Ministry for Primary Industries
Manatū Ahu Matua

“Fit-for-purpose” risk assessment

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This presentation

- Focus on food safety and biological hazards
- Positioning “risk assessment” in a risk management framework
- When is a biological “risk assessment” fit-for-purpose?
- Examples

[Risk assessment for chemicals]

- Risk assessment for chemicals is well codified - fit-for-purpose?
- ADI: threshold approach and point estimates
- “How much pesticide was in my food today?”
- “No more than necessary, and less than would be harmful to your health”
- Probabilistic approach to RfD requires detailed residue and consumption data

Risk Management Framework (RMF)

- Risk managers “own” the system
- Principles
- Steps
- Processes e.g. roles, methods, documentation

NZ Food Safety Authority (2007) / Codex / FAO

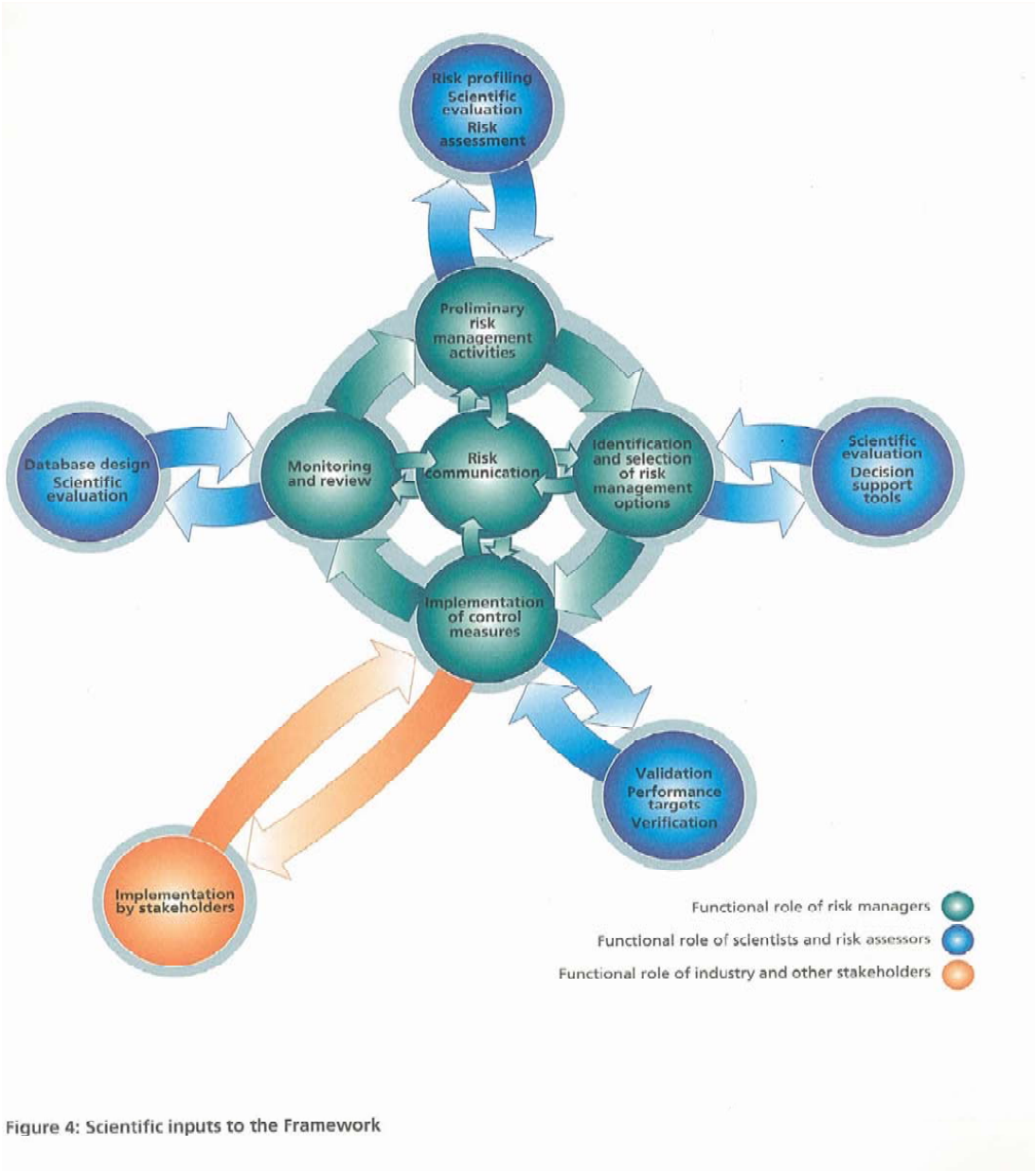
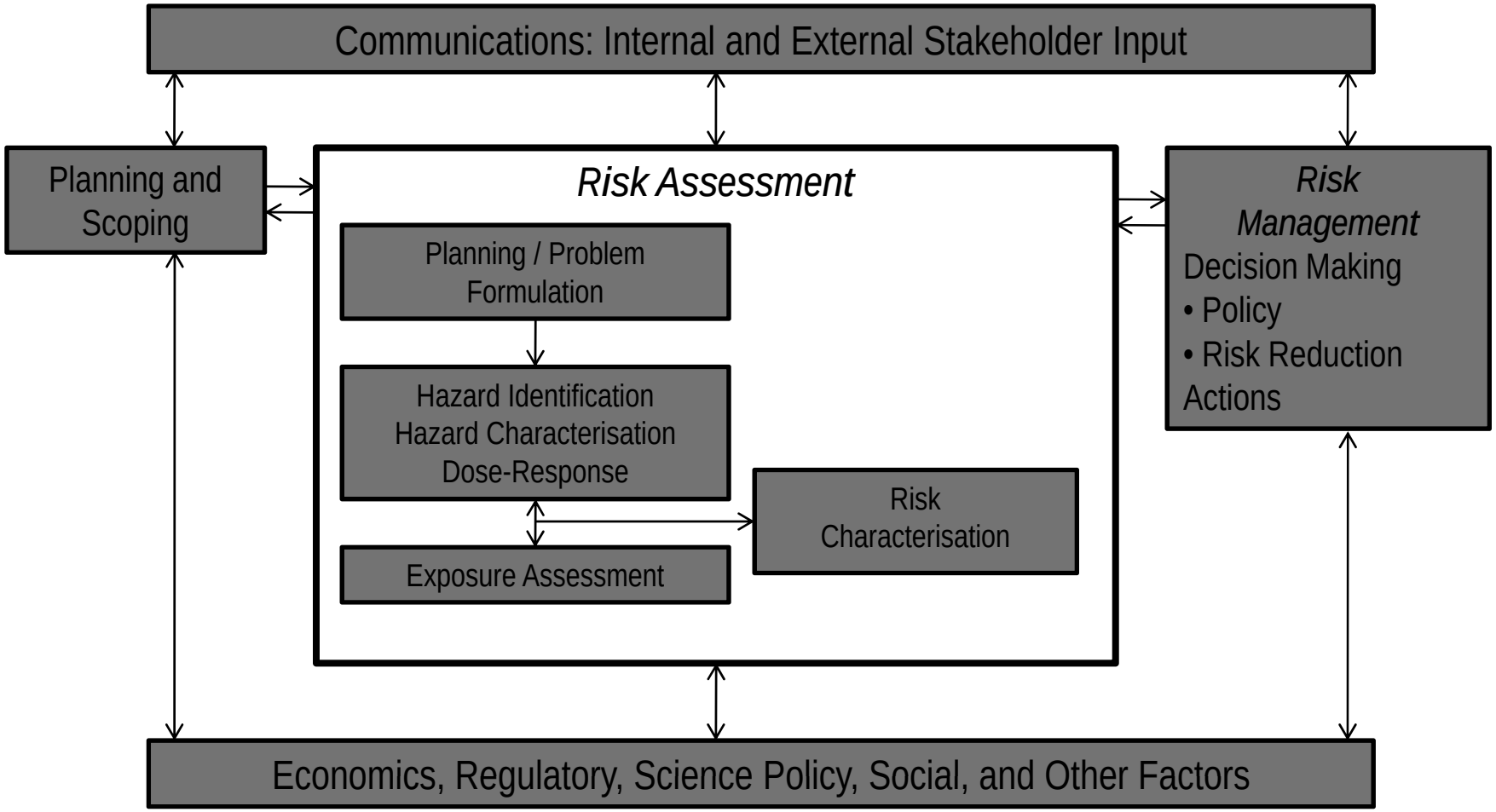
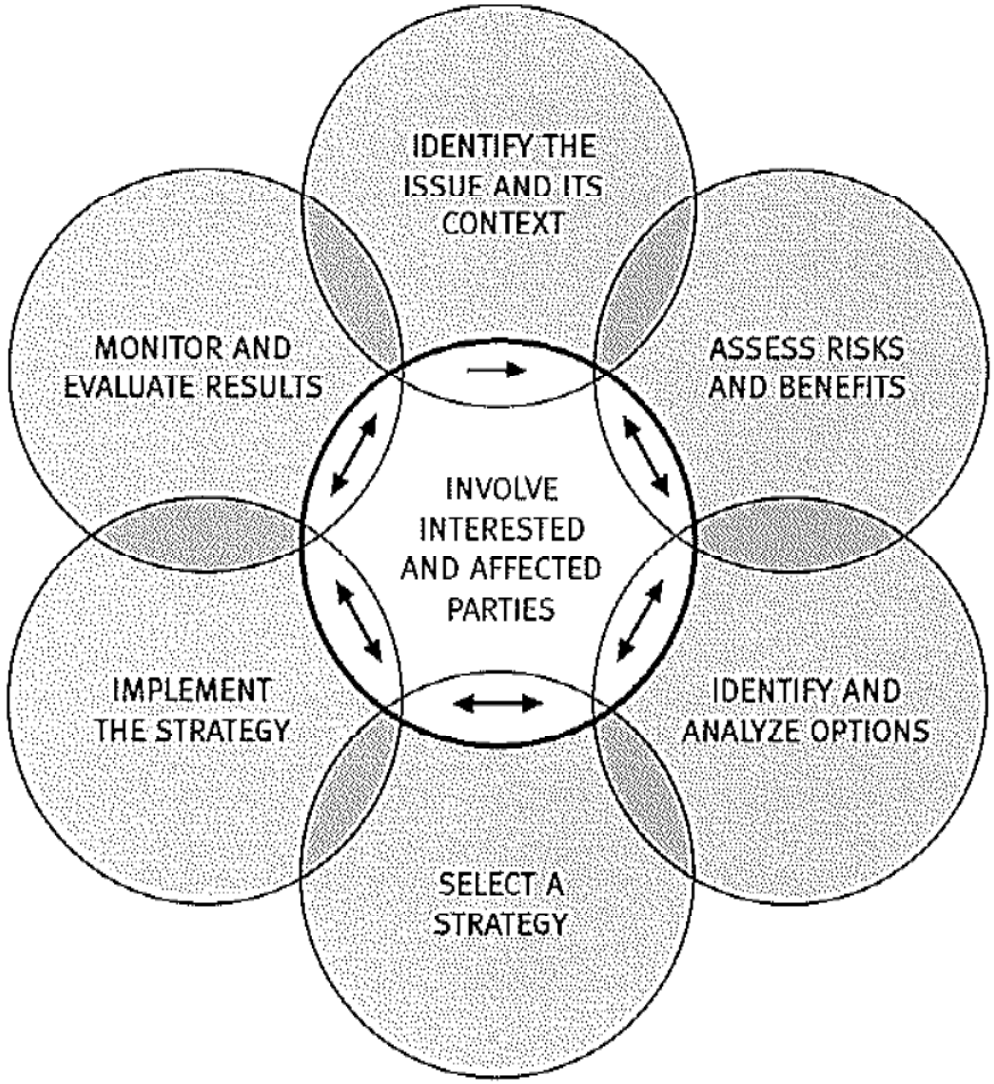


