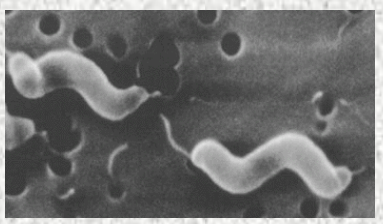
New approaches to source attribution: their role in reducing campylobacteriosis notifications in New Zealand



Nigel French

EFSA December 2008

Hopkirk Research Institute

Massey University

http://epicentre.massey.ac.nz/

EpiCentre

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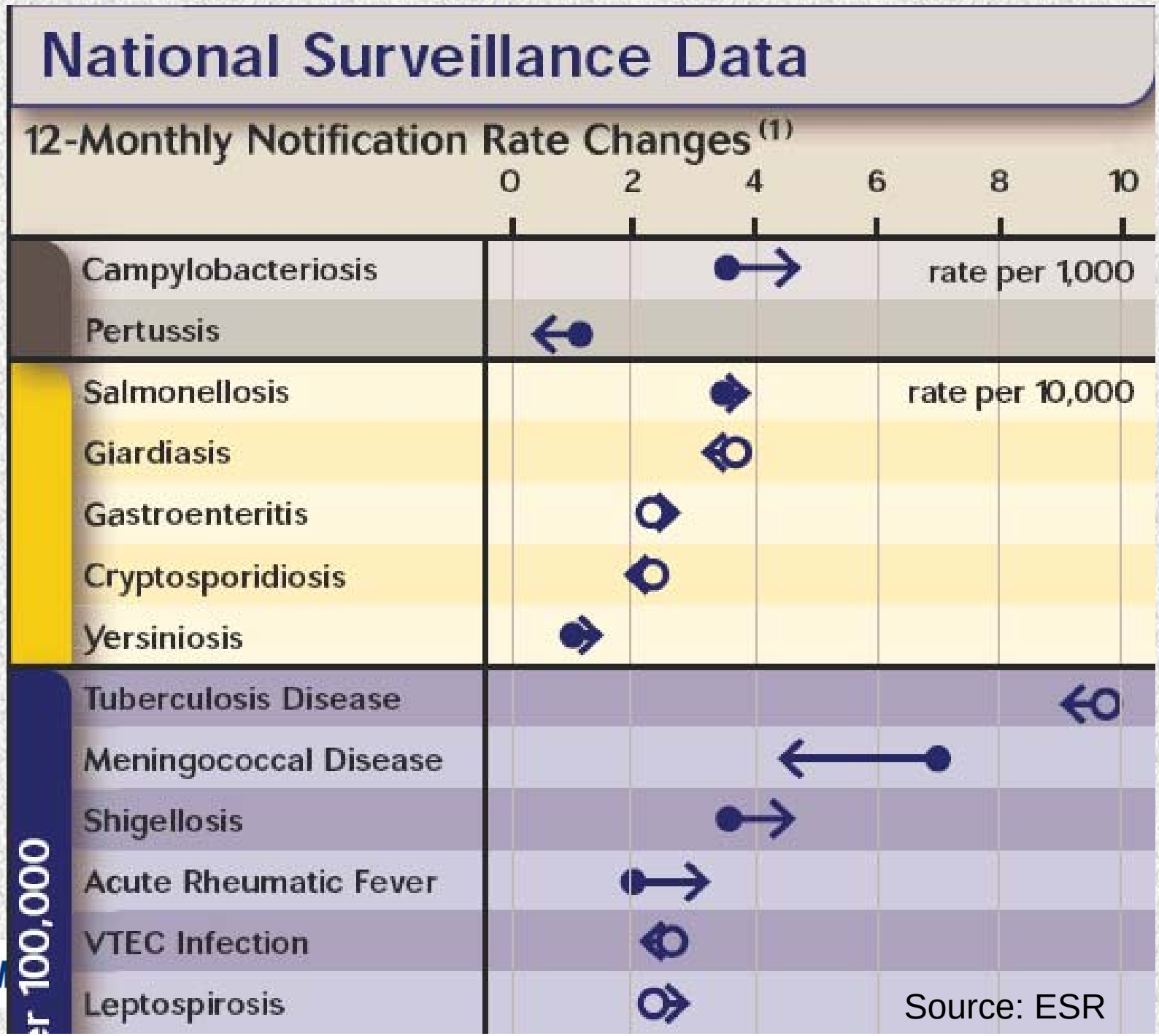
Outline

- Epidemiology
  - Recent studies of human case data
- Genotyping – human and animal reservoirs
  - MLST
- Source attribution modelling
- Recent trends – post intervention

National Surveillance Data



Source: ESR

Campylobacteriosis in NZ

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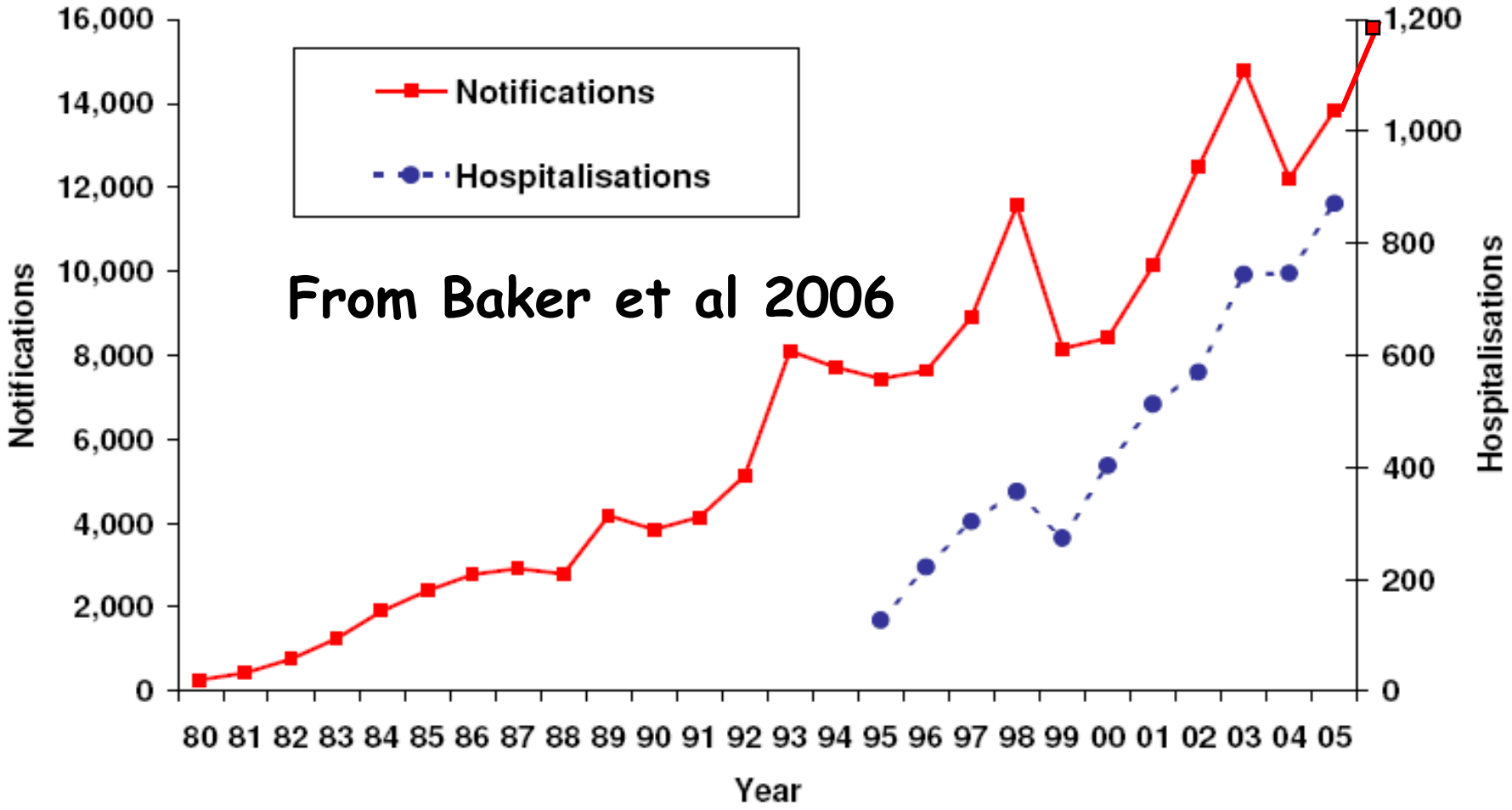
Figure 1. Annual number of notifications (1980–2005) and hospitalisations (1995–2005) for campylobacteriosis in New Zealand



Epidemiology: seasonal pattern

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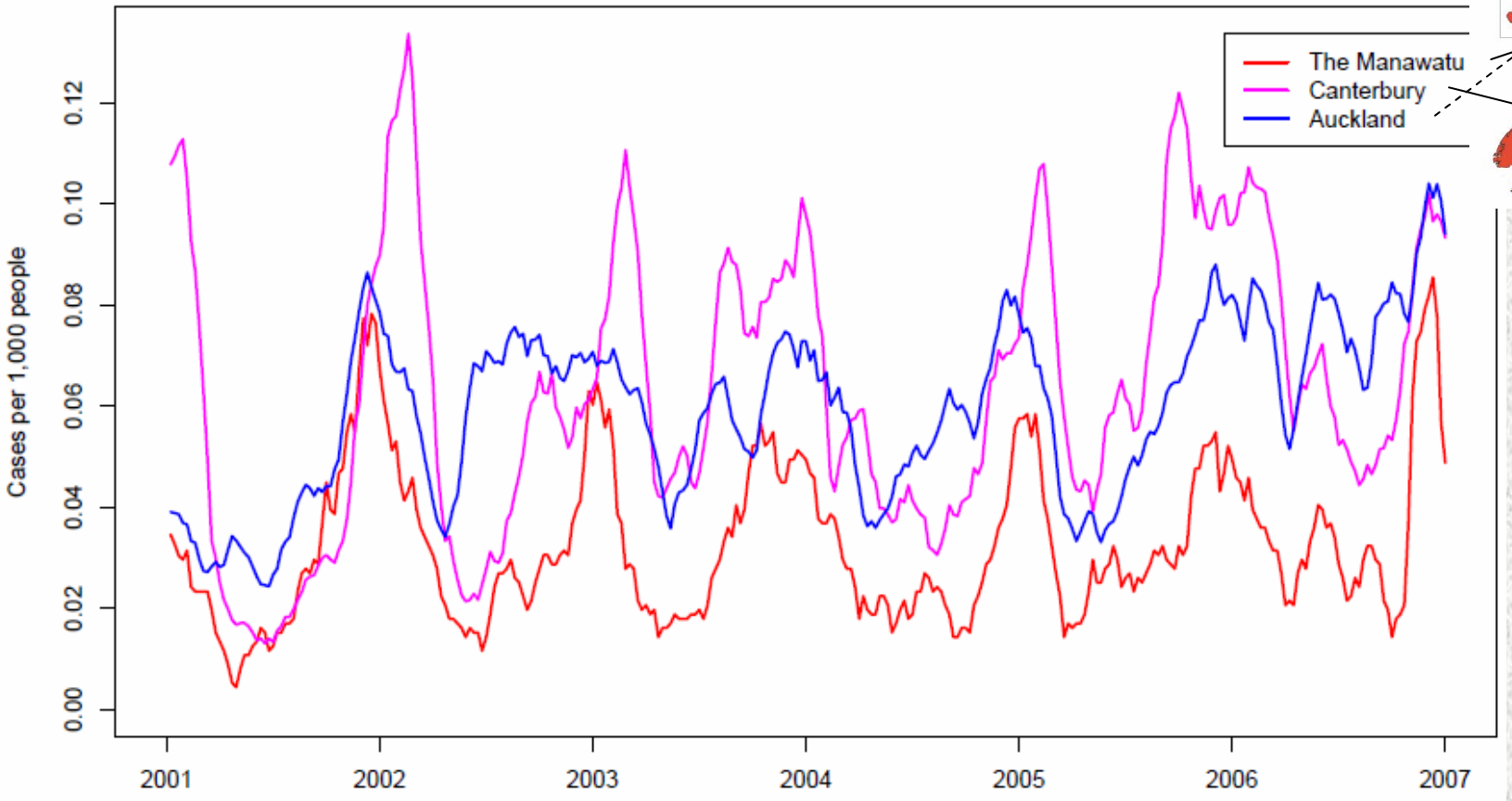
Smoothed Time Series: Cases per 1,000 People



Epidemiology: spatial pattern

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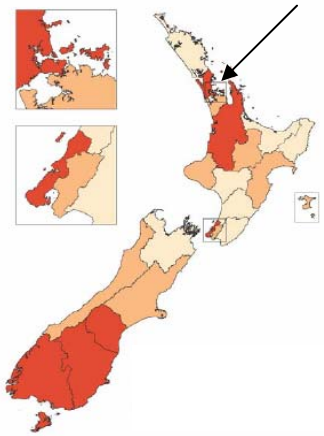
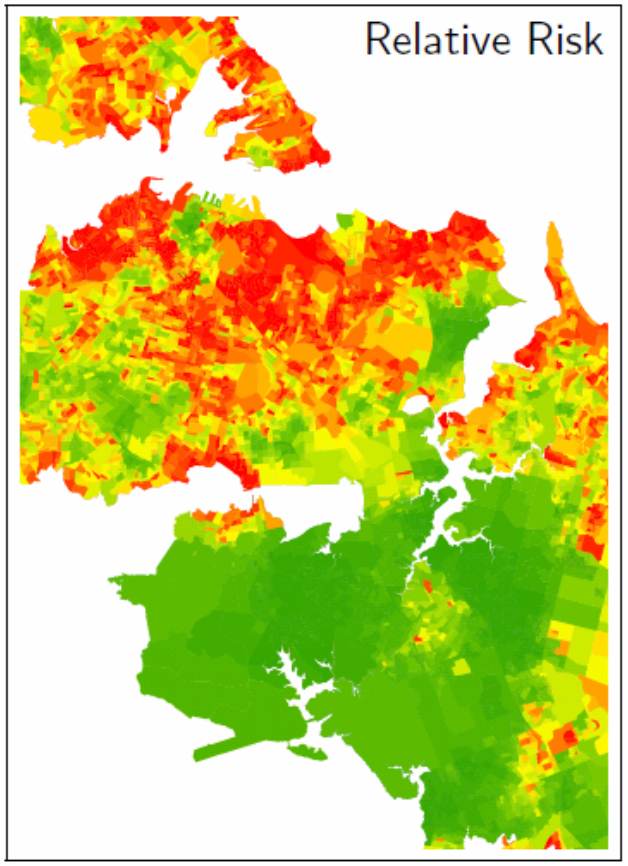
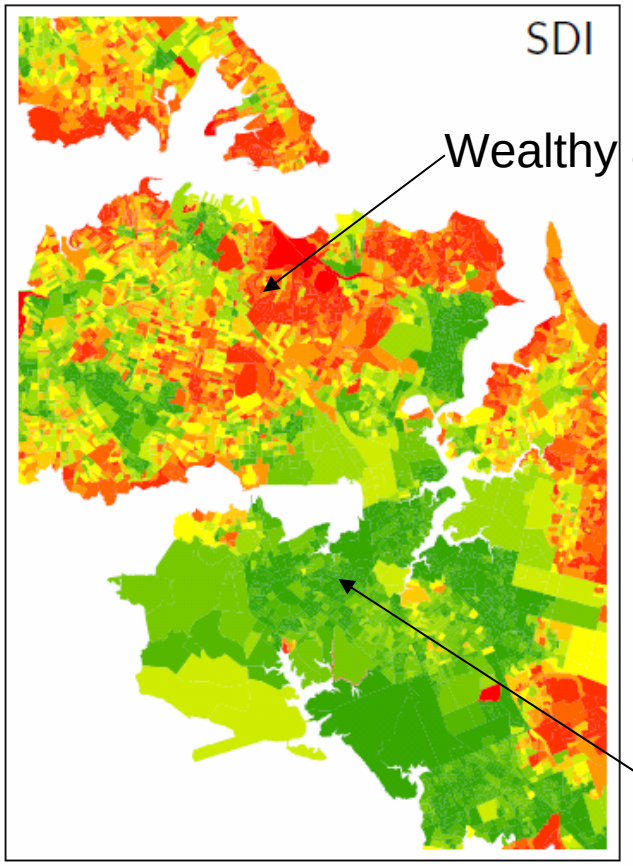
Comparison of Relative Risk vs SDI



