

New ways to tackle the threat of worms:

The development of vaccines



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Ruminant nematode vaccines

- research > 50 years
- practical outcomes
 - *cf.* other pathogens: disappointing
- few successes
 - irradiated vaccine
 - bovine lungworm



Anthelmintic resistance index

  Reports to some classes

  Widespread resistance to some classes

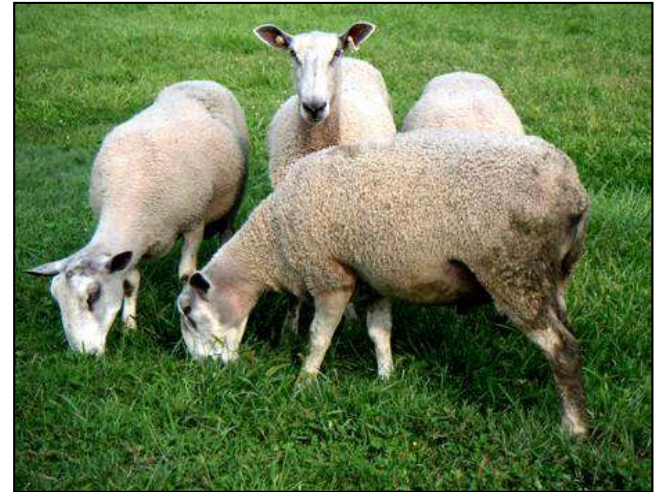
  Widespread resistance to all commonly used classes

  Relatively rapid resistance to all classes

Teladorsagia circumcincta- most important
gastrointestinal nematode of sheep in
temperate regions

Parasitic gastroenteritis: lambs

- weight loss, diarrhoea, anorexia



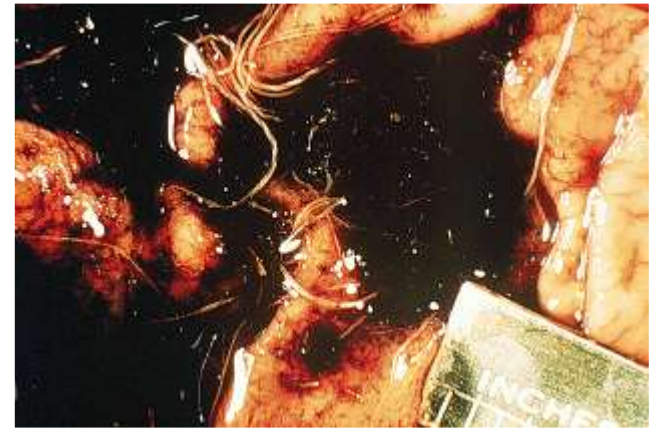
= £4.40 per lamb

ADAS 2013 “Economic impact of health and welfare issues in beef cattle and sheep in England”



Haemonchus contortus - most important gastrointestinal nematode of sheep in tropical/subtropical regions

- Acute disease can be fatal
- High FEC (2000 to 20000 EPG) - difficult to control
- Anthelmintic resistance widespread



Haemonchus vaccine development at Moredun

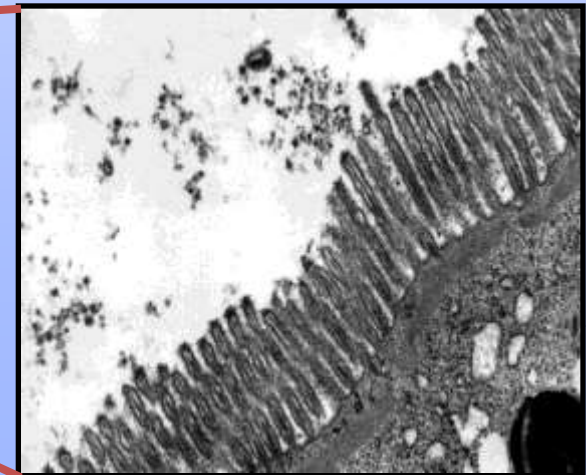
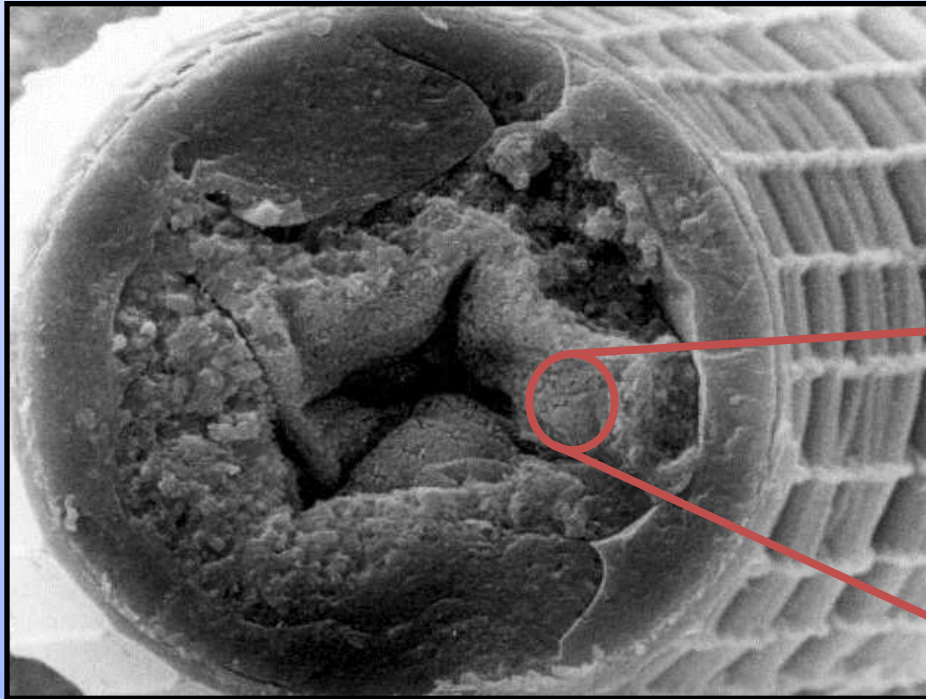


