Rapid detection of pandemic influenza in a background of seasonal influenza

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Outline

- Influenza-like illness (ILI) data collected by Scottish syndromic surveillance systems
- Brief overview of the methods of early warnings of disease aberrations
- The detection method we use in our analyses
- Application of our algorithm to the simulated pandemic influenza data
- Results: comparing the performances of three pandemic methods
- Summary and Future work

Seasonal Influenza-like illness (ILI) Surveillance in Scotland

Scottish Enhanced Respiratory Virus Infection Surveillance (SERVIS)

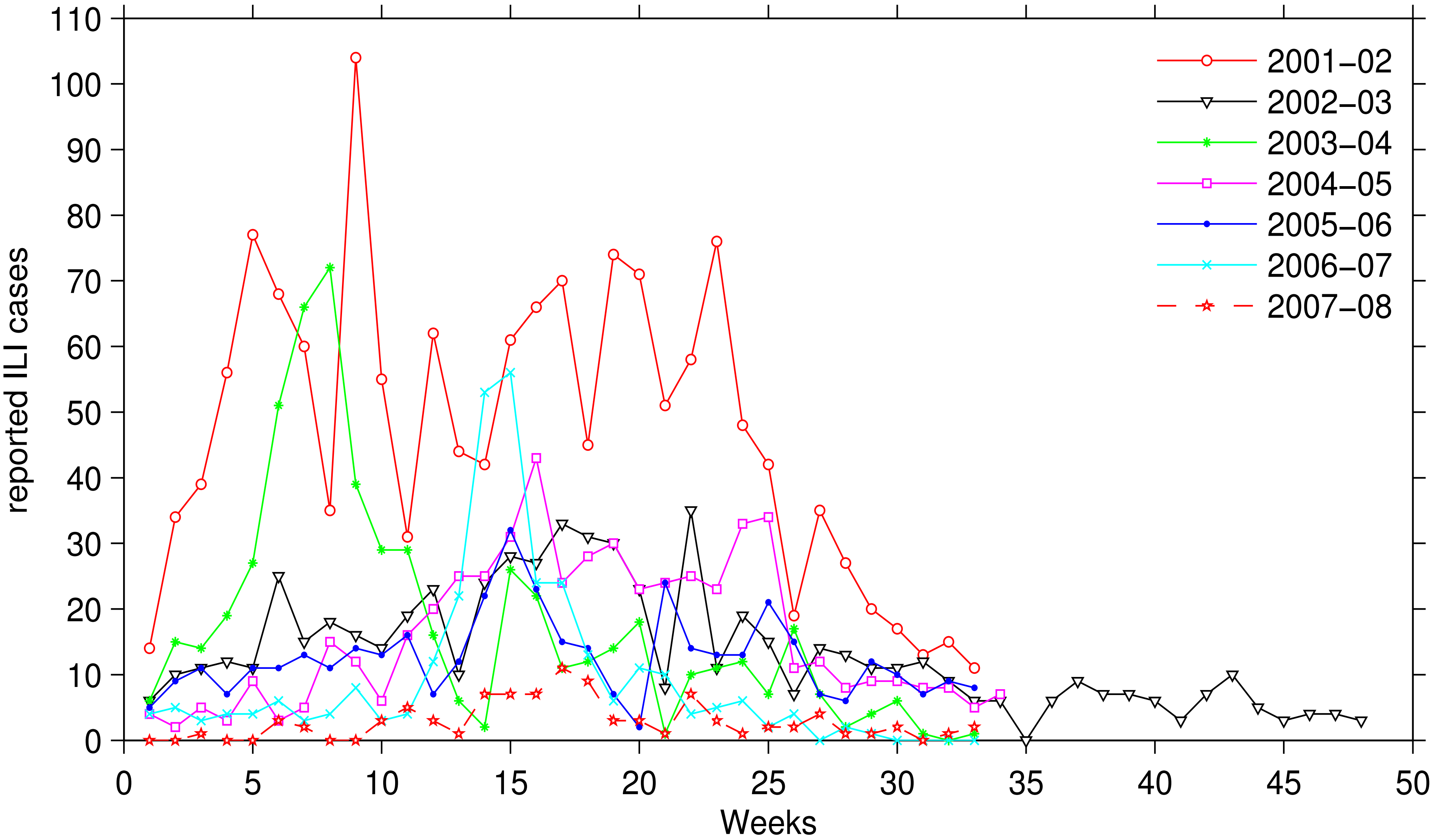
- introduced in 2000-01 season
- weekly reporting of ILI and acute respiratory infection (ARI) by age and sex
- 22-44 sentinel GPs from 13 Health Boards (HBs), covers 3% of population
- integrates clinical data from continuous morbidity recording GPs and virological testing

Flu-spotters

- reporting for 30 years
- weekly cases of seasonal influenza-like-illness (ILI)
- 80 GPs, covers 10% of population

PIPER (Pandemic Influenza Primary carE Reporting): to timely generate the vaccine uptake by risk groups in Scotland

Data: weekly ILI cases in Scotland

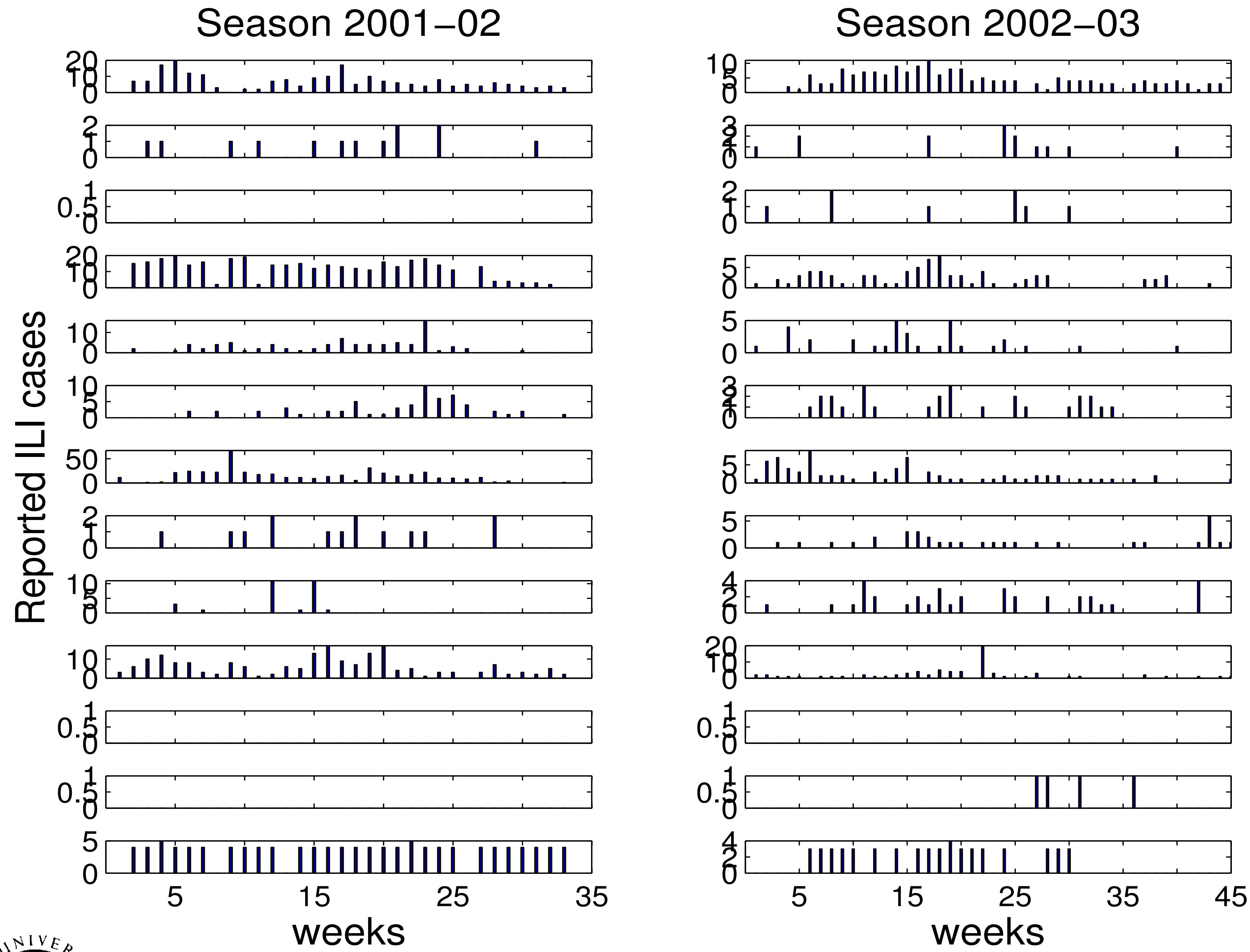


1st week of Oct

3rd week of May

Flu season

Data: weekly ILI cases by Health boards



Health Boards

1: Ayrshire & Arran
2: Borders
3: Dumfries & Galloway
4: Fife
5: Forth Valley
6: Grampian
7: Greater Glasgow & Clyde
8: Highland
9: Lanarkshire
10: Lothian
11: Orkney
12: Shetland
13: Tayside

1st week of Oct — 3rd week of May

Flu season

Detection methods for generating early warnings of adverse health using surveillance data

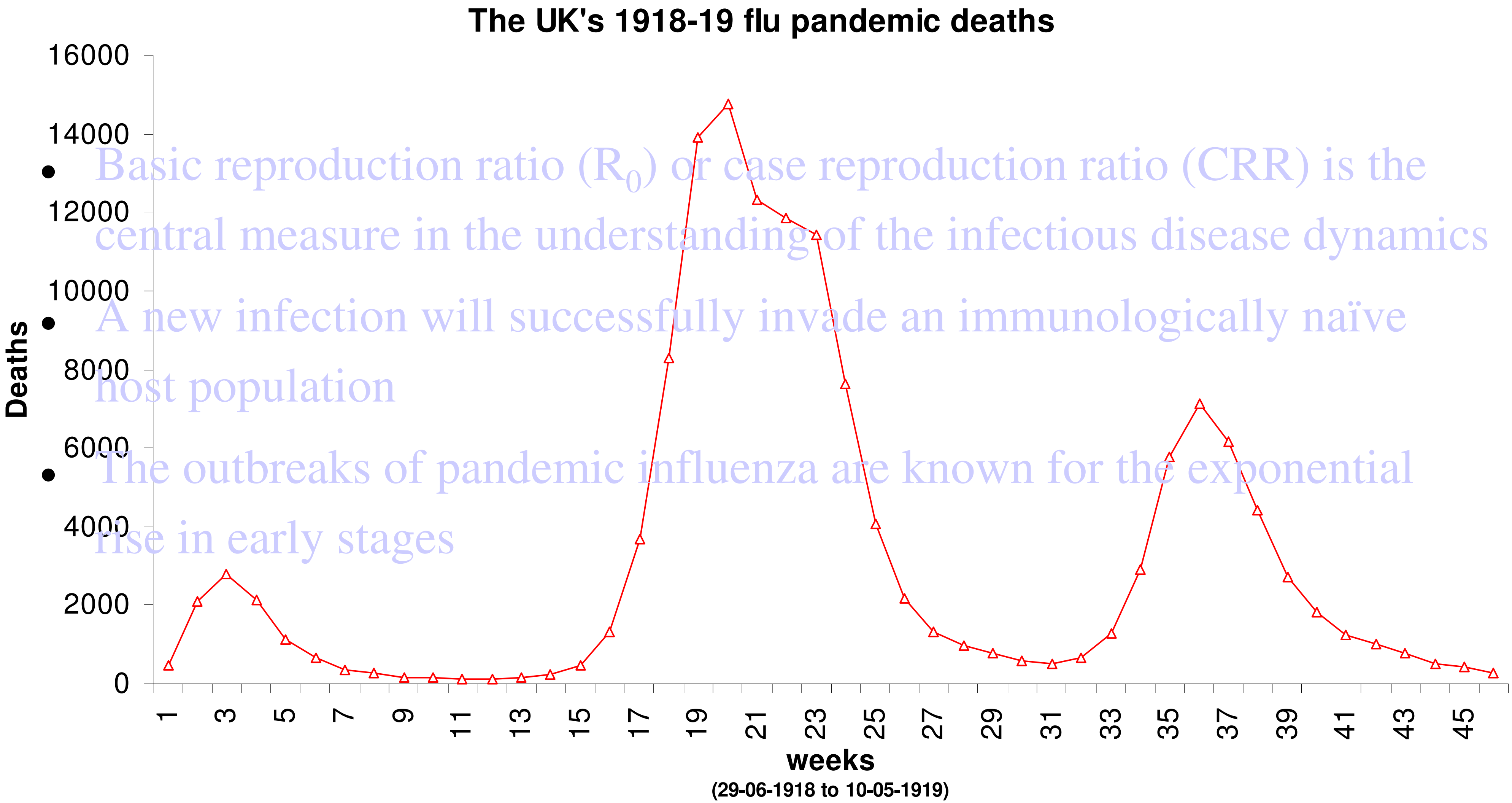
There are several statistical methods:

- Two main types: i) temporal methods (e.g., regression or time-series analysis); ii) spatial ones (e.g., the Scan statistics)
- the third type (i.e., spatiotemporal ones) is gaining popularity

Motivation behind developing a new pandemic detection algorithm

- Basic reproduction ratio (R_0) or case reproduction ratio (CRR) is the central measure in the understanding of the infectious disease dynamics
- A new infection will successfully invade an immunologically naïve host population
- The outbreaks of pandemic influenza are known for the exponential rise in early stages

Motivation behind developing a new pandemic detection algorithm



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- Basic reproduction ratio (R_0) or case reproduction ratio (CRR) is the central measure in the understanding of the infectious disease dynamics
- A new infection will successfully invade an immunologically naïve host population
- The outbreaks of pandemic influenza are known for the exponential rise in early stages
- Methods applied to ILI surveillance data for generating early warnings of a potential pandemic seem to largely ignore this natural candidate as their basis to do so.

