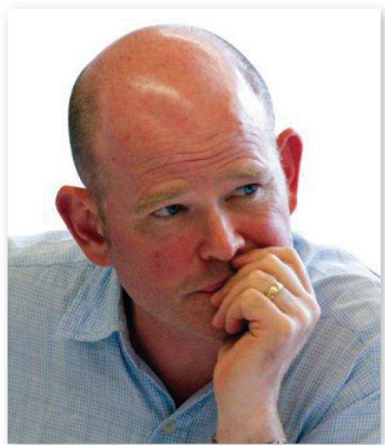




Professor Nigel French

Food Safety and Veterinary Public Health
Massey University
Palmerston North

Friday, June 9, 2017

(Room 7)

16:30 - 17:25 WS #70: Campylobacter - If The Chicken Doesn't Get You, the Groundwater Will

17:35 - 18:30 WS #82: Campylobacter - If The Chicken Doesn't Get You, the Groundwater Will
(Repeated)

Campylobacteriosis: if the chickens don't get you the groundwater will

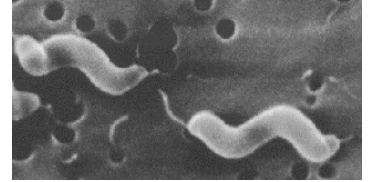
Nigel French

GPCME, Rotorua, June 9th 2017



Some questions to address

- Where are people getting infected from in New Zealand?
- How does this differ between urban and rural areas?
- What is the role of poultry compared to ruminants and wild birds?
- What is unique about New Zealand? – why do we have such high rates compared to other countries?
- How important was the emergence of the antimicrobial resistant strain of *Campylobacter jejuni* in 2014?
- What happened in Havelock North and how can we prevent it from happening again?
- What needs to be done to reduce the risk to New Zealanders from all campylobacteriosis?



My background

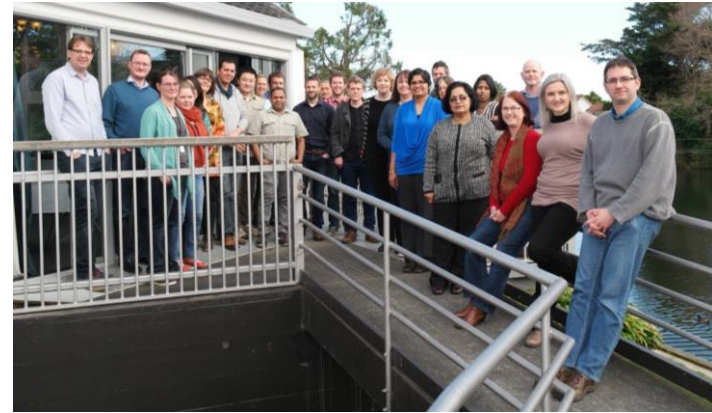
- Training:
 - veterinarian (Bristol)
 - epidemiologist (London)
- Research:
 - Molecular epidemiology
 - Infectious diseases
 - Food and water safety



^mEpiLab: Molecular Epidemiology and Public Health Laboratory

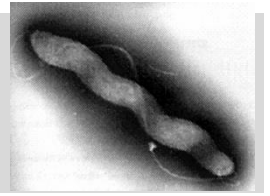
Research lab - we work on:

- Food safety
- Water quality
- Tools for surveillance
- Modelling to inform policy
- Molecular epidemiology of zoonoses
 - *Campylobacter*
 - STEC (*E. coli* O157)
 - *Cryptosporidium*, *Giardia*
 - *Leptospira*
 - *Salmonella*
- Run campylobacteriosis sentinel site
- Provide source attribution for MPI
- Outbreak investigation support



<http://mepilab.massey.ac.nz>

Campylobacteriosis



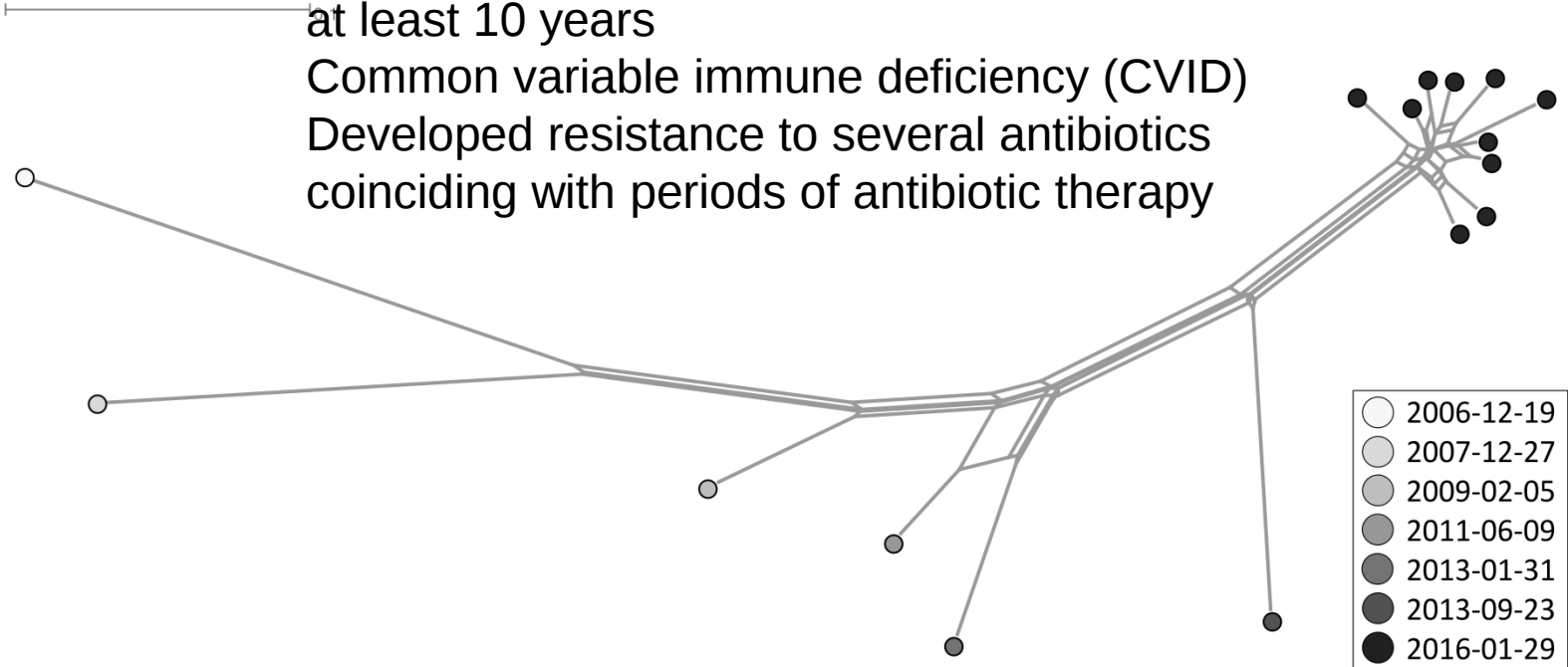
- Mainly *C. jejuni*, *C. coli*
- Diarrhoea, stomach pain, fever in most
- Vomiting and bloody diarrhoea in 1 in 3 cases
- ~ 1 in 15 cases hospitalised
- Complications
 - Guillain Barre syndrome



Long term infection

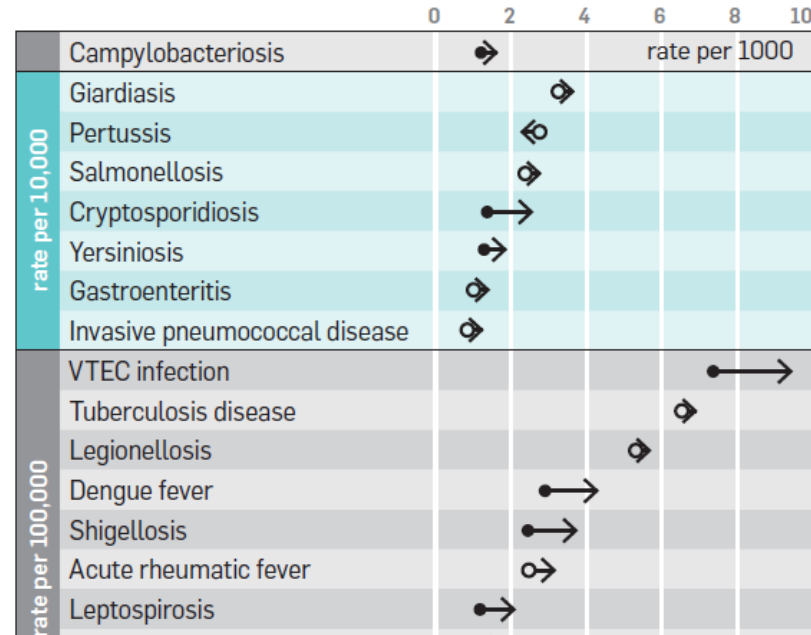
Patient in NZ colonised with same strain for
at least 10 years

Common variable immune deficiency (CVID)
Developed resistance to several antibiotics
coinciding with periods of antibiotic therapy



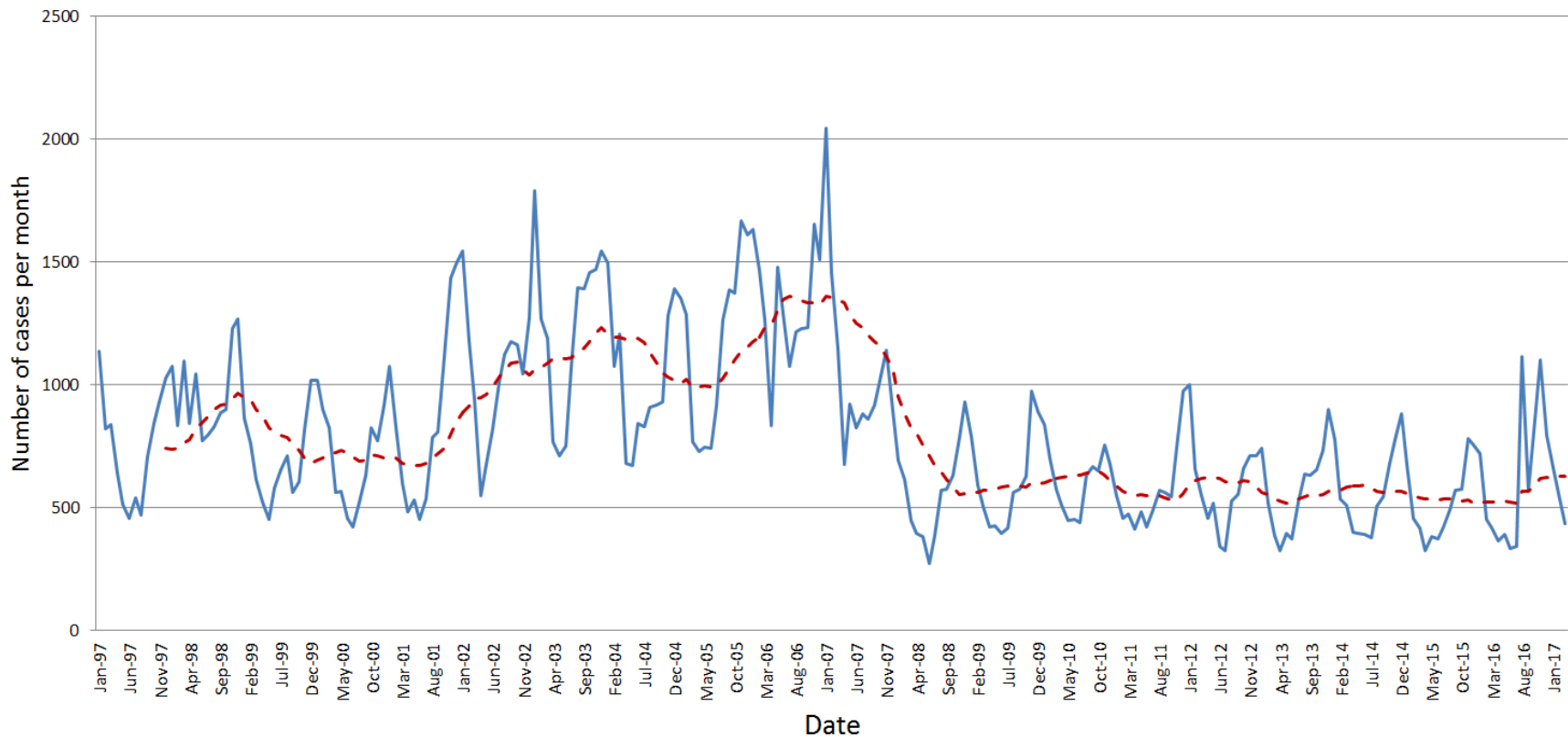
Campylobacteriosis still top of the list of notifiable diseases