Figure 4: Scientific inputs to the Framework



United States EPA (2012)

Health Canada (2009)



NZ Ministry of Primary Industries (2012)

Formalising the RMF approach

- Risk managers need to set the best course of action under uncertainty
- Start with questions, not data
- Several scientific approaches are available to establish the evidence base
- Provides for strong iteration between scientists / risk assessors and risk managers

Generating the evidence base (1): Principles

- Fully analyse and discuss risk management questions
- Decide on methodology that will provide a sufficiency of evidence (scope, depth)
- Tailor to data availability (cf. one-size-fits-all)
- Retain ability to make reasonable scientific assumptions
- Be timely (cf. paralysis by analysis) and credible (cf. opaque use of science)
- Ensure outputs are usable (cf. excessive uncertainty)

Generating the evidence base (2): Tools

- Converting information into scenarios and simulations that make risk insights easier to understand and action
- Estimating risk or evaluating interventions?
- A range of tools may do the job e.g.

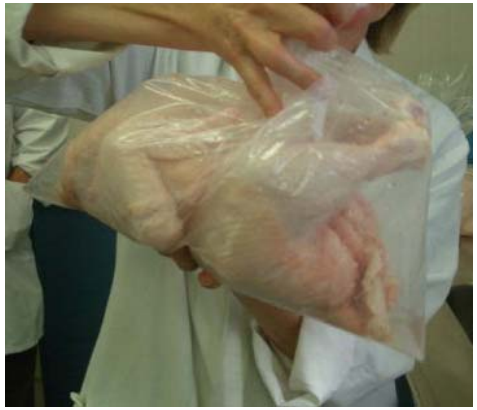
  - risk profiles (generated from existing knowledge)
  - comparative evaluation of exposure pathways
  - epidemiological studies
  - food source attribution models
  - risk assessment models

Reality check

"Humans are more sensitive detectors of pathogens than many laboratory methods"

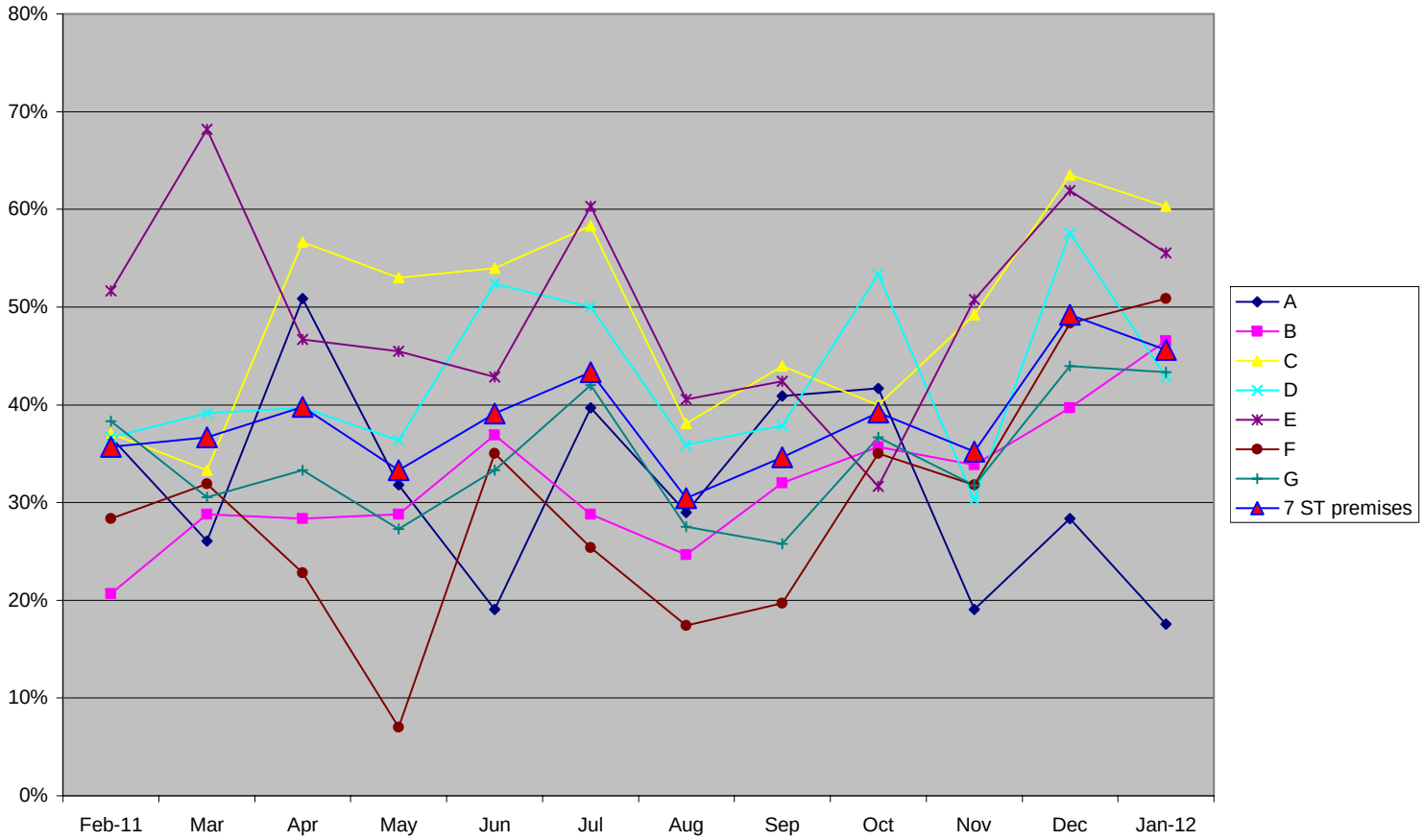
Data considerations (1)

- What steps in the food chain?
- Prevalence (presence/absence) or enumeration?
- Level of detection of culture system? (number of sample replicates affect prevalence rates)
- Molecular-based subtyping methods are powerful discriminating tools



The premises effect

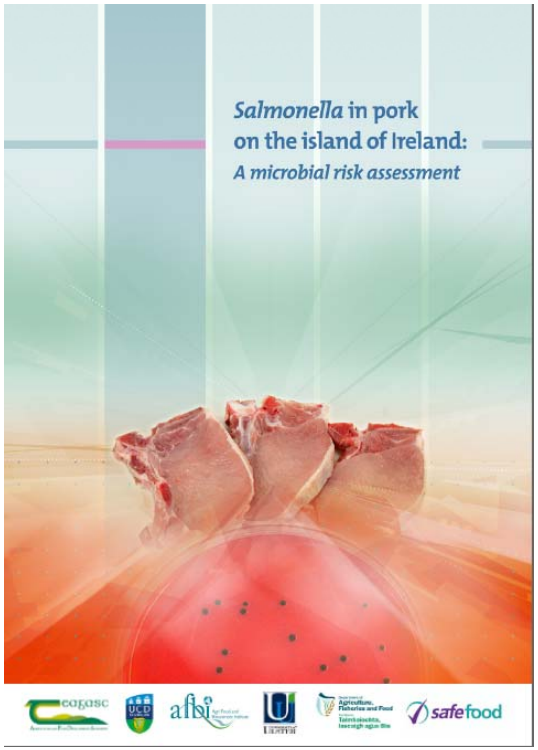
Campylobacter positive rinsates of different poultry premises



