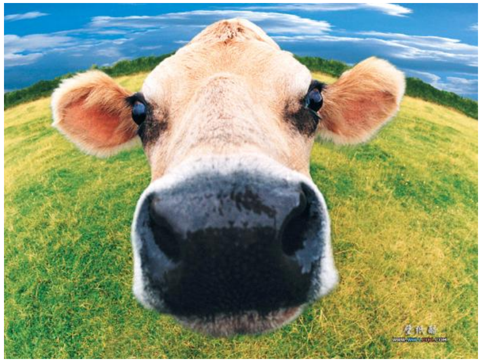


Developments in FMD-free countries

Marleen Werkman
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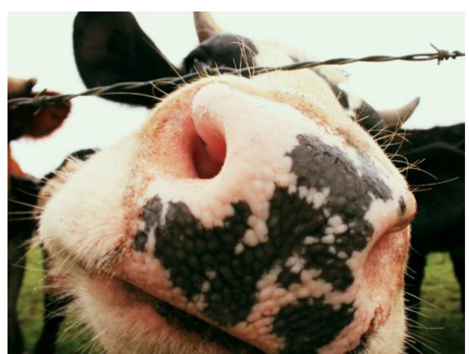


University of Warwick
Mike Tildesley
Matt Keeling
Marleen Werkman
Peter Dawson
Ben Hu (Pirbright)

Colorado State
Colleen Webb
Dan Grear
Michael Buhnerkempe

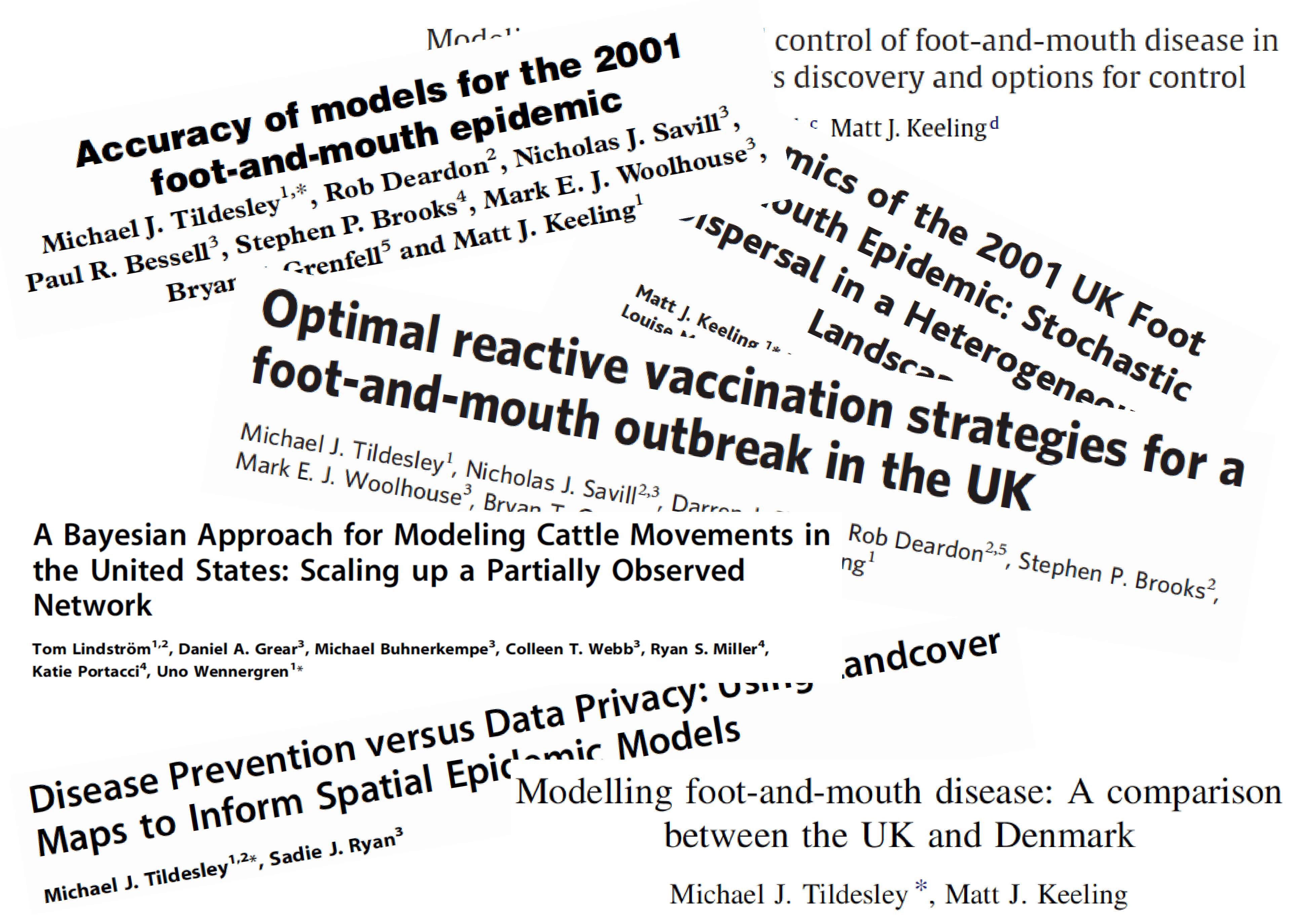
Penn State University
Matt Ferrari
Kat Shea

Linkøpings University
Uno Wennergren
Tom Lindström

USDA
Ryan Miller
Katie Portacci
Jason Lombard
Matt Farnsworth

Other
David Schley (Pirbright)
Chris Jewel (Massey University)
Ellen Brooks-Pollock (University of Cambridge)
Ruri Ushijima (University of Miyazaki)
Sadie Ryan (SUNY ESF)
Gary Smith (University of Pennsylvania)

Funding
The Wellcome Trust
NIH MIDAS
DHS
BBSRC


control of foot-and-mouth disease in
s discovery and options for control
Matt J. Keeling[d]
Accuracy of models for the 2001 foot-and-mouth epidemic
Michael J. Tildesley[1,*], Rob Deardon[2], Nicholas J. Savill[3], Paul R. Bessell[3], Stephen P. Brooks[4], Mark E. J. Woolhouse[3], Grenfell[5] and Matt J. Keeling[1]
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outh Epidemic: Stochastic
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Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK
Michael J. Tildesley[1], Nicholas J. Savill[2,3], Mark E. J. Woolhouse[3]
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A Bayesian Approach for Modeling Cattle Movements in the United States: Scaling up a Partially Observed Network
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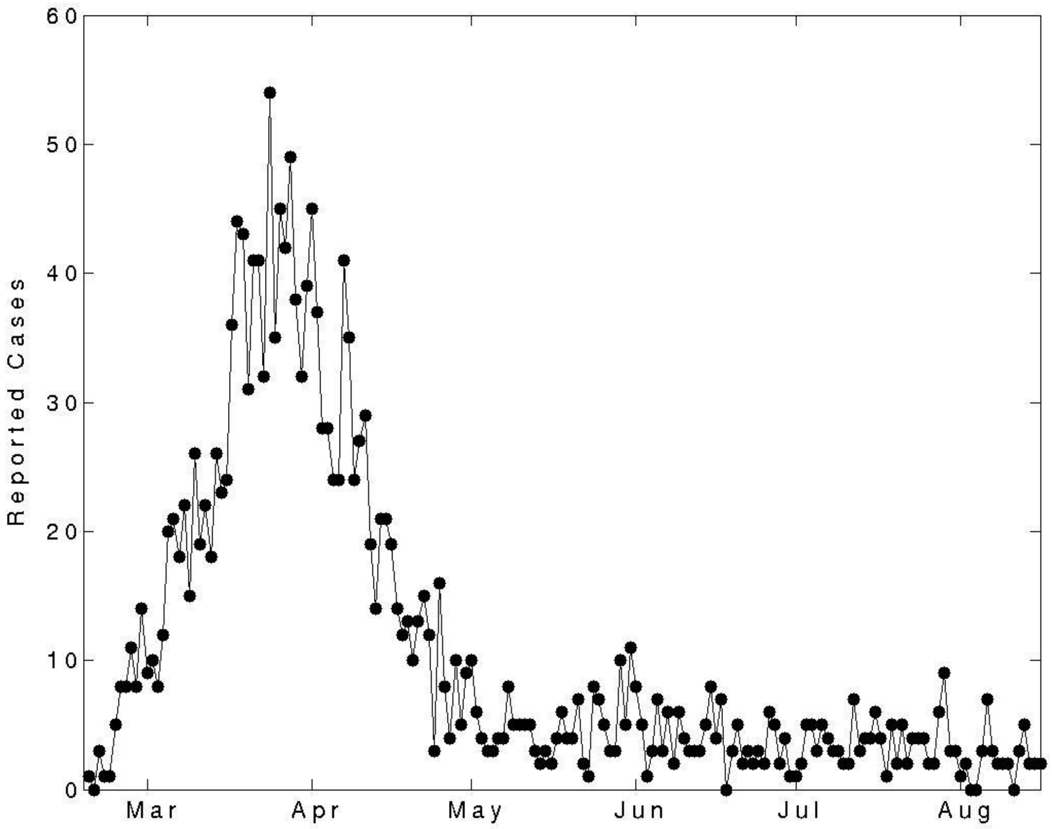
andcover
Disease Prevention versus Data Privacy:
Maps to Inform Spatial Epi
Models
Michael J. Tildesley[1,2*], Sadie J. Ryan[3]
Modelling foot-and-mouth disease: A comparison between the UK and Denmark
Michael J. Tildesley *, Matt J. Keeling

Dynamics of the 2001 UK Foot and Mouth Epidemic: Stochastic Dispersal in a Heterogeneous Landscape

Matt J. Keeling,[1*] Mark E. J. Woolhouse,[2] Darren J. Shaw,[2] Louise Matthews,[2] Margo Chase-Topping,[2] Dan T. Haydon,[3] Stephen J. Cornell,[1] Jens Kappey,[1] John Wilesmith,[4] Bryan T. Grenfell[1]

Science 2001, 294: 813-817

UK 2001 epidemic timescale



FMD entered the UK in early February.

Whilst the disease was "under control" by the end of April, the tail of the epidemic lasted until the end of September.

Over 10,000 farms were affected by the epidemic (either infected or culled as part of the control) and a total of 850,000 cattle and 4,000,000 sheep were culled.

The Keeling/Warwick Model

- Relatively simple model that was developed during the UK 2001 outbreak
- In this model, the risk of spread is based upon various parameters:

$S_{c,s}$ - The susceptibility of livestock (cattle, sheep, pigs etc.).