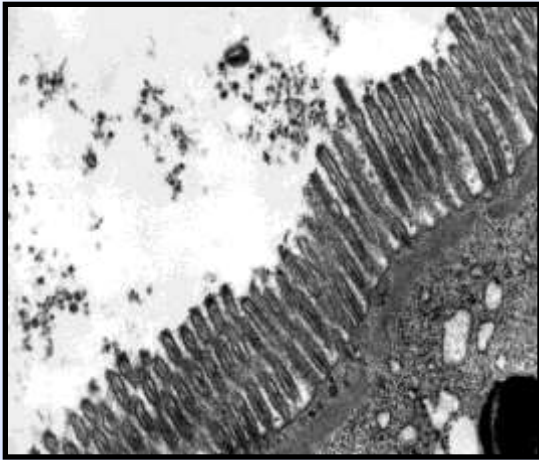
and Department of Food and Agriculture, WA



Haemonchus vaccine - gut antigen approach

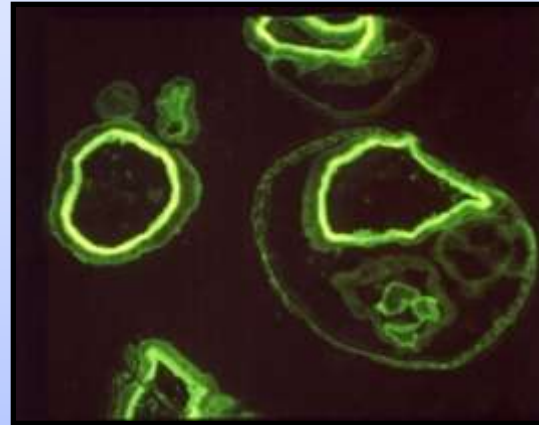
Because *Haemonchus* feeds on blood, molecules on the surface of the worm's gut are appropriate vaccine targets





When surface proteins from the worm gut are injected into a sheep.....

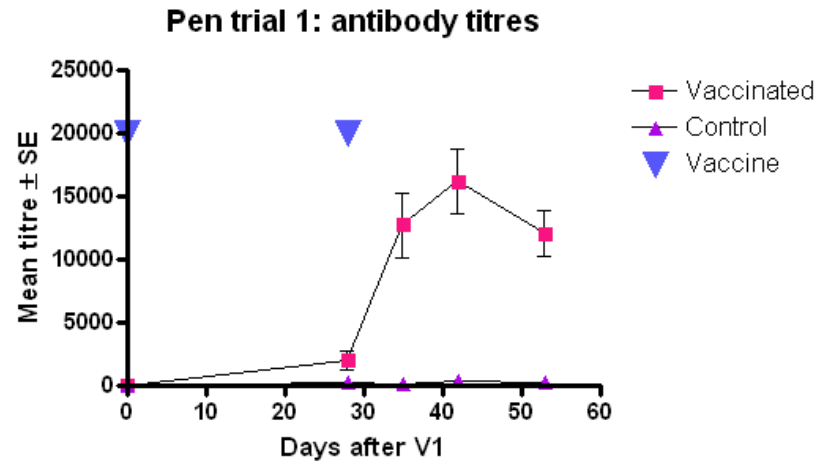
it responds and makes antibodies which circulate in the blood. If a vaccinated sheep gets infected, the parasites ingest blood so that antibodies bind to the worms intestines ...



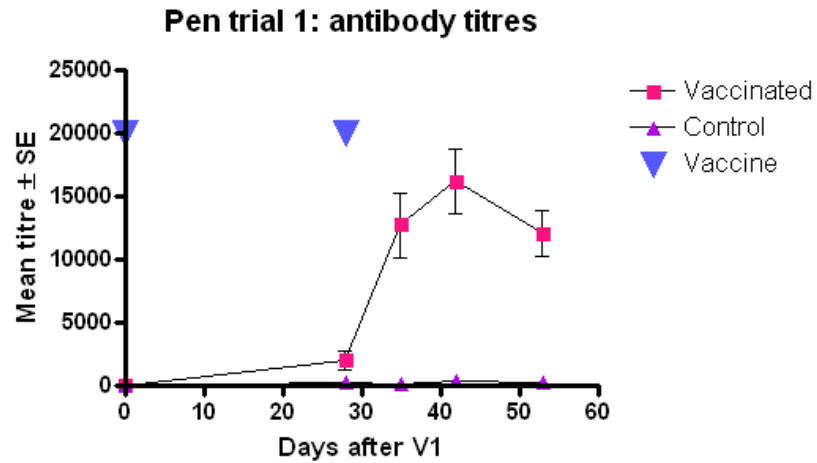
....leading to greatly reduced egg output and worm numbers.