>1M popⁿ





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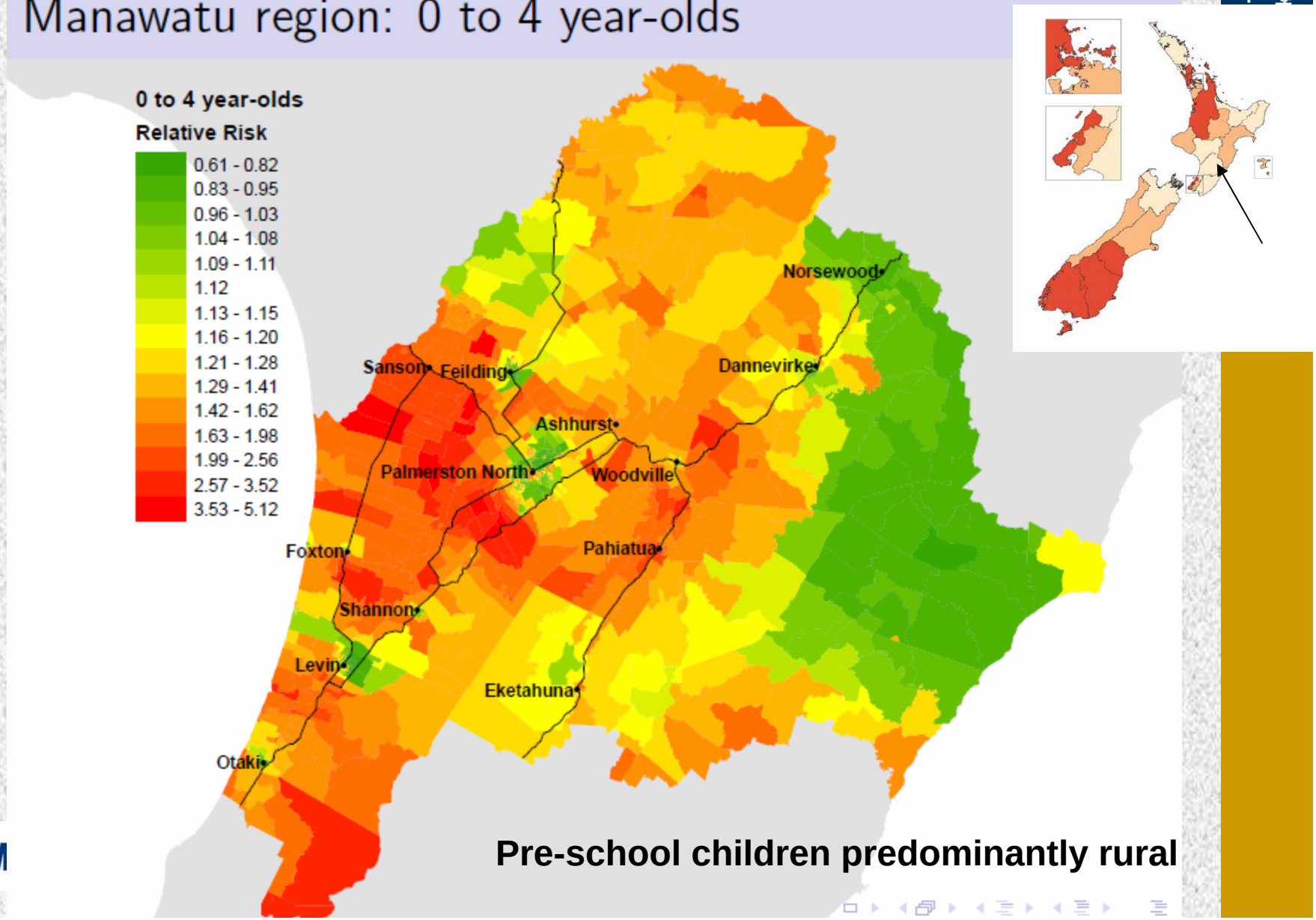
Spatial epidemiology - age

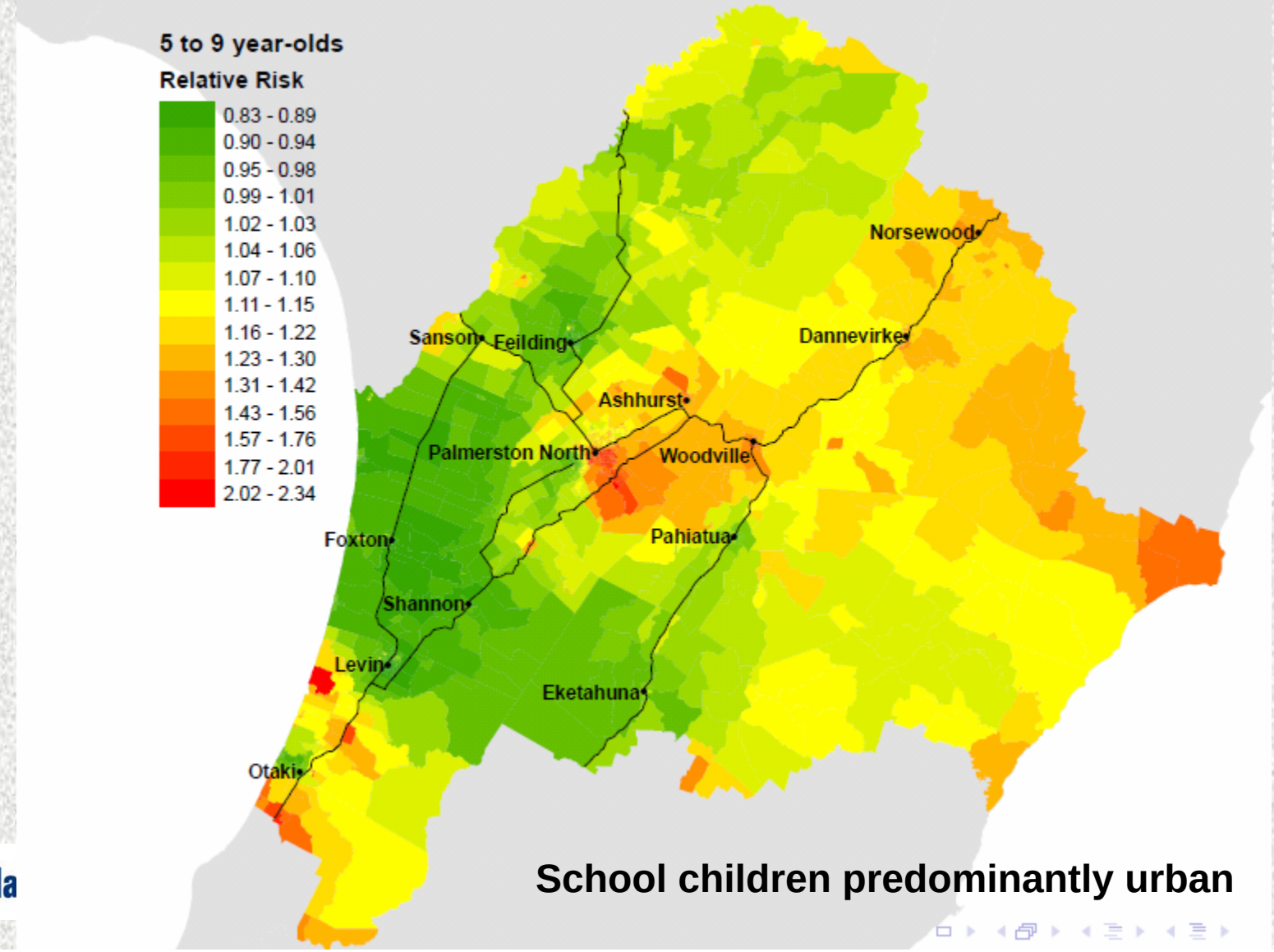
Manawatu region: 0 to 4 year-olds



Pre-school children predominantly rural

Spatial epidemiology - age

Manawatu region: 5 to 9 year-olds



School children predominantly urban

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Interventions in poultry industry demanded

THE NEW ZEALAND MEDICAL JOURNAL
Vol 119 No 1243 ISSN 1175 8716 2006

Regulation of chicken contamination urgently needed to control New Zealand's serious campylobacteriosis epidemic

Michael Baker, Nick Wilson, Rosemary Ikram, Steve Chambers, Phil Shoemack, Gregory Cook

Poultry ~ 40% of meat consumption

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Te Kunenga ki Pūrehuroa

Source attribution

- Essential for:
  - Managing public health risks
  - Prioritising resources
  - Directing research effort

Approaches to 'source attribution'

- (Analytical) epidemiology
  - Population-based epidemiological studies
- Simulation modelling / Risk assessment
- Molecular epidemiology
  - Microbial subtyping / source tracking
  - Applying molecular tools, population genetics and epidemiological modelling to inform public health policy
  - NZFSA and industry funded

Approaches to 'source attribution'

- (Analytical) epidemiology
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  - NZFSA and industry funded

Population-based epidemiological studies

- Cross-sectional, cohort, **case-control**, case-case.
- Can estimate relative risk / odds ratios / PAF for different exposures
  - e.g. *Campylobacter* and eating poultry, foreign travel, environmental, occupational

Source/ exposure ← **disease**

Issues with case-control studies

- Can be very valuable but…
- Prone to reporting bias
  - "I must have eaten chicken…."
- If high level immunity, similar exposures in cases and controls – low power

Chicken – confusing / conflicting evidence?

Risk/Protective factor	Odds ratio (CI)
Eating undercooked poultry (risk)	4.94 (1.03, 23.62)
Poultry eaten at a friend's house (risk)	3.18 (1.0, 10.73)
Consuming fresh chicken (as opposed to frozen) (risk)	1.8 (0.82, 3.82)
Eating poultry at home (protective)	0.36 (0.14, 0.9)
Freezing fresh chicken before consuming (protective)	0.58 (0.18, 1.83)
Buying frozen chicken (protective)	0.71 (0.34, 1.31)

Ikram 1994, New Zealand Campylobacter study

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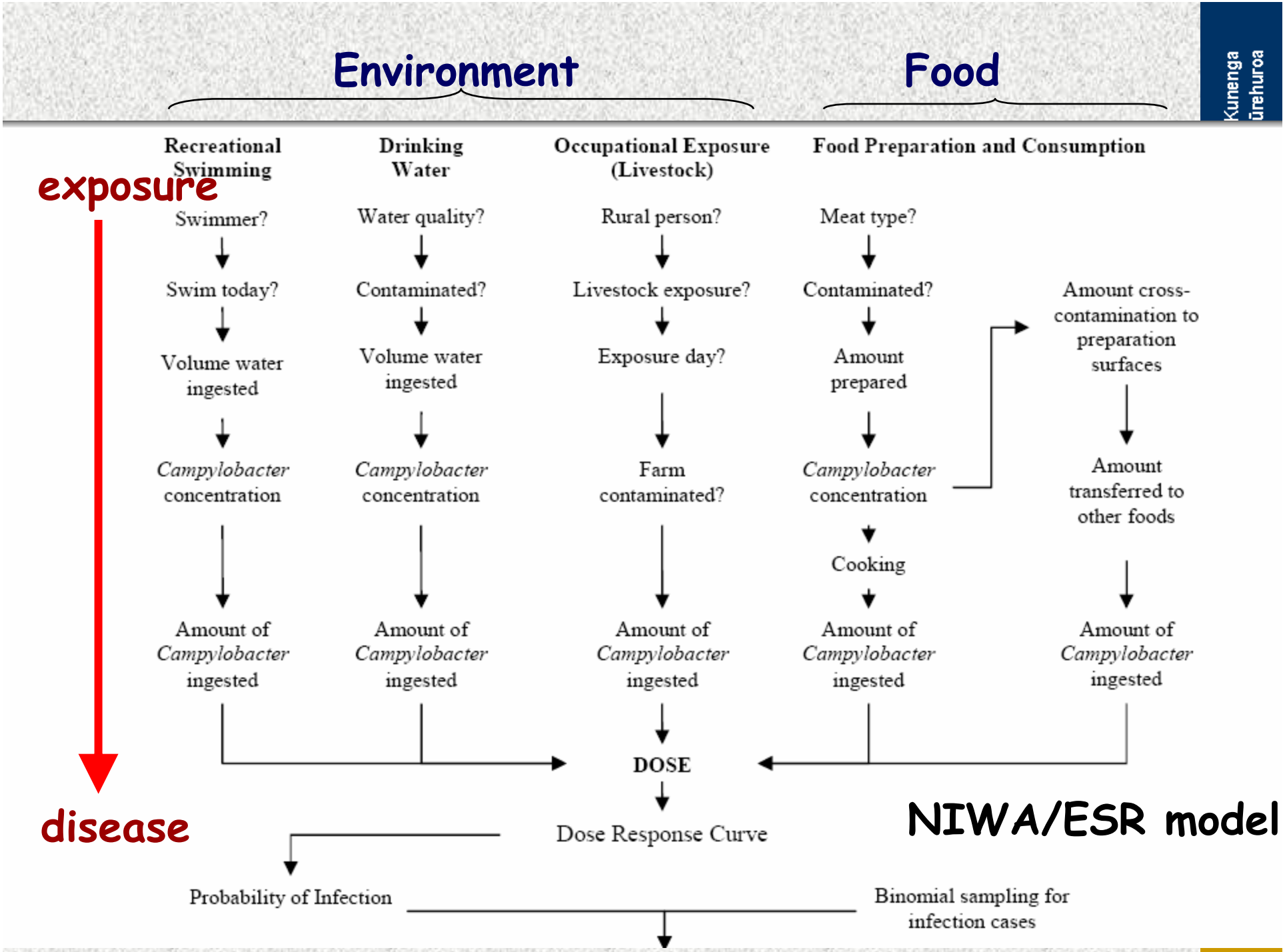
Approaches to 'source attribution'