National surveillance data 12-monthly notification rate changes¹

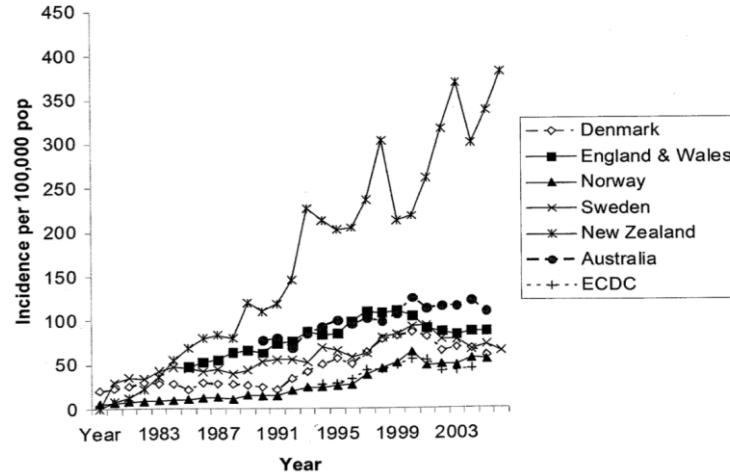
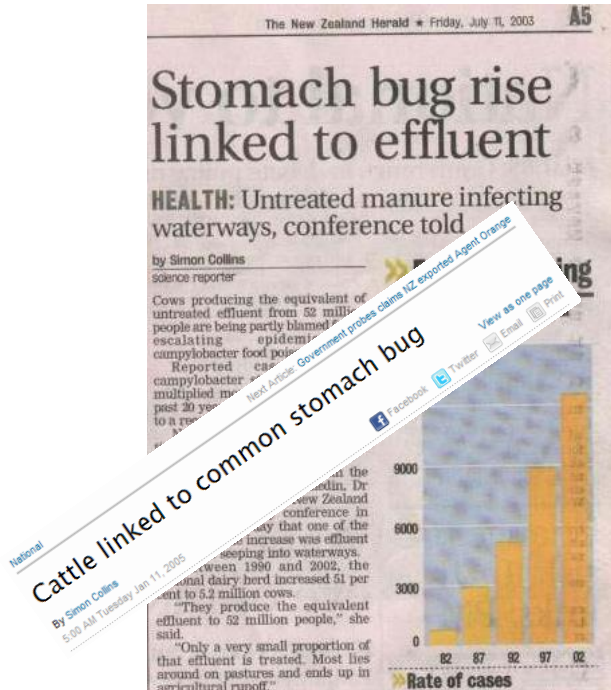


Source: ESR Ltd
Quarter to March 2017

Campylobacteriosis notifications



Campylobacter in NZ: 1980-2006



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

Manawatu sentinel site 2005-2017

- 'One health' approach: human, animal and environment
- Identify strain types common to particular sources
- Modelling (source attribution)

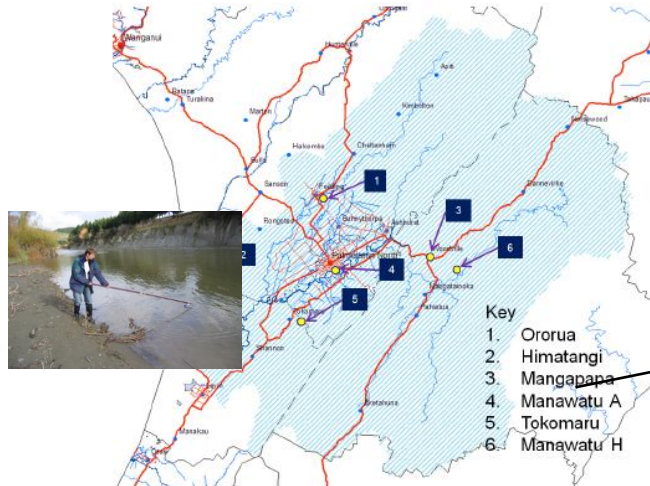
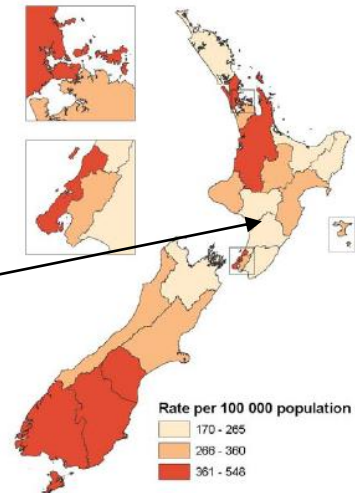
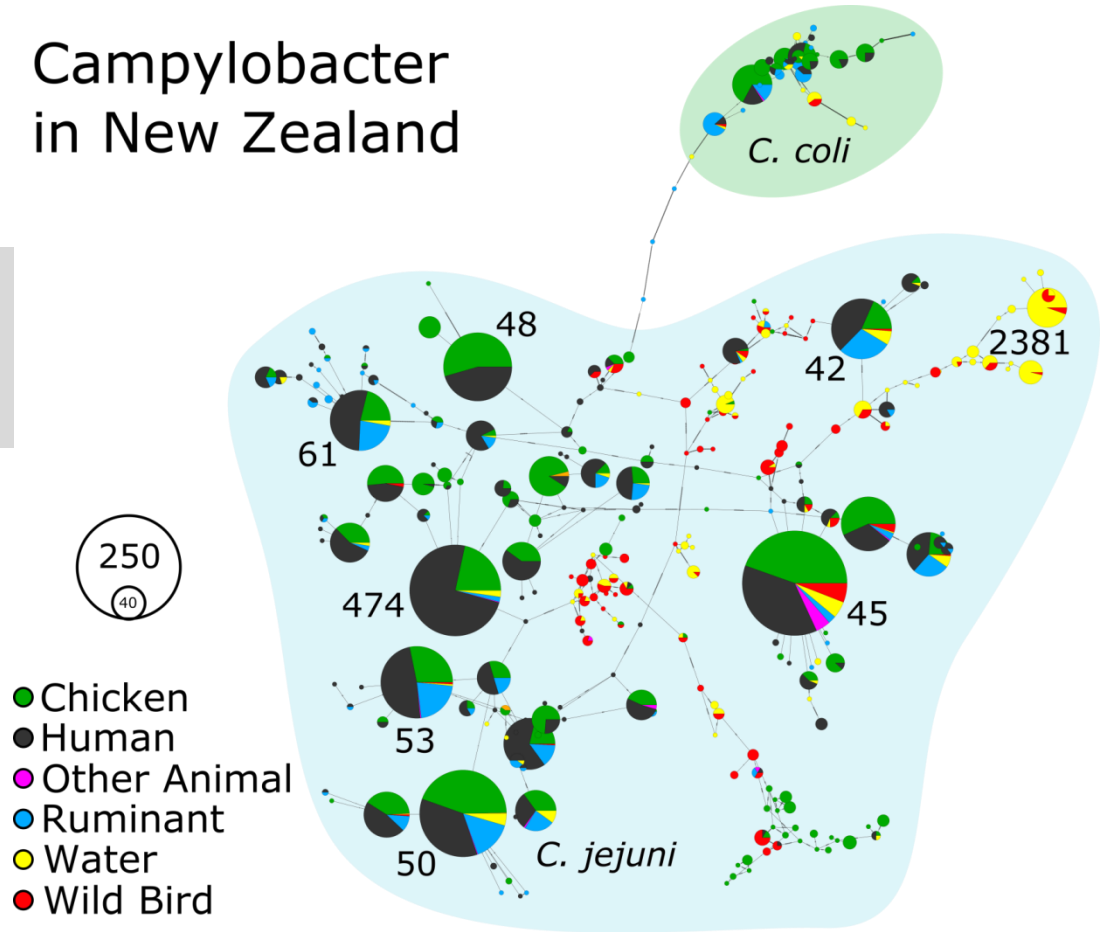


Figure 7. Campylobacteriosis notifications by DHB, 2004



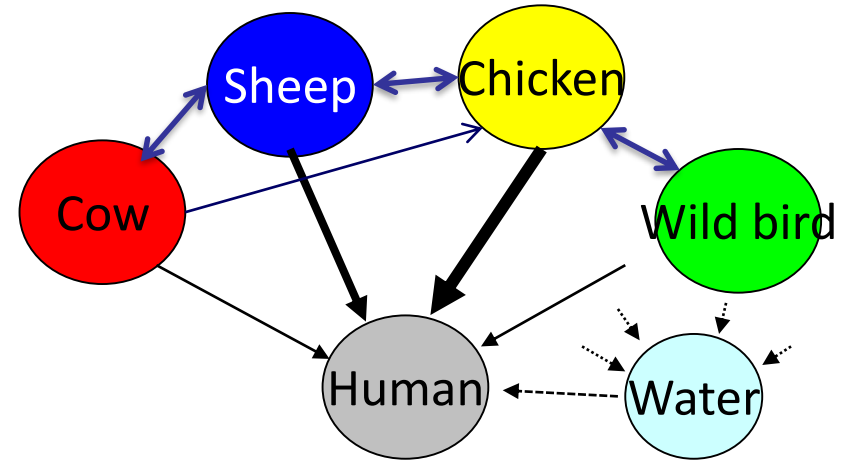
Campylobacter in New Zealand

Campylobacter strains
in different sources

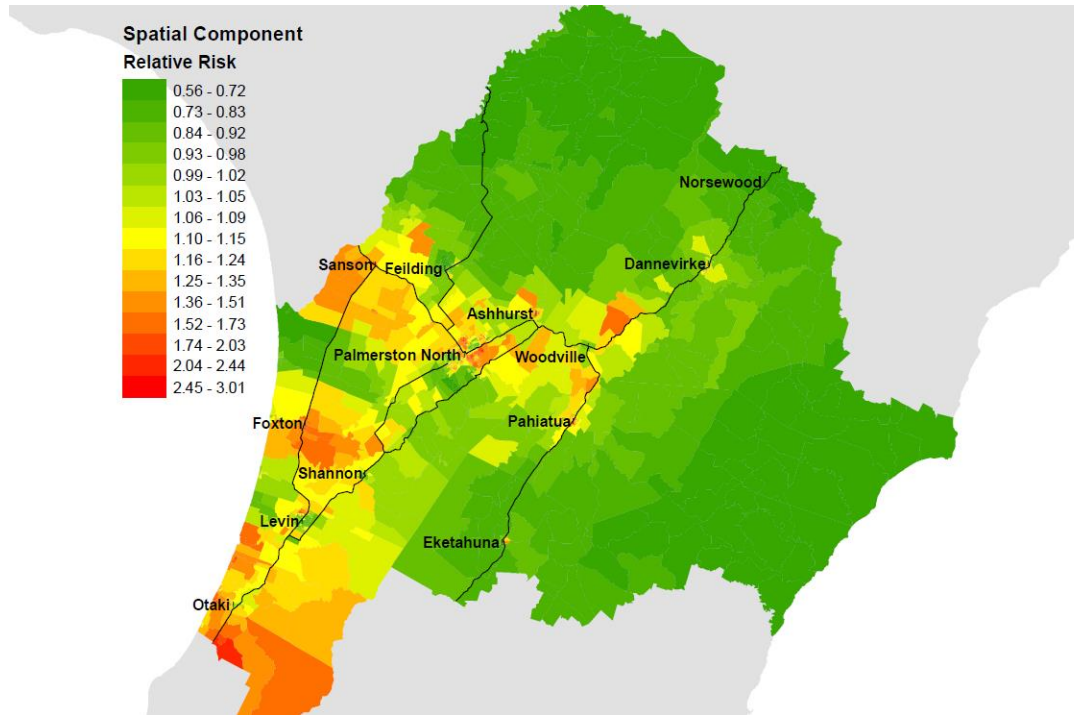


Identifying the source of infection

- Use DNA sequences to model 'gene flow'
- Used to find out source of human infections
- Flow into the human "island" from animal "islands"