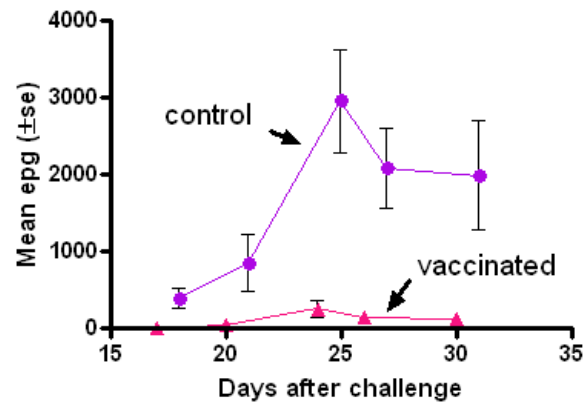
Pen trial example



Pen trial example



Pen Trial 1: Faecal egg counts of vaccinated and control sheep



Manufacture of a native *Haemonchus* vaccine for Australia

Where?

(must be from Australian *Haemonchus*)

Dept of Agriculture and Food, Albany, W.A



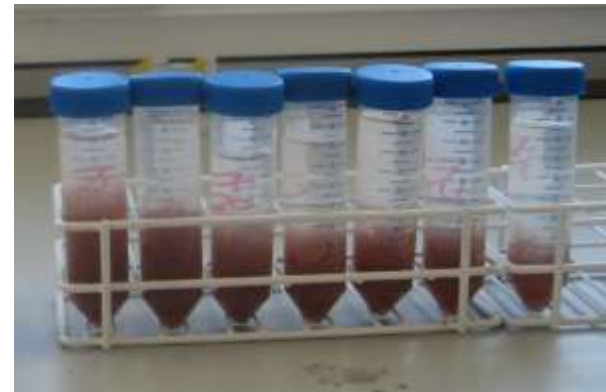
Vaccine production process: Field



Machine for rapid
recovery of adult
Haemonchus from
infected
abomasa



2 mins

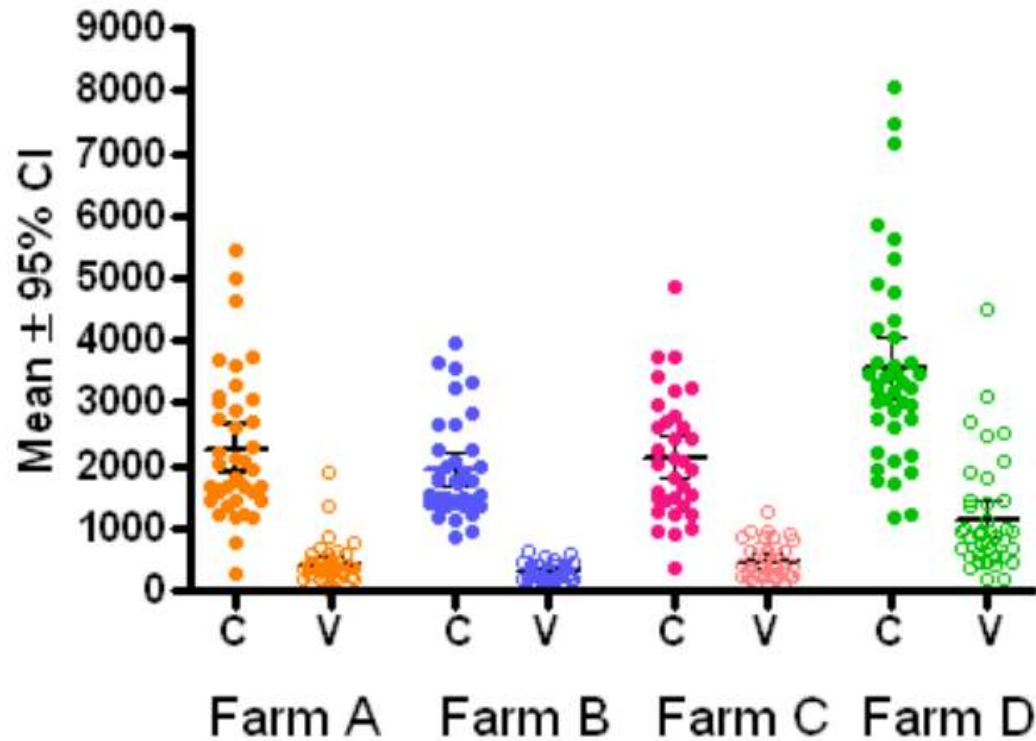


Good Manufacturing Licence granted by APVMA in 2010

Whole process from sourcing sheep to bottling vaccine



Effect of vaccine on Haemonchus egg output on four NSW farms from early Nov 2011 to late April 2012



>80% protection on each property

How good do nematode vaccines need to be?

