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Detection of Dairy Herds at risk for changing *Salmonella* Dublin status

Symposium in Applied Statistics 2012

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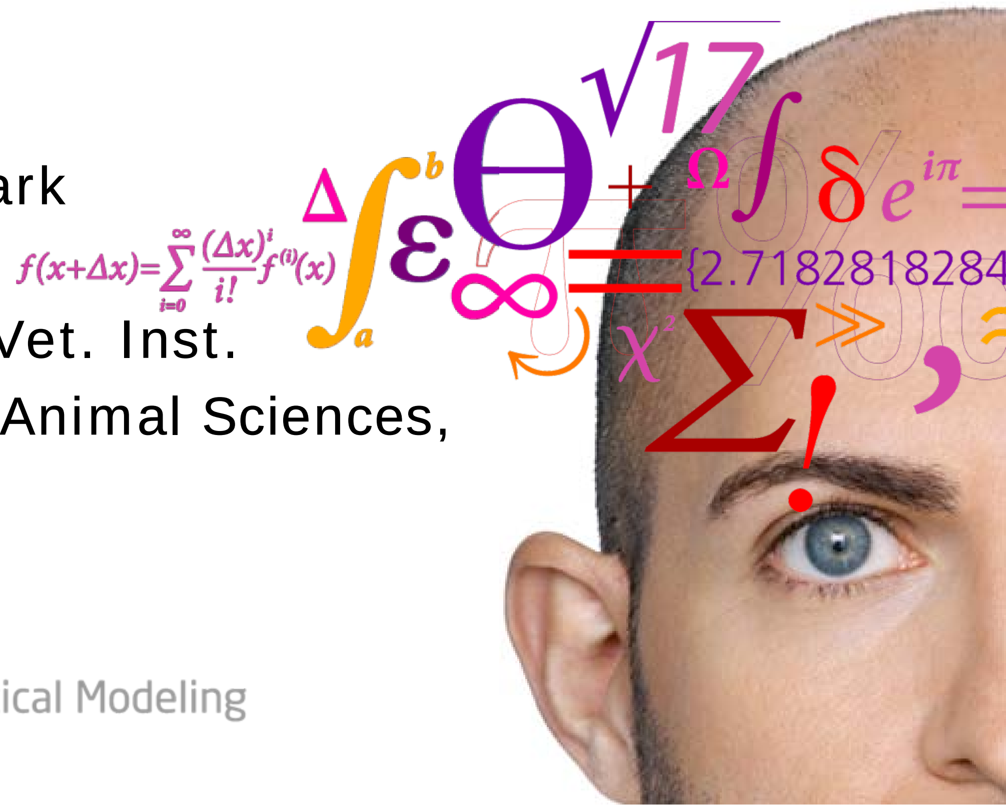

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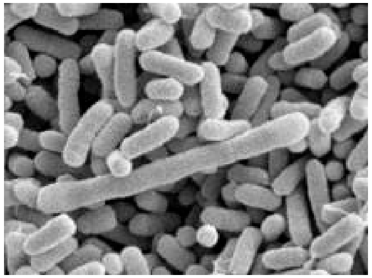
Background



- *Salmonella* Dublin (S. Dublin) is a specific serotype of the *Salmonella* bacterium

- *S.* Dublin is host-adapted to cattle, and the most prevalent serotype found in cattle in Denmark (~60-70% of all isolates)

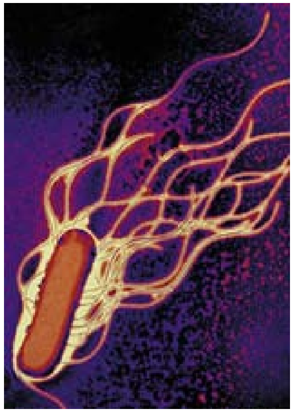
- *S.* Dublin is a rare but serious zoonosis that causes severe disease and deaths in humans every year (10-40 hospitalized cases per year in Denmark).

S. Dublin Symptoms

• Unthrifty calves • Fever • Diarrhoea (bloody)

• Pneumonia • Death • Abortions

The Salmonella Dublin surveillance and eradication programme in Denmark



- Eradication campaign until 2014

- Goal: *The Danish cattle population free from Salmonella Dublin in 2014*

- 2010-2012: Sanctions to improve motivation

- 2013-2014: Veterinary Authorities will handle infected herds through law enforcement

The Salmonella Dublin surveillance and eradication programme in Denmark

- Surveillance program since 2002:

- Cattle herds are classified as follows, based on Bulk Tank Milk/blood sample antibodies and trade contacts:

Level 1: Most likely **free** from salmonella

Level 2: **Too high antibody** levels or contact to other herds in Level 2 or 3

Level 3: **Clinical** *Salmonella* Dublin diagnosis and culture positive

Unknown: Only non-dairy herds with too **few samples** to classify (hobby herds)

The Salmonella Dublin surveillance and eradication programme in Denmark

- Surveillance program since 2002:

- Cattle herds are classified as follows, based on Bulk Tank Milk/Blood sample antibodies and trade contacts:

Level 1: Most likely **free** from salmonella

Level 2: **Too high antibody** levels or contact to other herds in Level 2

For the present work we do not distinguish between level 2 and 3

Reasons for assigning Level 1 to dairy herds

Salmonella Dublin Level 1 is given if:

1. Valid bulk tank milk antibody **measurements exists** – and
2. The last 4 bulk tank milk antibody measurements, gathered with at least 3 weeks in between, shows an **average ODC-value of less than 25** – and
3. The latest Salmonella Dublin measurement has **not shown an increase of more than 20**, compared to the average of the three preceding measurements - and
4. A number of circumstances mainly related to trade and missing data do not hold.

Otherwise, Salmonella Dublin Level 2 is given.

Bulk Tank Milk antibody measurements from dairy herds



- Collected routinely every three months.
- Thus, a very long period for an infection to develop before a dairy herd is possibly re-classified.
- Sanctions and law enforcement gives farmers an incentive to act if they suspect an infection is present.
- There is therefore a need to identify herds at risk of changing S. Dublin level, based on information a quarter earlier than re-classification takes place.

Risk Herds

- Are herds ’at risk of’ changing level from 1 to 2; we will start out with this loose definition.

- Risk herds are thus Level 1 (”Status 1”) herds.

Purpose of current study:

- To determine appropriate definitions for a risk herd, based on available factors one quarter prior to a possible level shift.

The probability of changing *S.* Dublin status

If $X_{i,t}$ denotes the BTM measurement for herd i at time t,

and $M_{i,t}$ the mean of the last 3 measurements, $M_{i,t} = \frac{1}{3}\sum_{j=1}^{3} X_{i,t-j}$

then the probability $p_{i,t}$ of a status change is given as

$$p_{i,t} = P(\frac{1}{4} X_{i,t} + \frac{3}{4}(\frac{1}{3}\sum_{i=1}^{3} X_{i,t-i}) > 25 \vee X_{i,t} - (\frac{1}{3}\sum_{j=1}^{3} X_{i,t-j}) > 20 \mid X_{i,t-1}, X_{i,t-2}, X_{i,t-3})$$

ie.

$$p_{i,t} = P(\frac{1}{4} X_{i,t} + \frac{3}{4} M_{i,t} > 25 \vee X_{i,t} - M_{i,t} > 20 \mid M_{i,t})$$

$p_{i,t}$ is modeled through a logistic regression:

$$\log it(p_{i,t}) = \sum \beta_k Z_{i,k,t}$$

through successive conditioning on the BTM measurements.

What makes herds become Risk Herds? - bulk tank milk measurements, trade, neighbors and herd size

- Bulk tank milk measurements:
  - High antibody levels;
  - Unstable development in measurements.
- Trade:
  - That animals are bought from herds that turn out to be Status 2 herds;
  - that many animals are bought;
  - that many herds are traded with.
- Neighbors:
  - That many neighbors are assigned Status 2;
  - That there are many neighbors.
- Size:
  - That the herd is large.

Available Data

- Quarterly bulk tank milk measurements 2002-2008 for 9397 dairy herds;

- Geographical coordinates for dairy and non-dairy cattle herds and their quarterly *S.* Dublin level;

- All perfomed trades at animal level 2002-2008;

- Data on herd sizes; Only 2004-2008 er usable.

BTM measurements and Alarm Herds

- BTM measurement enter covariates through $M_{i,t}$; obviously a high level of recent antibody levels will increase the risk of a Status 2 change.
- But also sudden (upwards) deviations from a stationary development could indicate an emerging infection. BTM measurements also enters through *Alarm Herd* status:

- Alarm Herd concept: A Status 1 herd A is an *Alarm Herd* at a timepoint t_0, if BTM measurements for A for at least the previous 4 time points do not vary more than a standard 95% confidence interval would predict, and the BTM measurement for A at time t_0 is above this level, and above an upward threshold $c > 0$.

