Biological control of rabbits in Australia – The co-evolutionary arms race between rabbits and their viruses

CSIRO HEALTH & BIOSECURITY
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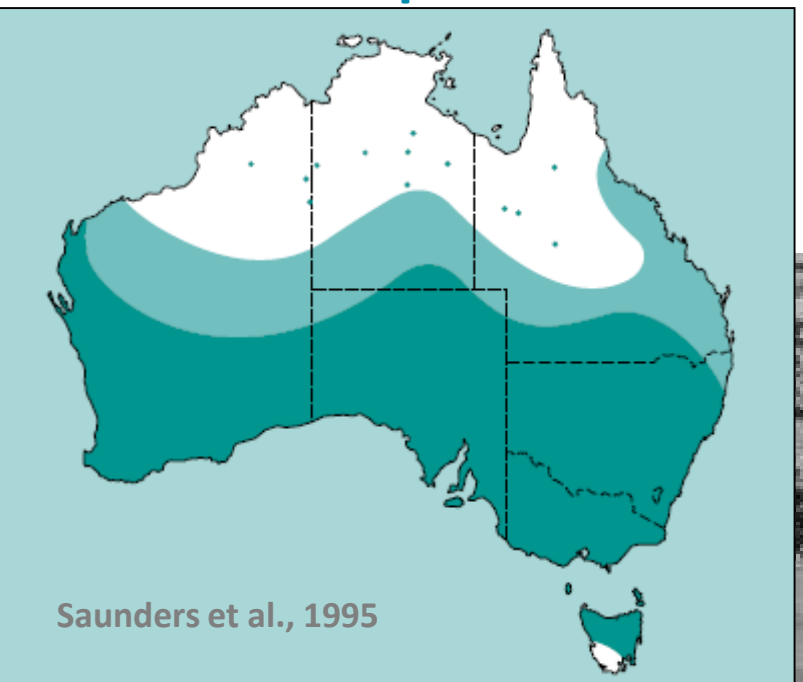
Tanja Strive, CSIRO

Rabbits in Australia

- Biological control of rabbits – history
    - Myxoma virus
    - Rabbit Haemorrhagic Disease Virus (RHDV)
    - host pathogen co-evolution
- current biocontrol initiatives
- other rabbit viruses

The European rabbit (*Oryctolagus cuniculus*): Australia's rabbit plague

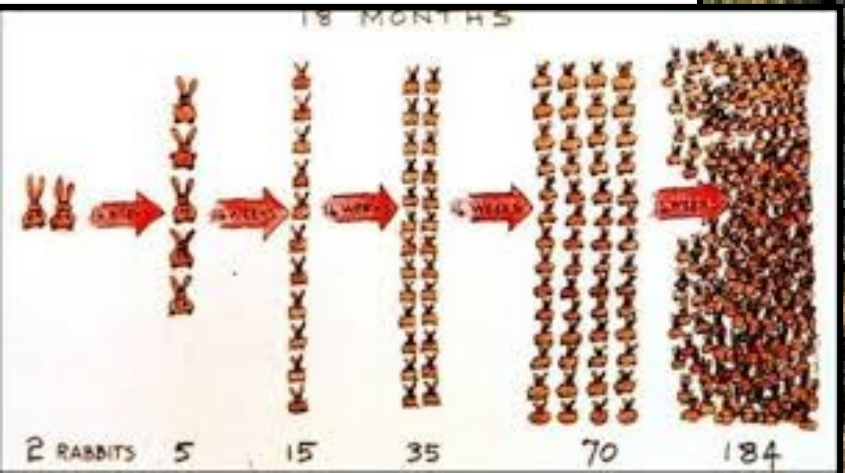
- Native to Europe
- 26 rabbits (released in VIC 1859)
- Colonised continent in 70 years
- Ideal environment
    - Few diseases
    - Fewer predators



Saunders et al., 1995

A perfect invader

- Gestation period 28 days
- Mating same day of giving birth
- Litter size 4-8
- Sexual maturity >3 months
- Young disperse widely
- Peak estimate: 0.5 – 10 billion rabbits
- Massive economic and ecological impacts




Rabbits impact over 300 EPBC Act listed threatened species and nine ecological communities. This includes 44 animal species (15 birds, 20 mammals, 6 reptiles, 1 invertebrate, 1 fish and 1 amphibian) and 260 listed plant species (Rabbit TAP 2016)
Rabbit exclosure on Macquarie Island
Image: Brian Cooke

Coventional Control of rabbits

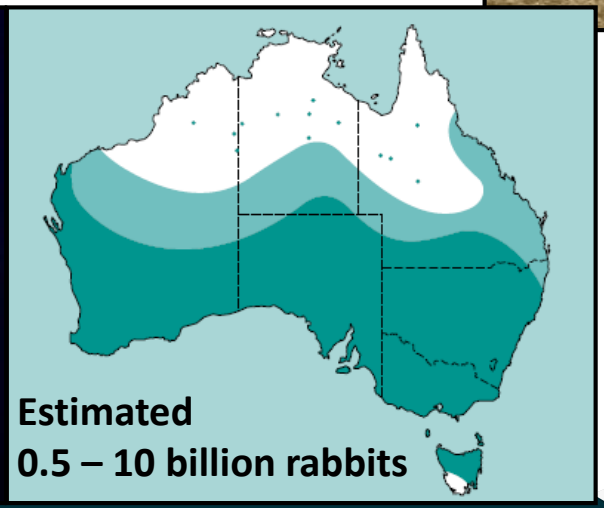
- Shooting/trapping
- Fencing
- Warren ripping
- Warren fumigation
- Poisoning

=> ineffective

Australia in 1930:

6.7 million km²

6.5 million people (in 1930)



Estimated
0.5 – 10 billion rabbits

What is biological control?

Biological control involves the use of another organism—predators, microparasites (e.g. bacteria, viruses, protozoa, fungi), or macroparasites (e.g. helminths, arthropods)—to control a pest population.

Efficacious

Reduces pest populations/impact

Safe (species specific)

Does not affect non-target species

Humane

Suffering minimised

Self-disseminating

Effective transmission

Persists in environment

Causes recurrent outbreaks without need to re-apply

Socially acceptable

Public acceptability

Biological control of the European rabbit (*Oryctolagus cuniculus*) - *early days*

1887:
Henry Parkes NSW-Government promised £24,000 rewards for eradication of rabbits

Pasteurella multocida (Chicken cholera)

Not species specific, did not transmit

Louis Pasteur
1822-95

Adrien Loir
1862-1941

Biological control of rabbits #1: Myxoma Virus (MYXV)

MYXV: an emerging disease of rabbits

Family: *Poxviridae*, Genus: *Leporipoxvirus* , *ds-DNA*

Natural host: Tapeti
***(Sylvilagus brasiliensis*)**
Mild infection

Jumped species to European rabbit
(*Oryctolagus cuniculus)*
Highly virulent disease

Myxoma virus initial spread

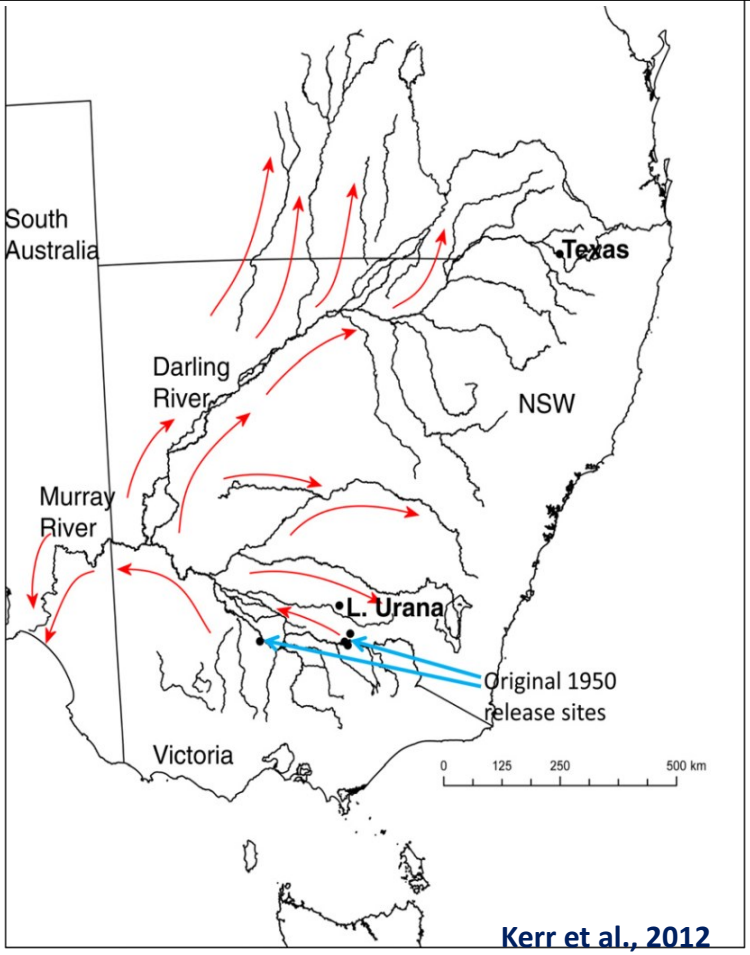
- Tested in Australia from 1937
- Release in 1950, initial spread slow

- Transmitted by mosquitoes (mechanical transmission)

- Spread limited to areas where vectors are available.

