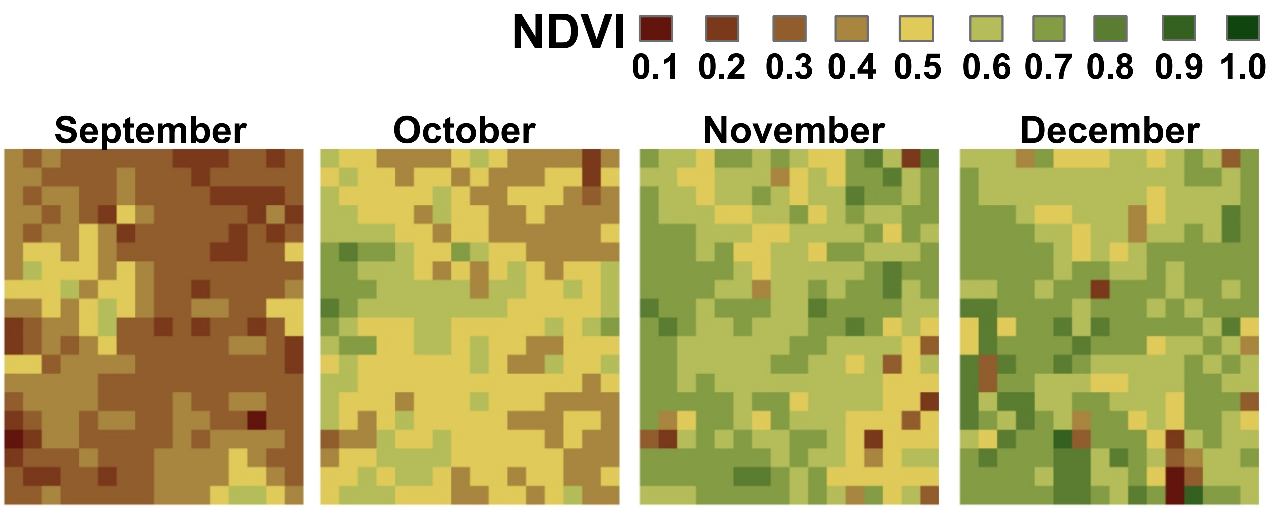


Blantyre, Malawi

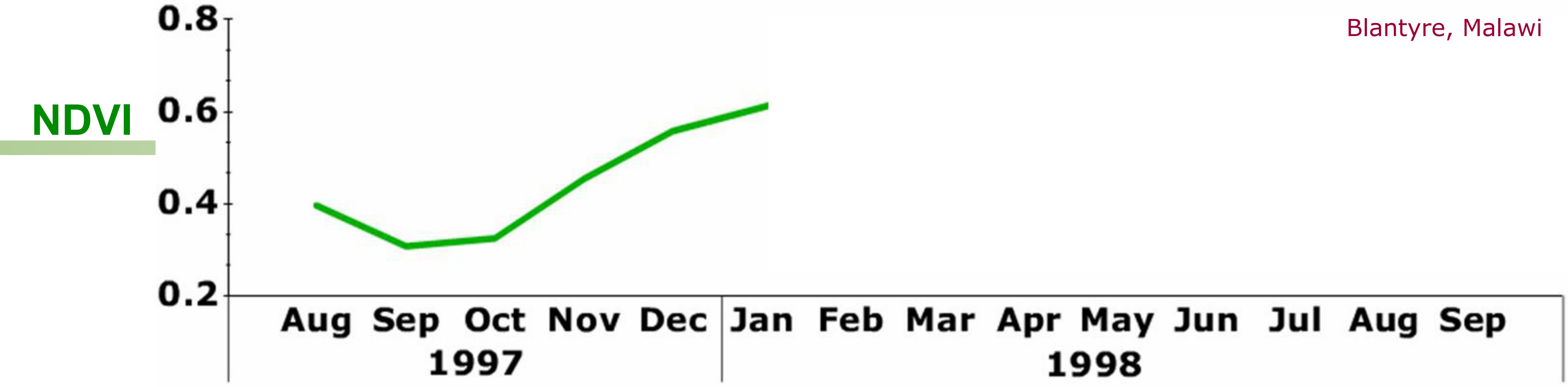


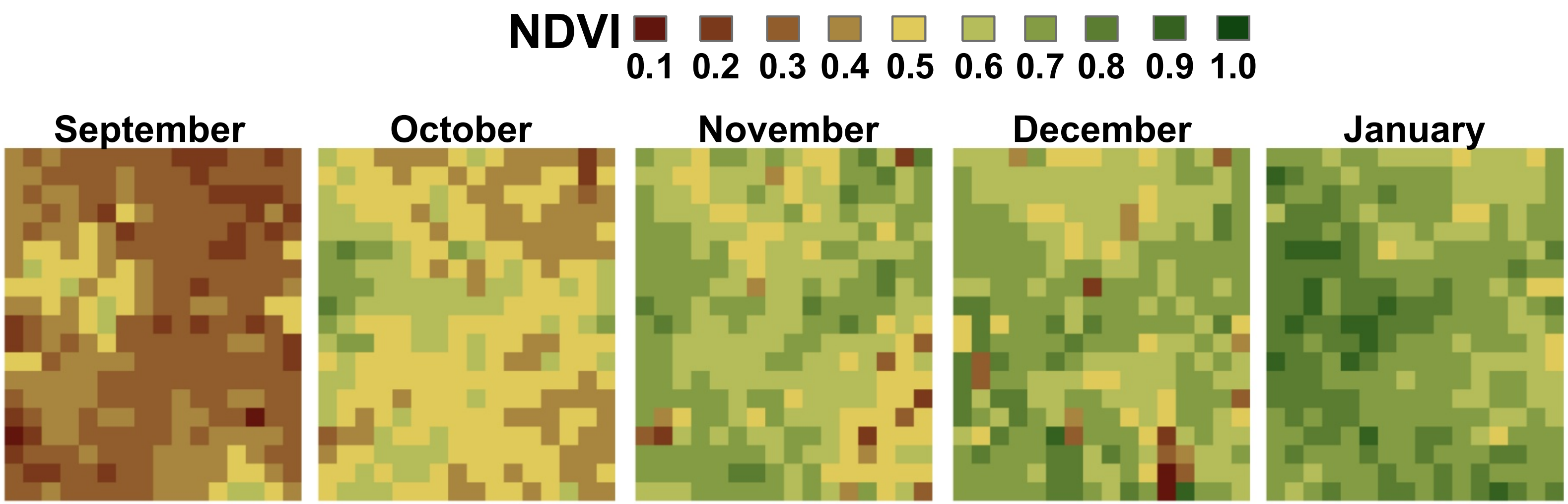
Blantyre, Malawi



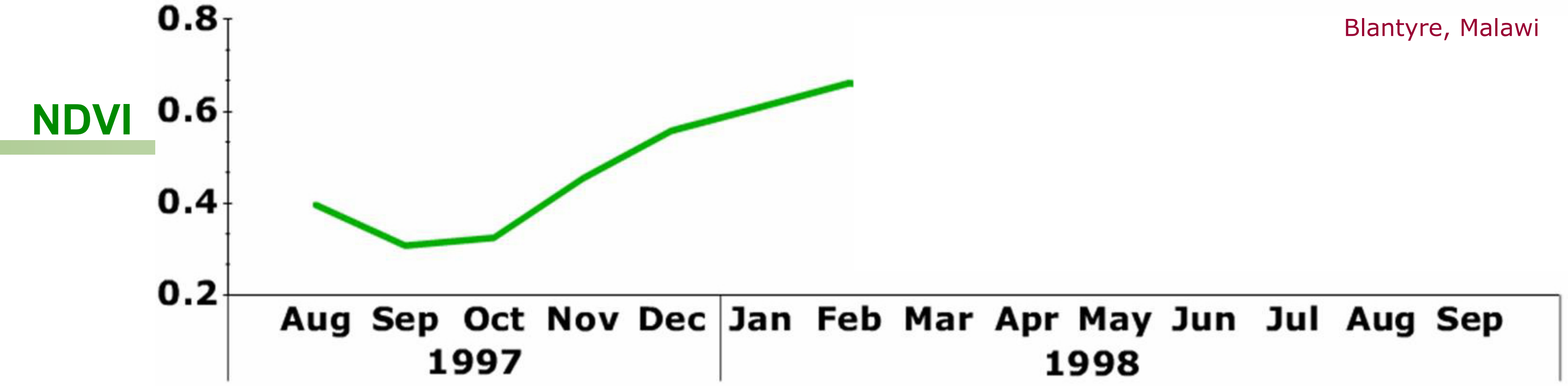


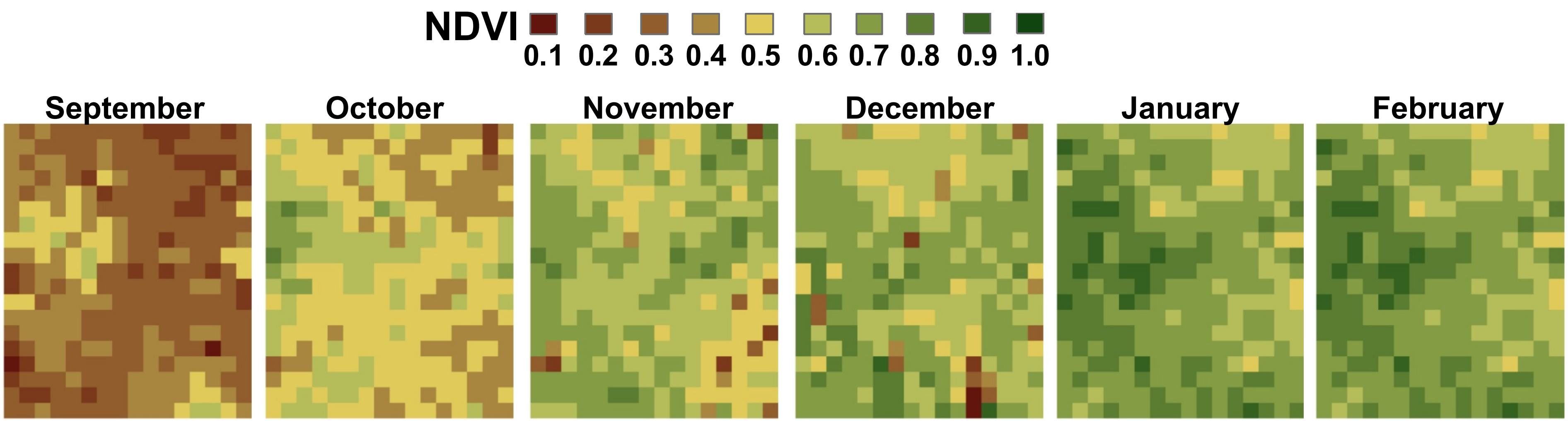
Blantyre, Malawi