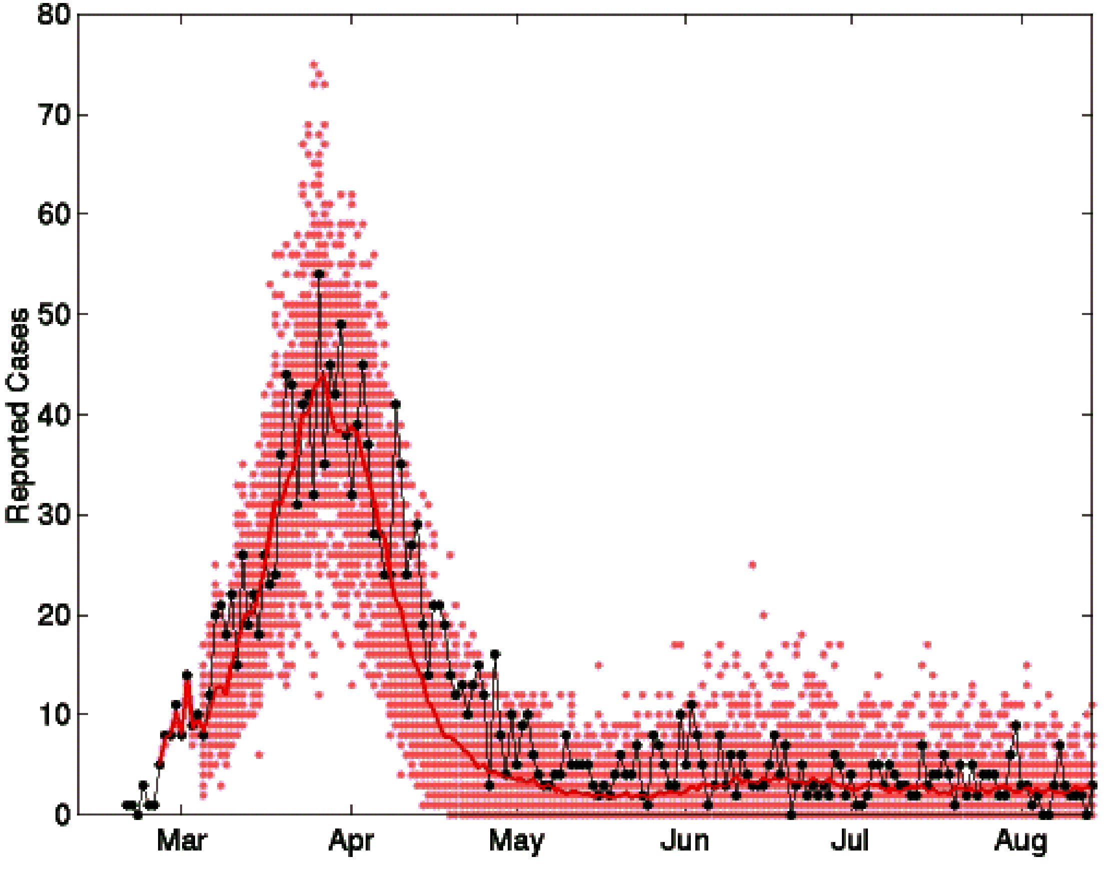
$N_{c,i}$ - number of livestock on a given farm.

T_c - transmissibility of livestock.

$K(d_{ij})$ - the distance kernel, giving probability of infection based on distance between farm *i* and farm *j*.

Comparison between model and data

Very good agreement between the observed cases (black) and the mean predicted epidemic (red line). The cloud of points indicates the stochastic uncertainty in predictions.



These simulations are iterated forward from end of February using the farms infected at that time.

Keeling *et al*. (2001) *Science*.

Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK

Michael J. Tildesley[1], Nicholas J. Savill[2,3], Darren J. Shaw[4], Rob Deardon[2,5], Stephen P. Brooks[2], Mark E. J. Woolhouse[3], Bryan T. Grenfell[6,7] & Matt J. Keeling[1]

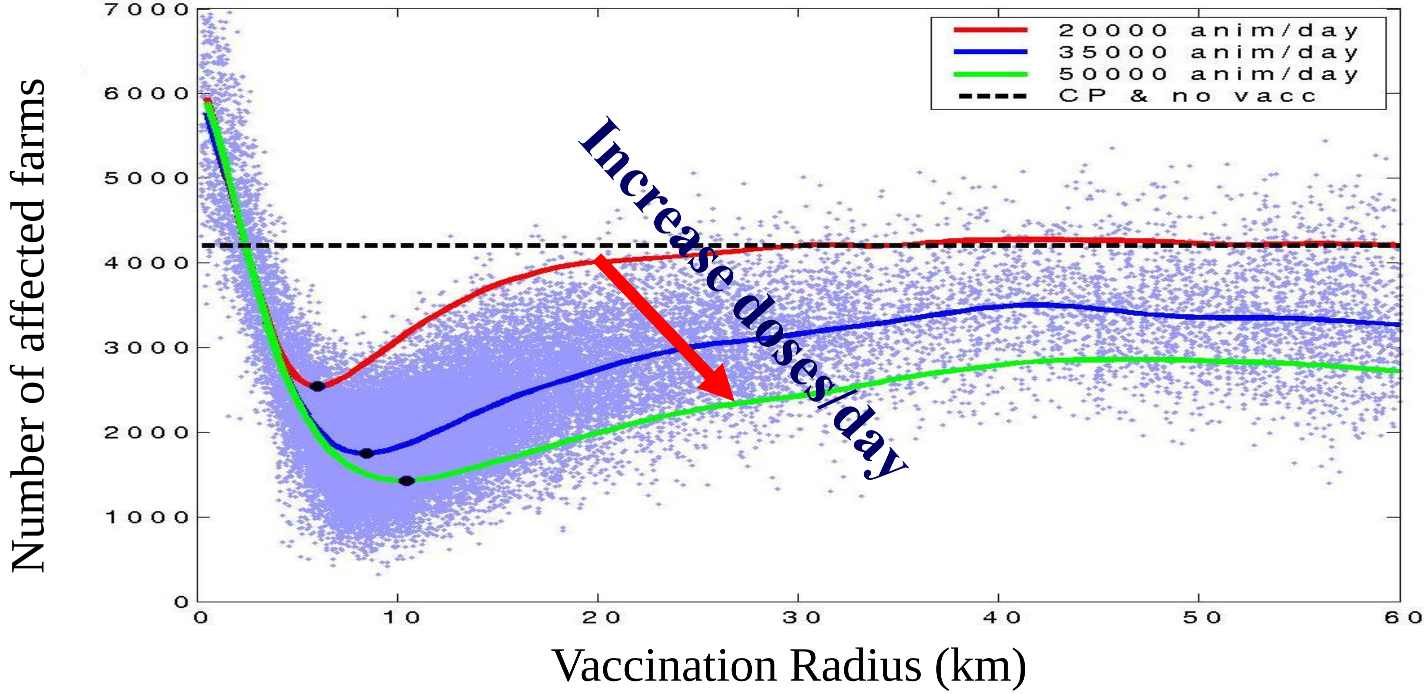
Nature 2006 440: 83-86

Optimizing the use of limited resources

- We investigated the effectiveness of ring vaccination – farms vaccinated within a given radius of infected farms.
- The optimal ring vaccination employed in an epidemic is highly dependent upon a range of factors:

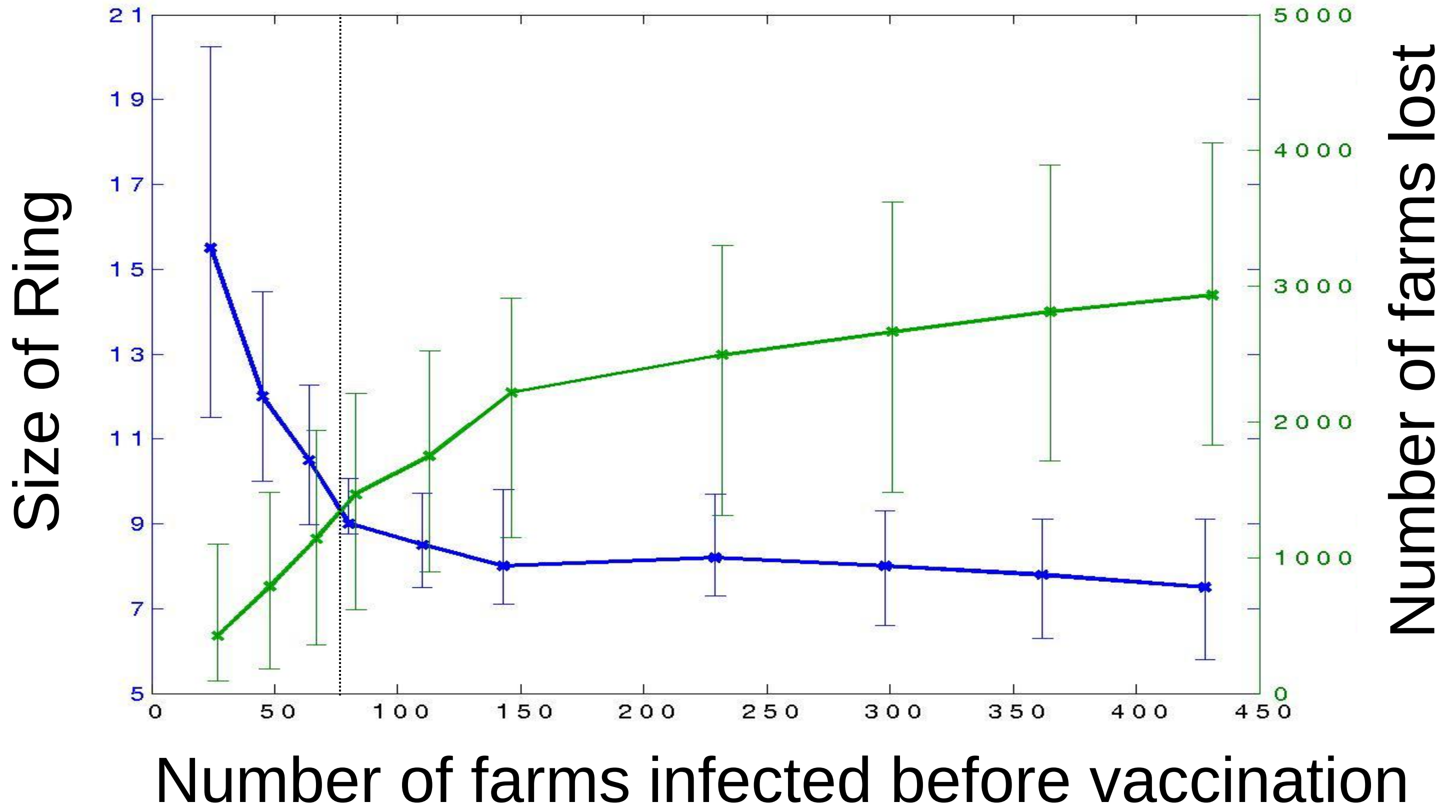
1. The number of animals you can vaccinate per day.
2. Time delay to the introduction of vaccination

1. The number of animals you can vaccinate per day.



As the number of doses increases, preference for larger vaccination rings around IPs with related drop in average epidemic size.

2. Time delay to vaccination introduction.



… so if more farms are infected when vaccination is introduced, epidemic size will be much bigger and vaccination rings are smaller (more farms to vaccinate around).

Tildesley *et al*. (2006) *Nature*.