- Subsequent introduction of rabbit fleas

  -European rabbit flea *(Spilopsyllus cuniculi)*
  -Arid adapted Spanish rabbit flea *(Xenopsylla cunicularis)*



Myxoma virus host-virus co-evolution

- Geared towards maximum transmission by biting insects:
  - High virus loads in skin lesions
  - Increased survival rates and survival times

=> More (longer) opportunity for mosquitoes and fleas to transmit disease
=> Classic example of 'Trade-off Theory' of virulence evolution

Outcomes:
- Reduced effectiveness as biological control agent
- Increase in rabbit numbers
- More severe Disease

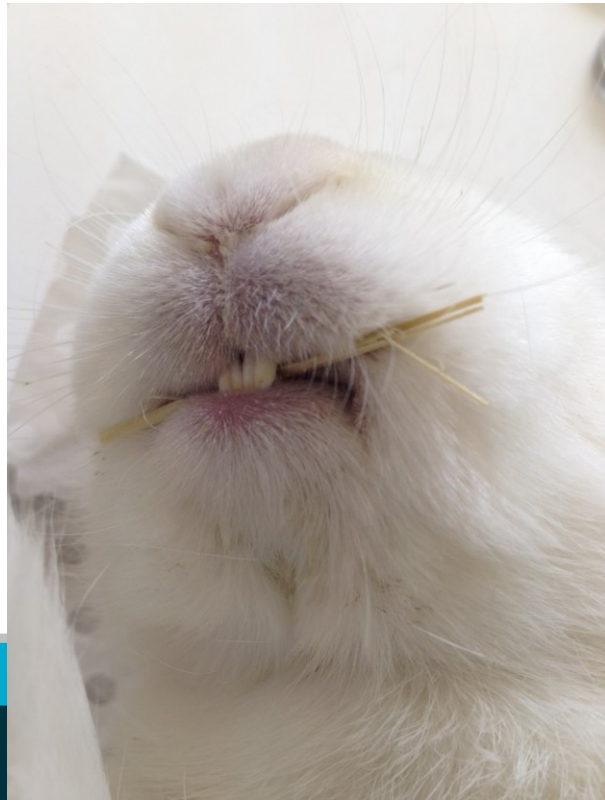
Biological control of rabbits #2: Rabbit Haemorrhagic Disease Virus

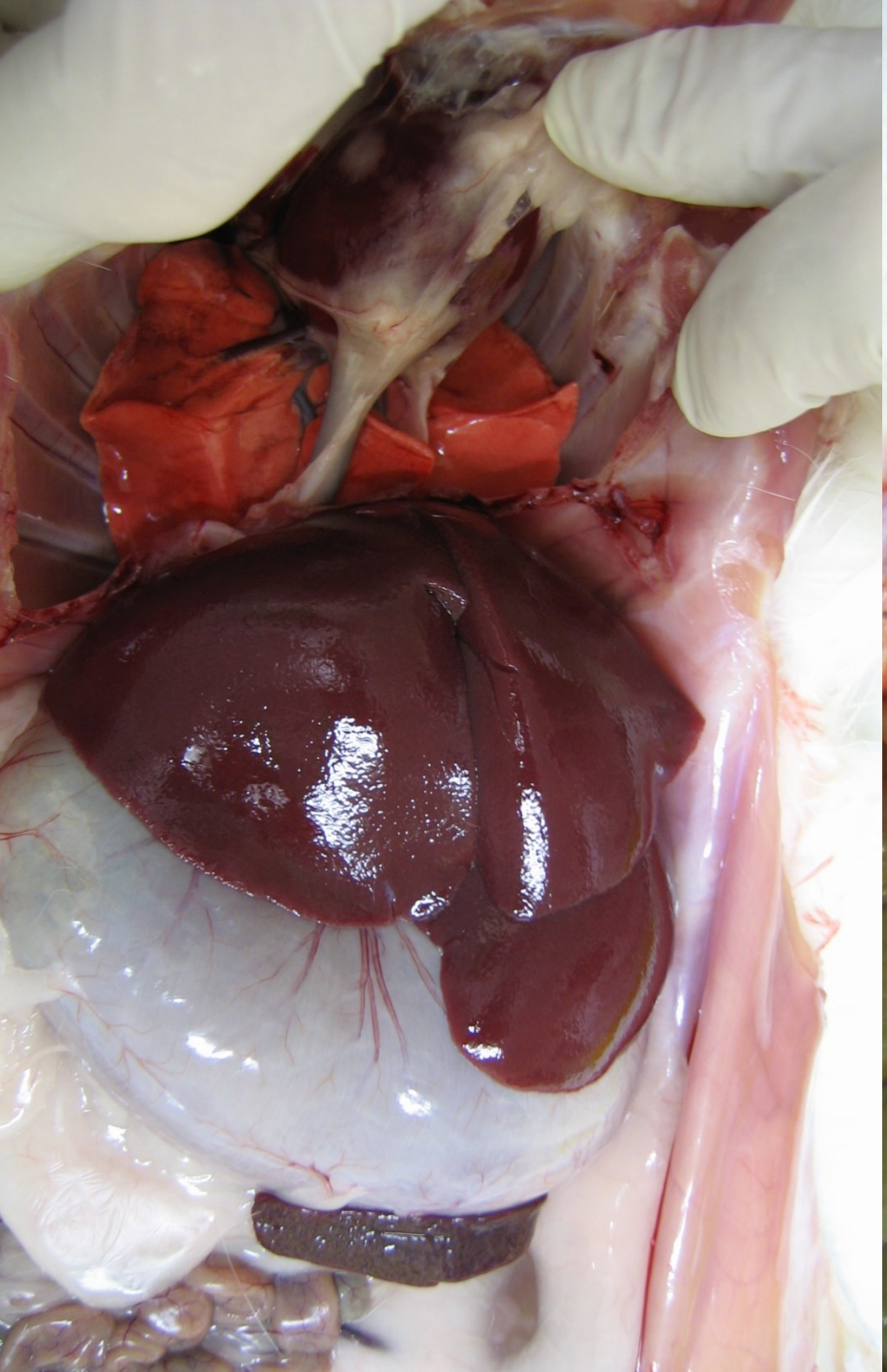
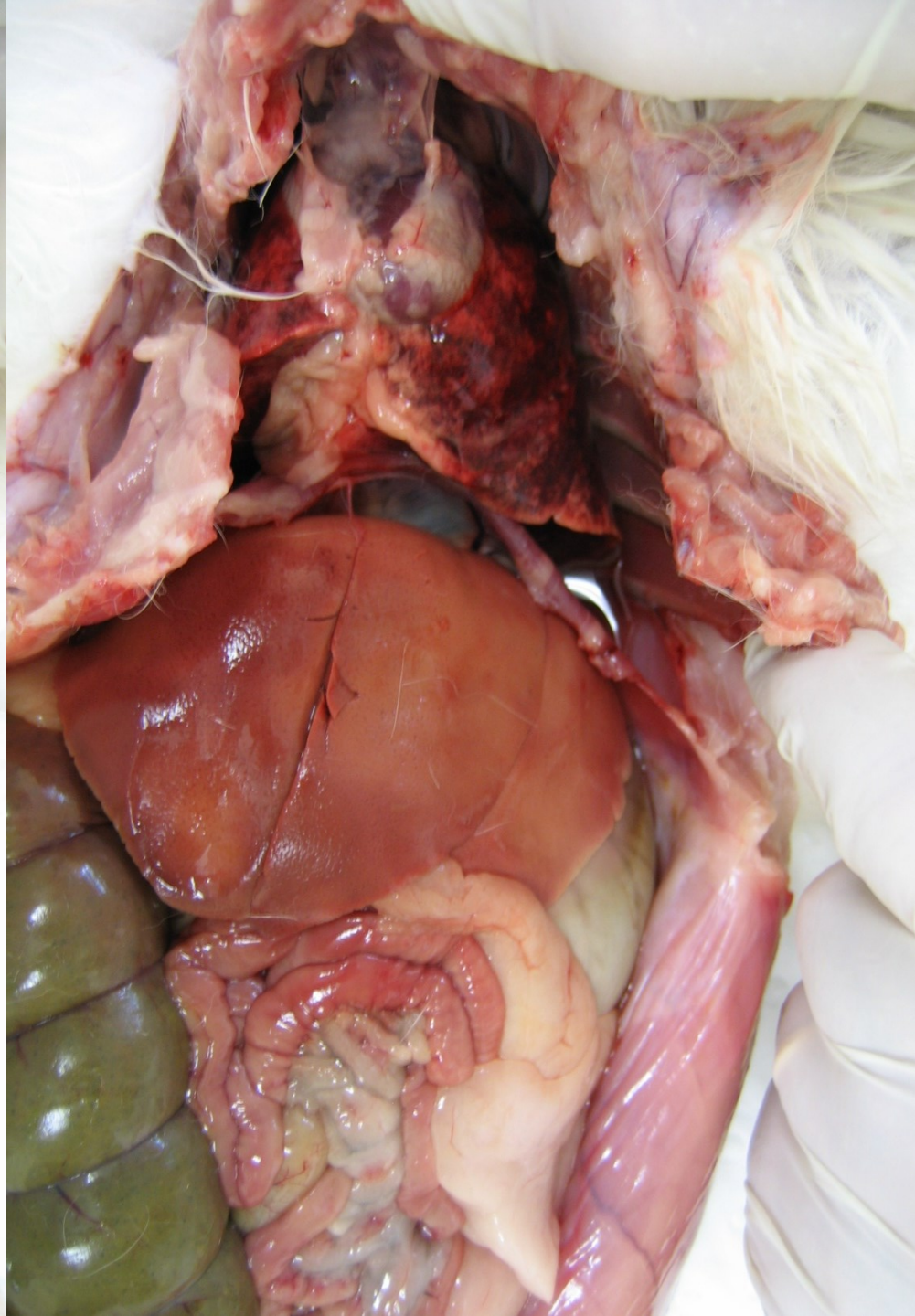
RHDV

Family: *Caliciviridae*, Genus: *Lagovirus* , *small RNA virus*

- Emerging disease of rabbits
- Likely evolved from non-pathogenic ancestors via mutation
- First described in China in 1984
- >95% case fatality

- Infectious hepatitis
- Massive hepatic necrosis and encephalopathy
- Disseminated Intravascular Coagulation
- Death usually within 36-72h post infection
- Short (if any) clinical signs
- Young rabbits innately resistant to lethal disease
- Does not grow in cell culture