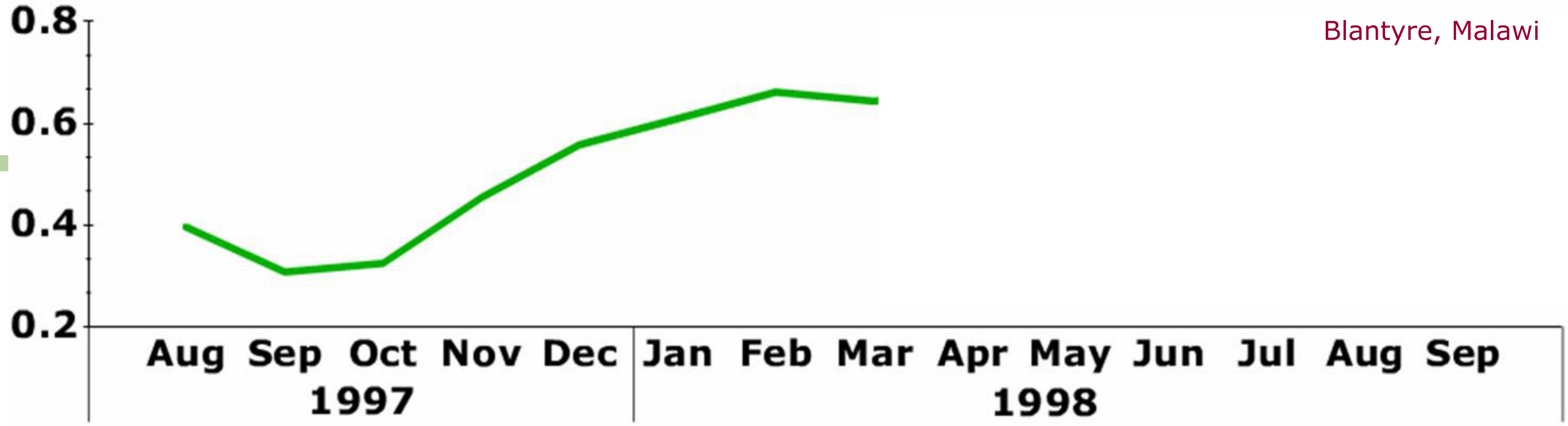
Blantyre, Malawi

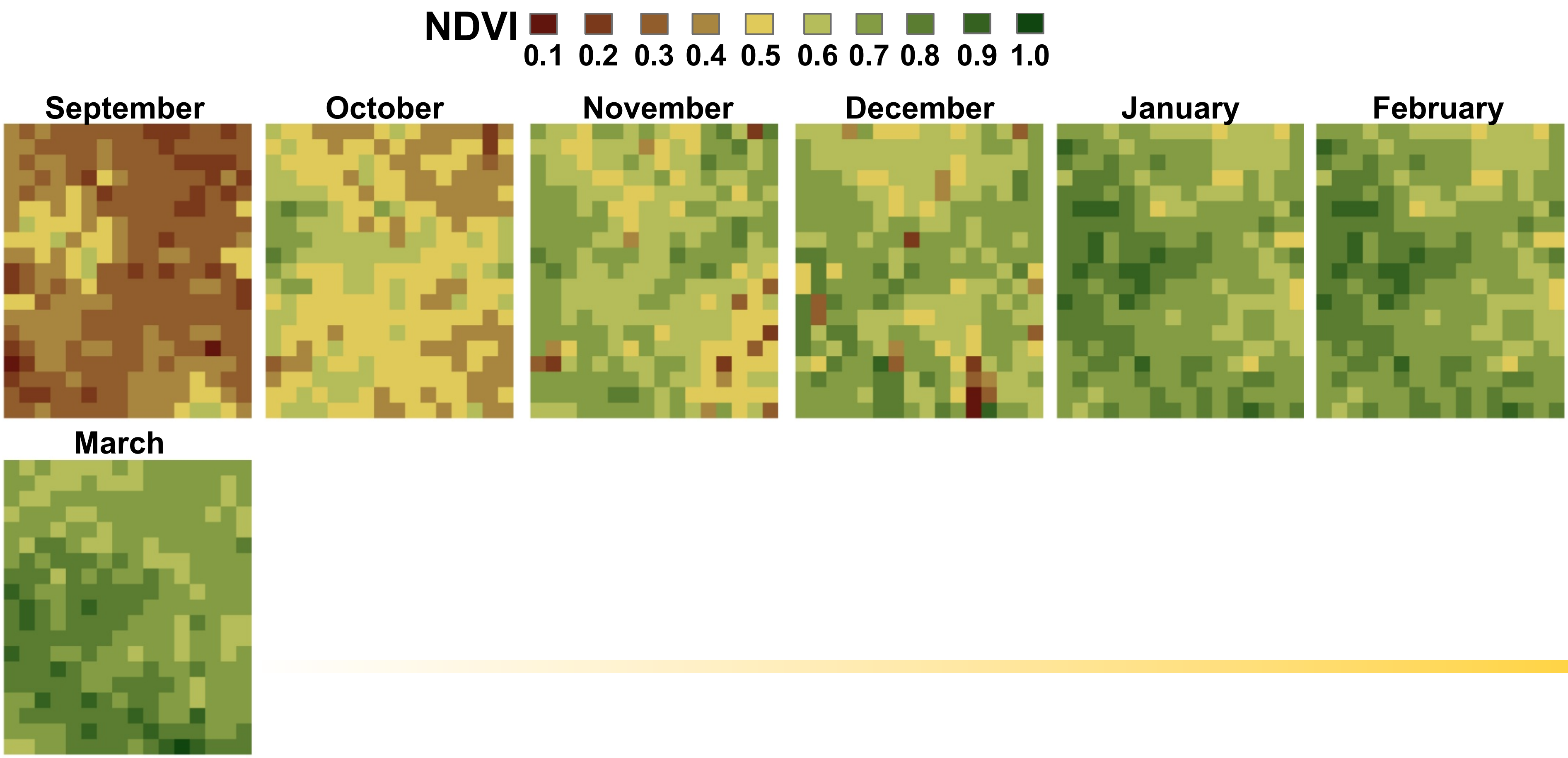




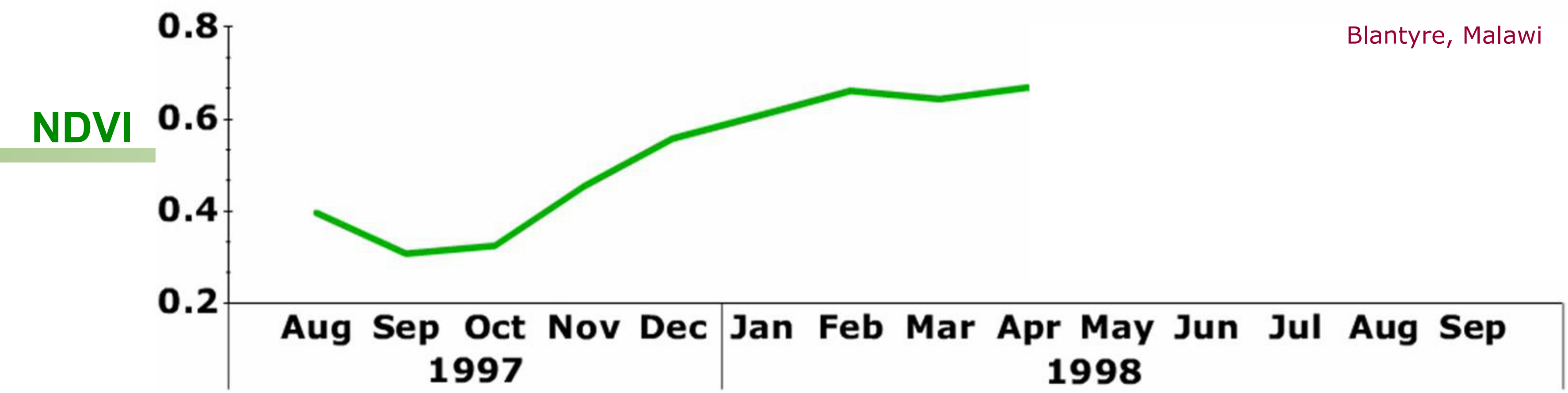
Blantyre, Malawi

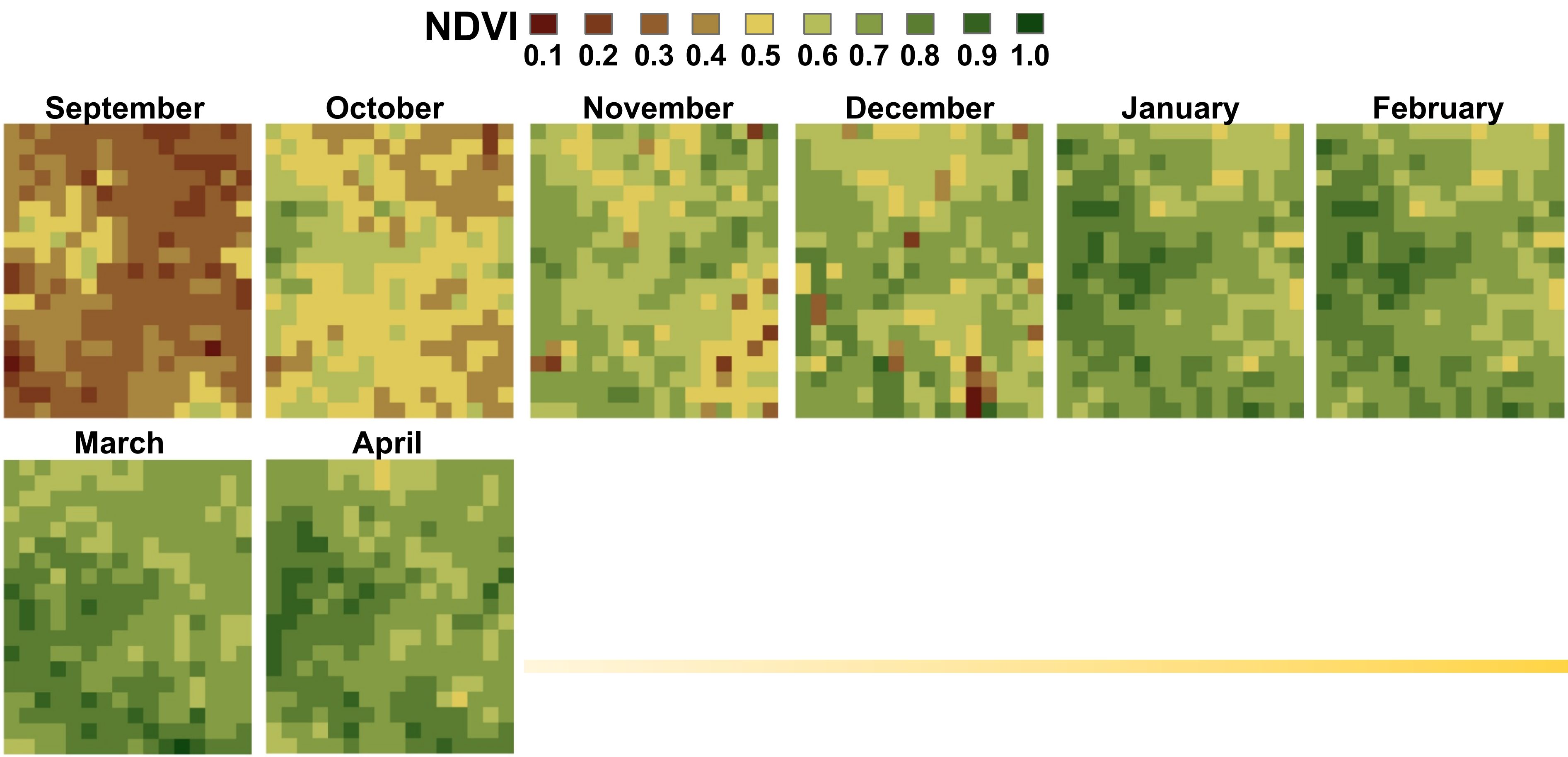
NDVI



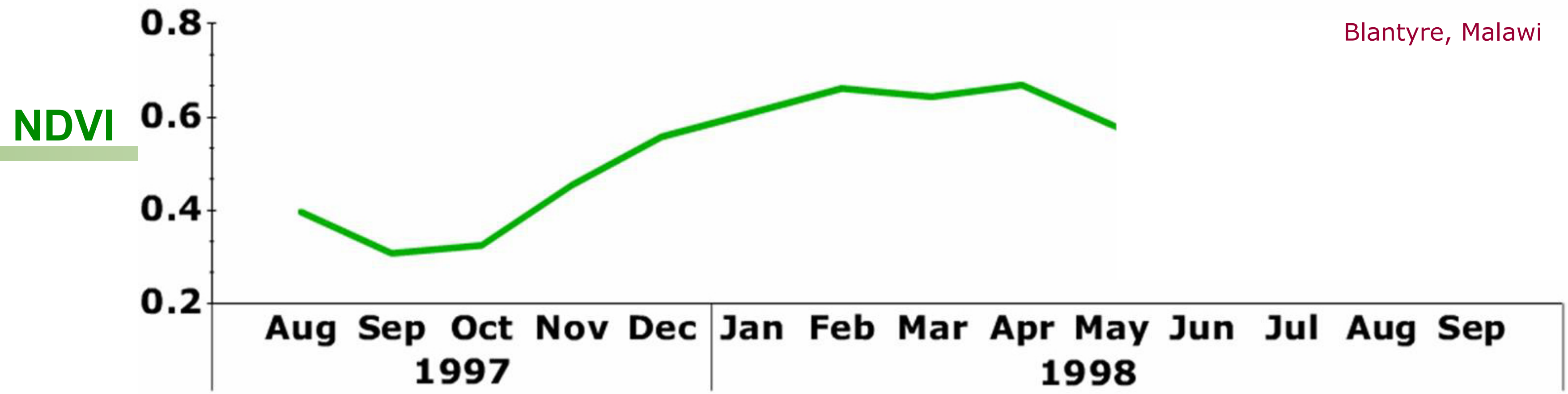


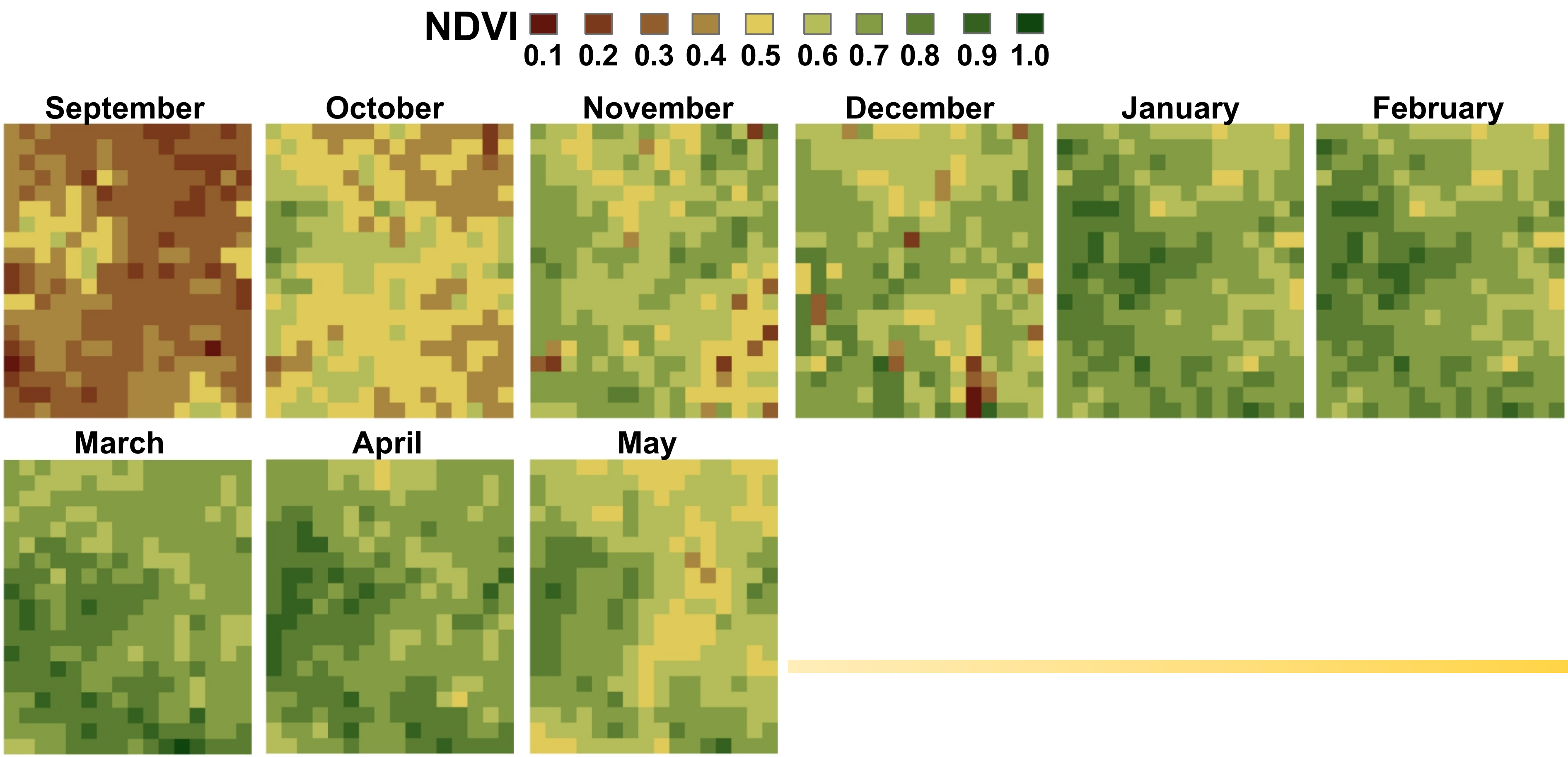