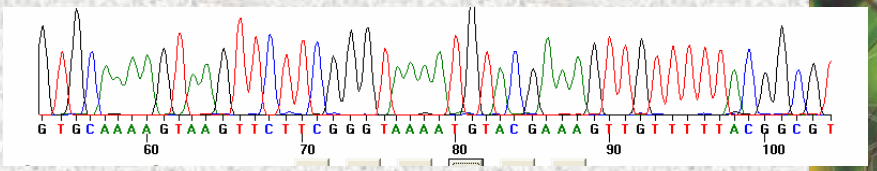
- (Analytical) epidemiology
- Simulation (RA) modelling
  - Multiple pathways / exposures
  - Food and environmental sources
  - Simulation of propagation of pathogen along pathway
  - Hazard or risk based (need D-RR)
  - Good for assessing interventions
- Molecular epidemiology


Environment
Food
exposure
disease
Recreational Swimming
Drinking Water
Occupational Exposure (Livestock)
Food Preparation and Consumption
Swimmer?
Swim today?
Volume water ingested
Campylobacter concentration
Amount of Campylobacter ingested
Water quality?
Contaminated?
Volume water ingested
Campylobacter concentration
Amount of Campylobacter ingested
Rural person?
Livestock exposure?
Exposure day?
Farm contaminated?
Amount of Campylobacter ingested
Meat type?
Contaminated?
Amount prepared
Campylobacter concentration
Cooking
Amount of Campylobacter ingested
Amount cross-contamination to preparation surfaces
Amount transferred to other foods
Amount of Campylobacter ingested
DOSE
Dose Response Curve
Probability of Infection
Binomial sampling for infection cases
NIWA/ESR model

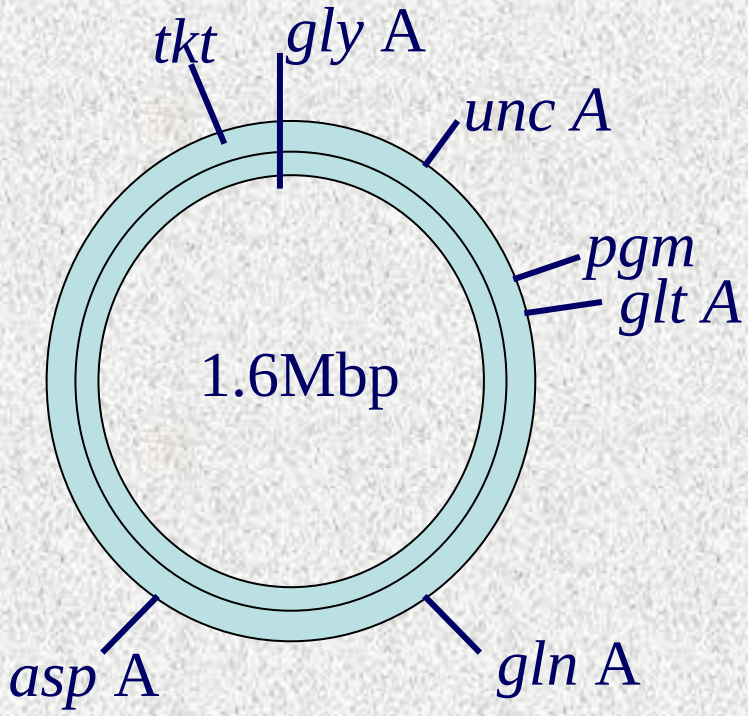
Approaches to 'source attribution'

- (Analytical) epidemiology
  - Population-based epidemiological studies
- Simulation modelling / Risk assessment
- Molecular epidemiology
  - Microbial subtyping / source tracking
  - Applying molecular tools, population genetics and epidemiological modelling to inform public health policy
  - NZFSA funded

Multi Locus Sequence Typing



- PCR highly conserved genes
- 7 housekeeping genes
- Use allelic variation to describe subtypes:
  - ST = sequence type – unique pattern of 7 alleles
  - Clonal complex = group of related STs identified by progenitor ST
  - Website: Oxford University *http://campylobacter.mlst.net*



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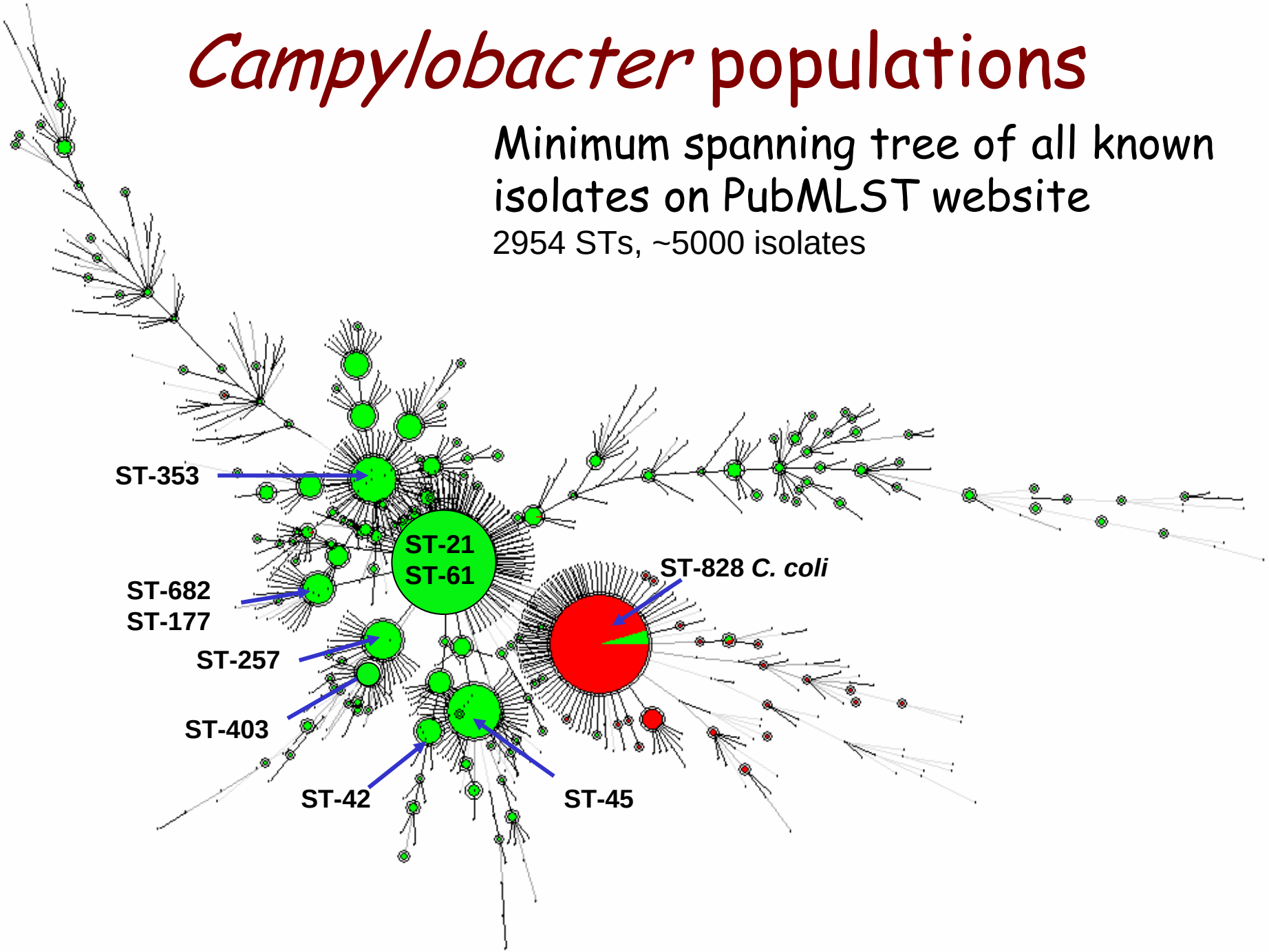
Campylobacter populations

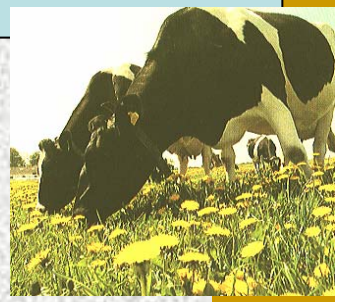
Minimum spanning tree of all known isolates on PubMLST website

2954 STs, ~5000 isolates



ST-61 complex

source	Frequency	Percentage
human stool	62	35.2%
cattle	53	30.1%
sheep	17	9.7%
ruminant offal/ meat	8	7.9%
lamb	8	4.5%
Chicken	3	1.7%



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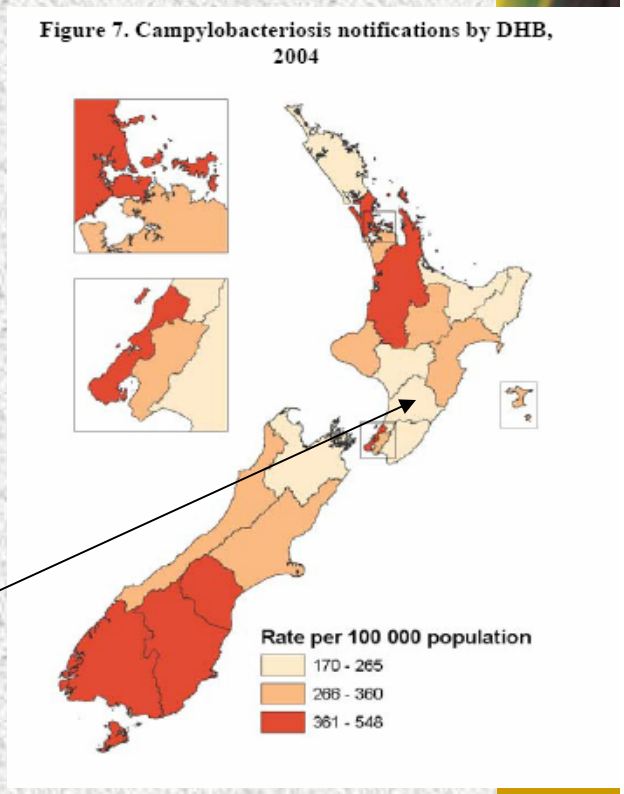
NZ Manawatu study 2005-

- Are human isolates the same as those found in different sources?
- Identify genotypes common to particular sources
- Modelling (risk attribution)
- Feasibility study: useful approach to embed within surveillance in NZ?



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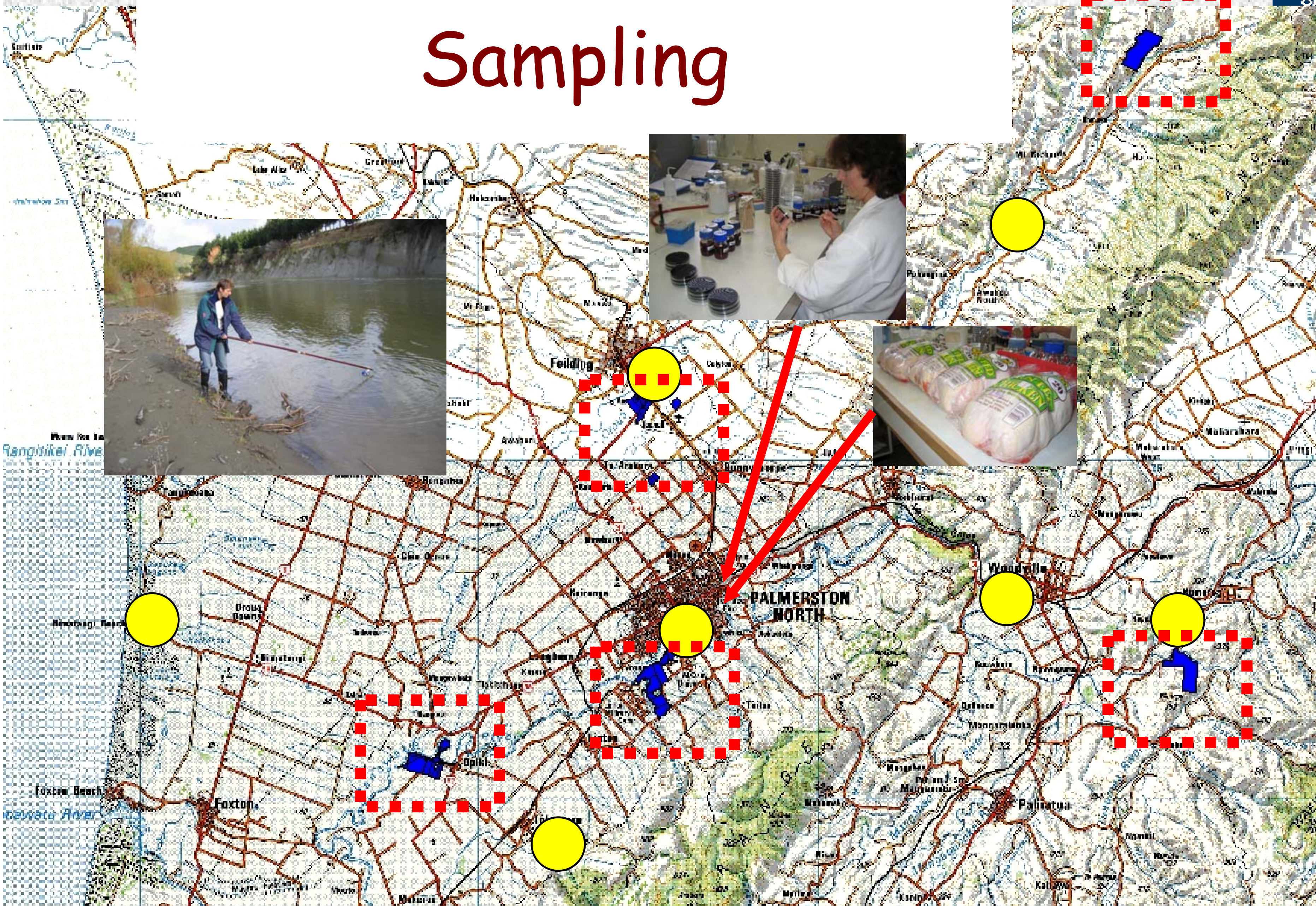
Sampling



ki Pūrehuroa

Numbers of samples/isolates: *C. jejuni*

- Human 520 (770 samples)
- Poultry 562 samples 75% +ve
- Red meat 1312 samples 12% +ve
- Ruminant faeces 278 samples 58% +ve
- Env. Water 335 samples 30% +ve
- Wild bird 192 samples 13% +ve