Methods: developing Pandemic detection algorithm

We propose a detection method,
based on the
Case Reproduction Ratio (CRR)
&
the number of HBs (N_{HB}) reporting increases in ILI cases
to detect
pandemic influenza outbreak

Methods: developing Pandemic detection algorithm

We propose a detection method,
based on the
~~Case Reproduction Ratio (CRR)~~
Weekly Case ratio (WCR)
&
the number of HBs (N_{HB}) reporting increases in ILI cases
to detect
pandemic influenza outbreak

Methods: Estimating Weekly Case Ratio (WCR) for seasonal ILI data

$$WCR_{week} = \frac{CASES_{week}}{CASES_{week-1}} \quad \left(WCR_{week} = 0 \quad if \quad week = 1 \right)$$

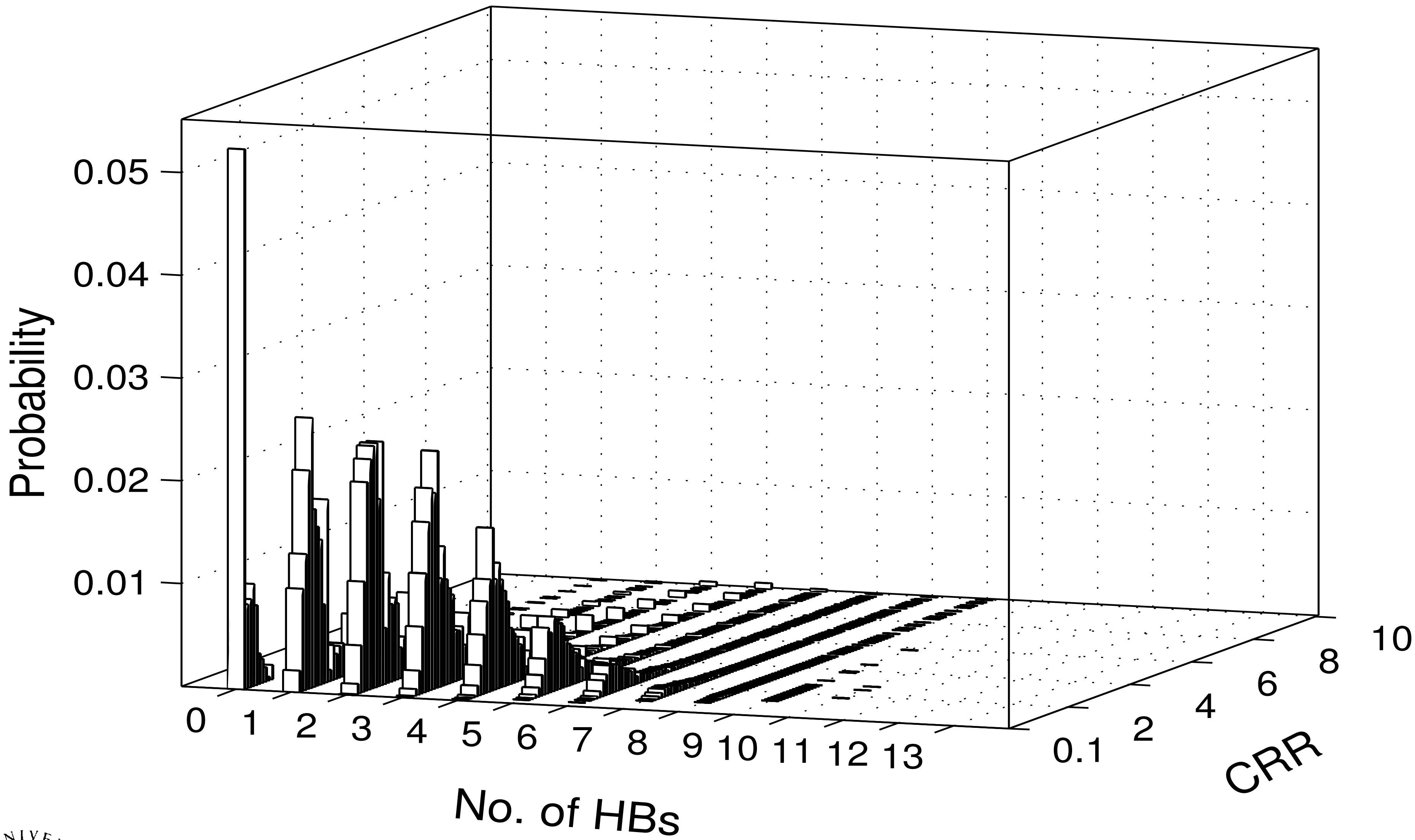
Methods: Estimating Weekly Case Ratio (WCR) and increases in case reporting in HBs

$$WCR_{week} = \frac{CASES_{week}}{CASES_{week-1}} \quad \left(WCR_{week} = 0 \quad if \quad week = 1\right)$$

$CASES_{week}$ is the sum of total ILI cases reported **to** the sentinel GPs of all 13 health boards in a given *week*

How many health boards have reported increase in ILI cases over previous week

Methods: joint probability of (WCR, N_{HB}) from the seasonal ILI data of 6 seasons



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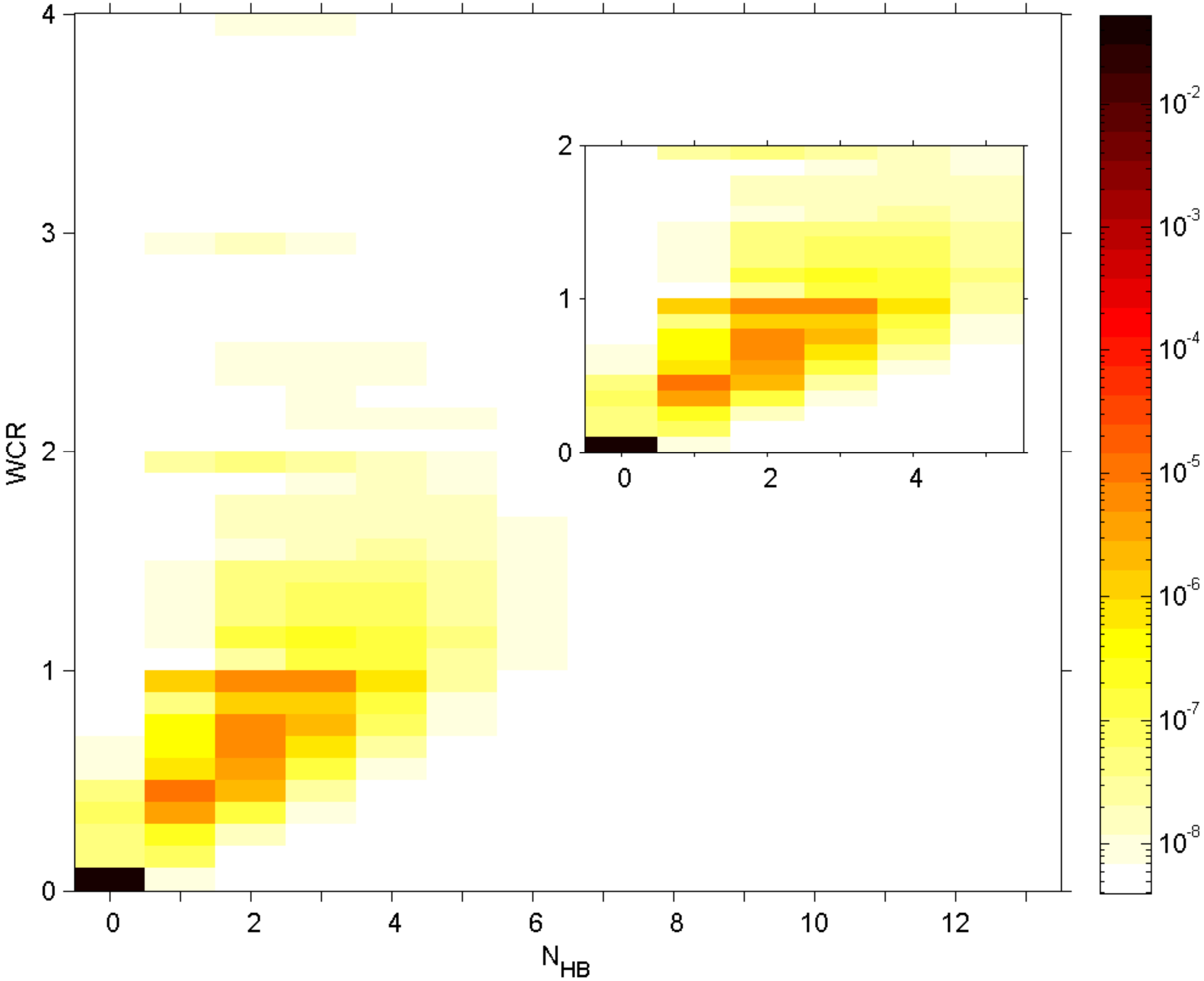
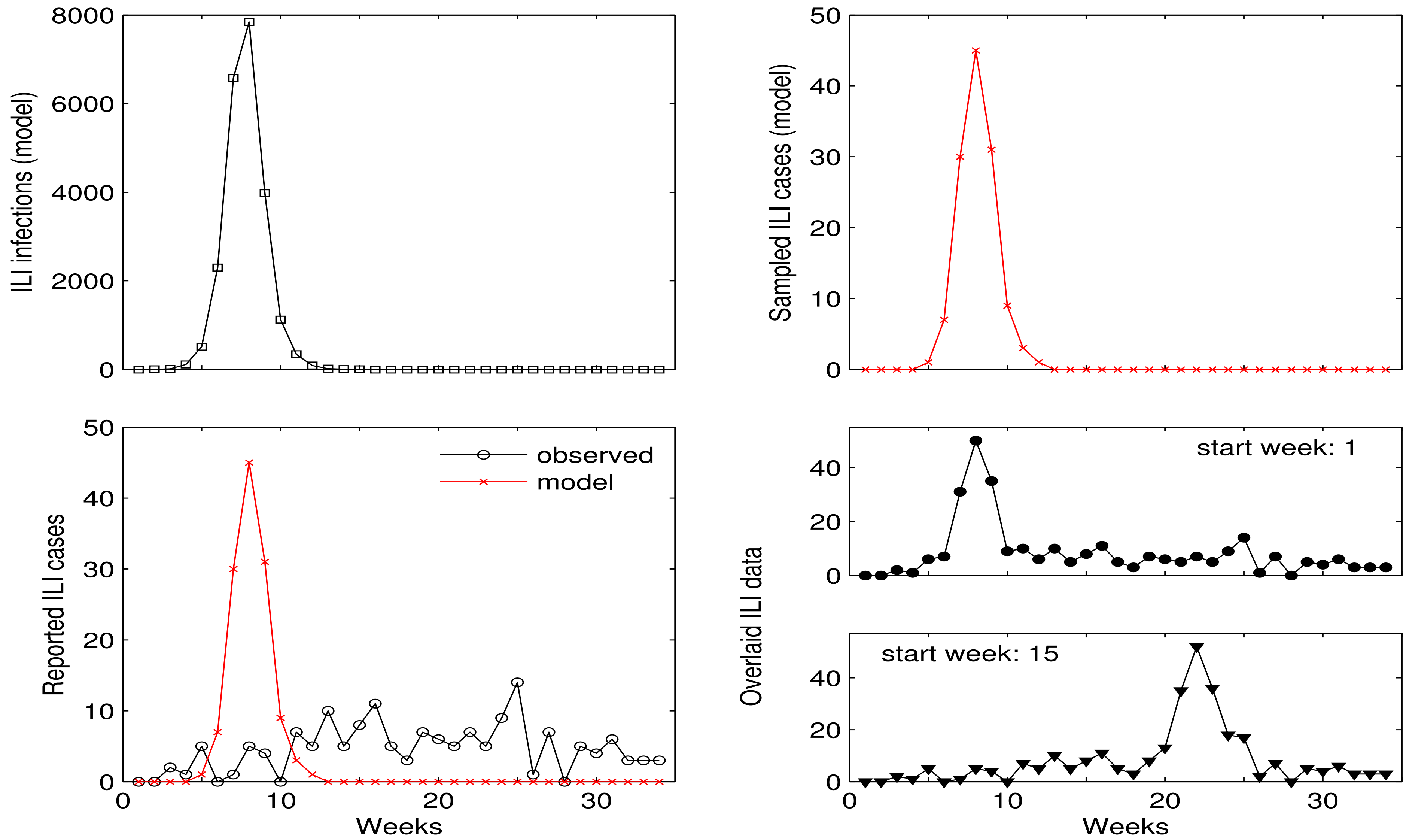