Blantyre, Malawi



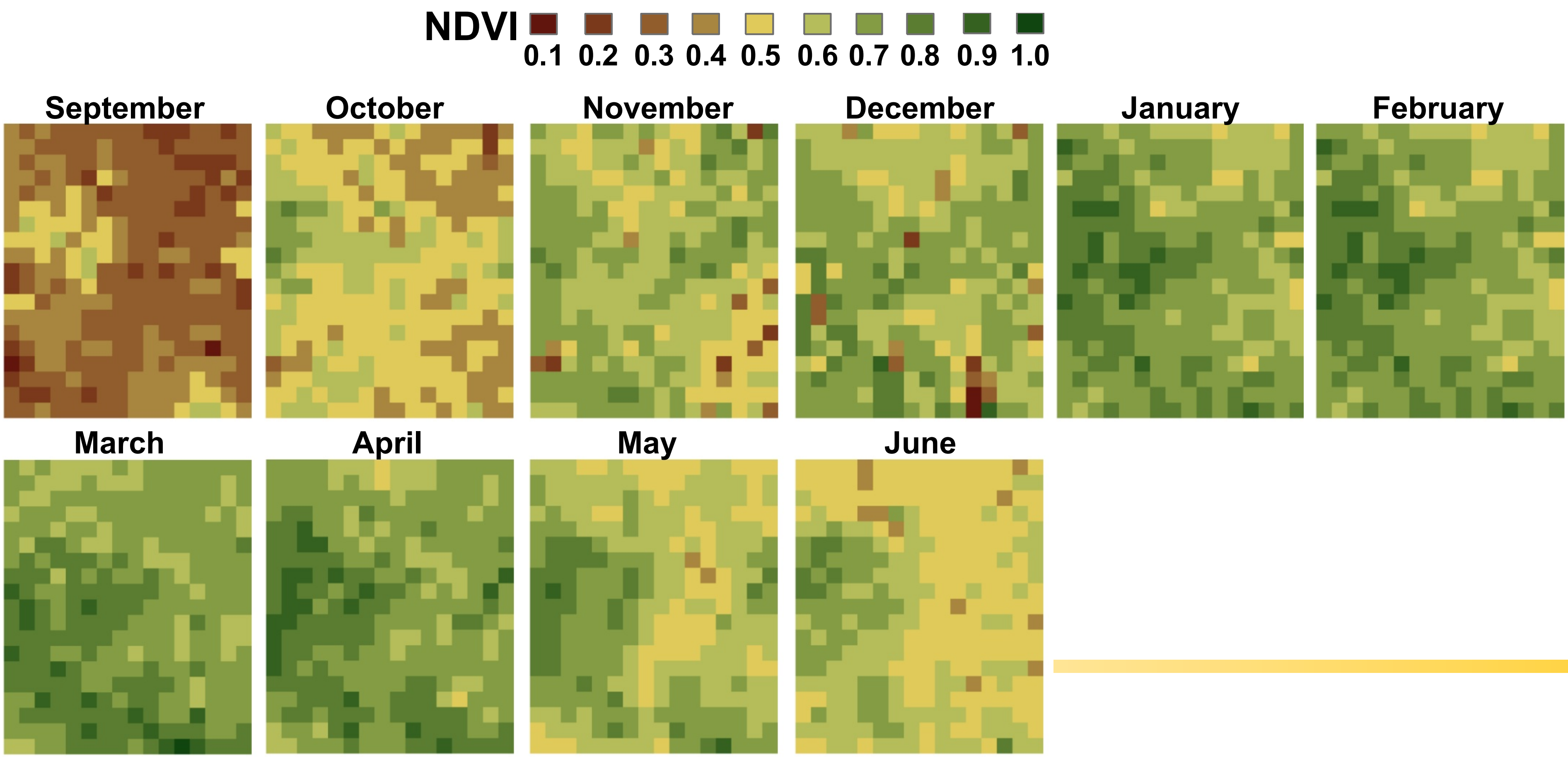


Blantyre, Malawi



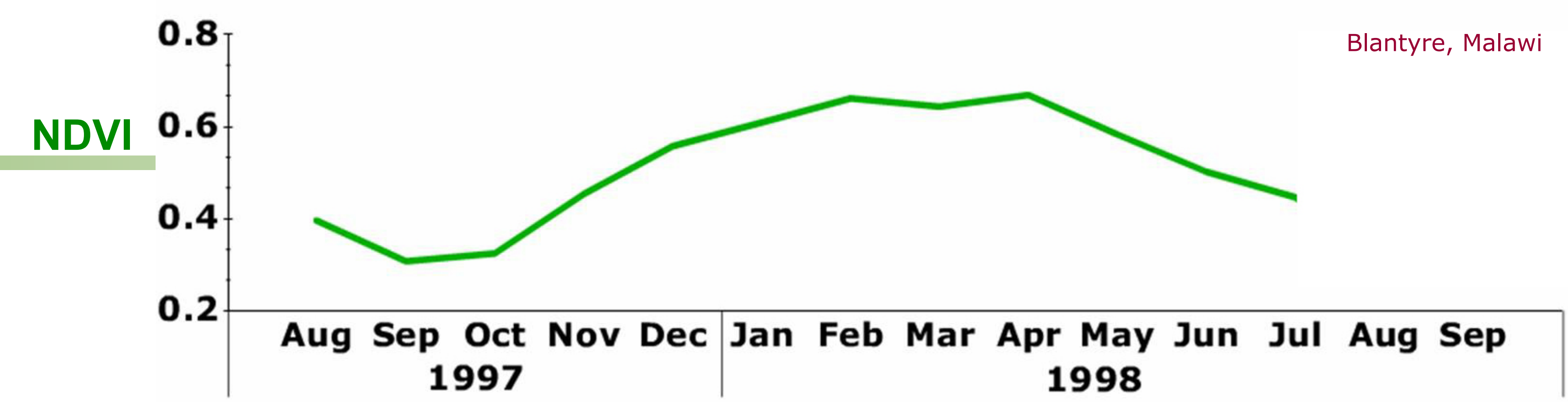


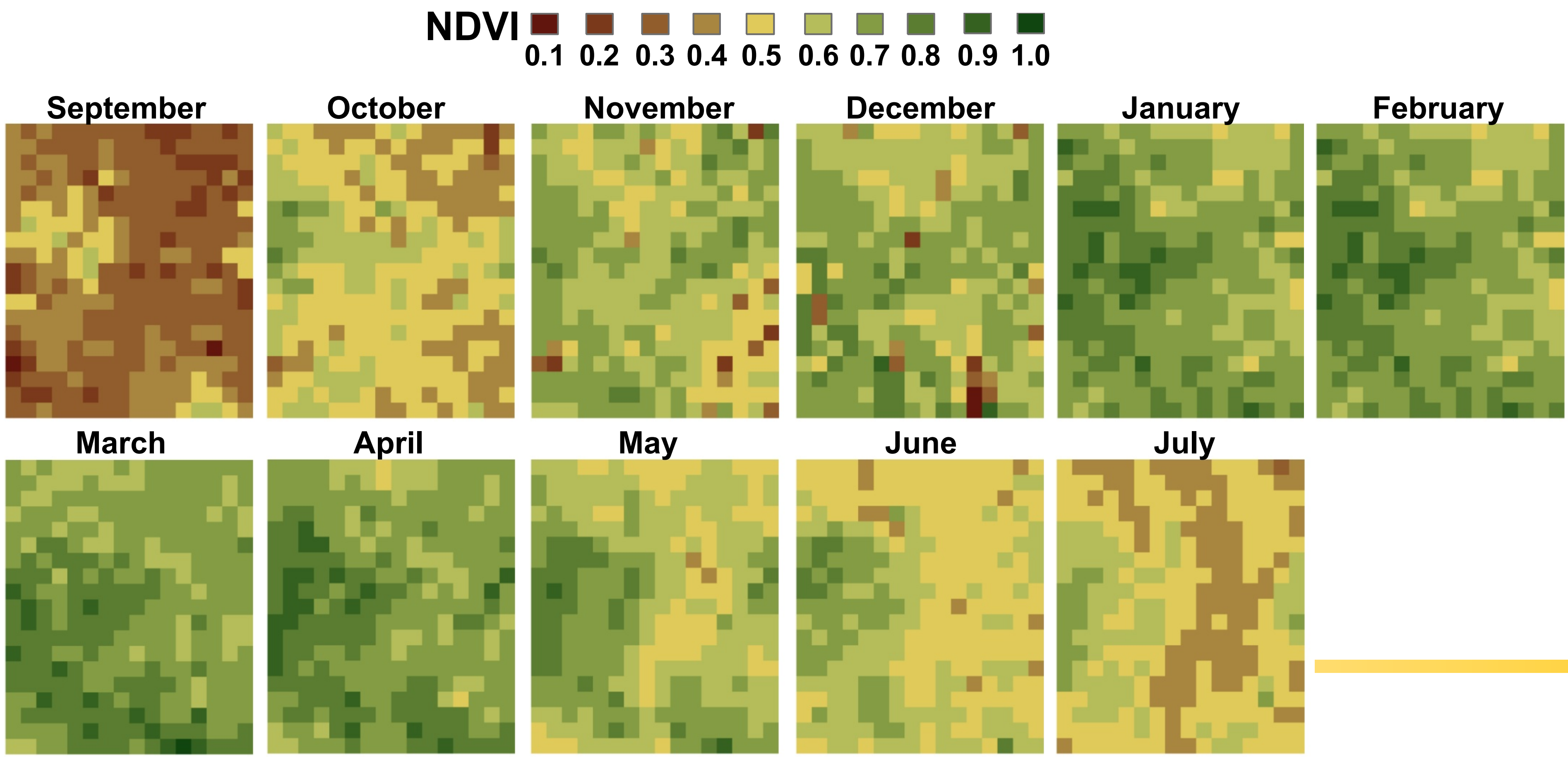
Blantyre, Malawi
NDVI
0.8
0.6
0.4
0.2
Aug Sep Oct Nov Dec
1997
Jan Feb Mar Apr May Jun Jul Aug Sep
1998