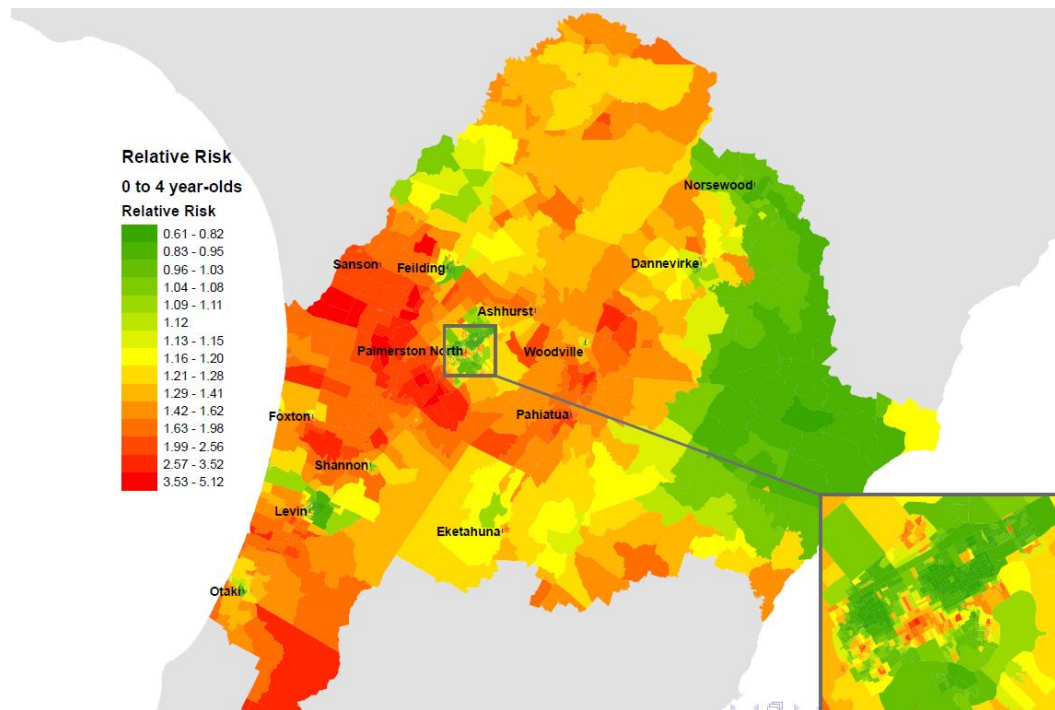


Relative risk surface of human campylobacteriosis notifications in the Manawatu

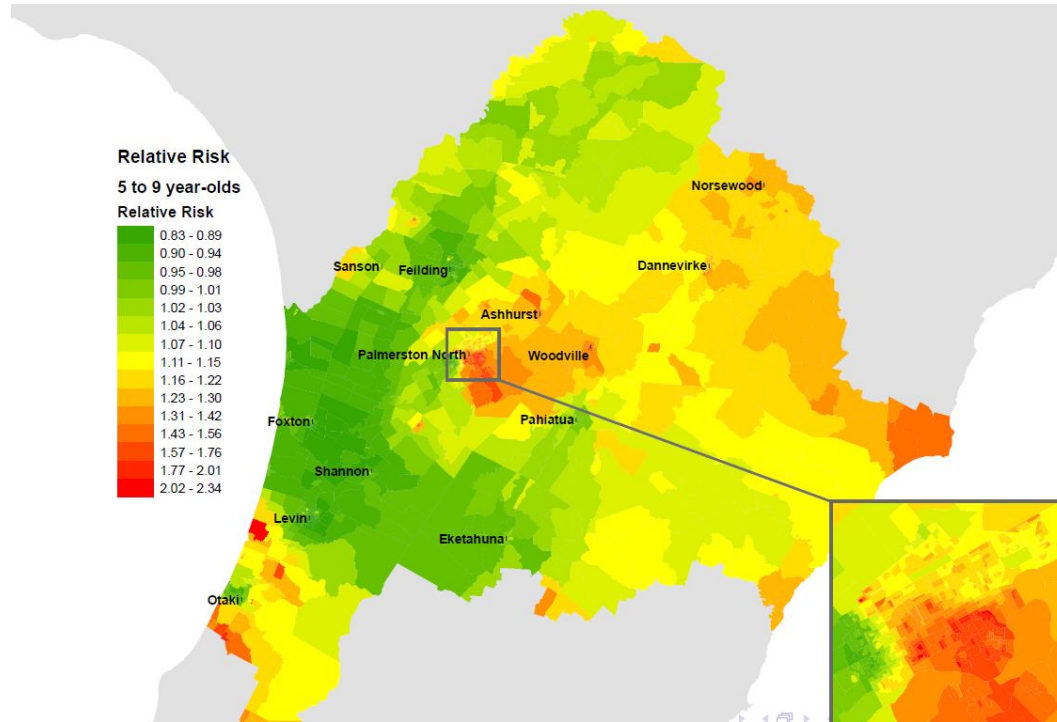


Red is higher risk
Green is lower risk

Pre-schoolers mainly in rural areas



Older children and adults in urban areas

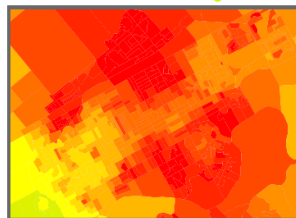
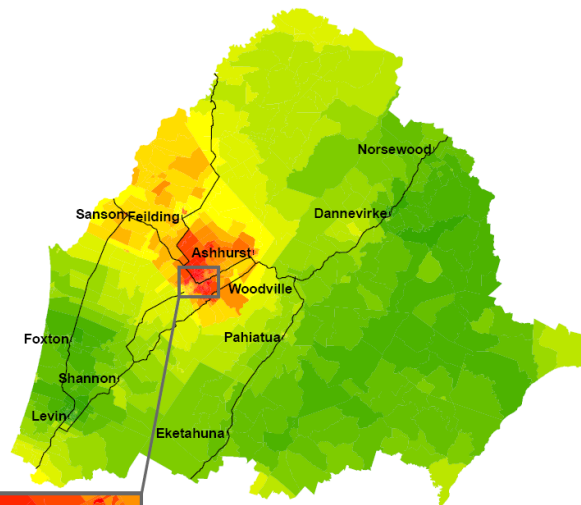
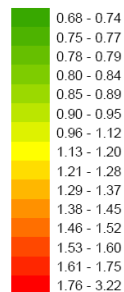


Poultry cases in urban areas



ST 474

Relative Risk

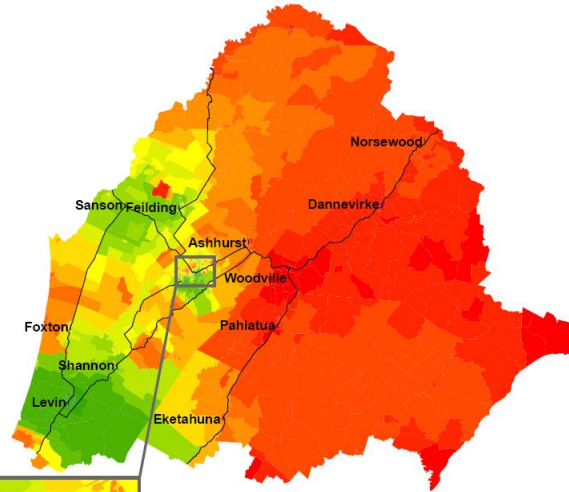
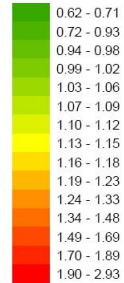


Ruminant cases in rural areas

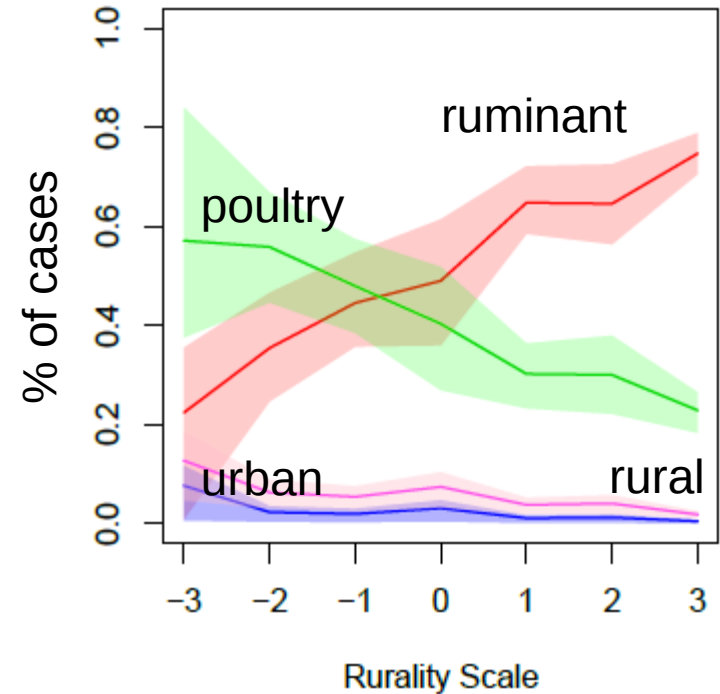
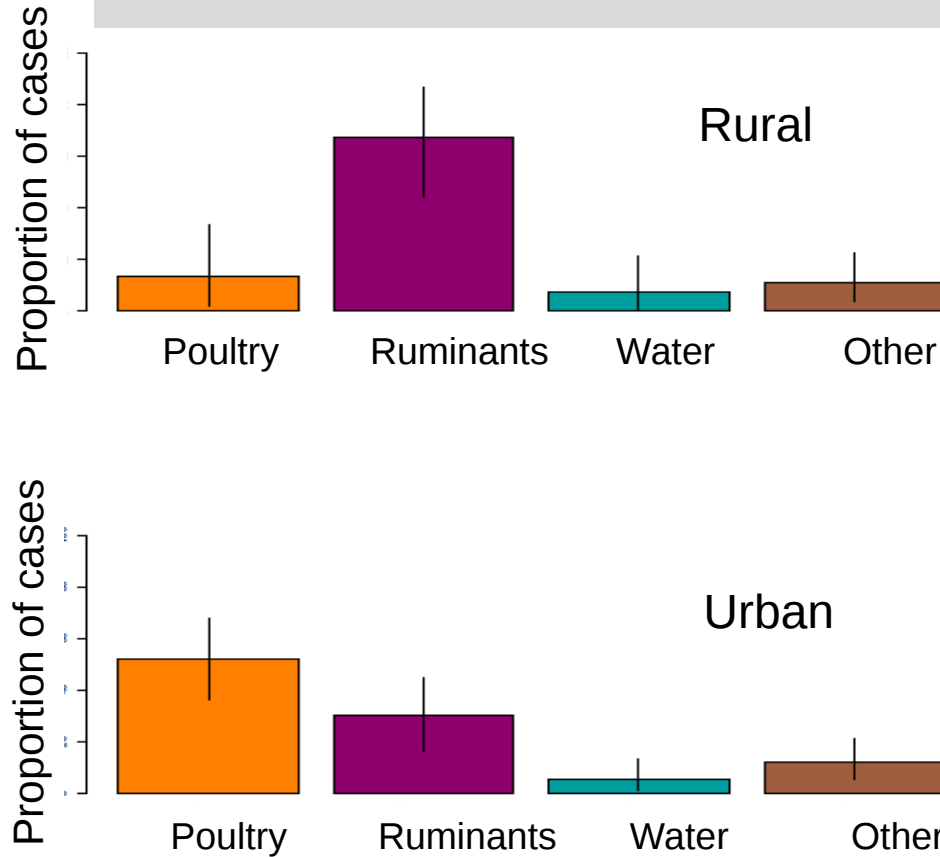


Ruminant STs

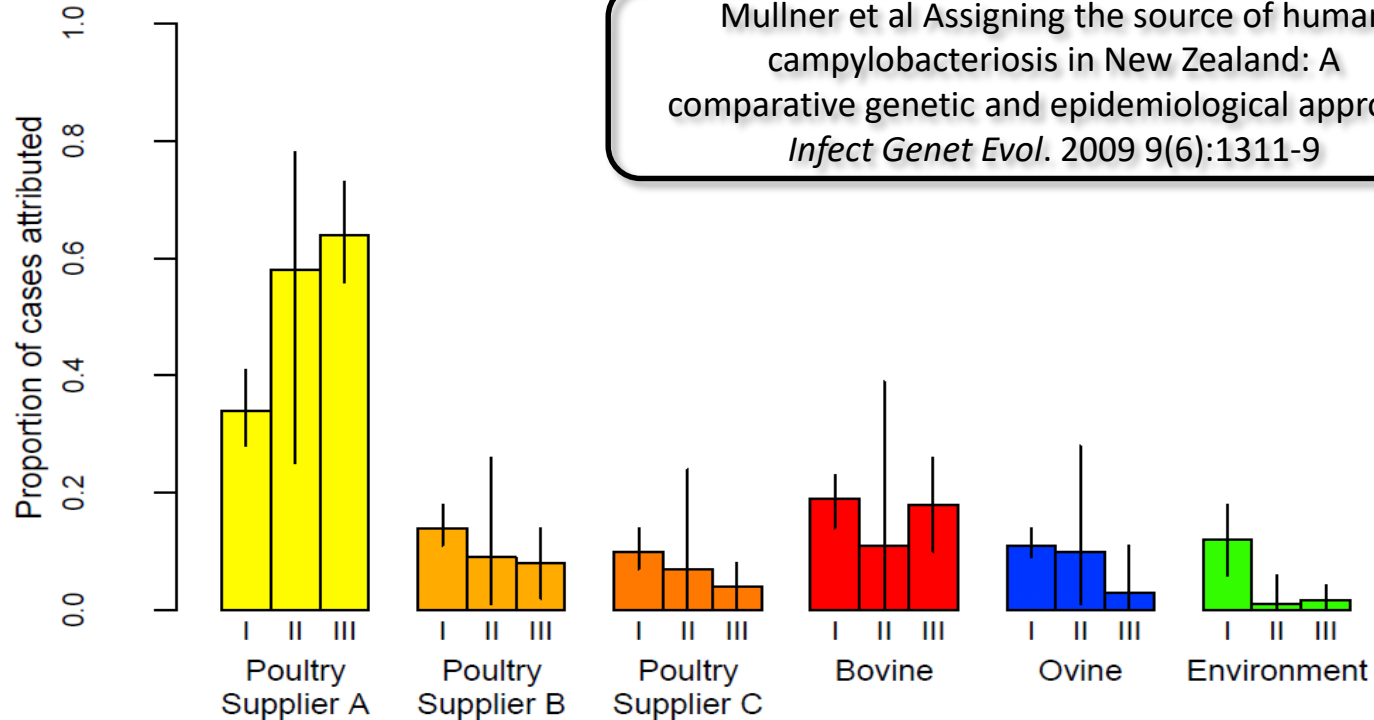
Relative Risk



Different sources for urban and rural dwellers



Poultry identified as main source of cases overall



Poultry industry interventions



- No single intervention
- Review of options presented to industry
- Spin / immersion chiller
- Evisceration equipment

