Te Kunenga ki Pūrehuroa

Massey University

Collaborating Centre for Veterinary Epidemiology and Public Health

– Paratuberculosis (PTB) –

Pathogen Typing and Modelling to Explore Transmission and Virulence

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IDReC | Infectious Disease Research Centre

EpiCentre

Agenda

Johne's disease (JD) = Paratuberculosis (PTB)

MAP = *Mycobacterium avium subsp. paratuberculosis*

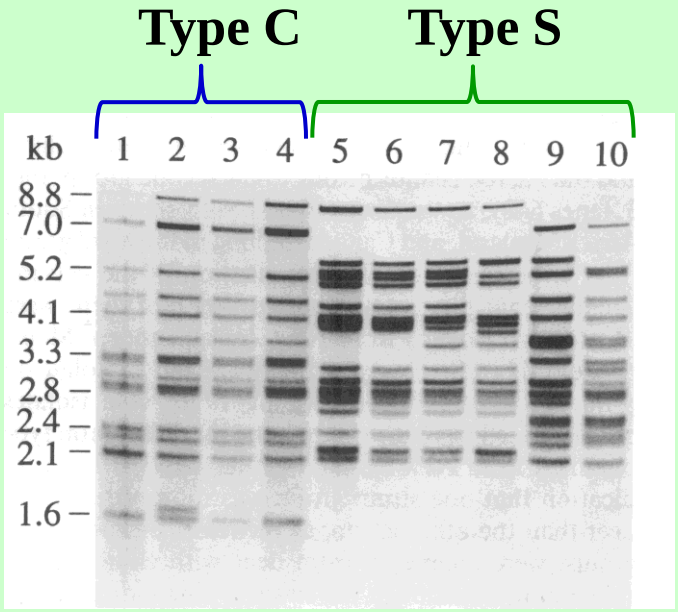
- MAP strain typing
- MAP strains in a farm-network
- MAP virulence
- MAP modelling

MAP Strain Typing

Strain type O'Brien, Mackintosh, Griffin (2006), DeLisle, Collins

- **Type C** (Type II)
  - *'Found in infected cattle and most infected deer'*
- **Type S** (Types I and III)
  - *'Found in most infected sheep and occasionally in infected deer'*

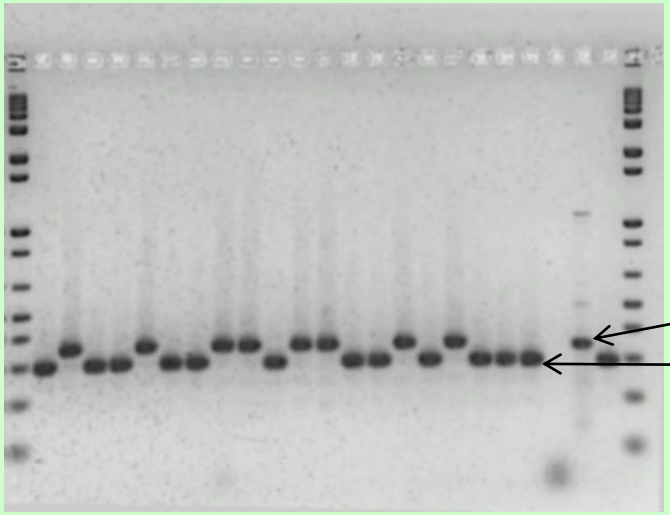
IS900 typing



VNTR + SSR typing

Collins, DeLisle et al. 2010

- 6 VNTR + 1 SSR loci
- Johne's Disease Research Consortium (JDRC)



JDRC data 2009-10:

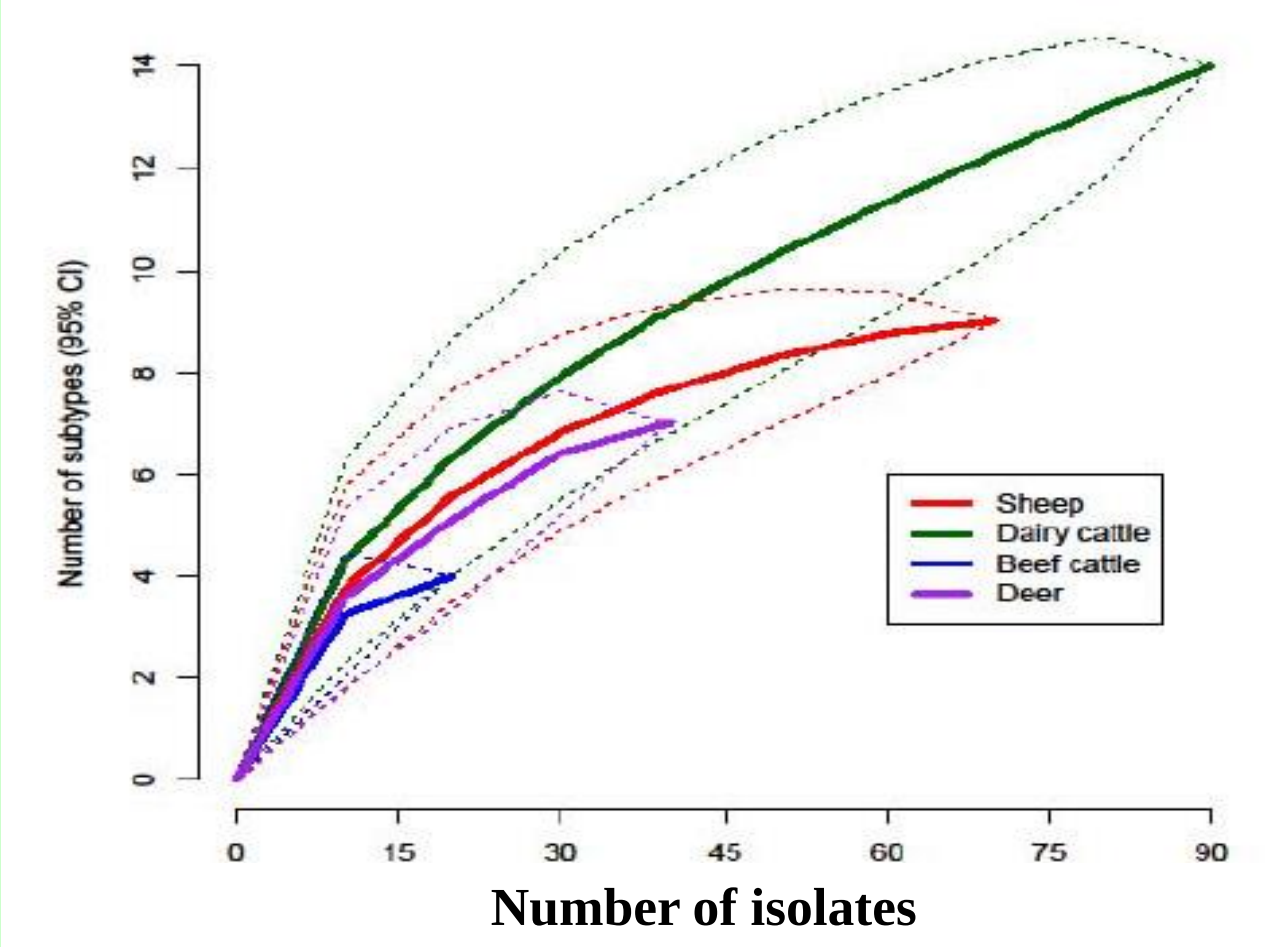
LIC: Voges et al.

Massey: Verdugo et al.