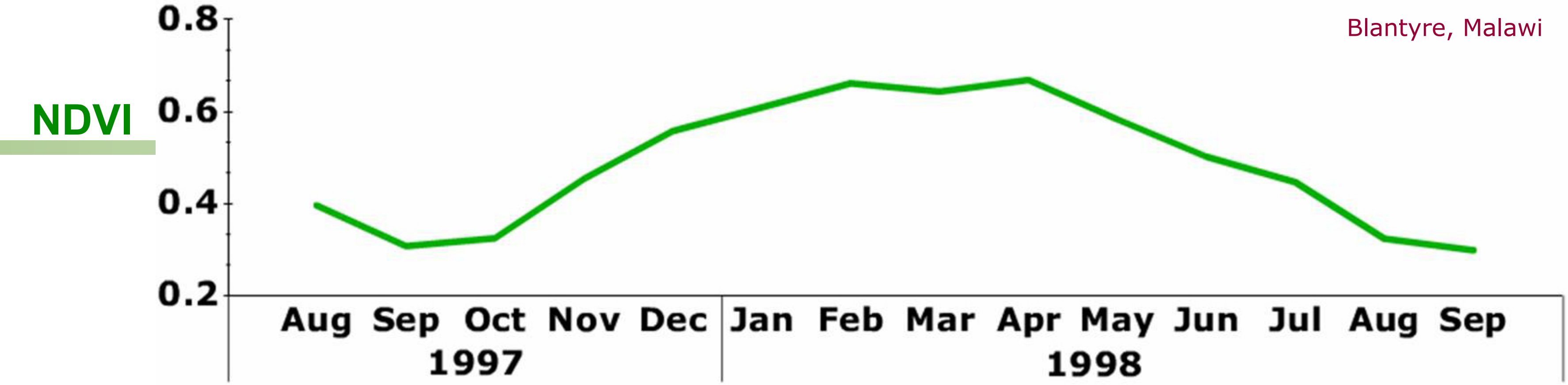


NDVI
0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
September
October
November
December
January
February
March
April
May
June

Blantyre, Malawi







NDVI
Blantyre, Malawi
0.8
0.6
0.4
0.2
Aug
Sep
Oct
Nov
Dec
1997
Jan
Feb
Mar
Apr
May
Jun
Jul
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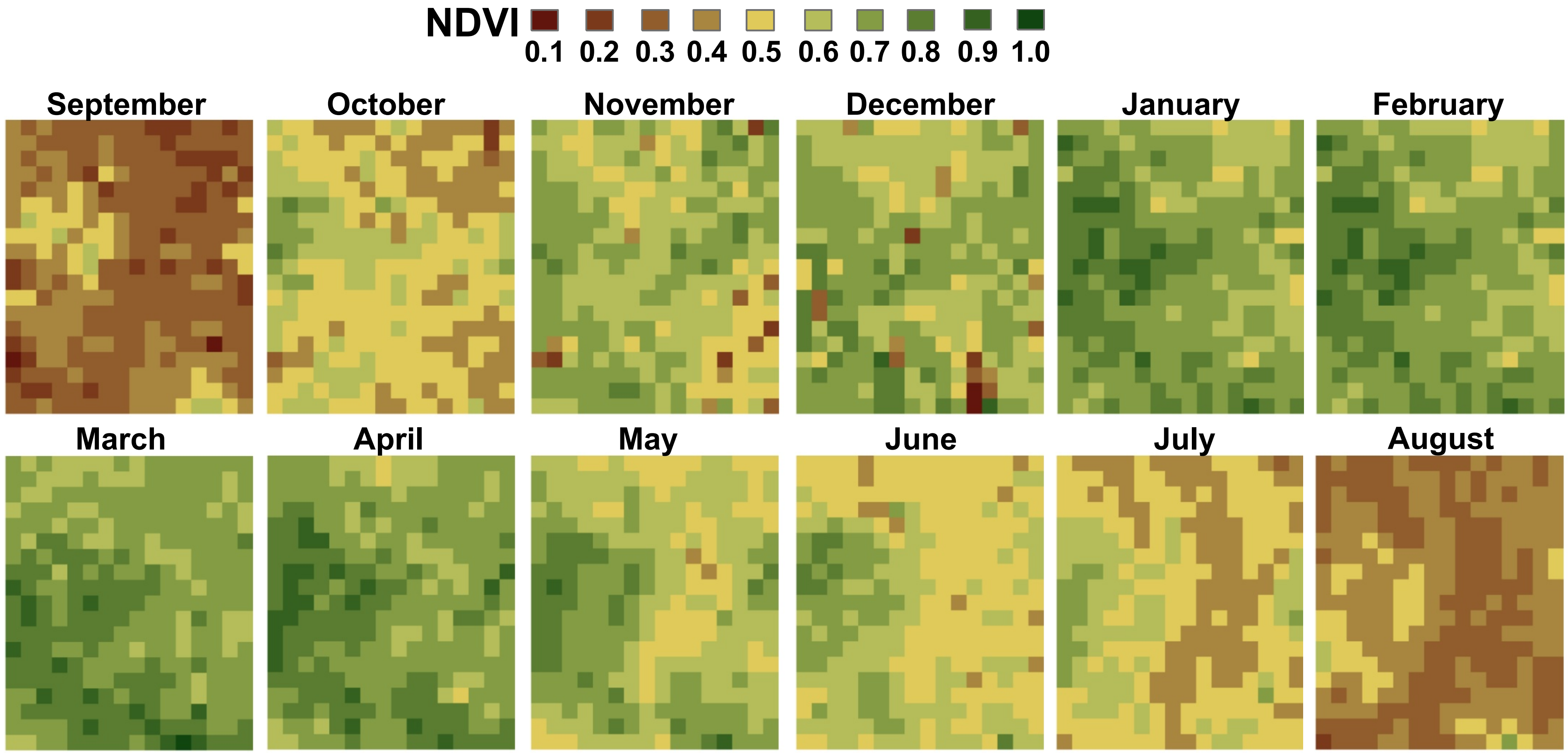
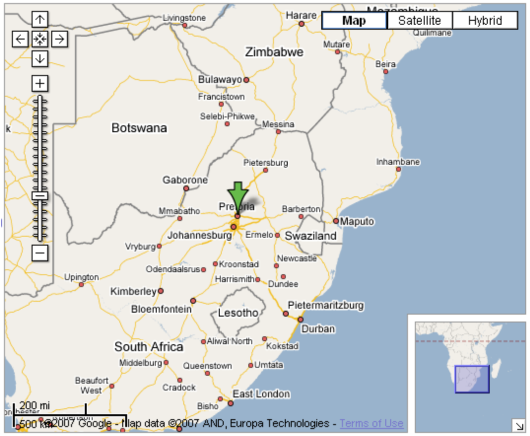
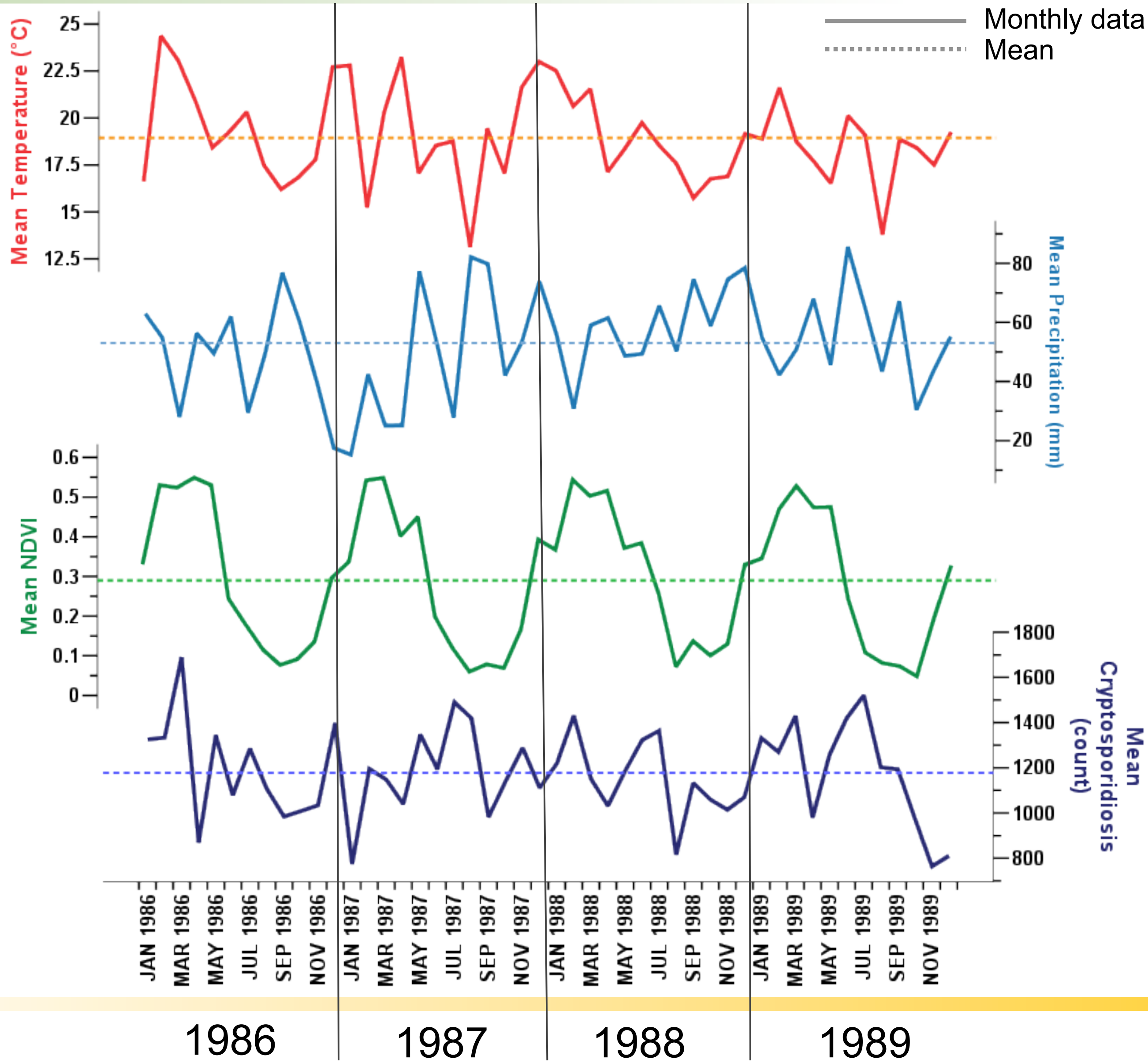
1998



NDVI
0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
September
October
November
December
January
February
March
April
May
June
July
August