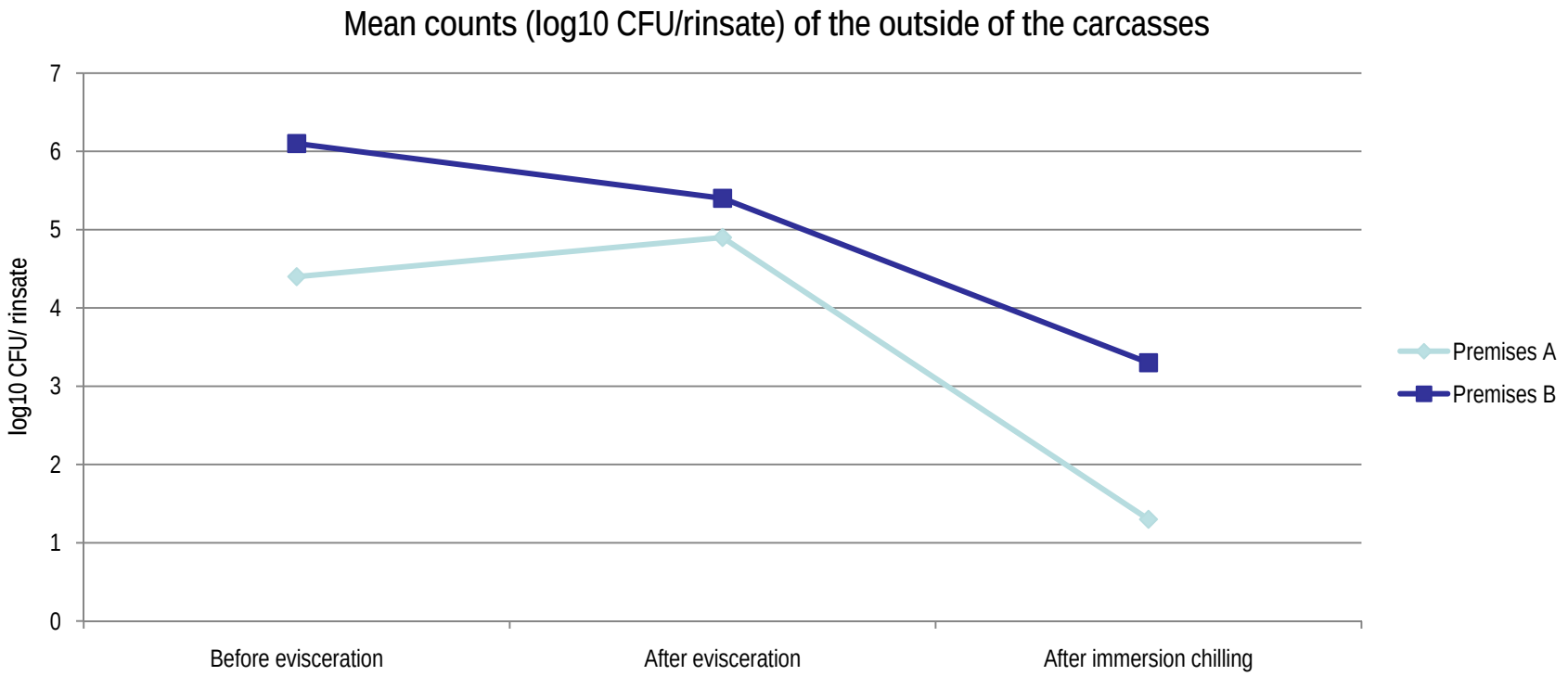
The premises effect

Plant	Sample size	No Positive	Prevalence %
A	180	0	0
B	180	4	2.2
C	180	0	0
D	180	20	5.5
E	405	35	8.6
F	120	8	6.7

UCD Institute of Public Health, Dublin



The premises effect



NZ MPI *Campylobacter* in poultry programme

Data considerations (2): Validation of tests (Ian Gardner, UPEI Canada)

- Diagnostic and analytic sensitivity and specificity not equivalent
- Culture often has poor sensitivity for food-borne pathogens
- Only one published meta-analysis of food hazard diagnostic tests: *Salmonella* spp. in pigs
- PCR replacing culture but challenges in validation
- Latent class analysis: assumes neither PCR or culture is perfect and and true contamination rate is unobserved (latent)
- STARD (Standards for Reporting of Diagnostic Accuracy)

invA-gene-based PCR for *Salmonella* in pigs

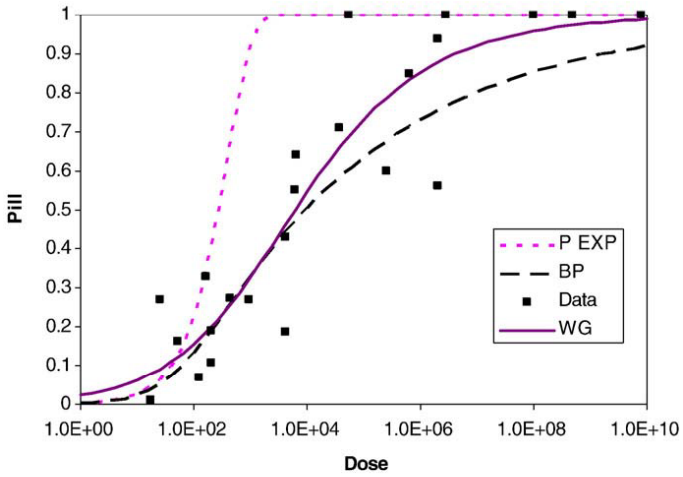
Mainar–Jaime et al.
Zoonoses and Public Health
2008; 55:112-118

	Culture +	Culture -
PCR +	28	39
PCR -	1	135
	29	174

Problem: PCR can never be more sensitive than culture, if culture is reference test

Data considerations (3): Dose response

- Few data sets
- Range of possible health endpoints
- Susceptibility of host e.g. genetic, immune status
- Extrapolation from high dose to low dose may be problematic
- Strain virulence can be significant
- e.g. *Listeria, Campylobacter*

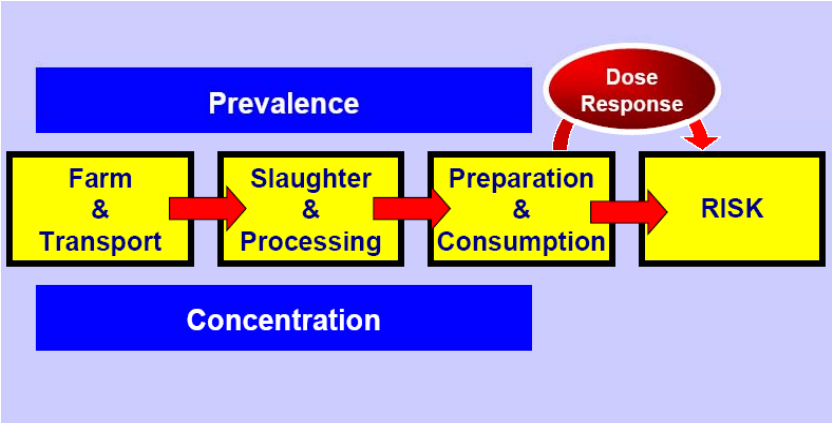


Data considerations (4): Uncertainty in risk assessment

- Lack of or incomplete information and knowledge: measurement sources, model sources and data gaps
- Explanation of uncertainties daunting in face of large number of input parameters and complex exposure pathways
- Hard to separate heterogenic (attribute) variability from uncertainty in risk computations
- Confidence intervals or credible ranges (Bayesian) for outputs are preferred cf. point estimates

Data considerations (5): Validation of risk assessments

- Is the risk assessment an accurate representation of the real world?
- Need to access data not used in model development
- Per serving risks vs. risks p. a. for a national population – latter requires additional data such as number of servings per year and YOPIs as proportion of total population



Risk profiling approach

Risk profile (Codex)

- “Description of a food safety problem and its context”
- Typically gathers hazard exposure pathway information, with risk information from published literature
- Many examples - screening” risk assessment?
- EFSA BIOHAZ Scientific Opinion 2012: Framework for risk ranking that utilised:

  - simple decision trees, with steps being treatments
  - qualitative outputs (low risk, moderate risk, qualified presumption of risk)

Risk profiling: Modernisation of meat inspection

265 Splitting backbones and final inspection — hogs ready for cooler, Swift & Co., Chicago, U.S.A. Copyright 1906 by H. C. White Co.