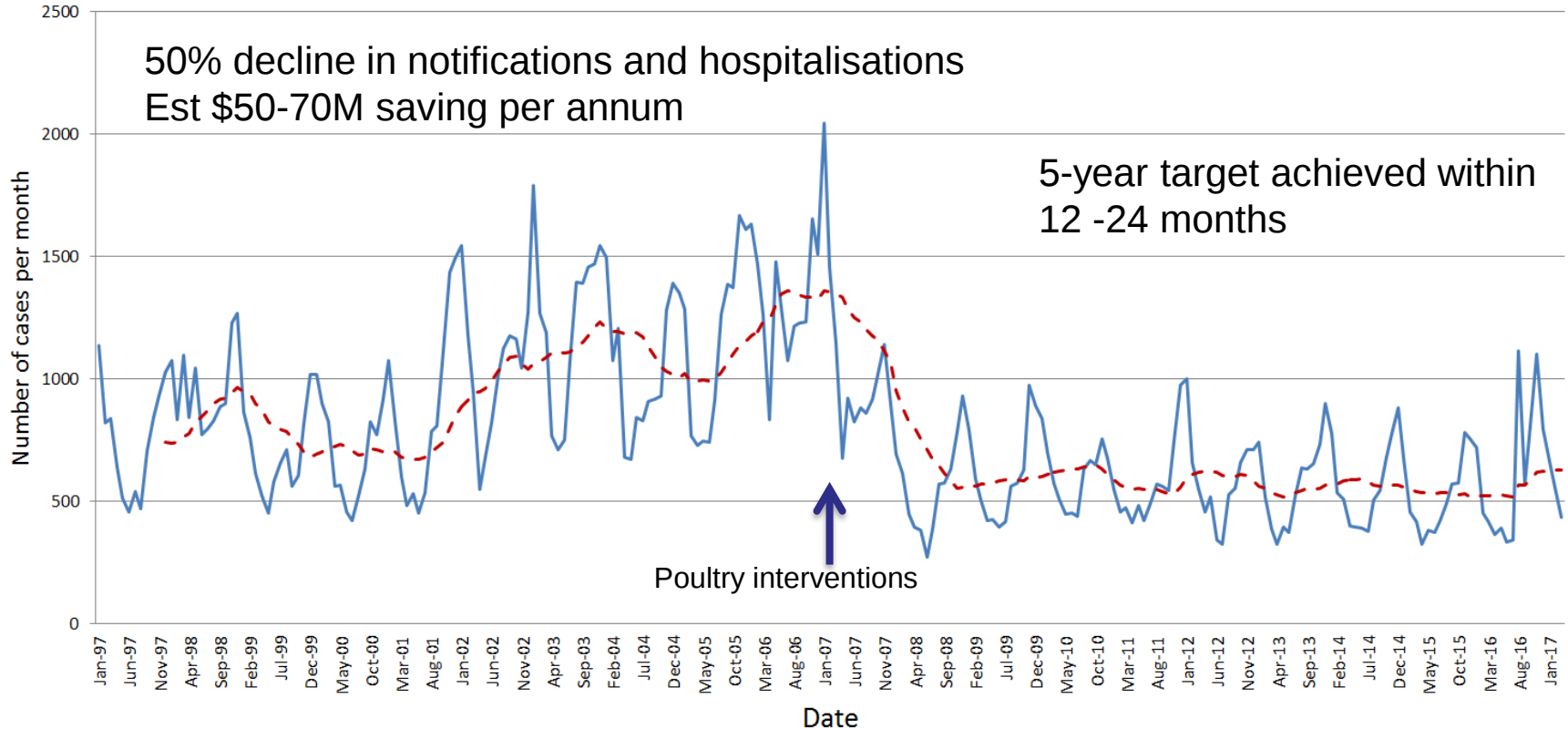
Risk management - Govt

- Set performance targets in consultation with industry
- Worked closely with industry, provide scientific review of interventions
- Mandated industry performance targets
- Added *Campylobacter* to National Microbiological database and analyse data

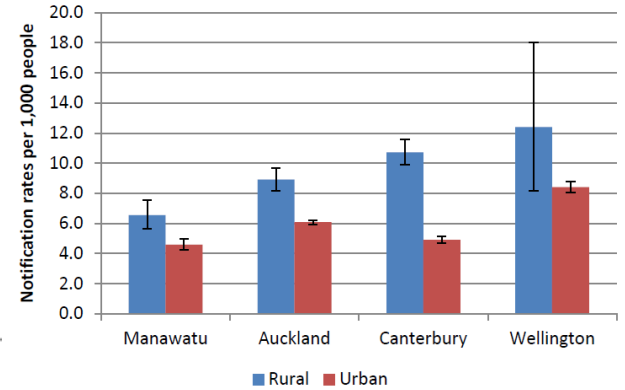
Marked Campylobacteriosis Decline after Interventions Aimed at Poultry, New Zealand

Ann Sears, Michael G. Baker, Nick Wilson, Jonathan Marshall, Petra Muellner, Donald M. Campbell,
Robin J. Lake, and Nigel P. French

Sears et al 2011,
Emerging Infectious Diseases 17, 1007-15

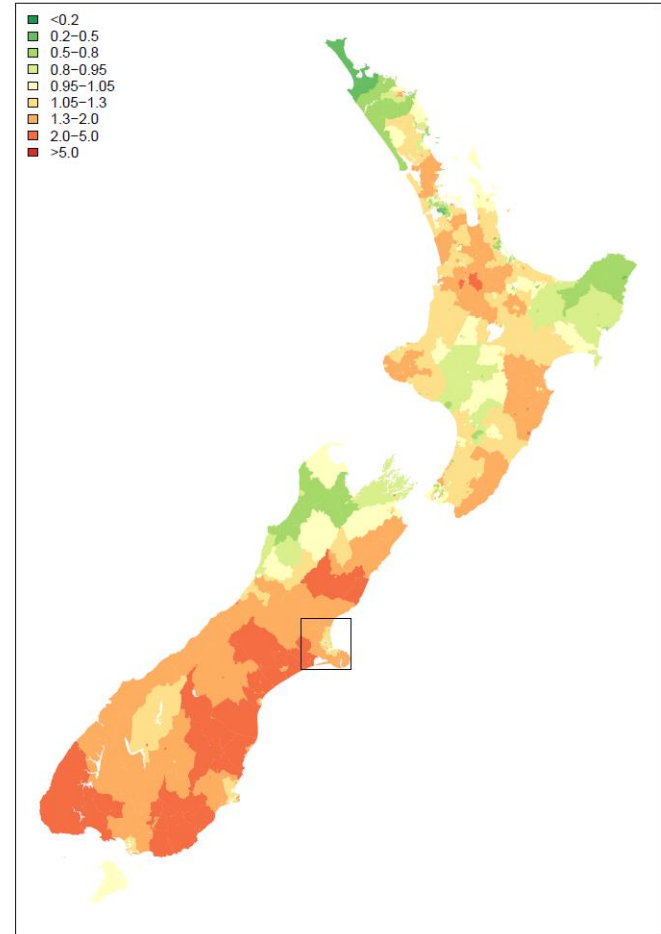


Dramatic change in epidemiology: now highest rates in rural under 5 year olds



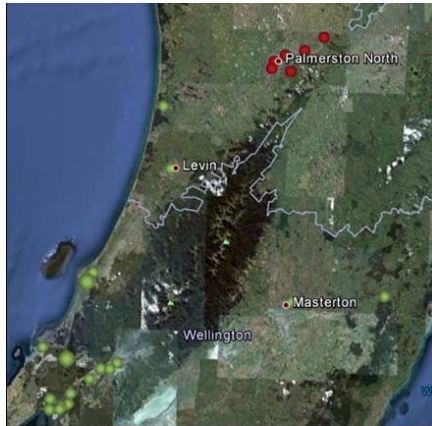
Why different epidemiology in rural areas?

Strong correlation
with density of
dairy cattle



Raw milk: mainly urban cases

Sampled Date	ST	Sex	Age Group	Ethnicity Grouping	Occupation	Probable food source
27-May-11	520	Male	20-29	European only	Maintenance Worker	Unpasteurised milk
23-May-11	520	Male	70+	European only	Resthome Resident	Unpasteurised milk
26-May-11	520	Female	70+	European only	Retired	Unpasteurised milk
27-May-11	520	Female	50-59	European only	Unknown	Unpasteurised milk
02-Jun-11	520	Male	50-59	European only	Truck Driver	Unpasteurised milk
02-Jun-11	520	Female	40-49	Maori only	Shop Assistant	Unpasteurised milk
02-Jun-11	520	Male	40-49	European only	Mechanic	Unpasteurised milk
07-Jun-11	520	Female	20-29	European only	Student	Unpasteurised milk



Dairy farmers go back to basics



They are passionate about producing high-quality milk the way it's meant to be and hope people will always have the right to choose to buy it before it gets "homogenised, pasteurised and bugged", says Mr Sproull, laughing.

Raw milk confidence despite outbreak

Richard Rennie
richard.rennie@tzx.com

THE chief executive of Village Milk remains confident consumer interest in buying raw milk will remain, despite a franchisee's milk supply being linked to a campylobacter outbreak.

The vat was turned off on raw milk supplies from Village Milk's Timaru franchisee late last month after milk from the property was linked to seven cases of campylobacter in the district.

The outbreak was traced to milk bought from the property of Stu and Andrea Weir, who have 20 cows supplying the unpasteurised product through a Village Milk vending machine.

The couple had been operating the franchise for only a month.

While Stu was confident the couple would be back selling raw milk by last weekend, Village Milk chief executive Mark Houston was more circumspect as he awaited the results of tests on cows and the farm's water supply.

The farm's water supply comes through the Timaru town supply.

Weir said changes to piping had possibly introduced dirt into the water system that was contaminated with campylobacter bacteria.

"We are quite relieved it is a water-borne issue and not the milk, and at the moment we are putting in an ultra-violet unit and have sent water samples away for testing.

"We are on the home straight hopefully."

He was optimistic he would be selling raw milk again in a few days.

While all cows are teat-sprayed with iodine before milking, he expected to find water had got to



BAD START: Stu and Andrea Weir had an outbreak of campylobacter traced to their milk after operating the Village Milk franchise in Timaru for only a month.
Photo: Stu Jackson

business had comprehensive procedures in place to minimise milk becoming infected with bacteria.

That included full washing of cows' teats, spraying with sanitiser before milking and wiping teats before applying cups.

But a leading disease expert is sceptical raw milk can be sold consistently free of campylobacter, given the bacteria's widespread presence in cattle faeces.

Massey University EpiLab director and food safety professor Nigel French said it was unrealistic to think milk could be produced and sold in the country without

"We are quite relieved it is a water-borne issue and not the milk, and at the moment we are putting in an ultra-violet unit and have sent water samples away for testing."

Stu Weir
Village Milk franchisee

Industries, which is examining regulations for the sector.

Village Milk tests for campylobacter every two months, but Houston said he was considering increasing the frequency.

Testing by the company had detected campylobacter in the past on another property, but the milk sales were halted before that milk made it to the vending machine, he said.

The problem was traced to the farm's water supply.

Houston expected to have test results today for milk and water.

"If it is water that is something

MPI caution to vendors

Richard Rennie
richard.rennie@tzx.com

THE Ministry for Primary Industries (MPI) is advising those who sell raw milk to tell customers the product might contain bacteria that could cause illness.

An MPI spokesman said even with stringent control measures there would always be a food-safety risk with raw milk, given three was no process to kill the bacteria that can cause illness.

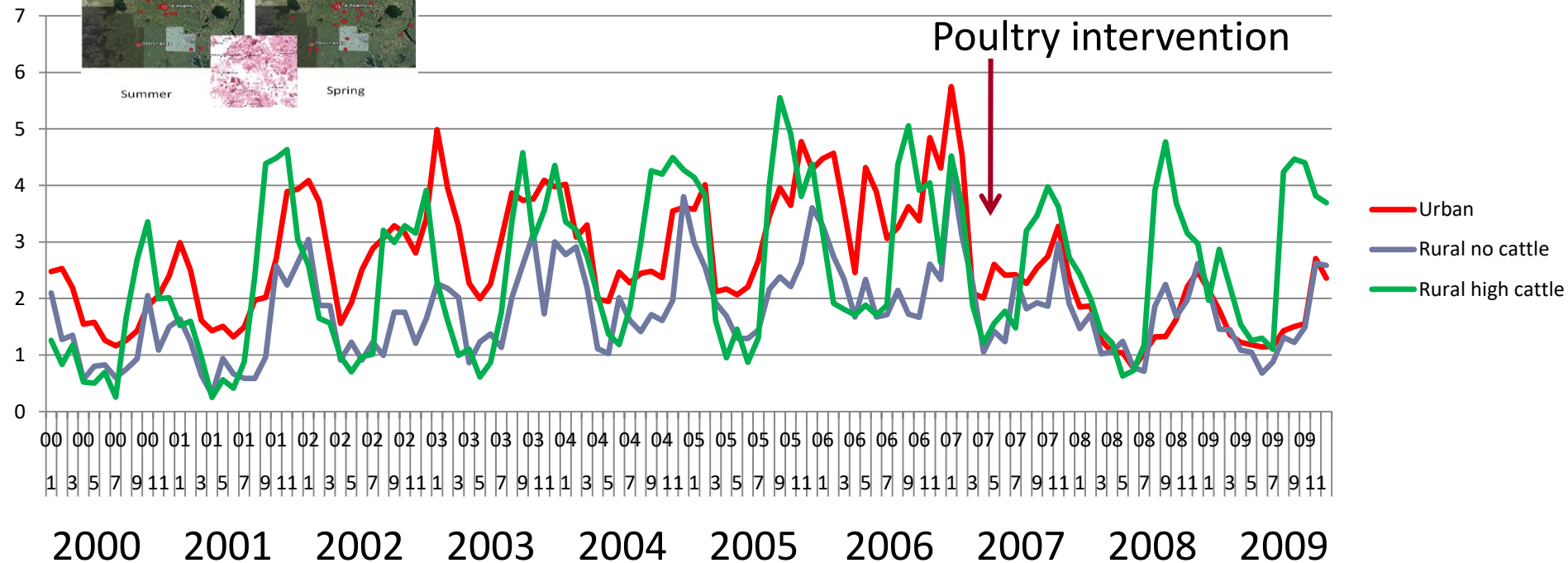
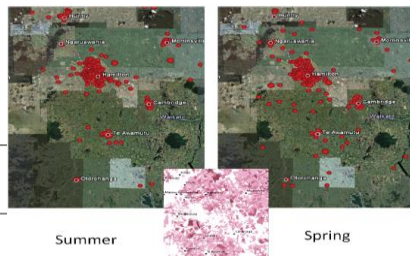
The ministry is advising producers to tell customers to heat the milk to 70C for one minute to reduce the risk of bacterial infection.