March 1st 2005 to Feb 29th 2008

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ST	# of cases	%	2006 rank
474	66	27.3	1
48	24	9.9	2
190	18	7.4	4
45	17	7.0	3
53	13	5.4	8
42	11	4.5	5
61	10	4.1	10
50	9	3.7	7
2026	9	3.7	11

Rare internationally

MLST Human cases in Manawatu

Red = Ruminant associated strains

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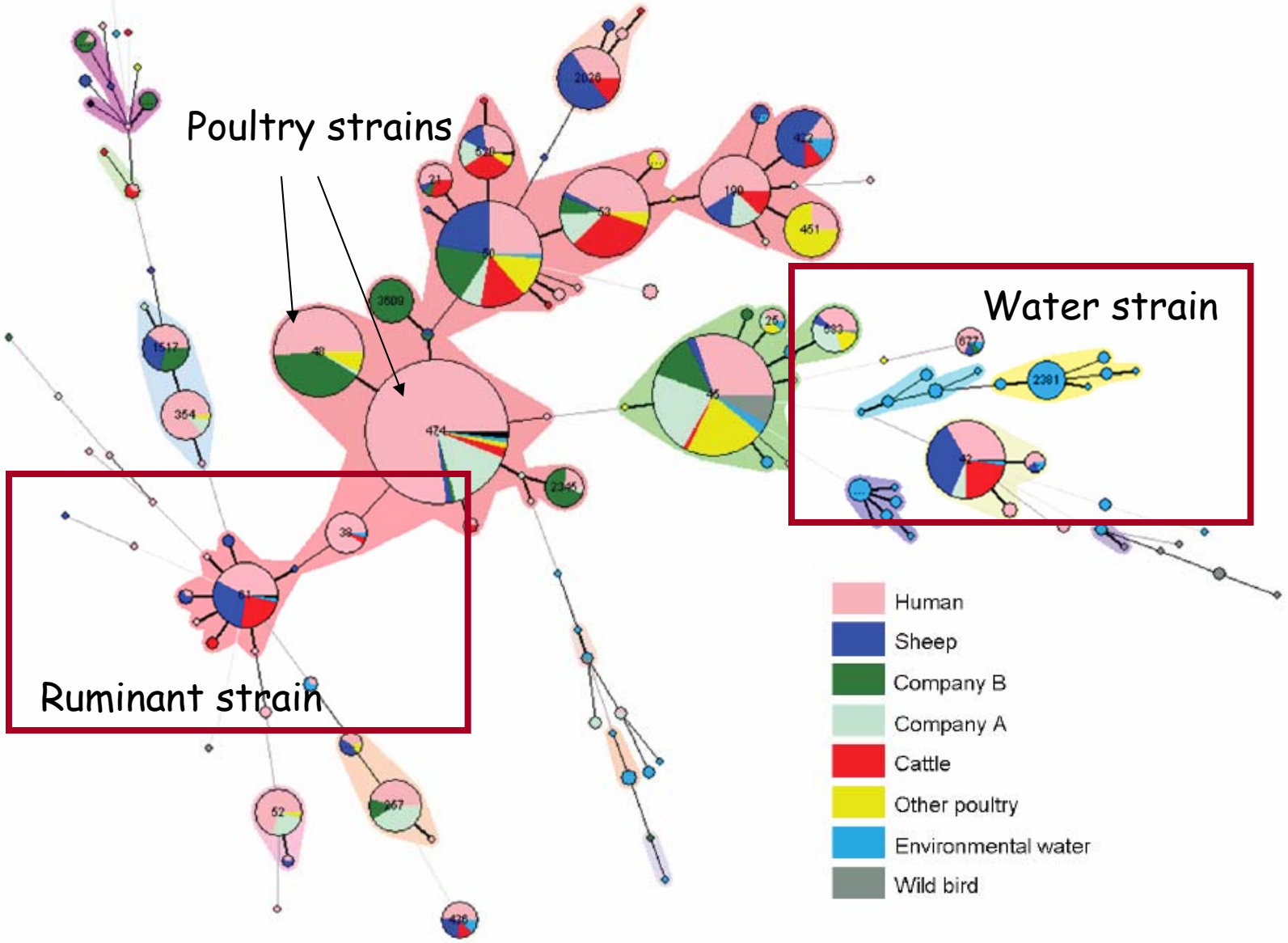
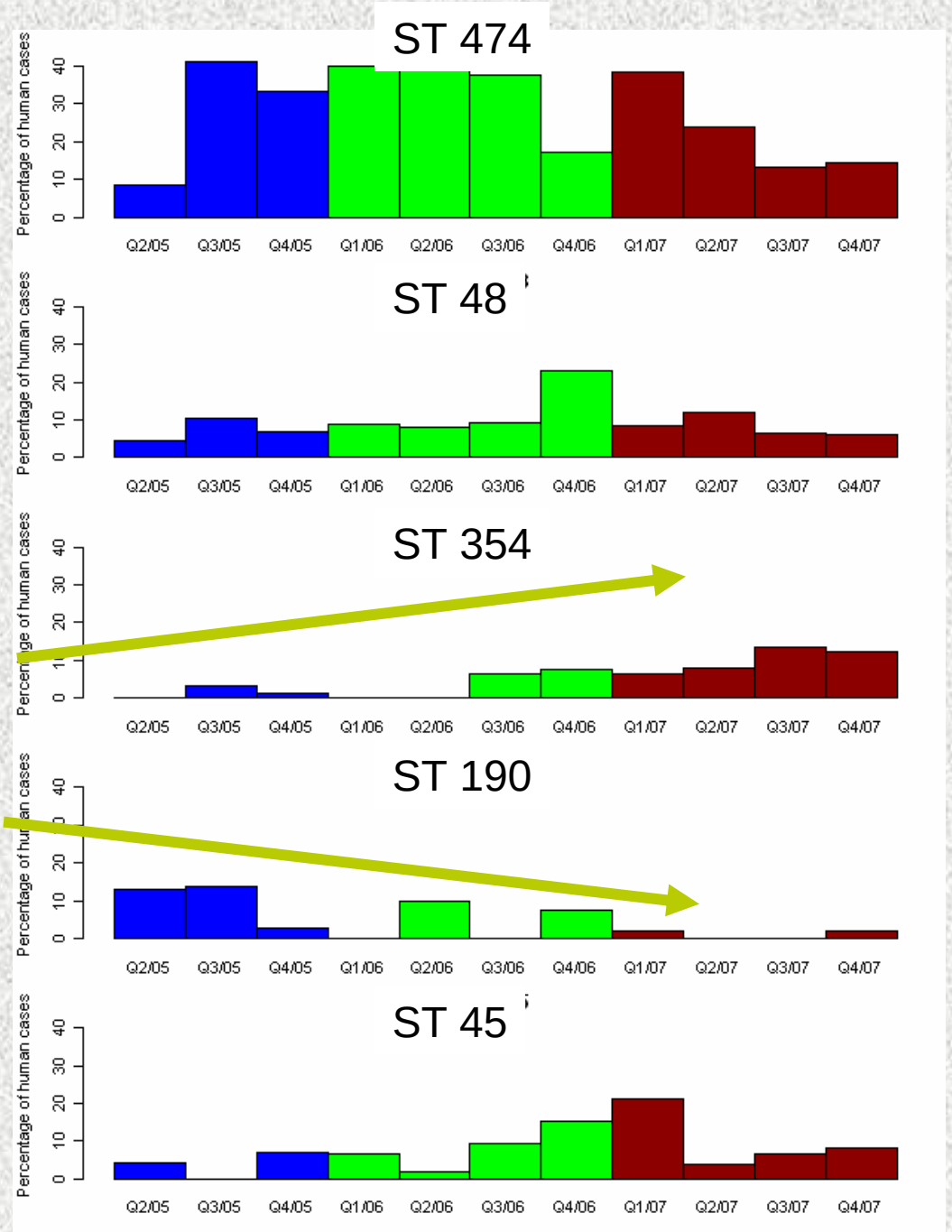
Minimum spanning tree: isolates from the Manawatu



Human cases over 3-year period



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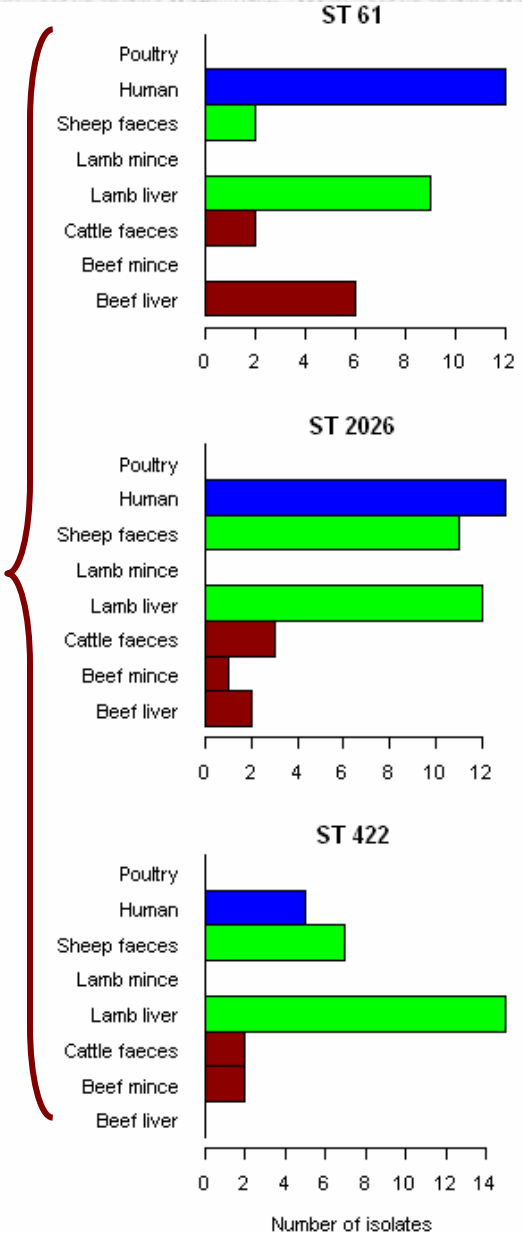
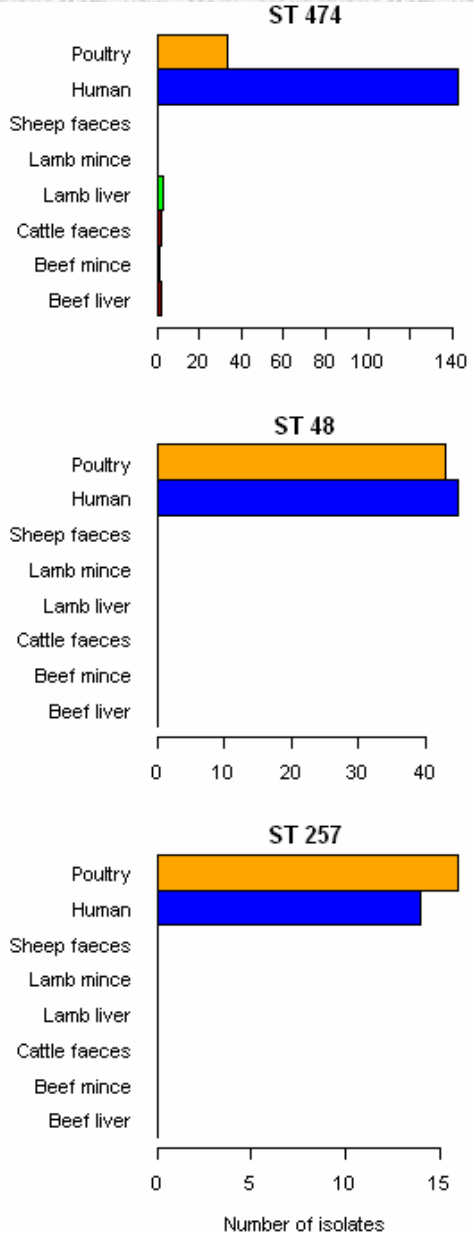
Host associated sequence types in NZ