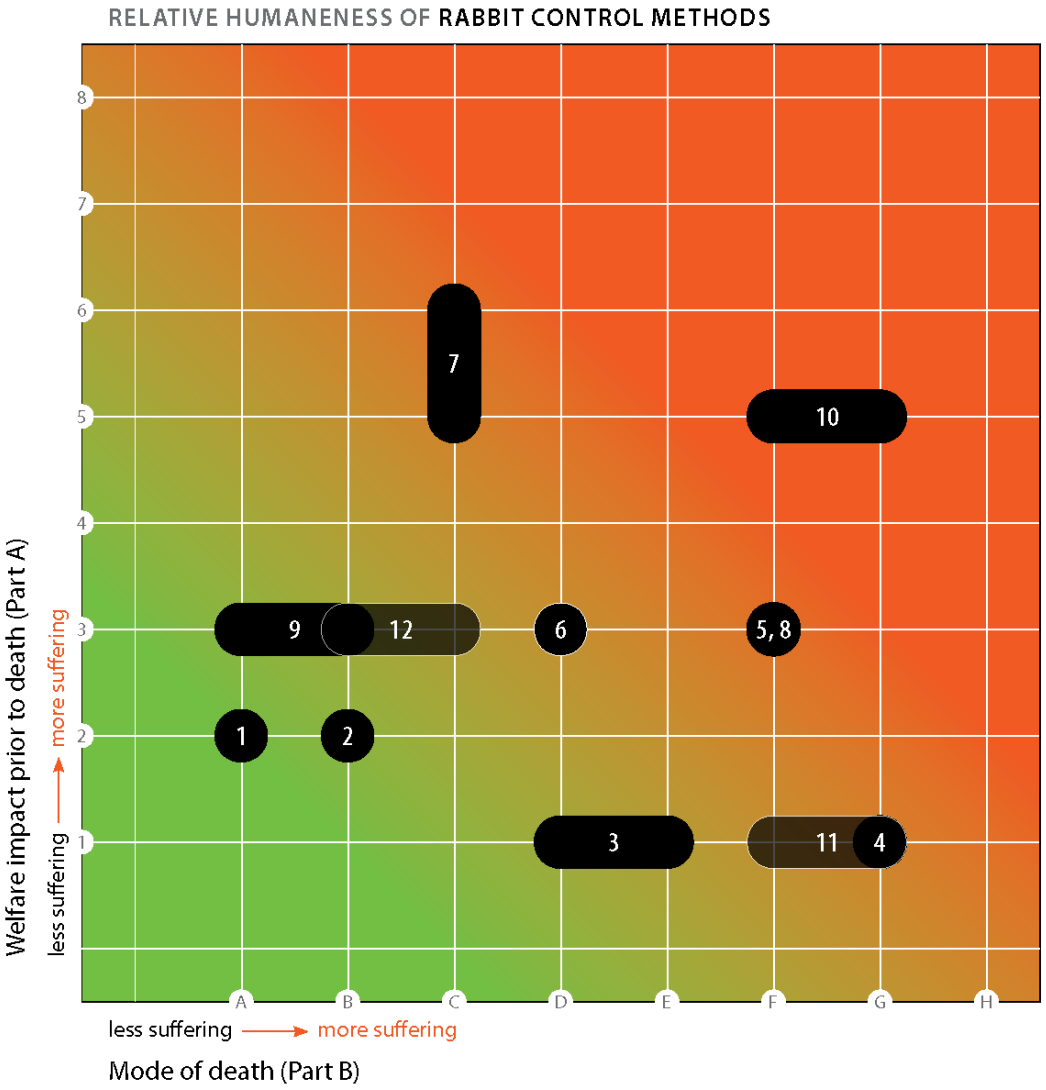



Animal Welfare

Is an integral component of pest animal control

Factor to be considered when choosing the appropriate tool for pest animal management

-> Weigh options available, including option of doing nothing



Workshop on the humaneness of pest animal destruction hosted by the RSPCA

1. Shooting (head)
2. Shooting (chest)
3. 1080 poison
4. Pindone anticoagulant
5. Chloropicrin
6. Phosphine
7. Padded foot hold trap
8. Warren ripping
9. Warren blasting
10. RHDV inoculation
11. Baits RHDV
12. LPG Warren fumigation

Scoring Matrix to assess the welfare impacts of approved rabbit control methods

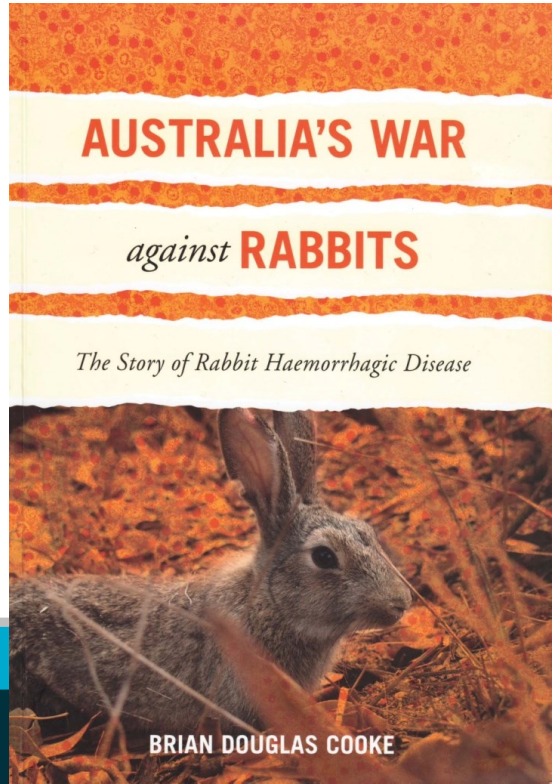
Sharp and Saunders 2012

RHDV in Australia

- Quarantine tests (AAHL) commenced in 1991
- Later: field transmission trials on Wardang Island
- Escaped in 1995 (Fly transmission!)
- Officially released in 1996
- Illegally introduced into NZ 1997

- Highly successful in reducing rabbit populations

- -> less effective in cooler climates

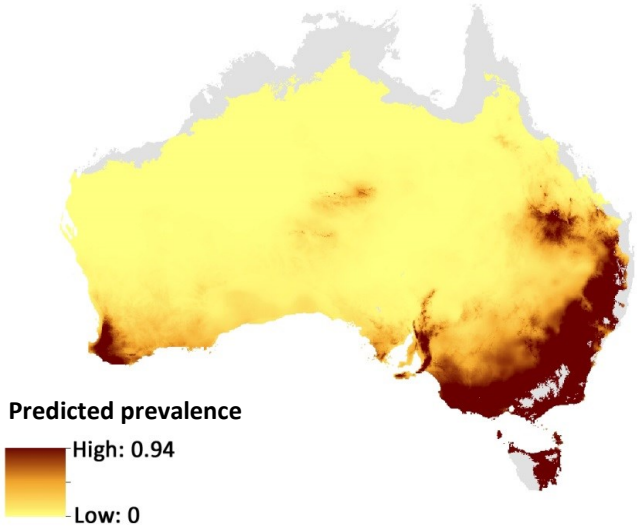


Interfering benign endemic caliciviruses

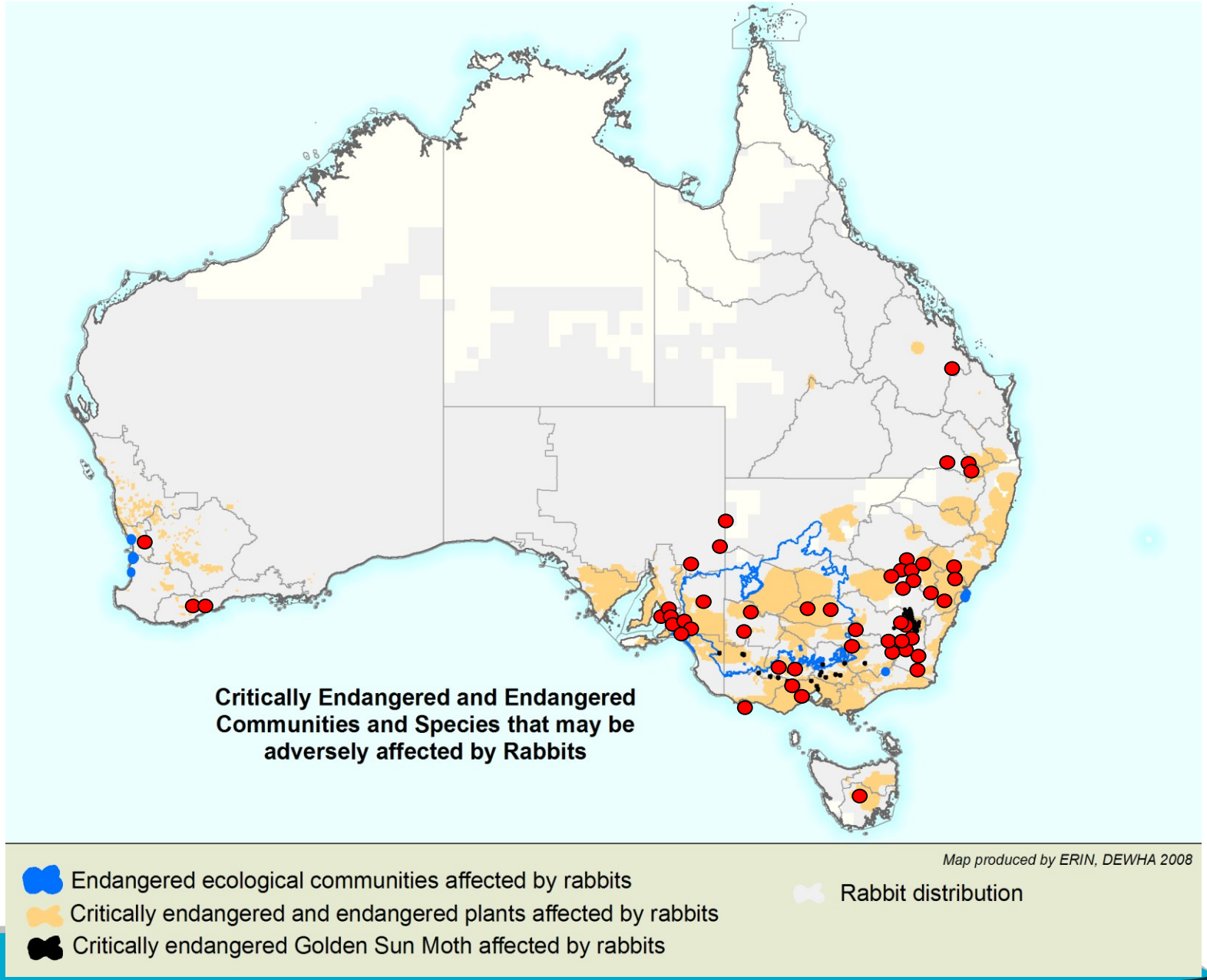
- Following release/escape RHDV was less effective in temperate areas

- Antibodies cross reacting to RHDV found in samples collected before virus release in 1996
- rabbits with these cross-reacting antibodies survived RHDV challenge

=> Hypotheses: Other virus(es) exist that are similar to RHDV but non-pathogenic and act as a partially protective vaccine to RHDV.



- Virus found in in 2007 Causes a non-clinical infection of the gut
- RCV is an imperfect natural vaccine against lethal RHD
  - Up to 50% protection max
  - Transient (approx 2 months)
- Survivors are then immune to RHDV for the rest of their lives


Critically Endangered and Endangered Communities and Species that may be adversely affected by Rabbits
Map produced by ERIN, DEWHA 2008
Endangered ecological communities affected by rabbits
Critically endangered and endangered plants affected by rabbits
Critically endangered Golden Sun Moth affected by rabbits
Rabbit distribution

Economic benefits of rabbit biocontrol

Myxoma virus
1950

Rabbit fleas
1968 and 1993

Calicivirus
(RHDV)
1996

Combined cumulative benefits estimated at $70 billion to the agricultural industries over 60 years.