Recent/Ongoing Work

Regionalized movement bans in the UK

- In case of a new outbreak in the UK, DEFRA policy is to introduce a nationwide movement ban
- Large inconvenience for farmers
- Is it justifiable after the experiences with the 2007 outbreak?
- Investigating the effectiveness of a regionalized movement ban in the UK
  - <20 km
  - County level

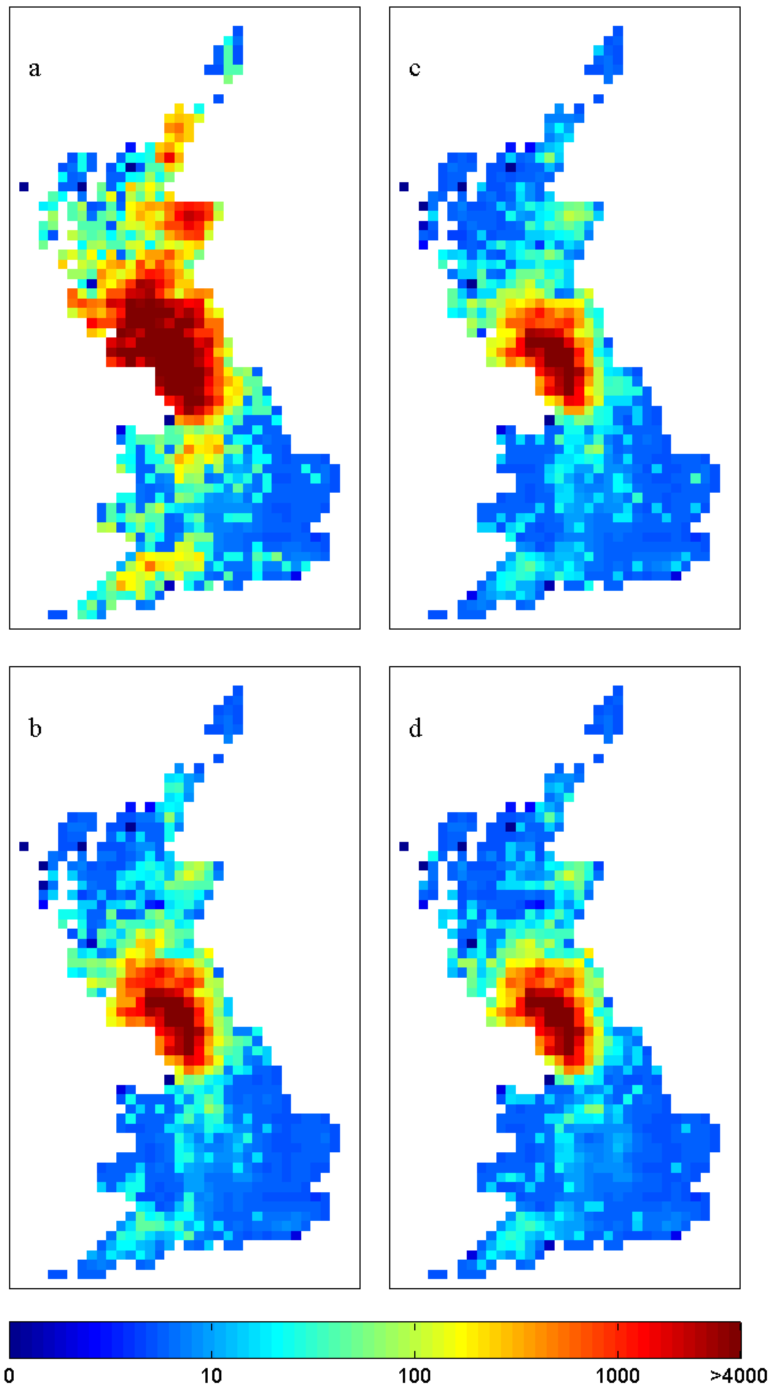
Infected farms

A = No restriction
max = 10261 farms
mean = 647 farms

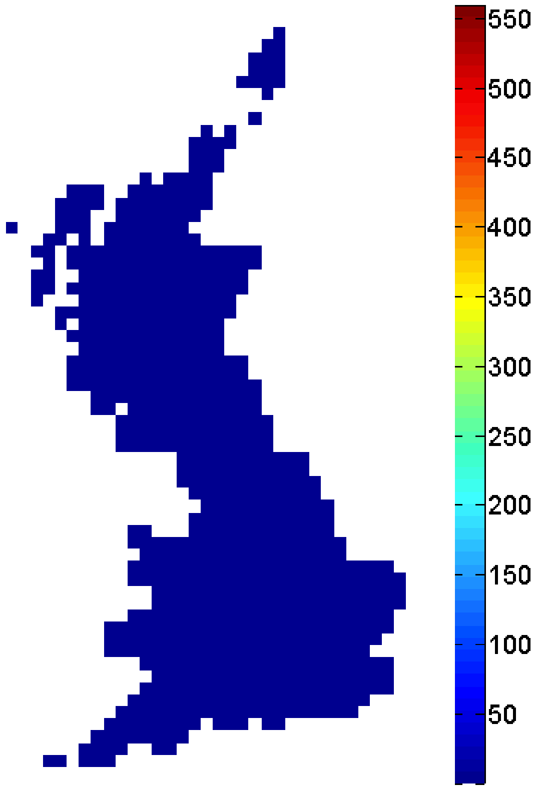
B = Closing down the infected grid
max = 5623 farms
mean = 191 farms

C = Closing down the infected county
max = 5657
mean = 173

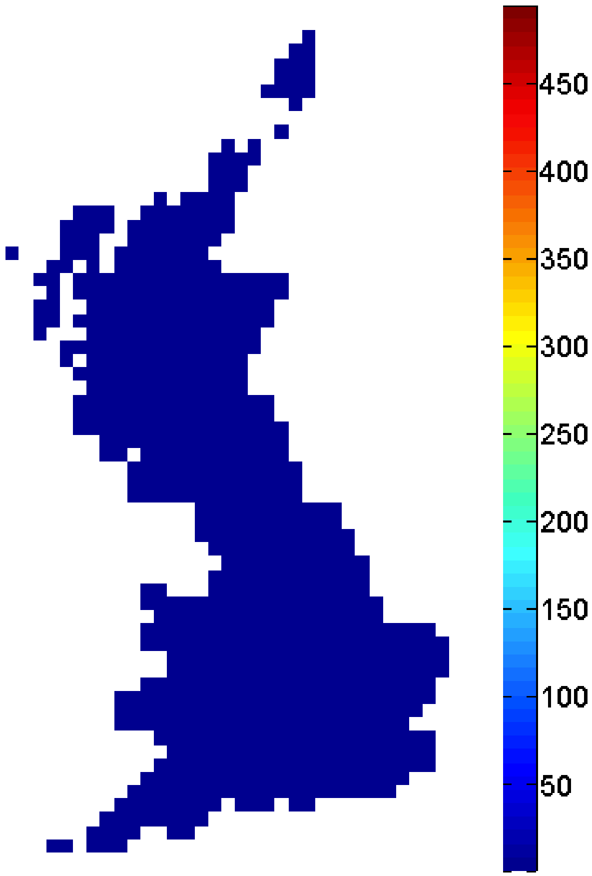
D = Nationwide movement ban
max = 5448 farms
mean= 169 farms



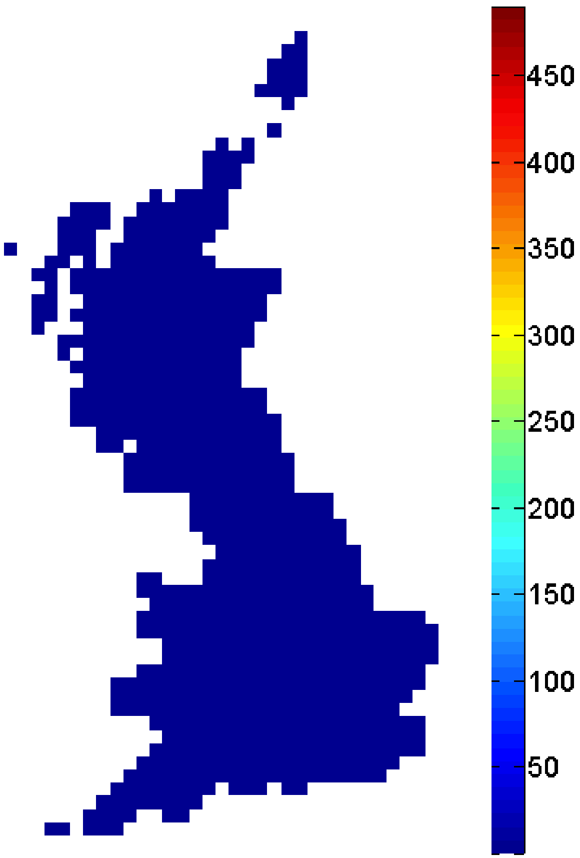
No restriction



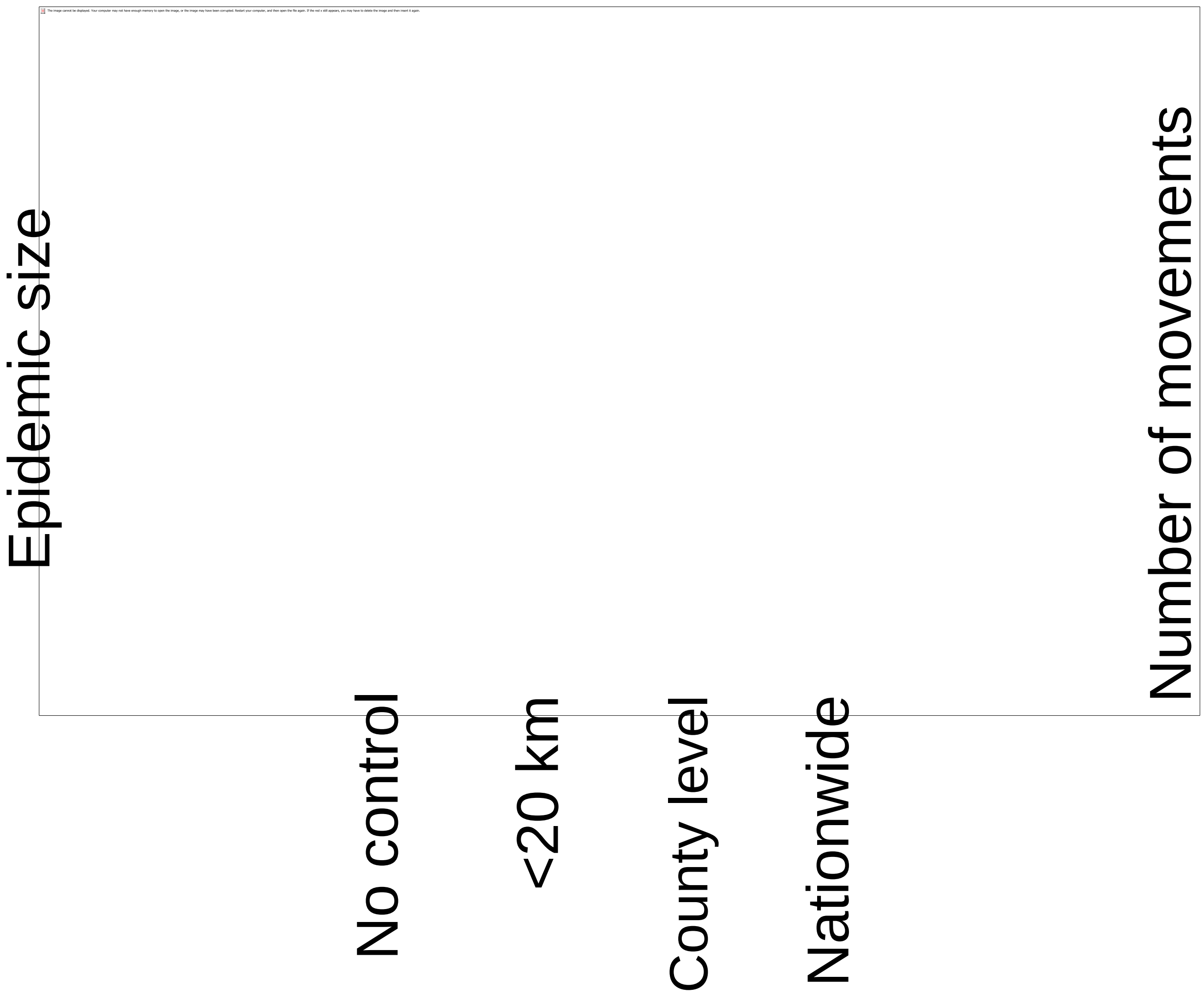
County ban



Nationwide ban

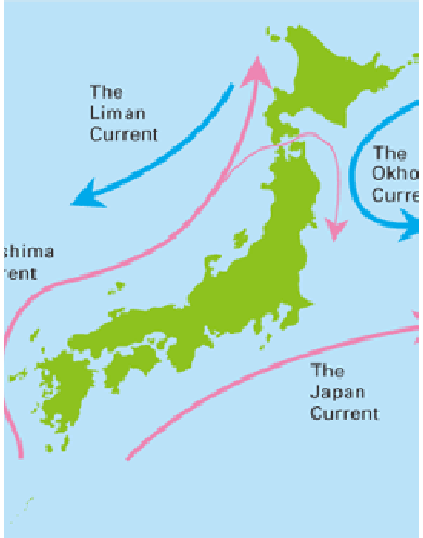


Epidemic size vs. movements



Outbreak Japan

- Ruri Ushijima (university of Miyazaki) and David Schley (Pirbright)
- 20 April to 5 July 2010
- Vaccination to kill
- Pigs and cattle got infected



What can we learn from the Japan outbreak

- Pig transmission kernel (Ben Hu, warwick/Pirbright, David Schley, Pirbright)
- Estimation of country specific susceptibility and transmission for cattle
- Effects of vaccination policy
- Investigating possible control strategies (Ruri)

Uncertainty

- In the UK we are very fortunate to have detailed location data, farm size data and live animal movement records.
- This is not the case in all countries
  - Data do not exist
  - Data are not available because of privacy concerns
- What are the effects and possible solutions of missing data?