Ruminant associated

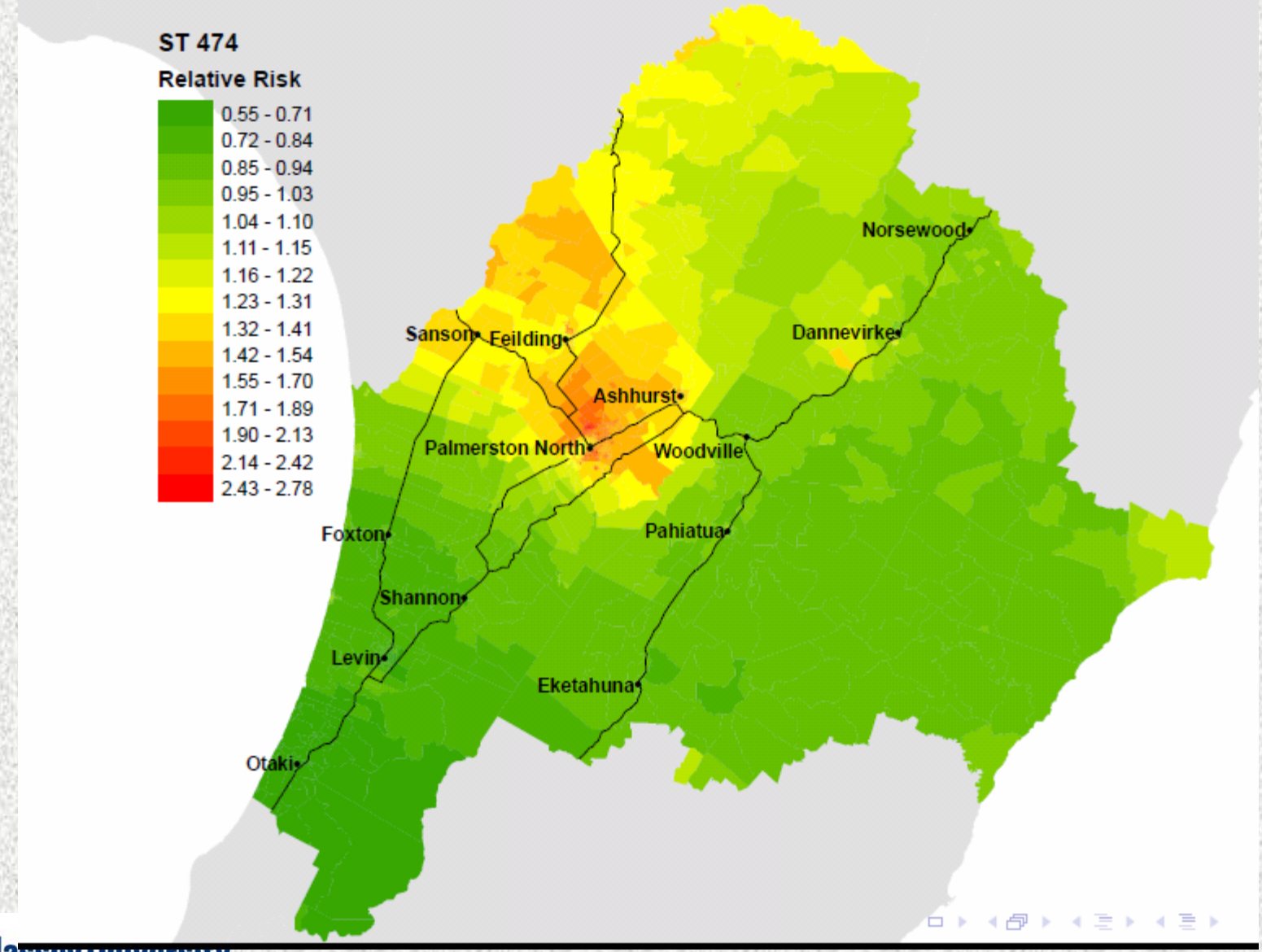




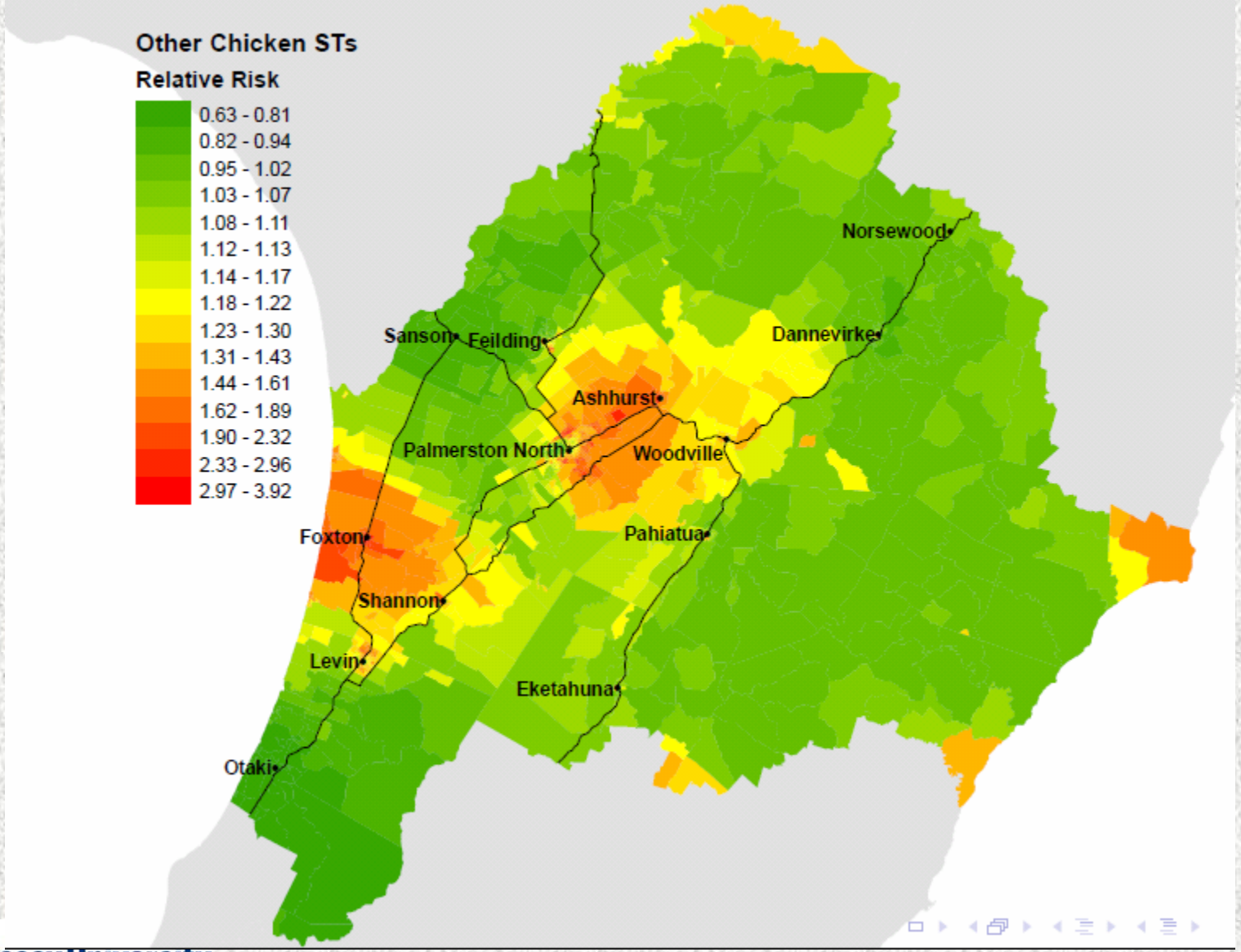
Poultry associated

Te Kunenga ki Pūrehuroa

Manawatu region: ST 474



Manawatu region: Other poultry associated STs



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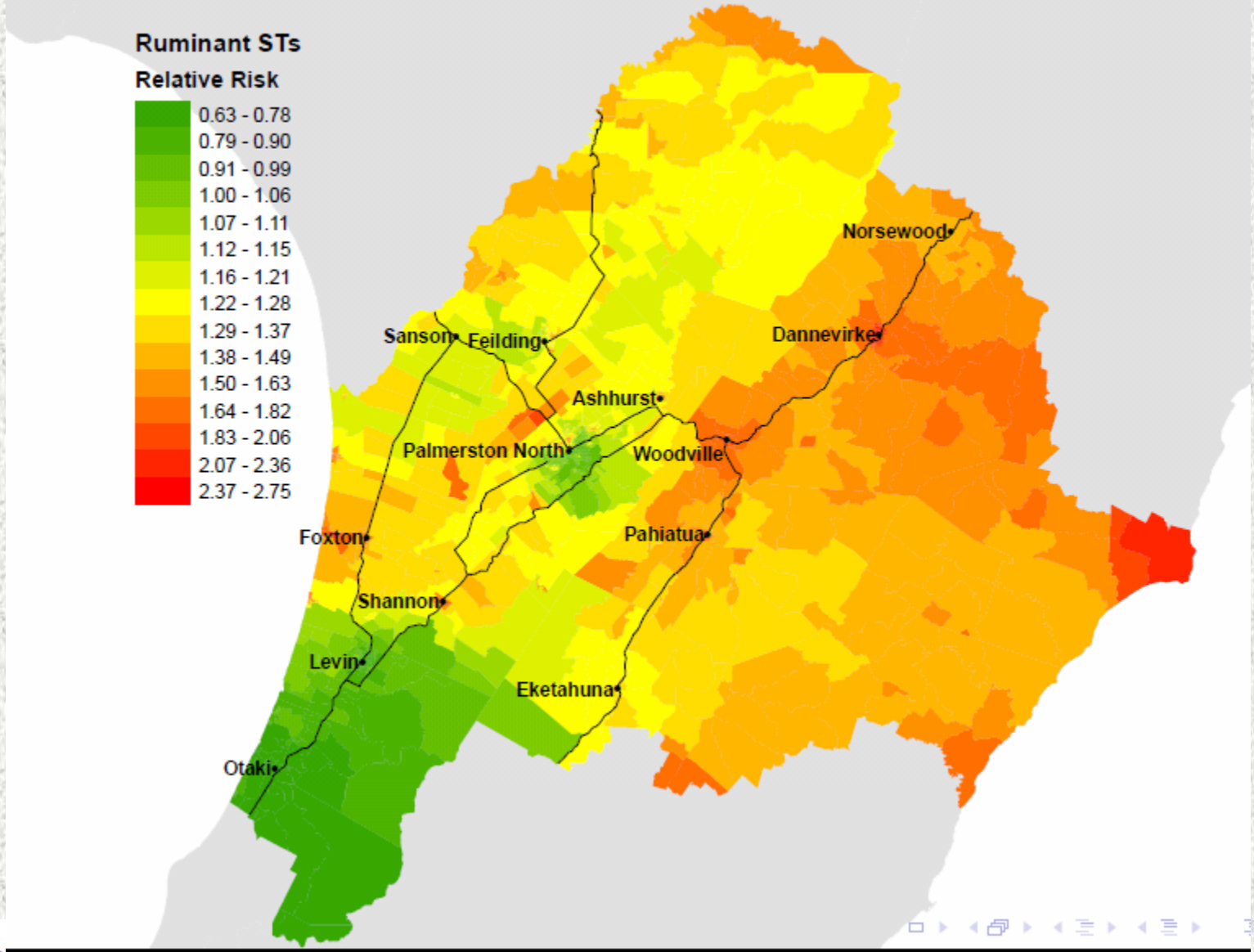
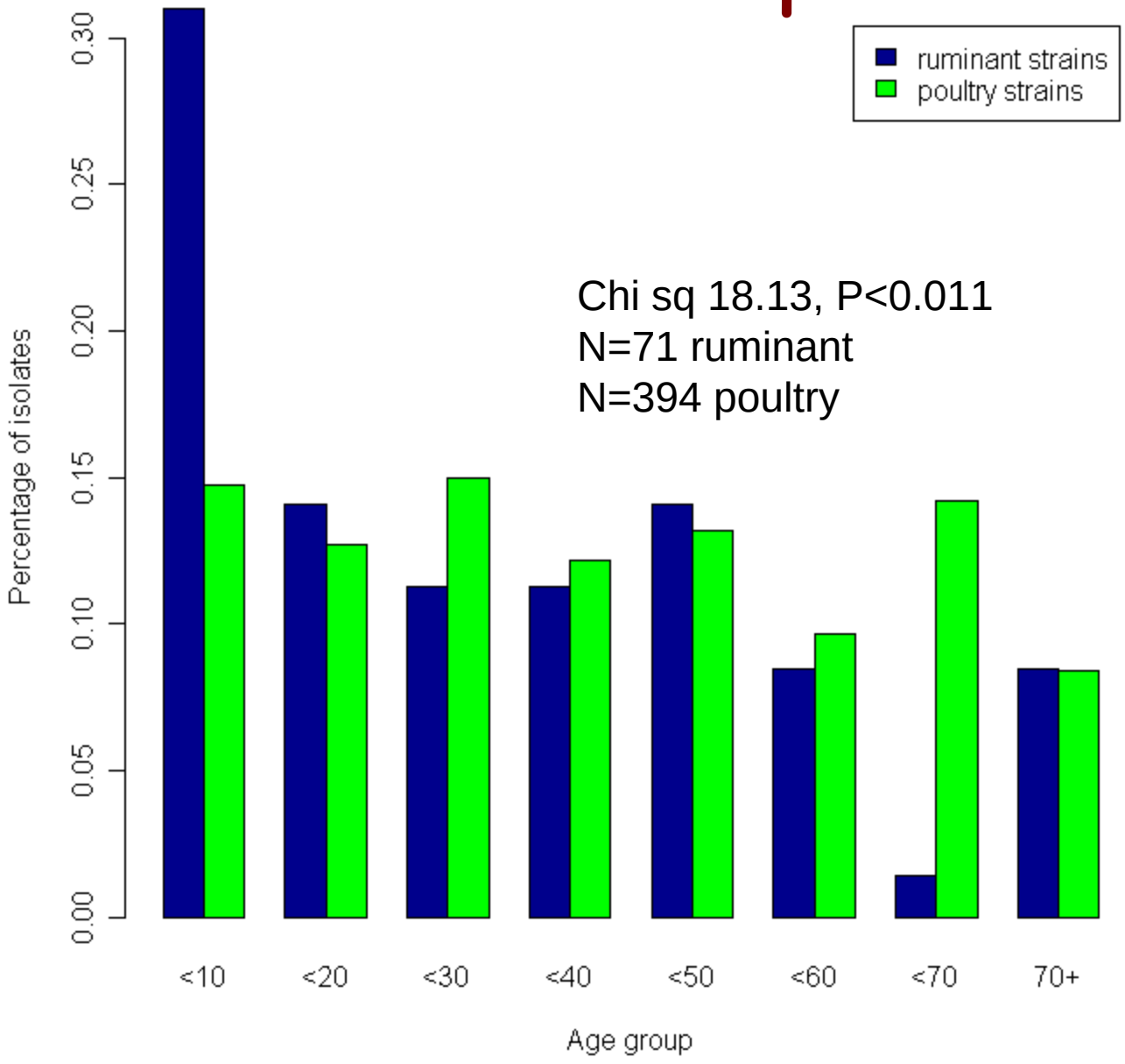
Manawatu region: Ruminant associated STs