(Cooke et al., 2013, Aust Econ Hist Rev)

Environmental benefits of RHDV (examples)

Large scale landscape recovery (Pedler et al 2016) => Top-down and bottom up effects

241–365% increase in occurrence

Dusky hopping-mouse (*Notomys fuscus*)

Plains mouse (*Pseudomys australis*)

Crest-tailed mulgara (*Dasycercus cristicauda*)
70 fold increase in occurrence
20 fold range extension

2000

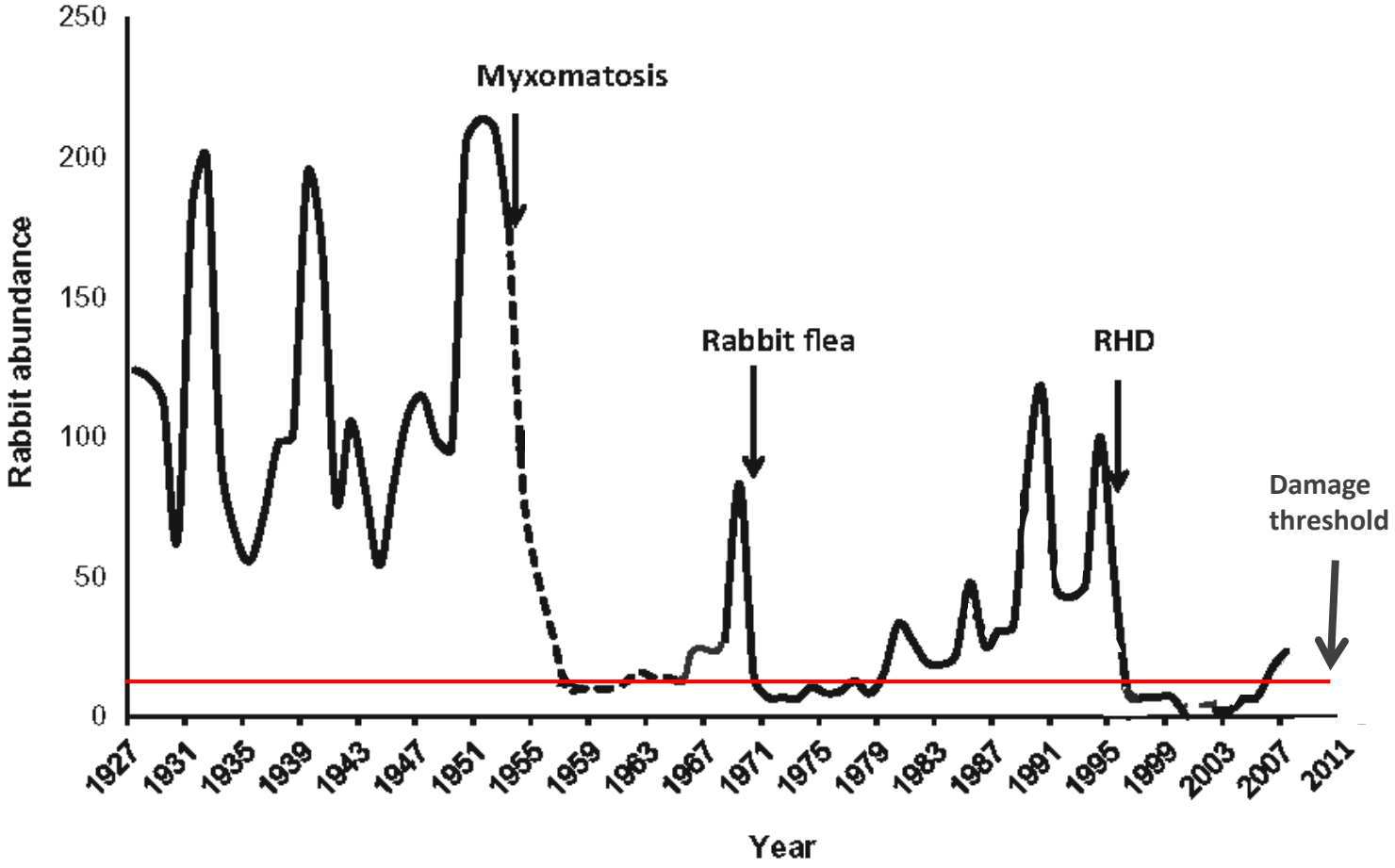
Photo: David Lord

2012

Photo: David Lord


Photos: Tanja Strive
Hattah Kulkyne National Park 2009

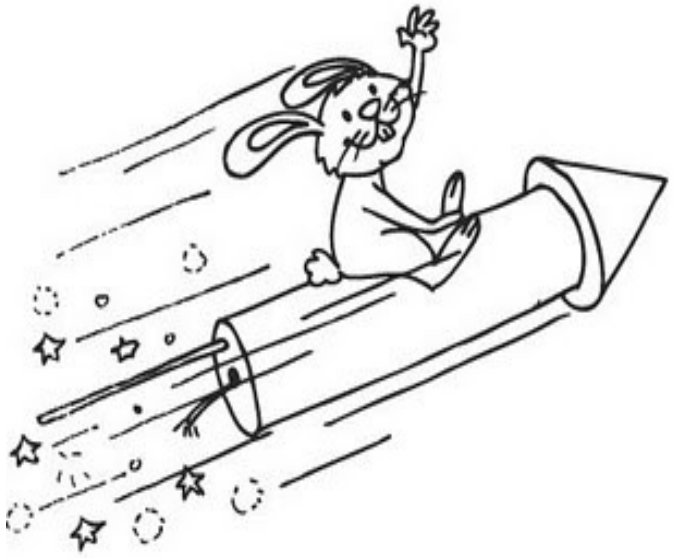
Biological control: Not a silver bullet !



- An ongoing battle (host-pathogen co-evolution)

(Cooke et al., 2013, Aust Econ Hist Rev)

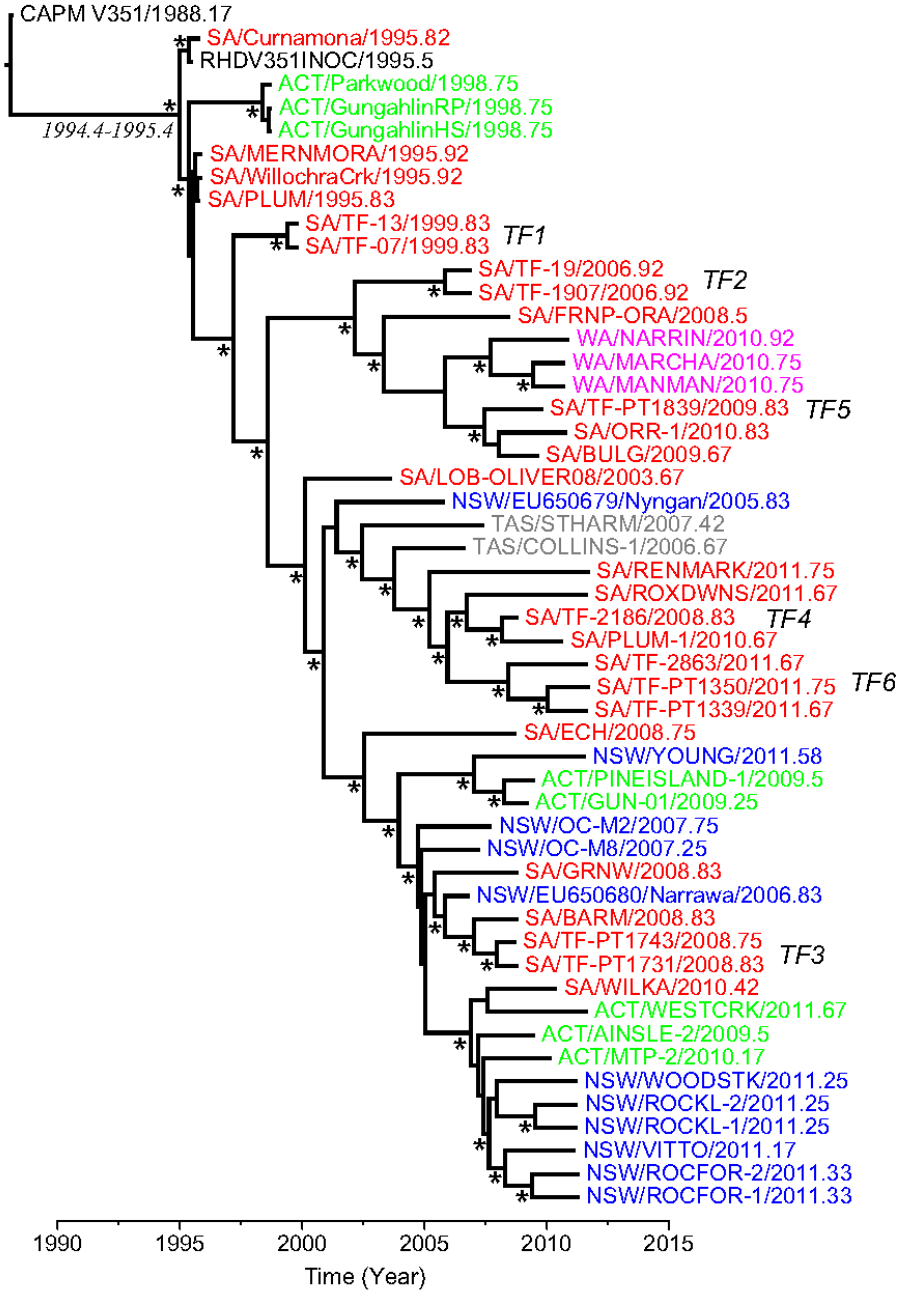
Host Pathogen Co-evolution of RHDV?



Are Australian rabbits developing genetic resistance to infection with RHDV?