- Sterile immunity not always necessary
- *Haemonchus* vaccine needs to reduce egg counts by only 65% to be superior to “best practice” anthelmintic control programs

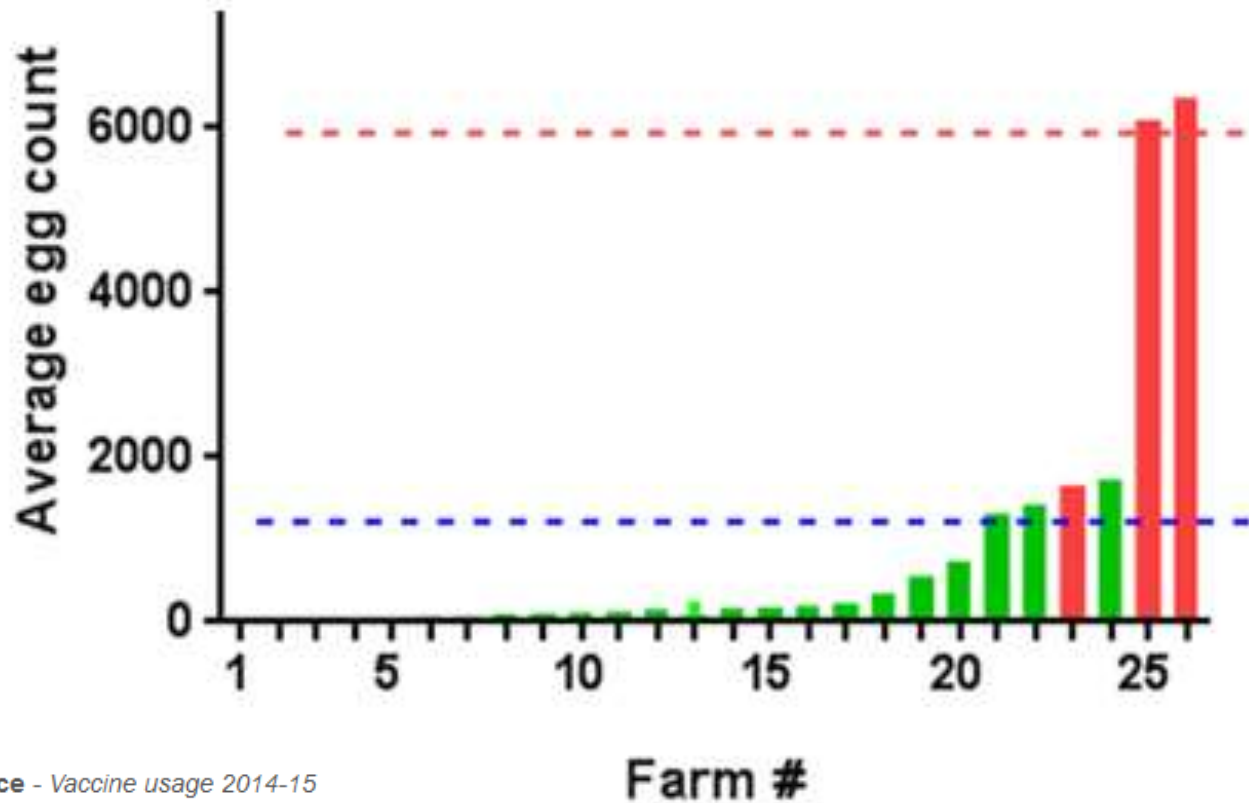


APVMA
Registered
October 1st,
2014



All 300,000
doses of vaccine
sold by word of
mouth within
10 days

No large
pharma
involved



First year performance - Vaccine usage 2014-15

About 50,000 lambs on some 35 New England properties between Walcha and Tenterfield NSW received a course of Barbervax. Two worm egg count kits were supplied to each customer to monitor the vaccine performance.

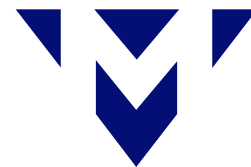
The results are shown in the graph.

Red bars - Farm did not follow label advice.

Green bars - Farm followed label advice correctly.

Blue dotted line - Drench threshold advised by Wormboss.