Alarm Herds

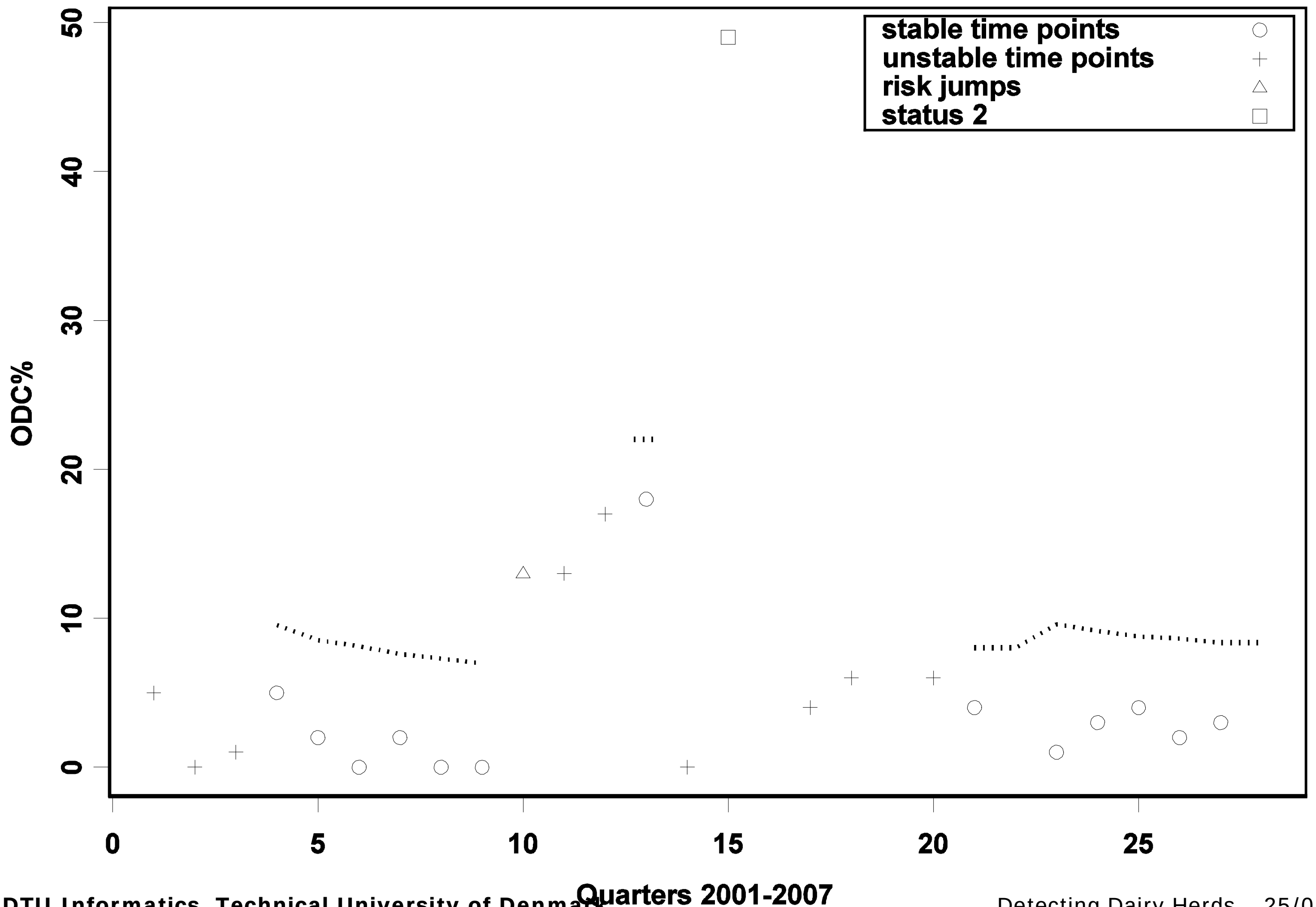
- Alarm Herds are Level 1 herds: The jump from the steady progression should be big (to a level > *c*),but not so big that it triggers a Status 2 classification.

- Time points where BTM measurements for A for at least the previous 4 time points do not vary more than a standard 95% confidence interval would predict are called *stable* timepoints.

- When a herd leaves a stable state to become unstable, we say that a *jump* has occurred.

- When a herd becomes an Alarm Herd, we say that a *risk jump* has occurred.

A BTM measurement progression example



Estimation of *c*

- We included Alarm Herd status in the basic logistic regression model with varying values of c (integer ODC values), to gain a series of competing models;

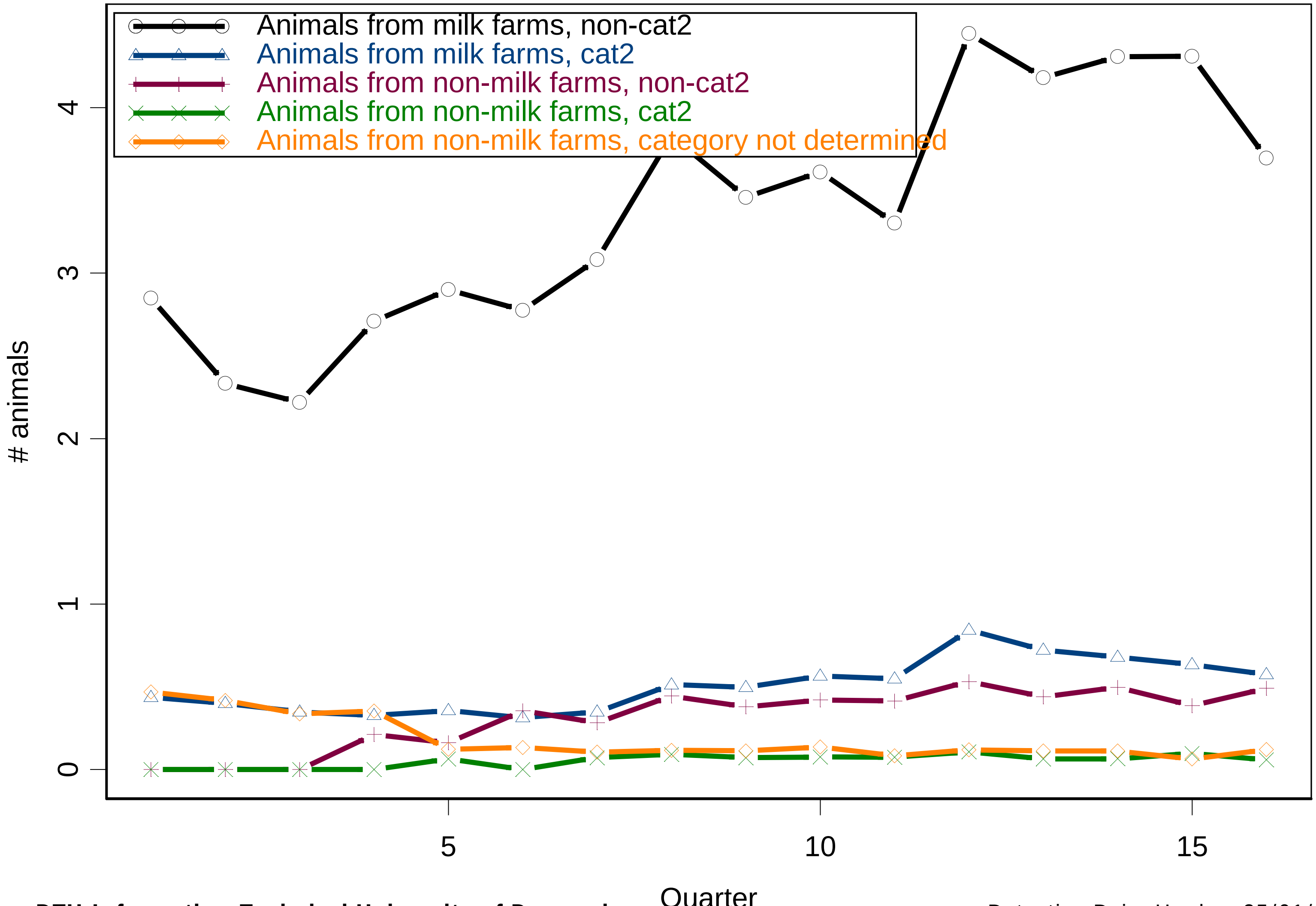
- We chose the model with the optimal Akaike Information;

- Consequently, we estimated *c* to be 13.