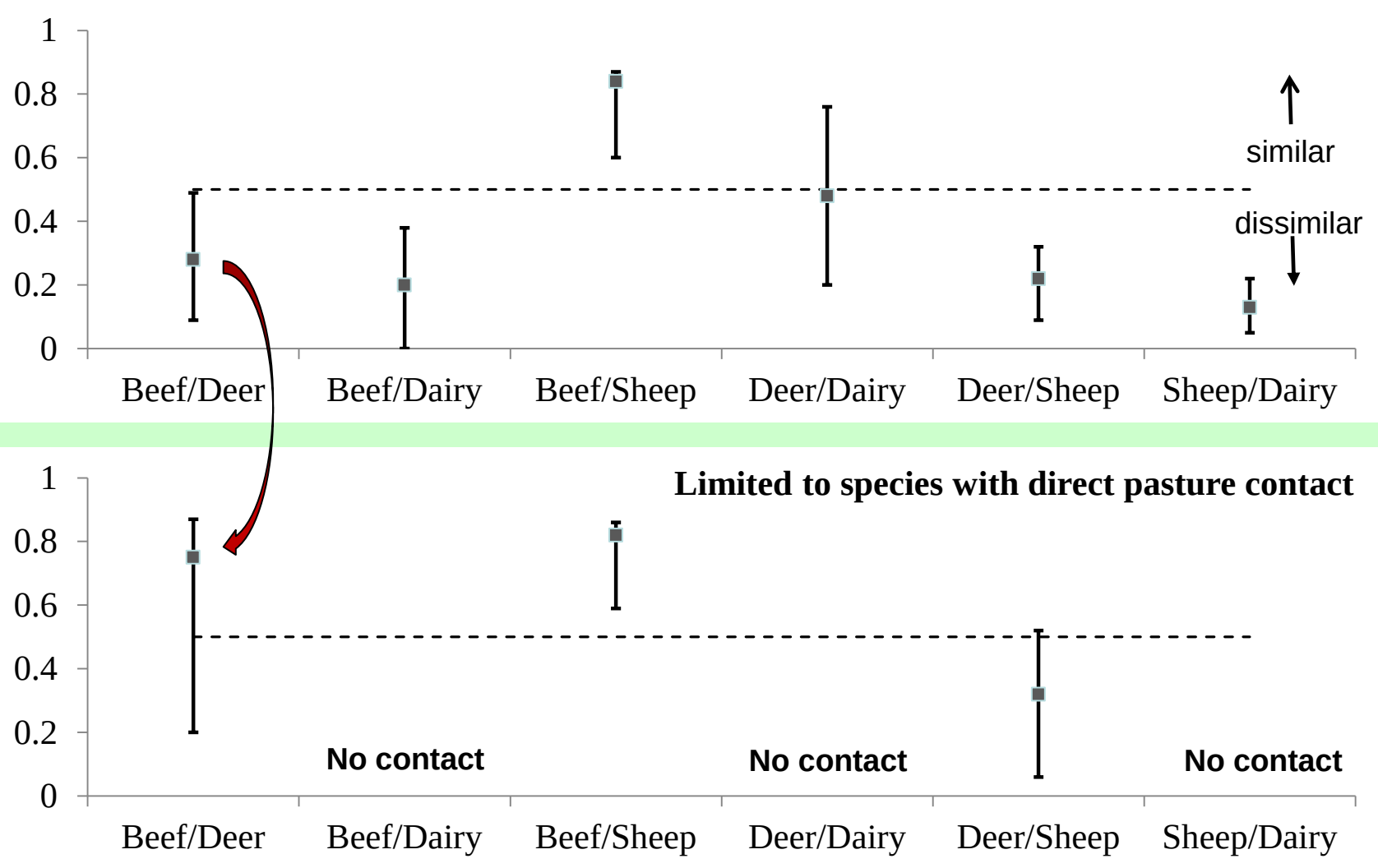
	BEEF	DEER	SHEEP	DAIRY
	- 97 farms -			
Farms	20	32	55	55
Isolates	26	68	68	184
Type C	13	65	9	169
Type S	13	3	59	15
Profiles	6	9	13	14
Type C	4	7	4	12
Type S	2	2	9	2

Strain diversity in the population (‘*rarefaction*’)

Number of ST-Profiles



Strain Similarity (‘proportional similarity index’)



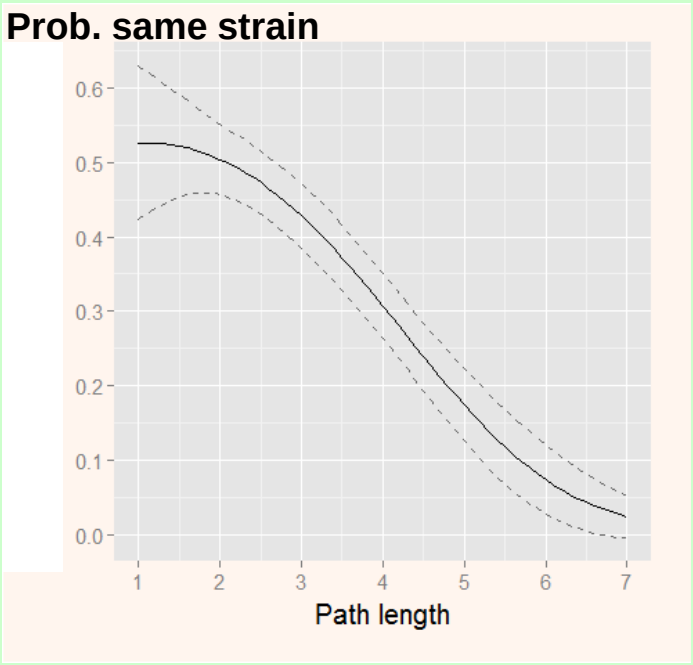
MAP strains in a farm-network

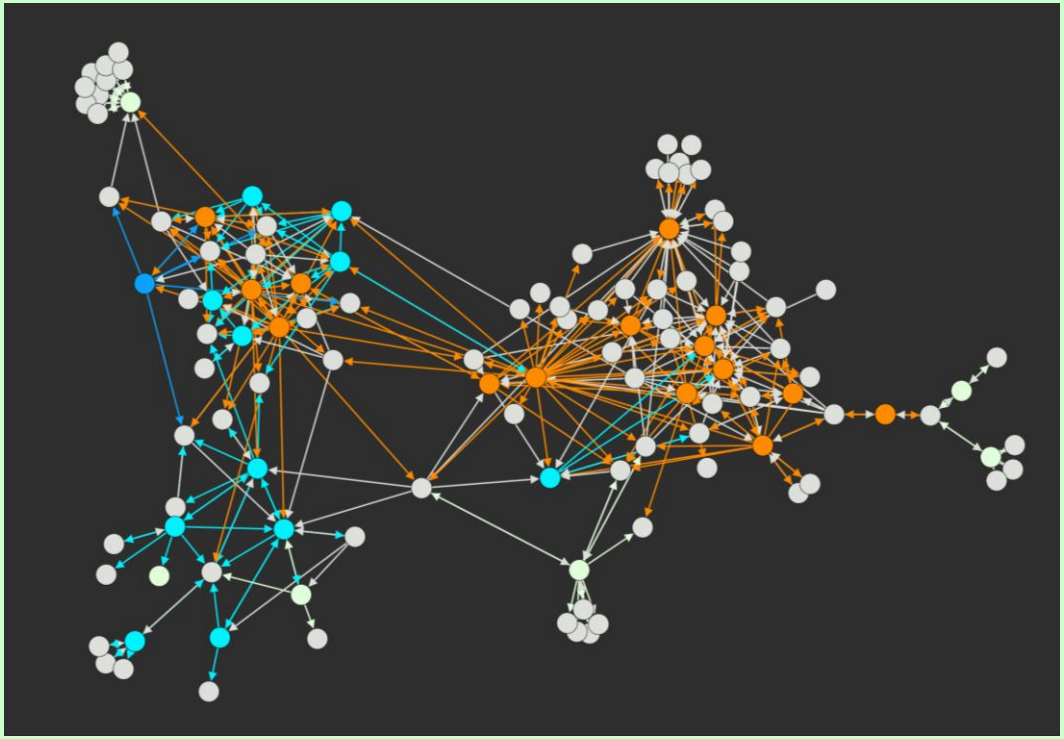
Marquetoux et al. 2014. Social network analysis and preventive veterinary medicine: application to a livestock movement network in New Zealand (PhD manuscript)

Probability of sharing same ST ~ path length + path length^2

Farm-to-farm transmission: *comparing strains of two connected farms*

112 farms of Landcorp Ltd.
68 other farms (out-movements)
3,531 movements 2006 – 2010
7 strains
45 isolates from 33 farms

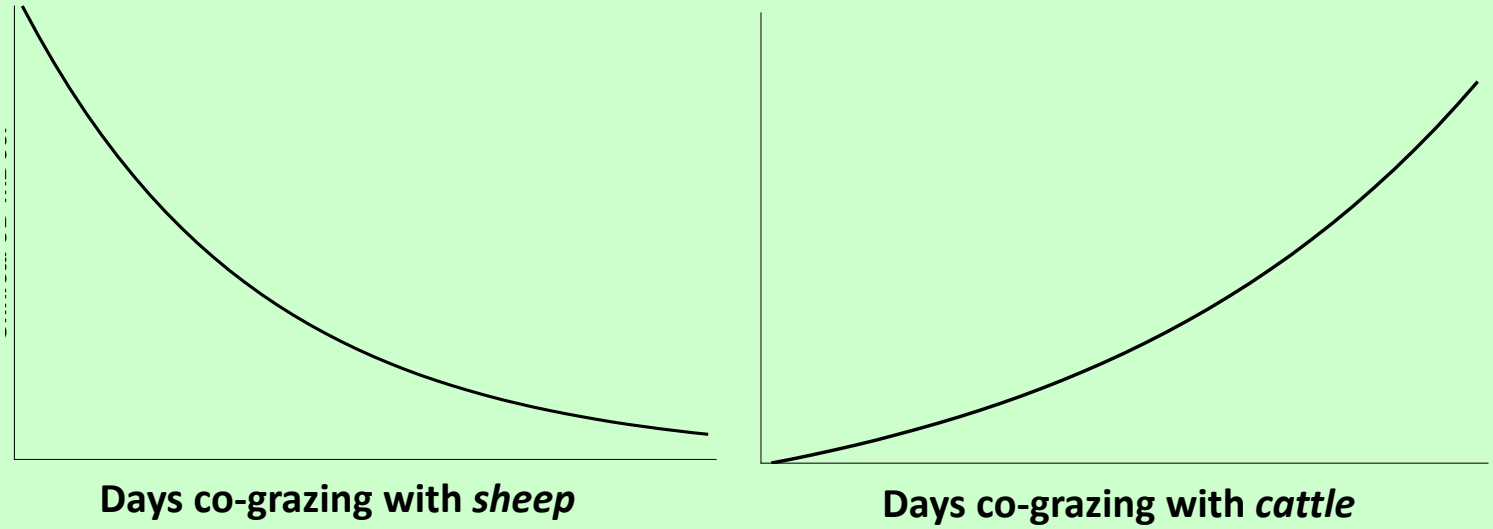




MAP Virulence

Ovine strain less virulent than bovine strain for cattle or deer?