Disease Prevention versus Data Privacy: Using Landcover Maps to Inform Spatial Epidemic Models

Michael J. Tildesley[1,2]*, Sadie J. Ryan[3]

1 Centre for Complexity Science, Zeeman Building, University of Warwick, Coventry, United Kingdom, **2** US National Institute of Health, Fogarty International Center, Bethesda, Maryland, United States of America, **3** Department of Environmental and Forest Biology, College of Environmental Science and Forestry, State University of New York (SUNY-ESF), Syracuse, New York, United States of America

Plos Computational Biology 2012 8(11)

Landcover data

In many countries, precise locations of farms are not available.

It may be possibly to capture farm demography using other data in the public domain.

We use land cover in the UK to determine whether we can accurately predict farm locations.

Farm Locations

We use Land Cover Map 2000 to obtain surrogate farm locations for UK livestock farms (to compare with the 2000 UK Agricultural Census).

Land Cover Map 2000 defines land use in one of 10 classes:

Class	Sub-class
1-2. Woodland.	
3. Arable and Horticulture.	
4-5. Grassland. →	14. Improved Grassland 15. Neutral Grass
6. Mountain/Heath/Bog.	
7. Urban.	
8-10. Water/Coastal.	

Land use data is available in parcels of 25 square metres.

Farm Locations

We investigate the effects of knowledge of farm locations upon epidemiological predictions using three data sets:

1. Random farm locations within a County.

2. LCM 2000 sub-classes to determine farm locations within a County.

3. True (recorded) data.

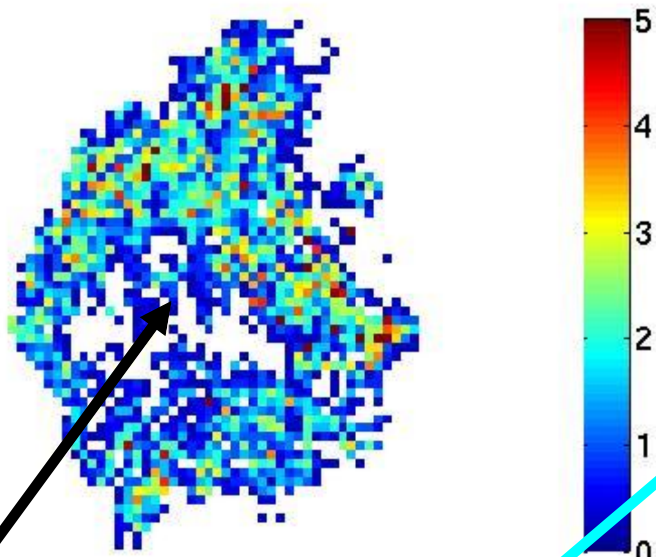
Farm Locations

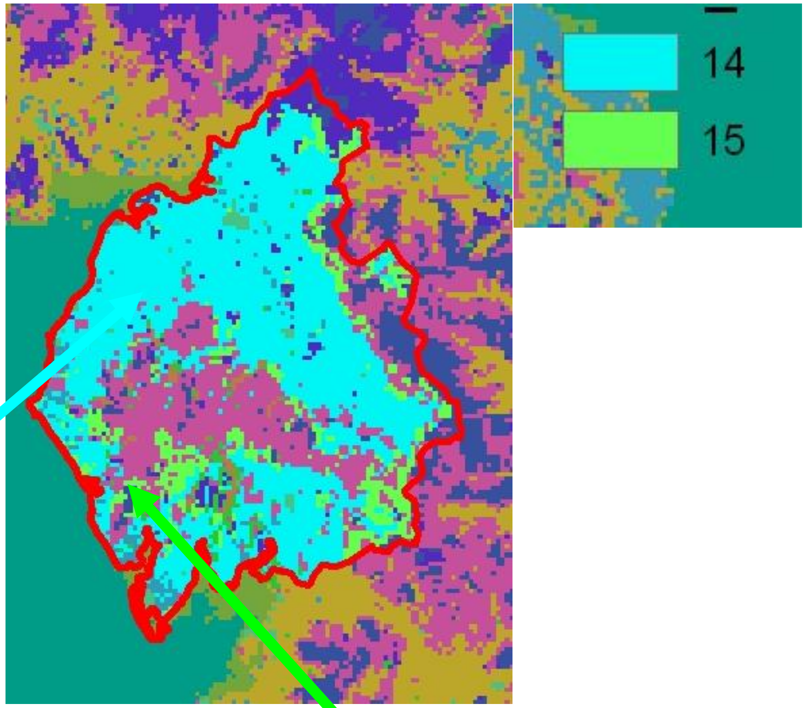
We simulate epidemics in Cumbria on these three data sets, using the same parameters for each data set.

	Epidemic Size (farms)	Duration (days)	Opt. Ring Cull radius (km)	Opt. Vacc. Radius (km)
Random	196	106	1.6	34.0
LCM Sub-classes 14-15	1480	228	3.6	48.8
True Data	1605	224	3.6	50.0

Farm Locations

So what are we capturing in the sub-class data that we are missing in less well-resolved data sets?





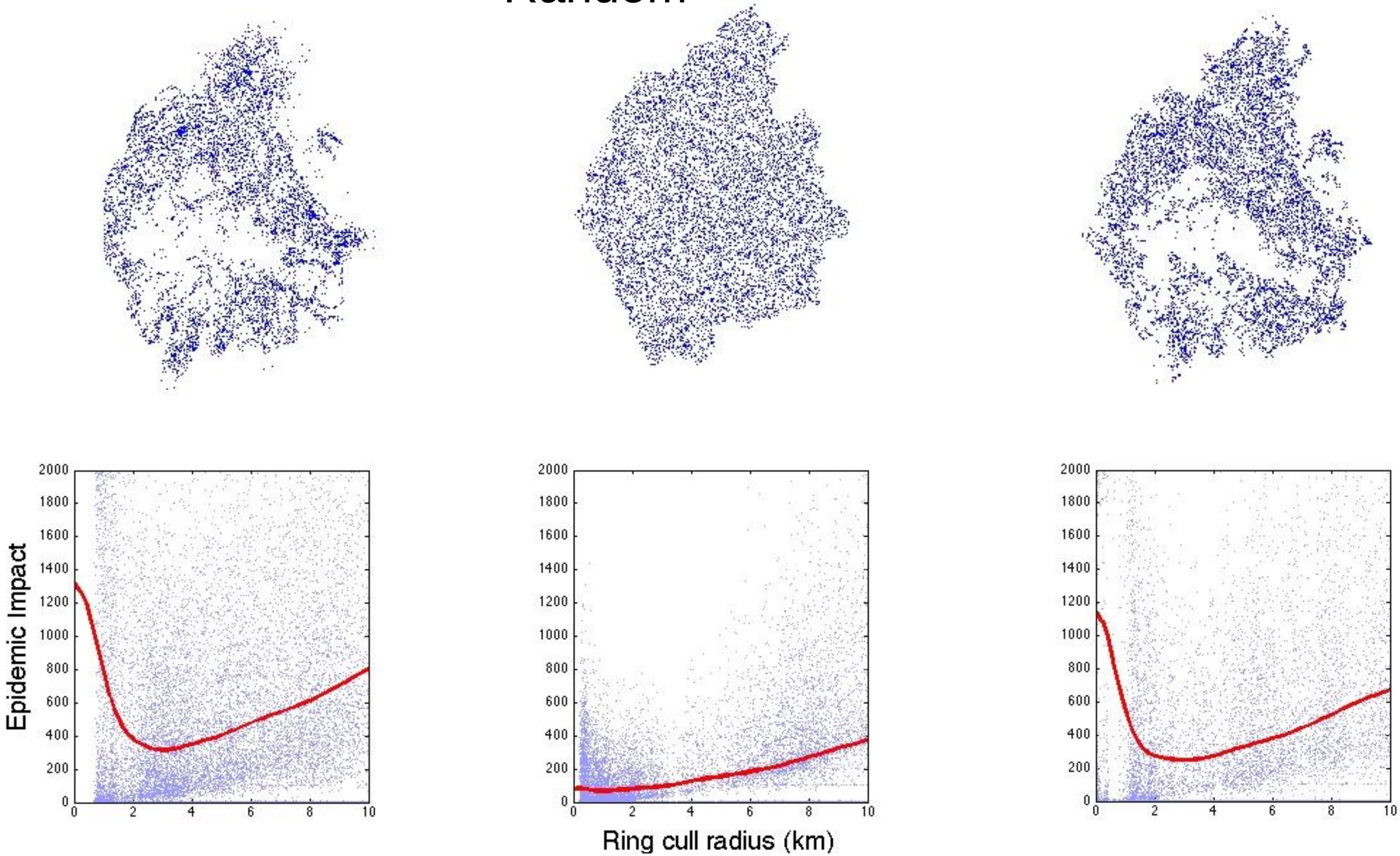
Lake District

14. Improved Grassland

15. Neutral grass

Farm Locations

Truth Data Random Land Cover



Highly resolved land use data could potentially act as a proxy for true farm locations.

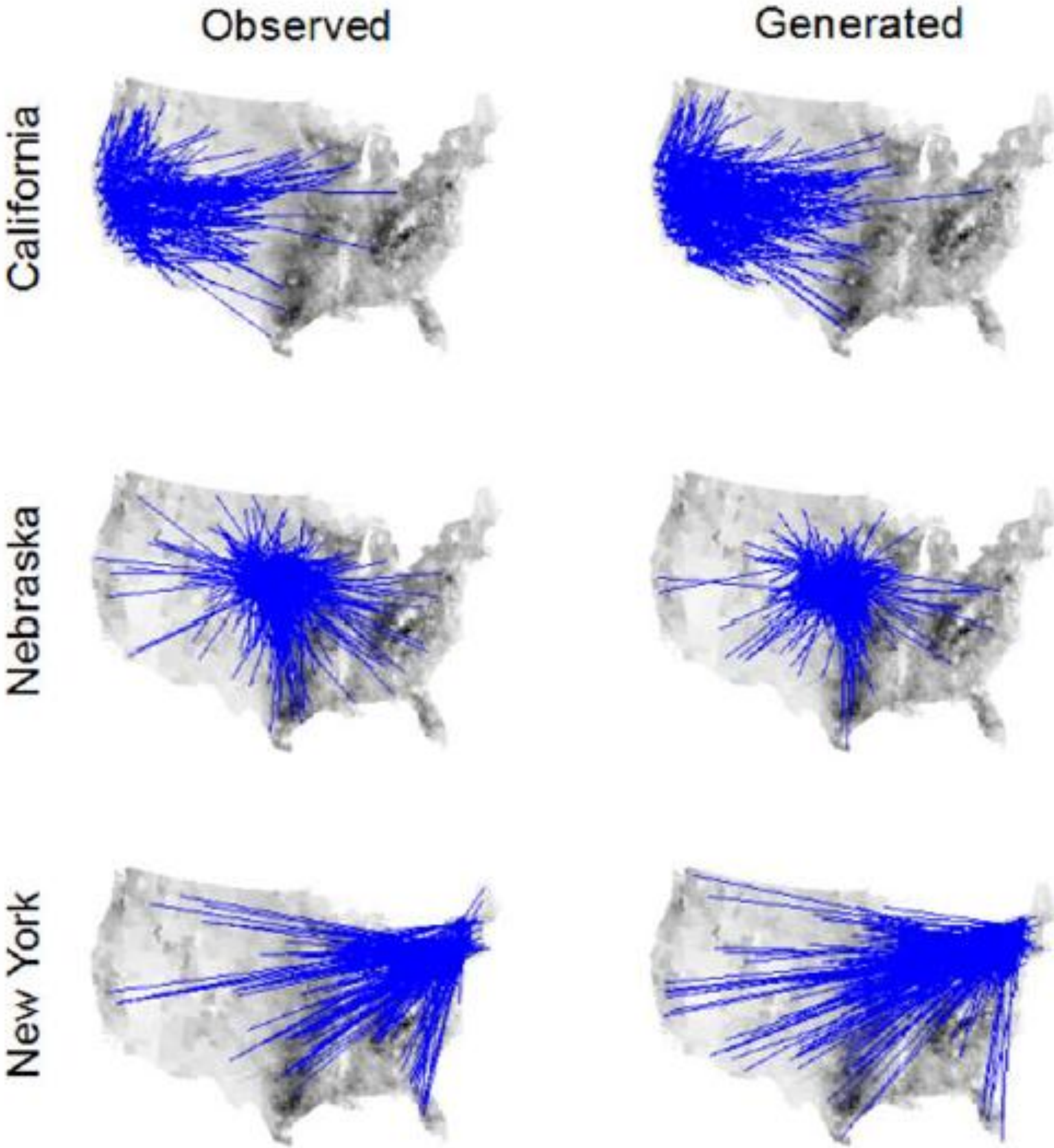
A Bayesian Approach for Modeling Cattle Movements in the United States: Scaling up a Partially Observed Network