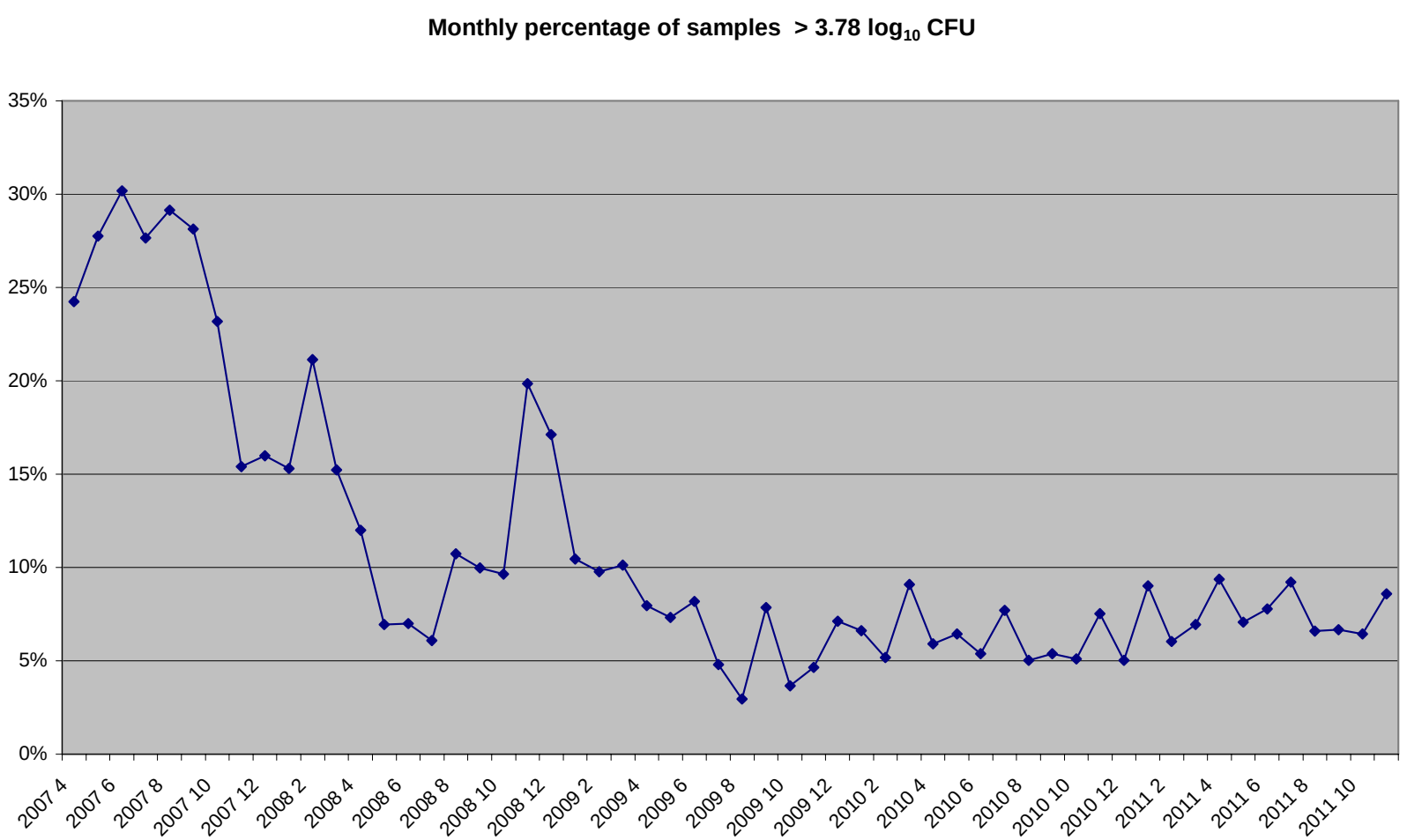
Post mortem meat inspection

- Global paradigm shift : focus on post mortem inspection to focus on process control
- Risk profiling / modelling exposure pathways rather than risk assessment has driven change:
  - Equivalence – grossly-detectable abnormalities
  - Equivalence - hazard control at specific steps
  - EFSA BIOHAZ meat inspection scientific opinions
  - Risk assessments for specific pathogens (*Salmonella*, *Campylobacter*, STECs) have had impact on choice of interventions for contaminants

NZ *Campylobacter* performance target

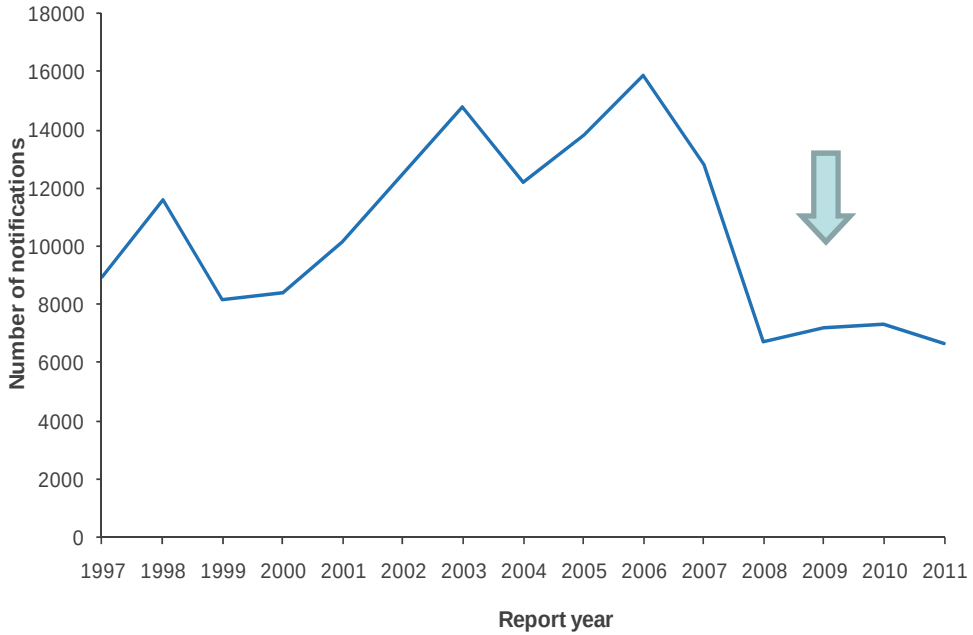
- Represents an approximate one log reduction in level of hazard control cf. 2007 baseline (4 logs to 3 logs)
- System accredited and verified by MPI
- High count limit, quarterly limit and moving window
- MW failure when seven or more out of 45 samples from three successive processing periods are greater than 3.78 log $_{10}$ cfu/carcass
- Integrated industry and regulator response in case of non-compliance, with possible escalation to premises closure

NMD: *Campylobacter* prevalence > 3.78 log $_{10}$ cfu/carcass



Plateau of human notifications of campylobacteriosis per 100 000 population

- 2009: 166
- 2010: 168
- 2011: 152



Campylobacter risk management

- Marked improvement in national NMD statistics following introduction of regulatory target but variable performance at premises level
- Link to Codex “performance objective’ (PO) concept?
- Increased stringency in CPT could target:

  - a further improvement in national performance and /or

  - an improvement in poorest performing premises
- Risk assessment needed to inform decision

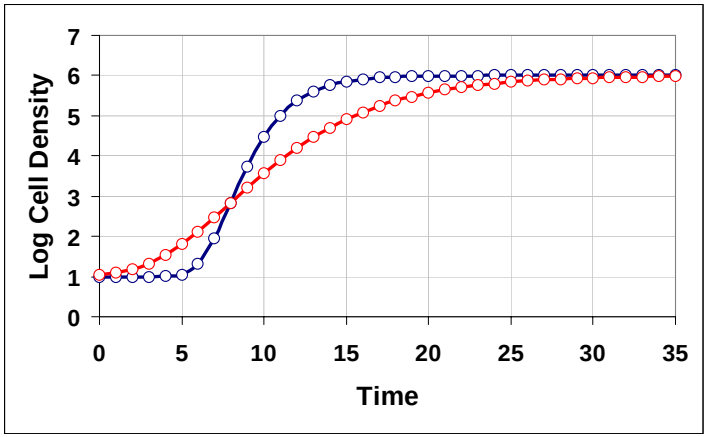
Simplified risk assessment models

Simplified risk assessment models (1)

- Marcel Zwietering: Quantitative risk assessment: Is more complex always better? Simple is not stupid and complex is not always correct. International Journal of Food Microbiology 134 (2009) 57–62
- While promoting probablistic methods, accept that probability values will be approximate in simplified models
- Limit number of steps in exposure pathway
- Limit number of scientific assumptions
- Characterise variability to extent practical
- Minimise opportunities for uncertainty

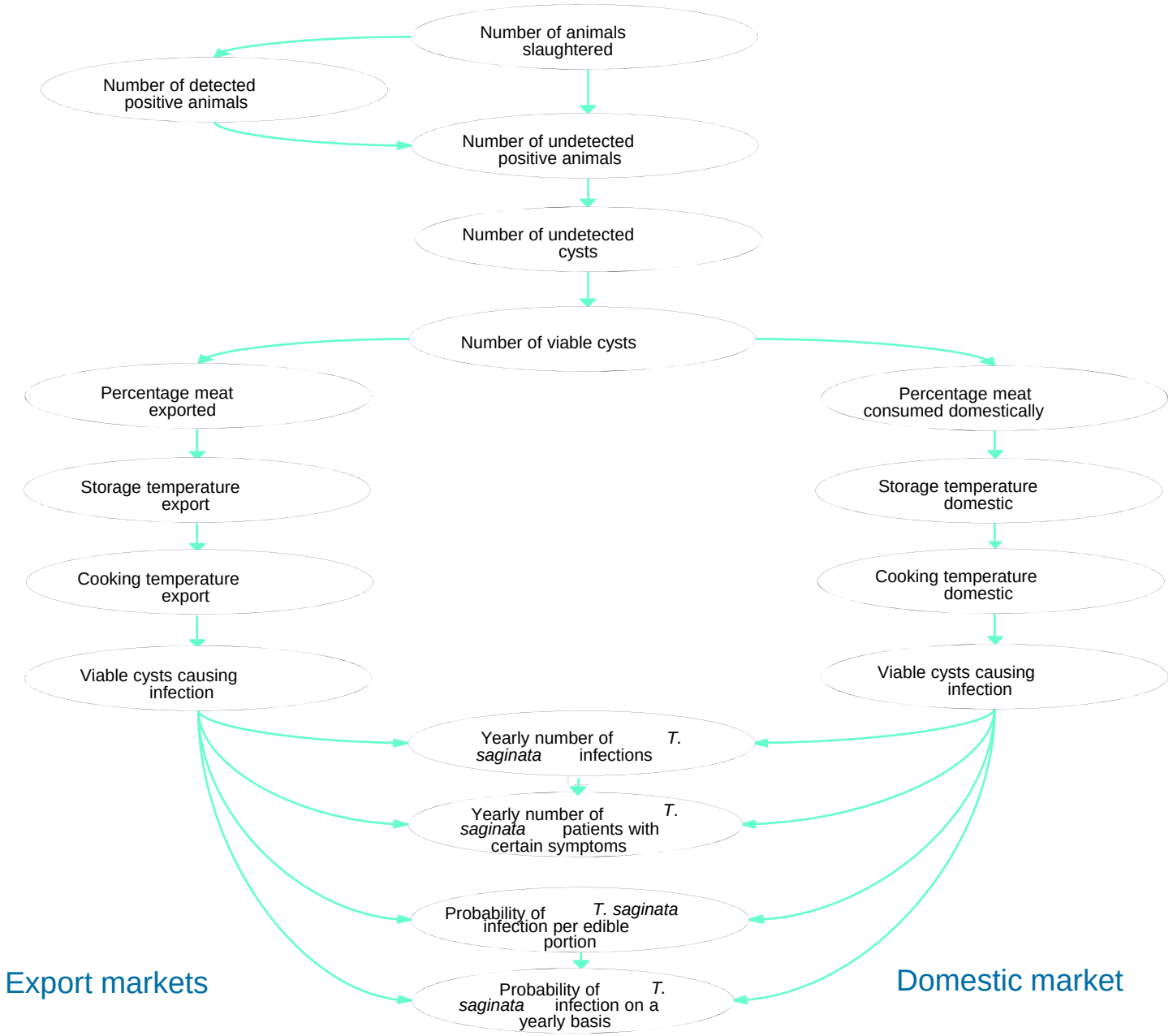
Simplified risk assessment models (2)