Clinical PTB incidence of deer (Hunnam et al. 2007)



2. Mackintosh et al 2007: Infecting deer experimentally
3. Gollnick et al. 2007: Infecting bovine macrophages
4. Verdugo et al. 2010: Prevalence of enlarged visceral lymph nodes
5. Verdugo et al. 2013: Clinical incidence in co-grazed vs. isolated species

Testing a virulence hypothesis

- JDRC sheep intervention study
- Farms: 13 Merino + 7 farms (Romney, Corridale, mixed)
- PM of low BCS cull-ewes (n = 343)

Low BCS ewes

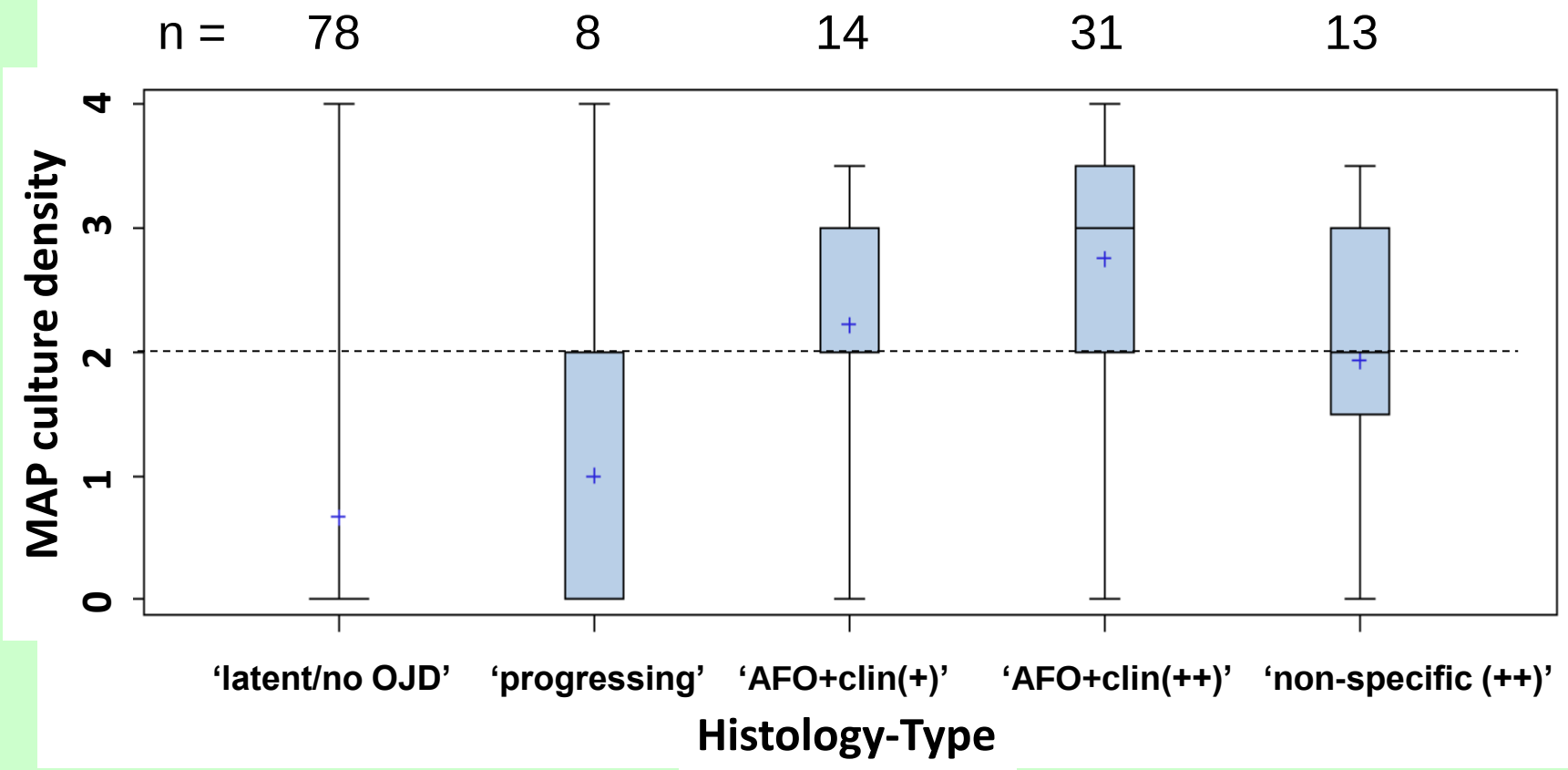
Gross pathology

+ 91% lab pos

- 12% lab pos

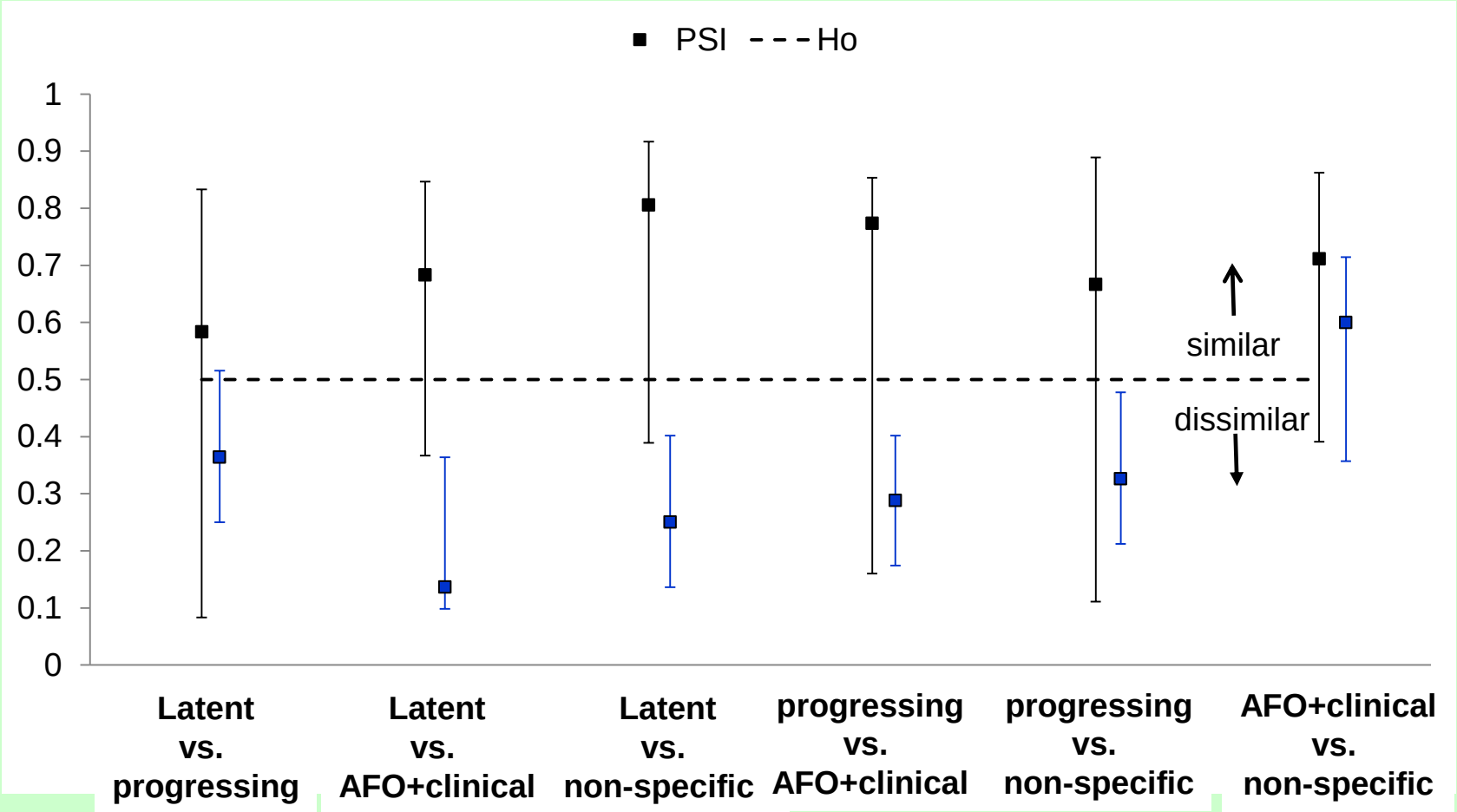
Lab=histo/Elisa

"Gold standard" for virulence <u>histology</u> *vs.* MAP culture density



Association between virulence and genotype n=49

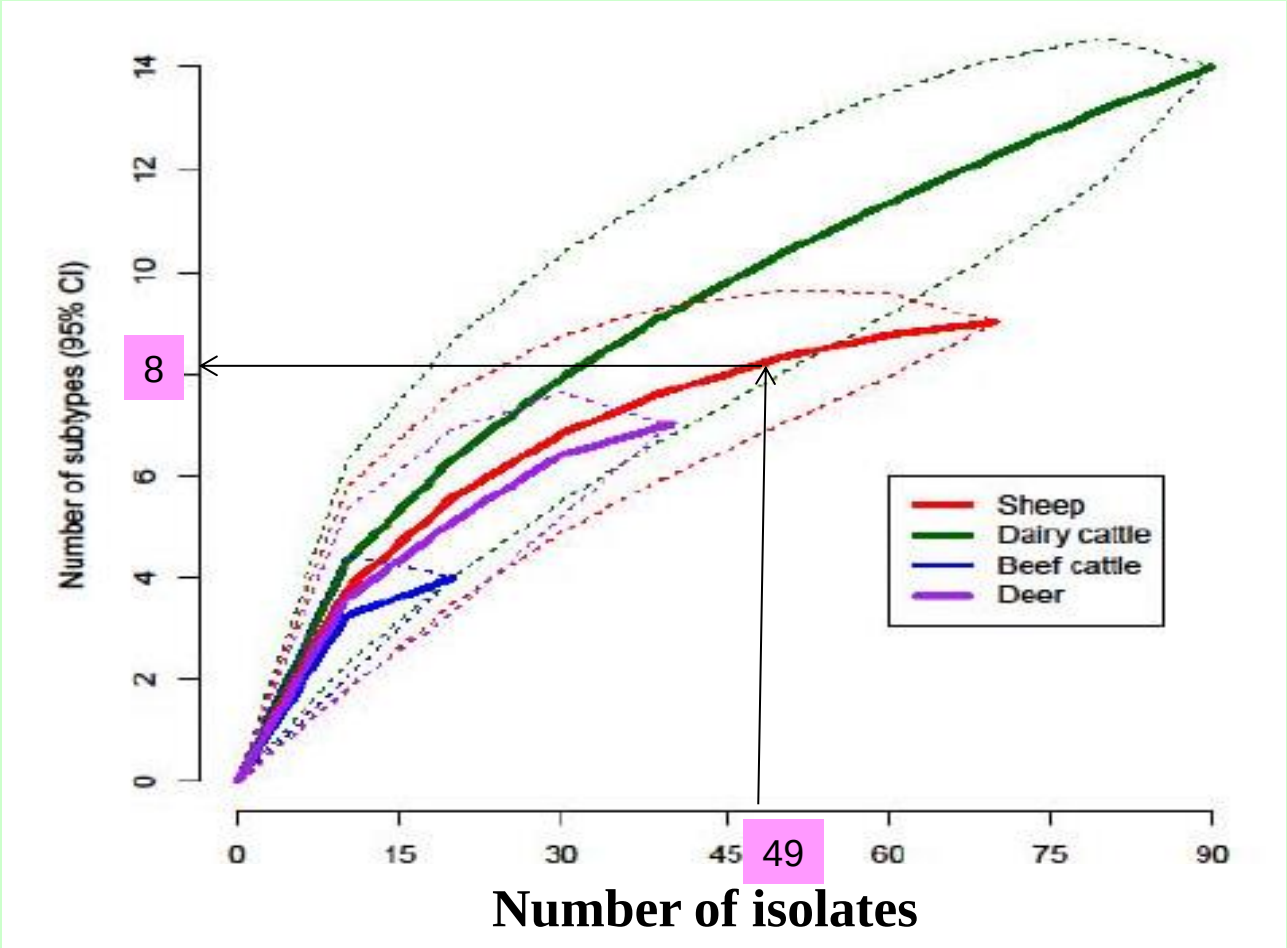
- **Proportional similarity index (PSI ± 95%CI)**