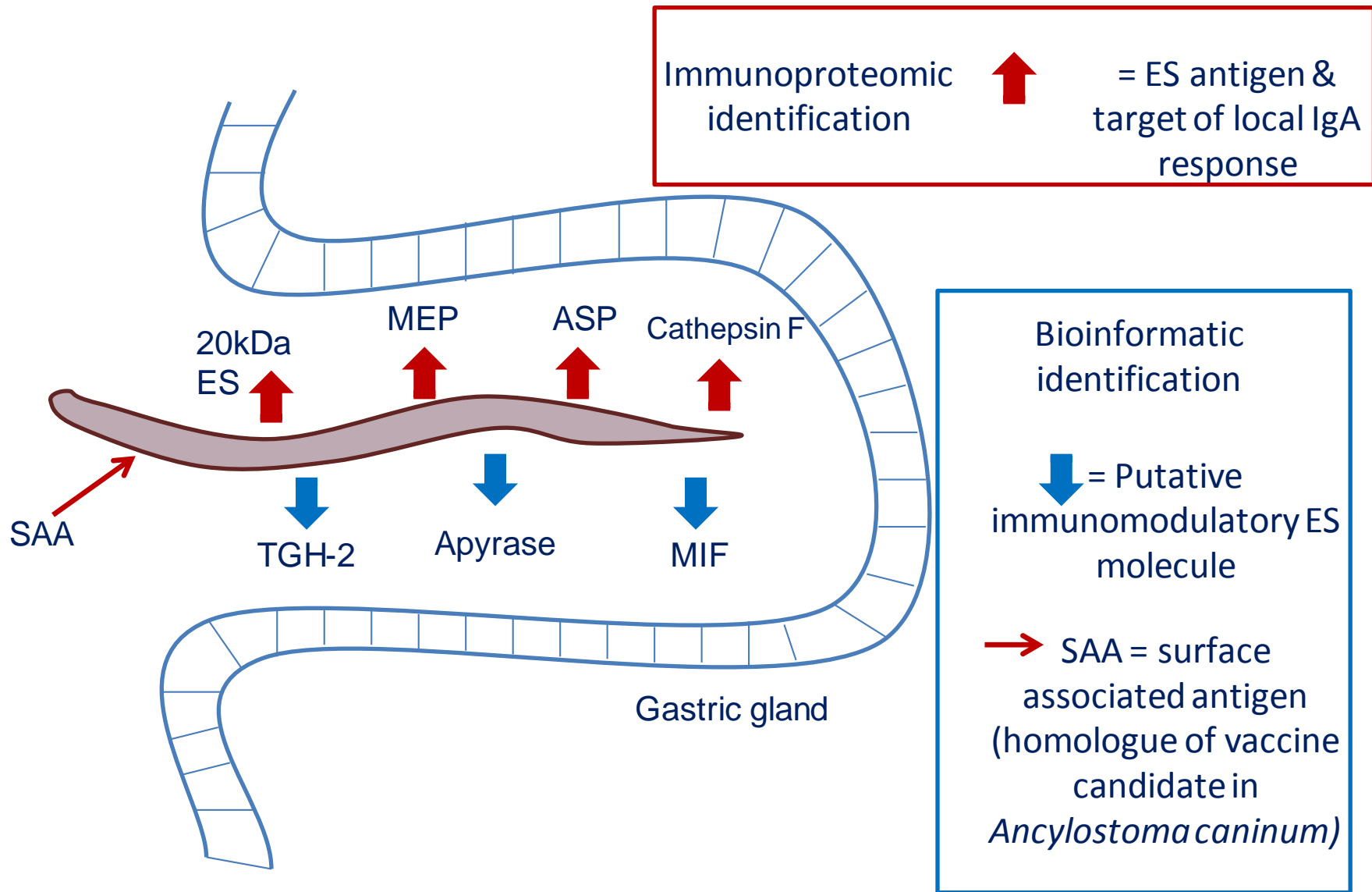
Red dotted line - Disease and or deaths by Barbers Pole likely.



Teladorsagia circumcincta vaccine development

- Gut vaccine approach has not been successful thus far
- Natural immunity does develop against *T. circumcincta*
- Route to a successful vaccine may be to mimic that immunity