Methods: simulated pandemic ILI cases

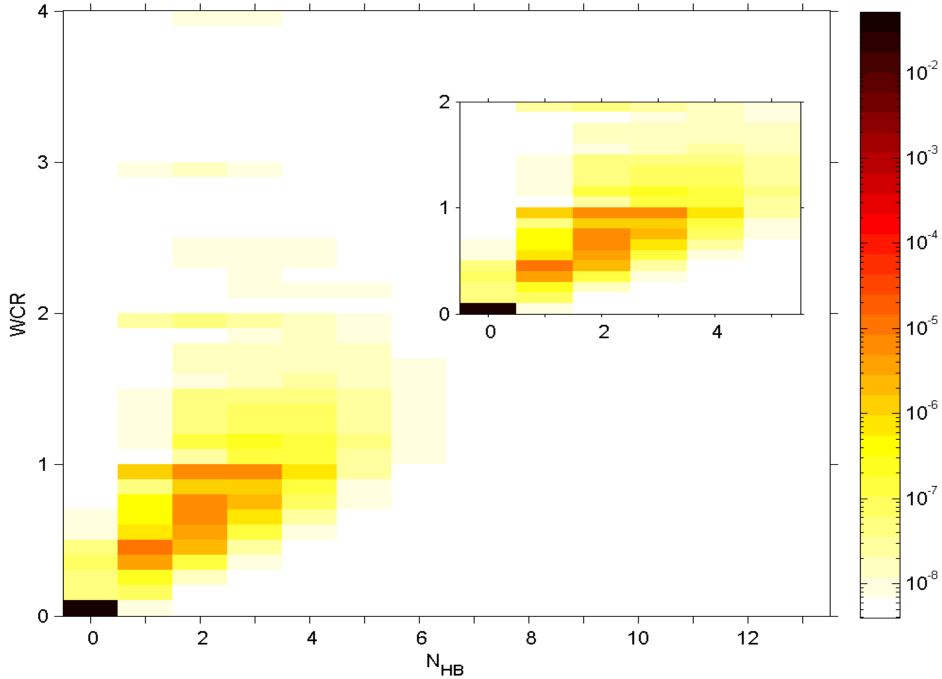
- We use simulated pandemic influenza data from Neil Ferguson's spatially explicit, individual-based pandemic model
- Seeded randomly at one location in GB
- R_0=1.7
- 10 runs of simulated pandemic
- Occurrence of the first infections in Scotland marks the start of pandemic influenza infection in Scotland
- Pandemic reporting is at 0.5% of infections as if they were coming through the participating sentinel GPs of the SERVIS health boards

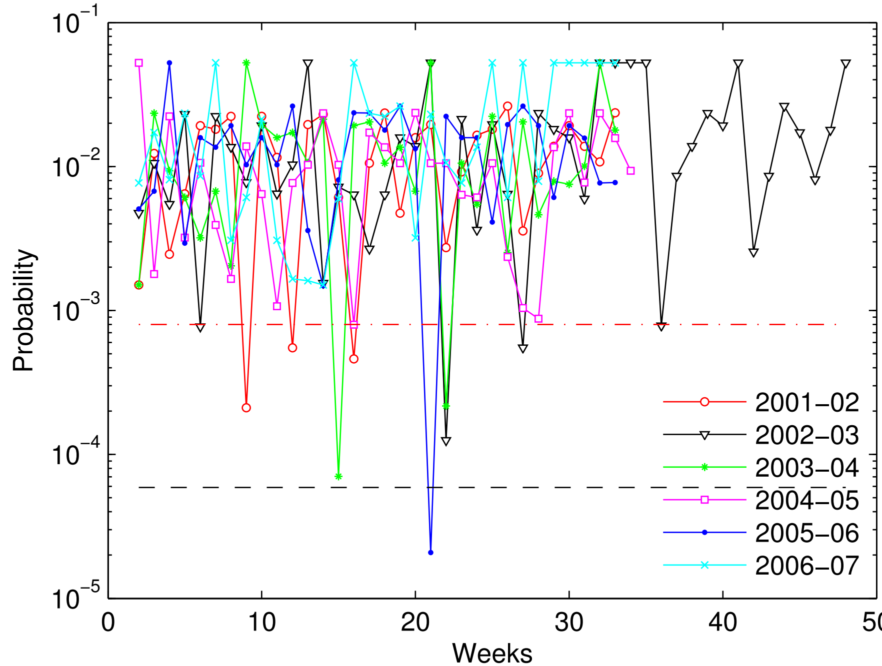
Methods: reported (model) pandemic ILI cases



Results: specificity of the detection algorithm

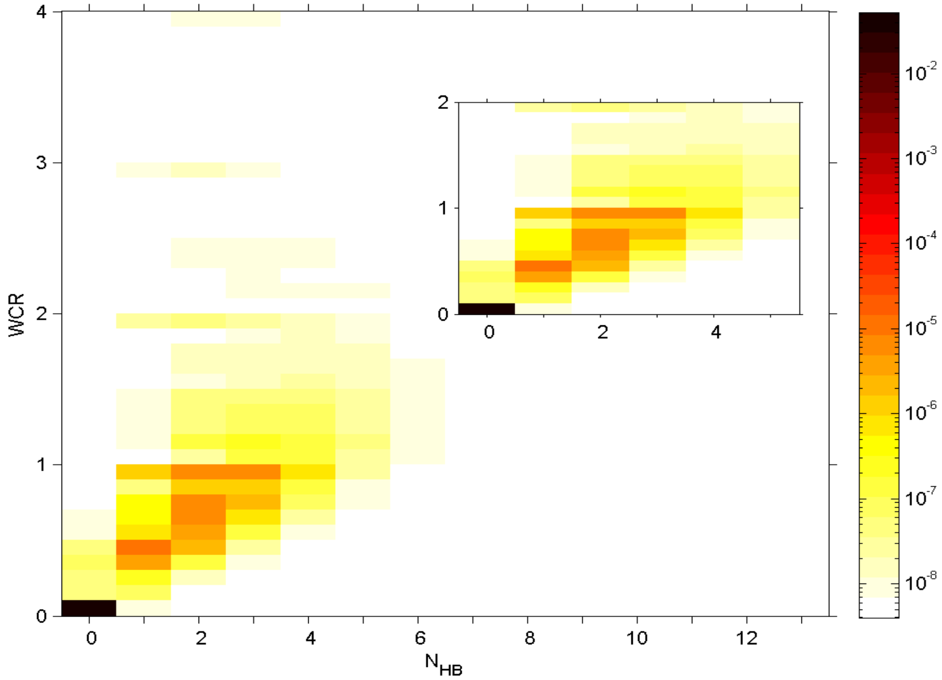
(Specificity is a measure of not detecting pandemic when no pandemic is occurring)

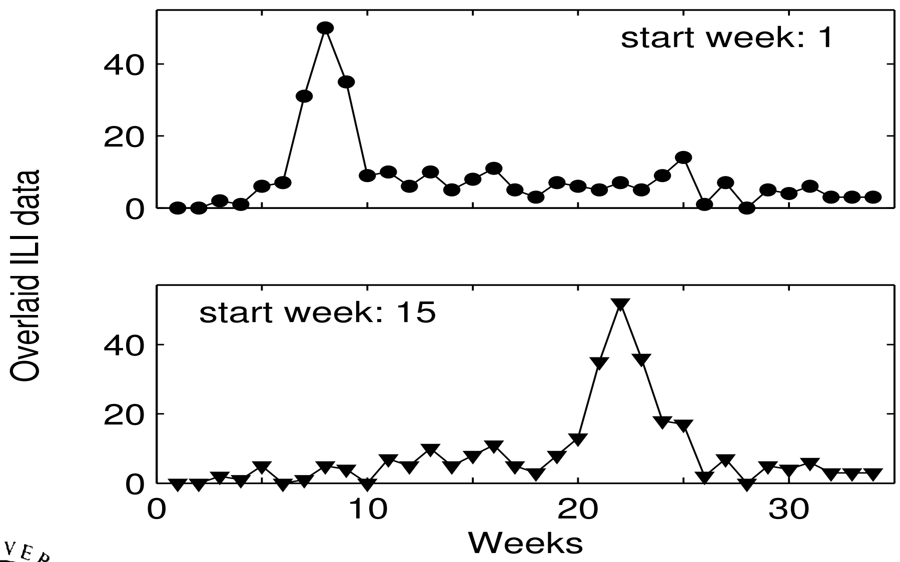


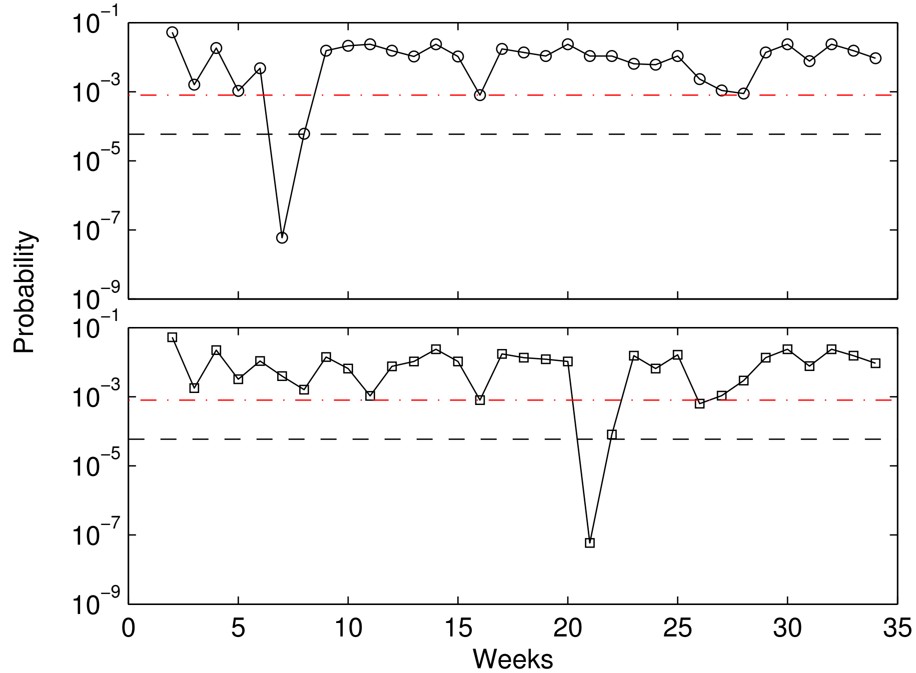


We obtain the probability values of weekly pairs of (WCR, N_{HB}) from the seasonal ILI data for each season. Dashed line is for specificity of 99%, while the dot-dash line for 95%.