Trade information

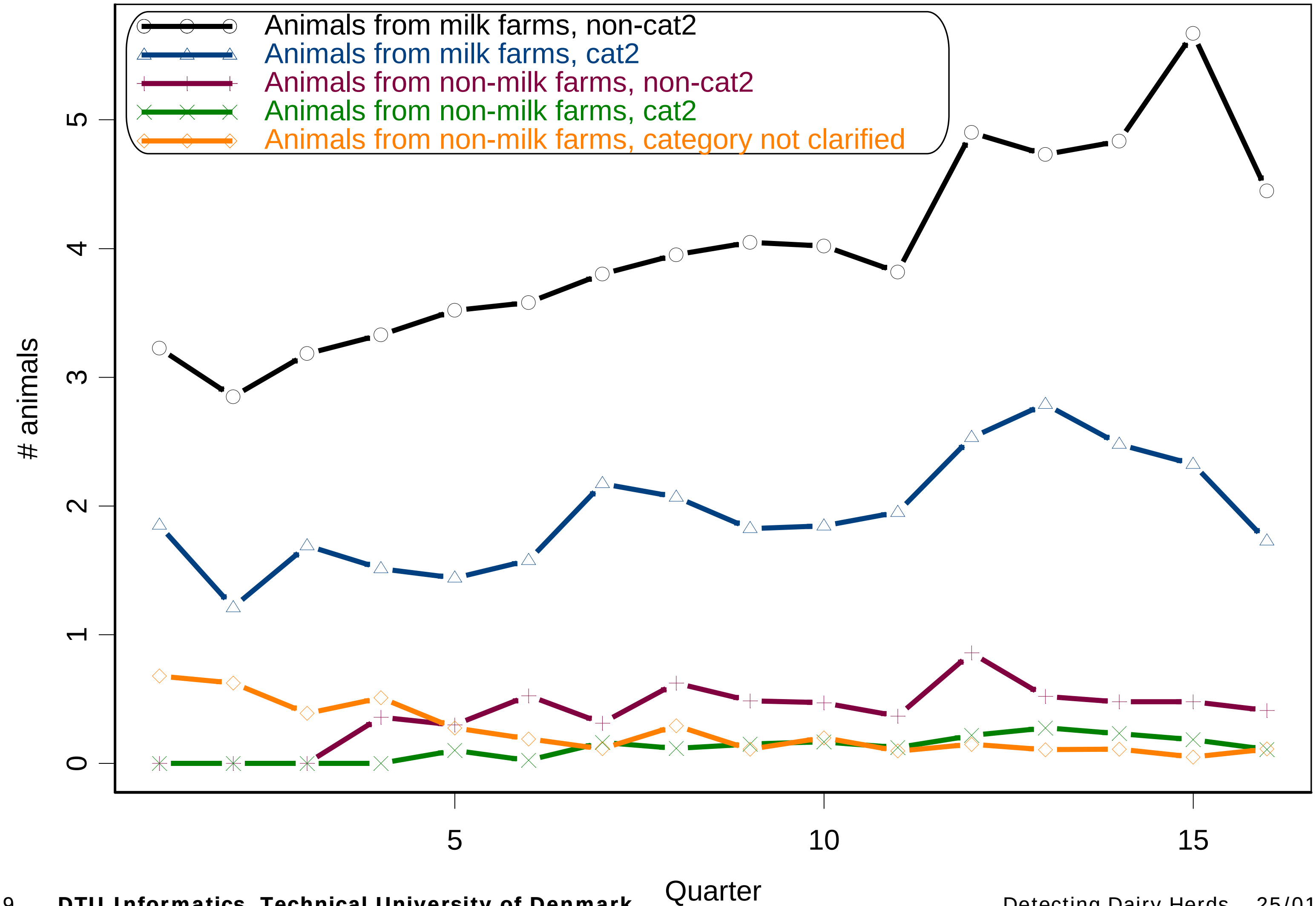
Trade

Milk producing non-cat 2 herds purchases 2004-2007



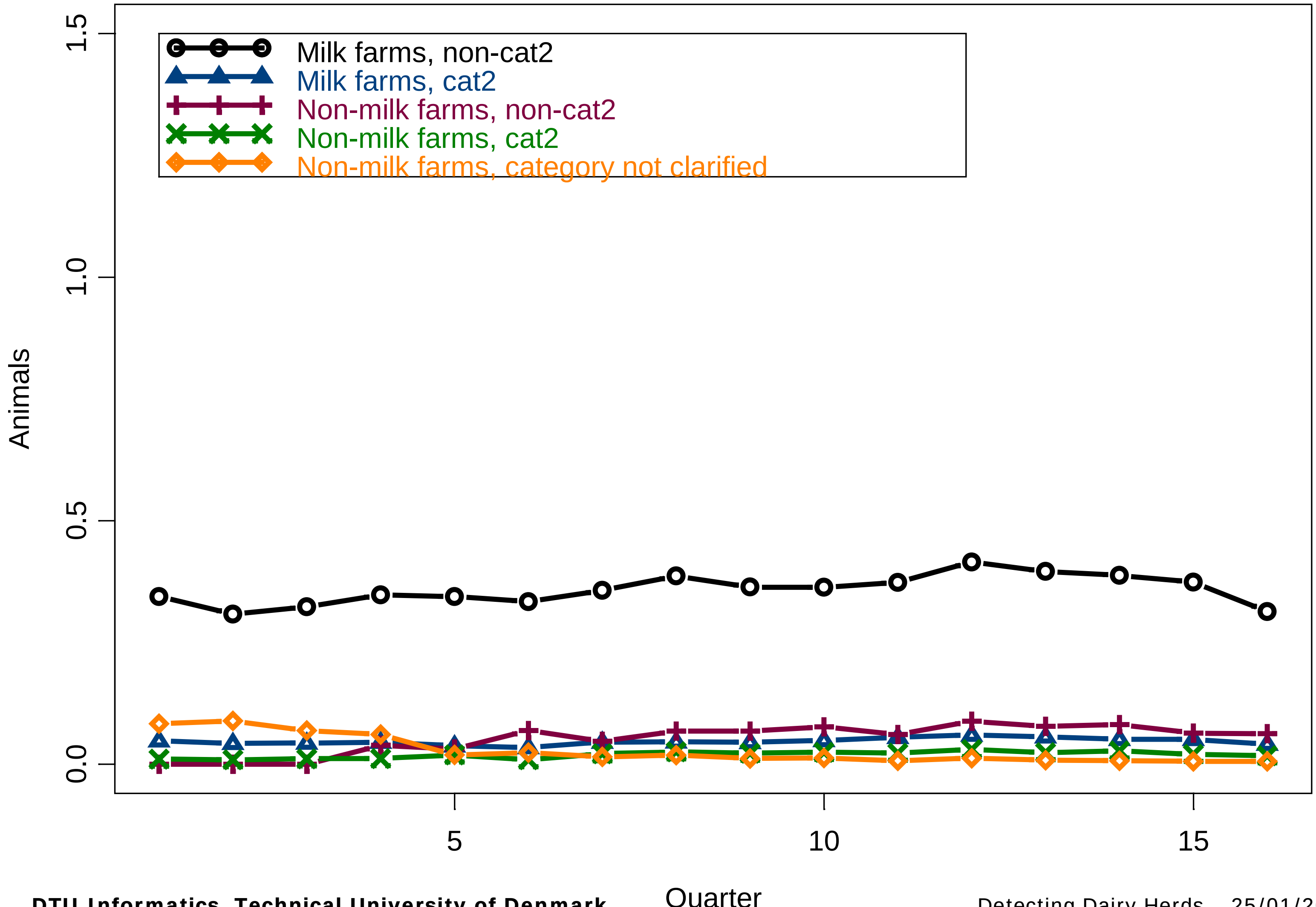
Trade II

Milk producing cat 2 herds purchases 2004-2007



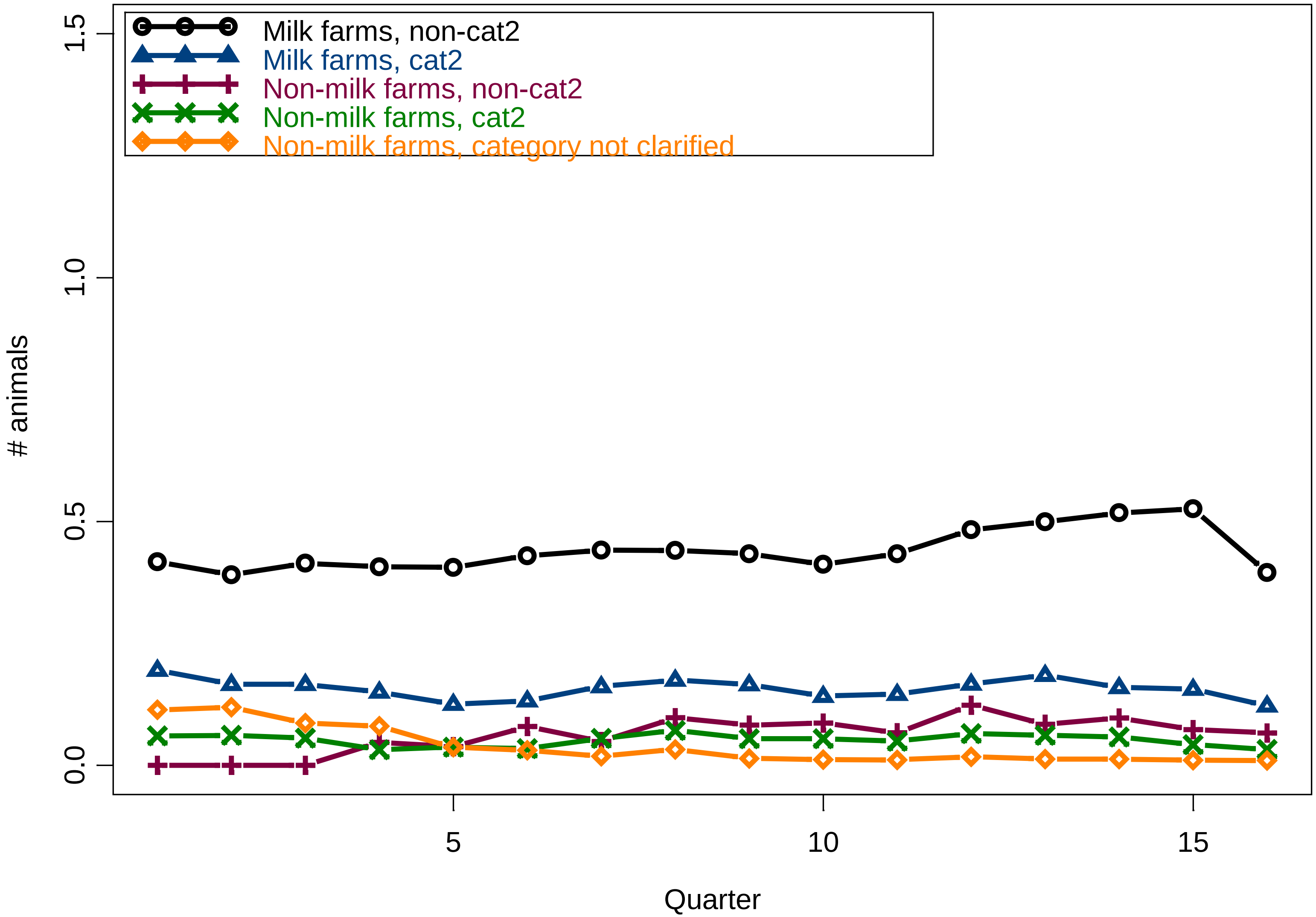
Trade III