- Key data points: farm / processing / retail
- Cannot do reverse calculations to test value of “upstream” interventions (link to PO discussion)
- Utilise predictive microbiology for intermediate steps if needed

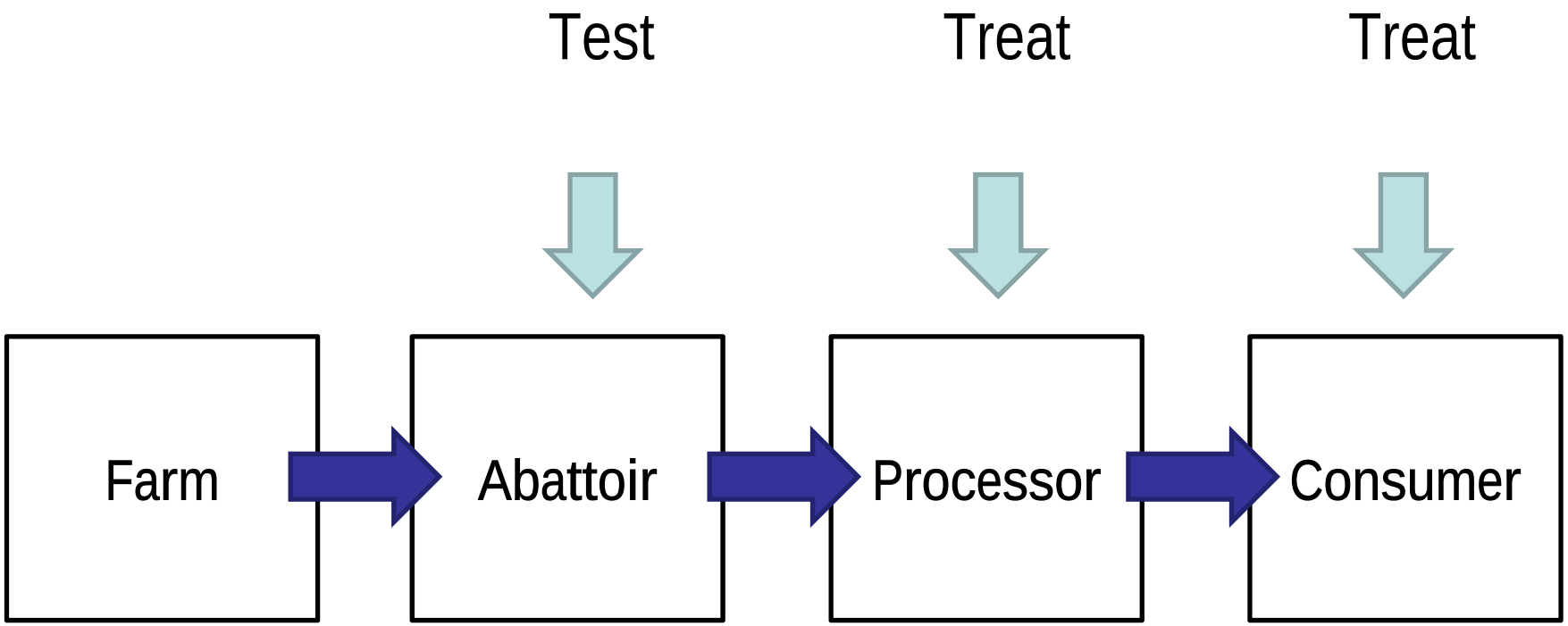


Modernisation of meat inspection: Beef tapeworm

- Traditional meat inspection for *Taenia saginata* cysts is highly intensive but highly ineffective at low infection rates
- Detailed “NZ-only” probabilistic risk assessment model as basis for decisions on equivalence
- Domestic and export consumer exposure pathways
- Detailed data on sensitivity of post mortem inspection procedures of decreasing intensity


Number of animals slaughtered
Number of detected positive animals
Number of undetected positive animals
Number of undetected cysts
Number of viable cysts
Percentage meat exported
Storage temperature export
Cooking temperature export
Viable cysts causing infection
Percentage meat consumed domestically
Storage temperature domestic
Cooking temperature domestic
Viable cysts causing infection
Yearly number of *T. saginata* infections
Yearly number of *T. saginata* patients with certain symptoms
Probability of *T. saginata* infection per edible portion
Probability of *T. saginata* infection on a yearly basis
Export markets
Domestic market

Simple model: minimise pathway steps



Simple (Codex?) model for modernisation of meat inspection: *Taenia saginata* in beef

Colour code:

Estimates to be entered by user
Values calculated by programme

4,272,082	Cattle population
0.0069%	Prevalence
4	Number of cysts of lightly infected animal
4%	Probability of detecting one cyst
15.1%	Probability of detecting an animal if infected
0.001%	Percentage of the population that is infected and detected
84.9%	Probability of not detecting an animal if infected
0.006%	Percentage of the population that is infected and not detected
250	Number of animals that are infected and not detected
1001	Number of undetected cysts
30%	Probability cyst is viable
298	Number of viable cysts
12%	Probability cyst survived freezing.
37	Number of viable cysts that survived freezing
32%	Probability cyst survived cooking
12	Number of viable cysts that survived freezing and coooking
29%	Probability of infection
3	Number of people infected

Taenia saginata in beef: Another simulation

Colour code:

Estimates to be entered by user	
Values calculated by programme	

4,272,082	Cattle population
0.0069%	Prevalence
10	Number of cysts of lightly infected animal
4%	Probability of detecting one cyst
33.5%	Probability of detecting an animal if infected
0.002%	Percentage of the population that is infected and detected
66.5%	Probability of not detecting an animal if infected
0.005%	Percentage of the population that is infected and not detected
196	Number of animals that are infected and not detected
1960	Number of undetected cysts
30%	Probability cyst is viable
583	Number of viable cysts
12%	Probability cyst survived freezing.
73	Number of viable cysts that survived freezing
32%	Probability cyst survived cooking
23	Number of viable cysts that survived freezing and coooking
29%	Probability of infection
7	Number of people infected

Taenia saginata in beef: Detecting an outbreak

The probability of detection depends on the number of cysts and the distribution

Probability of detection per cyst	4.0%	The effectiveness of inspection. Assumes 100% specificity.
Mean number of cysts per animal	10	The average level of infection of animals in the herd.
Probability of detecting an infected animal	**33.5%**	
Number of animals inspected before first positive detected	**2**	

Simulated infected herd

	Number of cysts	Probability of non-detection infected animal	Probability of detection at least one cyst	Cysts per animal detected	Infected animal detected?	Total number of infected animals detected?	Total number of cysts detected	Infected herd detected?
Cow 1	5	82%	18%	0	0	0	0	0
Cow 2	8	72%	28%	0	0	0	0	0
Cow 3	11	64%	36%	0	0	0	0	0
Cow 4	13	59%	41%	0	0	0	0	0
Cow 5	10	66%	34%	2	1	1	2	1
Cow 6	10	66%	34%	2	1	2	4	1
Cow 7	8	72%	28%	0	0	2	4	1
Cow 8	9	69%	31%	0	0	2	4	1
Cow 9	10	66%	34%	0	0	2	4	1
Cow 10	7	75%	25%	0	0	2	4	1

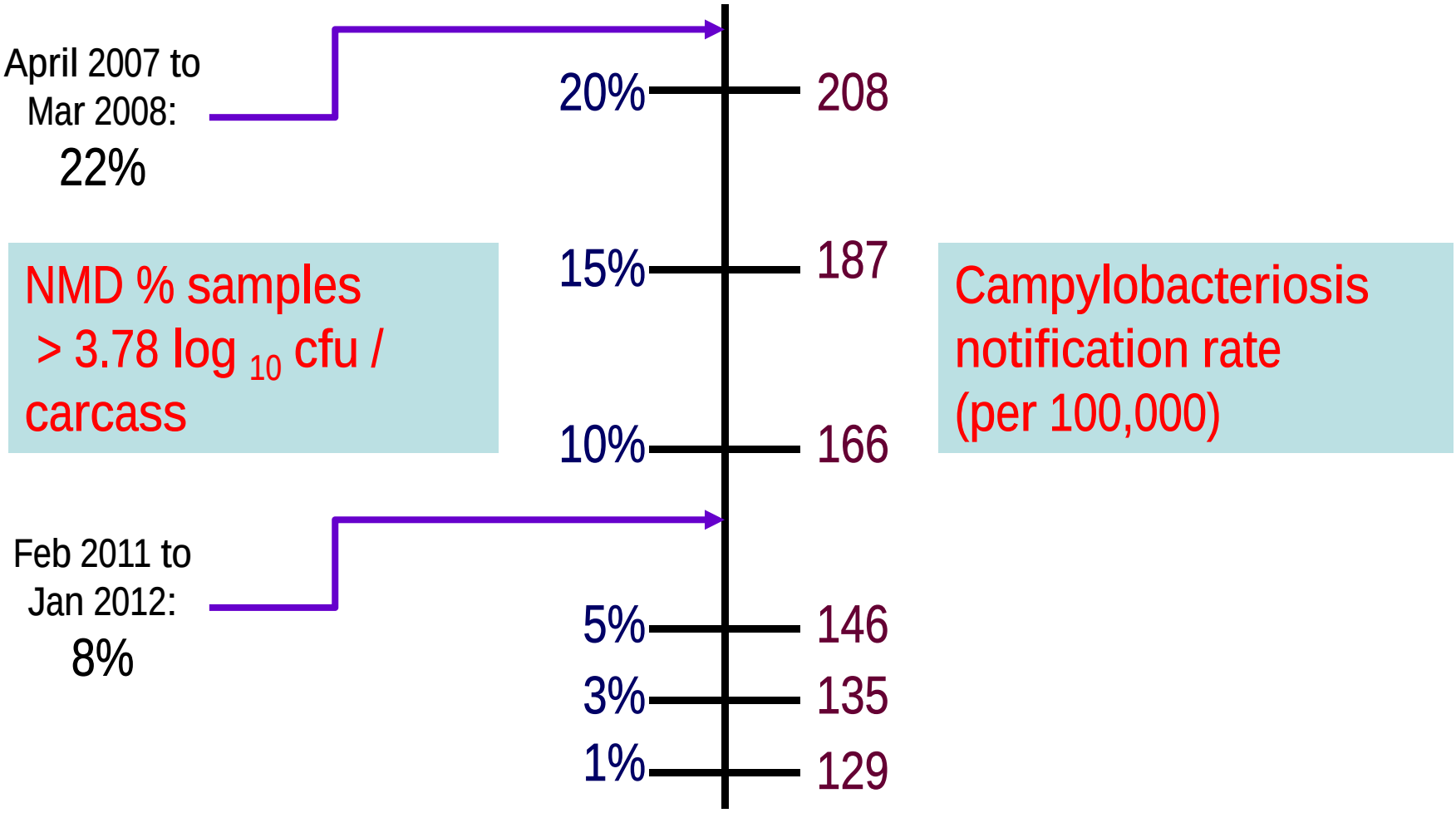
Simple risk assessment: *Campylobacter* CPT