Data Normalization: Pretoria, South Africa





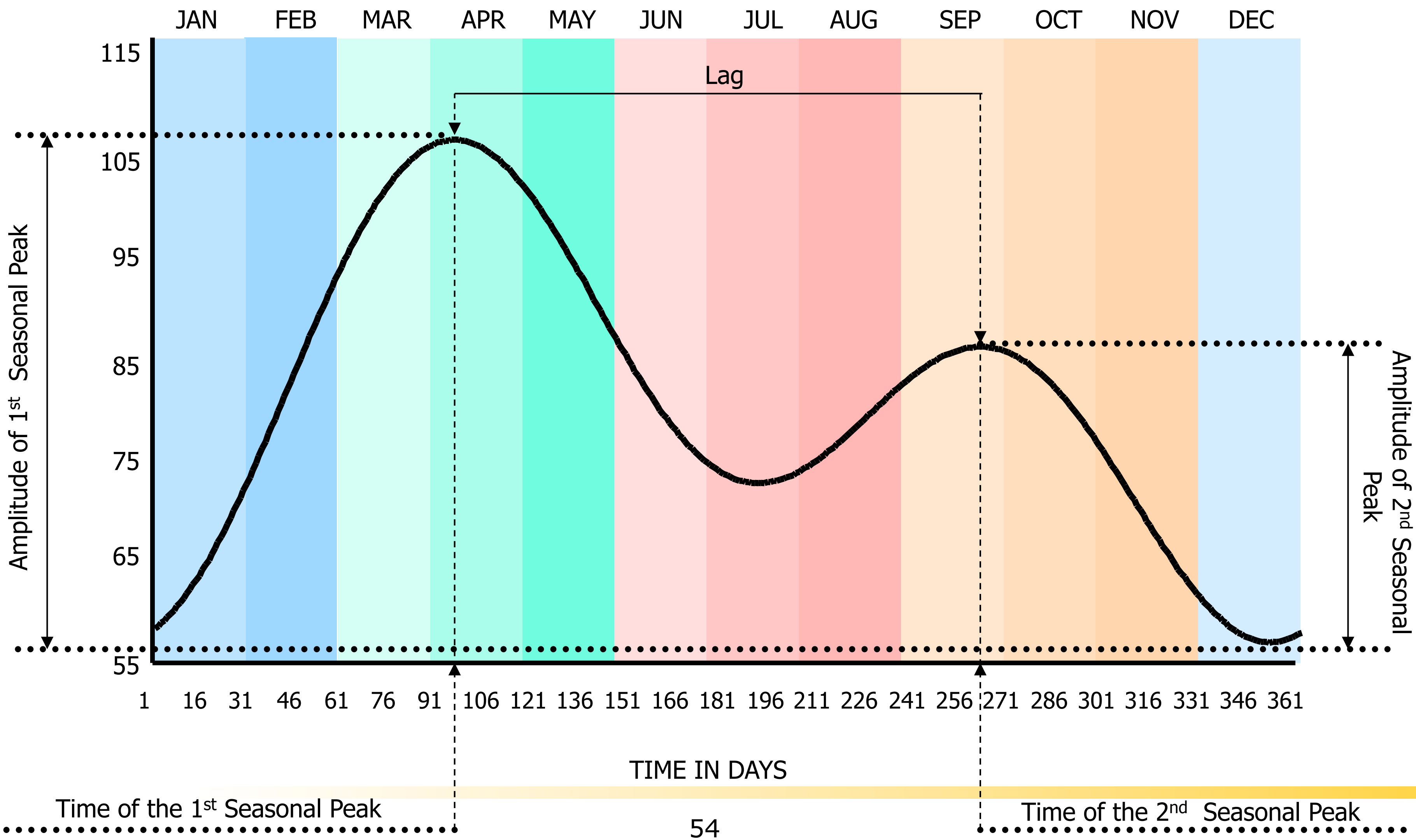
Results

- Temperature and precipitation are significant predictors of CP z-score
- Results vary by climate subgroup, sensitive to distance from equator, and stable with a lag of 1 month

Exposure Variables	Overall	Parameter by Climate Subgroup			
		A	B	C	D
Temperature	**0.272**	**0.248**	0.082	**0.360**	**0.346**
Precipitation	**0.322**	**0.422**	0.256	**0.231**	0.214
Mean NDVI	0.361	-0.830	-1.645	**2.140**	0.945

Table 3: Regression parameters of the effect of exposure on health outcomes for all studies and by climate subcategory. Bold indicates significance ($p<0.05$).

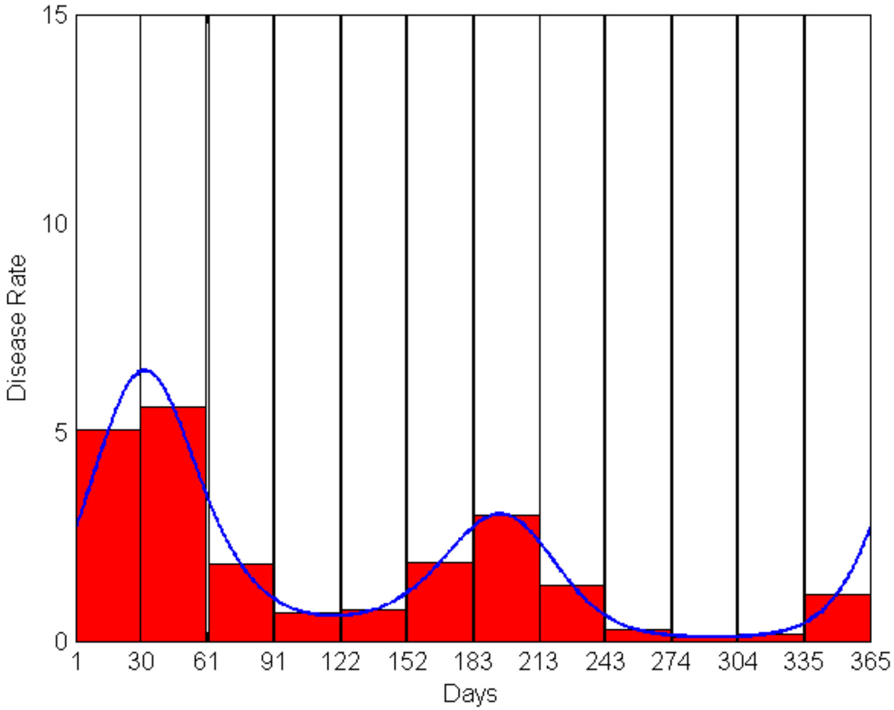
Seasonal pattern with two peaks

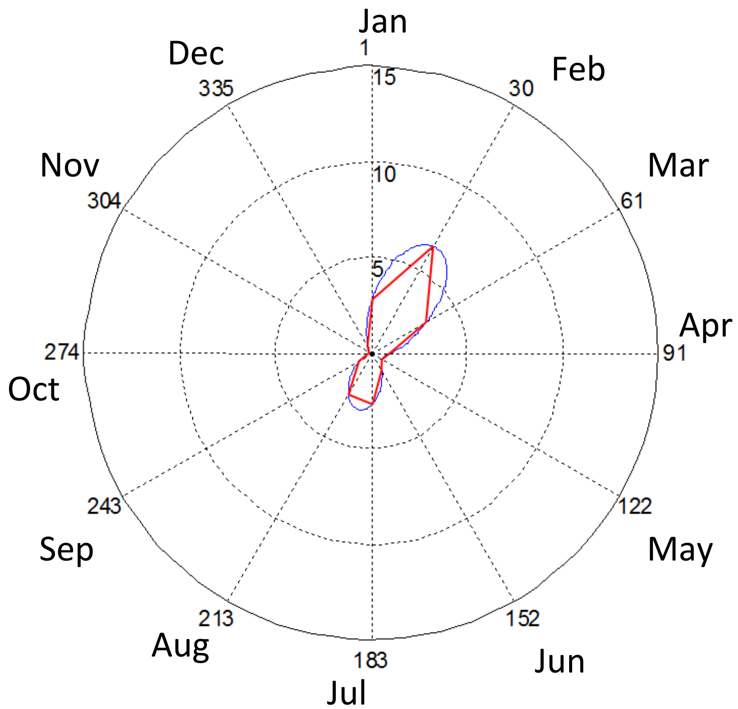


UNEQUAL DOUBLE ANNUAL PEAK

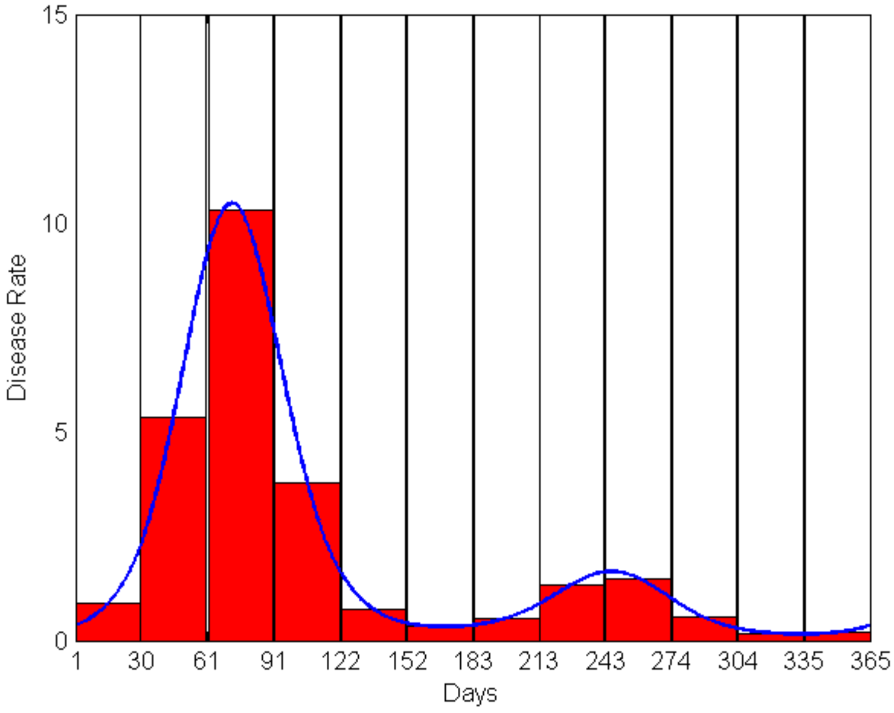
The progression of two **unequal** peaks throughout the year

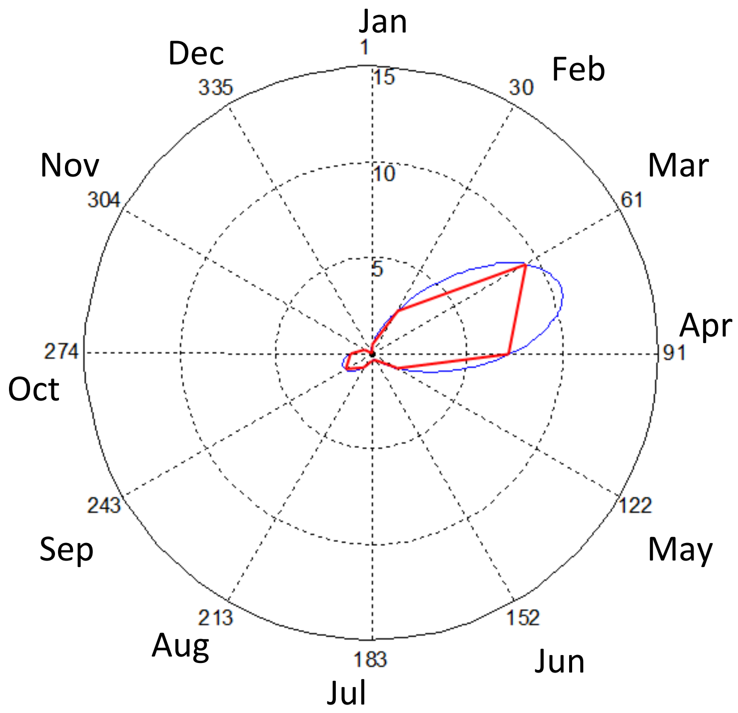
$\beta_1 = 1, \beta_2 = 0, \beta_3 = 1, \beta_4 = 1$