Case-case comparison



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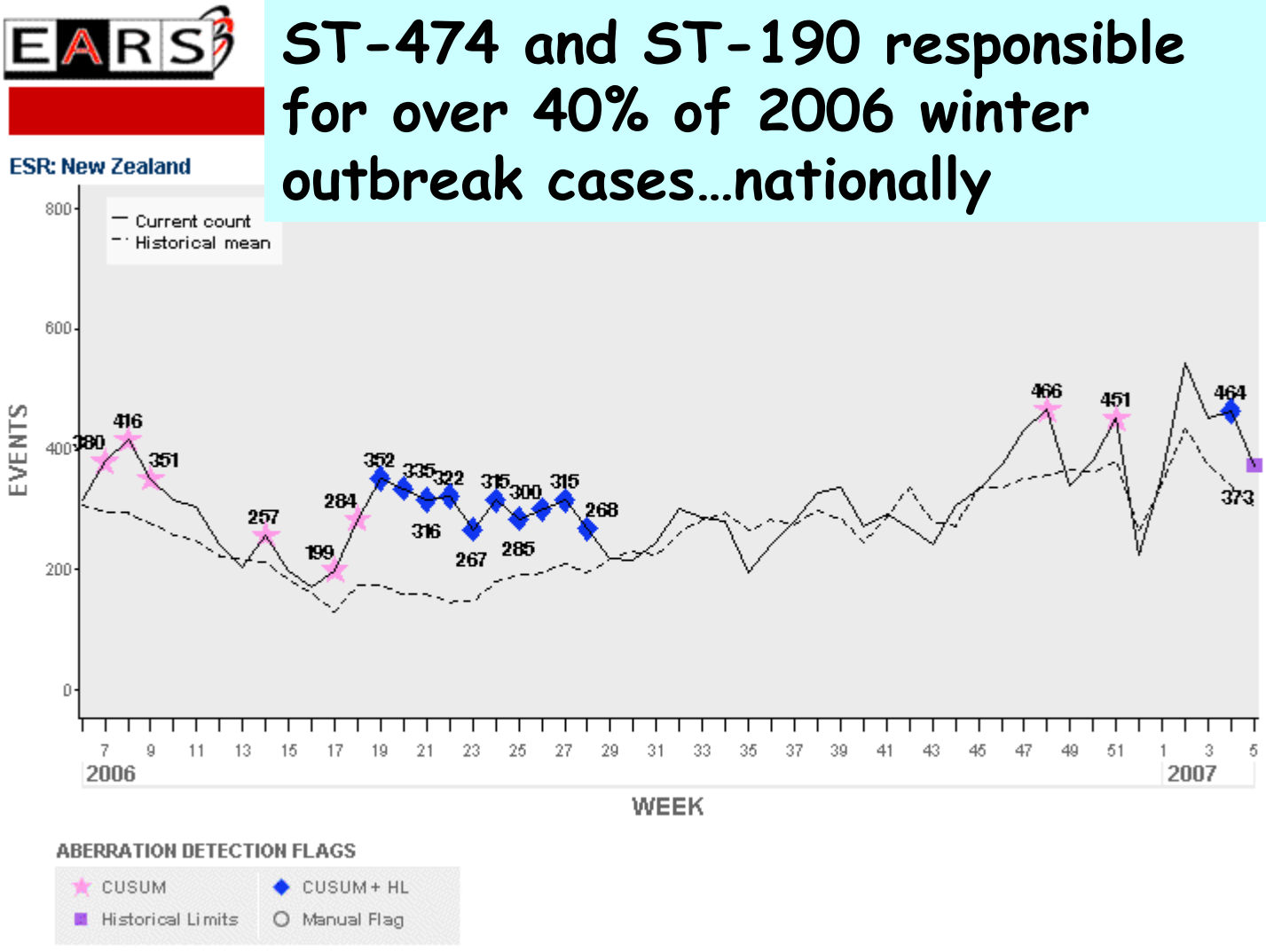
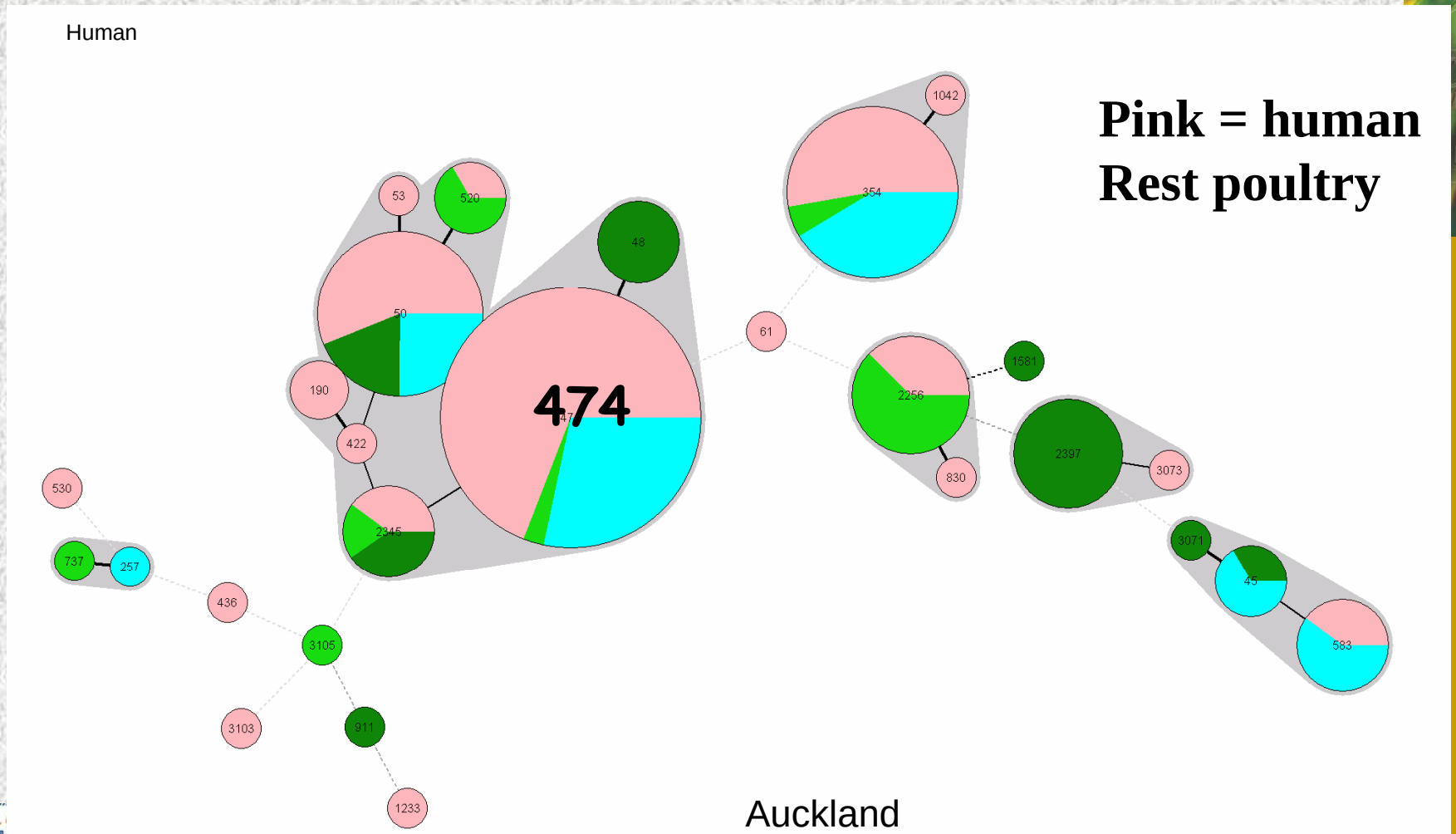
Generalised outbreak

ST-474 and ST-190 responsible for over 40% of 2006 winter outbreak cases…nationally



Te Kunenga ki Pūrehuroa

Auckland MLST (T. Wong)



Source attribution

- Molecular tools and modelling
  - Proportional similarity
    - Area of overlap
  - Dutch model
    - Simple deterministic assignment
  - Hald model
    - Bayesian model assignment with uncertainty
  - Island model
    - Population genetics approach

"I need 148 get-well cards."

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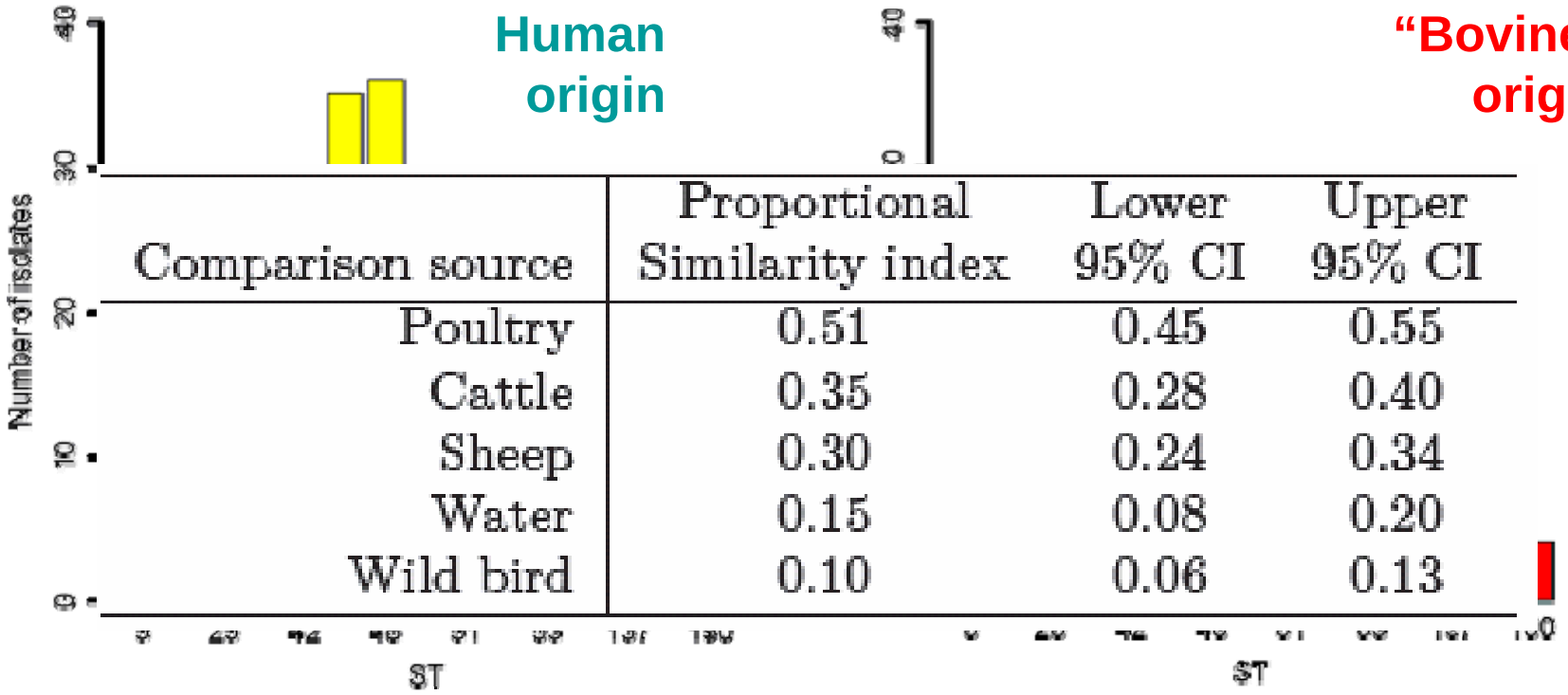
Proportional Similarity Index (PS)

The PS estimates the area of overlap between the frequency distributions of e.g. bacterial sub types from different sources.



Comparison source	Proportional Similarity index	Lower 95% CI	Upper 95% CI
Poultry	0.51	0.45	0.55
Cattle	0.35	0.28	0.40
Sheep	0.30	0.24	0.34
Water	0.15	0.08	0.20
Wild bird	0.10	0.06	0.13

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NEW ZEALAND FOOD SAFETY AUTHORITY

The Hald model (Hald et al 2004)

Number of cases of type *i* attributable to food source *j*

$$\lambda_{ij} = p_{ij}(M_j a_j)q_i$$

p_{ij} = matrix of prevalence of different strain types

M_j = relative amount of food consumed

a_j = relative 'danger' of food (or environmental) sources.

q_i = relative 'virulence' of strains.

Estimates number of cases with measure of uncertainty (Bayesian inference)

Modified Hald Model

- Model prevalence uncertainty
- Hierarchical model for bacterial parameters (q)
- Exponential prior for source specific parameters (a)
- Omit food consumption weights (M)
- Include potentially pathogenic subtypes

Island model (Wilson et al 2008)

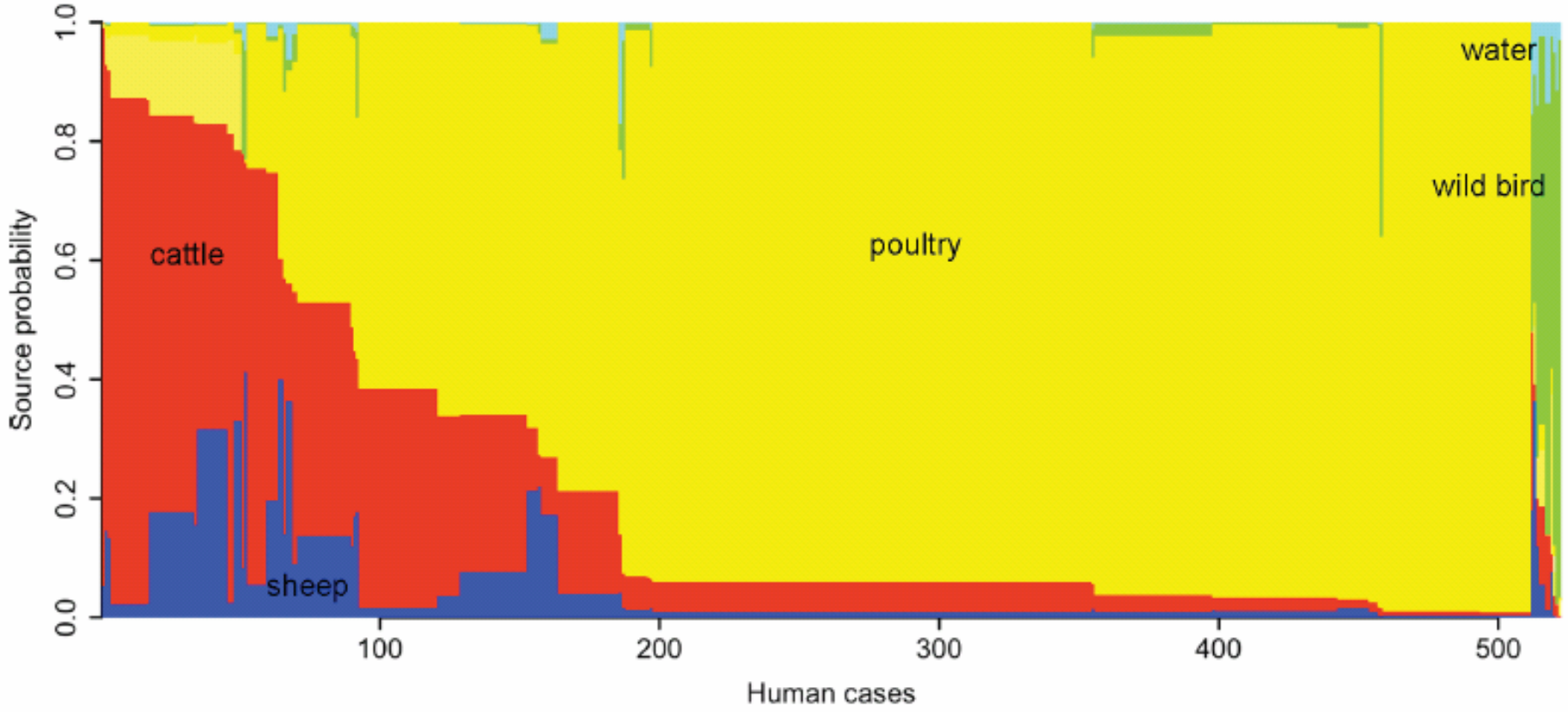
- Population genetics approach
- Genealogical method based on 'coalescent'
  - Cross-validation
- Use MLST data in animal populations ("islands") to estimate:
  - Mutation rates
  - Recombination rates
  - Migration rates (inter-host transmission)
- From these estimate 'migration' into human population
  - Source attribution