Methods: detection of (model) pandemic outbreaks







Methods: the *d*-week upper Cusum method

$$Cusum_t^+ = \max\left\{0, \frac{X_t - \tilde{X}_t}{\tilde{s}_t} - k + Cusum_{t-1}^+\right\},$$

where $Cusum_{t \le d+7}^+ = 0$. The letter d stands for the delay in calculating the moving average $\tilde{X}_t$ and standard deviation $\tilde{s}_t$ from the moving series of 7-week data preceding the most recent d weeks. That is, from the series of $X_{t-d-7}, \cdots, X_{t-d-1}$.

The parameter ***k*** is the reference size of the deviation.

Ref.: Montgomary, D.C. **Introduction to Statistical Quality Control**, 3rd Edition (1997), John Wiley & Sons, New York

Methods: the *d*-week upper Cusum method

$$Cusum_t^+ = \max\left\{0, \frac{X_t - \tilde{X}_t}{\tilde{s}_t} - k + Cusum_{t-1}^+\right\},$$

- **Main model parameters are:** *d* **and** *k.*
  (the best choice we found : d=0 and k=1)
- *A 7-week window is used for the moving average and standard deviation*
- *The method is defined for t>d+7*
- *A pandemic detection occurs when* $Cusum_t^+$ *is goes above a pre-determined detection threshold (12.5 for Sp=99%; 7.5 for Sp=95%)*

Methods: the ILI rate threshold method

- **Pandemic detection occurs when the weekly ILI rate η (cases per 100,000 population) crosses a pre-determined threshold value.**

  (η=34 for Sp=99%; and η=24 for Sp=95%)

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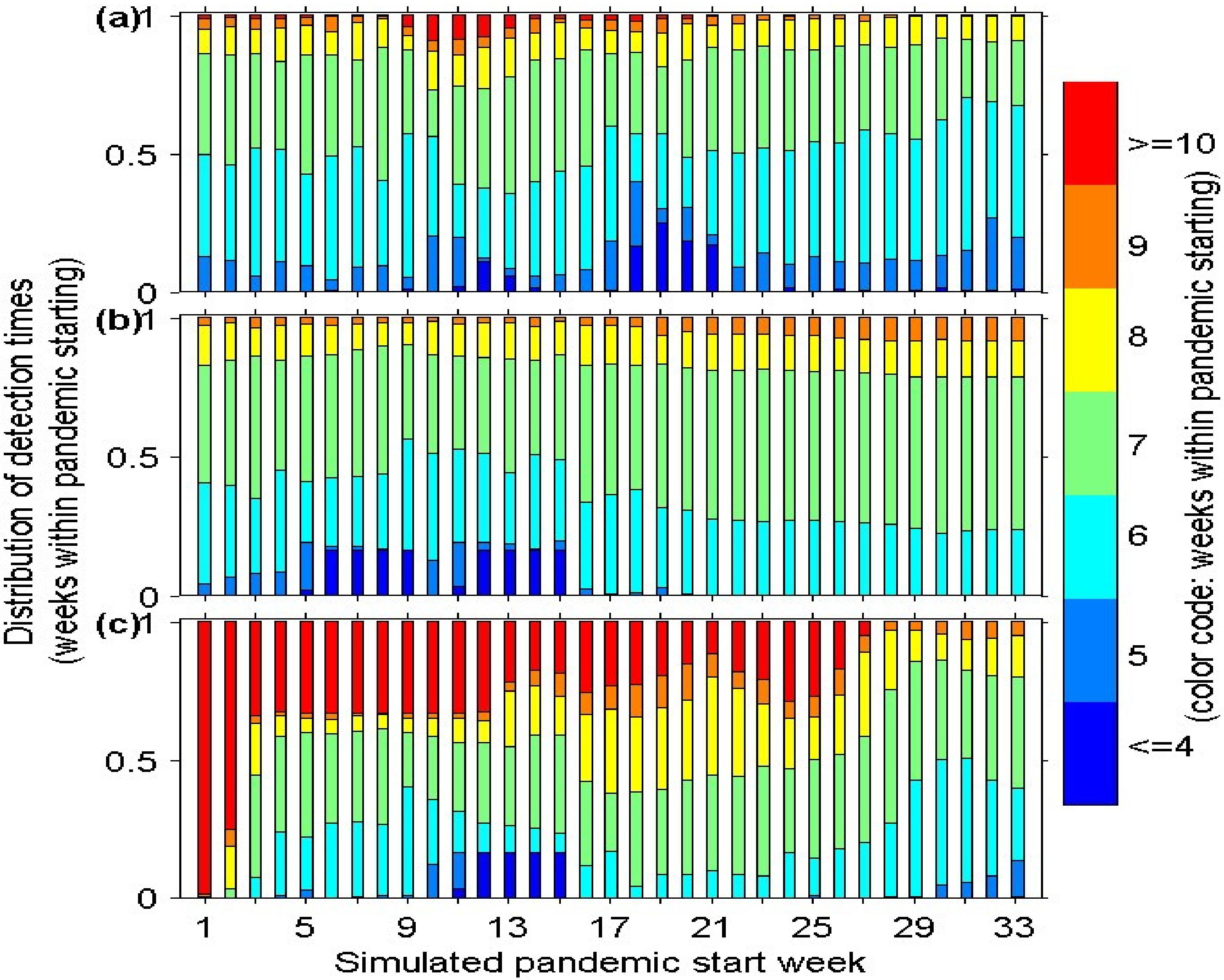
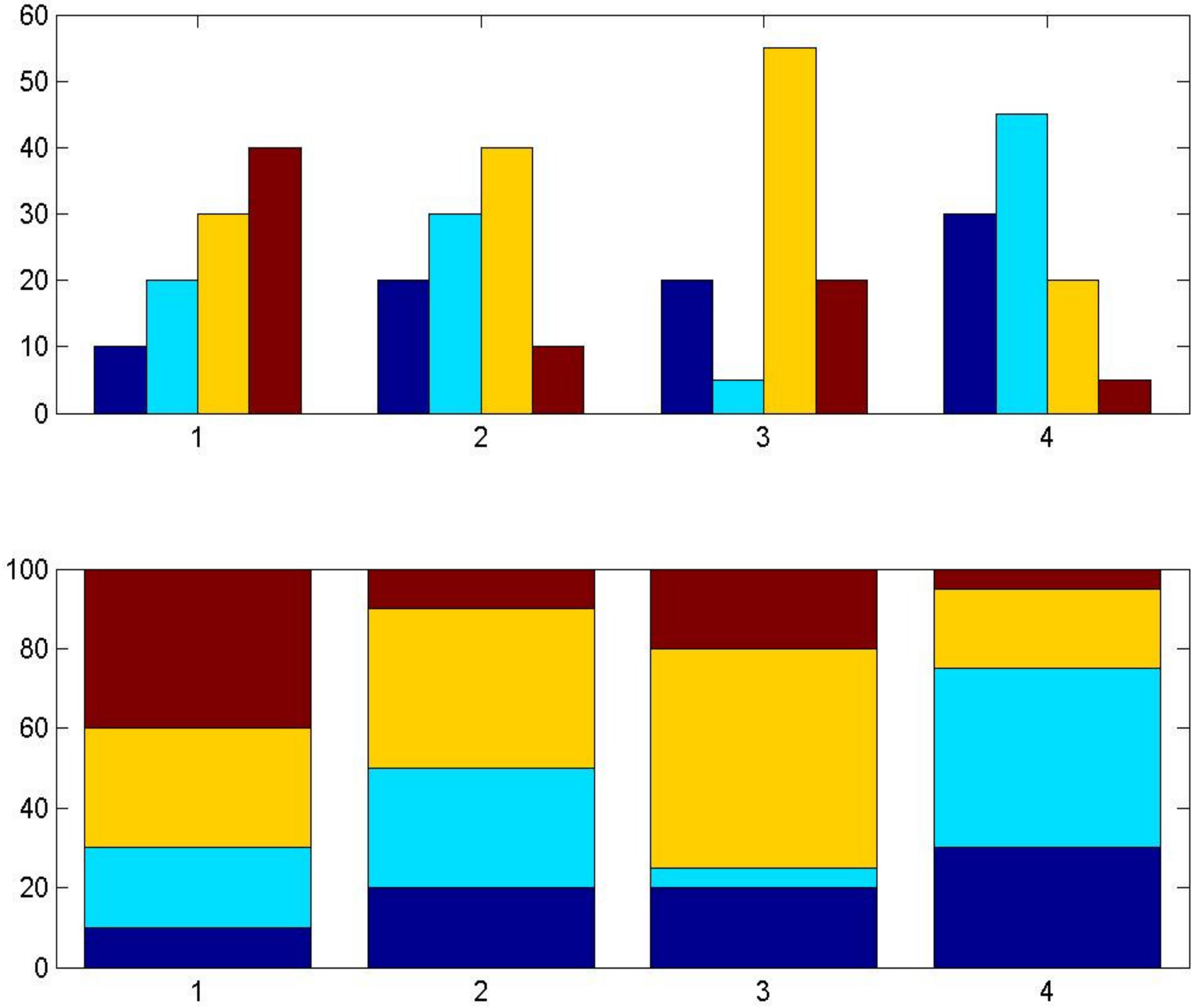
Results: distributions of detection times as a function pandemic start weeks



Plots (a): WCR detection method; (b) the ILI rate threshold method; and (c) the Cusum method (Specificity=99%, pandemic reporting =0.5%)

Illustration: the distributions of detection times for the first few pandemic start weeks



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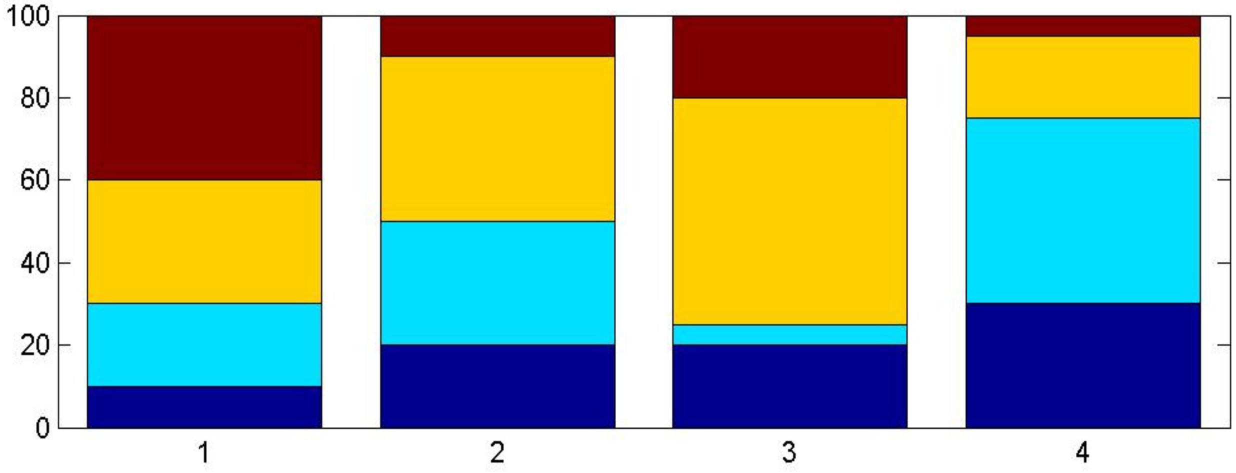