Testing raw milk for illness-causing bacteria was often problematic because raw milk had almost always been consumed by the time people got sick and there was nothing for investigators to test, the spokesman said.

MPI is reviewing the policy and rules applying to raw milk sales.

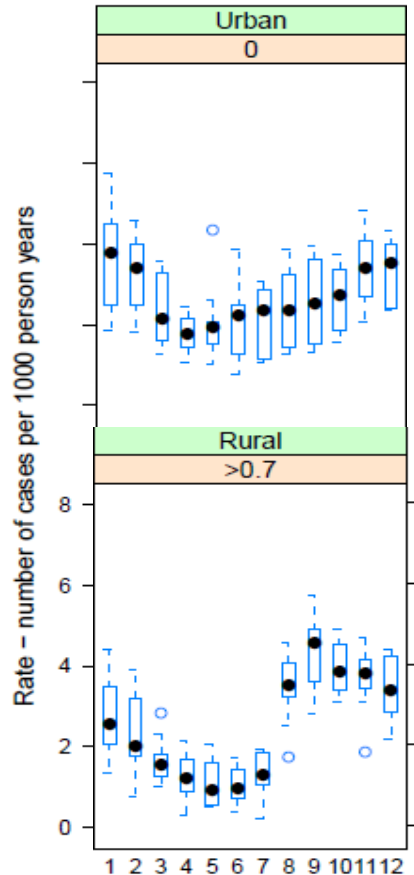
The ministry received 1600 submissions on the issue almost two years ago, with the majority supporting continuing sales of raw milk.

An investigation into the outbreak in Timaru is under way and MPI was unable to say how long it would take.



Seasonality and dairy density

Urban



Young children

During calving season

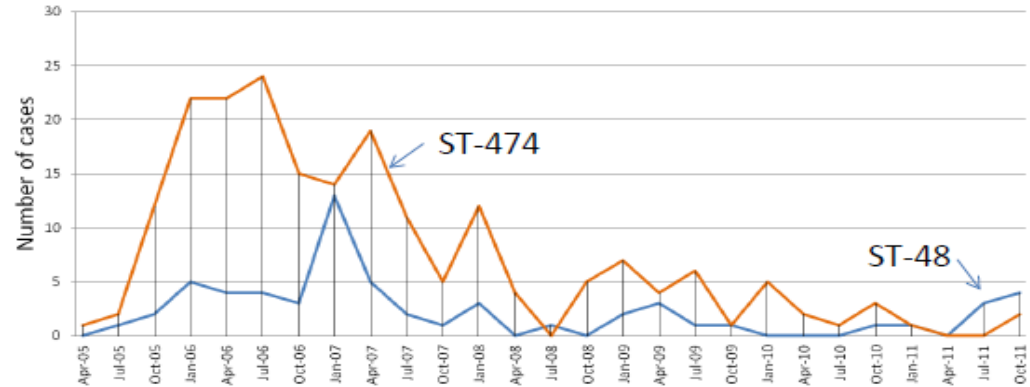
Direct contact

Hand mouth behaviour

High dairy rural

Rise and fall of the epidemic strain *C. jejuni* ST 474 and the increased use of whole genome sequencing

- ST-474 found in 25-30% of human cases early in 'epidemic'
- Predominantly one poultry supplier
- Early studies revealed rapid evolution
- Why did it emerge in poultry?
- Why did it decline?



Biggs et al 2011, PLoS One, 6 (11) e27121
French et al, 2014. *Campylobacter Ecology and Evolution*, 221-240.

Did the poultry supply become infected with *Campylobacter* ST-474 from ruminants?

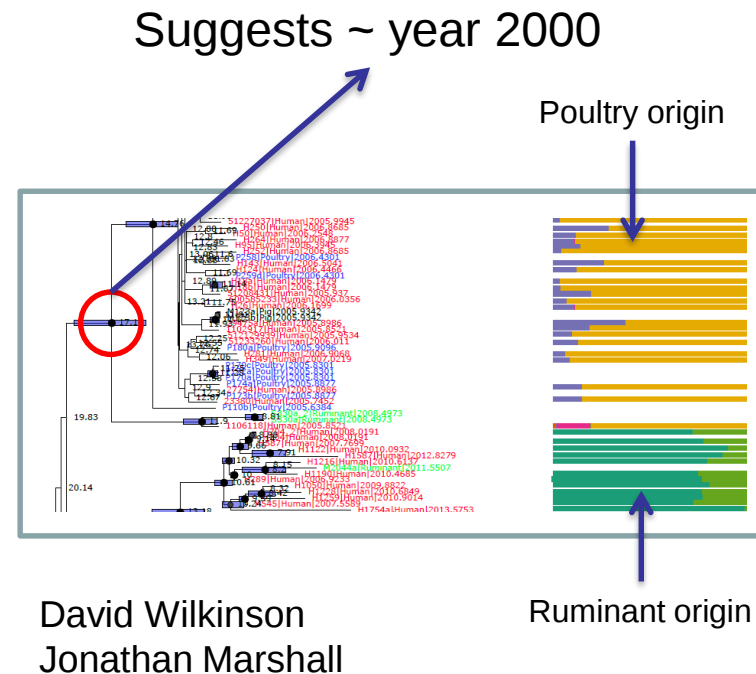
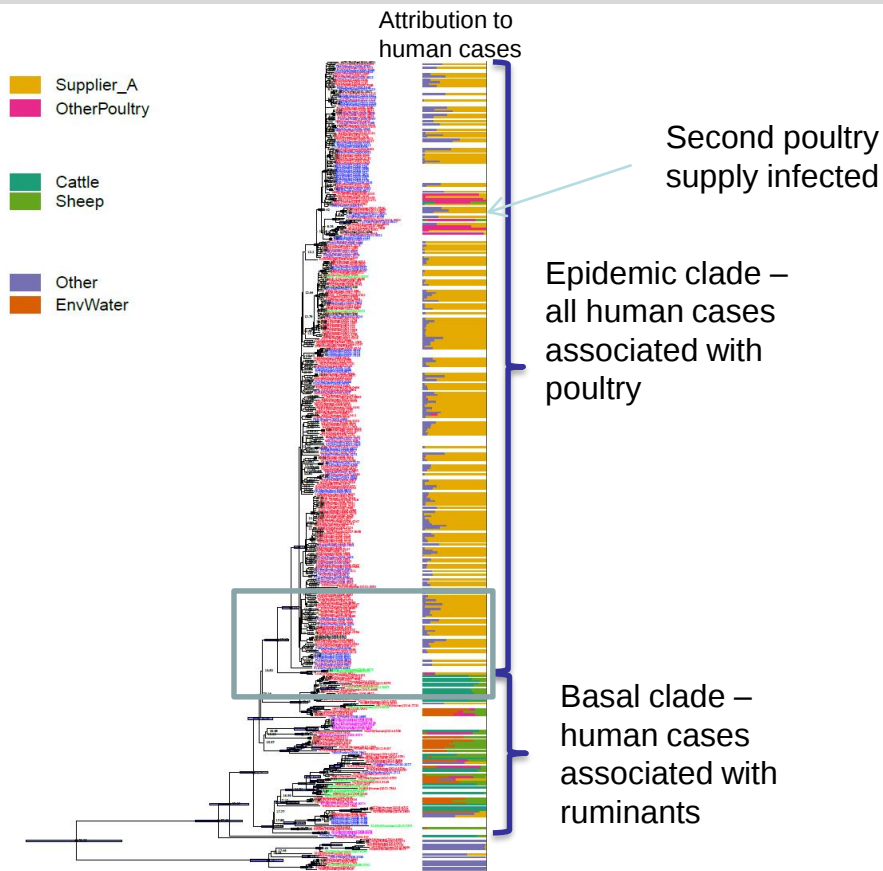
- Evidence:
 - ST-474 belongs to a group (CC 48) associated with ruminants elsewhere in world
 - Early isolates contained 'cattle gene'
 - Evolutionary analysis supports jump from ruminants to poultry – epidemic strain
- Example of host switching with major consequences for public health?



?



(If so) When did the poultry supply become infected?



Arrival of ST-6964 in 2014 and Antimicrobial Resistance (AMR)

(not a
superbug!)

SUNDAY STAR+TIMES November 22, 2015 NEWS A3

Superbug found in chicken

Scientists are alarmed at the unprecedented discovery of a strain that resists drugs and has crossed into humans around NZ, writes Susan Edmunds.

A new superbug has been found in chicken from three of New Zealand's four major poultry suppliers. Groundbreaking research reveals the new antibiotic-resistant strain of campylobacter spreads to humans, which could make it hard to treat serious cases of infections.

Campylobacter occurs naturally in the gut of chickens but is the leading cause of food poisoning with about 7000 cases reported in New Zealand each year.

The antibiotic-resistant strain was first found in 2014 and has now been identified in human cases in Manawatu, Auckland and Wellington.

The study, by Nigel French of Massey University and ISIR microbiologist Debbie Williamson, found three of the major poultry suppliers in the North Island tested positive for the strain. A fourth was still waiting for test results. The pair would not name the companies.

The resistance means two antibiotics – fluoroquinolones and tetracyclines – would fail in treating the infection. But another antibiotic, which is more

Which comes first? The chicken or the campylobacter

Humans ingest the bacteria from surfaces or improperly cooked meat

Campylobacter spreads through handling, left in fridges

Consumers buy fresh chicken

Campylobacter develops in the gut

Photo: CHRIS MCKEEN / FAIRFAX NZ
Graphic: NEIL BOND

Emergence of ST-6964

(in collaboration with Dr Debbie Williamson, MDU and ESR ERL)

- August 2014: first two human cases of new *C. jejuni* ST-6964 detected in sentinel site
- Found straight away in 3 poultry companies
- Resistant to tetracycline and fluoroquinolones
 - Sharp increase in AMR and ST 6964 in human cases across NZ (ESR study)
 - Chicken liver outbreak, Wellington
 - No overall increase in human cases?



AMR in Campylobacter in NZ: Poultry

New Zealand Veterinary Journal 58(5), 229-236, 2010

229

Scientific Article

Low levels of antibacterial drug resistance expressed by Gram-negative bacteria isolated from poultry carcasses in New Zealand

EJ Pleydell^{*,§}, L Rogers^{*}, E Kwan^{*} and NP French^{*}

Drug	Disc ^a (µg)	Res (%) ^b	Zone size (mm)														
			≤6	7–15	16	17	18	19	20	21	22	23	24	25	26	27	≥28
Erythromycin	15	0.5	1				1			2	3	4	8	19	12	21	122
Ciprofloxacin	5	0											1	1	1	2	188
Enrofloxacin	5	0											1		3	4	185
Nalidixic acid	30	0			2	2	3	8	12	13	19	24	22	33	17	12	26
Chloramphenicol	30	0								1	1				9	10	172
Tetracycline	30	0													1		192

^a Concentration of drug within the disc

^b Percentage of isolates with zone sizes within the resistant category for that drug

Very low by international standards
Low use of Abs in New Zealand poultry industry

Poultry survey 2015

- Samples:
 - 193 pooled caecal samples
 - 1 week of slaughter
 - 62 farms, 158 sheds
- 37% +ve for ST-6964 tet/cip resistant strain
- 0% +ve on South Island
- All 3 main NI companies +ve (27-62% of samples)
- Also isolated from breeder 'parent' stock



Human survey 2015

- ESR survey (Debbie Williamson)
- May-August 2015

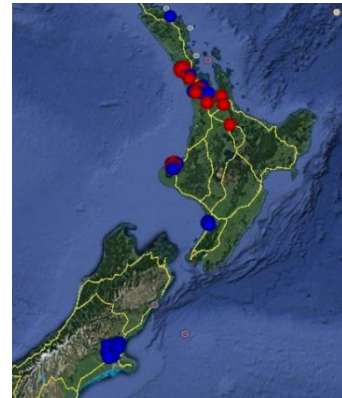
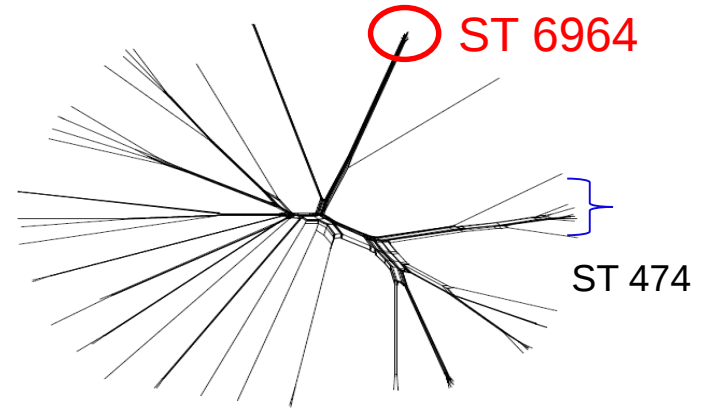
Island	Number tested	Number tet/cip resistant	% resistance
North Island	137	33	24.1%
South Island	101	7	6.9%
Total	238	40	16.8%

- 76% ST-6964
- Wellington outbreak (chicken liver)

Key questions?