Peter Elsworth & Brian Cooke
University of Canberra PhD student
QLD-DPI

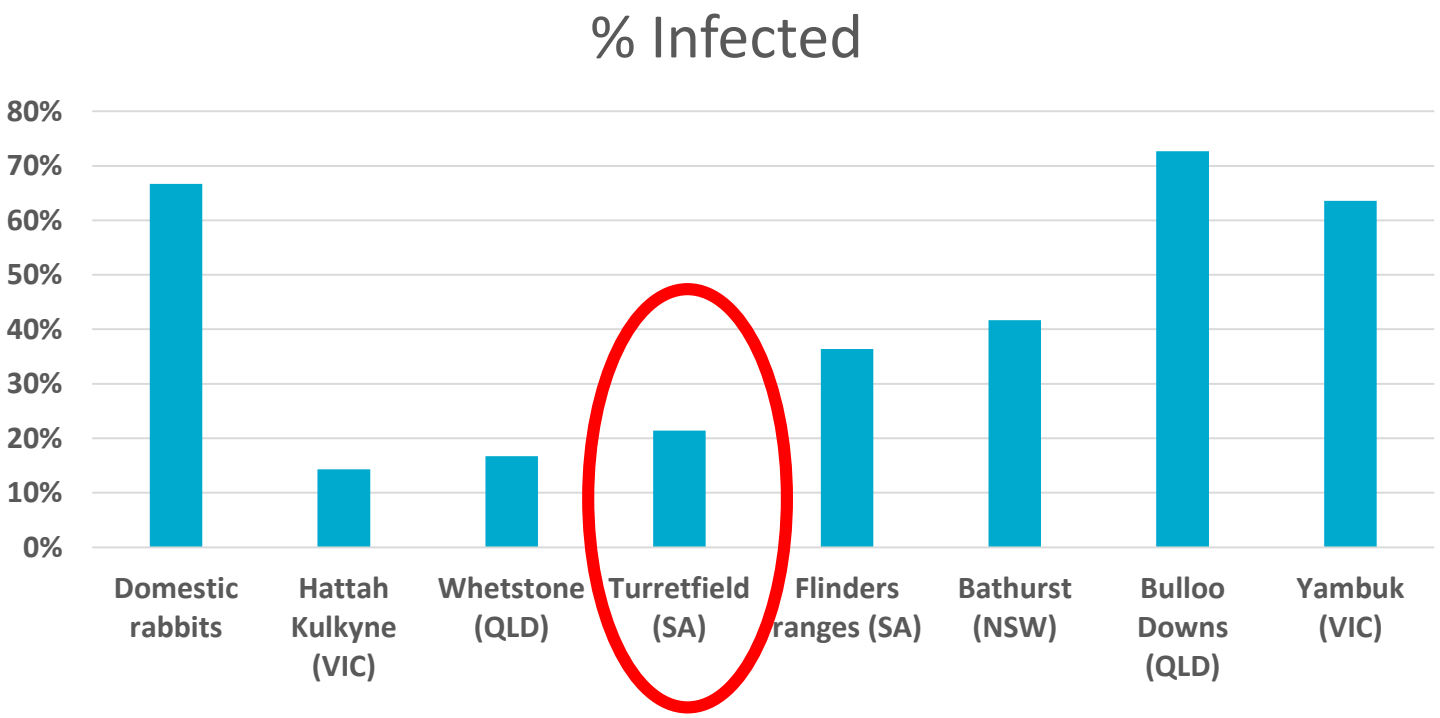
Evolution of RHDV in Australia



Despite >3000 releases of the original Czech strain only a single viral lineage has sustained field transmission in the long term

Kovaliski et al., Mol Ecol 2014
Eden et al., J Virol 2015

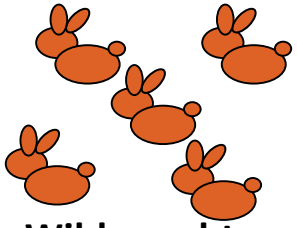
Wild rabbits from certain populations are more resistant to infection (low doses)



Yet field mortality of RHDV has remained high in these populations….

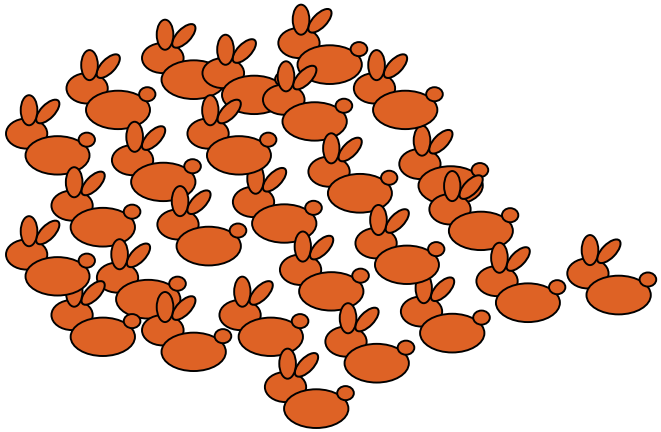
Elsworth et al, Epidemiol Inf 2012

Is RHDV evolving to counter developing resistance?



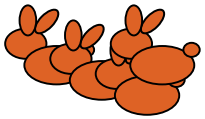
Wild caught
Turretfield rabbits
2008 (n=11)

breed



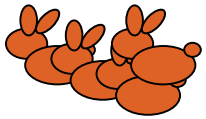
n=80

Oral infections (high dose)