OPEN ACCESS Freely available online PLoS GENETICS

Tracing the Source of Campylobacteriosis

Daniel J. Wilson[1¤a*], Edith Gabriel[2¤b], Andrew J. H. Leatherbarrow[3], John Cheesbrough[4], Steven Gee[4], Eric Bolton[5], Andrew Fox[4,5], Paul Fearnhead[1], C. Anthony Hart[6†], Peter J. Diggle[2]

Source attribution in New Zealand: Island model



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Source of human cases, Lancashire, England

Te Kunenga ki Pūrehuroa

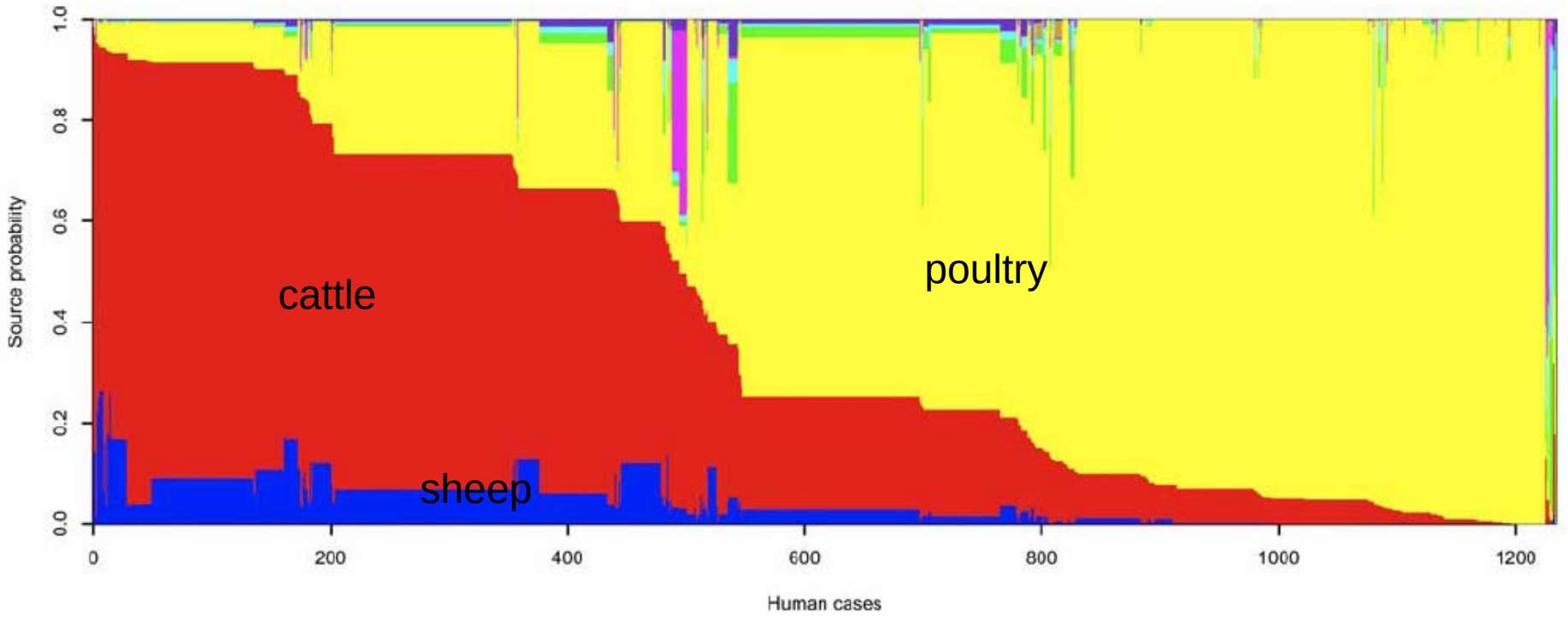

Figure 2. Probability of source for human cases. The source probability for 1,231 human cases (vertical columns) is depicted for Chicken (yellow), Cattle (red), Sheep (blue), Pig (pink), Bird (green), Rabbit (purple), Sand (beige) and Water (cyan). The isolates have been ordered horizontally to aid visualization.

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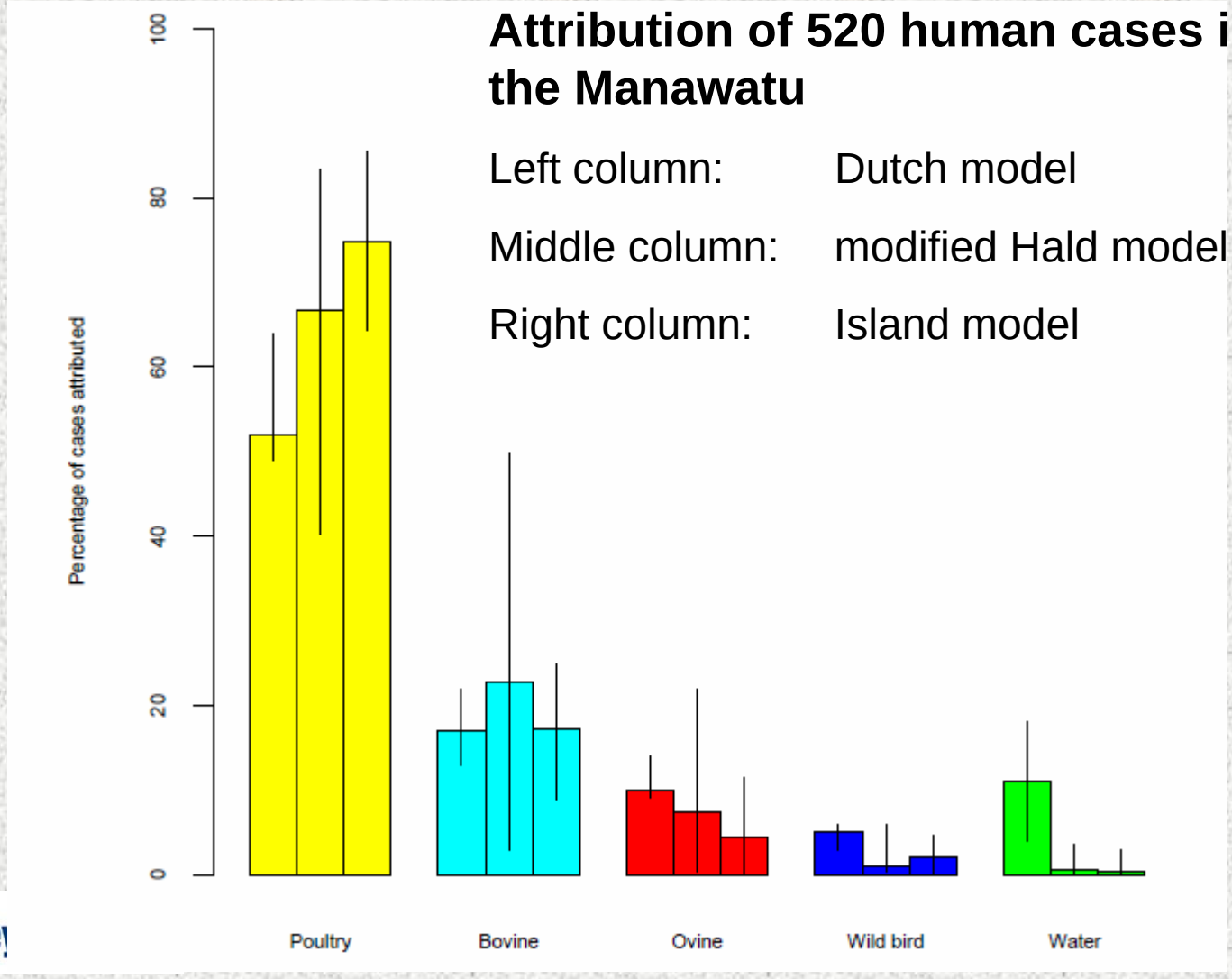
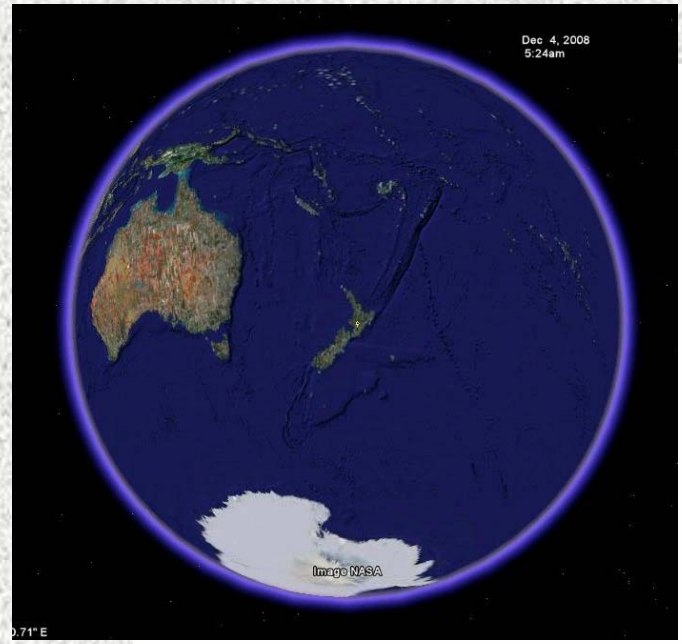
D. Wilson, Lancaster University, UK

Source attribution: comparing models



Comparing models

- PS index and Dutch models easy to compute
- m. Hald and Island models include more of information from data – more complex
- m. Hald model captures food and pathogen factors
- Island model can assign all human cases
- Therefore… recommend multiple, comparative approach…



NEW ZEALAND FOOD SAFETY AUTHORITY

Campylobacter in Poultry – Risk Management Strategy 2007 - 2010

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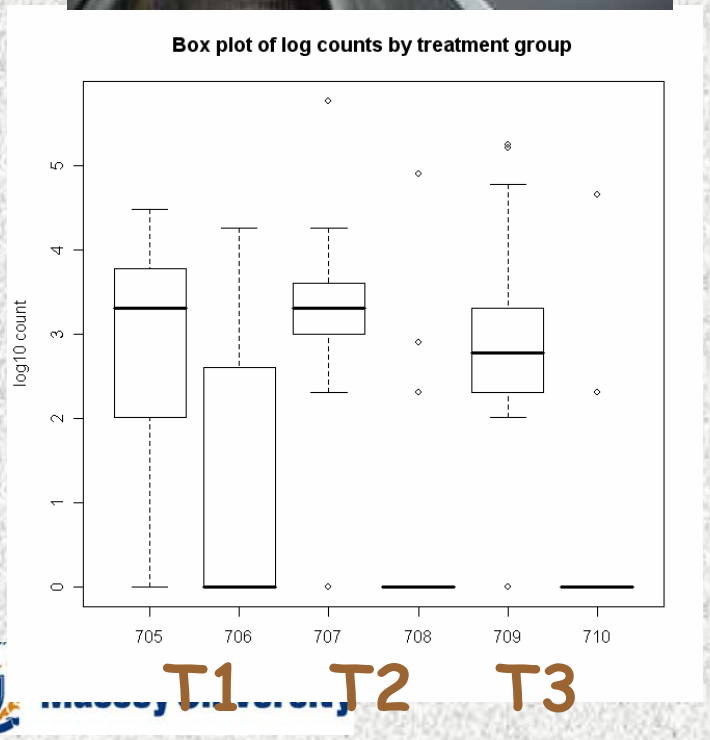
Poultry industry intervention trials



Post spin-chill:

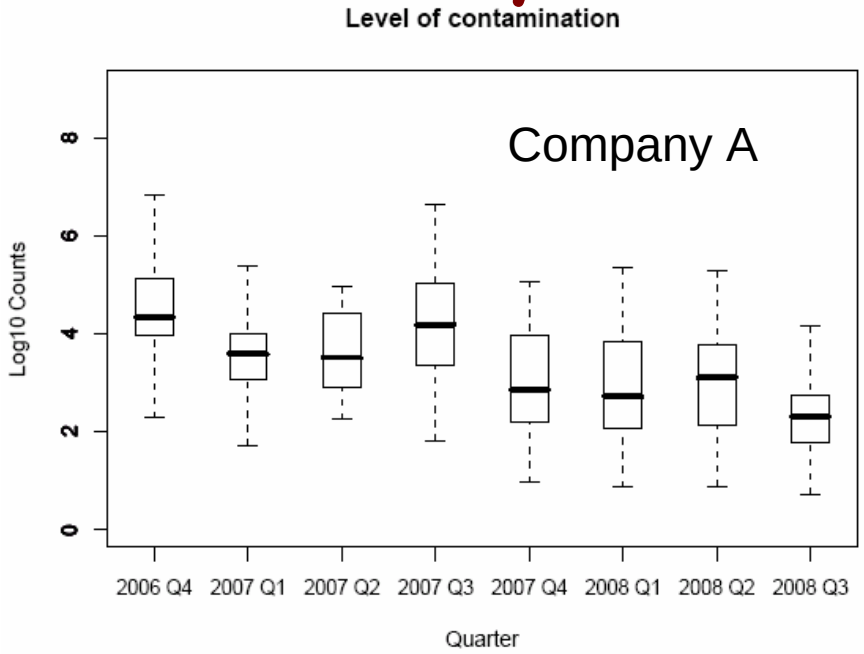
Tasker blue (Sulphuric acid and copper)

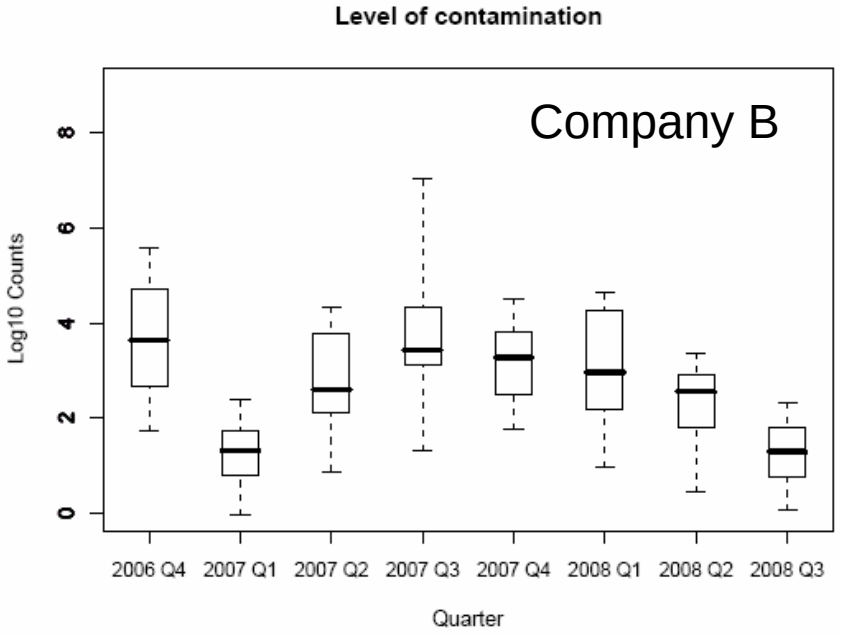
Sanova (ASC)