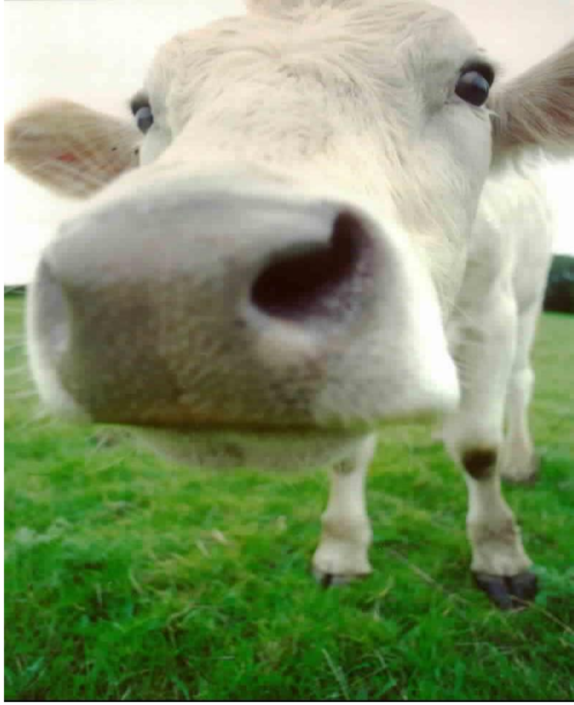
Tom Lindström[1,2], Daniel A. Grear[3], Michael Buhnerkempe[3], Colleen T. Webb[3], Ryan S. Miller[4], Katie Portacci[4], Uno Wennergren[1*]

Plos One 2013 8 (1)

Bayesian approach to generate cattle movement network

- 10% of all between state movements were sampled (Interstate Certificate of Veterinary Inspection)
- Predicting unobserved movements based on:
  - Distance
  - Number of premises per county
  - Historic imports of animals


Observed
Generated
California
Nebraska
New York



FMD-free countries Modelling the spread of FMD in the USA

For the UK we have information on:

- the location and size of all livestock farms
- the movement of all animals
- Farm specific epidemic data from 2001 and 2007

For USA we have limited information:

- the number of farms and animals in each county
- no information on livestock movements

There are NO epidemic data but vitally important:

Geographic Uncertainty

Network Uncertainty

Disease Parameter (Model) Uncertainty

USA Model

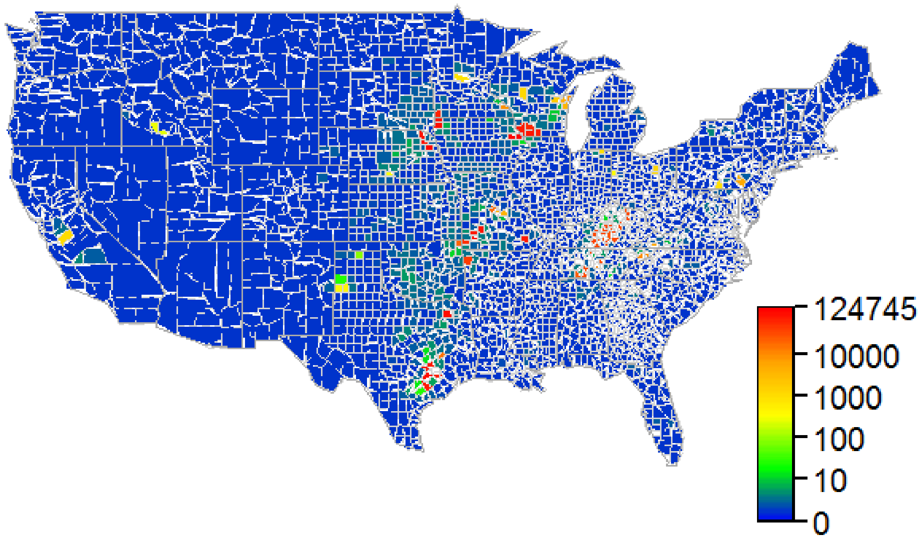
Previous approach inappropriate:

- Stochastic Metapopulation-Network model

  Precise farm locations are unknown
- 3109 counties (nodes)
- Disease spreads through local transmission (kernel) and movement networks.

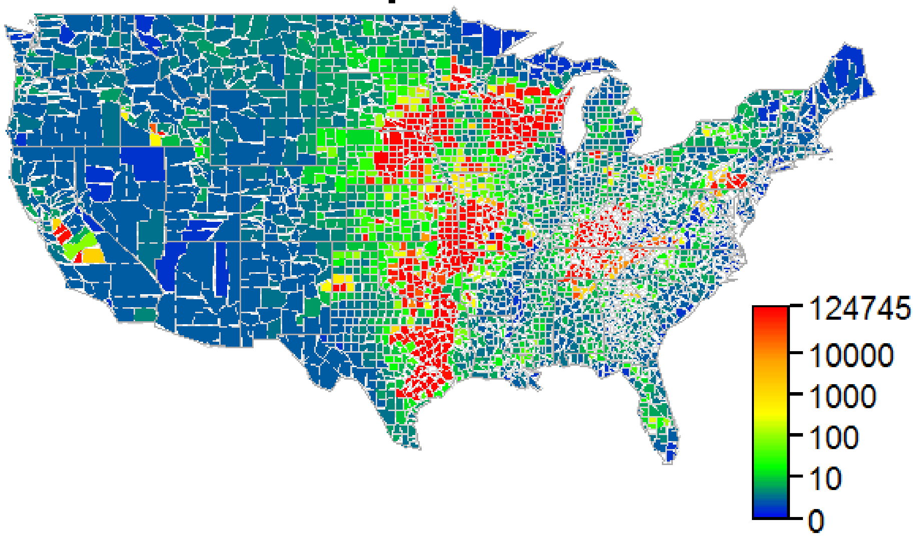
No movement control

Median Epidemic Size



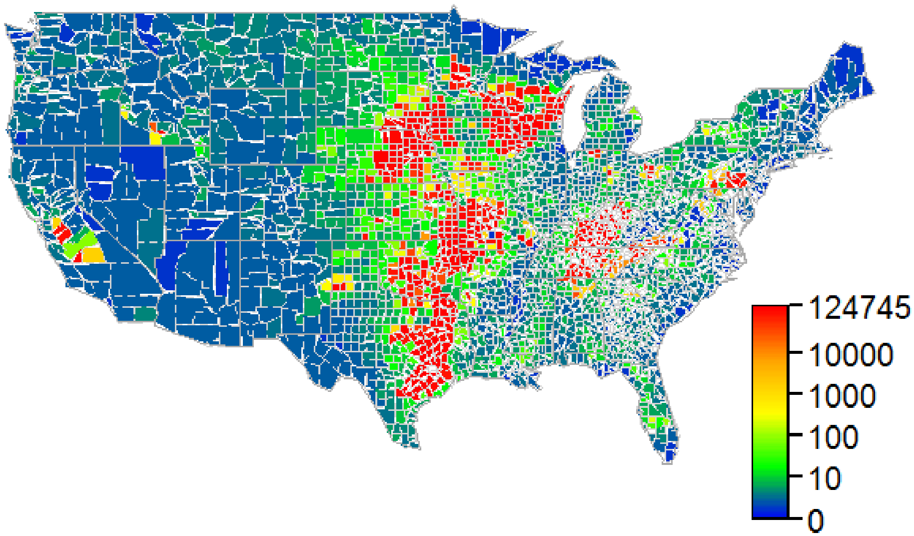
Color Scale shows number of farms infected over entire country given that the "colored" county is the source.

95% Level Epidemic Size

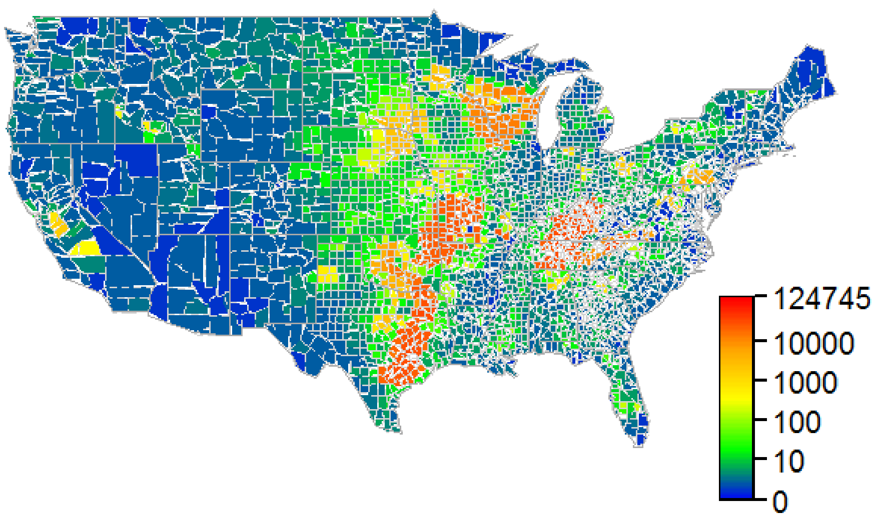


County Level Movement Ban

95% Level, No Ban



95% Level, County Ban



A ban on livestock movements in infected counties has a significant effect upon disease spread.

But we only have 10% of the data.

So what implications does this have upon epidemiological predictions?

Uncertainty

- Each epidemic is different
  - Between countries
  - Within countries
- Different virus strain
- Farming practices (countries/regions/outbreak situation)

How to deal with uncertainties in data?