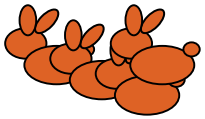
RHDV Czech strain

n=20



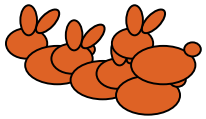
TUR 07

n=20



TUR 06

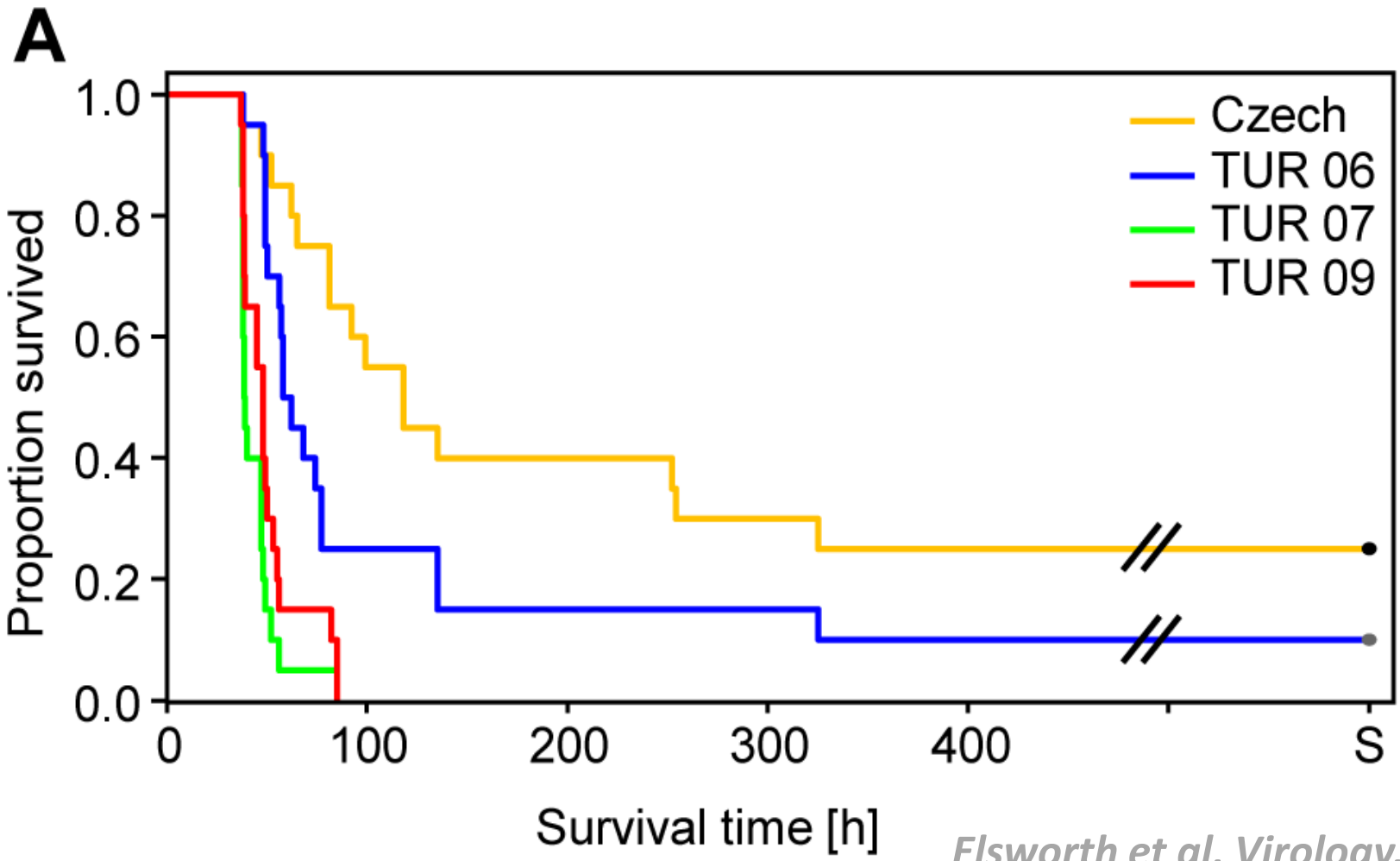
n=20



TUR 09

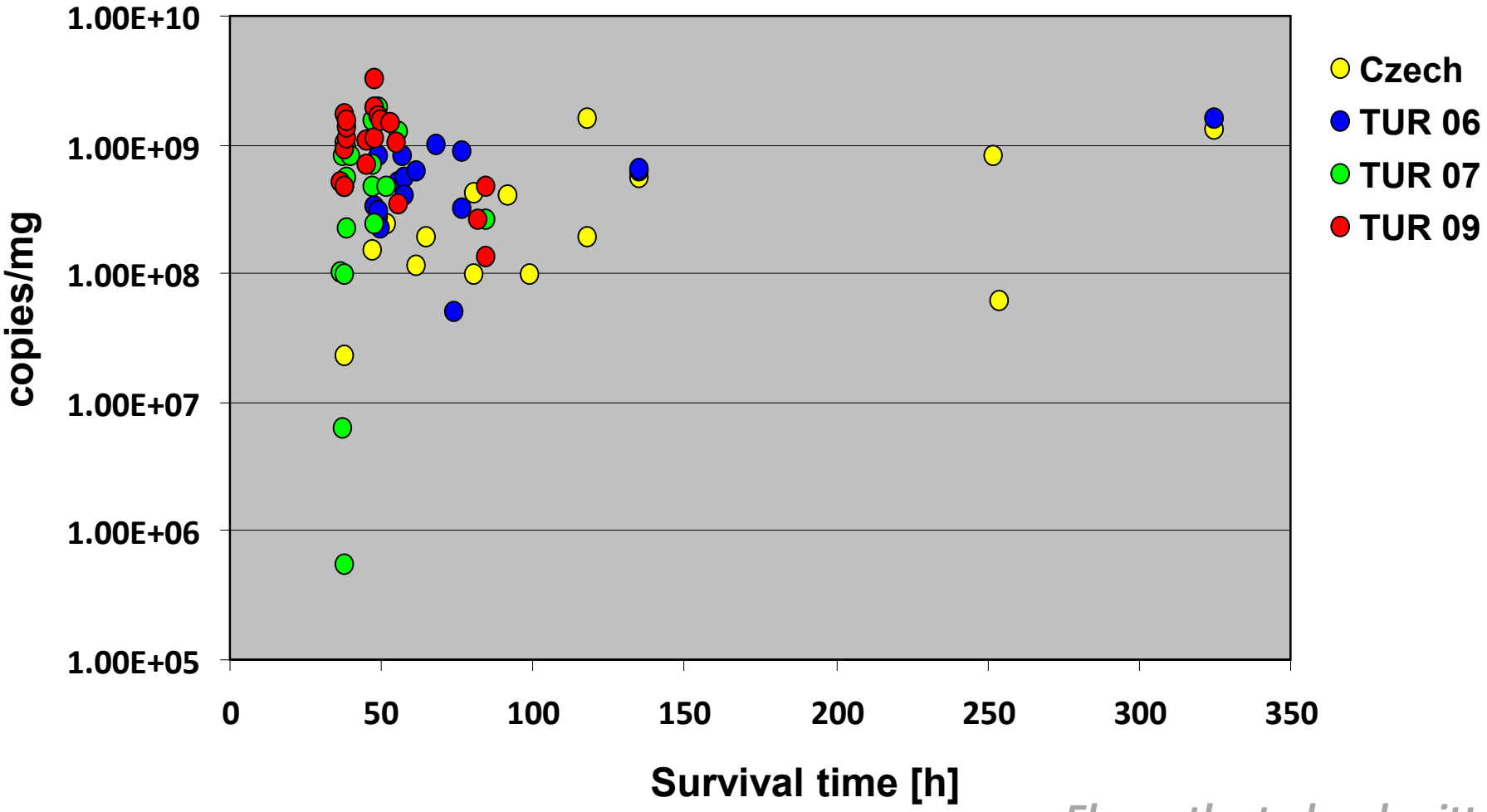
n=20

Survival curves



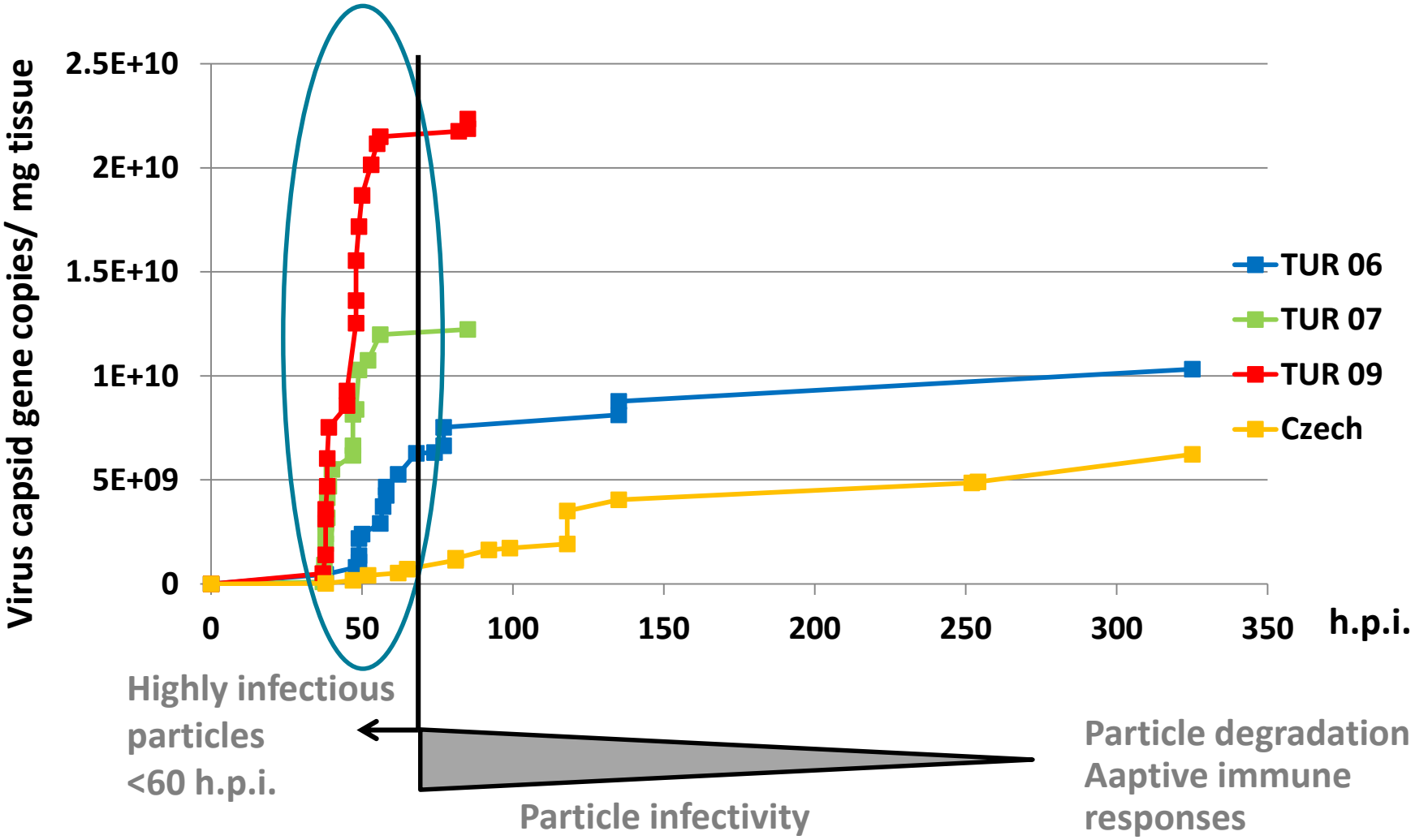
Elsworth et al, Virology, in print

Virus load in the liver



Elsworth et al, submitted

Cumulative virus produced in dead rabbits



More recent field strains

- Kill more rabbits
- Faster
- Produce higher titres of infectious virus in the liver (<60h)

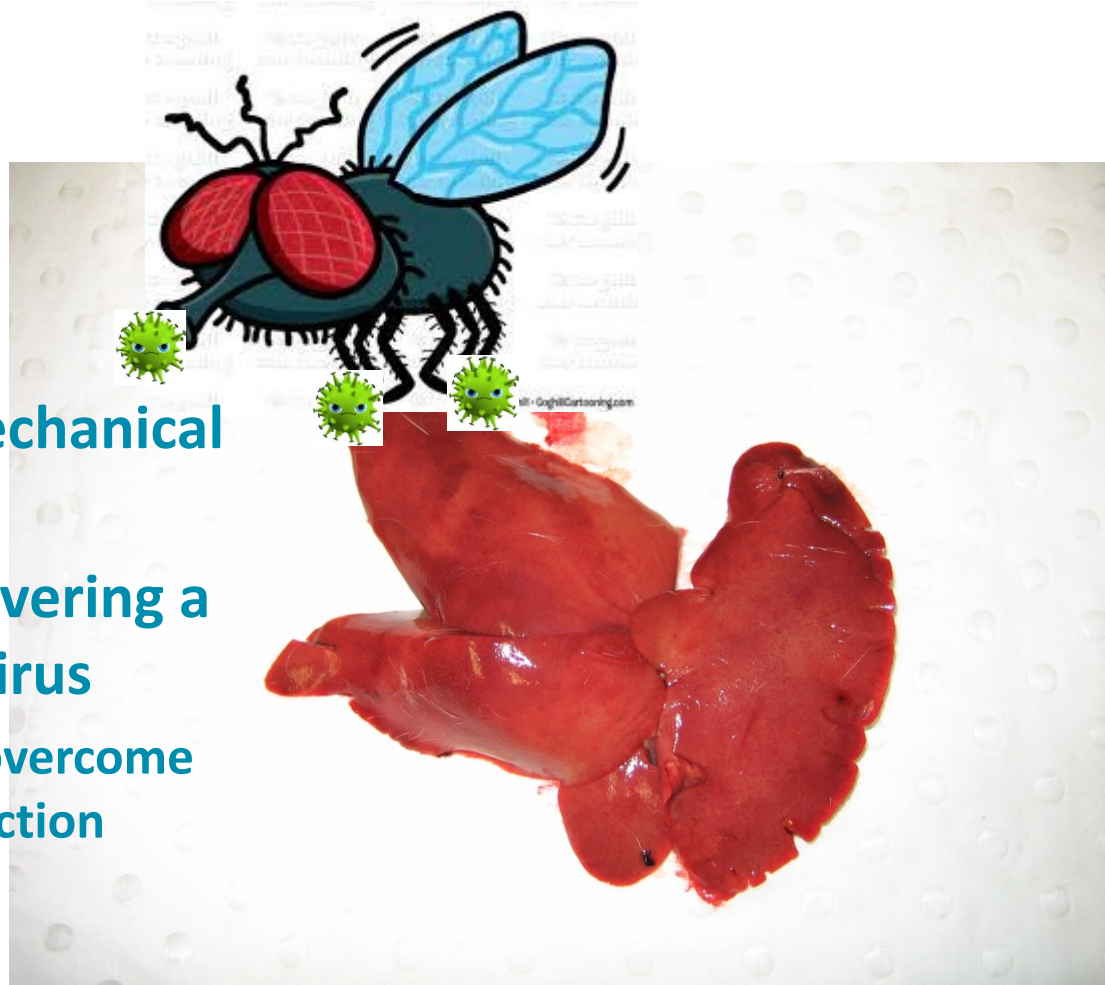
RHDV transmission

1. Contact (shedding) *(Morisse et al 1991)*
2. Mechanical insect transmission (flies feeding on carcasses) *(Asgari et al 1999 McColl et al 2000)*

Why is RHDV evolving to maintain high virulence?

Why is RHDV evolving to maintain high virulence?

- Increases likelihood for mechanical insect transmission
- Increases likelihood of delivering a higher dose of infectious virus
  - => possible mechanism to overcome increased resistance to infection

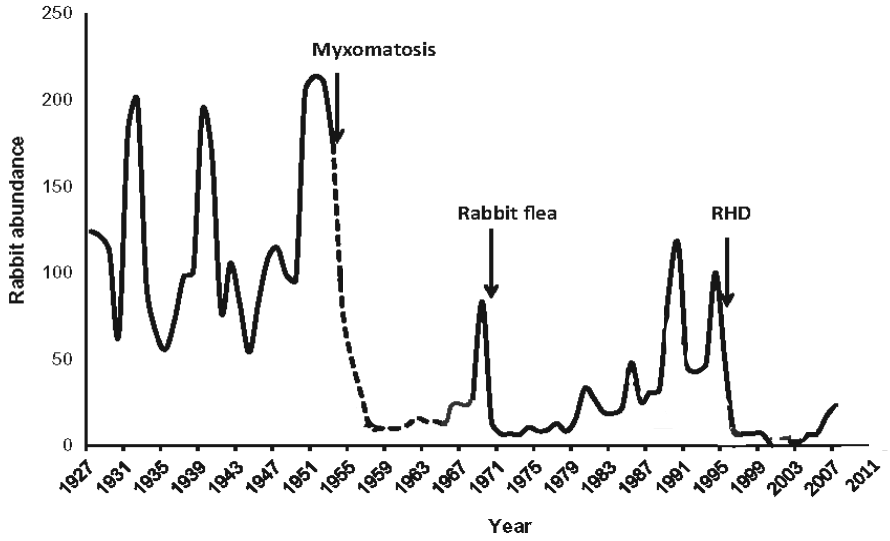


- **Selection towards maximum transmissibility (similar to MYXV)**
- **Rabbit carcass is main source of virus transmission (not the diseased animal)**

How can such high case fatality rates be sustainable?