Expected genotype diversity among 49 isolates

expected = 8 *vs.* observed = 3 STs

Number of ST-Profiles

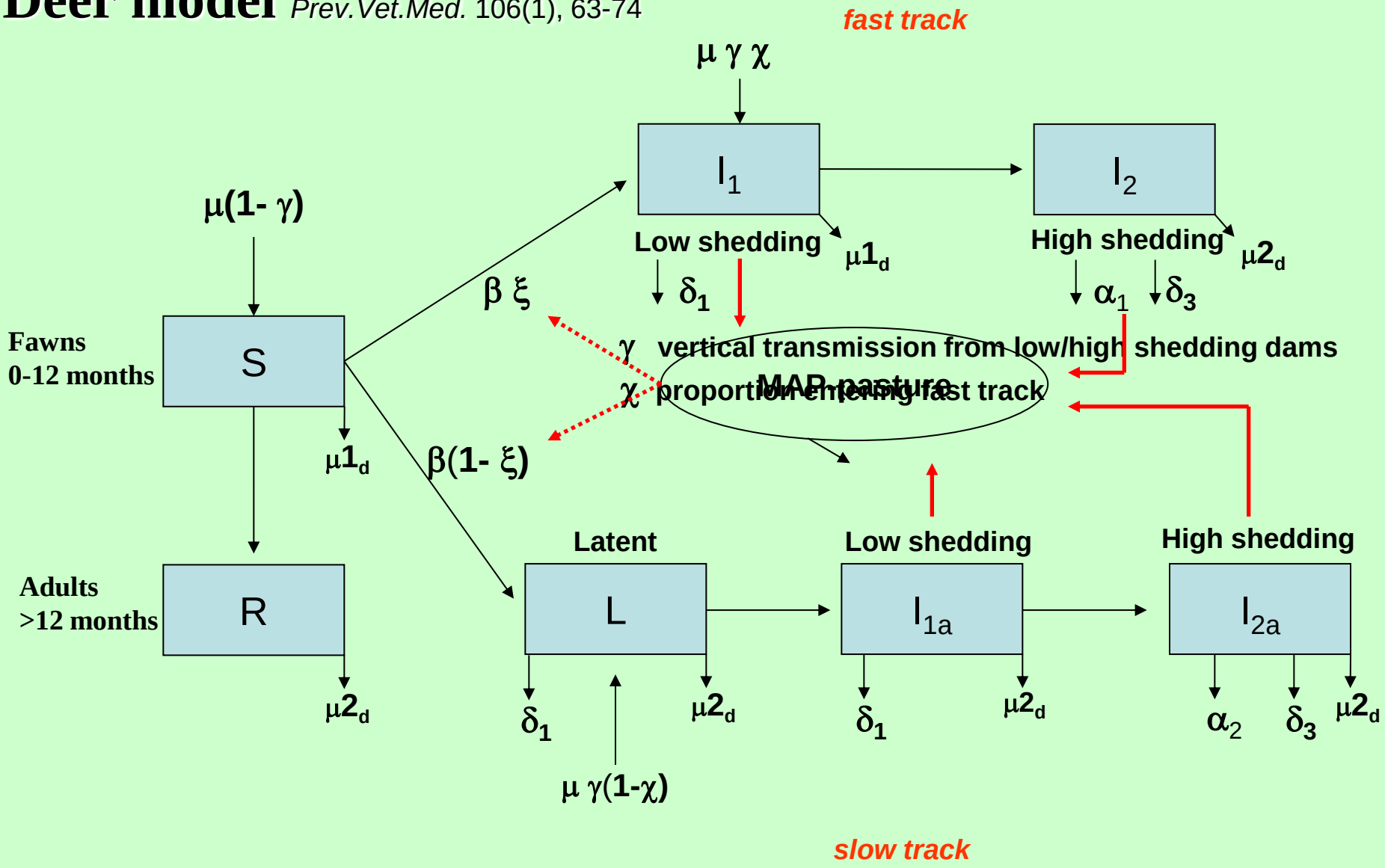


ST-Distribution: population vs virulence study

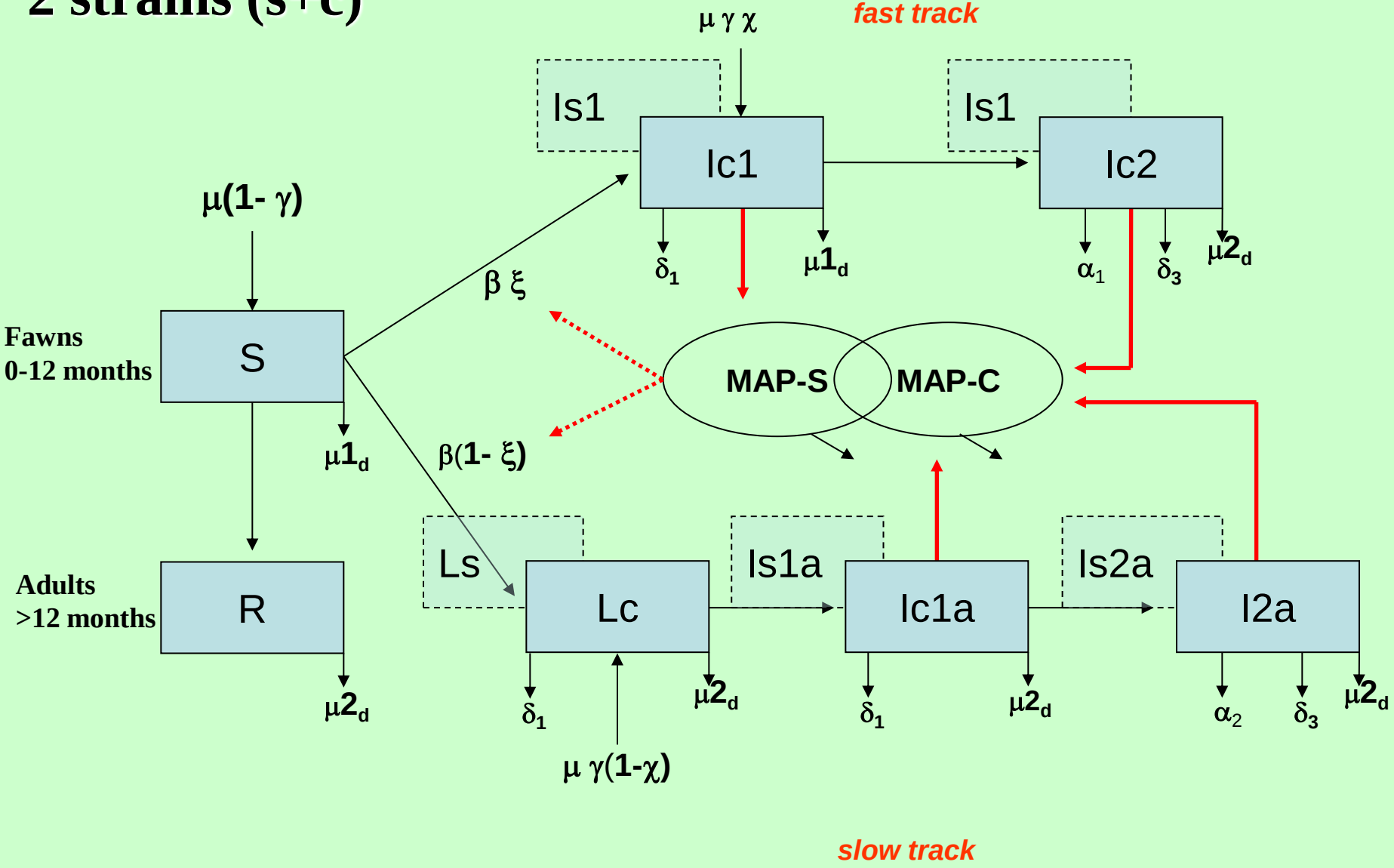
ST sheep	Population	%		Study	%
331113	6	8%		3	6%
331213	1	1%			
332224	2	3%			
332225	2	3%			
431113	51	67%	***	45	92%
431213	5	7%			
432224	5	7%		1	2%
531113	2	3%			
731113	2	3%			
Total	76			49	

MAP Modelling

Deer model *Prev.Vet.Med.* 106(1), 63-74

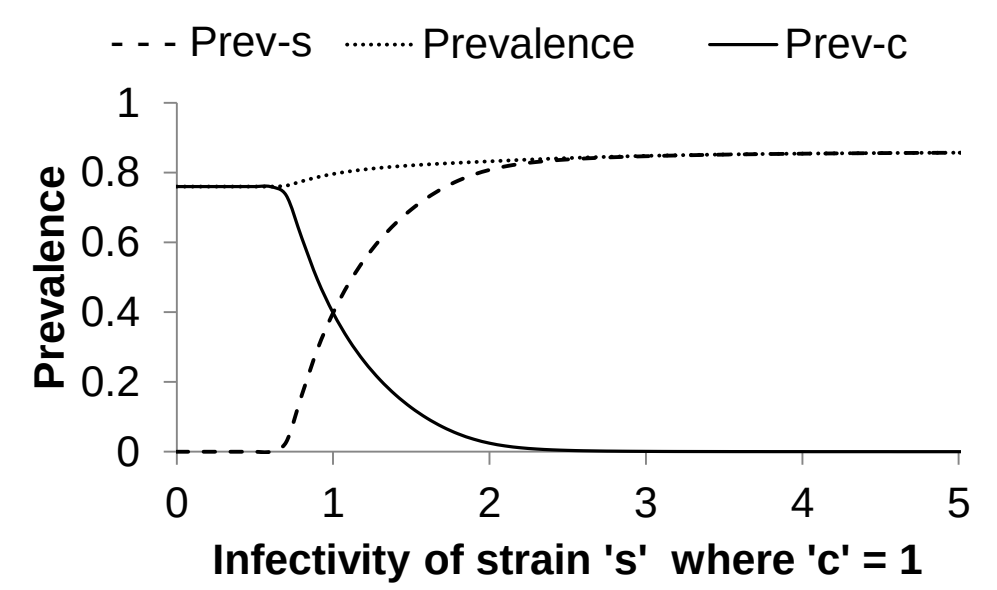


2 strains (s+c)


μ γ χ
fast track
Is1
Ic1
Is1
Ic2
μ(1- γ)
β ξ
δ1
μ1d
α1
δ3
μ2d
Fawns
0-12 months
S
MAP-S
MAP-C
μ1d
β(1- ξ)
Ls
Lc
Is1a
Ic1a
Is2a
I2a
Adults
>12 months
R
μ2d
δ1
μ2d
δ1
μ2d
α2
δ3
μ2d
μ γ(1-χ)
slow track

Strain competition in deer

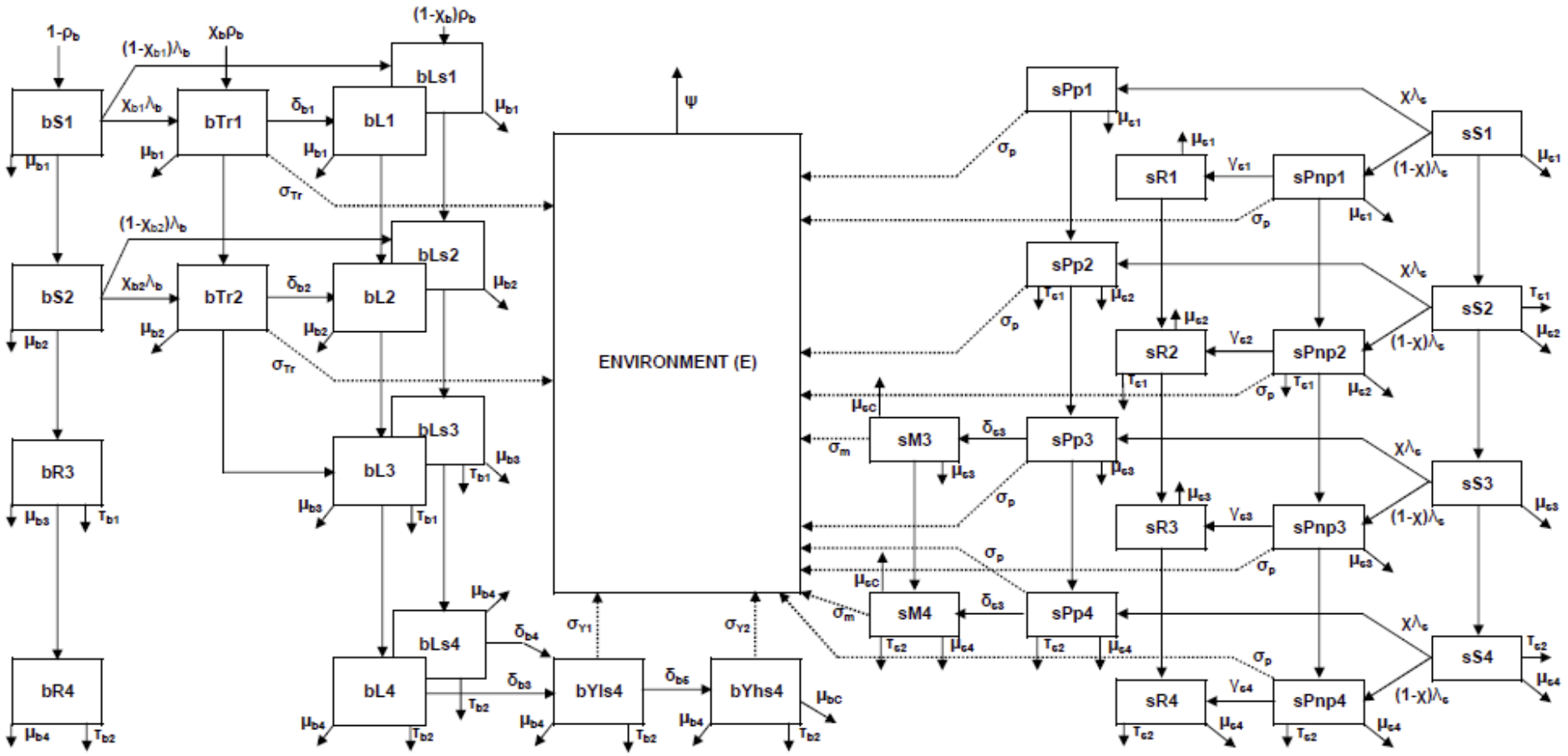
- Only strains with similar infectivity are able to survive:



- 90% ST in deer = bovine → ovine STs less virulent for deer ?
- 80% beef cattle isolates = ovine + no PTB → less virulent?