Trade partners for milk producing non-cat 2 farms 2004-2007



Trade IV

Trade partners for milk producing cat2 farms 2004-2007

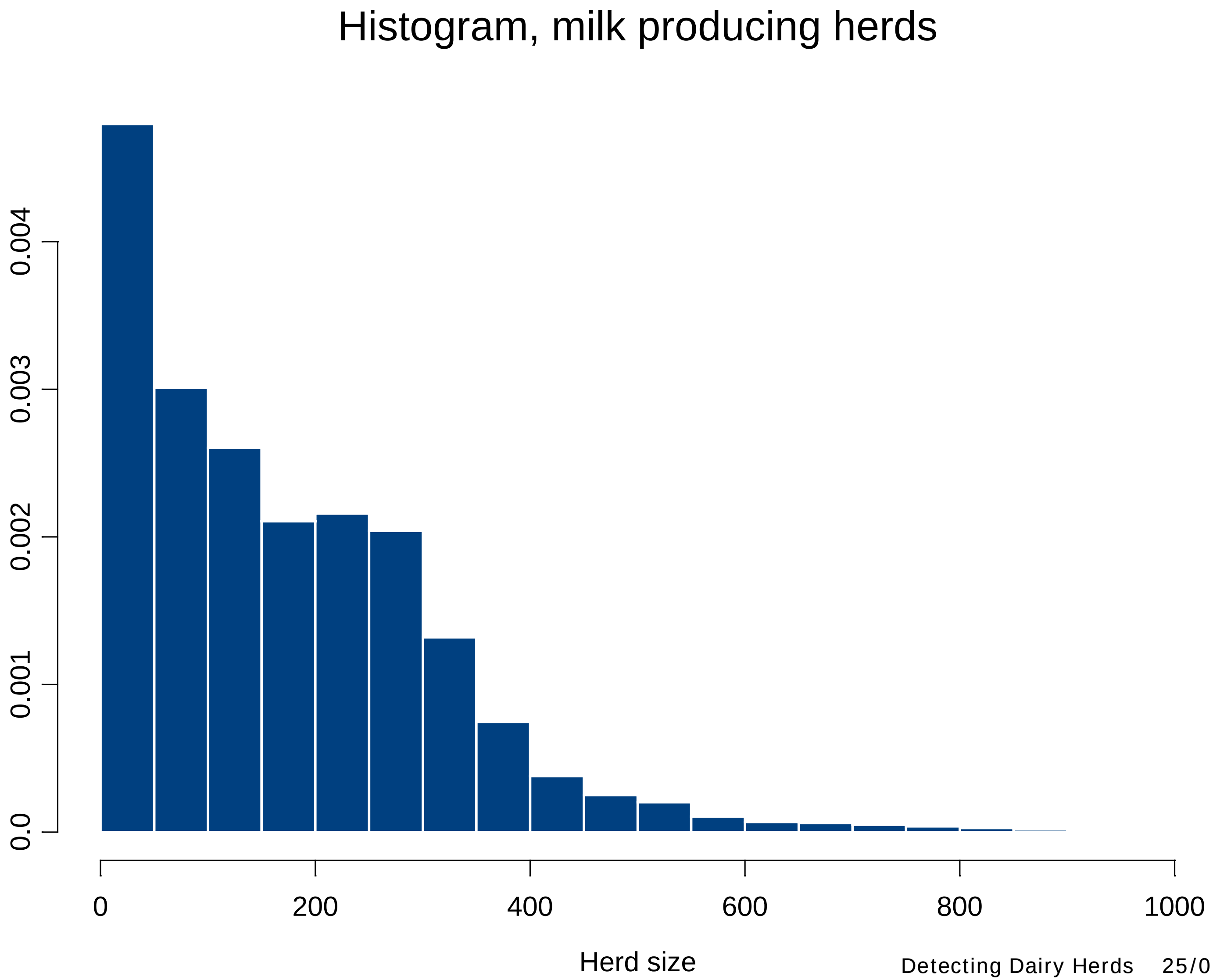


Neighbor herds and animals

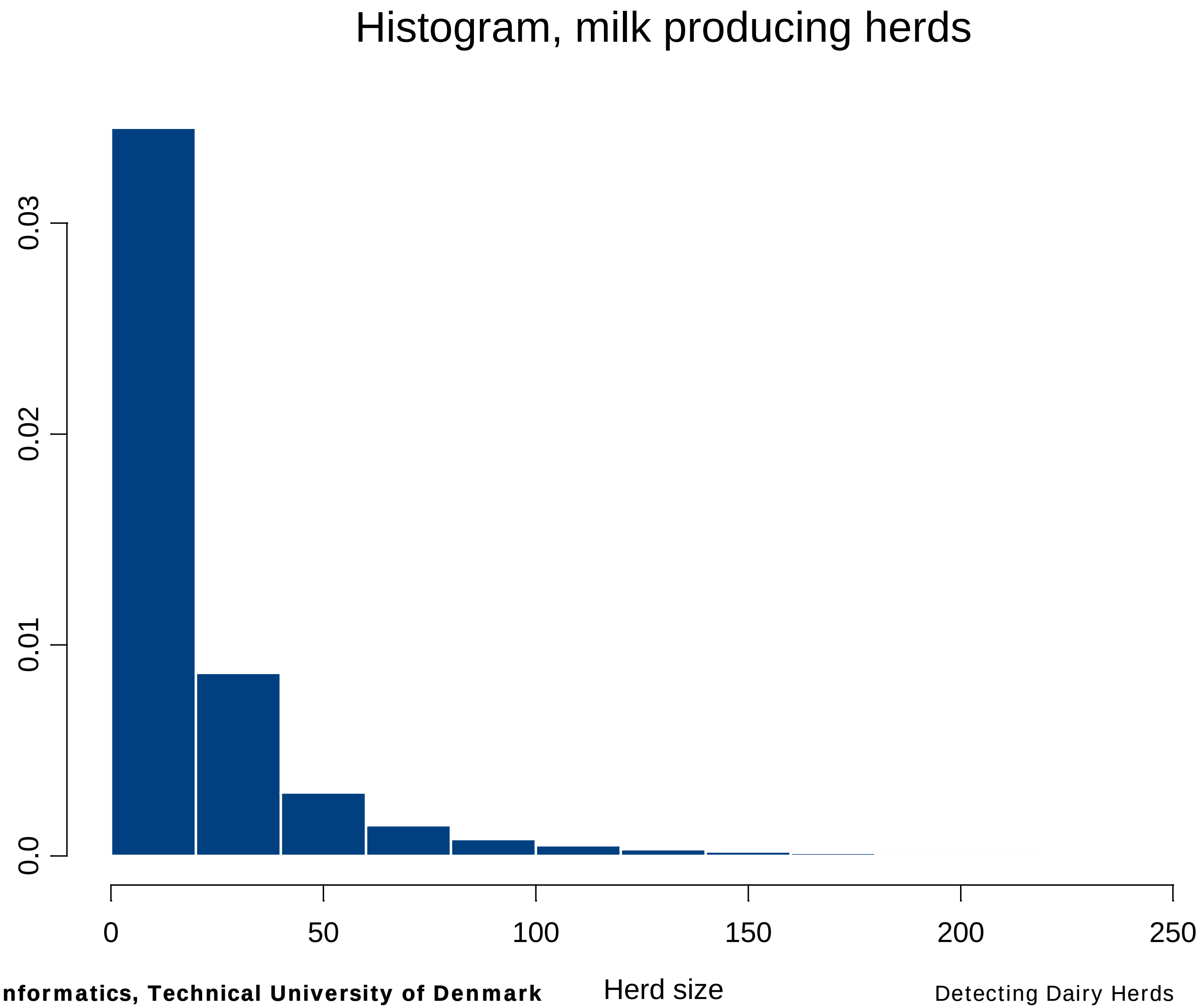
Neighbors – What is a neighbor?