- Population immunity
- Young rabbits innately resistant to lethal infection
- (but become infected and seroconvert)
- 100% case fatality in susceptible adult rabbits ≠ 100% mortality at population level
- Adult rabbits 'dispensable'

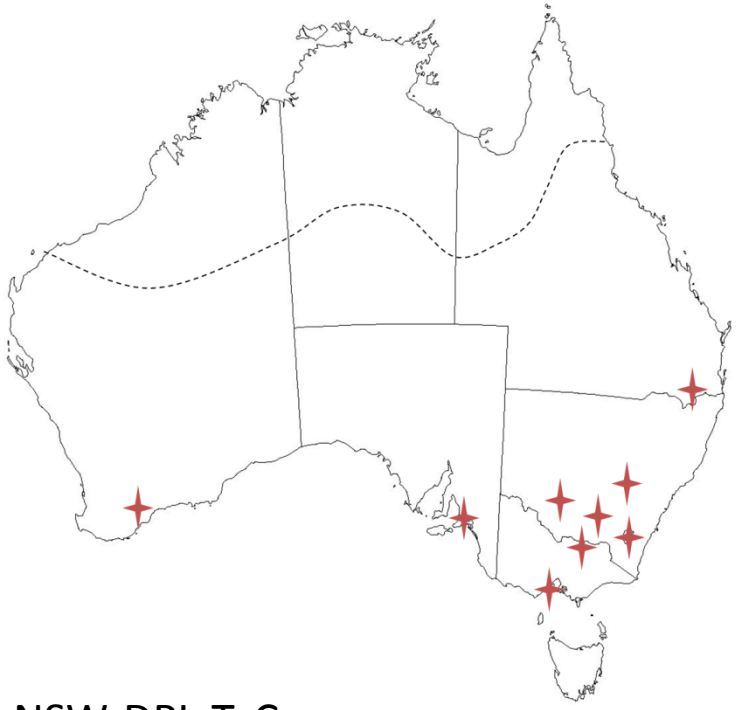
What's next?


Myxomatosis
Rabbit flea
RHD
Rabbit abundance
Year
250
200
150
100
50
0
1927
1931
1935
1939
1943
1947
1951
1955
1959
1963
1967
1971
1975
1979
1983
1987
1991
1995
1999
2003
2007
2011

“K5”: RHD-Boost

K5: RHDVa (Korea) proposed for release

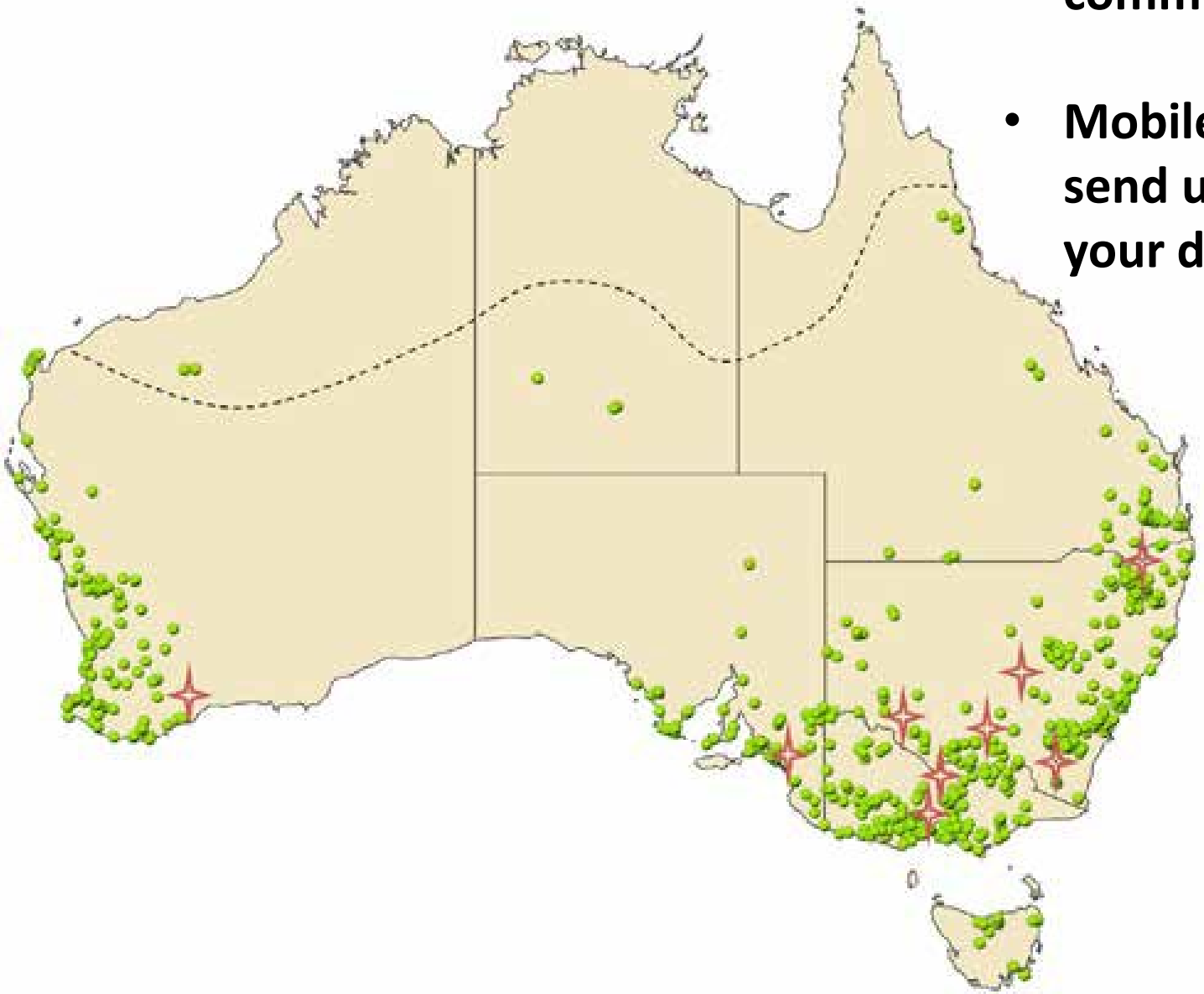
(performed better in genetically resistant wild rabbits and cross protection of non-pathogenic caliciviruses)



NSW-DPI T. Cox

- **APVMA approval, release planned for Autumn 2017 (=NOW!)**
- **>18 paired sites with intensive pre- and post release monitoring: Quarterly shot samples (n=20, serum, tissues, spotlight counts) since**
- **Expected to slow increase in rabbit numbers (NOT like initial impact)**

“K5”: RHD-Boost

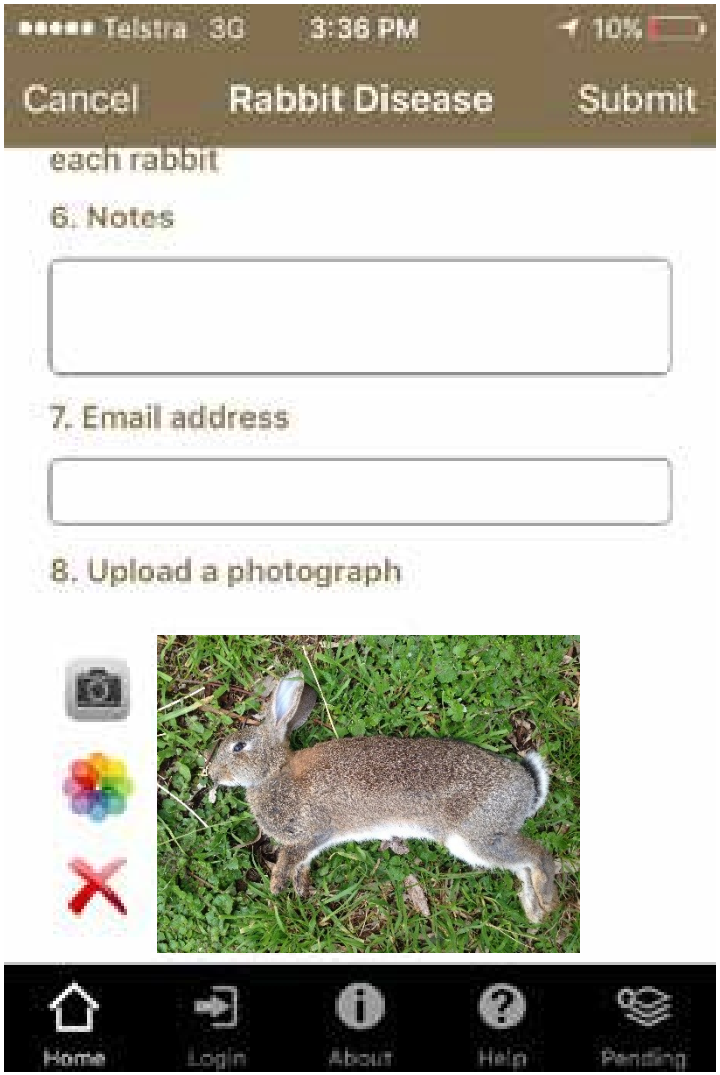


- Plus >600 community led sites
- Mobile phone App: send us a piece of your dead rabbit!

Feral Scan App: Rabbit Scan

“K5”: RHD-Boost


Telstra 3G 3:35 PM 11%
Cancel
Rabbit Disease
Submit
5. Do you want to submit a sample?
No
Yes
5a. Please enter your postal address, and a sample kit will be sent to you
John Smith. 15 Sampson Road, Suburb, Town, Postcode.
5b. Please place your rabbit in a plastic bag and label the bag (eg. Rabbit-1). Record the bag label below, and place the rabbit in a freezer until a sample kit arrives. Please submit a new record for each rabbit
Home
Login
About
Help
Pending