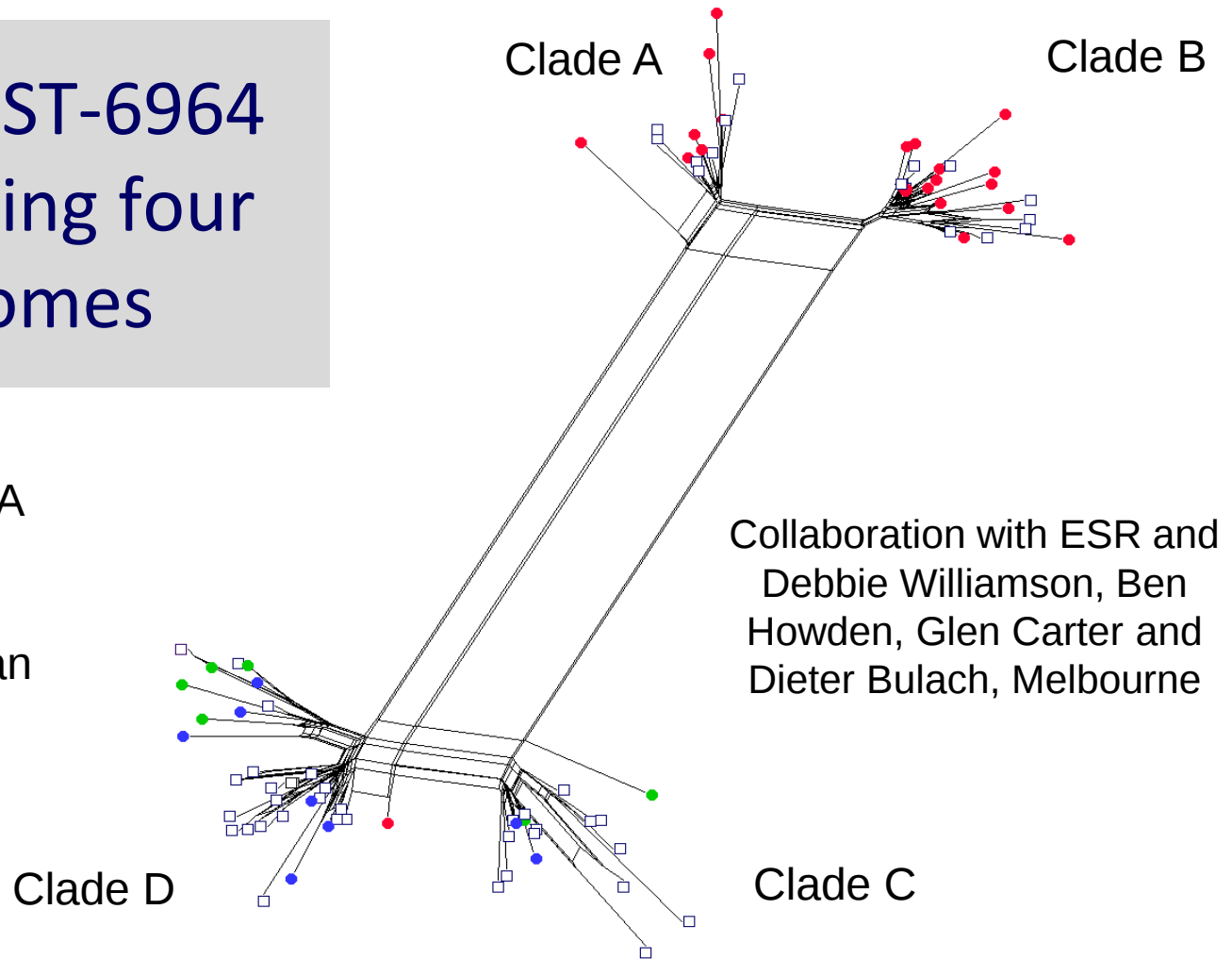
- Genetic basis for resistance?
- How long has it been in NZ?
- How has it been transmitted between poultry companies?
- What has driven the emergence?
- What is the main source of human infection?
- How is it evolving?

These can best/only be addressed by
Whole Genome Sequencing

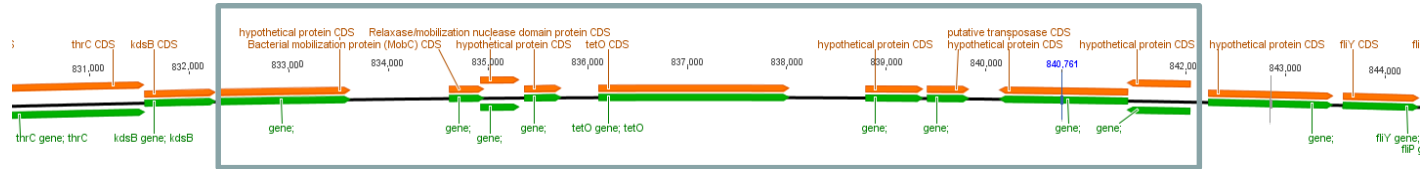


Sequencing of ST-6964 (N=230) including four reference genomes

Green=Poultry A
Blue=Poultry B
Red=Poultry C
Squares=Human



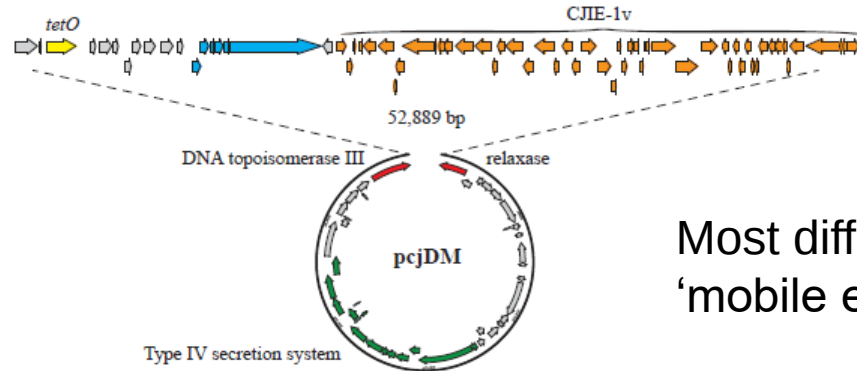
Tetracycline resistance genes and phage inserted into chromosome, leaving 'remnant' plasmid



Over 100 *tetO* insertion alleles in *C. jejuni* (Cody et al 2015).

Remnant plasmid

Absent from poultry
supplier C isolates



Most differences in
'mobile elements'

Key questions

- Genetic basis for resistance?
 - *tetO* plasmid and C257T mutation in *gyrA*
- How long has it been in NZ?
 - ~mid-late 2013.
- What drove the emergence?
 - Reverse zoonosis initially?
 - Limited tetracycline use in breeder flocks?
- How has it been transmitted between poultry companies?
 - Shared parent and grandparent stock? Feed?
 - Local spread seems likely
- Source attribution
 - All companies causing human infection



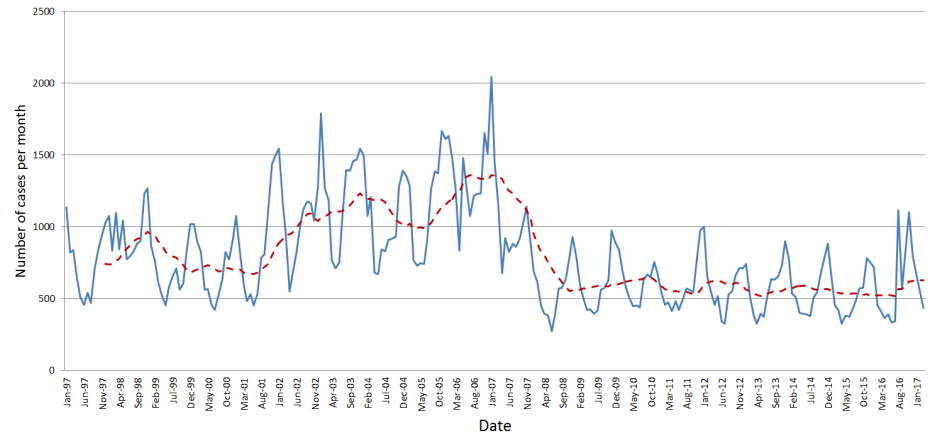
Fig. 2. Social network analysis of feed-related contacts in the New Zealand

Poultry farm network
(from Lockhart et al 2010)

Required cooperation and support
from poultry industry

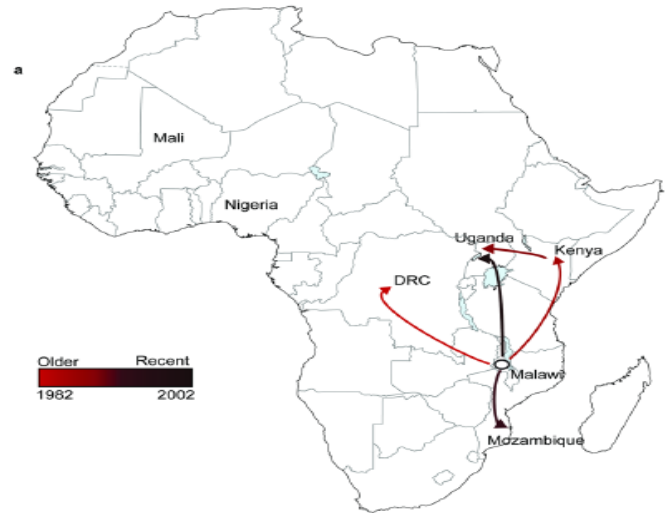
Public health significance?

- Resistant to two classes
 - Unless invasive, Abs not recommended
 - Erythromycin drug of choice (ST-6964 sensitive to Ery)
 - ...but FQs still given by some GPs?
- New strain hasn't caused increase in notifications



Public health significance?

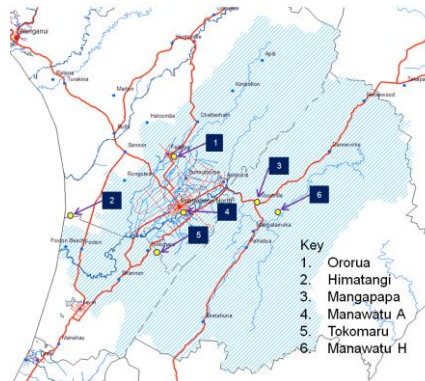
- Could have been worse...
 - *Salmonella* Enteritidis or resistant *S. Typhimurium*?
- Resistance still low compared to other countries
 - But shown it can change very rapidly...



Spread of ST 313

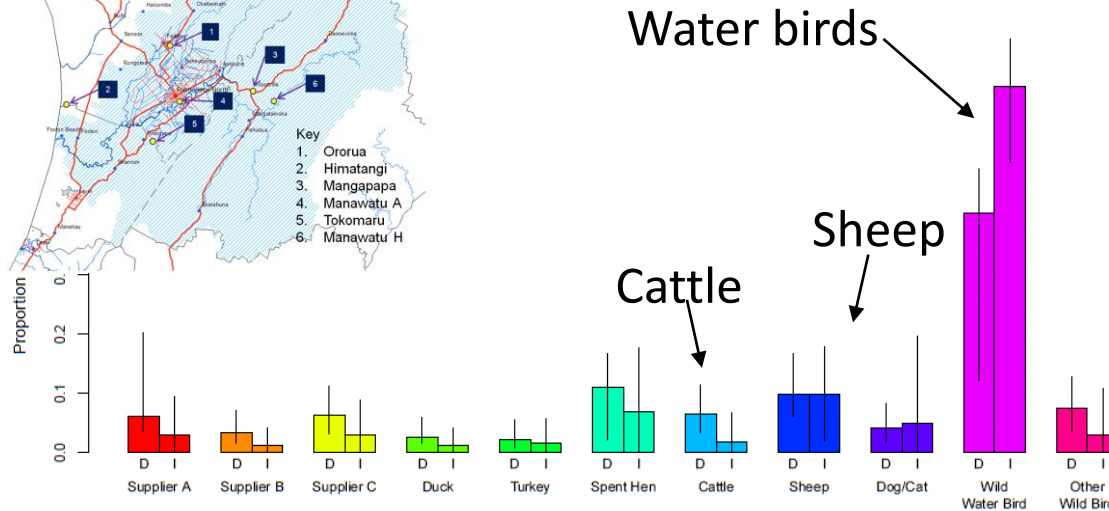
Campylobacter jejuni sources in water

Most *Campylobacter jejuni* in water in Manawatu from wildlife – even in dairy catchments



Dairy=227,658

Beef=181,196



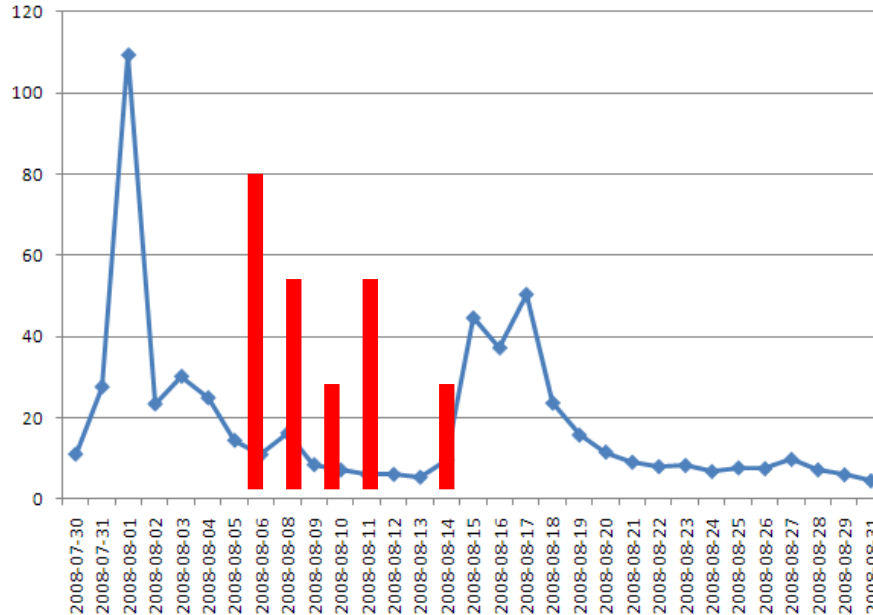
ST 2381

NZ drinking water outbreaks: Campylobacter

- 1986
 - Ashburton, 19 cases in two weeks attributed to poorly chlorinated drinking water drawn from river
- 1990 –
 - 44 cases linked to livestock contaminating camp water supply
- 1997 –
 - 67 cases linked to drinking water contaminated with river water
- 2008 –
 - Pahiatua, Manawatu 9 cases linked to rainfall and river flow
- 2012 –
 - Darfield incident 110 cases
- 2016 –
 - Havelock North 5000 cases