Adaptive Management/Ensemble Modeling

Adaptive Management

- Critical decisions are necessary in the face of uncertainty

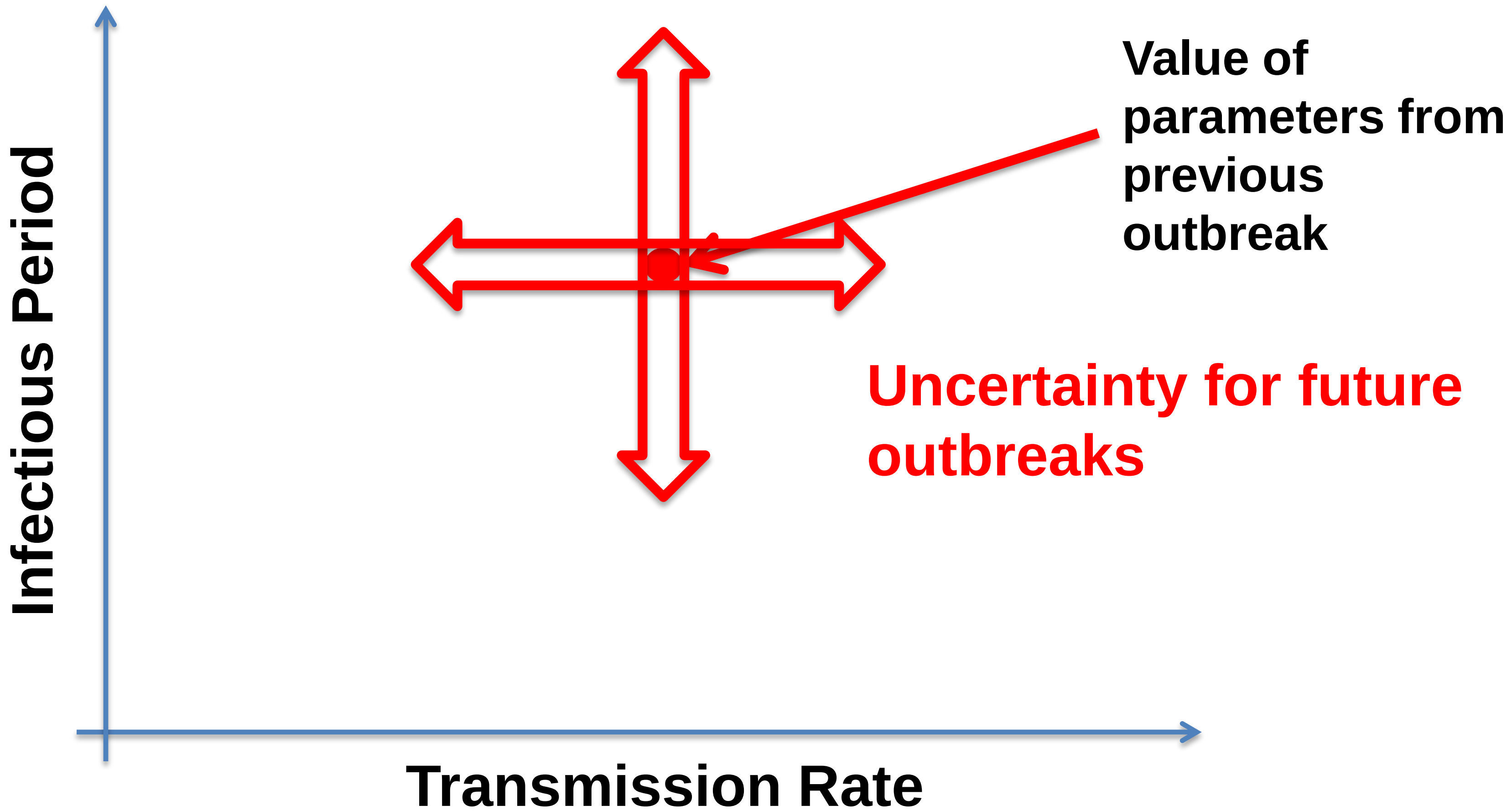
- Assessing the cost of making the right decision depends on
  - the projected outcome of the intervention conditional on each model, AND
  - likelihood of each model being correct

Questions

- How limiting is model uncertainty to the development of policy?
  - Though there may be things we want to learn to advance biological understanding, if they all support the same management alternative, it doesn't represent a limitation to policy.
- What would be the value of resolving that uncertainty in terms of improved management outcomes?
  - How much we might be willing to invest in learning?

Uncertainty in Model Parameters

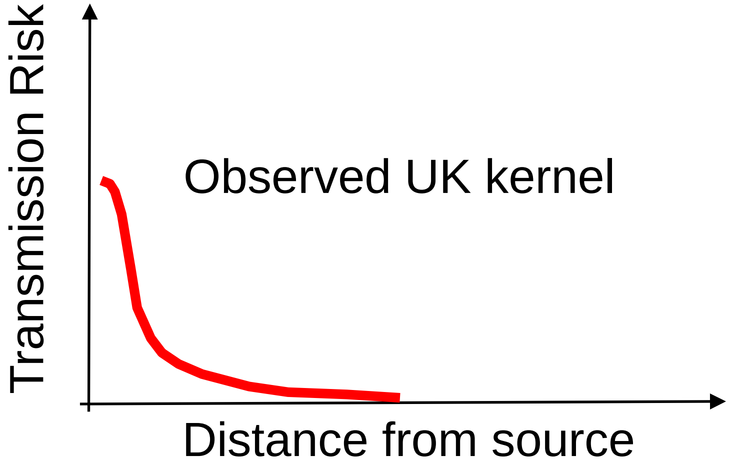
Let's consider uncertainty in two parameters:



We need to decide on a control policy at the start of new outbreaks, before we can resolve this uncertainty.

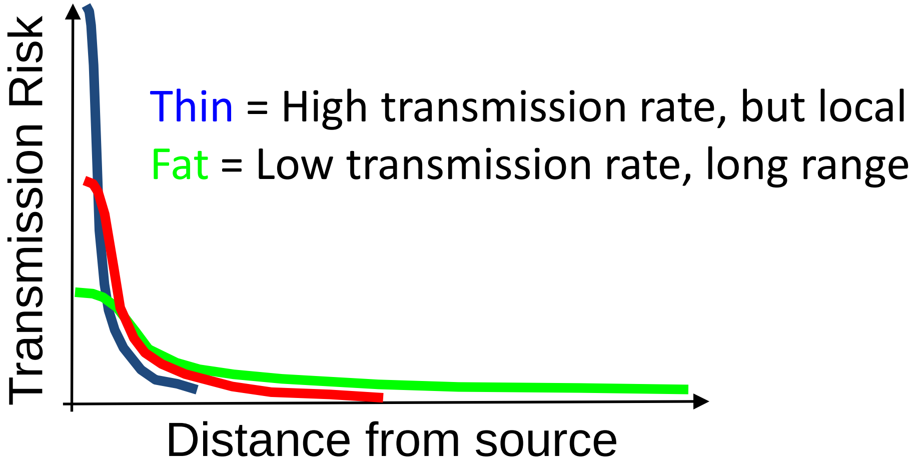
A Simple Example

Alternative Models



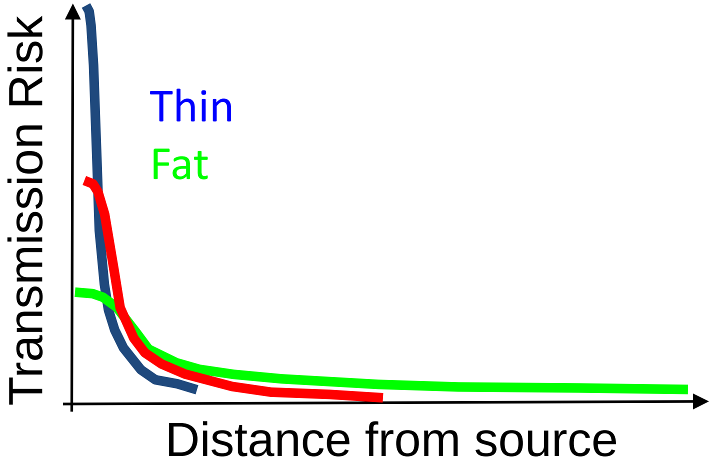
A Simple Example

Alternative Models



A Simple Example

Alternative Models



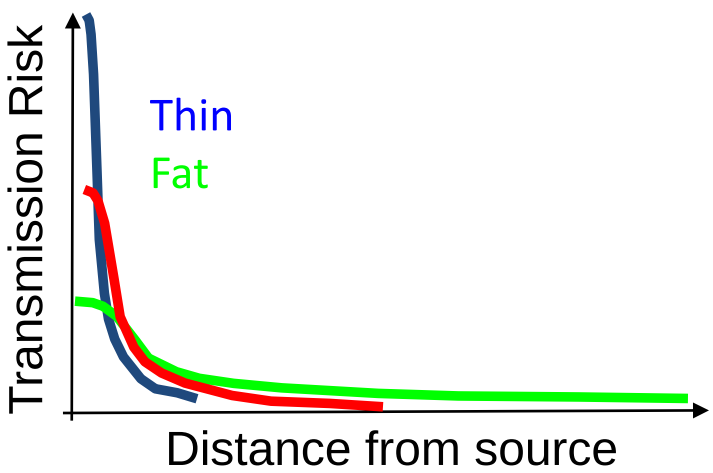
Candidate Interventions

1. Cull Infected Farms (IP)
2. Cull IPs+their contacts(DC)
3. Cull IPs + DCs + neighbouring farms (CP)

severity

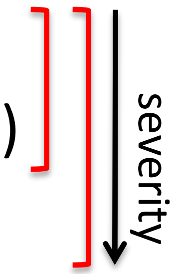
A Simple Example

Alternative Models



Candidate Interventions

1. Cull Infected Farms (IP)
2. Cull IPs+their contacts(DC)
3. Cull IPs + DCs + neighbouring farms (CP)



Objective

Minimize total cost epidemic
Total cost = 1000 * cattle culled + 100 * sheep culled
-- based on compensation costs from 2001 outbreak

Cost Matrix

Calculate cost of each strategy for each possibly model

Assign each model a weight

– belief in likelihood of model being correct.

Determine best policy to introduce at the start of an outbreak, given the underlying uncertainty.

Cost Matrix

		Interventions			
Kernel	weight	IP	DC	CP	Best
thin	.25	8.4	5.5	8.2	5.5
fat	.25	28.4	22.1	37.8	22.1
UK	.5	512.9	190.1	116.2	116.2
		265.7	103.0	69.6	65.0

- Cost in units of ~ £5 million

Cost Matrix

Kernel	weight	IP	DC	CP	Best
		Interventions			
thin	.25	8.4	5.5	8.2	5.5
fat	.25	28.4	22.1	37.8	22.1
UK	.5	512.9	190.1	116.2	116.2
Average		265.7	103.0	69.6	65.0

- Cost in units of ~ £5 million
- Best conditional intervention is to cull contiguous premises

Cost Matrix

		Interventions			
Kernel	weight	IP	DC	CP	Best
thin	.25	8.4	5.5	8.2	5.5
fat	.25	28.4	22.1	37.8	22.1
UK	.5	512.9	190.1	116.2	116.2
		265.7	103.0	69.6	65.0

- If uncertainty were resolved *a priori* we could choose best conditional intervention
- Expectation, relative to *a priori* weights is 65.0
- The Expected Value of Perfect Information (EVPI) is 69.6-65.0 = 4.6, or 6.6% of naïve strategy.