- Simple pathway model: Estimates changes in NMD results with different interventions *at premises level*
- Simple regression model: Estimates human health risk using NMD data *at national level*
- Alert tool: Simulates alerts and responses for individual premises

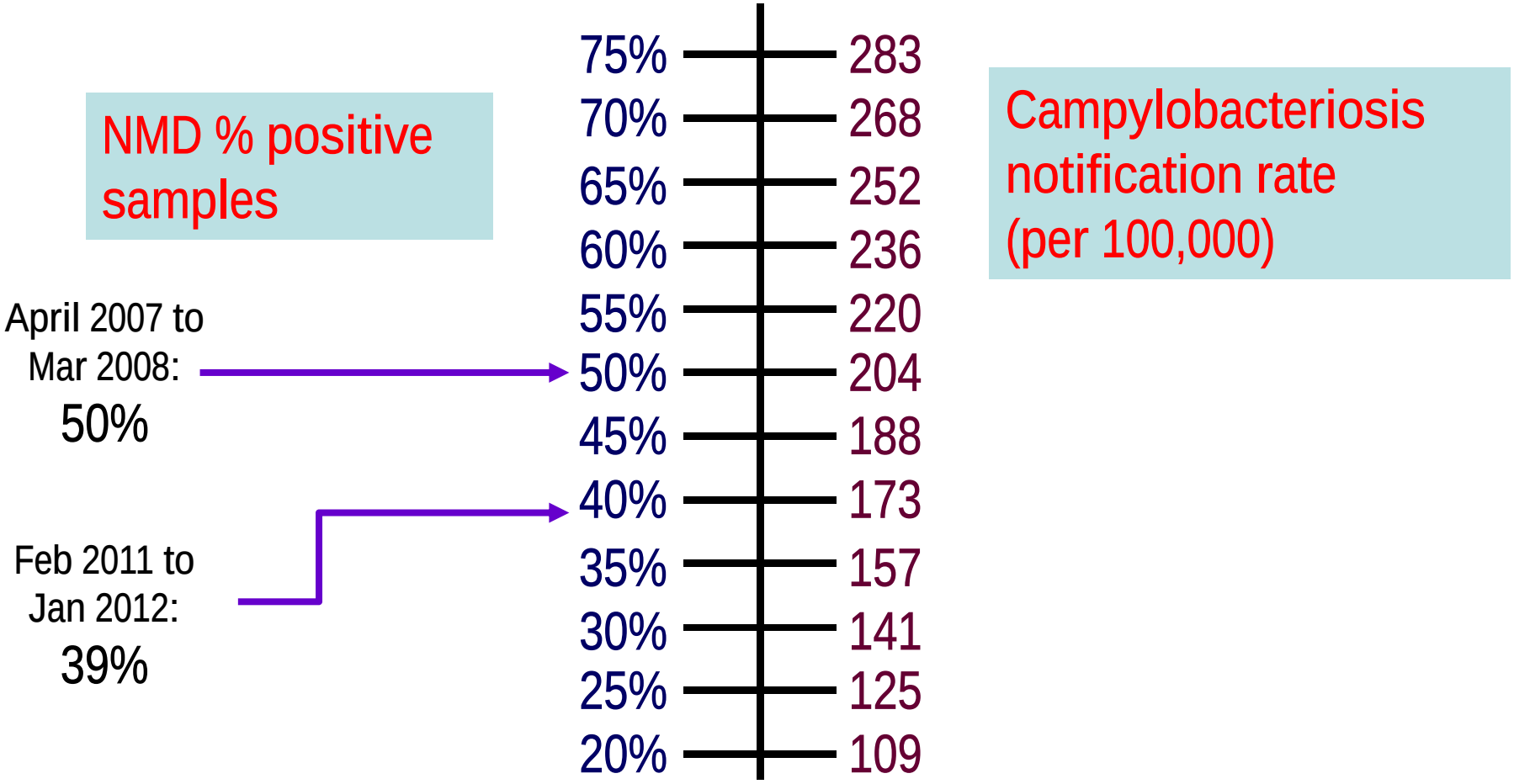
Simple pathway model: Screen example

	Data entry		
	Changes to routine process		
	Level immediately after processing step		
		Unit	**Distribution**
On farm (Caecal prevalence)	50%	Percentage	
Change			
	50%		
Pre scalding	8.21	CFU log_{10} \ rinsate	Triangular
Additional Change		CFU log_{10} \ rinsate	
Scalding and defeathering Effect	-1.67	CFU log_{10} \ rinsate	Triangular
Additional Change		CFU log_{10} \ rinsate	
	6.54		
Evisceration Effect	-0.18	CFU log_{10} \ rinsate	CDF-Based indepen
Additional Change	0.00	CFU log_{10} \ rinsate	
	6.36		
Spin chilling Effect	-2.71	CFU log_{10} \ rinsate	CDF-Based indepen
Additional Change		CFU log_{10} \ rinsate	
	3.65		

Regression model for human illness (1)

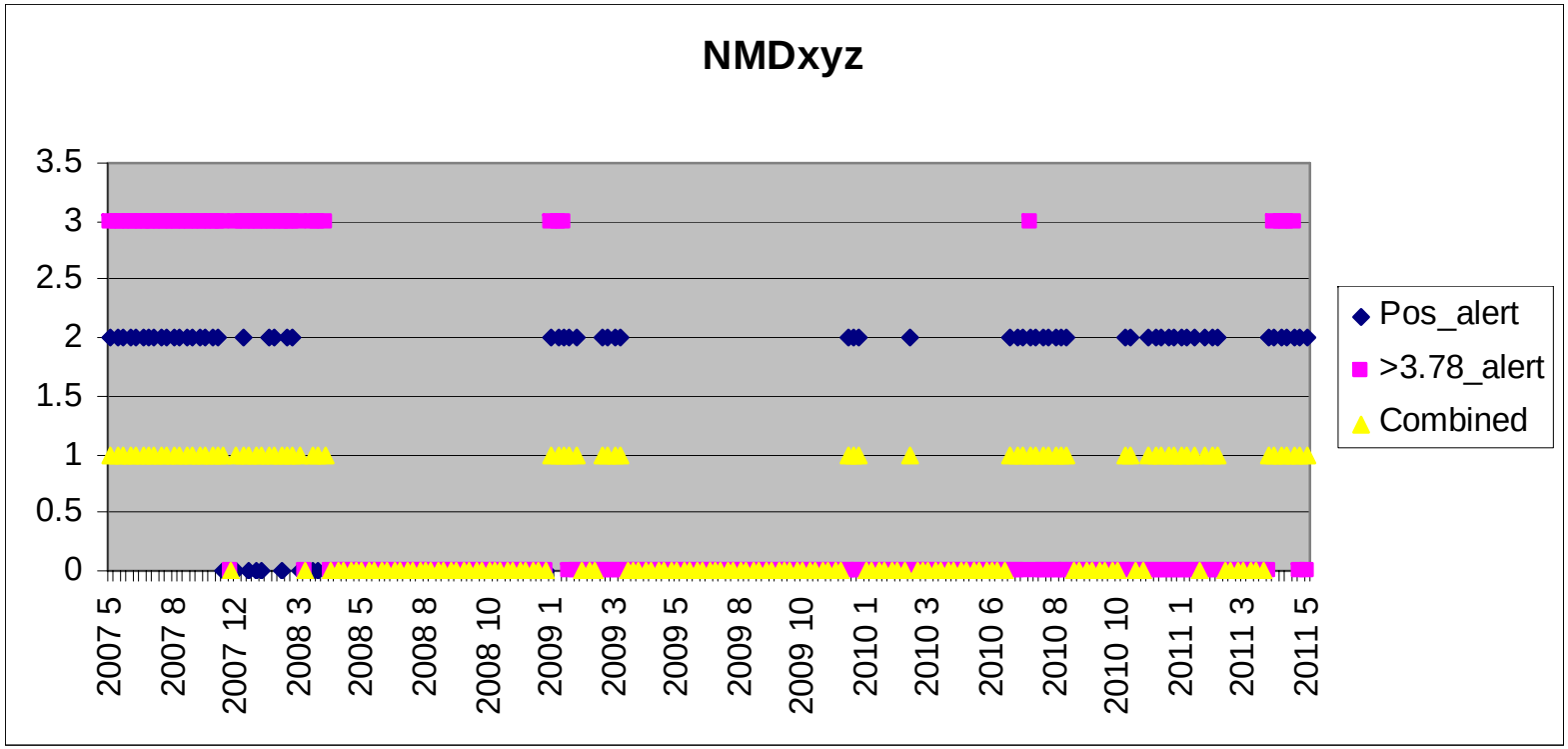


Regression model for human illness (2)