Manawatu drinking water outbreak in 2008

Water flow

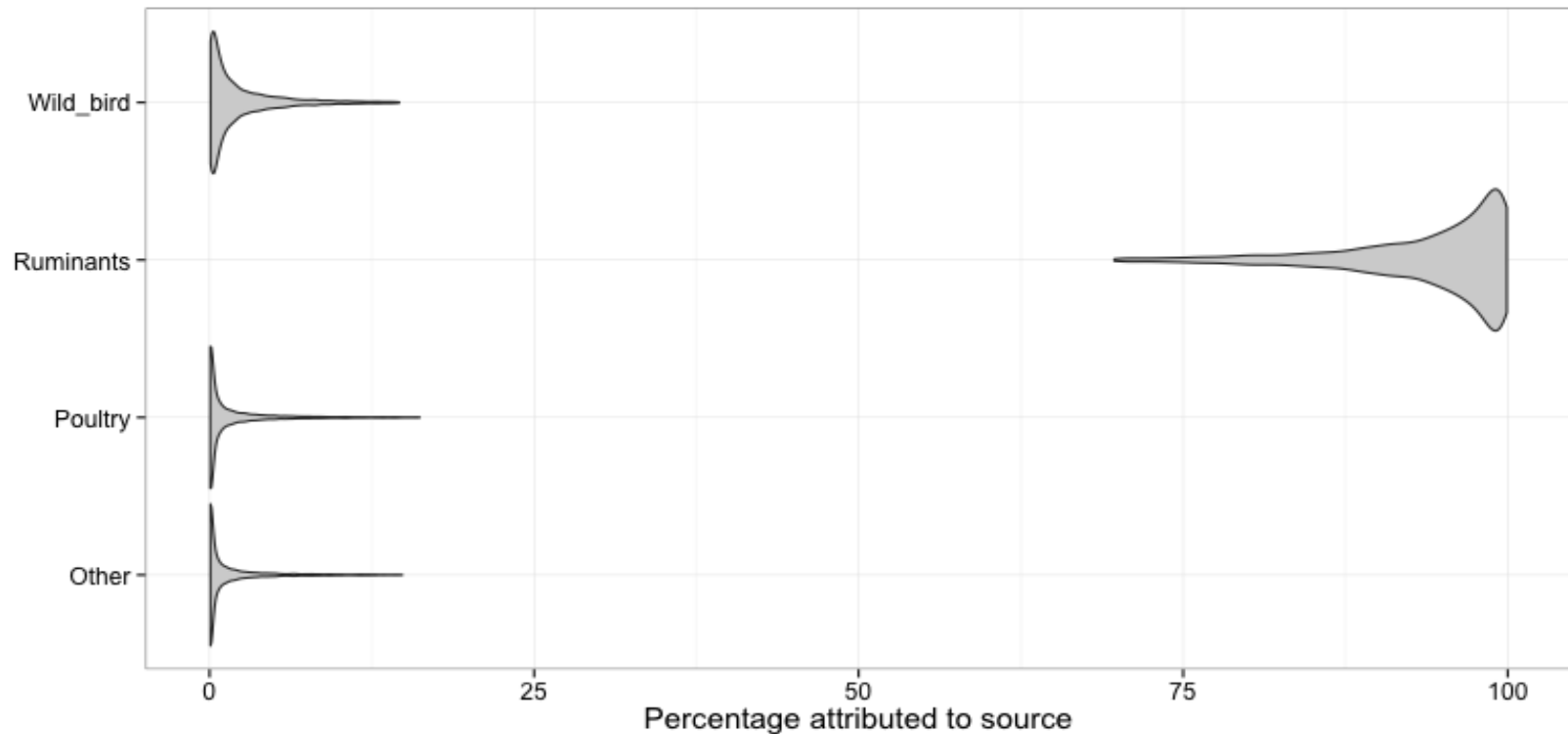


Comments on
drinking water



Muddier than usual "toxic in it's self"
smells of dirt, brown
water been brown, "crap"

Attribution of Pahiatua 2008 human *C. jejuni* isolates



Darfield contaminated water supply

Stomach bug lays 110 low in Darfield

CAROLINE KING AND GEORGINA STYLIANOU

Last updated 05:00 25/08/2012



Darfield teen Chloe Walker has had a bucket by her side for a week.

The 13-year-old is among more than 110 people to have been hit with gastroenteritis, a serious stomach illness, in the Darfield area after drinking contaminated water.

Chloe's family were using boiled water after a notice was issued by the Selwyn District Council. The council's warning came after E. coli was found in some parts of the local water supply.

However, on one occasion Chloe "forgot" to use boiled water. She drank a glass of tap water and used some to brush her teeth.

Not just a mild case of diarrhoea....

Chloe said the stomach pains were soon crippling.

"I would pretty much be in tears with the pain because it was so bad. Every time I got the pain I'd get goose bumps and feel cold," she said.

She also suffered intense headaches and was "too scared" to eat.

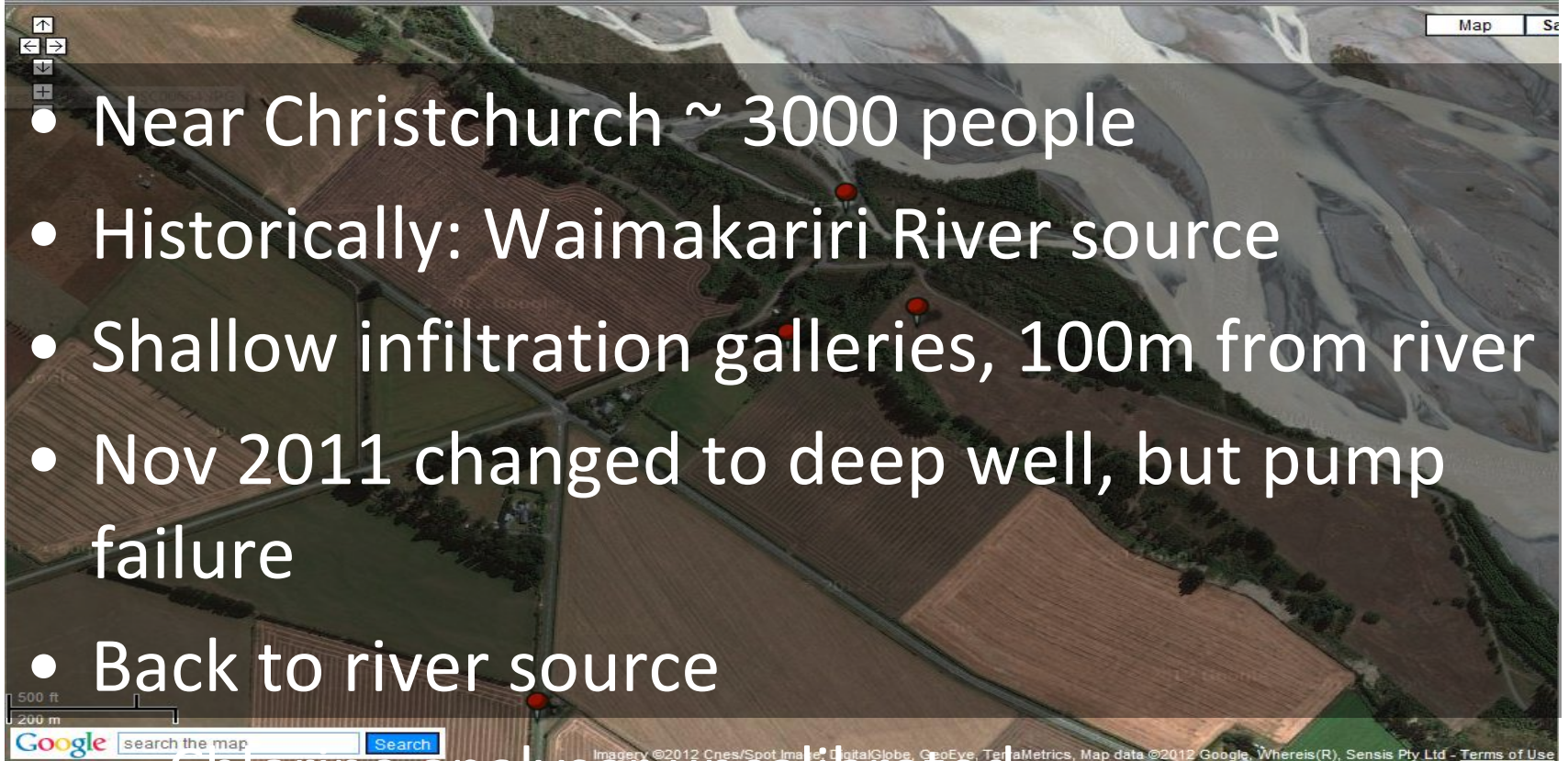
Chloe's mother, Michelle Walker-Jones, bought some painkillers from the local pharmacy, where she works.

"[But] nothing was really helping me. I'd just had enough of it. I just wanted to go back to school," Chloe said.

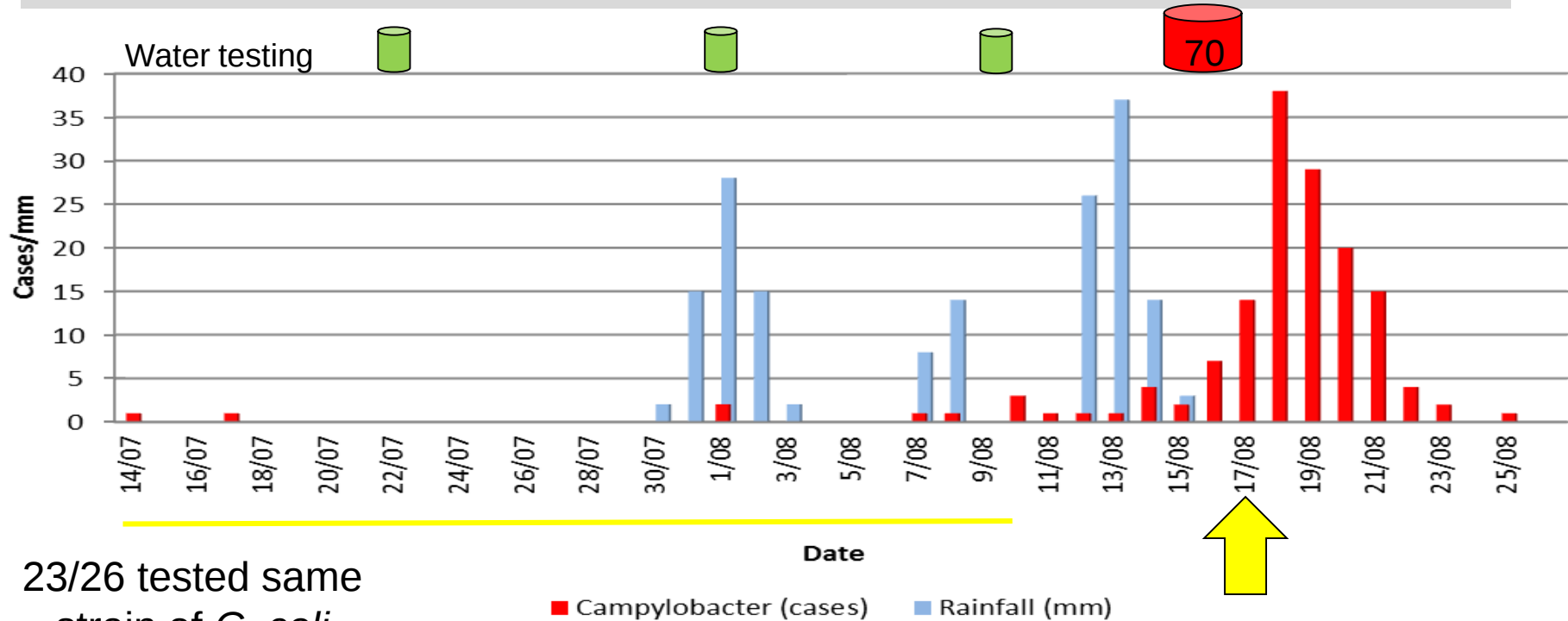
Walker-Jones said the pharmacy had been inundated with people affected by gastro since Monday.

Darfield outbreak 2012

- Near Christchurch ~ 3000 people
- Historically: Waimakariri River source
- Shallow infiltration galleries, 100m from river
- Nov 2011 changed to deep well, but pump failure
- Back to river source



Darfield 2012 outbreak





The infiltration gallery in use at the time of the *E. coli* transgression was located in a small recess in an unsecure privately owned paddock, where no animals are thought to have grazed for a couple of months. There is uncertainty about whether the paddock was flooded during the heavy rains. The gallery intake was unlikely to have provided significant levels of filtration given the typically high permeability gravels that occur in the alluvial deposits in the area.