Model Weights

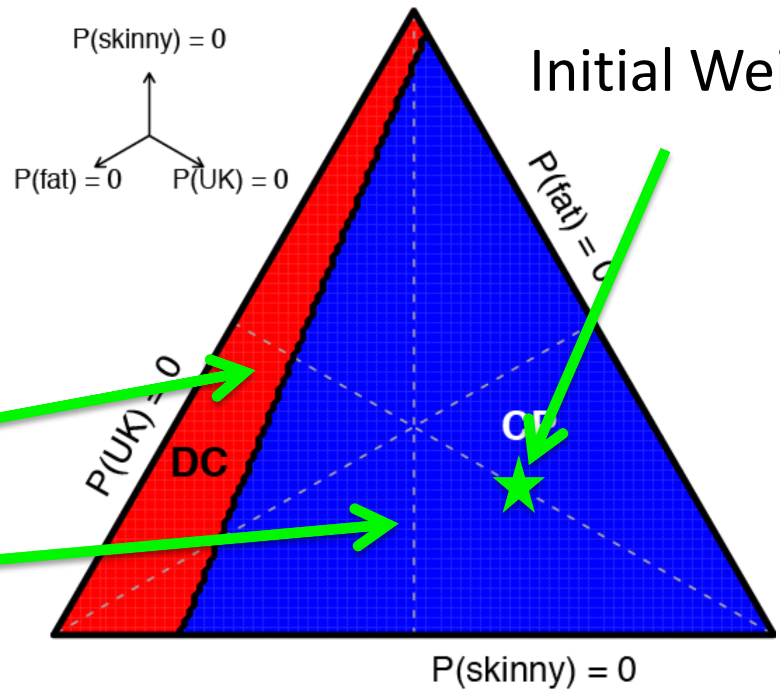
The optimal strategy is dependent upon the model weights.

What happens as we vary the weights on the three models?

Initial Weights

DC culling optimal

CP culling optimal



Model Weights

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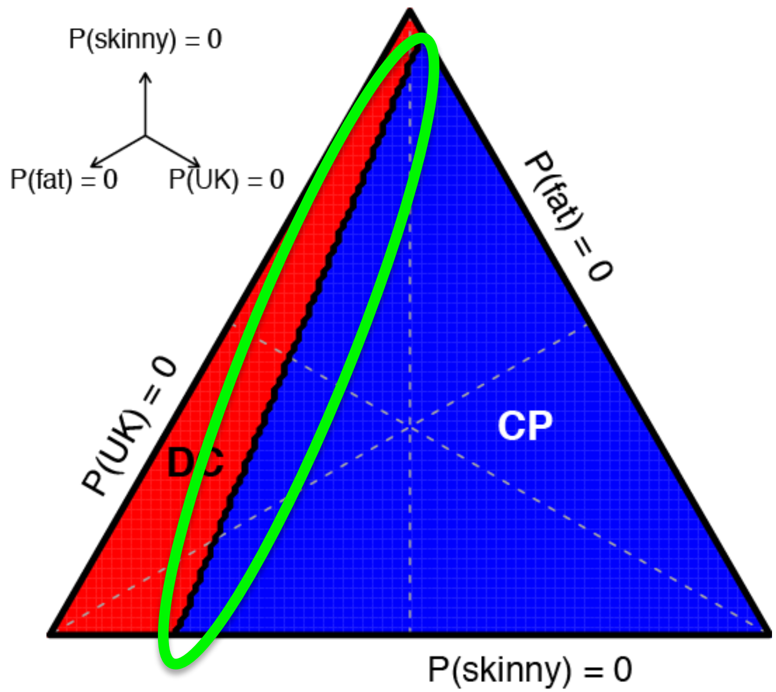
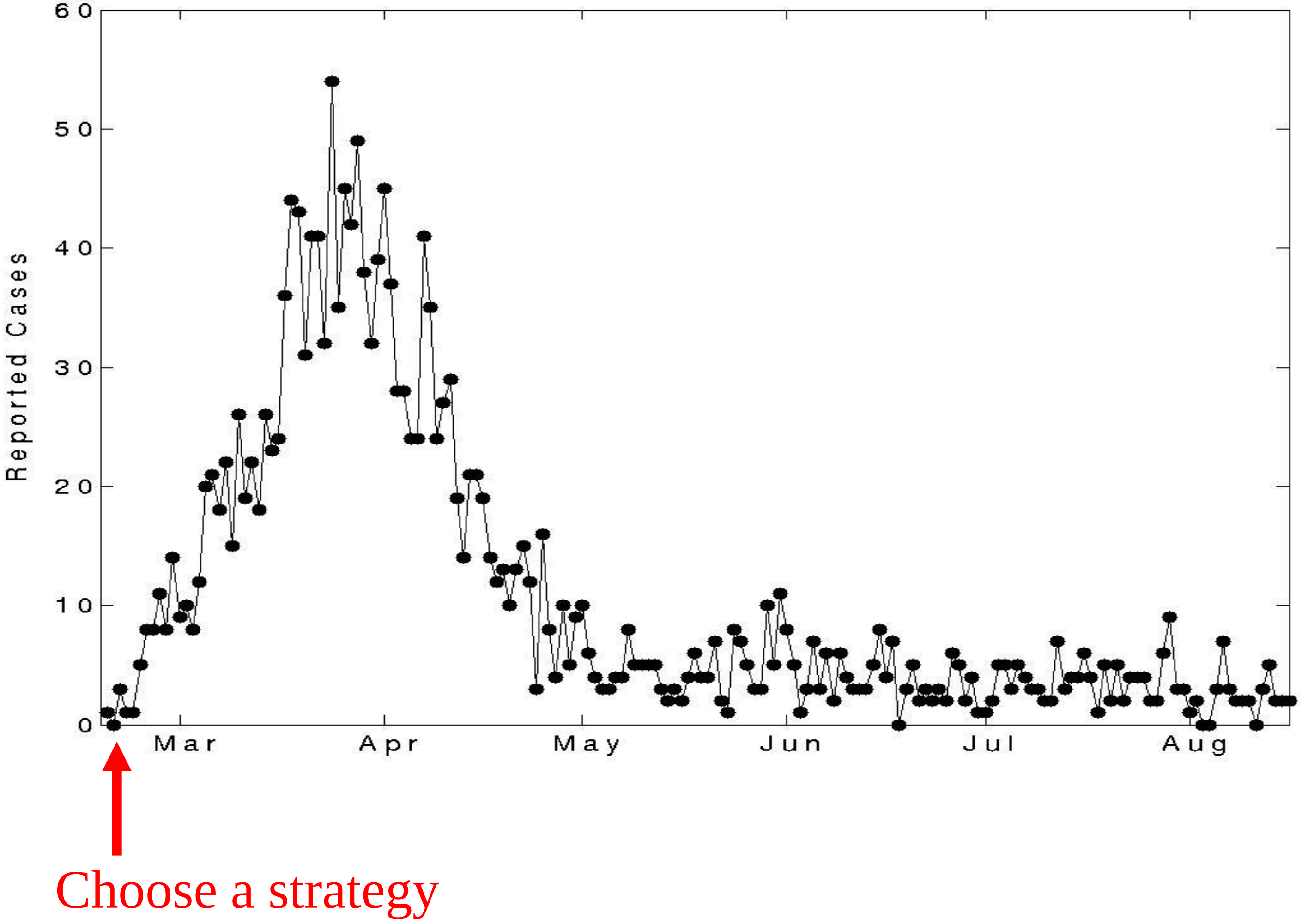
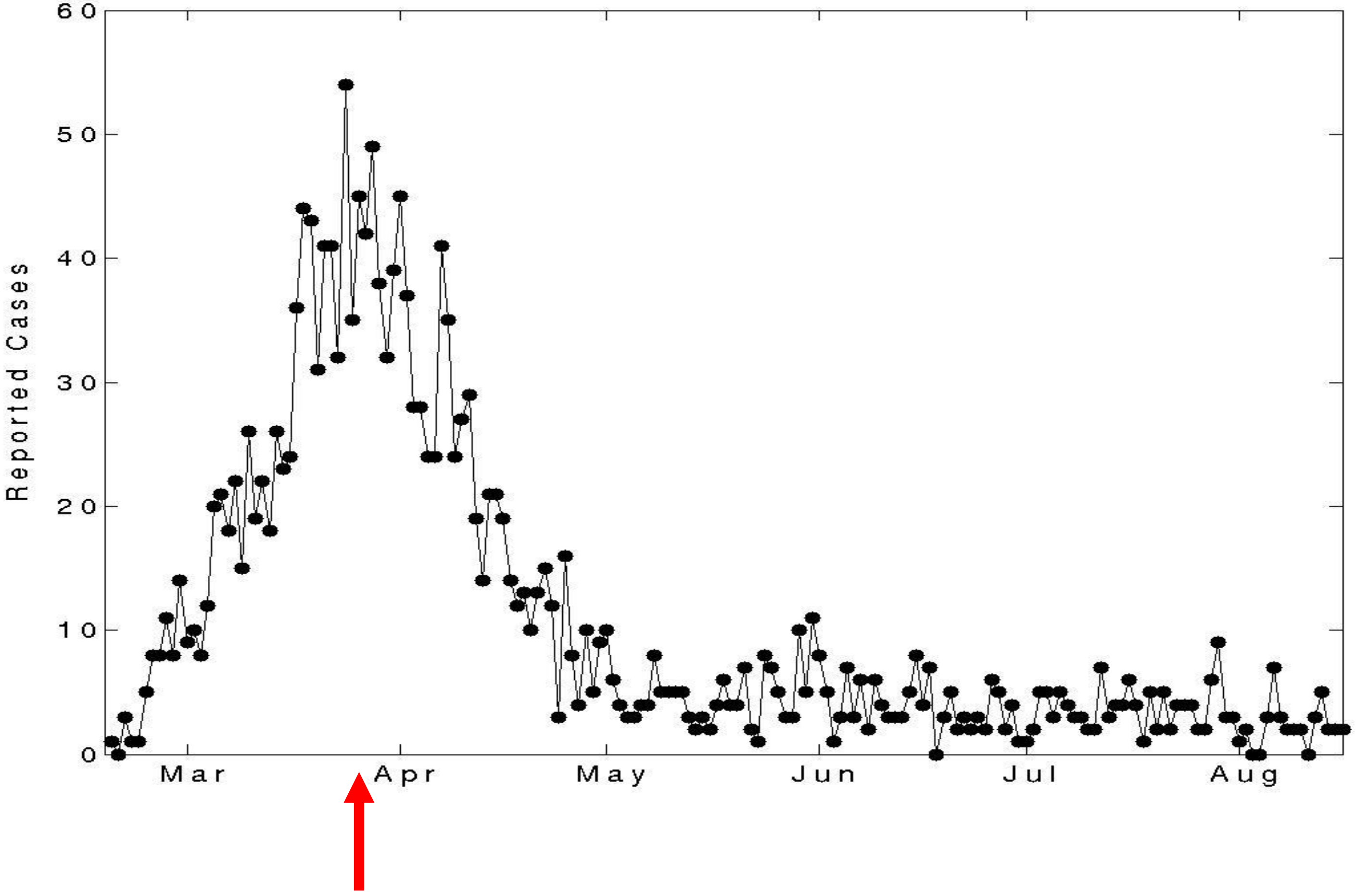


If true parameters are in this region, it is vital to resolve model uncertainty as soon as possible.