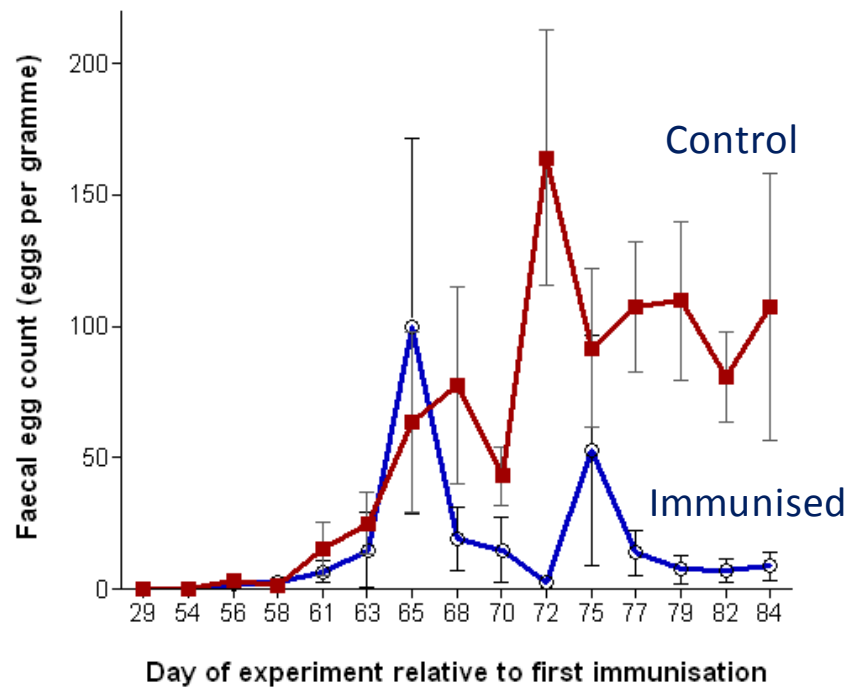




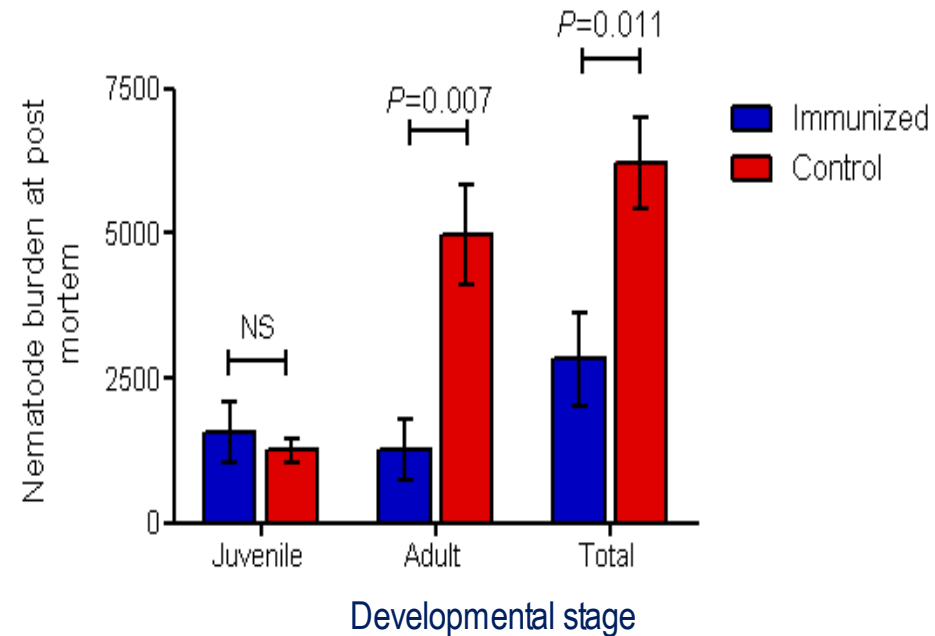
We generated recombinant versions of 8 molecules and combined them and tested in independent vaccine trials

Teladorsagia circumcincta recombinant antigen cocktail Trial 1

Cumulative faecal egg count reduced
by 70% ($P < 0.001$)

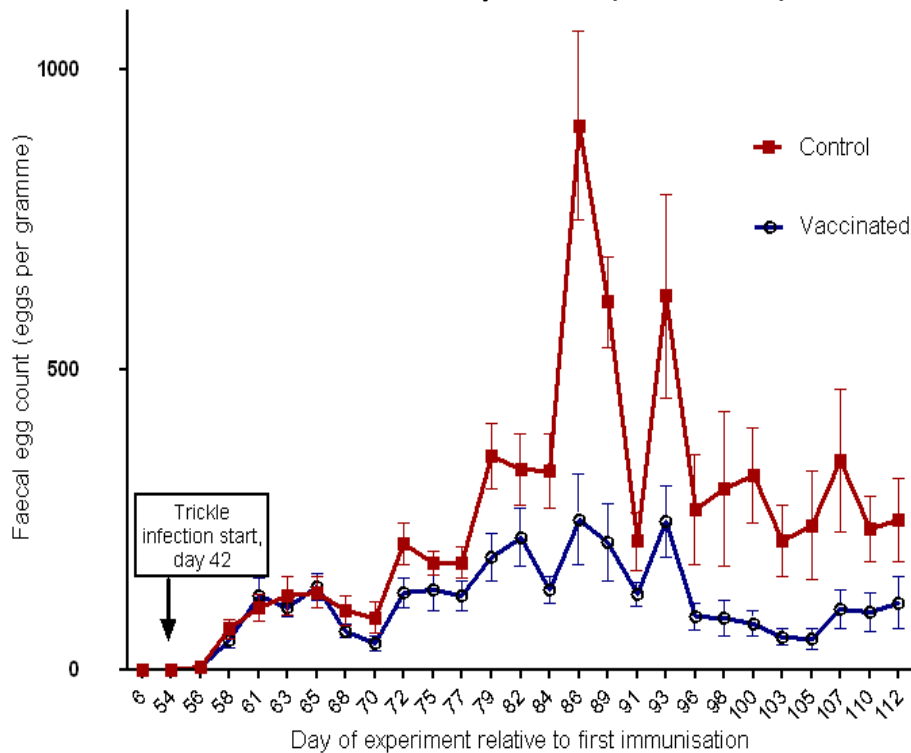


Adult worm burden reduced
by 75% ($P = 0.007$)