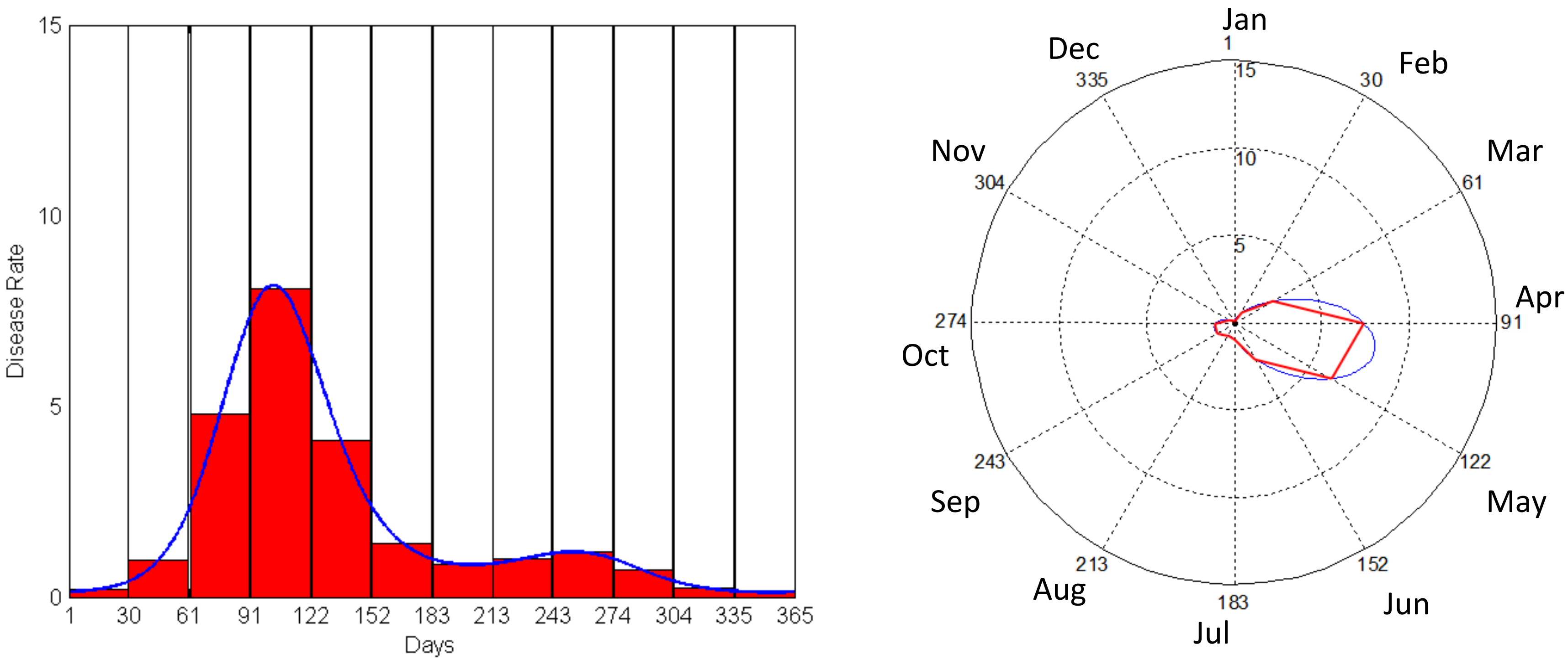


$\beta_1 = 1, \beta_2 = 0, \beta_3 = 1, \beta_4 = -1$

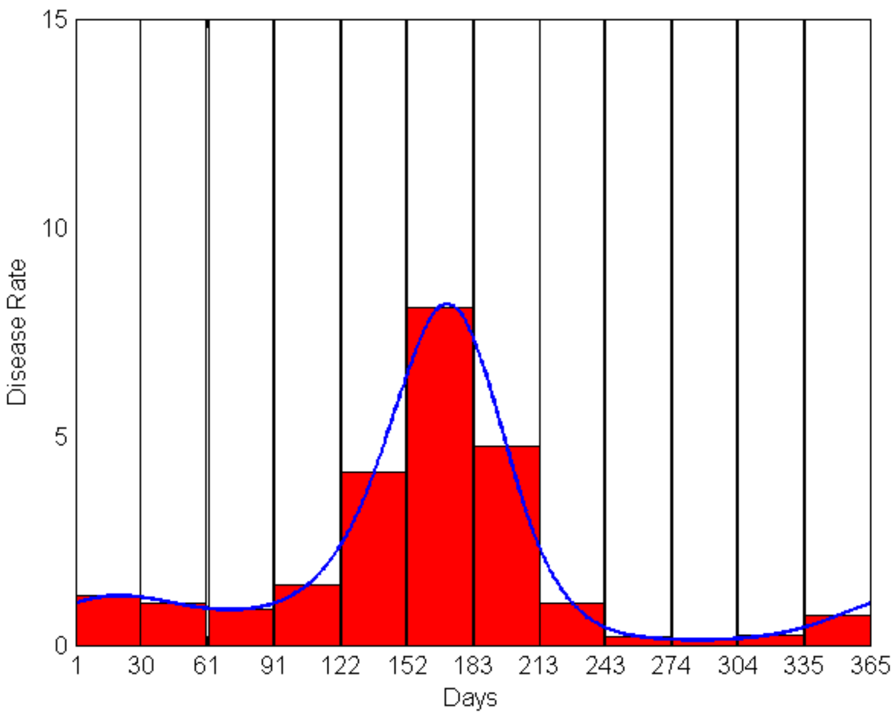


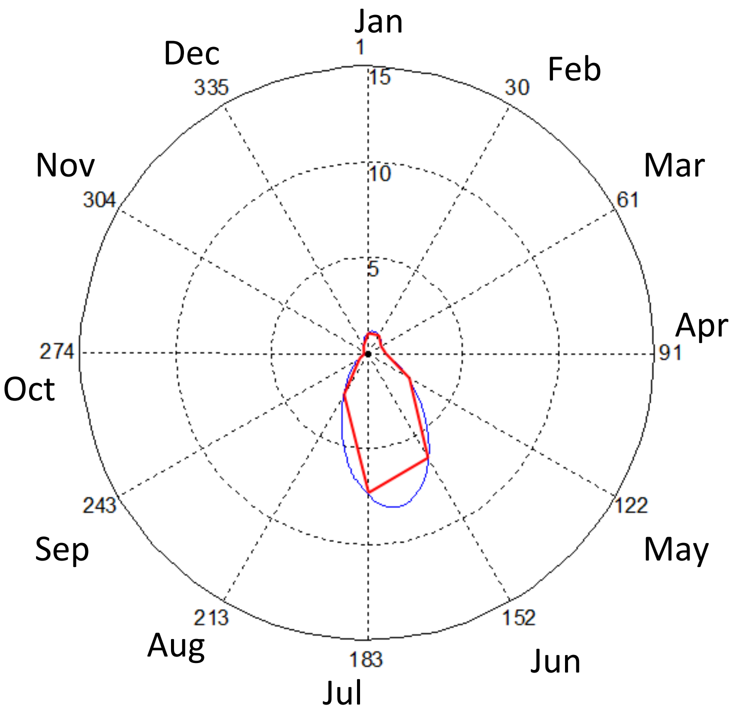


$\beta_1 = 1, \beta_2 = -1, \beta_3 = 0, \beta_4 = -1$

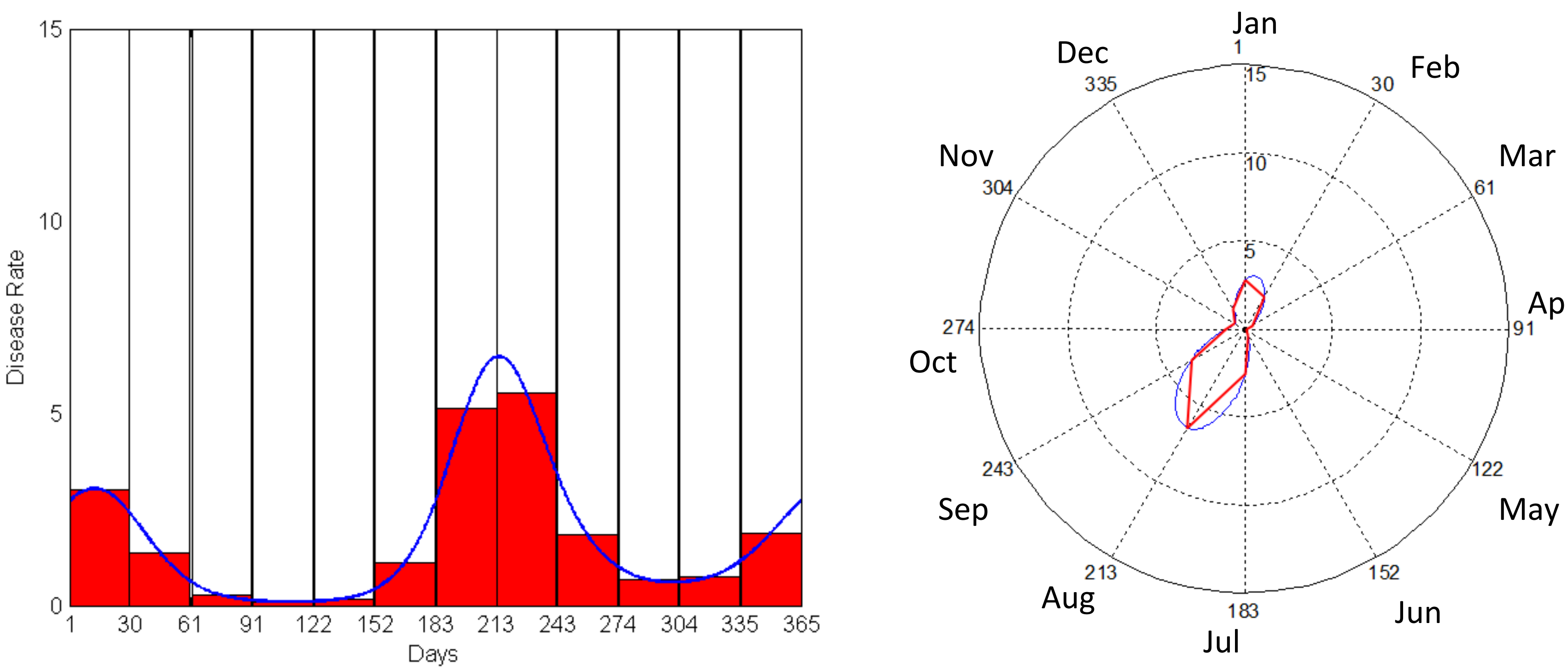


$\beta_1 = 1, \beta_2 = -1, \beta_3 = 0, \beta_4 = 1$

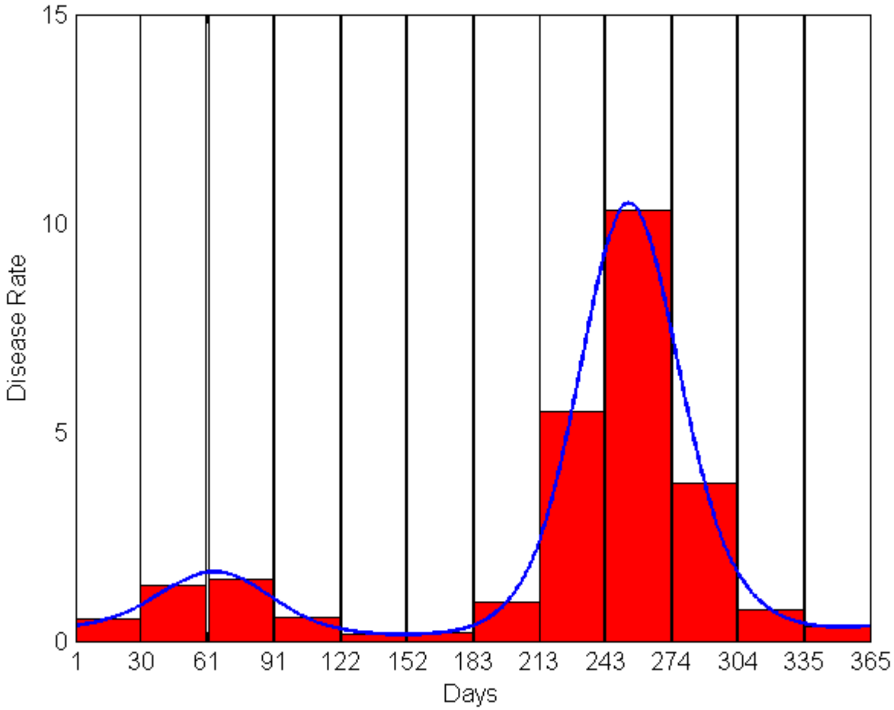