CPT alert modelling tool

Acceptance number	20	6
	MW_Positives	MW_>3.78



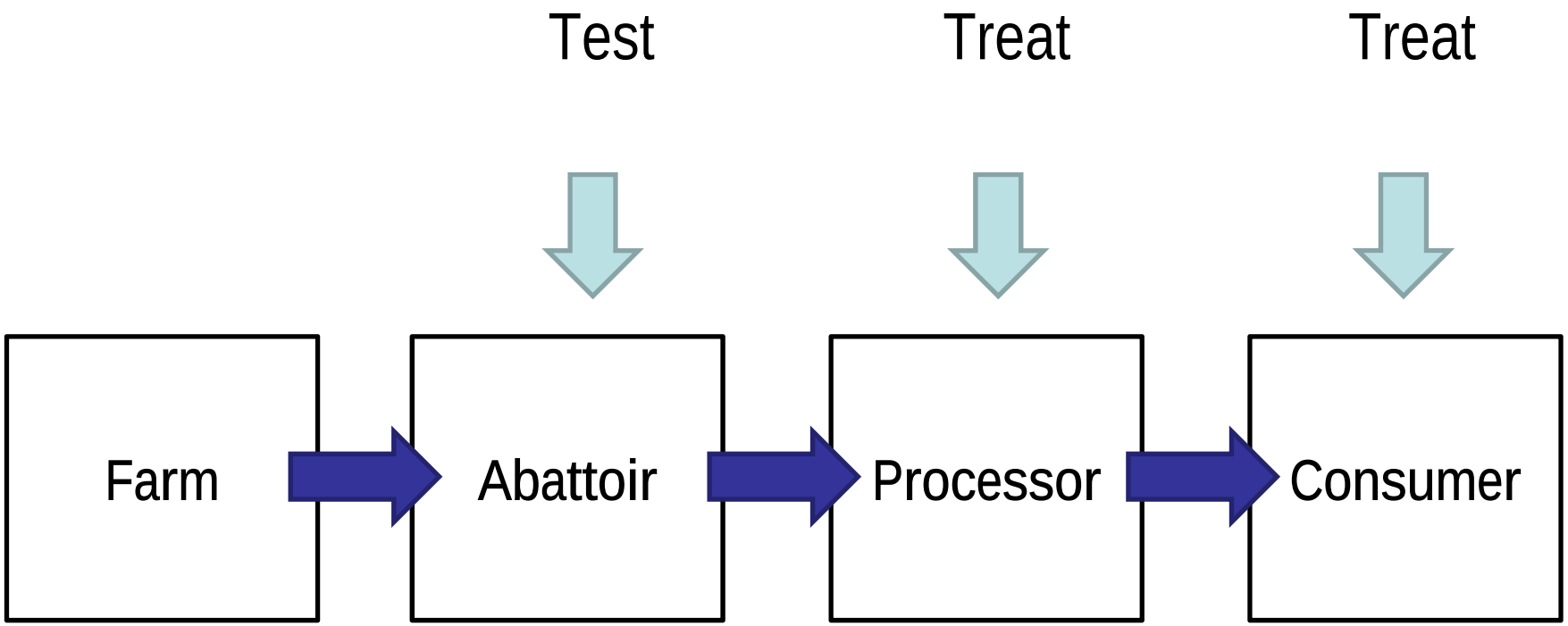
Alert tool: MW > 3.78 log10; Ac = 8

MW_Positives	MW > 3.78	Alerts
23	8	59
24	8	49
25	8	37
26	8	32
27	8	29
28	8	28
29	8	27
30	8	25
35	8	16
40	8	12

Trichinella spp. in pig meat

- Extremely low likelihood in pigs in many countries and readily available control measures
- Codex and OIE work programme
- Any residual risk must be extremely low
- Can a “negligible risk compartment” (OIE) be established at farm level?

Simple model: Minimise pathway steps



Assumptions for risk assessment

- The digestion test has a very high (close to 100%) sensitivity in terms of detecting animals that have a level of infection sufficient to cause human illness
- Only 1:1000 edible portions of infected pig meat remain infective after application of heat treatment and/or preservation at the processor and consumer parts of the food chain
- All infections are regarded as being severe

0.90

PIG TRICHONELLA SURVEY DATA AND POSSIBLE UPPER LIMIT OF EXPOSURE

INPUTS	OUTPUTS
Enter the total number of pigs used for fresh pork or small goods slaughtered per year	The prevalence could be as high as the following (the upper 1 sided confidence limit)
10,000,000	**0.00002%**
Enter the number of pigs that have been tested with negative results	The number of infected meals prior to cooking could be as high as the following
10,000,000	**115**
Select the confidence upper limit	The number of infected meals after cooking could be as high as the following
	0

0.90

PIG TRICHONELLA SURVEY DATA AND POSSIBLE UPPER LIMIT OF EXPOSURE

INPUTS		OUTPUTS	
Enter the total number of pigs used for fresh pork or small goods slaughtered per year	10,000,000	The prevalence could be as high as the following (the upper 1 sided confidence limit)	0.00046%
Enter the number of pigs that have been tested with negative results	500,000	The number of infected meals prior to cooking could be as high as the following	2,303
Select the confidence upper limit		The number of infected meals after cooking could be as high as the following	2

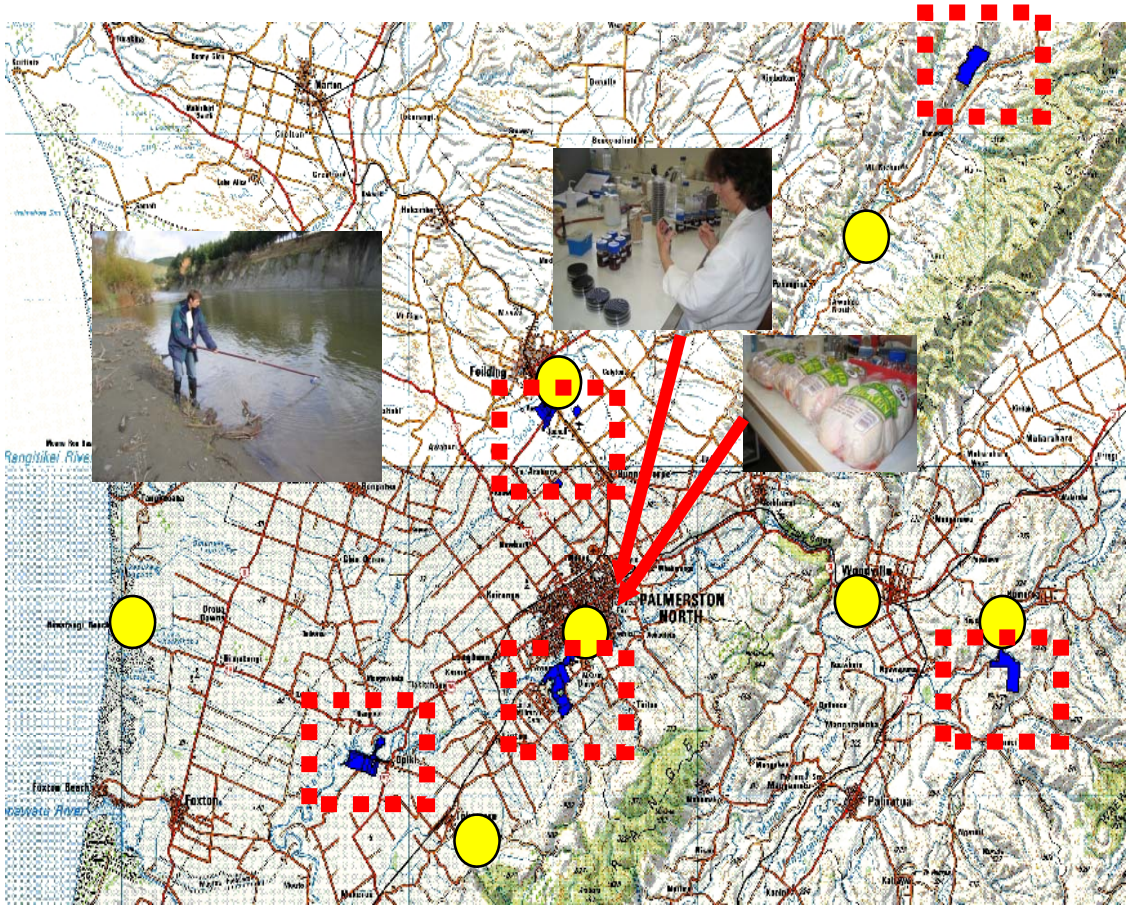
Food source attribution

Food source attribution

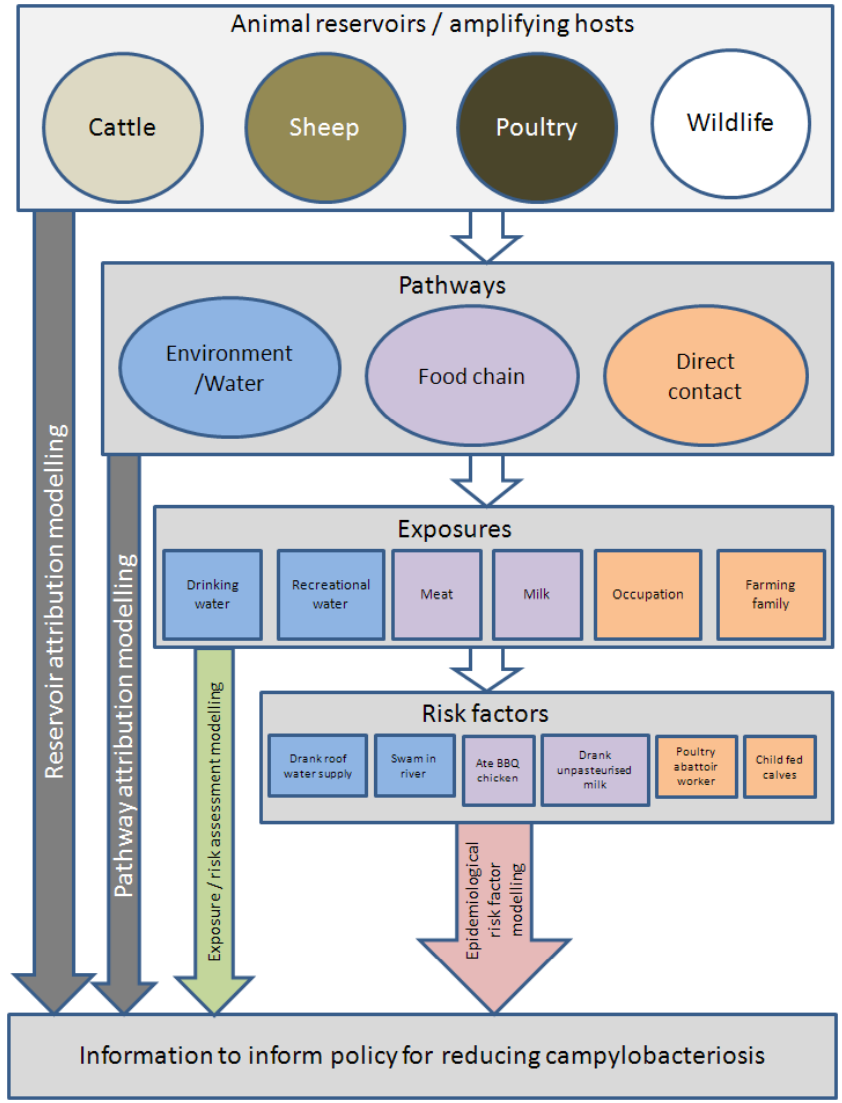
- Rapidly developing discipline
- Utilises human illness data and modelling of exposures from specific sources to attribute risks
- Molecular sub-typing adds a powerful tool e.g. PCR
- rMLST (new generation) uses high throughput sequencing of whole genomes to analyse many more genomic loci
- Informed by outbreak investigations (inherent investigation bias) and case-control studies (identify risk-factors for sporadic infections but require knowledge of population attributable fractions)