- Ersbøll & Nielsen (2008): 4.9 km is the average 'range of influence' for local spread of Salmonella.
- We define Neighbors to be herds with a distance of less than 4.9 km from the herd in question.
- Counted for all dairy herds in Denmark, dynamically (ie., a time series).
- We consider both the number of herds and the number of animals within this radius.
- The neighbor effect is a hidden geographical component, in that clusters of herds will have many Neighbors (well known places in Jutland).

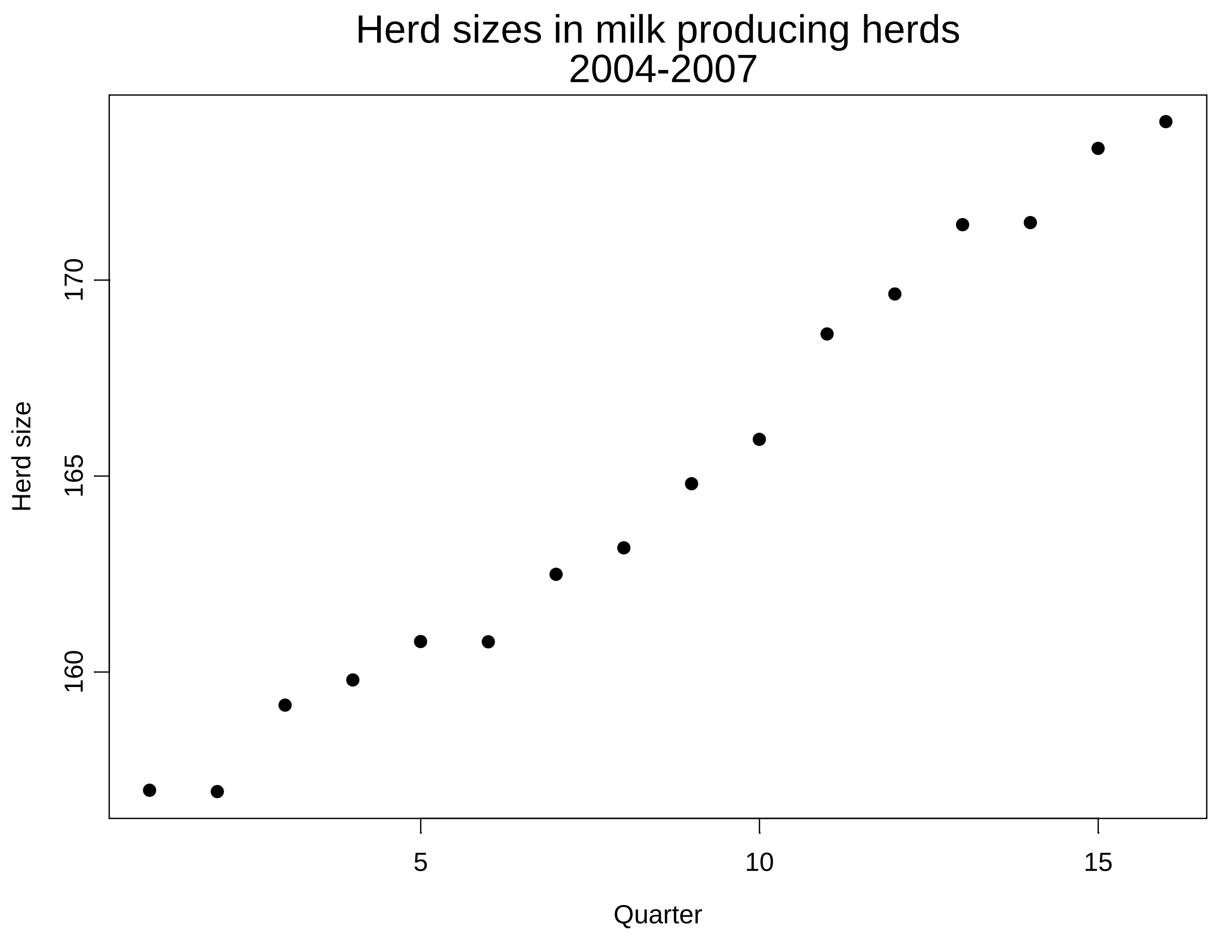
Herd Sizes, dairy herds



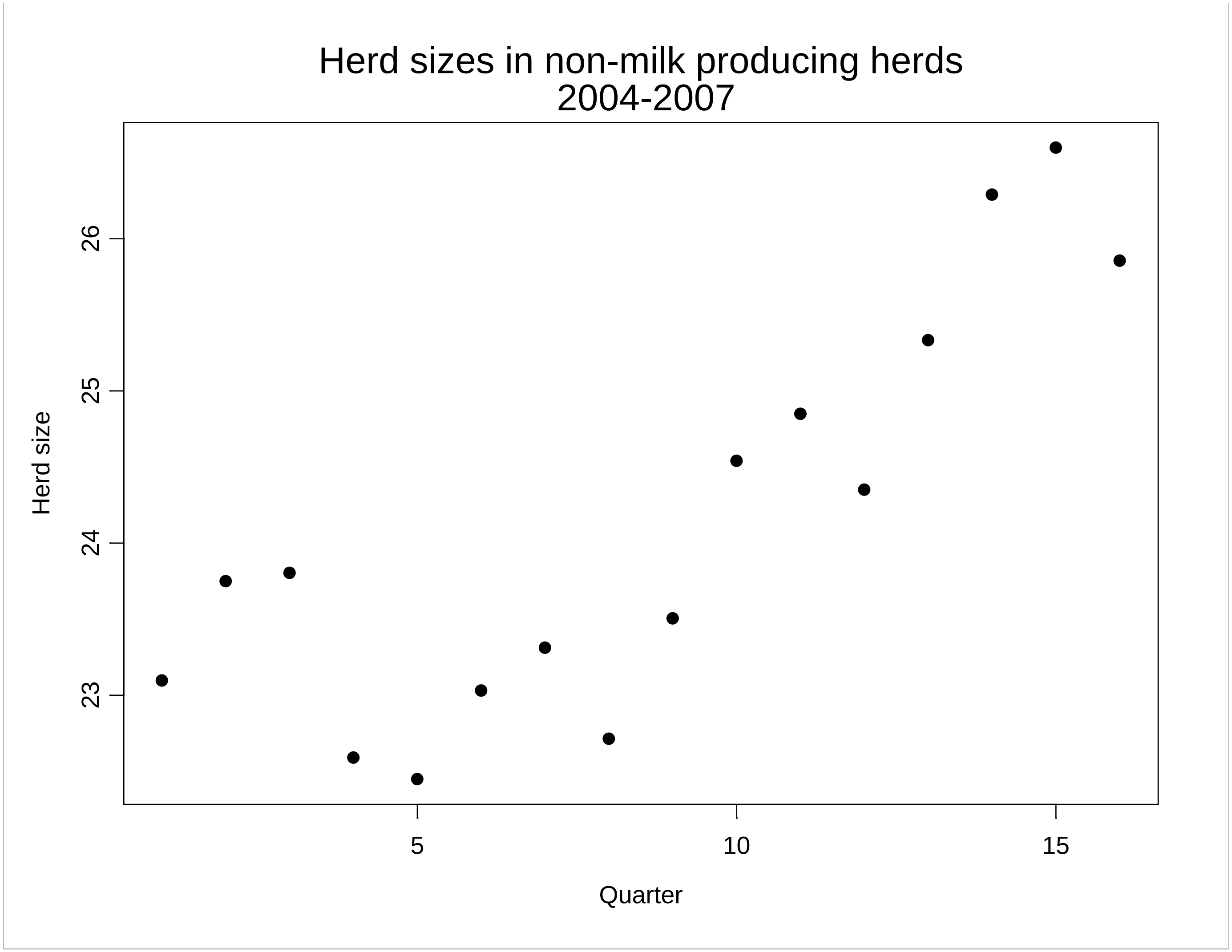
Herd sizes, non-dairy herds (used as neighbors only)