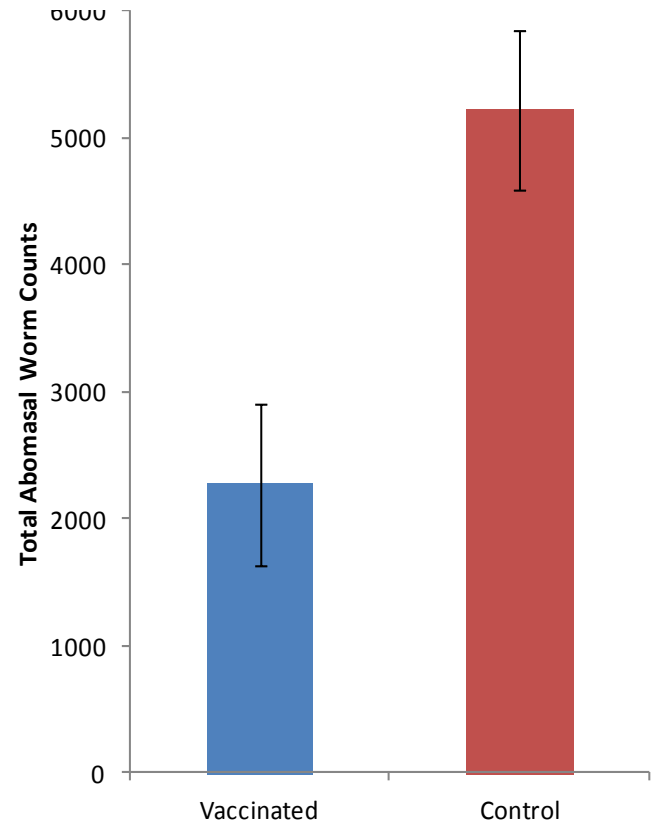


Teladorsagia circumcincta recombinant antigen cocktail Trial 2

Cumulative faecal egg count
reduced by 58% ($P=0.024$)



Worm burden reduced by 56%
($P=0.020$)



Nisbet, A.J., McNeilly, T.N., Wildblood, L.A., Morrison, A.A., Bartley, D.J., Bartley, Y., Longhi, C., McKendrick, I.J., Palarea-Albaladejo, J., Matthews, J.B., 2013. Successful immunization against a parasitic nematode by vaccination with recombinant proteins. *Vaccine in Press*

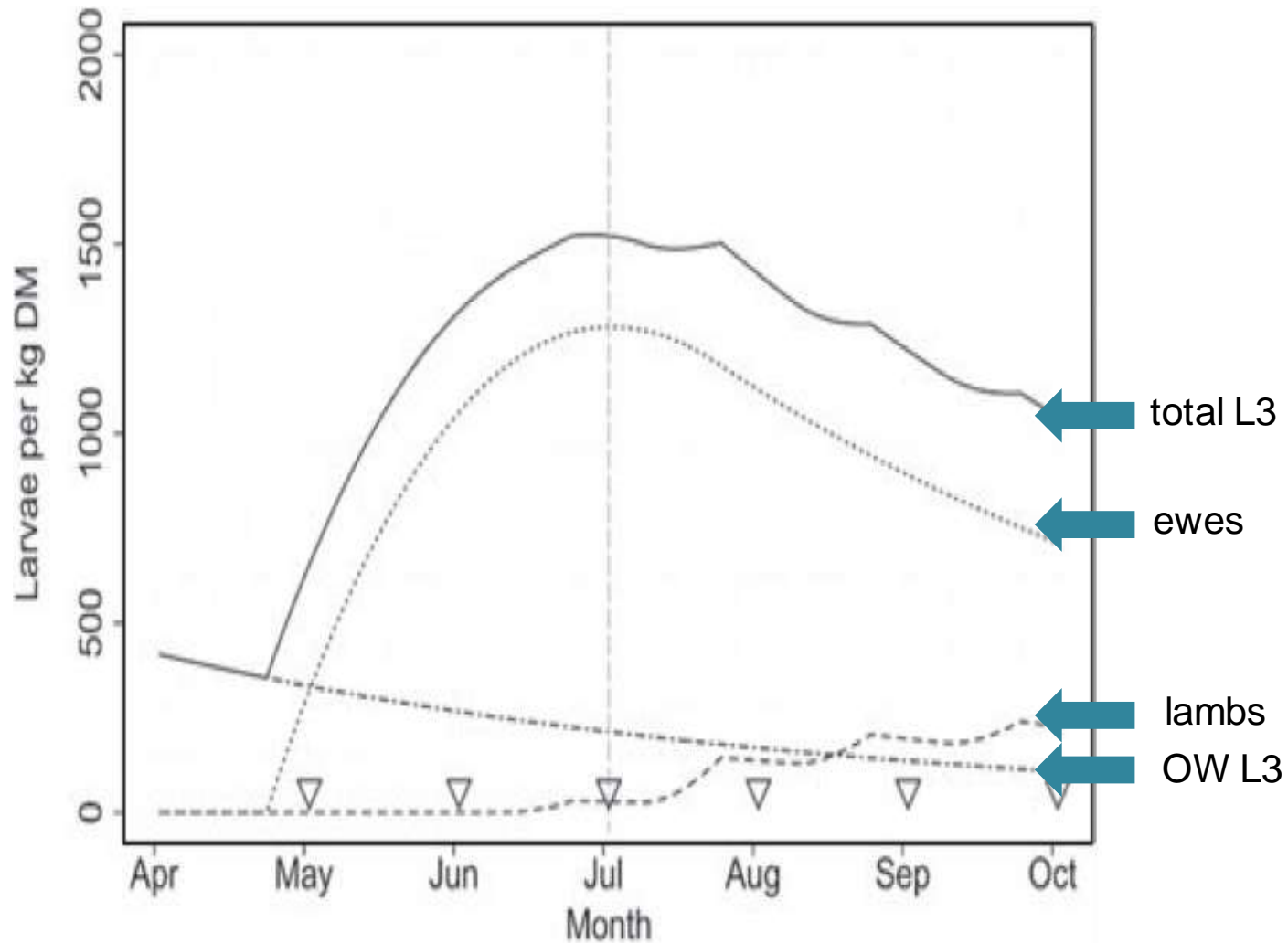
The way forward with the *Teladorsagia* vaccine...