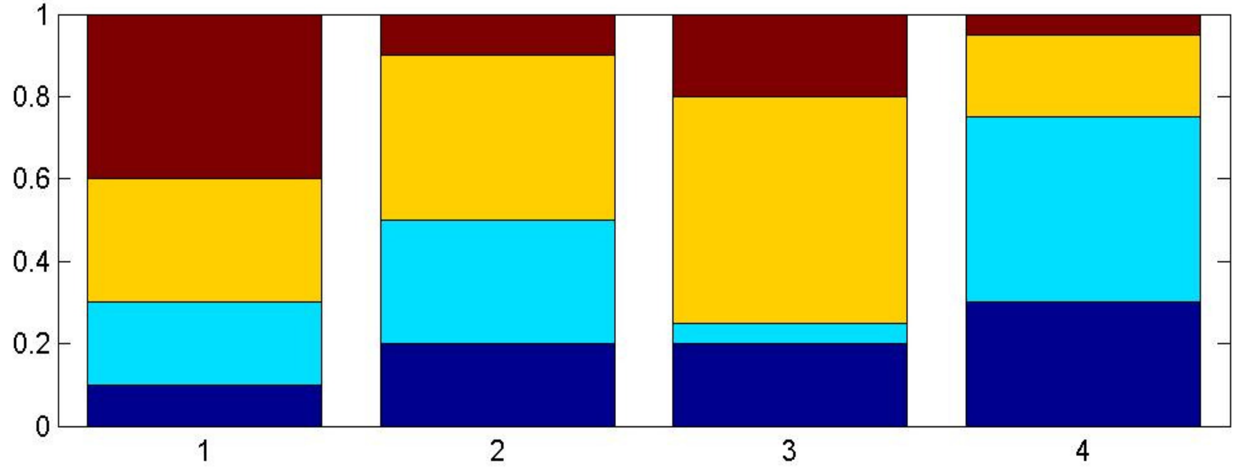

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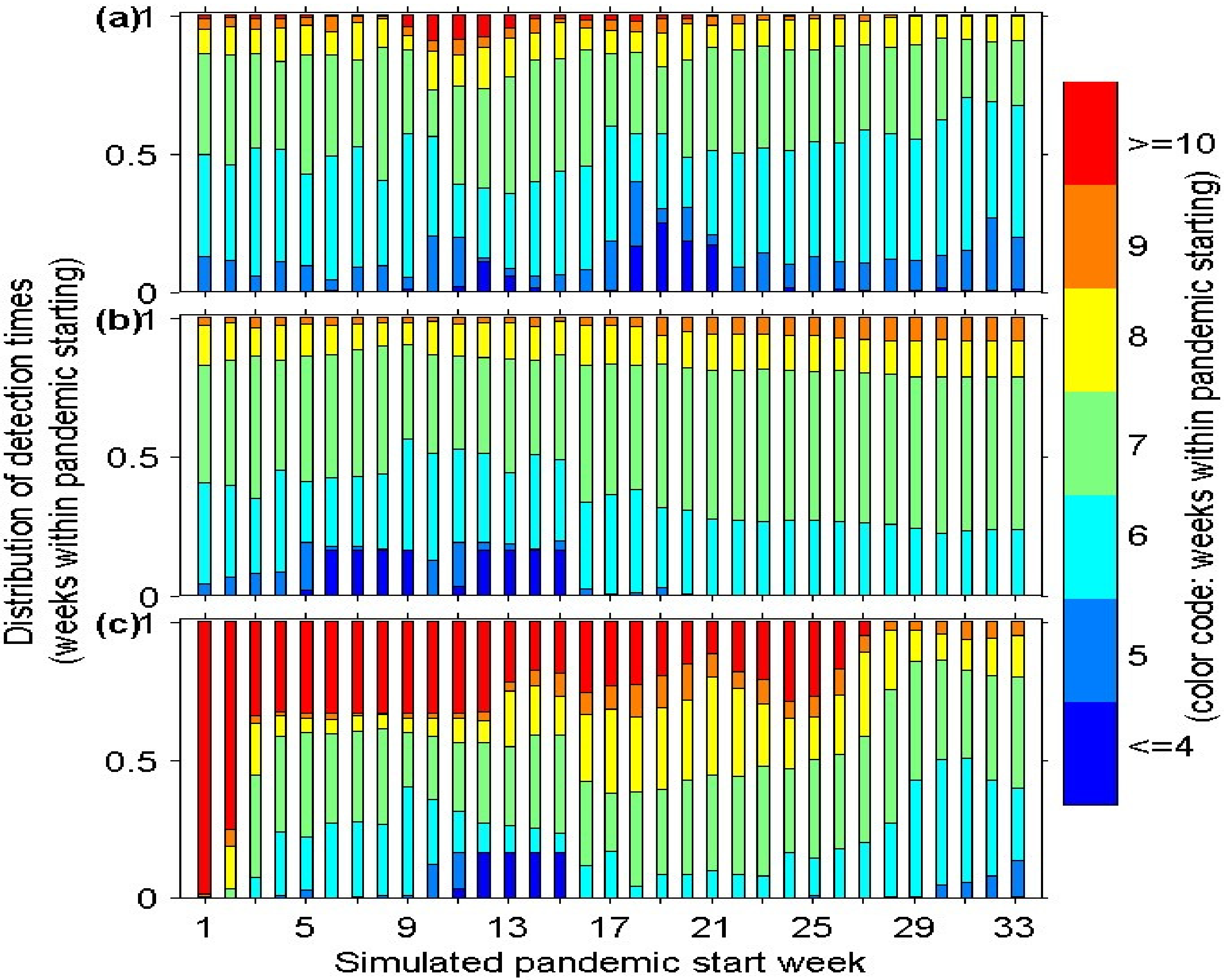
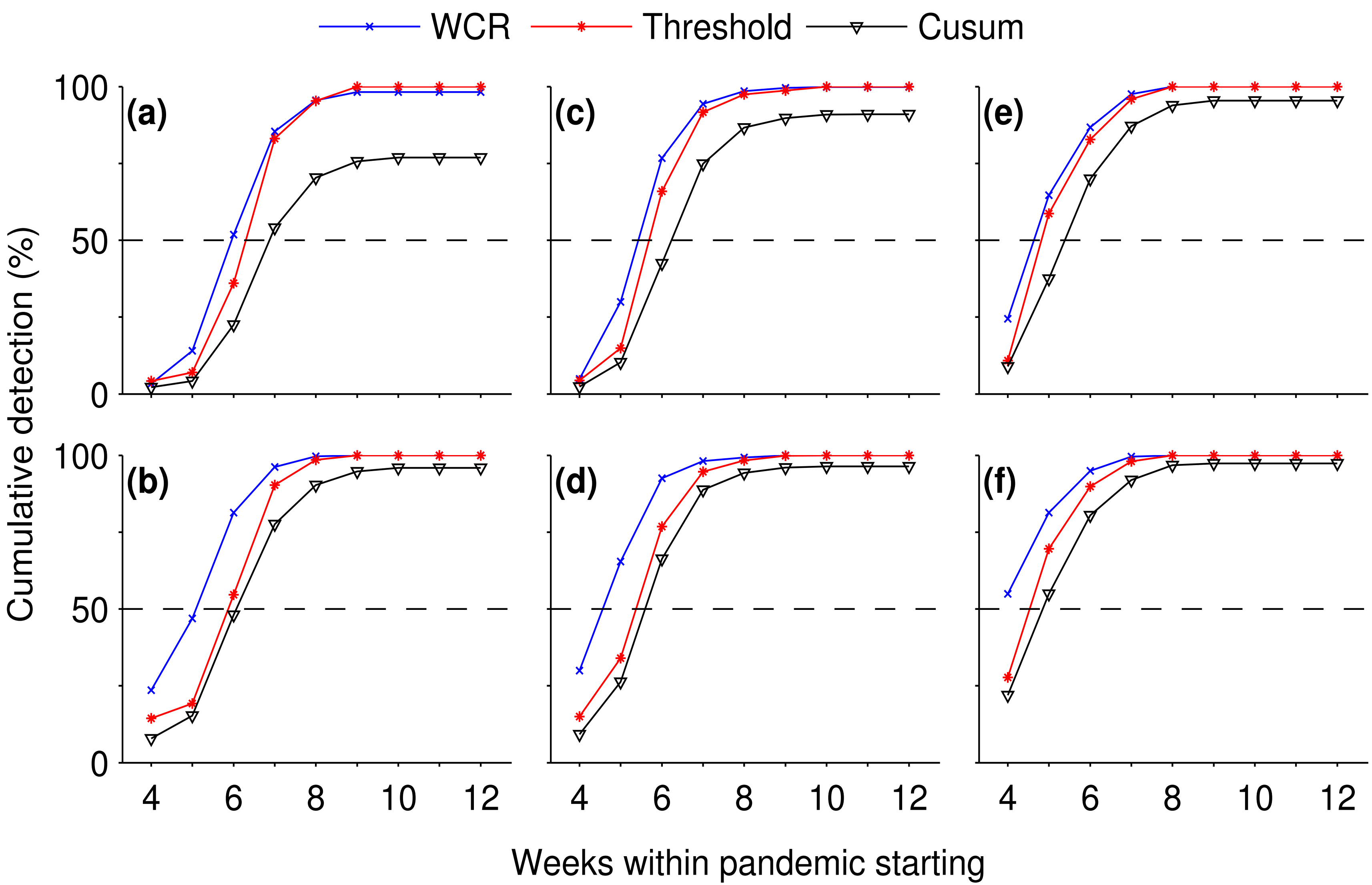


Plots (a): WCR detection method; (b) the ILI rate threshold method; and (c) the Cusum method (Specificity=99%, pandemic reporting =0.5%)

Results: effect of specificity and pandemic reporting on pandemic detections in early weeks



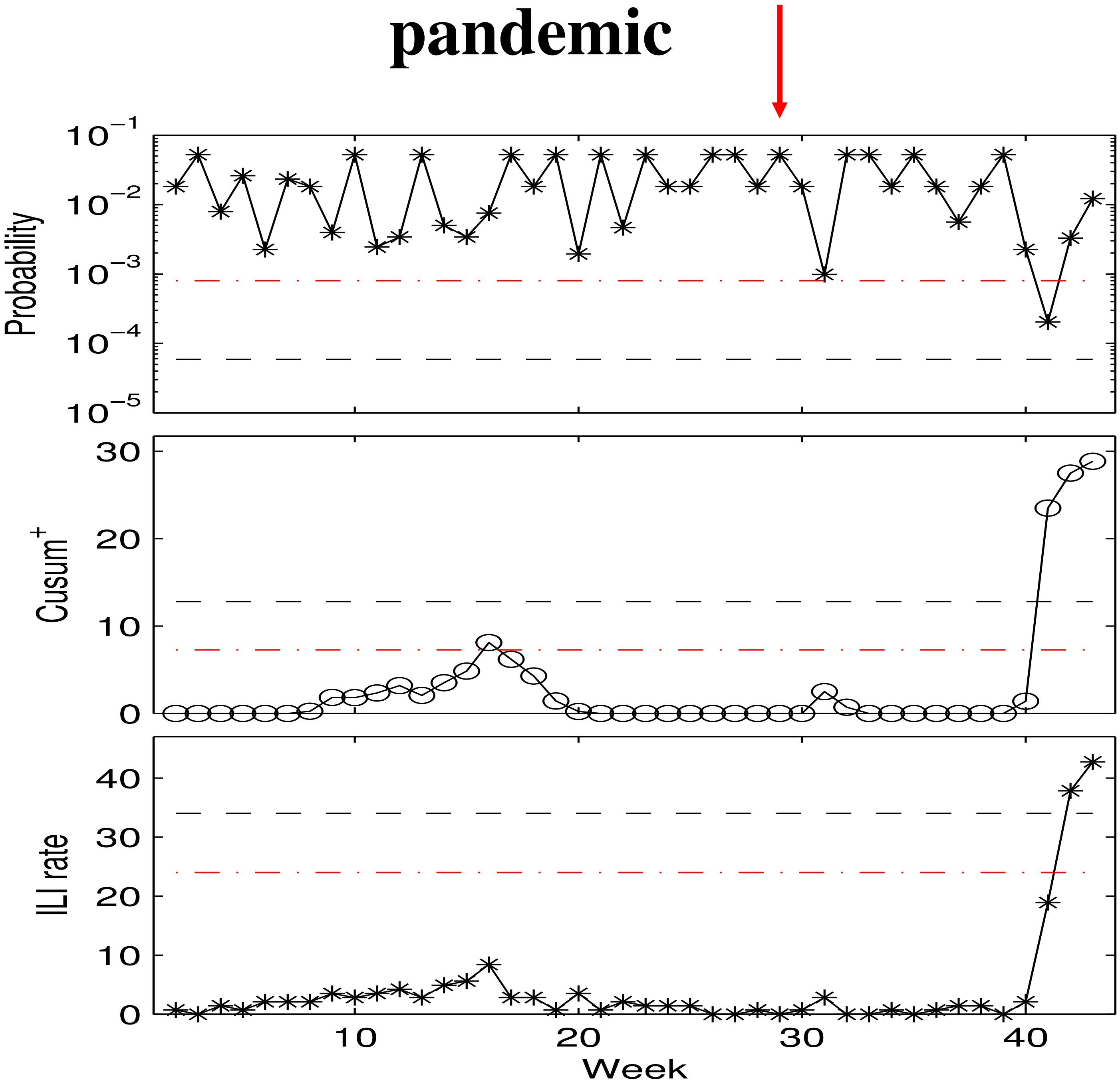
Pandemic case reporting rates (columns – left to right): 0.5%, 1% and 5%.