Dynamic herd sizes, dairy herds



Dynamic herd sizes, non-dairy herds



Explanatory variable	Type of effect	Mean of explanatory variable	Regression coefficient ± S.E.	P
Intercept	Main effect	1	4.90 ± 0.20	<0.0001
Season , 1st quarter	Seasonal effect	0.27	-6.80 ± 0.30	<0.0001
Season , 2nd quarter	Seasonal effect	0.26	-7.14 ± 0.32	<0.0001
Season , 3rd quarter	Seasonal effect	0.26	-6.62 ± 0.29	<0.0001
Mean of last 3 (Mean3)	Main effect	5.34	0.12 ±0.016	<0.0001
Mean3, 1st quarter**	Interaction	5.25*	0.071± 0.021	<0.0001
Mean3, 2nd quarter	Interaction	5.27*	0.11 ± 0.022	<0.0001
Mean 3, 3rd quarter	Interaction	5.47*	0.067 ± 0.021	<0.0001
Trade contacts with Status 2 herds	Main effect	0.037	0.44 ± 0.21	-
Animals traded with Status 1 herds	Main effect	2.62	5.30e-3 ± 3.44e-3	-
Animals traded with Status 2 herds	Main effect	0.29	0.033 ± 0.010	-
Neighbour Status 2 dairy herds	Main effect	4.28	0.066± 0.033	-
Neighbour animals from Status 2 dairy herds	Main effect	816	4.01e-4 ± 1.61e-4	-
Alarm1	Main effect	0.019	0.58± 0.32	0.001
Mean3× Animals traded with Status 2 herds	Interaction	2.51	-1.14e-3 ± 6.41e-4	<0.0001
Mean 3 × Neighbour animals from Status 2 dairy herds	Interaction	5370	-1.27e-5 ± 5.70e-6	<0.0001
Trade contacts with Status 2 herds × Animals traded with Status 2 herds	Interaction	0.40	-9.33 e-3± 6.21e-3	<0.0001
Neighbour Status 2 dairy herds × Neighbour animals from Status 2 dairy herds	Interaction	8250	-1.69e-5 ± 0.73e-6	<0.0001

Remarks I

- No effect of trade two quarters back.

- Interaction across groups of covariates with M_t only.

- Alarm Herd status (one quarter back) has a large impact;

- Effect of animals (traded and neighbors) decreases when level of M_t increases; those with a high level of M_t have a risk independent of animals purchased and animals traded.

- Independent of M_t:

  Trade contacts with Status 2 herds and

  Alarm Herd status.

Remarks II

- **Trade with Status 1 herds** has an effect through the number of purchased animals, while **trade with Status 2 herds** has an effect both through the number of trade partners and the number of purchased animals.

- Status 1 trade contacts is not significant.

- Neighbors has an effect through **Status 2 dairy neighbor farms** and **Status 2 dairy animals**.

- Non-dairy neighbours and Status 1 dairy neighbors are not significant.

Model based on 2007 data only

Table 2 Explanatory variables, regression coefficients and P-values in the final logistic regression model for a change in herd classification from Status 1 to Status 2 in the Danish surveillance programme for S. Dublin in dairy herds, base on data from 2007

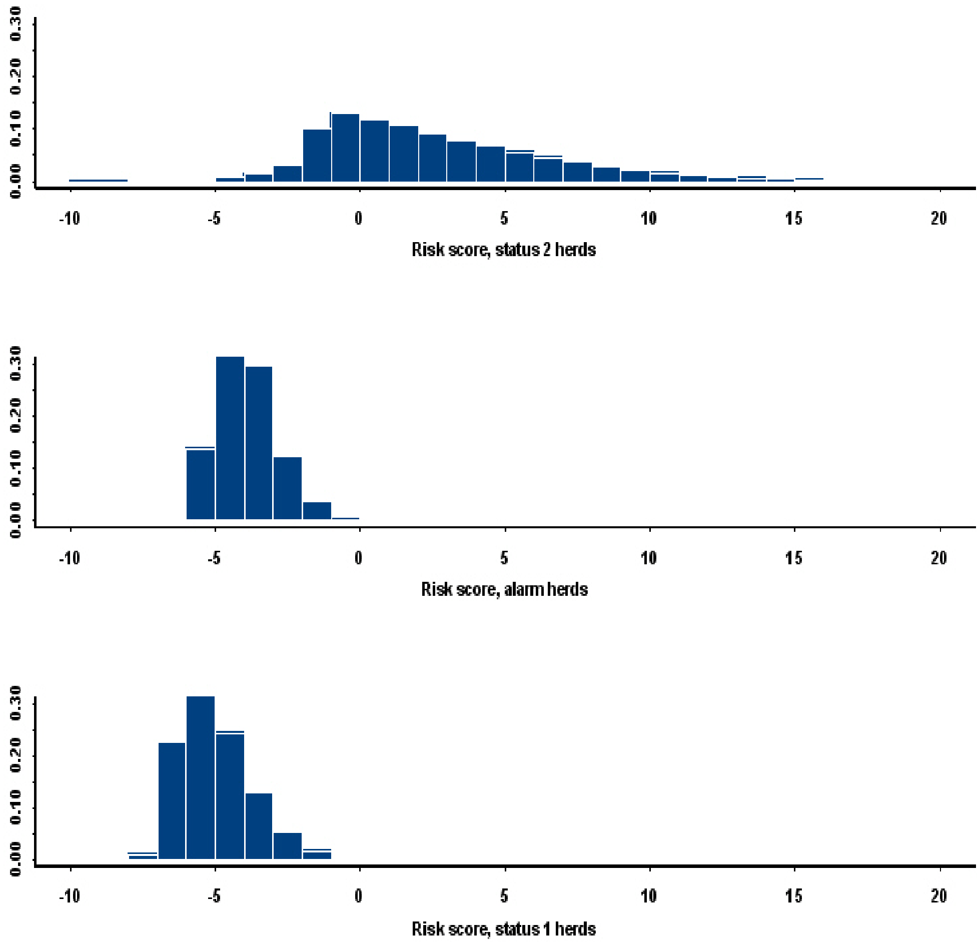
Explanatory variable	Type of effect	Mean of explanatory variable	Regression coefficient ± S.E.	p
Intercept	Main effect	1	-7.05 ± 0.39	<0.0001
Mean3	Main effect	6.50	0.22 ± 0.02	<0.0001
Trade contacts with Status 2 herds	Main effect	0.048	0.70 ± 0.37	0.0006
Number of animals in neighbouring Status 2 dairy herds	Main effect	758	0.0179 ± 0.0113	0.003
Alarm1	Main effect	0.023	1.08 ±0.69	0.006