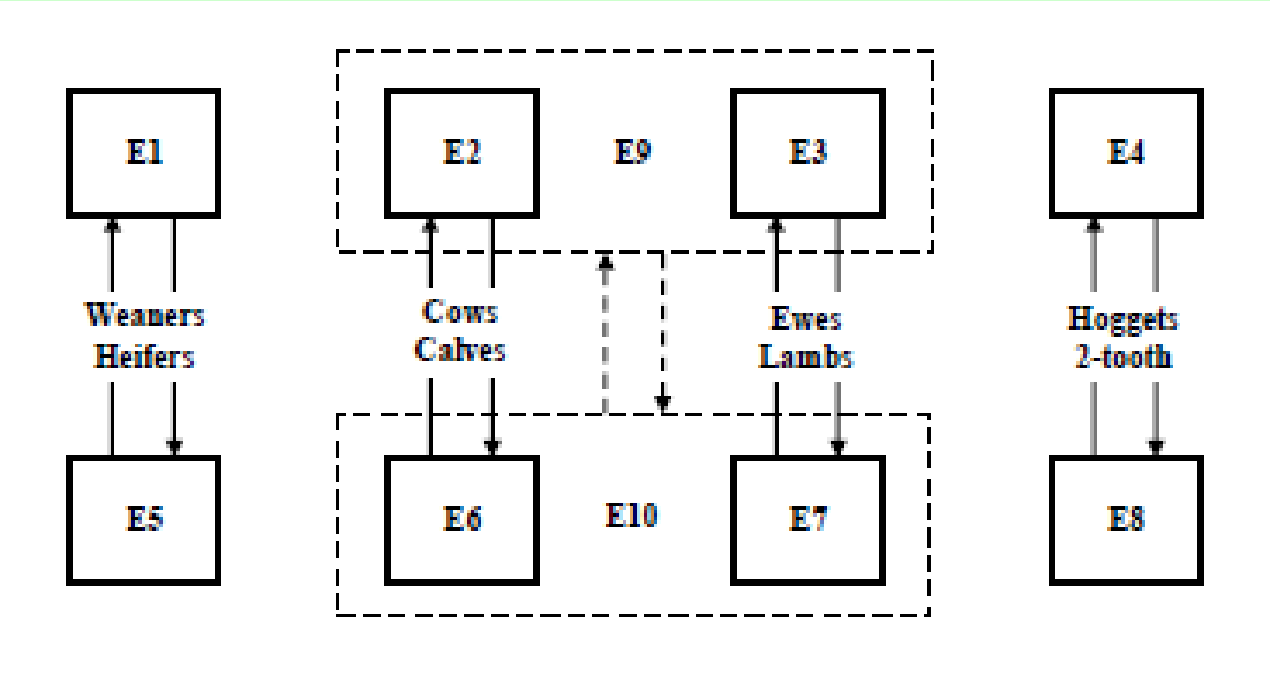
Sheep & Beef model Verdugo,PhD 2013

- Cattle (left) and sheep (right) with grazing contact (centre)
- Environment subdivided in paddocks



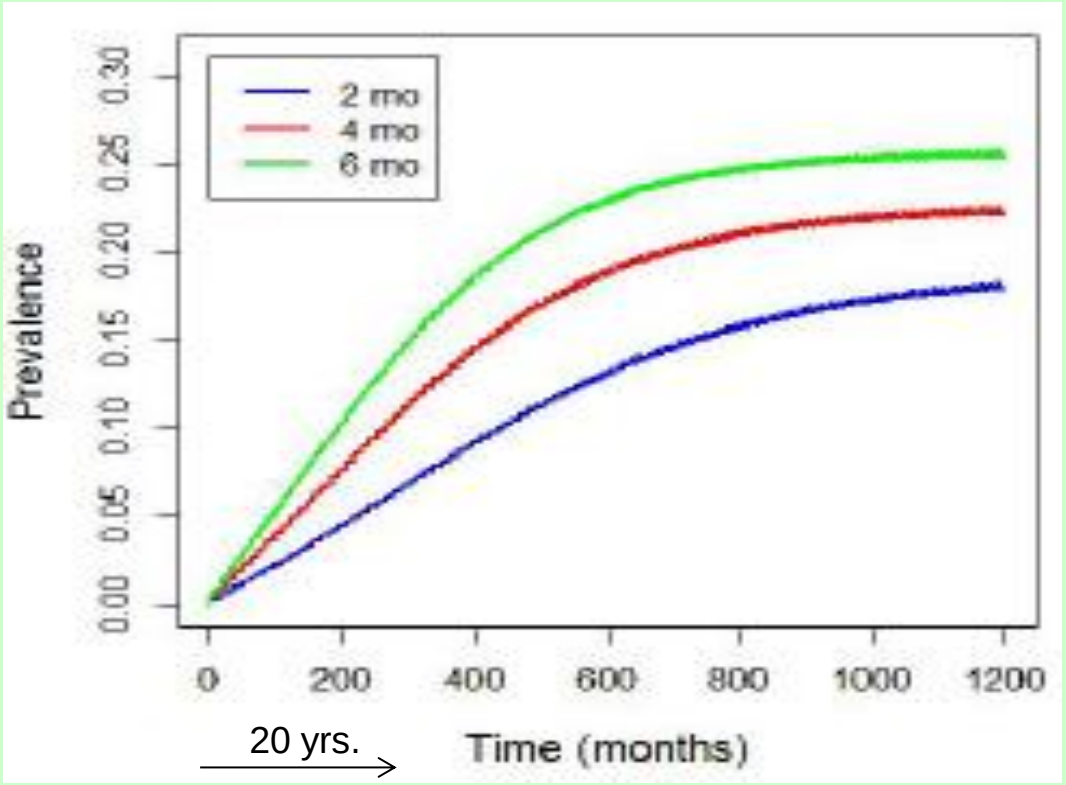
Sheep & Beef model Verdugo,PhD 2013

- Environment subdivided in paddocks
- Rotational grazing with/-out co-grazing periods



MAP transmission to naive beef cattle gazing with infected sheep

Prevalence by length of co-grazing period

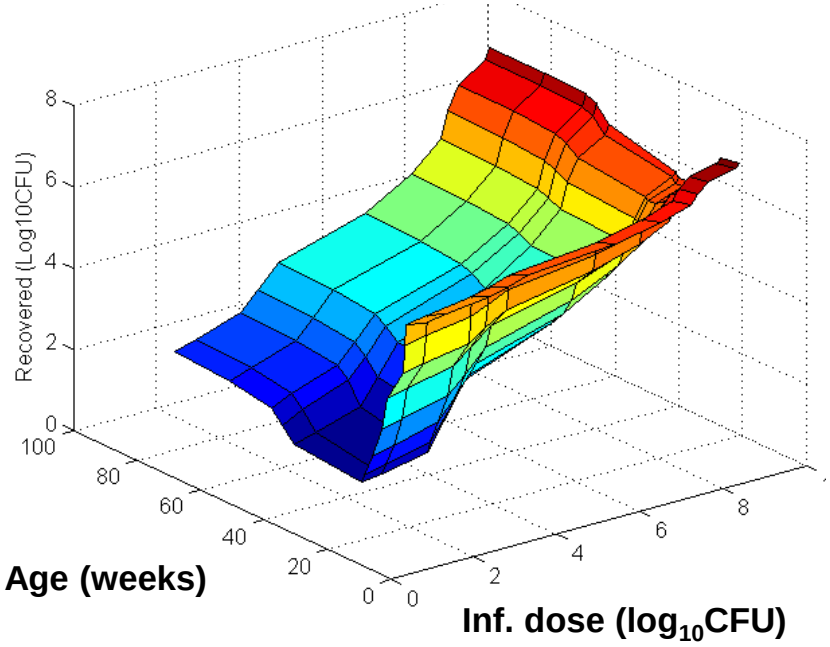


Sheep model (ovine Johne's disease OJD)