Massey University EpiLab 2005-2012

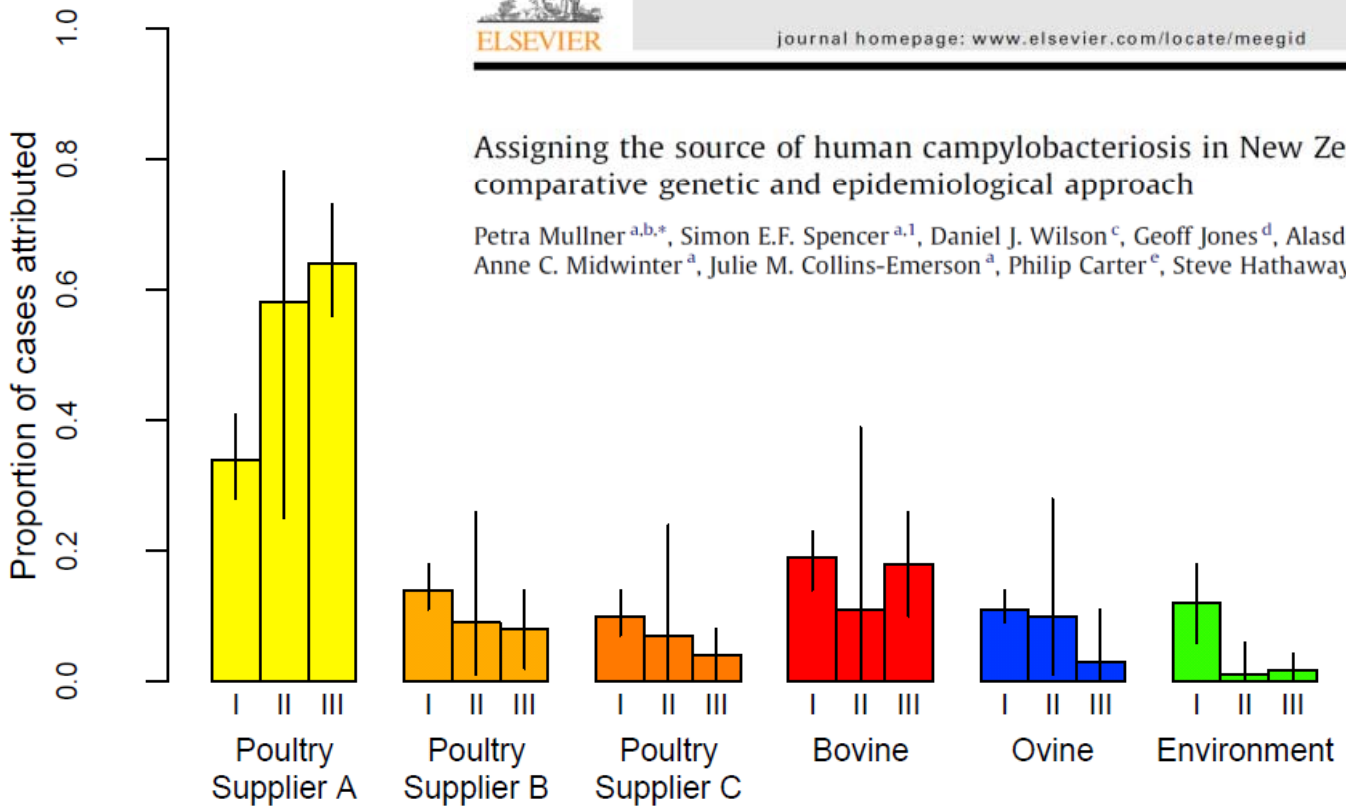
- Manawatu sentinel site
- Identify genotypes common to particular sources
- Modelling (reservoir attribution)



Modelling approach



Campylobacter source attribution

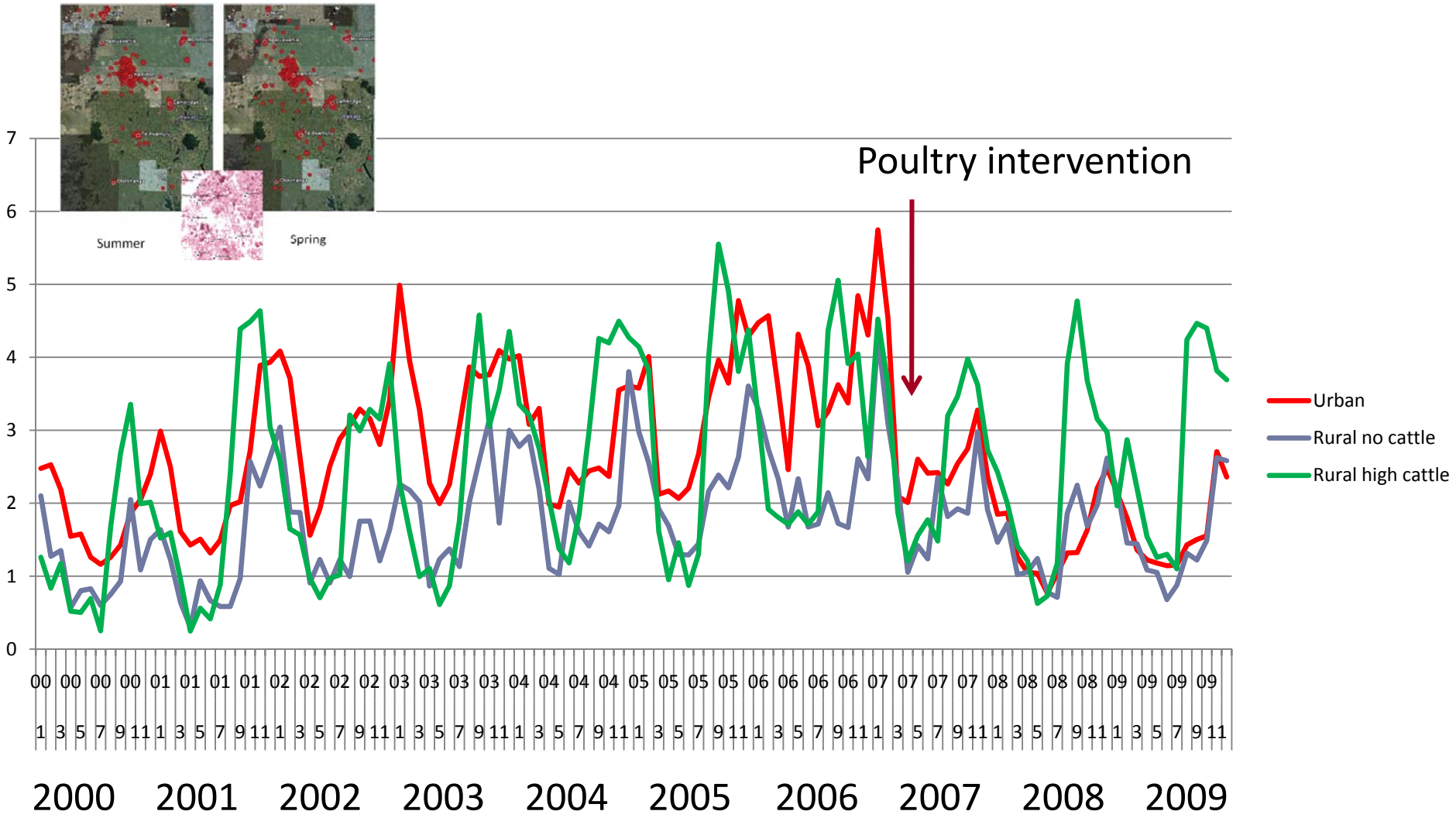


Infection, Genetics and Evolution

journal homepage: www.elsevier.com/locate/meegid

Assigning the source of human campylobacteriosis in New Zealand: A comparative genetic and epidemiological approach

Petra Mullner [a,b,*], Simon E.F. Spencer [a,1], Daniel J. Wilson [c], Geoff Jones [d], Alasdair D. Noble [d], Anne C. Midwinter [a], Julie M. Collins-Emerson [a], Philip Carter [e], Steve Hathaway [b], Nigel P. French [a]



Dynamic changes in source attribution

Summary

- Fit-for-purpose “risk assessment” is using the right tool to adequately answer the risk managers questions
- Simplify where possible and practical
- Creative combinations of tools strengthen the evidence base for illuminating risks associated with biological hazards in food

Acknowledgements

- Peter van der Logt, MPI : Modelling *Taenia saginata*
- Terry Ryan, MPI: Modelling *Trichinella*
- Nigel French and EpiLab team: Food source attribution for *Campylobacter*
- *Campylobacter* risk management working group, MPI