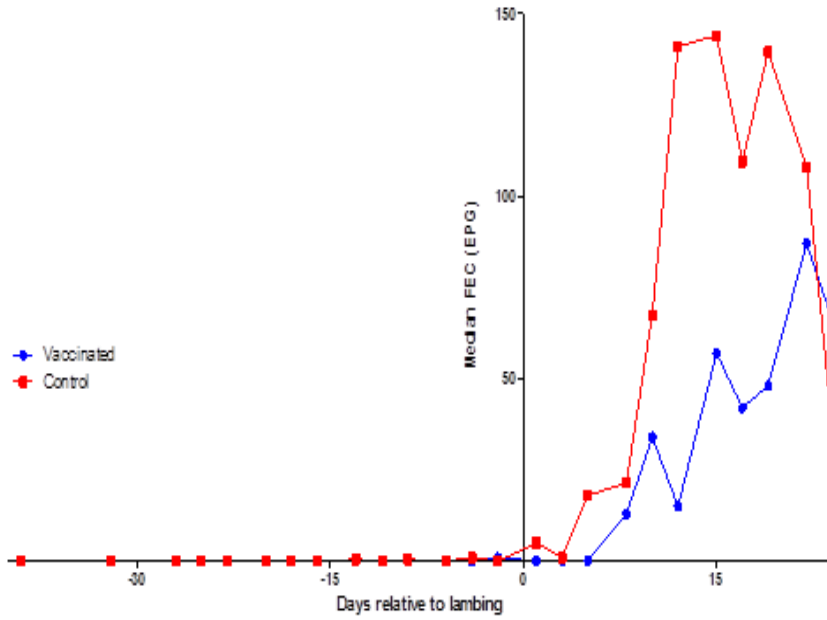
- Protection higher than in any other system using a recombinant vaccine against a parasitic nematode in the definitive host
- Efficacy variable in younger lambs

Is there a practical solution?



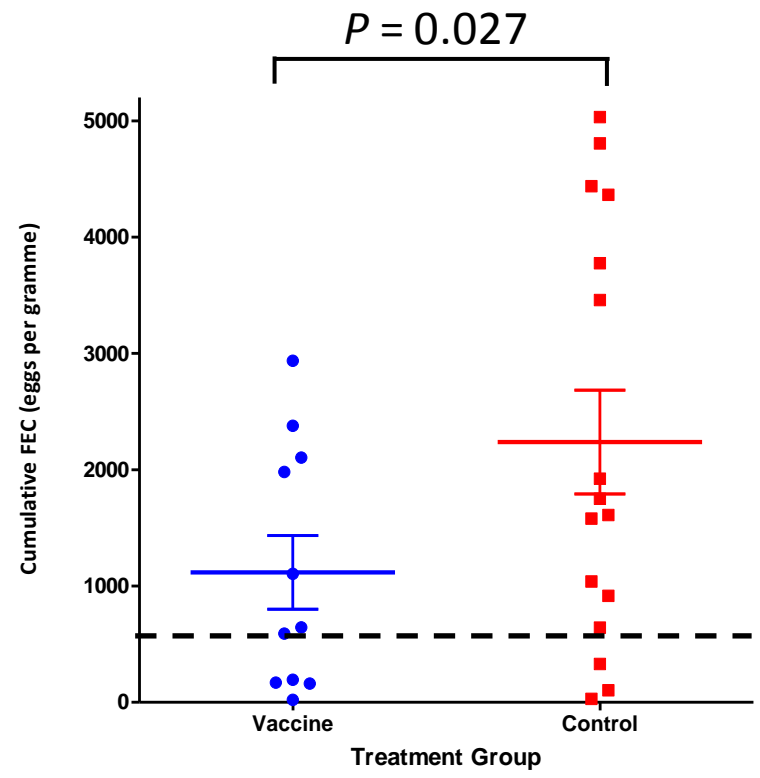
Can vaccination overcome the PPRI?





Median FECs during trickle infection period

Cumulative FEC during trickle infection period



$P = 0.027$

Conclusions and future directions

- *Haemonchus* control by vaccination is now a reality
- *Teladorsagia* control by vaccination is a possibility
- Other species.....*Nematodirus*, *Trichostrongylus*...



Acknowledgements



David Smith, George Newlands, Jacqui Matthews, Tom McNeilly, Dan Price, Yvonne Bartley, MoreDun Proteomics Facility, MoreDun Bioservices



United States Department of Agriculture

Dan Zarlenga



Steve Paterson



Brown Besier