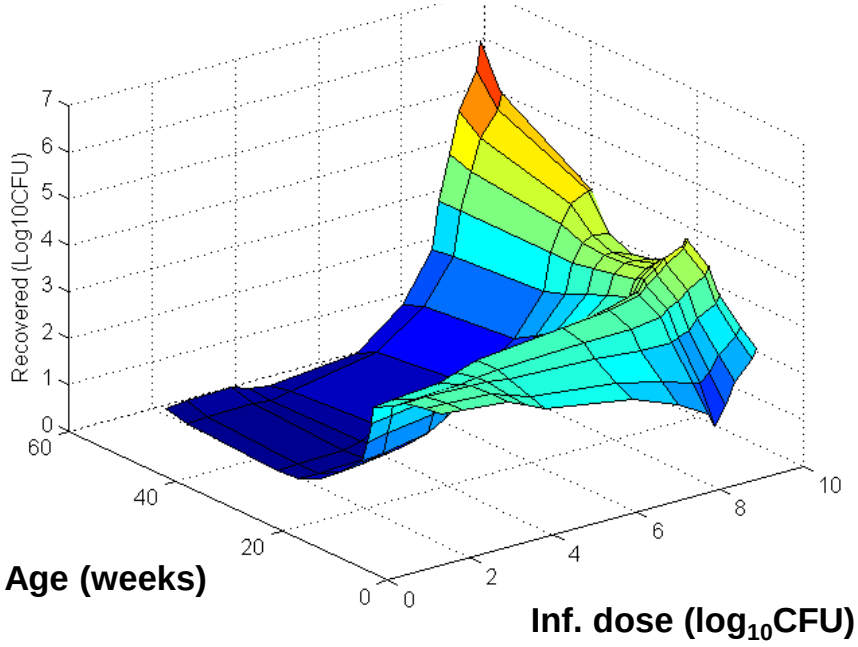
Model parameters from meta-analysis (7 papers)