Risk Scores

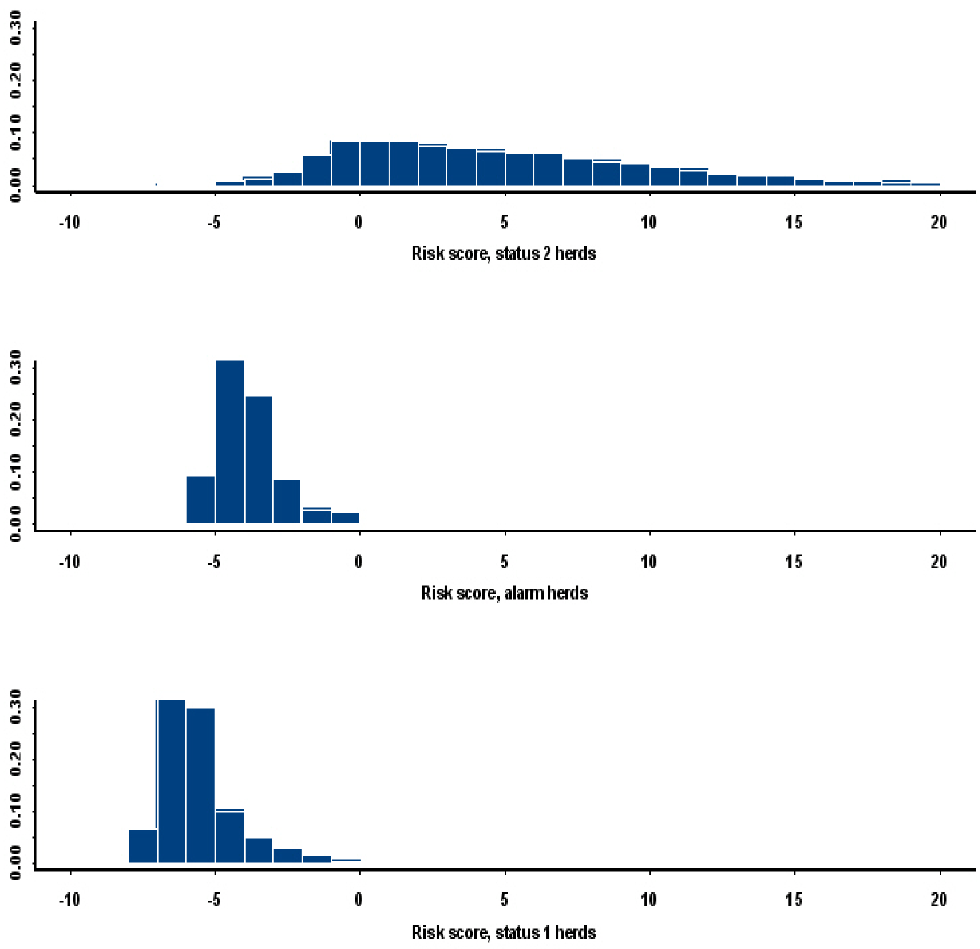
- We used the linear predictor as a risk score index.

- Which index value is high enough to consider a given herd to be a ’risk herd’, where the farmer should intervene if possible?

Risk Scores – big model

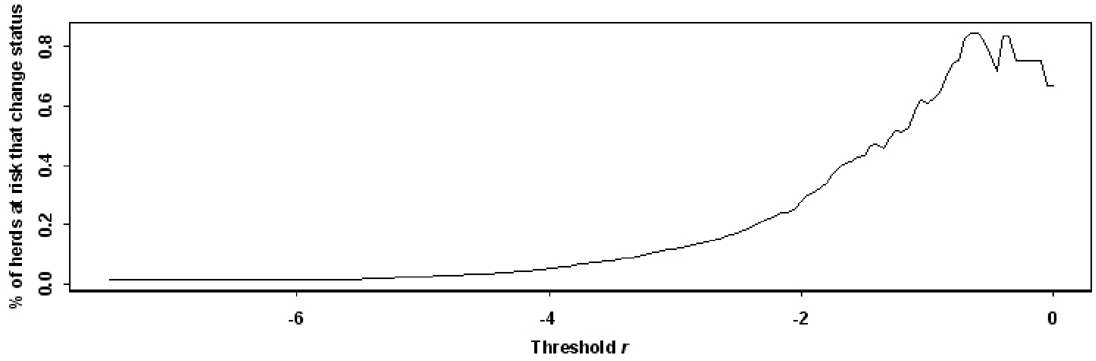


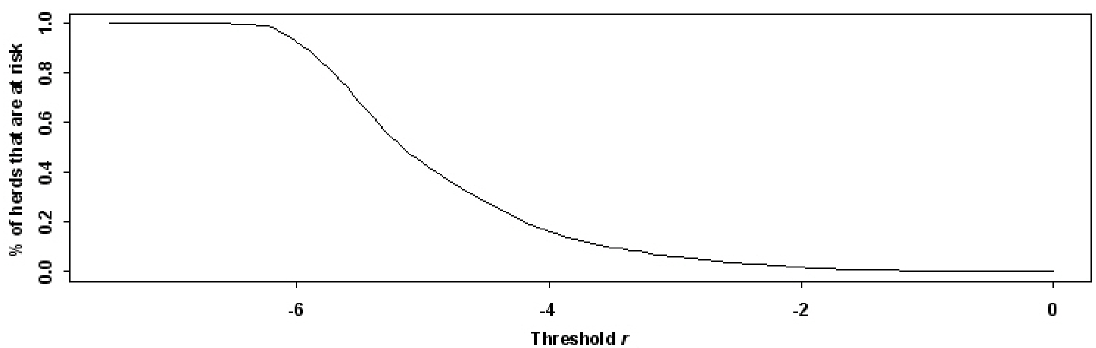
Risk Scores – small model



Definitions of risk herds

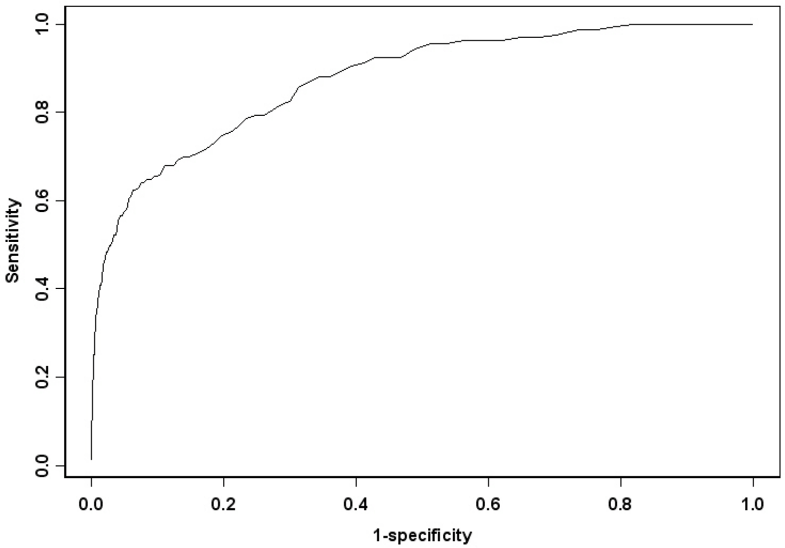
- A threshold *r* that defines a herd to be a risk herd if the risk score is > *r* represents a trade-off between number of herds at risk and the frequency with which they change status:



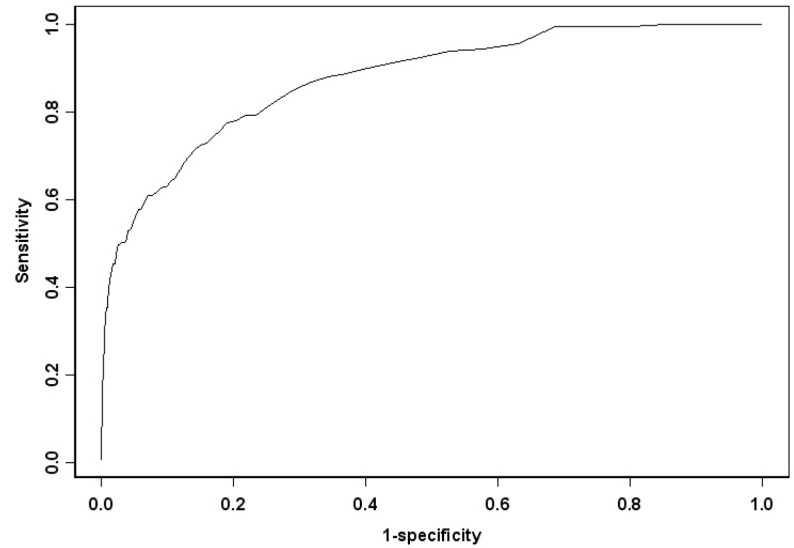


Predictive power

Coefficients re-estimated based on 2004-2006 data, and used to predict 2007 data: ROC curves when threshold varies



Big model



Small model

Small model versus big model

- Tempting to choose the simpler model;
- Predictive power is similar and model is much less complicated;
- However, the model could not be reproduced in full when applied to different cohorts of the data; we have no explanation for this.
- We recommend use of the big model.