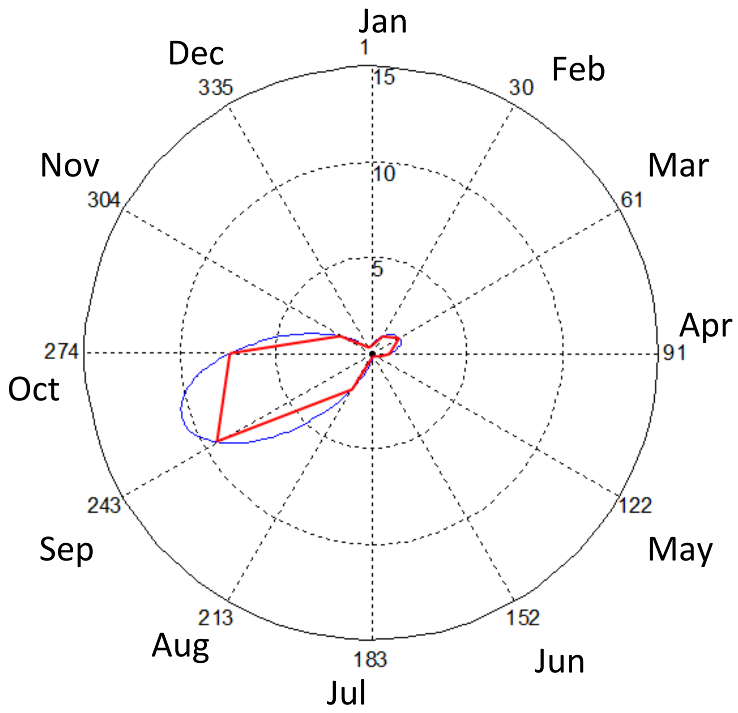


$\beta_1 = -1, \beta_2 = 0, \beta_3 = 1, \beta_4 = 1$

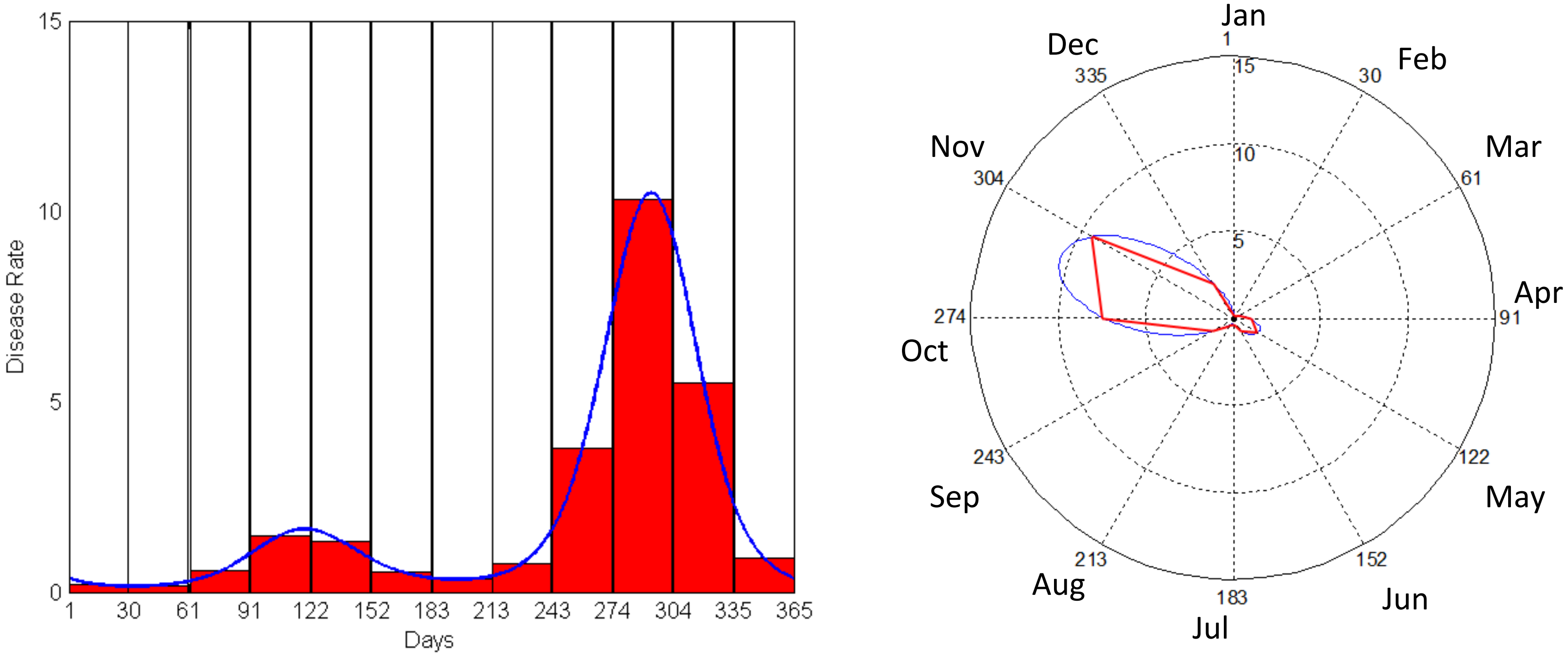


$\beta_1 = -1, \beta_2 = 0, \beta_3 = 1, \beta_4 = -1$





$\beta_1 = -1, \beta_2 = 0, \beta_3 = -1, \beta_4 = -1$



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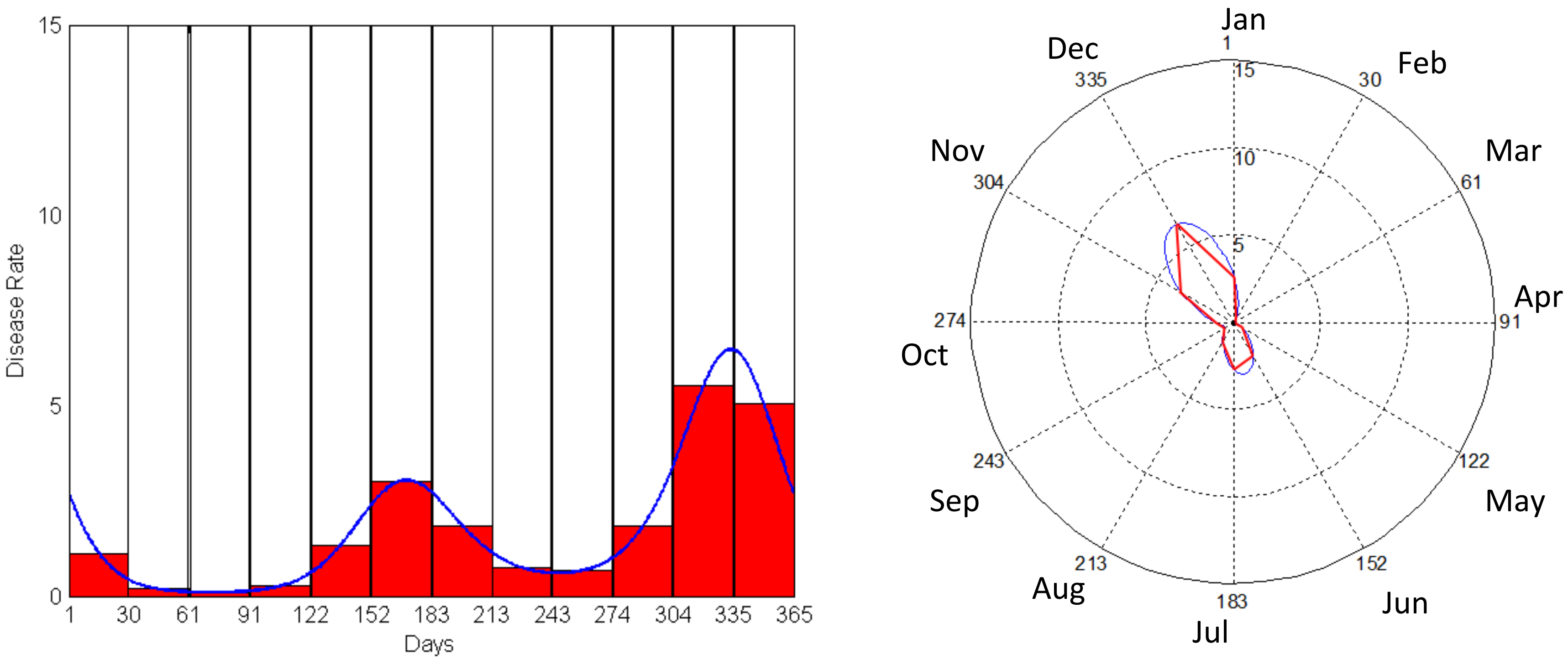
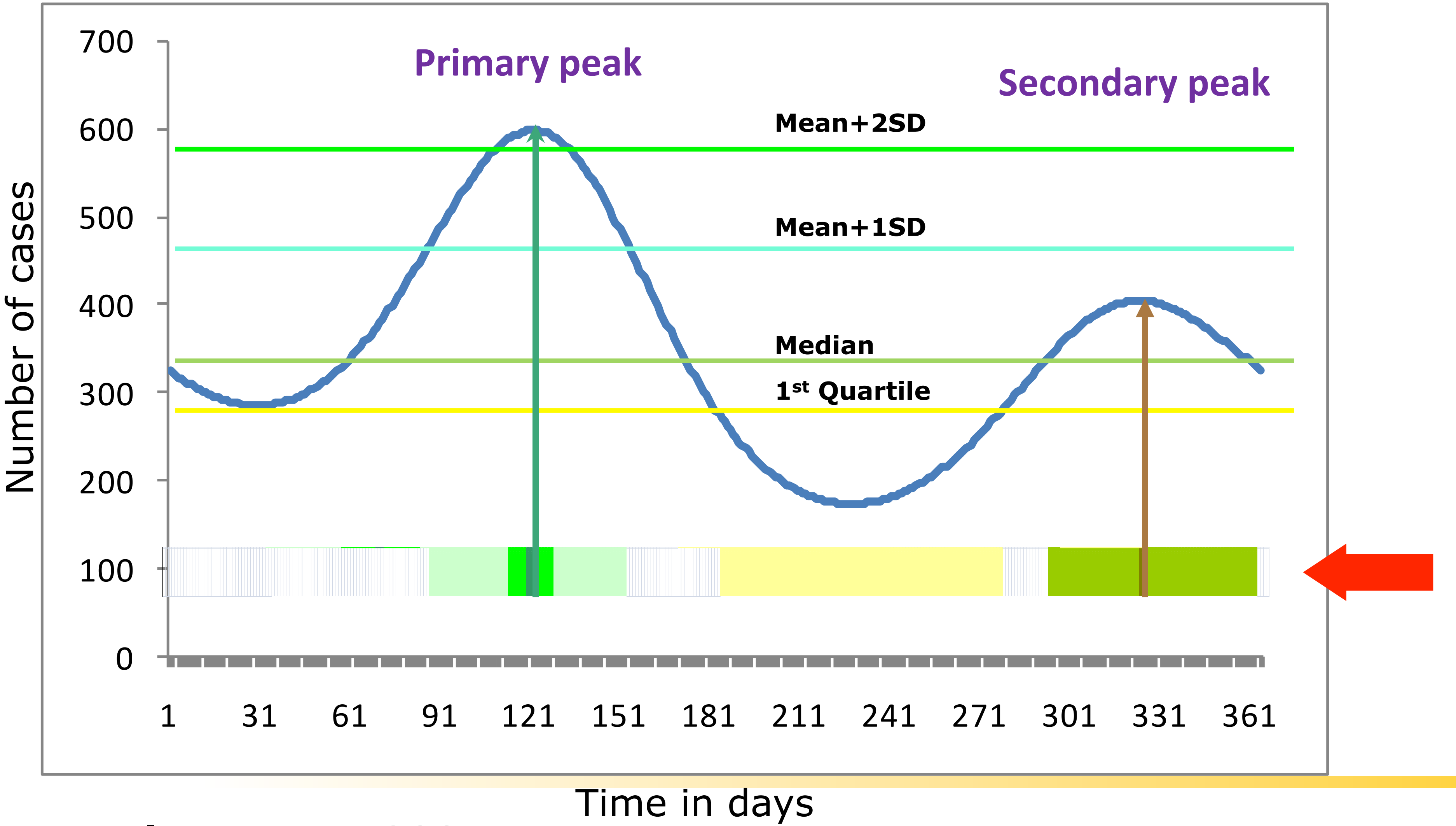