Brotherston et al. 1961/62; Gilmour et al. 1965/65/66/77; Reddacliff et al. 2003

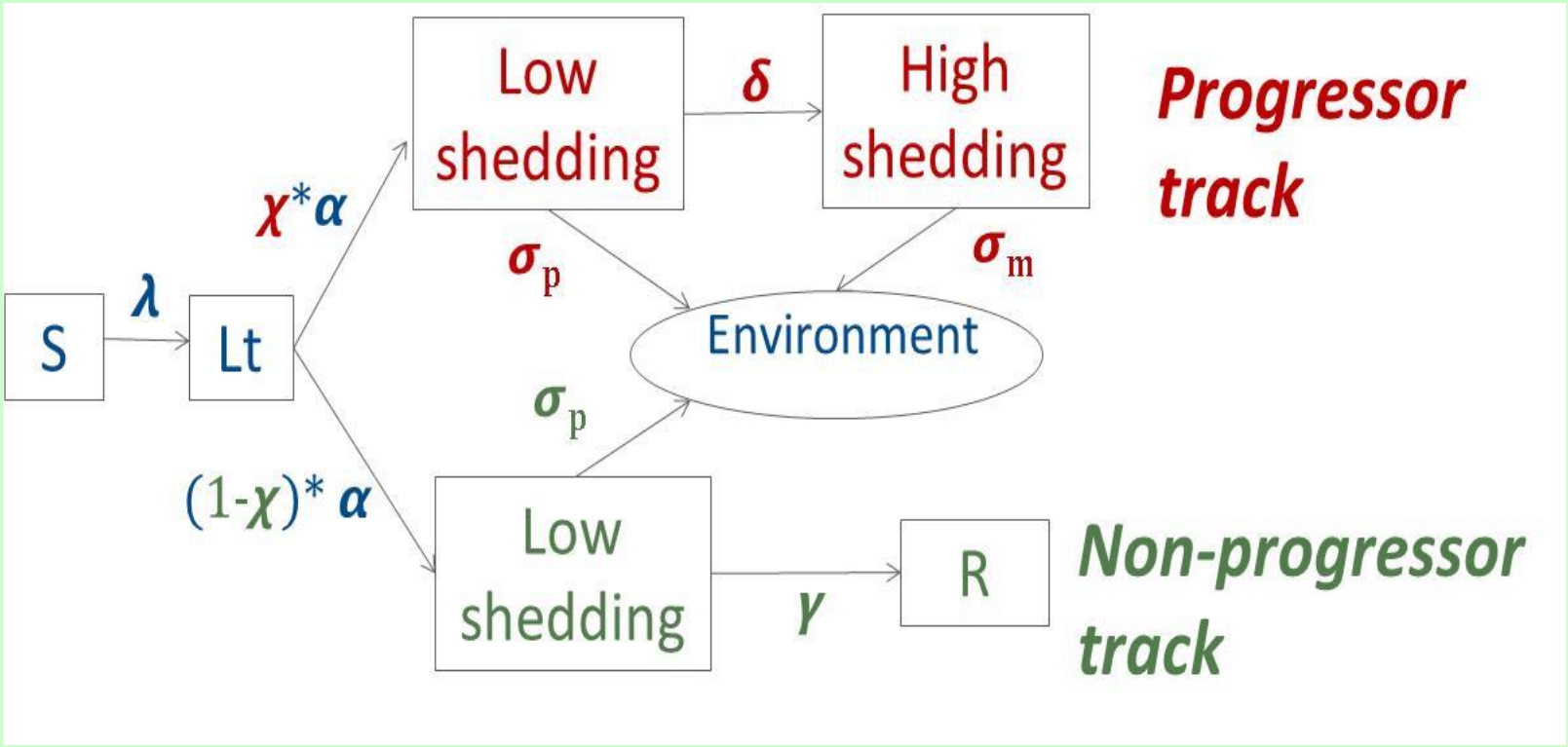
Tissue burden: intestines



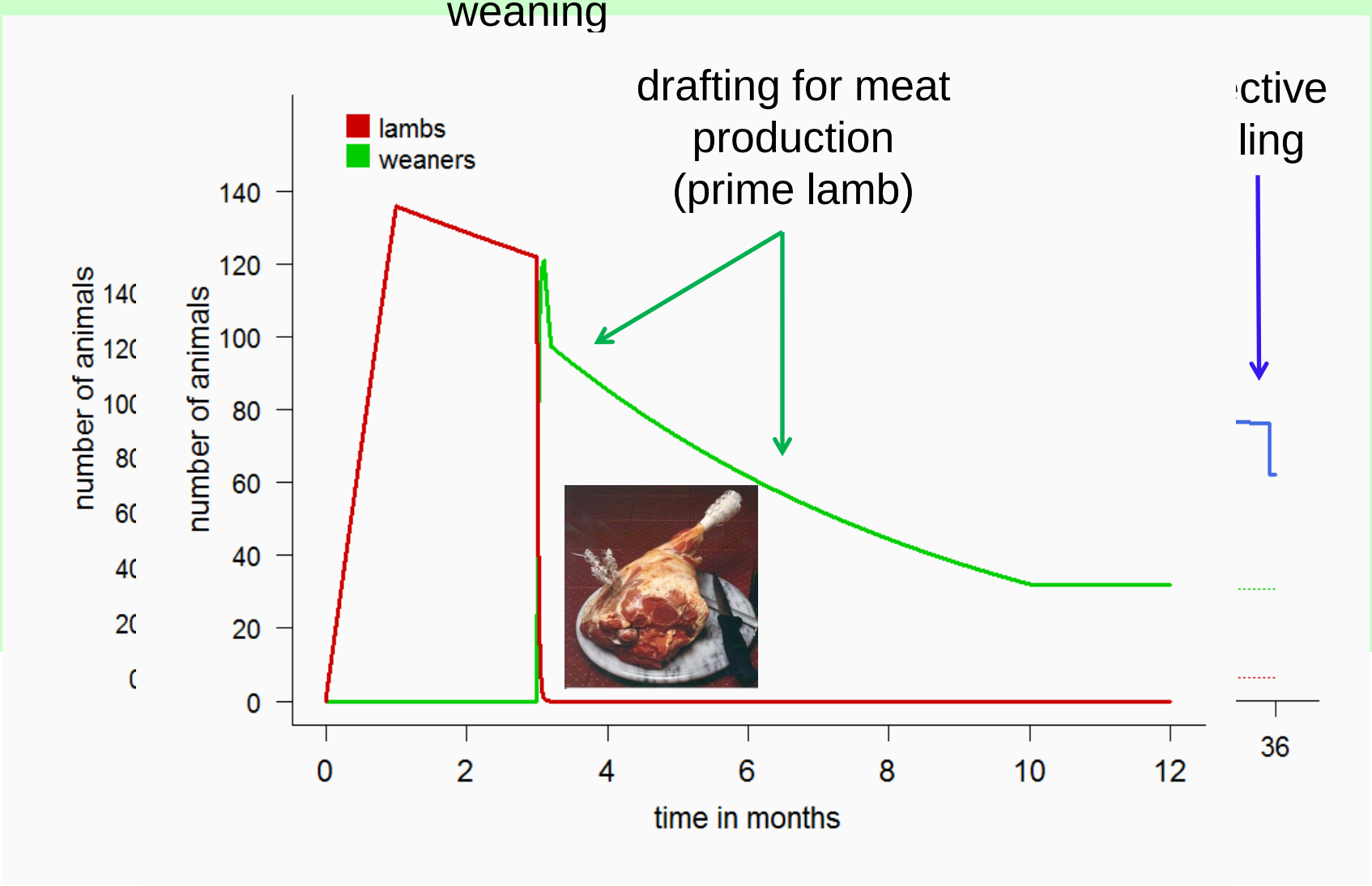
Tissue burden: lymph nodes



OJD Model Structure



Modeling productive offtake



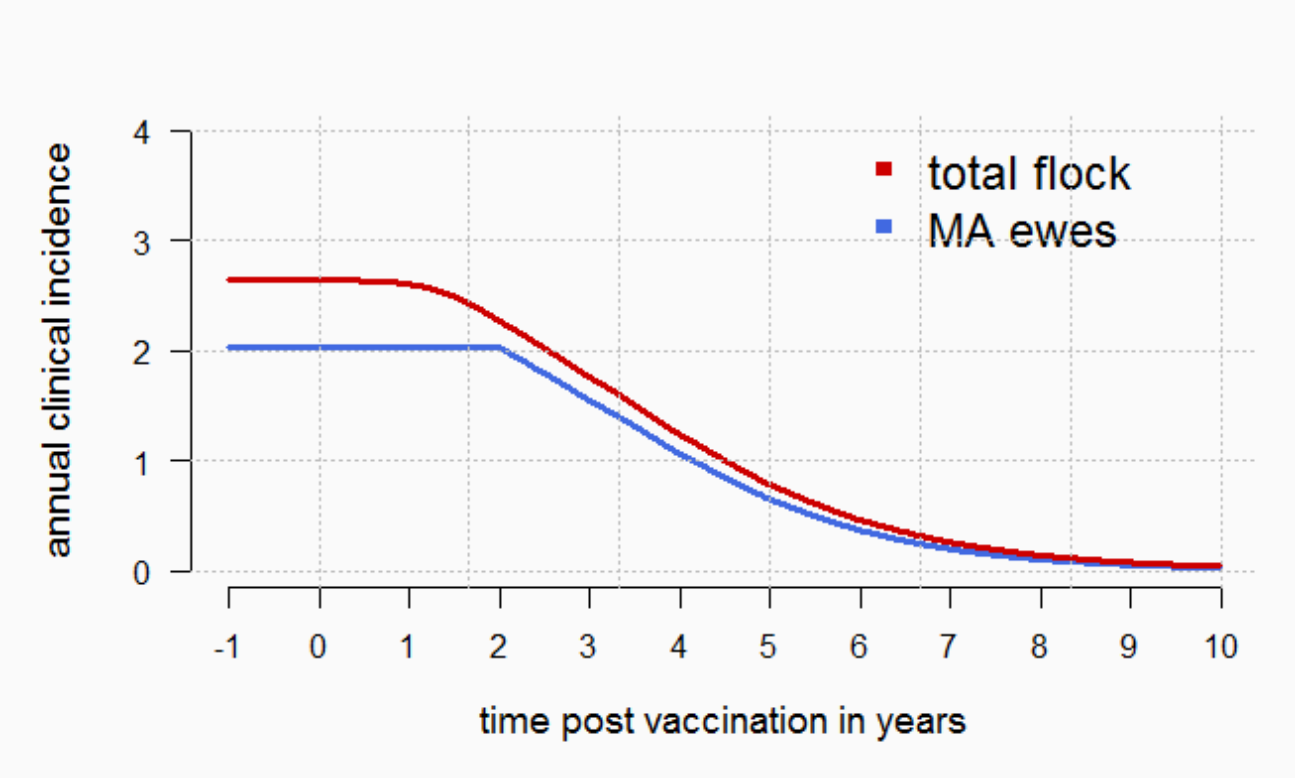
Model validation

Parameter	Industry NZ	Value model
Lambs tailed/ewe	132 %	131 %
Lambs slaughtered by Dec.	21%	20%
Lambs slaughtered/ewe	101%	92%

Source: Beef+Lamb NZ, statistics New Zealand

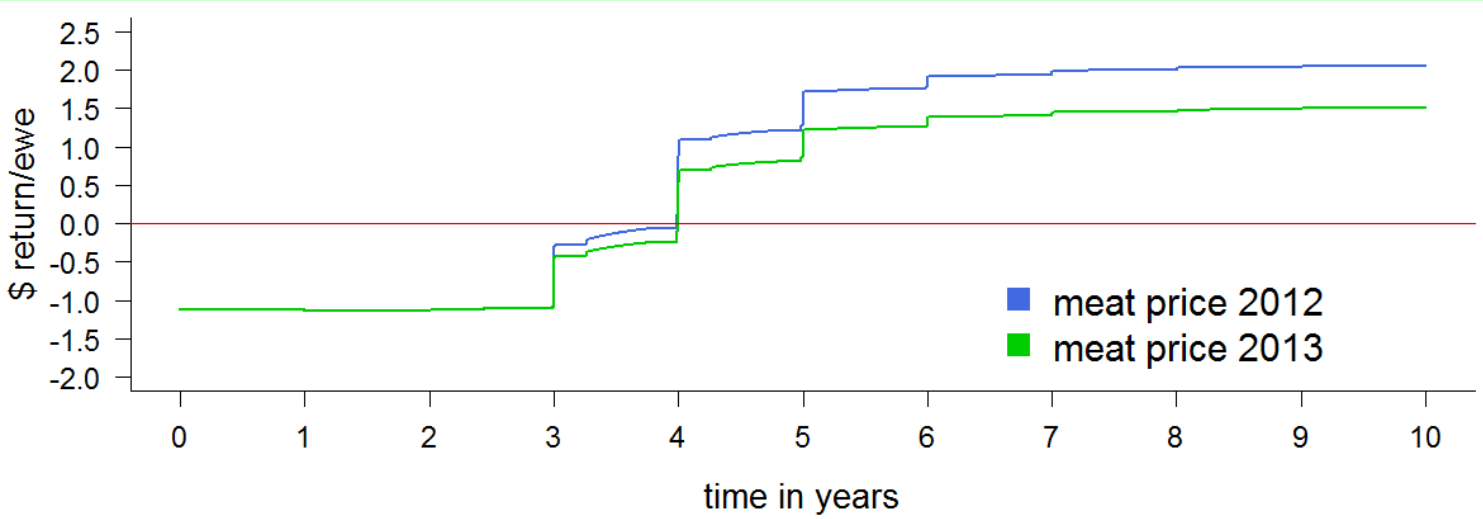
Modelling intervention: vaccination