Specificity (rows): 99% (top) and 95% (bottom)

Results: performance summary of three methods in terms of sensitivity & median detection times

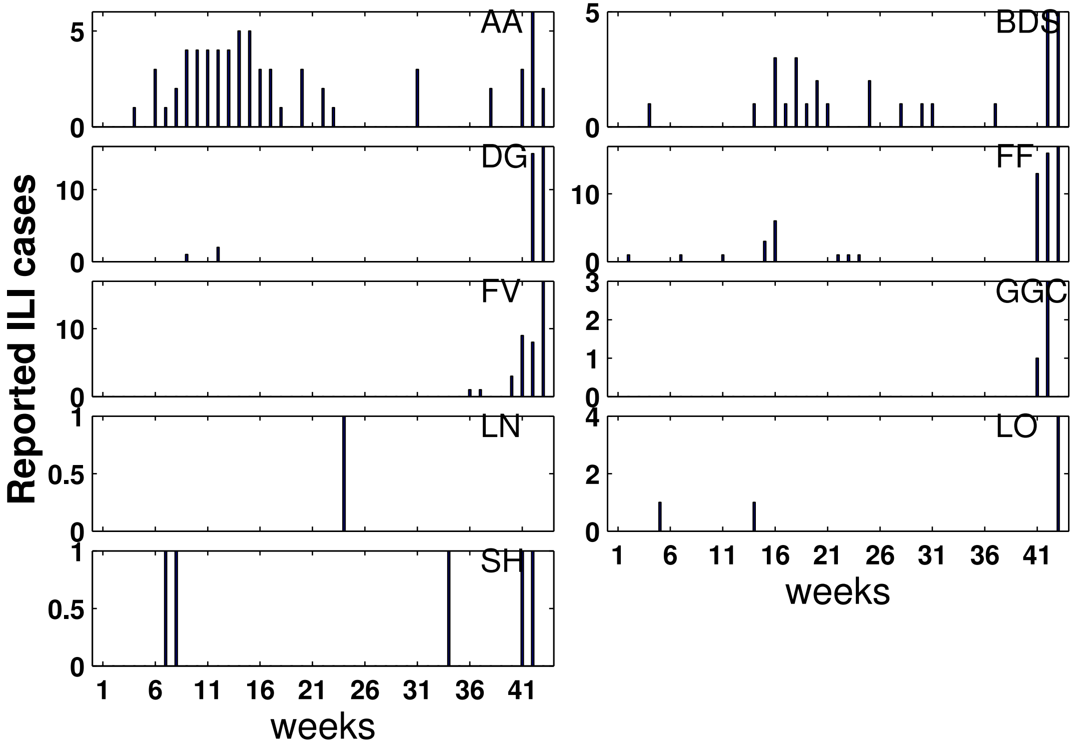
Case reproting rate		WCR method	Threshold method	Cusum method
specificity = 95%				
0.5%	Sen	100	100	96
	MDT	5	5	6
1.0%	Sen	100	100	97
	MDT	4	5	5
5.0%	Sen	100	100	97
	MDT	3	4	4
specificity = 99%				
0.5%	Sen	98	100	77
	MDT	5	6	6
1.0%	Sen	100	100	92
	MDT	5	5	6
5.0%	Sen	100	100	95
	MDT	4	4	5

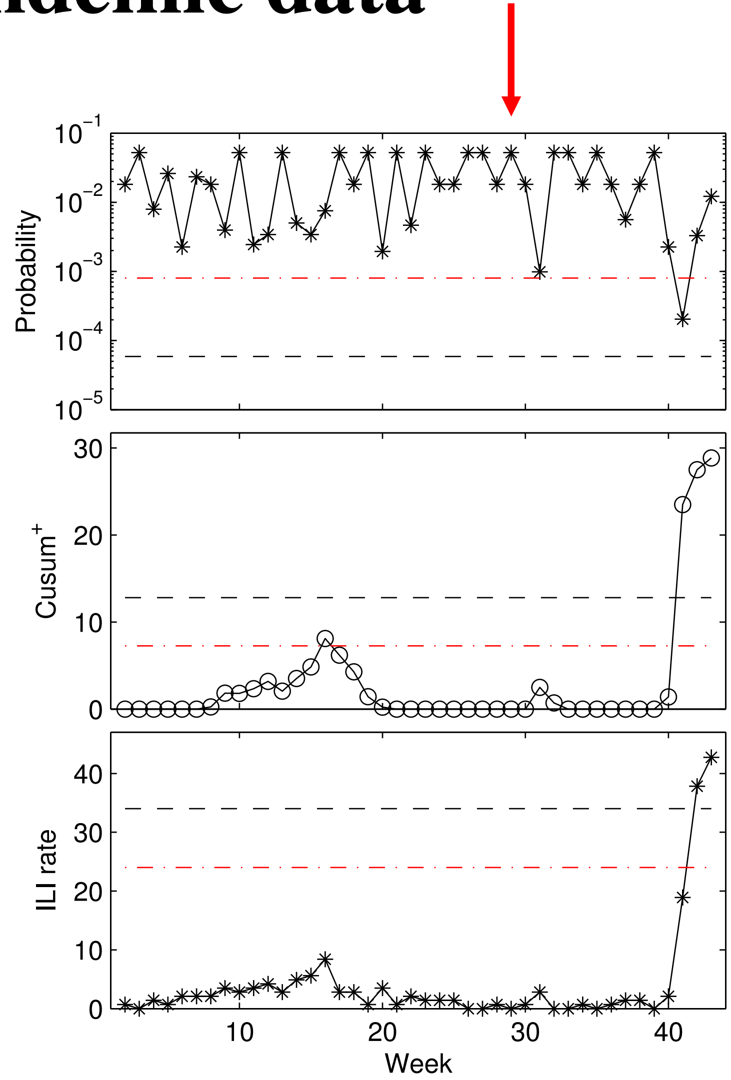
Results: detection of the 2009 influenza A(H1N1)v pandemic



Our method and the Cusum method detect the pandemic **12** weeks after the first cases were reported

Results: performance comparison with the 2009 influenza A(H1N1)v pandemic data





Our method and the Cusum method detect the pandemic **12** weeks after the first cases were reported

Summary

Scotland has several existing influenza surveillance systems; syndromic data are available for developing and testing new detection tools. (This work has helped us to make some recommendation about the increased number of the sentinel GPs used now; the number has gone up to about 950.)

We have developed a detection algorithm based on the Weekly Case Ratio.

WCR-based method appears to provide a rapid and sensitive detection tool for the outbreak of pandemic influenza.

As well as, statistically and computationally simple to implement to syndromic surveillance systems.

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Discussion

Although our algorithm performs better than the Cusum and the ILI rate threshold methods in detecting pandemics in the early weeks of simulated pandemics, it did not perform that well when applied to the 2009 influenza A(H1N1)v data.

At least, several reasons for this poor performance:

- the 2009 influenza A(H1N1)v pandemic started in the end of an influenza season, and was mild in severity;
- the observed data are very patchy (the network of the sentinel GPs was at their sparsest level);
- spatiotemporal heterogeneity in the real pandemic cases than the [synchronous] pattern predicted by the pandemic model;

Future challenges

- Apply the algorithm to other syndromic data (e.g., the NHS24/NHSDirect calls data, the ARI data, the PIPeR data) that are structured in space and time
- Improve criterion for detection (e.g., weighted WCR, ILI increases at spatial unit of GPs rather than HBs, daily reporting versus weekly)
- Evaluate detection efficiency with other modelling approaches to pandemic influenza outbreaks
- Relationship between the number of participating SERVIS sentinel GPs and the detection times: how many and where?
- The Cost-effectiveness analysis of the detection process. Do we need to have the entire population under constant surveillance?
- The modelling of seasonal influenza in Scotland to have greater flexibility with the number and the locations (in urban/rural, or high/low deprivation area) of sentinel GPs in order to be able to evaluate the cost-effectiveness of the surveillance.
- Analysis of the sero-surveillance data

Acknowledgments

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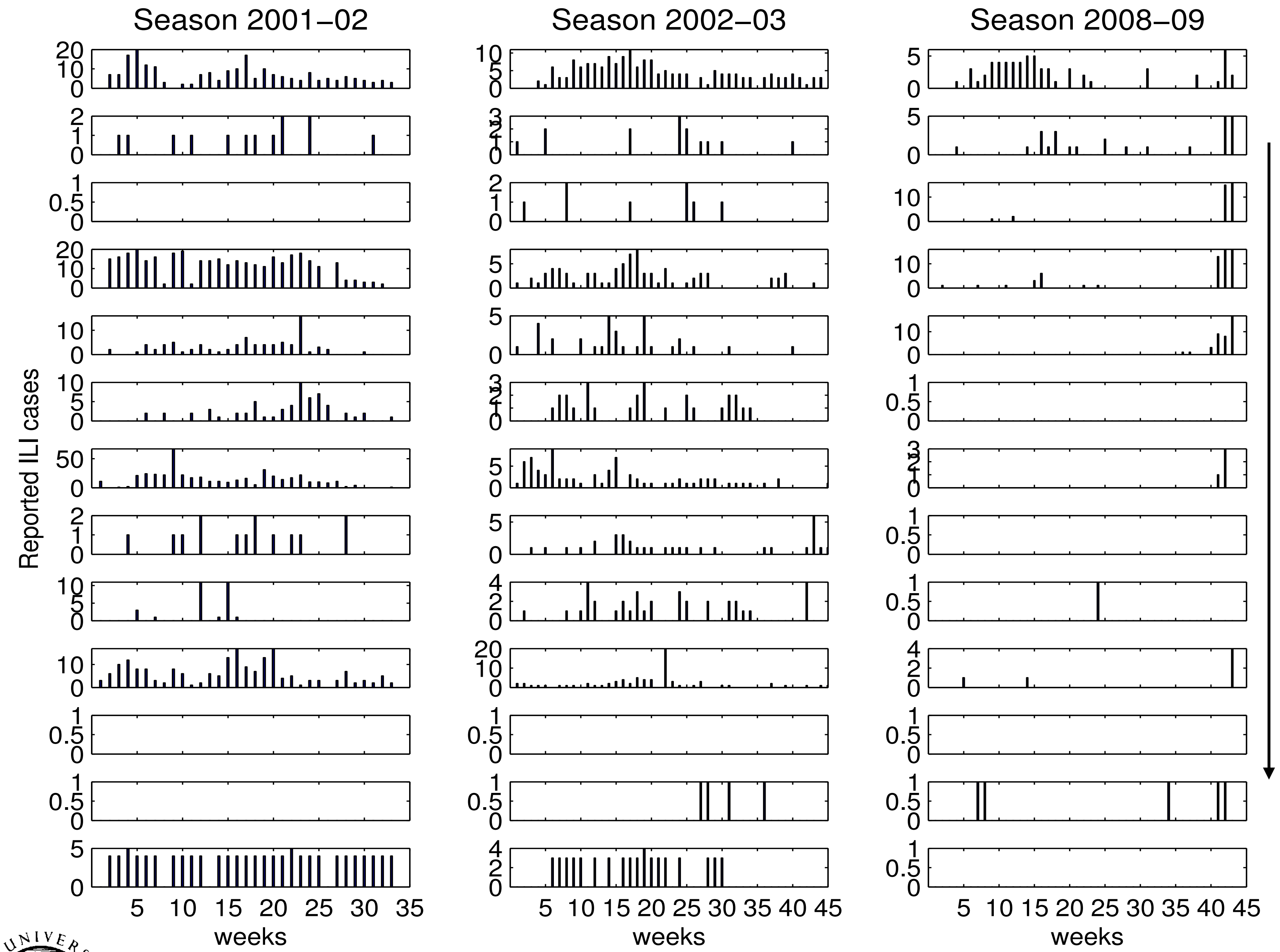
Ann Smith
Jim McMenamin

Chris Robertson

Neil Ferguson, **Imperial College London**, for simulated pandemic data.