Adaptive Management

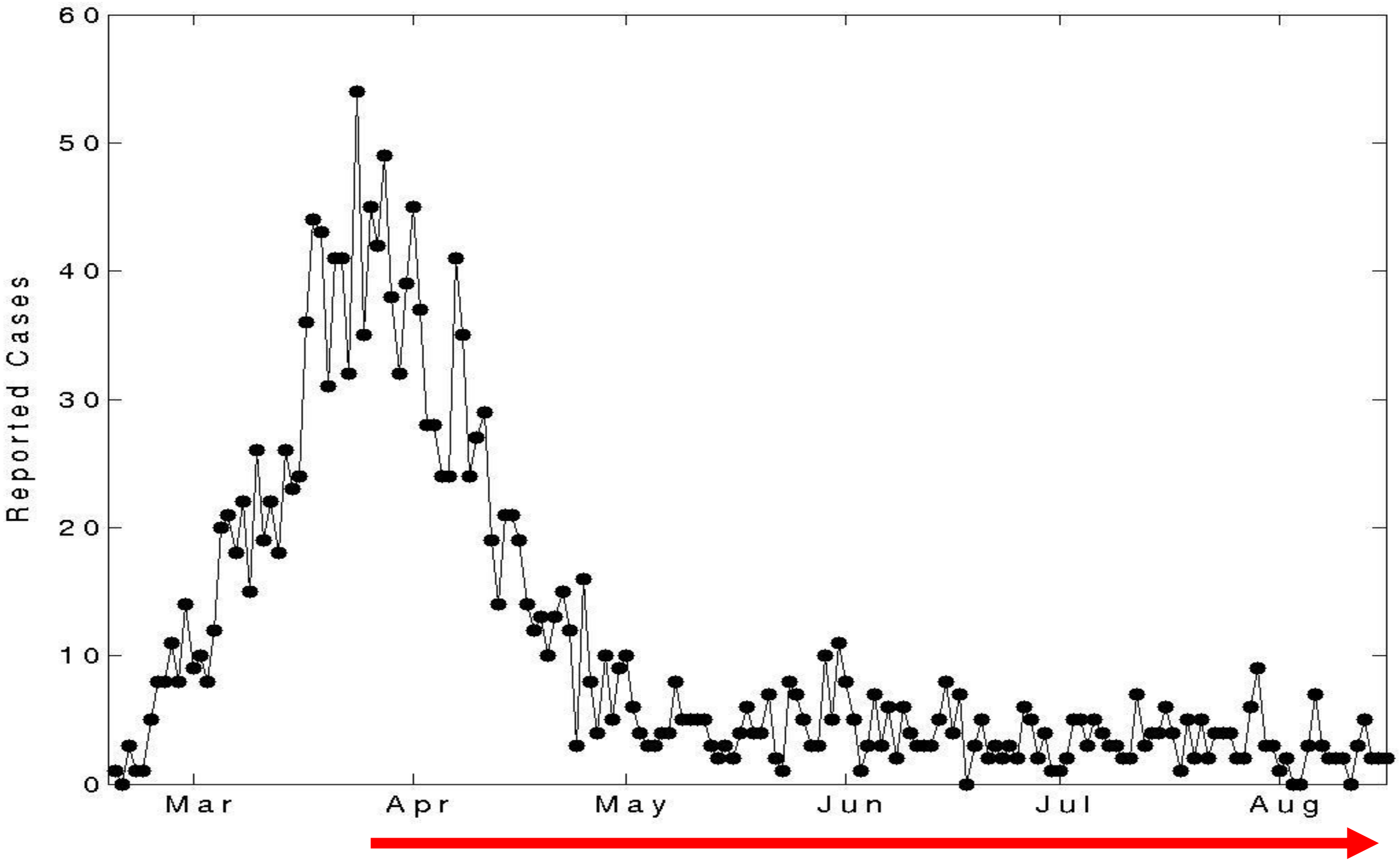


Adaptive Management



Observe and resolve model uncertainty

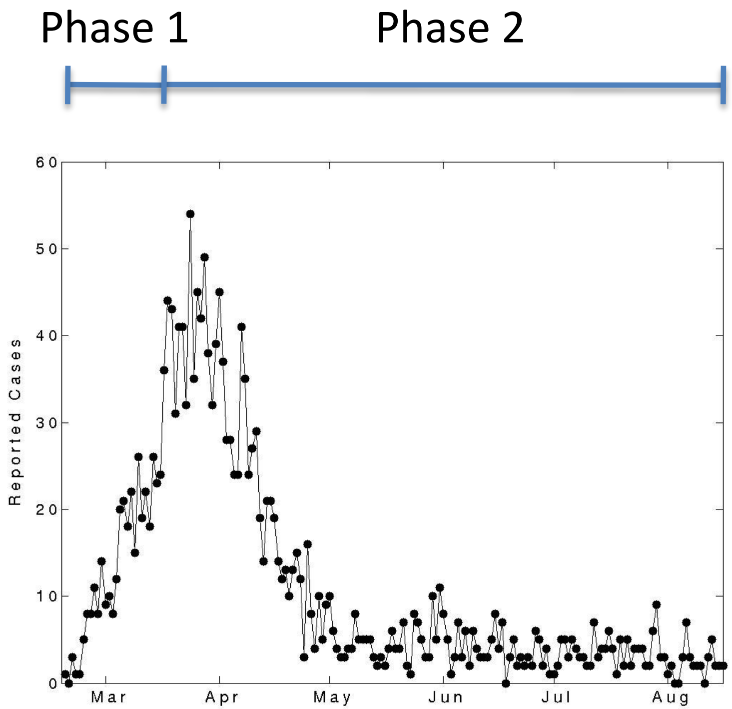
Adaptive Management



If required, modify strategy and use until eradication

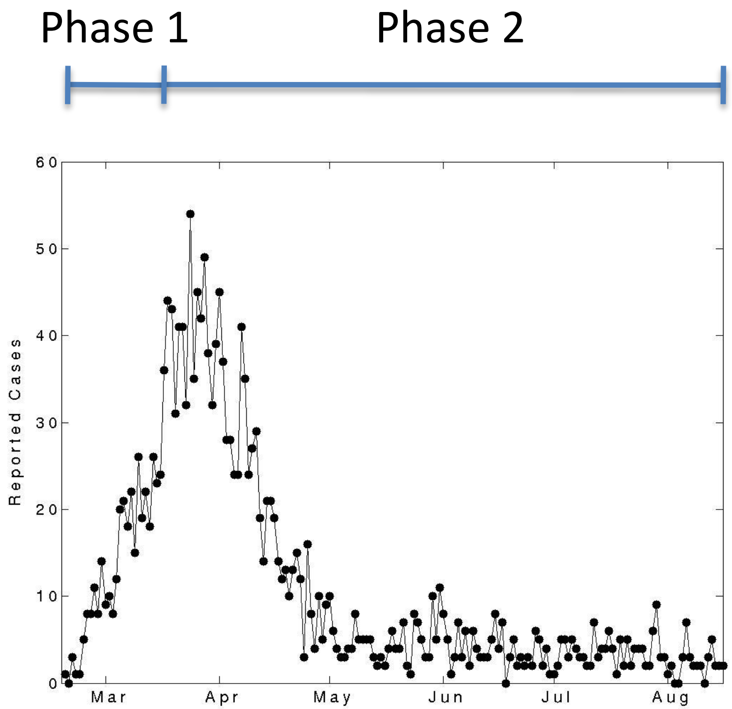
Expected Value of Adaptive Strategy

- Consider 9 possible 2-phase combinations (IP/IP, IP/DC, IP/CP, DC/IP etc).



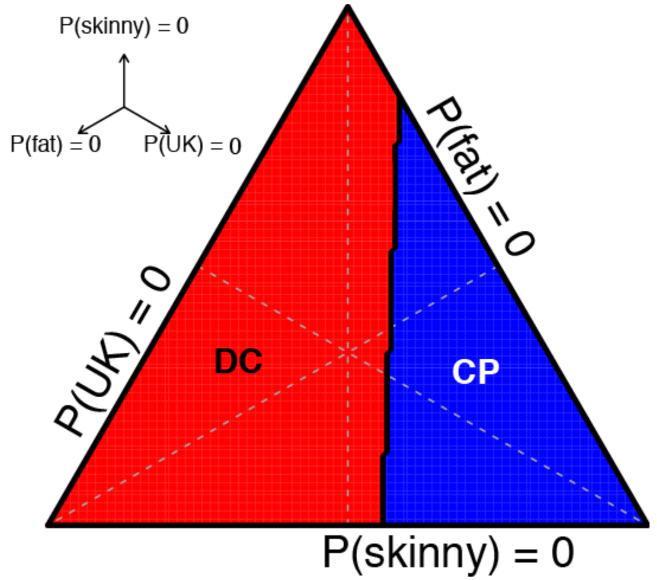
Expected Value of Adaptive Strategy

- Consider 9 possible 2-phase combinations (IP/IP, IP/DC, IP/CP, DC/IP etc).
- What is the best 1st phase intervention, when there is an opportunity to update?



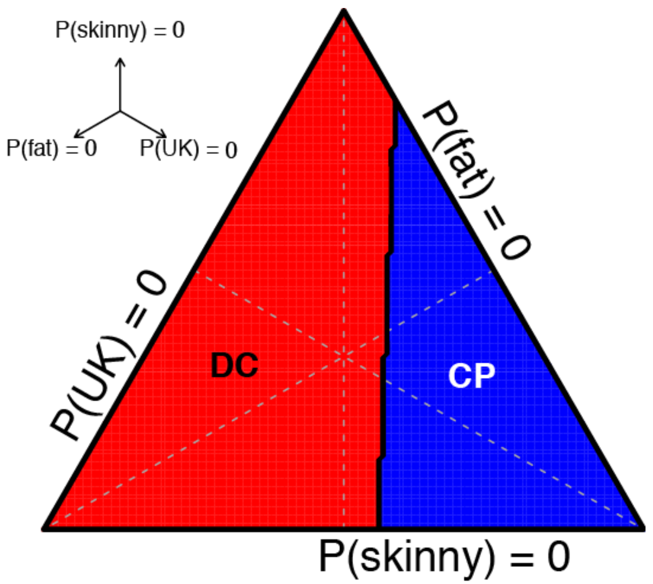
Expected Value of Adaptive Strategy

- DC culling is optimal 1st stage strategy for a broader range of initial weights



Expected Value of Adaptive Strategy

- DC culling is optimal 1st stage strategy for a broader range of initial weights
- Dependent on initial weights AND timing of decision point
  - Later means less time to recover costs



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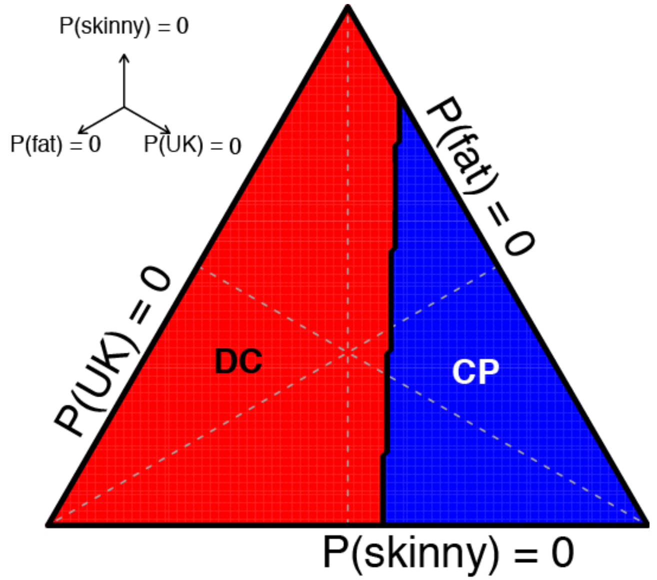

- May consider multiple decision points, but may be pressure on policy makers not to “change their minds” too often!!!

Weather predictions

- Multiple models are informing weather forecast
- Competing models into complementary models
- Give one prediction
- Can we do something similar for disease models?

An Ensemble Approach

- This method can be used determine an optimal control policy for multiple competing models as well as for multiple parameter sets within a single model.

- It may be advantageous to use multiple models to predict spread and impact of control – too much reliance upon a single model could be dangerous
  - preserve model differentiation

- An adaptive management approach provides a method for determining ***a single control policy*** in the case where models predict different optimal control policies.

Epidemic vs. endemic

- Very different situations
- However, knowledge and experiences from epidemic can be used in countries where the disease is endemic and vice versa.
- Endemic situation not studied in great detail yet in mathematical models
- Normally just one strain in case of an epidemic, whereas endemic countries have often multiple strains
- Vaccines: how effective are they
- Detailed data of countries where locations and farm sizes are available could be used to test the importance of details and the effects of not having perfect data on disease epidemics.

Solutions for missing, incomplete data or uncertainty

- Sensitivity analysis
- Incomplete movement data: Bayesian
- Farm locations missing: Metapopulation model or landcover data
- Disease outbreak data: Historic data (other countries), adaptive management and ensemble approach