- Vaccinating 30% of the weaners at 3 months of age
- Keeping only vaccinated animals for replacement

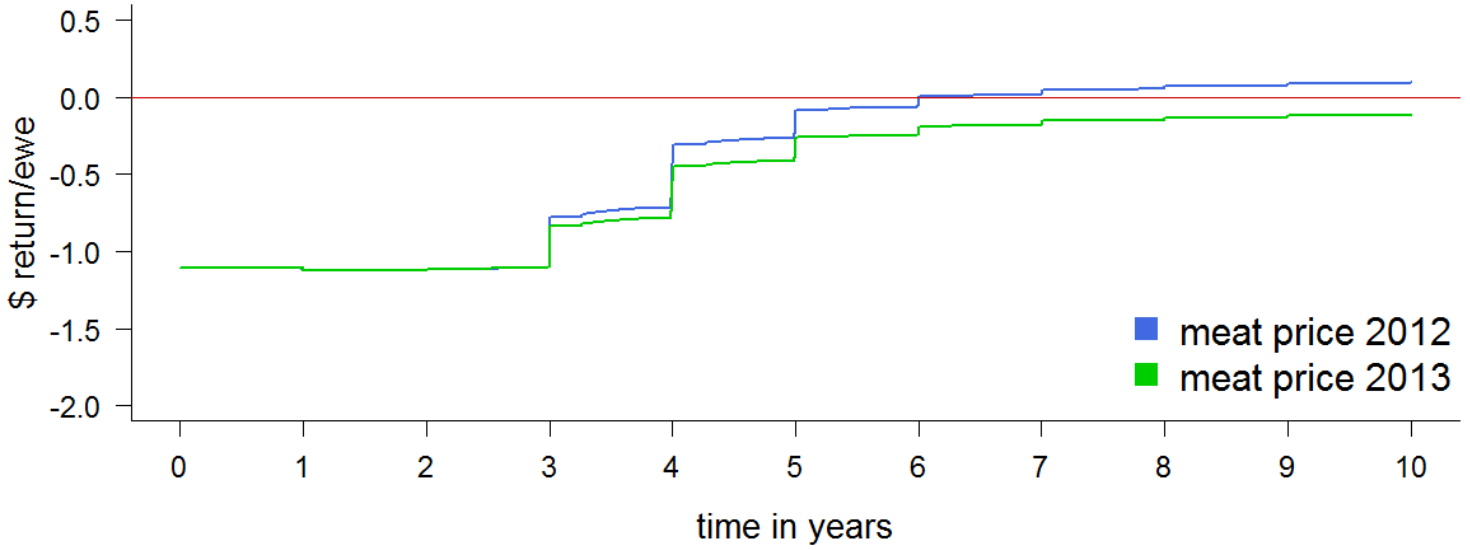


Cost effectiveness of vaccination

JD mortality 1.8%



JD mortality 0.75%



Strain typing + modelling: opportunities

- Understanding pathogen dynamics
  - Strain competition
  - Interaction with vaccination, genetic selection, breeding for resistance
- Comparing the efficiency of interventions
- Evaluating financial returns

Acknowledgements

- JDRC, the Merino Breeders Association and Education NZ for funding
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