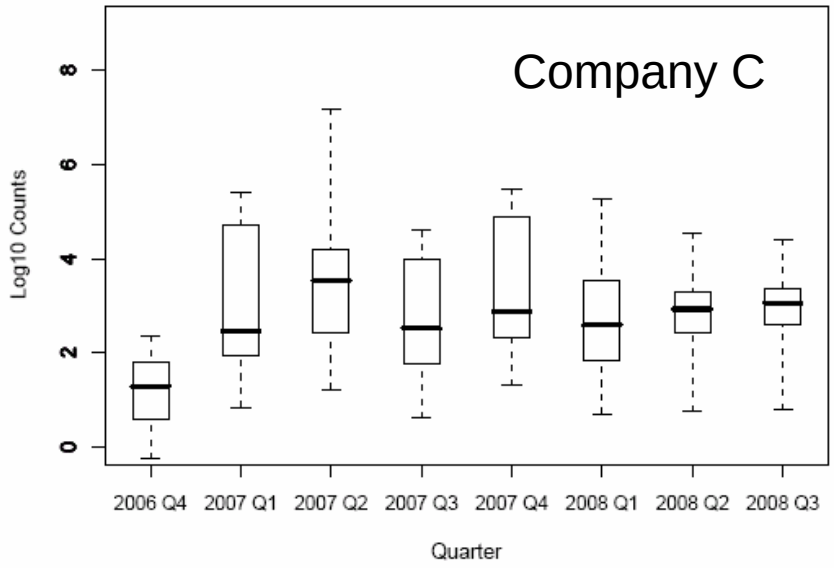
Pre spin chill:

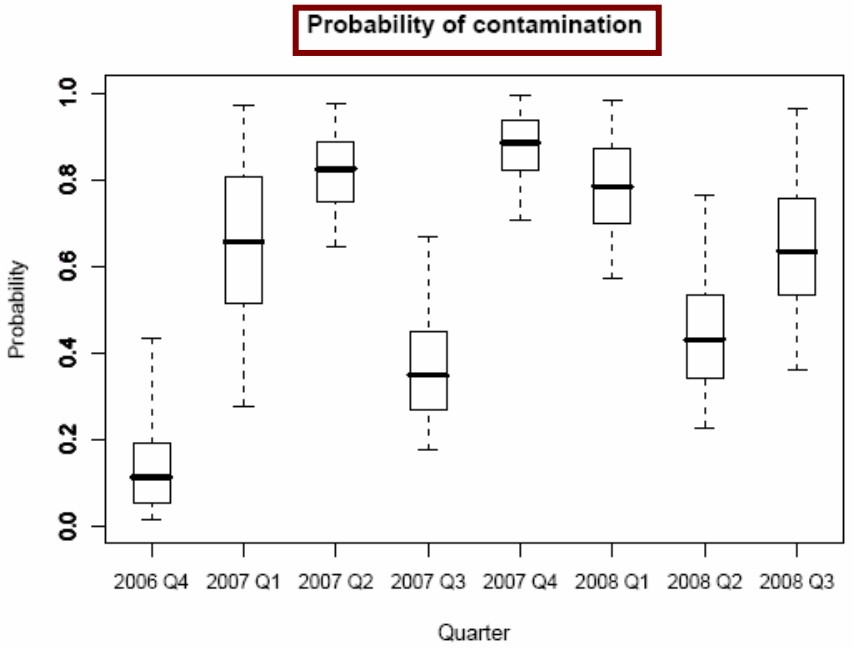
Inspexx (hydrogen peroxide and peroxyactic acid)

Poultry - count data at retail









Dramatic drop in risks from chicken - 07 Jun 2008 - NZ Herald: New Zealand National news - Windows Internet Explorer

http://www.nzherald.co.nz/section/1/story.cfm?c_id=1&objectid=10514955

Dramatic drop in risks from chicken - 07 Jun 2008 - NZ...

Winner 2008

National Story

Myspace Facebook RSS

Dramatic drop in risks from chicken

5:00AM Saturday June 07, 2008
By Geoff Cumming

Consumers can feel less nervous about putting chicken on the table after a dramatic reduction in food-poisoning rates.

Notifications of campylobacter cases have fallen by more than a third in the past year, suggesting poultry producers are finally limiting the spread of the bacteria on farms and in processing plants.

The downturn is accelerating – notifications in the first four months of this year are down by more than half.

Contaminated chicken is the biggest single source of campylobacter illness, which causes vomiting, diarrhoea, fever, headaches and muscle pain.

New Zealand's reported rates of the illness are higher than those of comparable countries, and chicken is blamed for about 50 per cent of cases.

Up to 1000 people are hospitalised each year because of campylobacter

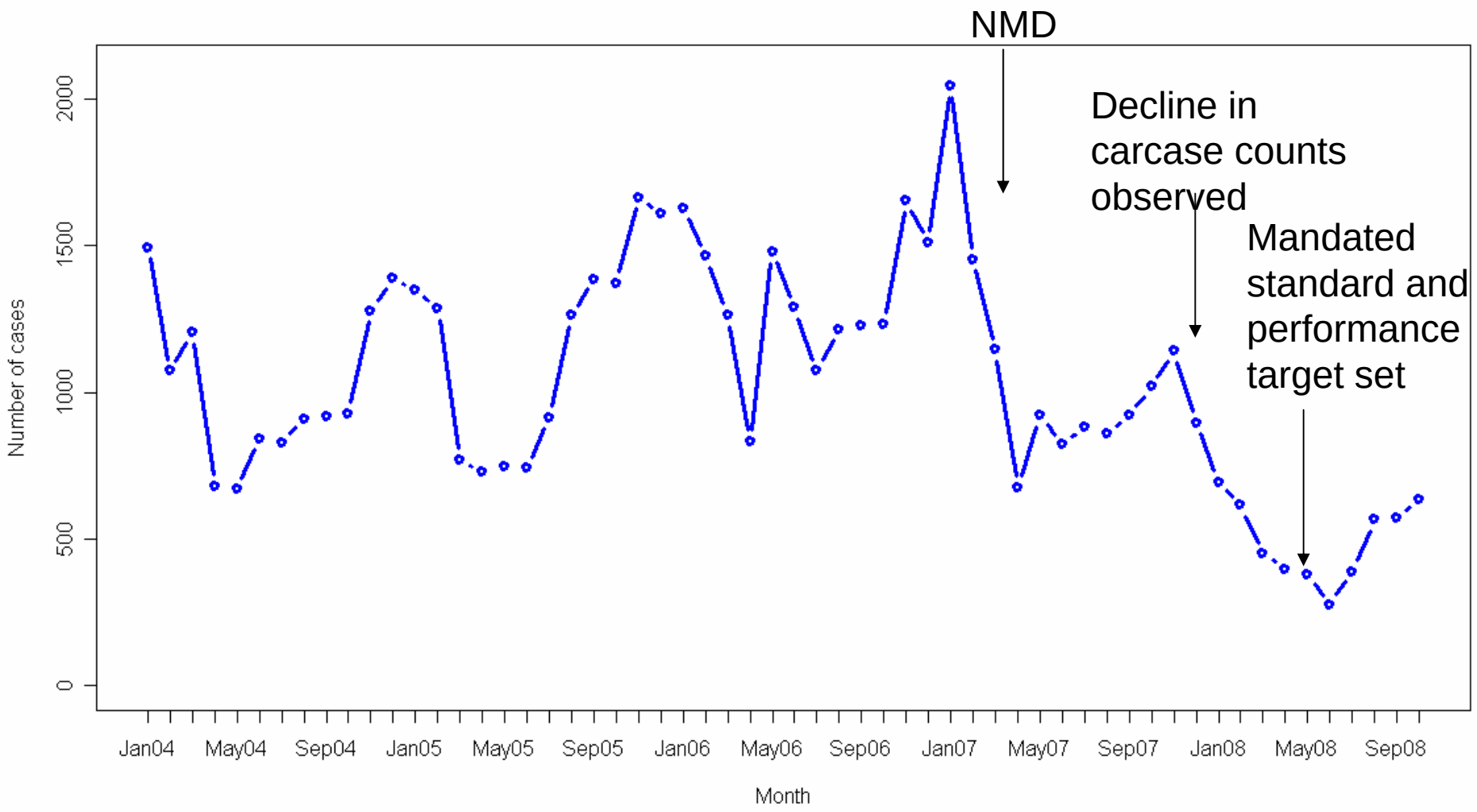
National Headlines

- Schools boycott Labour's big plan over funding
- Migrants contribute much more than locals
- Fraudster link shocks sports star
- Officers sprayed and beat man, jury told
- UPDATED 8:56AM Judge questions legality of abortions
- NEW 9:49AM Police no closer to finding truck driver who hit girl
- UPDATED 9:14AM Gas leak spurs Turangi evacuation
- NEW 9:12AM Victim fights rapist's parole at High Court
- Three in court after video store robbery
- Plea change for Jhia murder allowed
- Japanese student dies after road accident
- UPDATED 8:25AM Falling oil price may ease petrol price threat
- All Blacks still pull in crowds
- The 'awful, senseless' death of a loving family man (+photos)
- President vouches for visa chief's character
- Bill changes limit growth of civilian roles in police force
- Labour leaflet decision upheld
- Health board slashing electricity, gas and water use

Internet

start | privat - Mi... | Presentati... | EndNote X | 2 Micros... | 4 Micros... | Dramatic d... | EN

Recent trends in NZ



Early Aberration Reporting System

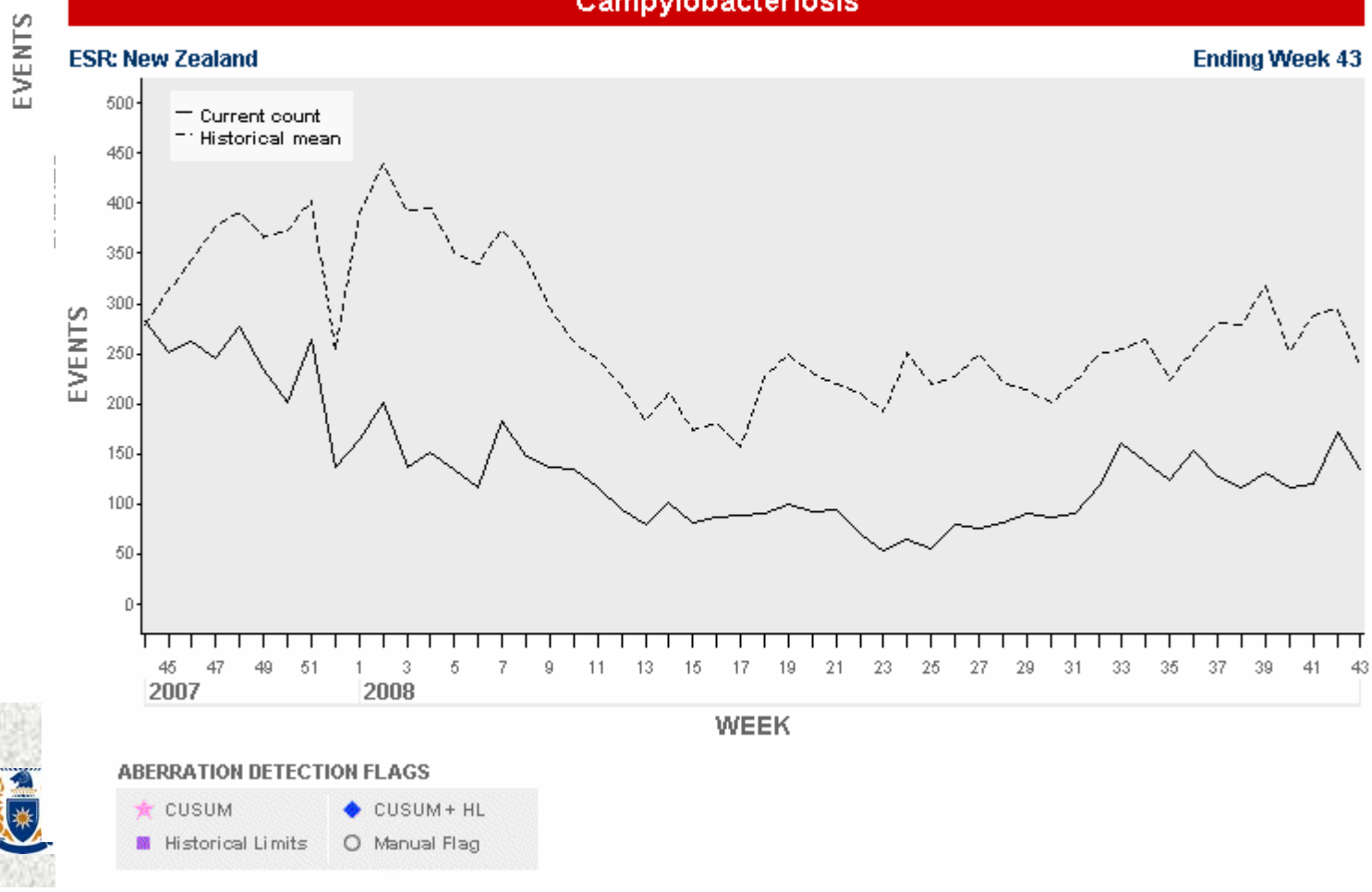
Salmonellosis

ES Early Aberration Reporting System

Cryptosporidiosis

Early Aberration Reporting System

Campylobacteriosis



50% reduction

Te Kunenga ki Pūrehuroa

Conclusions

- NZ has unique epidemiology
  - Rural ruminant exposure in young children
  - Urban poultry across all ages
  - Dominant strain: ST474
- Source attribution modelling
  - Tools advanced in recent years
  - Applied to *Campylobacter* identified food, particularly poultry, most important source, cattle second
- Focussing on poultry – early signs of success
- Environmental exposures less well defined
  - May become more important
  - Ruminants and wildlife

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Te Kunenga ki Pūrehuroa