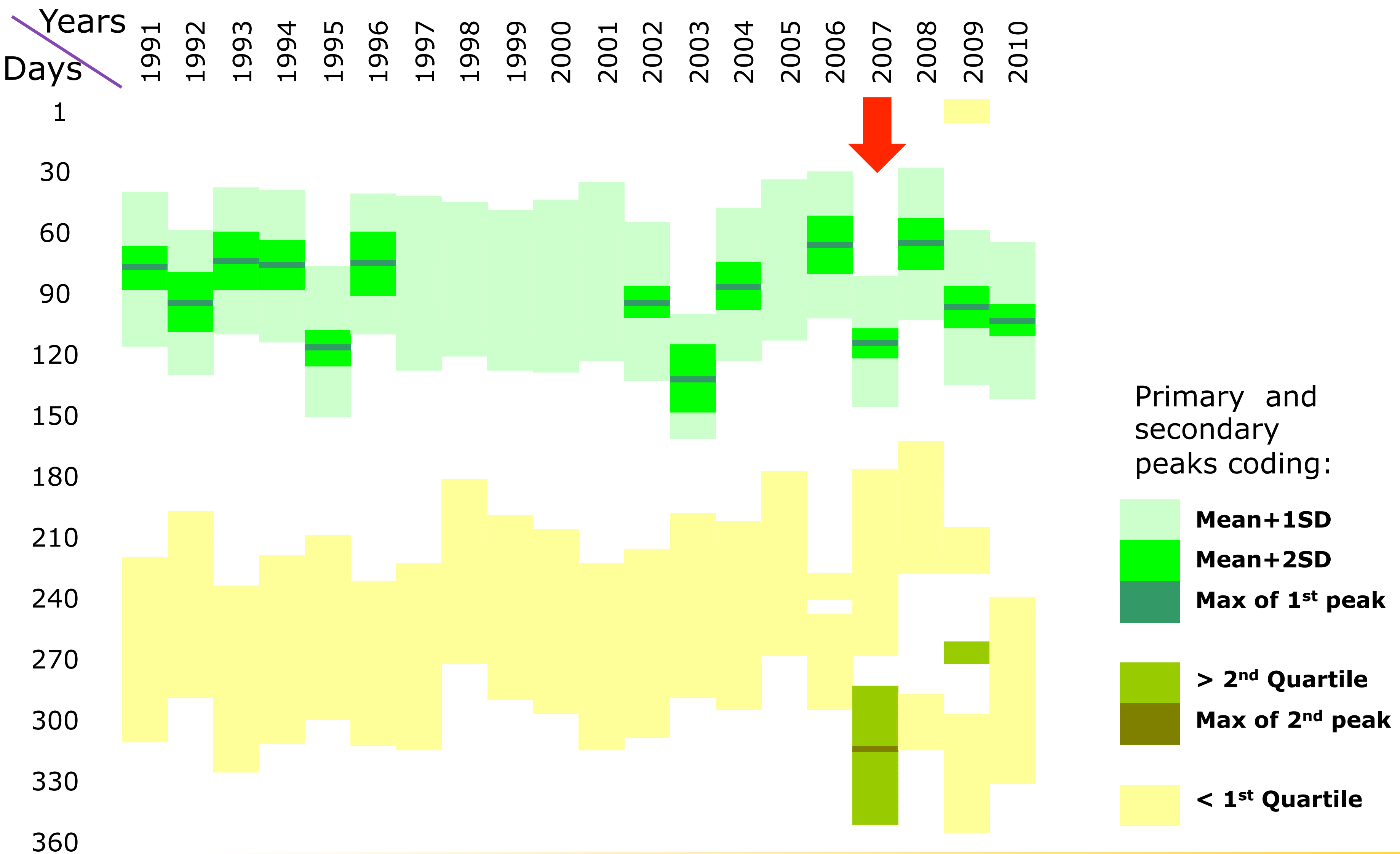
Peak Timing for Semi-Annual Seasonality

$$\log [Y(t)] = \beta_0 + \beta_1 \sin(2\pi\omega t) + \beta_2 \cos(2\pi\omega t) + \beta_3 \sin(4\pi\omega t) + \beta_4 \cos(4\pi\omega t) + e(t)$$

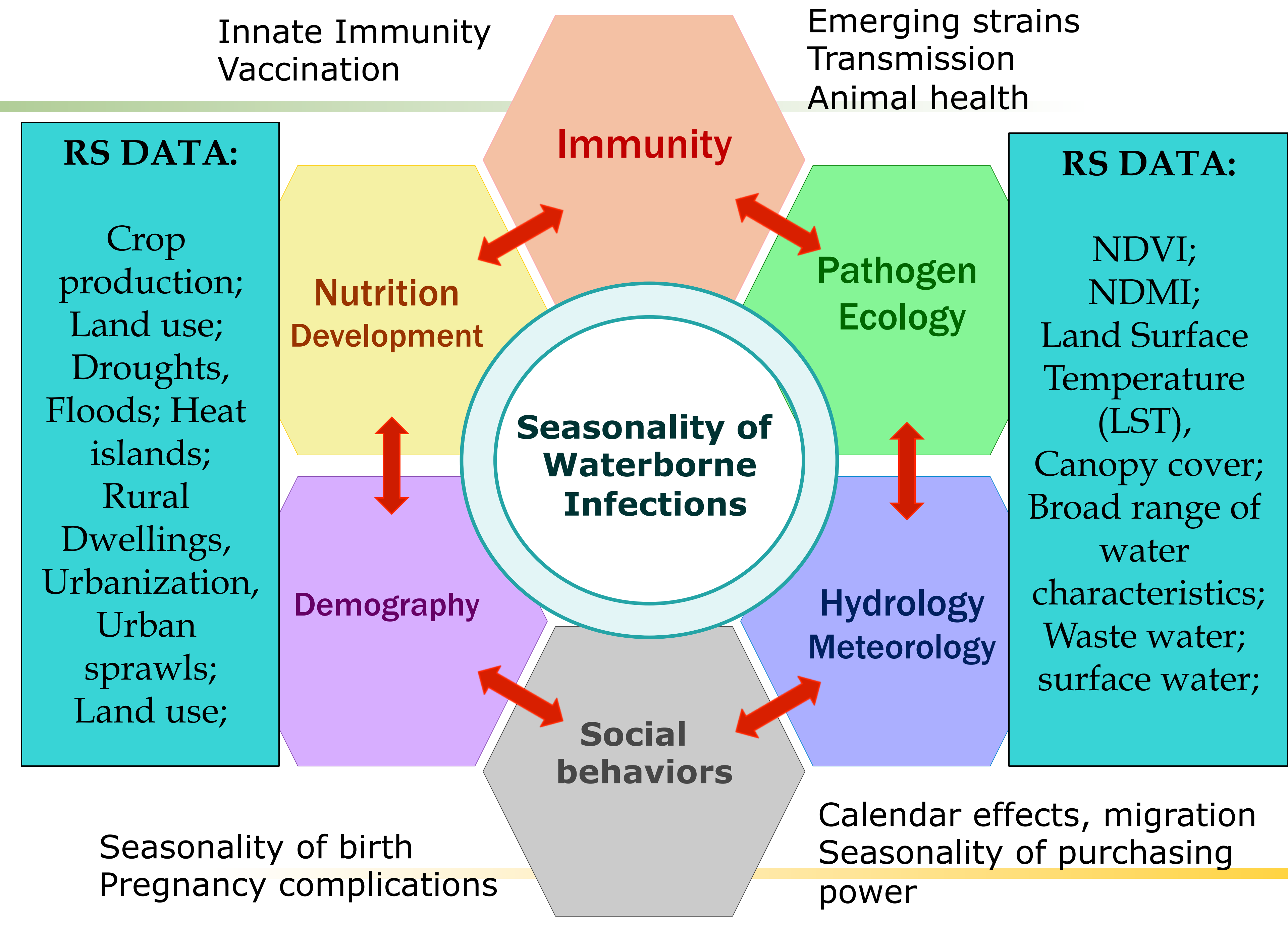


Ross River Fever, 2007

Seasonality of Ross River Fever in Australia



Mor S, Naumova EN. Assessing seasonality of vectorborne and zoonotic infectious diseases. In the proceedings of the First OneHealth Symposium. Melbourne, Australia. February 13-15, 2011.


Innate Immunity
Vaccination
Immunity
Emerging strains
Transmission
Animal health
RS DATA:
Crop production; Land use; Droughts, Floods; Heat islands; Rural Dwellings, Urbanization, Urban sprawls; Land use;
Nutrition
Development
Pathogen Ecology
RS DATA:
NDVI; NDMI; Land Surface Temperature (LST), Canopy cover; Broad range of water characteristics; Waste water; surface water;
Seasonality of Waterborne Infections
Demography
Hydrology
Meteorology
Social behaviors
Seasonality of birth
Pregnancy complications
Calendar effects, migration
Seasonality of purchasing power

Seasonality Research

- determine factors governing seasonality
- design cross-sectional and prospective studies geared to estimate the burden of waterborne diseases considering seasonality
- prioritize allocation of resources
- improve primary data collection with refined temporal resolution
- assess the effect of interventions
- assess the effect of environmental factors
- consider social calendars in modeling seasonality
- enhance the validity of near-term and short-term forecasts

Several essential aspects of seasonality are outlined:

the need for preservation of information relevant to episodes of waterborne infections at the finest temporal resolution,

the importance of considering social calendars in modeling seasonality,

the rationales why seasonality has to be taken into account in designing cross-sectional and prospective studies geared to estimate the burden of waterborne diseases.

Mentioned and Relevant Publications

1. Naumova EN, MacNeill IB. **Seasonality assessment for biosurveillance systems**. In: Advances in Statistical Methods for the Health Sciences: Applications to Cancer and AIDS Studies, Genome Sequence Analysis, and Survival Analysis. Edited by N. Balakrishnan, Jean-Louis Auget, M. Mesbah, Geert Molenberg. Birkhauser, Boston. 2006; (pp. 437-450)
2. Wenger JB, Naumova EN. **Seasonal synchronization of influenza in the United States older adult population**. *PLoS ONE*. 2010 (on-line)
3. Lofgren E, Fefferman NH, Naumov YN, Gorski J, Naumova EN. **Influenza seasonality: underlying causes and modeling theories review**. *Journal of Virology*. 2007; 81(11): 5429-36.
4. Naumova EN, Jagai J, Matyas B, DeMaria A, MacNeill IB, Griffiths JK. **Seasonality in six enterically transmitted diseases and ambient temperature**. *Epidemiology & Infections*. 2007. 135(2):281-92.
5. Lofgren E, Fefferman NH, Doshi M, Naumova EN. **Assessing seasonal variations in multisource surveillance data: annual harmonic regression**. D. Zeng et al. (eds.): BioSurveillance 2007. Lectures Notes in Computer Science (LNCS) 4506, Springer. 2007; pp. 114-123.
6. Lofgren ET, Wenger JB, Fefferman NH, Bina D, Gradis S, Bhattacharyya S, Naumov YN, Gorski J, Naumova EN. **Disproportional effects in populations of concern for pandemic influenza: insights from seasonal epidemics in Wisconsin, 1967-2004**. *Influenza and Other Respiratory Viruses*. 2010; 4(4): 205-12 [Epub ahead of print]
7. O'Neill EA, Naumova EN. **Defining Outbreak: Breaking out of the confusion**. *JPHP*. 2007, Dec; 28(4):442-55.
8. Muchiri JM, Ascolillo L, Mugambi M, Mutwiri T, Ward H, Naumova EN, Egorov A, Cohen S, Else JG, Griffiths JK. Seasonality of Cryptosporidium oocyst detection in surface waters of Meru, Kenya as determined by two isolation methods followed by PCR. Water & Health. 2009; 7(1):67-75.
9. Fefferman NH, Naumova EN. **Innovation in Observation: A Vision for Early Outbreak Detection**. *Emerging Health Threats*. 2010. [Epub ahead of print]
10. Naumova EN, Christodouleas J, Hunter PR, Sued Q**. Temporal and spatial variability in cryptosporidiosis recorded by the surveillance system in North West England in 1990 - 1999**. *Water and Health*. 2005; 3(2):185-96.
11. Naumova EN. **Mystery of seasonality: getting the rhythm of nature**. *Journal of Public Health Policy*. 2006; 27(1): 2-12.
12. Lofgren E, Fefferman NH, Naumov YN, Gorski J, Naumova EN. **Influenza seasonality: underlying causes and modeling theories review.** *Journal of Virology*. 2007; 81(11): 5429-36.
13. Jagai JS, Castronovo DA, Monchak J, Naumova EN. **Seasonality of cryptosporidiosis: a meta-analysis approach**. *Environmental Research*. 2009 May; 109(4):465-78.

Acknowledgements

National Institute of Environmental Health Sciences, R01 ES013171
(PI - Dr. Elena N. Naumova, Tufts University, Boston USA)
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National Institute of Child Health and Development
and NIH Fogarty International Center Grant, R01 HD38327
(PIs – Kang and Ward)

CDC/IMRC: Environmental Indicators of Enteric Infection
(PI – Naumova[USA] and Balraj [India])

Drs. Sempertegue, Estrella (Baca Ortiz Children Hospital, Quito Ecuador)

Denise Castronovo, Jim Monchak (Mapping Sustainability, Inc. USA)

Tufts Institute of the Environment (TIE)

Graduate students (former and current):
Rajiv Sarkar, Andrea Brown, Jyotsna Jagai, Ken Chui,
Siobhan Mor, Steve Cohen, Julia Wenger, Alex Liss