The Havelock North incident, August 2016

>5000 people affected

Untreated groundwater

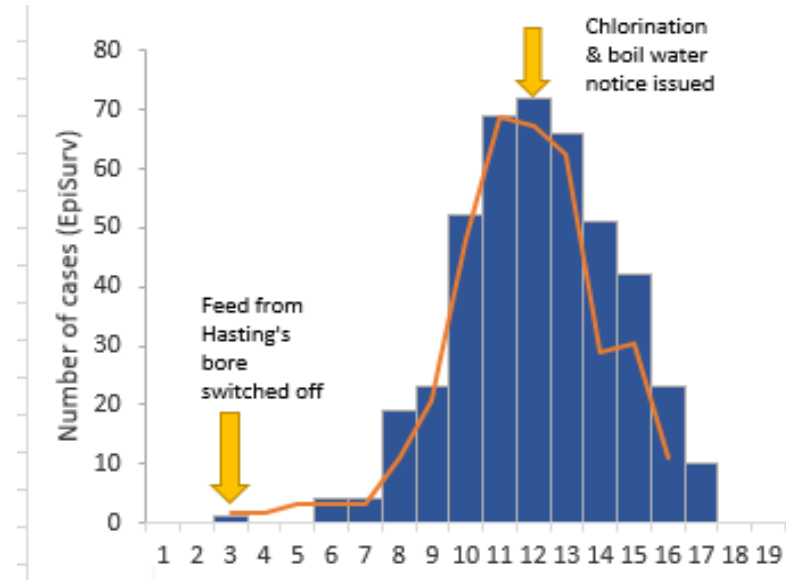
Campylobacter jejuni ST42 predominant cause

One of the largest waterborne outbreaks in the developed world ever....



Early timeline

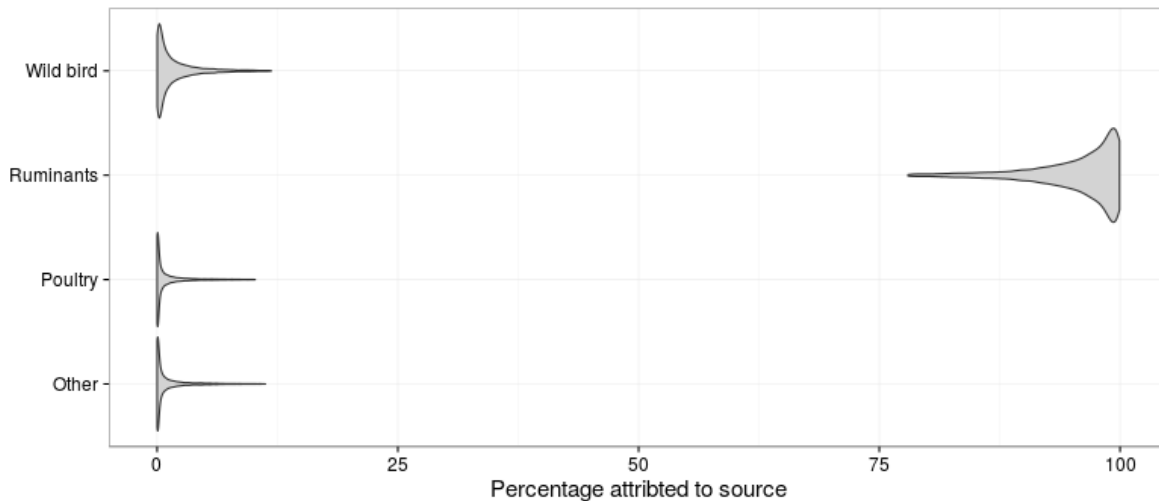
- Campylobacteriosis incubation 1-10 days (2-5)
- Major rainfall on 5th and 6th August
- Local flooding
- Onset dates started to rise on 8th August
- 9th August routine testing showed no contamination of water supply
- 11th August further tests taken, results on 12th showed contamination
- Cases peaked on 12 August, chlorination and boil water notices were issued.



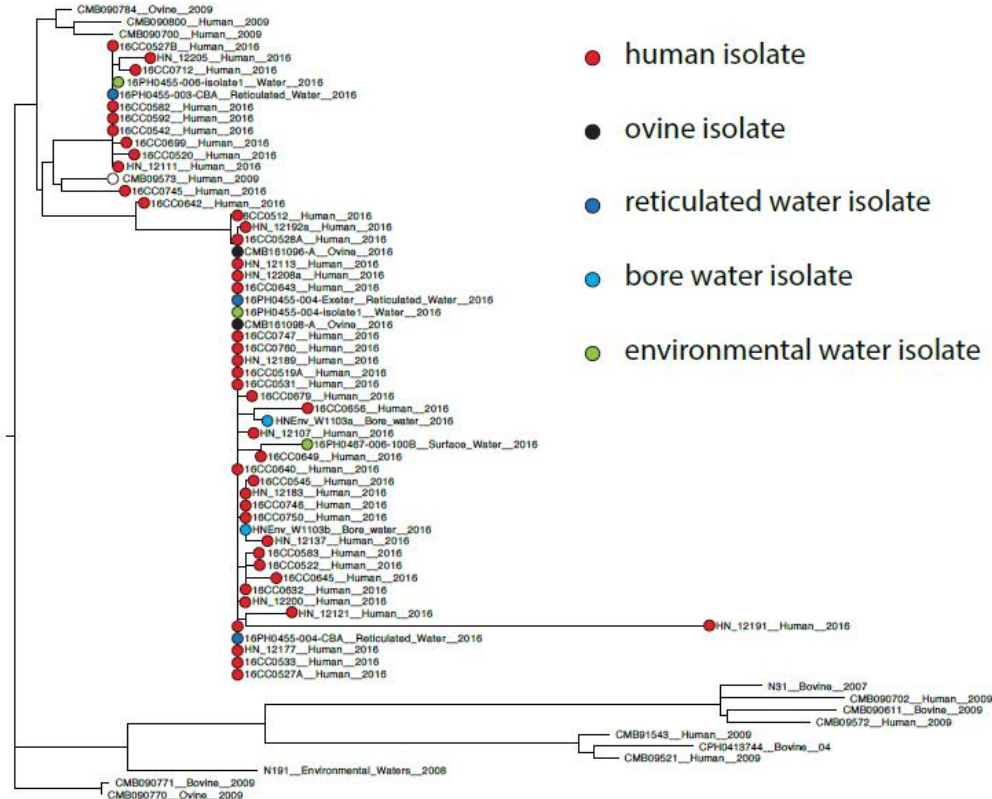
Ruminants highly likely to be source

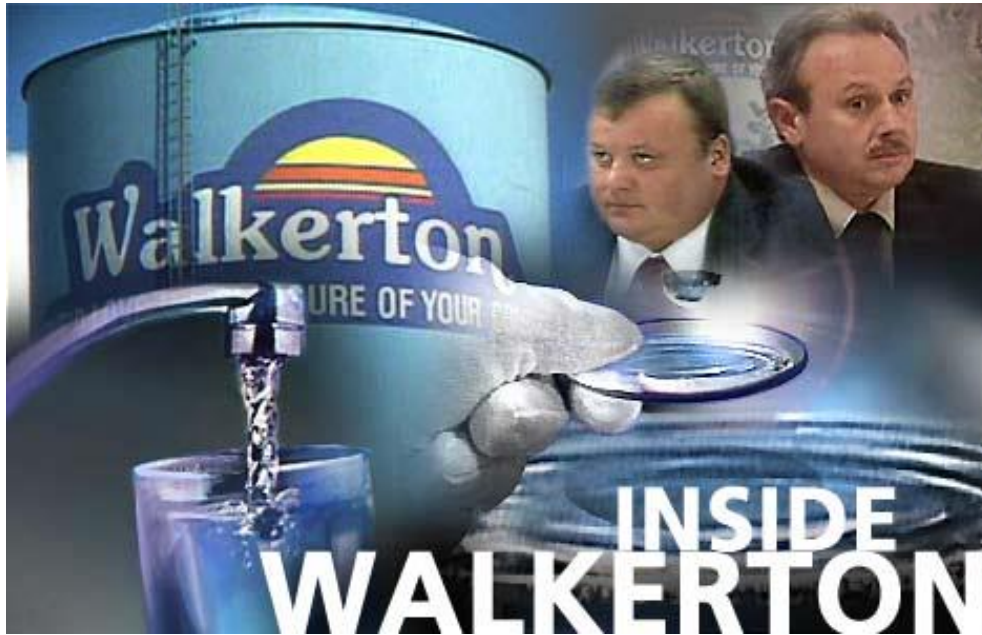


Heavy rainfall and
run-off



New technology pinpointed source





Town of 5,000 people

Could be a lot worse....

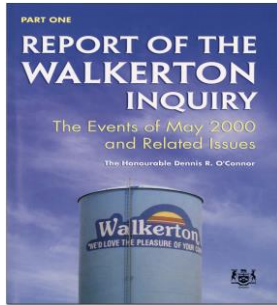


Walkerton, Canada, 2000



faeces

Campylobacter jejuni
E. coli O157



7 deaths
2300+ illnesses
>CAN\$65 million direct cost



Town water
source



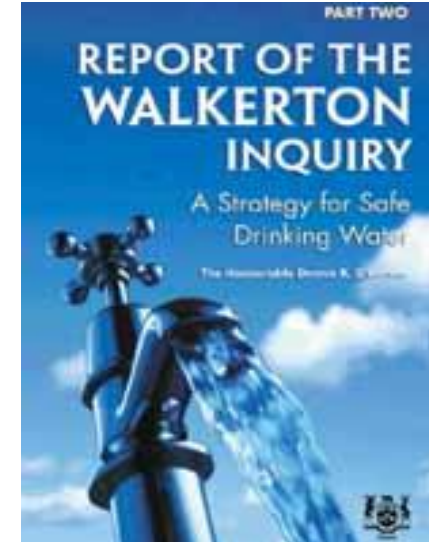
Treatment
failure



Town
drinking supply

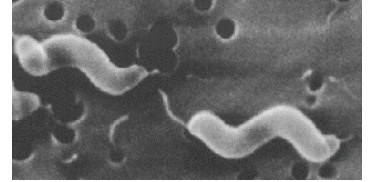
Walkerton inquiry report

- “I conclude that the primary, if not the only, source of the contamination was manure that had been spread on a farm near Well 5..... The manure was applied in late April 2000, before a period of significant rainfall occurring from May 8 to 12.DNA typing of the animals and the manure on the farm revealed *E. coli* O157:H7 and *Campylobacter* strains on the farm that matched the human outbreak strains predominating in Walkerton in May 2000.”
- “I conclude that the entry point of this contamination into the municipal drinking water supply was through Well 5. The overburden in the area of Well 5 was shallow, and there were likely direct pathways – such as fence post holes and a reversing spring by the north side of Well 5 – through which the contamination travelled from the surface to the bedrock and the aquifer.”

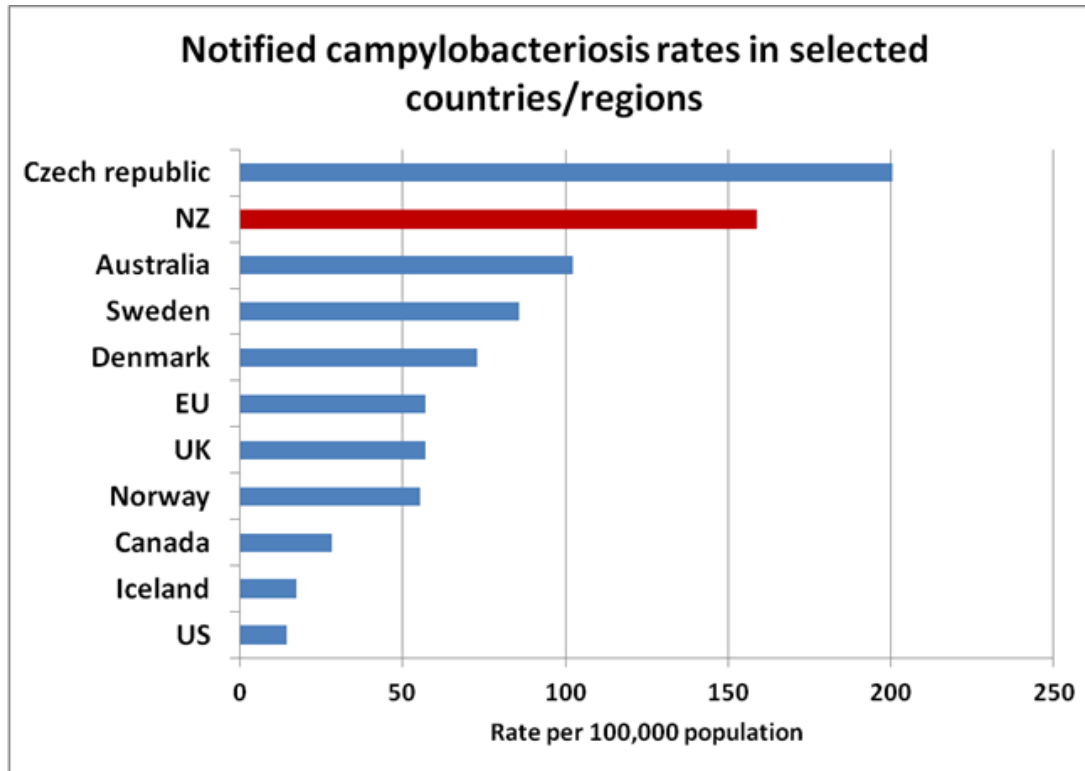


Some questions to address

- Where are people getting infected from in New Zealand?
- How does this differ between urban and rural areas?
- What is the role of poultry compared to ruminants and wild birds?
- What is unique about New Zealand? – why do we have such high rates compared to other countries?
- How important was the emergence of the antimicrobial resistant strain of *Campylobacter jejuni* in 2014?
- What happened in Havelock North and how can we prevent it from happening again?
- What needs to be done to reduce the risk to New Zealanders from all campylobacteriosis?



NZ vs the World (2013)



Still ~90% chickens in supermarket +ve for Campy

Need to reduce further

Export market will drive this

Protect/clean water supplies