The Funding support from the **Scottish Funding Council** & **ICHAIR** is also gratefully acknowledged.

Time series of weekly ILI cases in different Health boards



Health Boards

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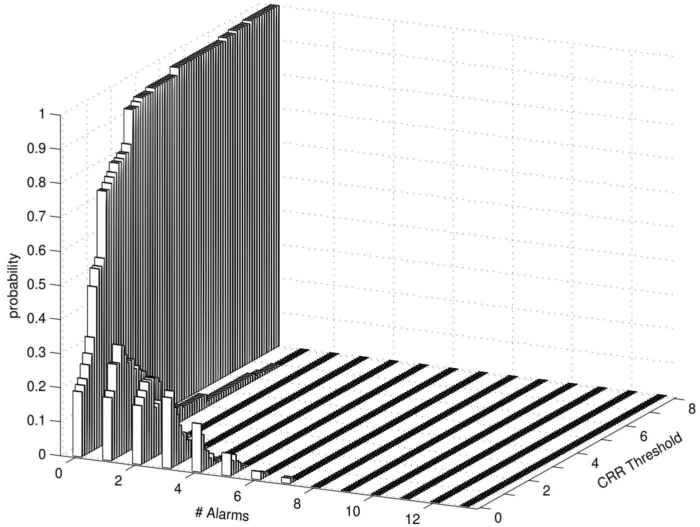
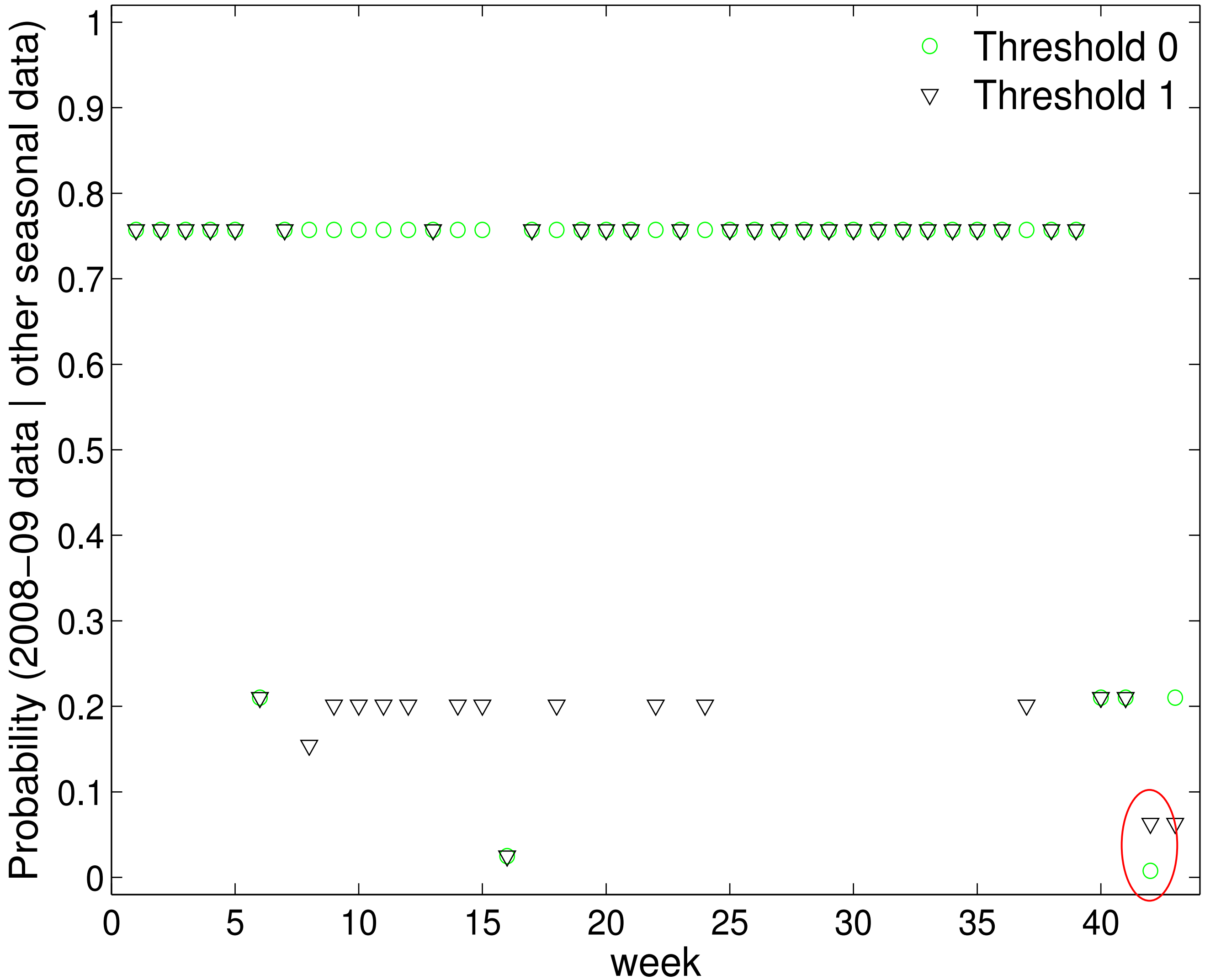
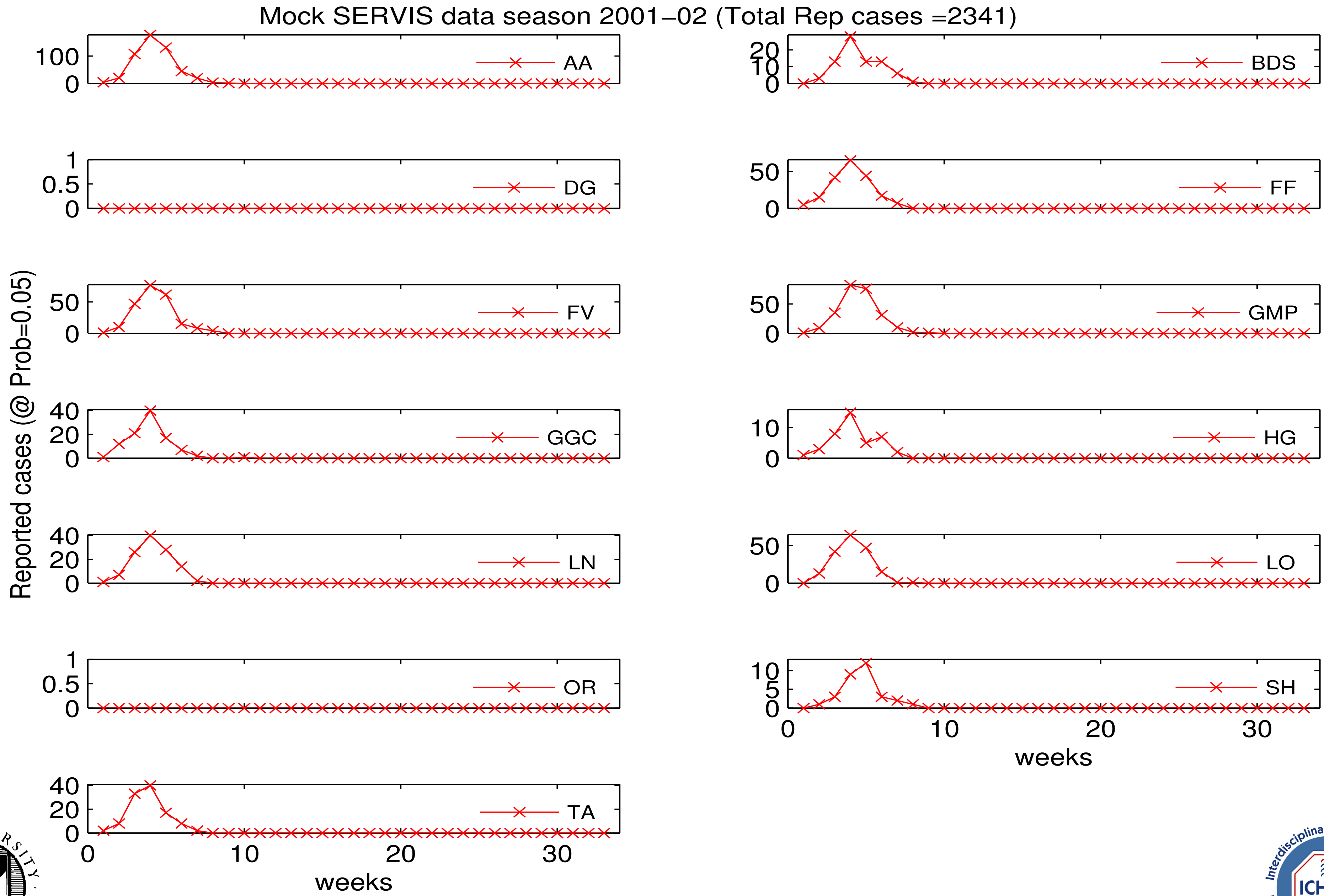
Comparing probability of SERVIS 2008-09 data



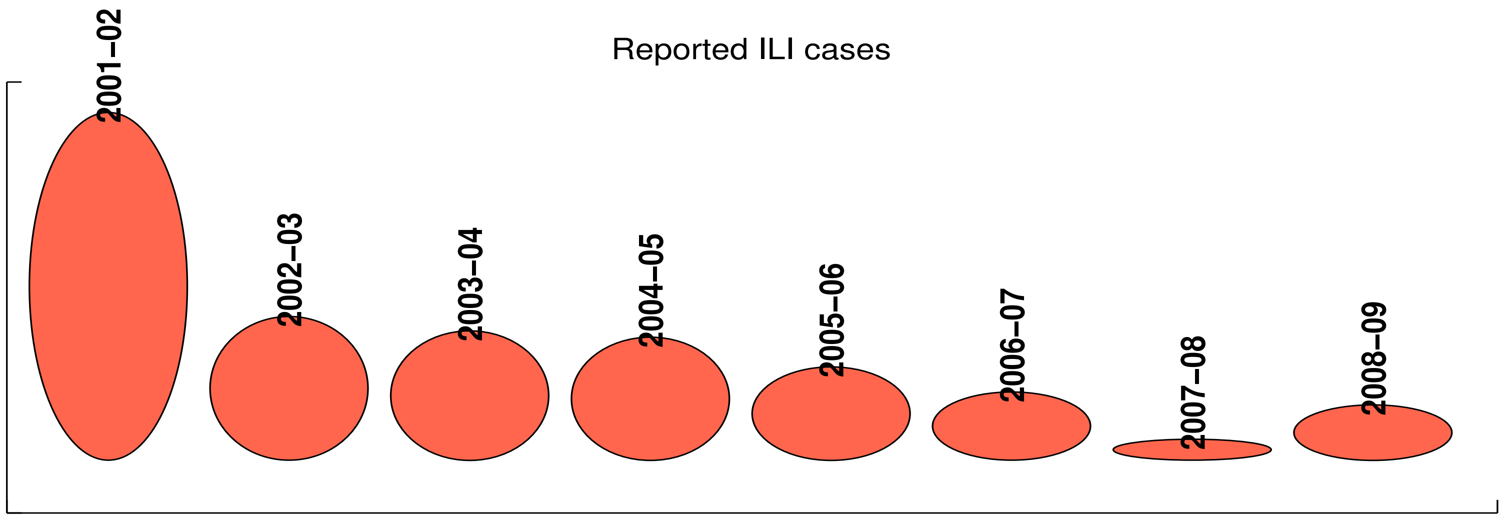


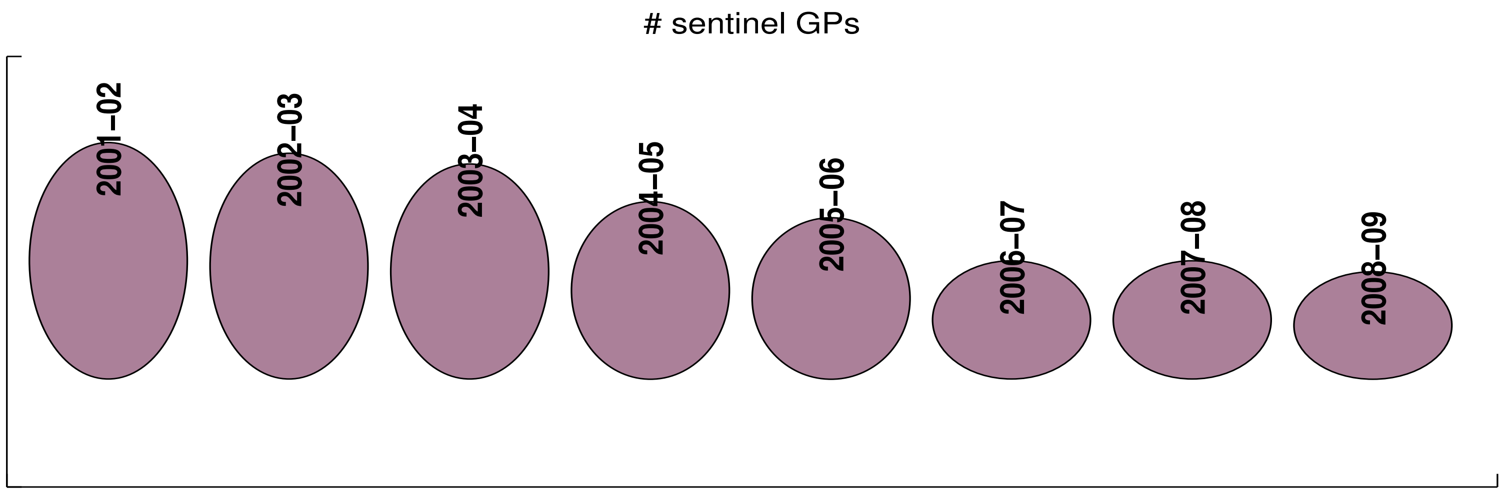
Mock SERVIS data sampled from model pandemic infections