Predictive power and relative importance

- Threshold is optimized based on predictive power of the big model as

$$r = -1.05$$

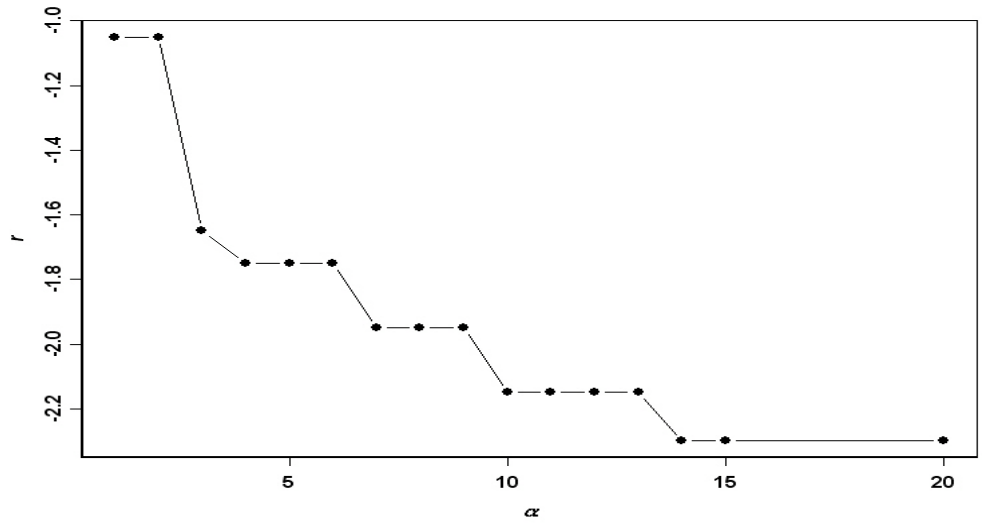
- However, it is much more important to predict those that change status than those that do not.

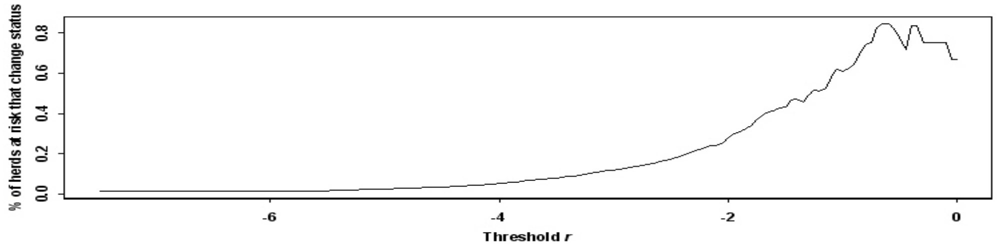
- Let α denote the importance of predicting a status change correctly relative to a non-change, and let **C** be the event “change of status”, and **PC** the event that a herd is classified as a Risk Herd. Instead of optimizing average predictability, we optimise the importance function

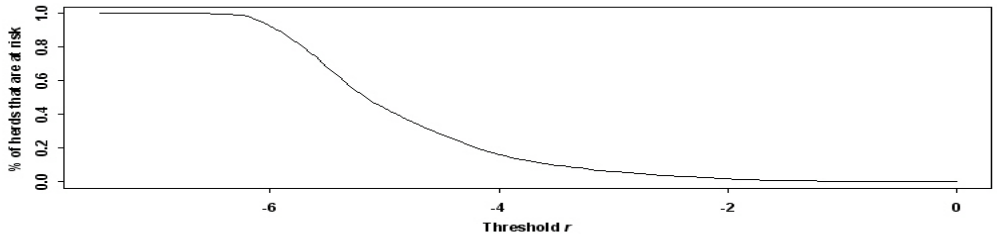
$$\alpha P(C|PC)P(PC)+P(C^{\neg}|PC^{\neg})P(PC^{\neg})$$

where “ ¬ ” signifies negation.

Threshold value as a function of importance







Suggested estimation of α based on farmer incentive

- Loss if a Status 2 herd is not correctly predicted:

```
 Price[3 months in Status 2]
-Price[3 months in Status 2]*
 P(Interventions fail)
-Price[Interventions]
```

- Loss if a Status 1 herd is not correctly predicted:

```
Price[Interventions]
```

$$\hat{\alpha} = \frac{\text{Price[3 months in Status 2]* P(Interventions succeed)}}{\text{Price[Interventions]}} - 1$$

Suggested estimation of α based on societal costs

Replace Price[3 months in Status 2] by

R_0[Price[3 months in Status 2]

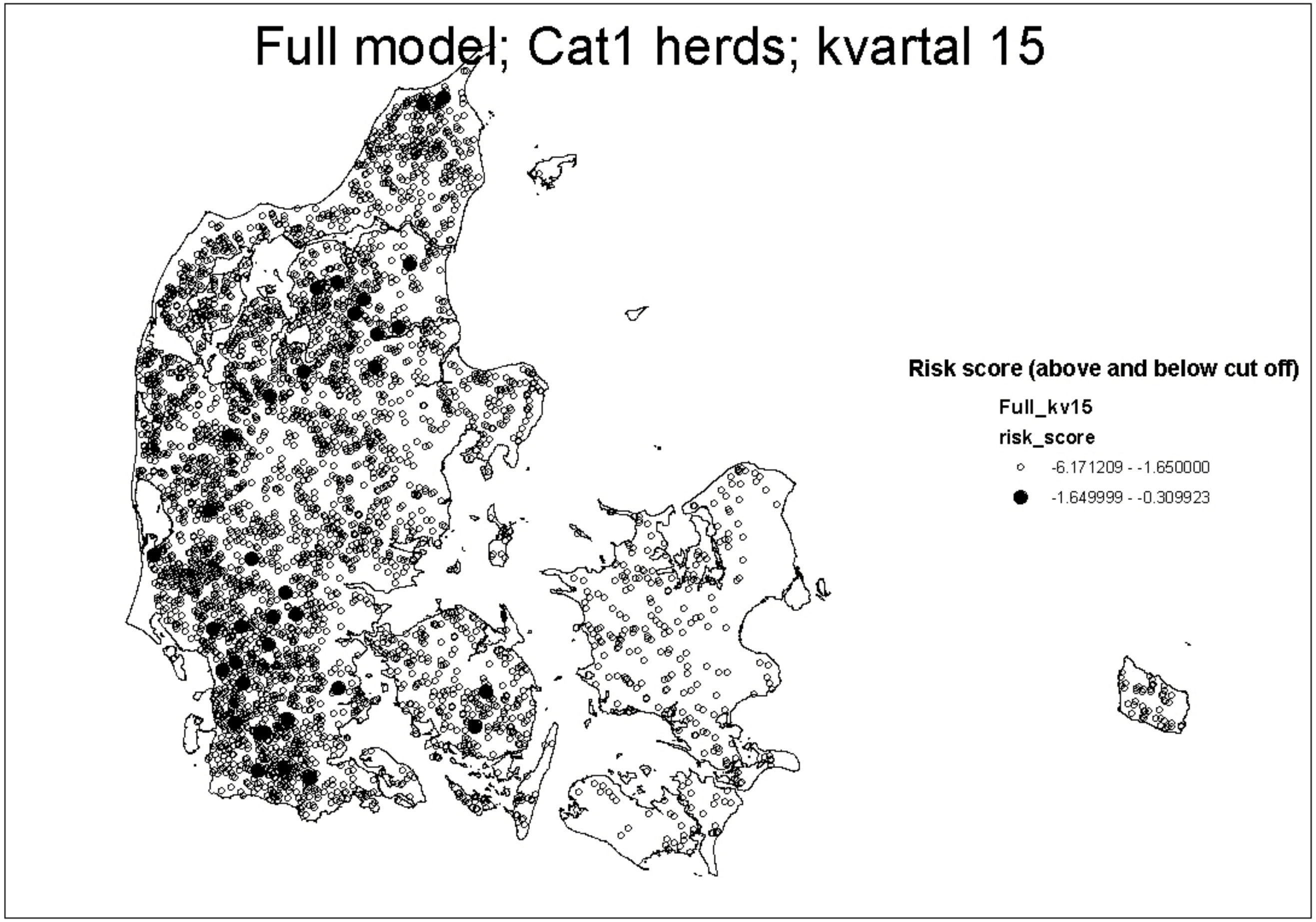
+cost(human infections) per herd]

where R_0 denotes the average excess number of infected herds due to delayed identification.

Higher α and lower threshold *r*.

These cost values are not known and dependent on legislation

Geographical distribution of risk herds ($\alpha=5$) 3rd quarter 2007.



Conclusion

- We suggest that risk herds may be defined as herds with a risk score over a threshold *r, with r taking a value from -1.05 and lower, depending on the nature of sanctions and the importance of detecting status changes.*

- *Potential uses if risk index: replacement of the current classification system; potential legal conflicts should be clarified.*

- *Alternatively, a mandatory notice to the farmer on a risk herd classification, allowing voluntary interventions;*

- *Coming legislation should encourage farmers to intervene. However, cost to society is higher than the cost to individual farmers due to spread of disease, so a higher* α *value and thus lower threshold r could apply.*

Acknowledgement

- We thank Jørgen Nielsen from the Danish Cattle Federation for providing register data from the Danish Cattle Database. Thanks Jørgen.