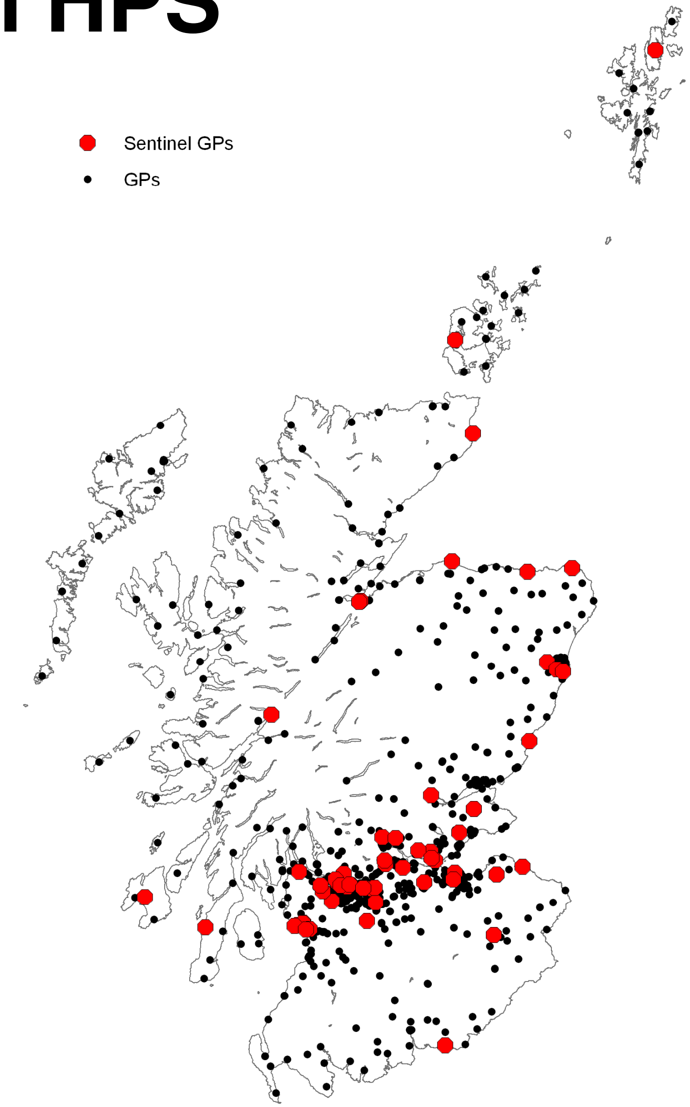
Historical Patterns of ILI surveillance in Scotland

(reported cases and sentinel GPs)





SERVIS Data from HPS

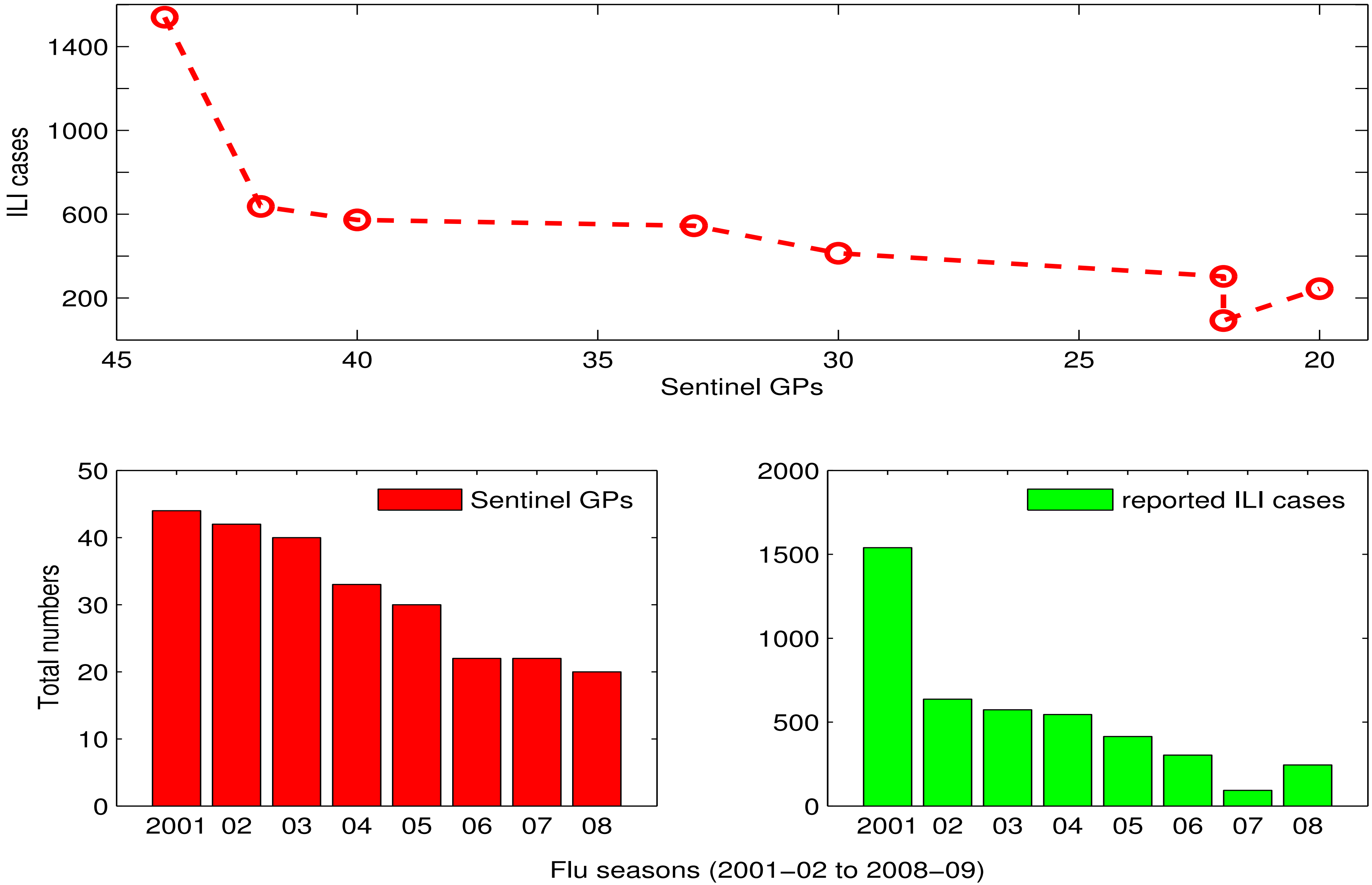


A sentinel GP reports

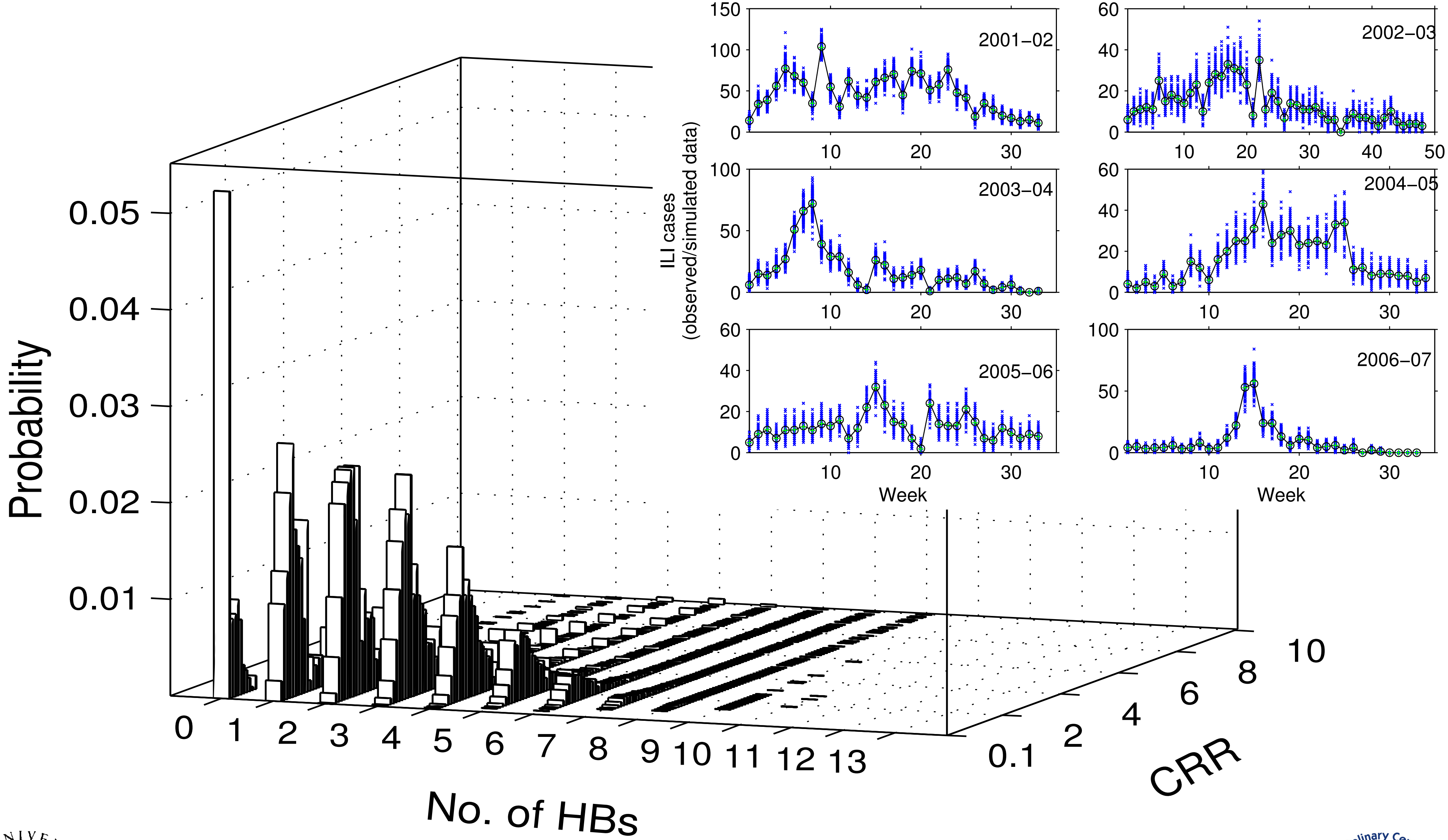
weekly ILI and ARI cases by

- - age category
  - sex
- catchment size
- location
- Health Board

Trends observed in SERVIS data



Methods: joint probability of (WCR, N_{HB}) from the seasonal ILI data of 6 seasons



X_w=Pois($CASES_w$)