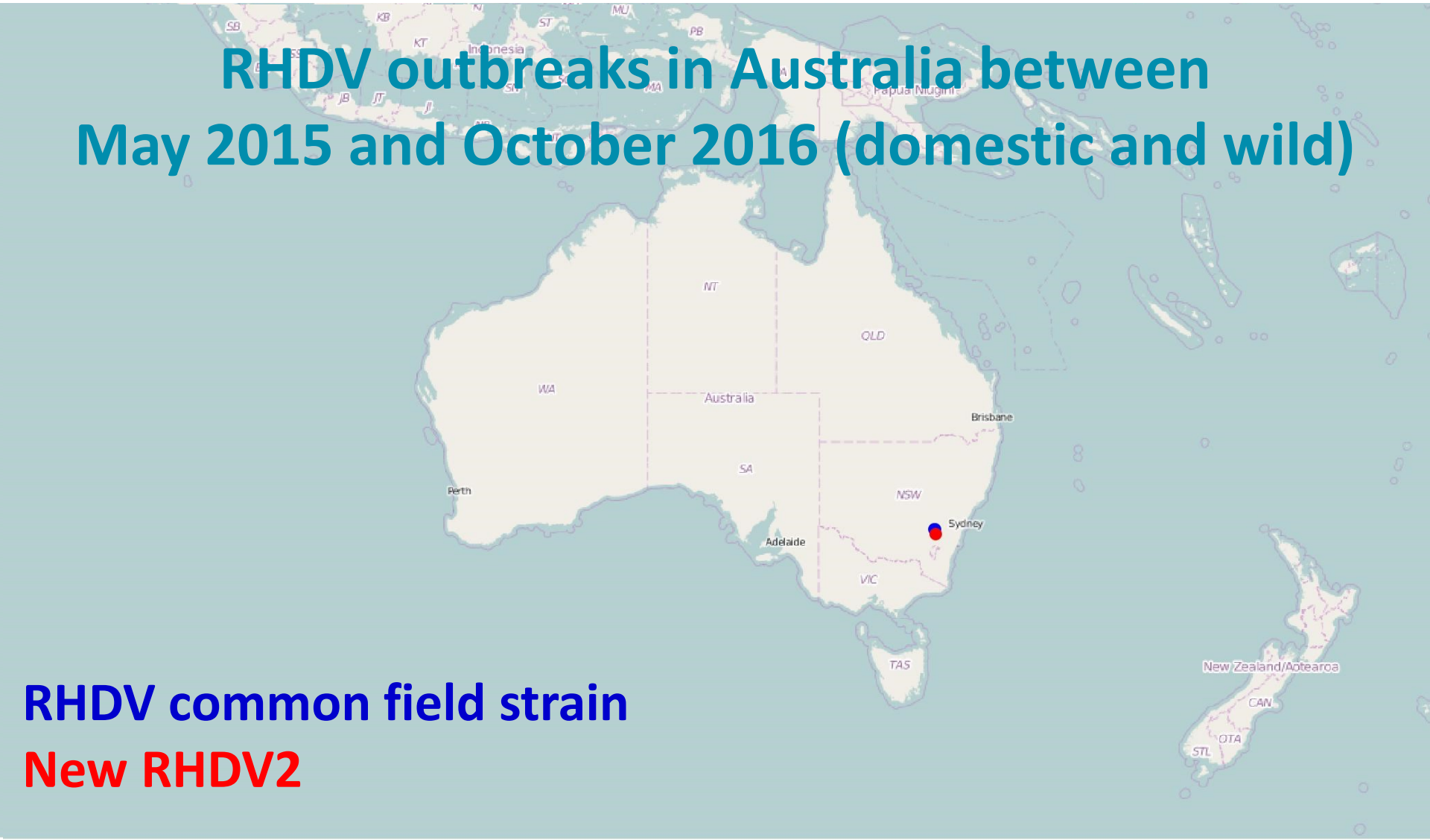

Telstra 3G 3:36 PM 10%
Cancel
Rabbit Disease
Submit
each rabbit
6. Notes
7. Email address
8. Upload a photograph
Home
Login
About
Help
Pending

What else is going on?
=> RHDV2

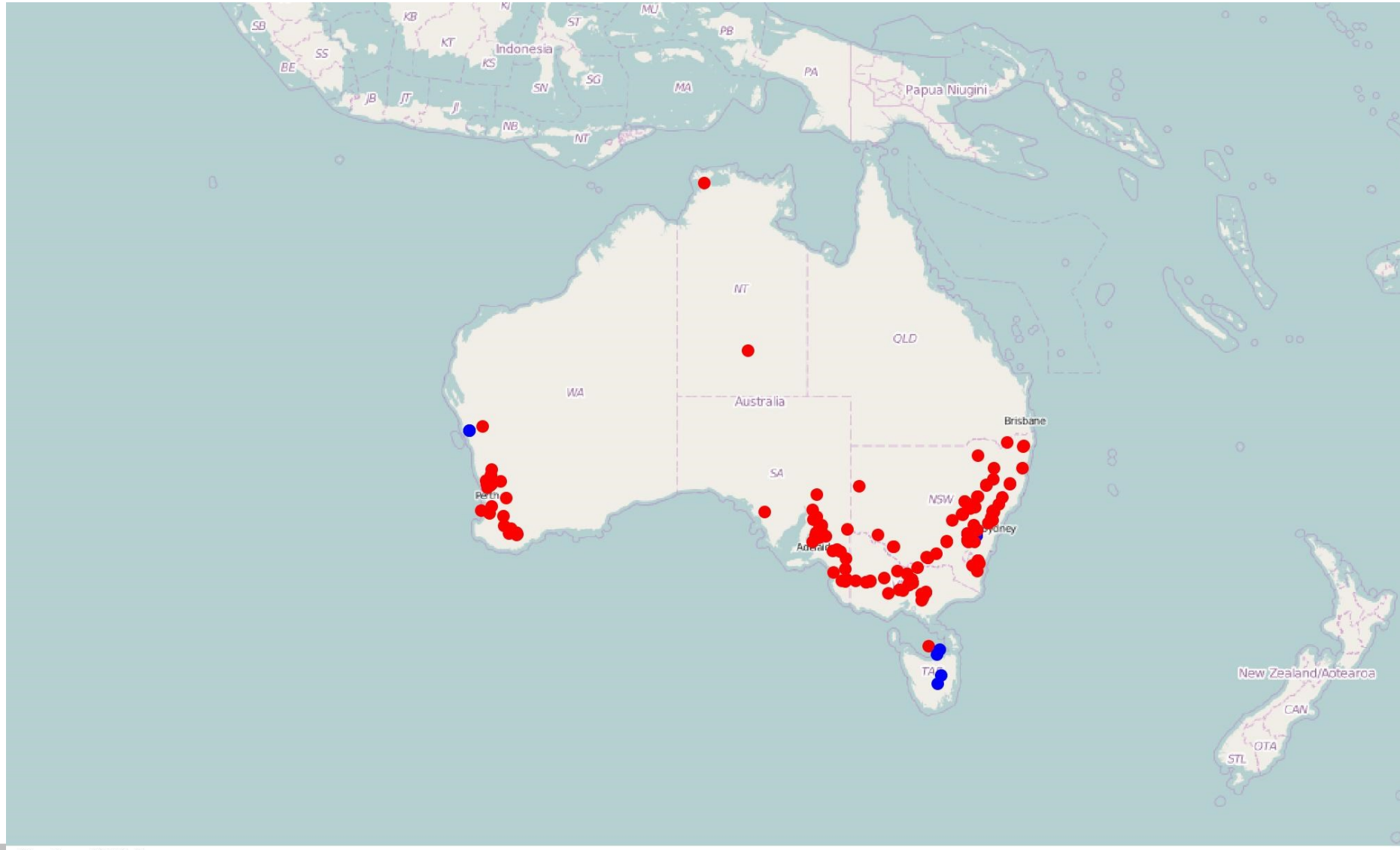
- A new rabbit calicivirus (related but different)
- Emerged in Europe since 2010
- Can overcome immunity to other strains (to some degree)
- Can kill young rabbits
- Initially reported to be moderately virulent (10-70% case fatality rate)
- Can affect lagomorph species other than rabbits
- Route of entry unclear

- Found in Australia in May 2015

Autumn (May) 2015



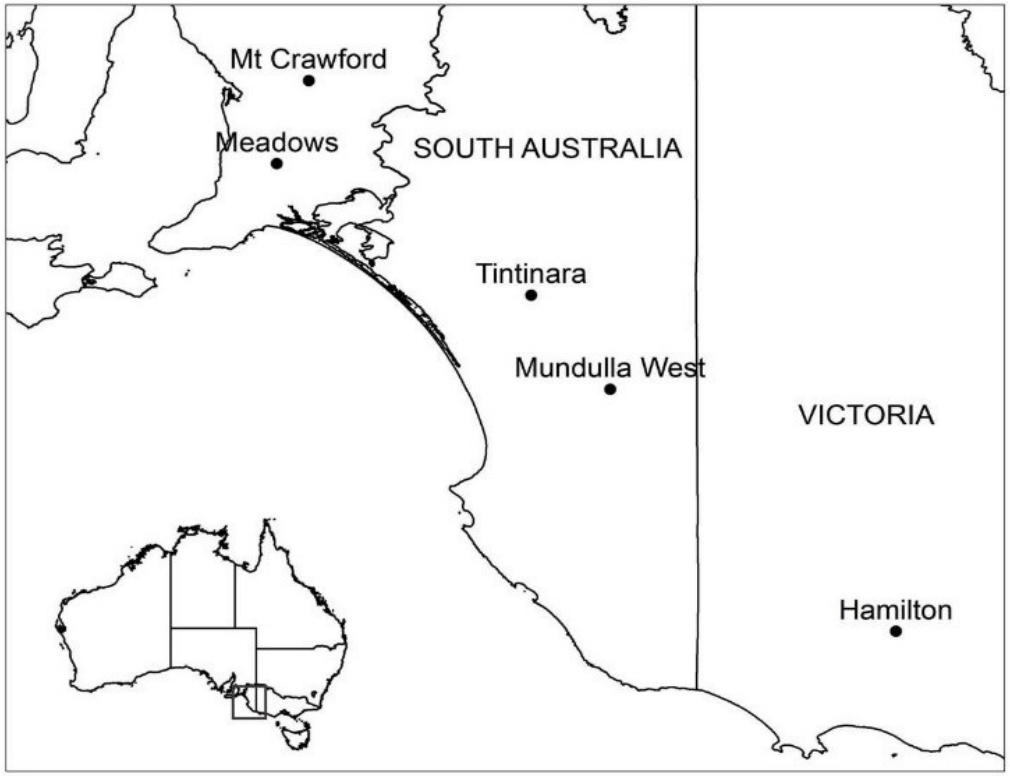
Spring (Oct) 2016



Spring 2016

RHDV2 can infect and kill rabbits and hares

- **Several hares found dead in VIC and SA (n=8)**
- **confirmed to have high loads of RHDV2 in the liver**
- **Unclear if rare spillover or if hares are an alternative host**



Hall et al., 2016

What we know about RHDV2 in Australia

- Within 18 months RHDV2 has become the dominating strain causing RHDV outbreaks in all states ecxept TAS
- Reports of young and vaccinated rabbits dying
- Pilot studies indicate very high levels of virulence (7/7 died within 4 days)

- Very fortunate to have the national RHDV monitoring network in place!!
- Has enabled excellent sample coverage
- Long term monitoring sites will allow assessment of initial RHDV impact (Analysis in progress)
- Differential diagnostic tools developed: molecular, serology (European collaboration)

What we don't know about RHDV2 in Australia (and what we need to find out)

- Experimentally quantify
- Virulence (adults + kittens)
- Ability to overcome immunity to other strains (and vice versa)
- Determine efficacy of current vaccine, need a new vaccine!

- Understand field epidemiology, transmission and evolution of RHDV2
- Include flies into monitoring
- Impact on rabbit populations (national monitoring program, in progress)
- Which role do hares play?
- What does all this mean for the planned K5 release?
- Can we harness RHDV2 as a tool?

Get involved!

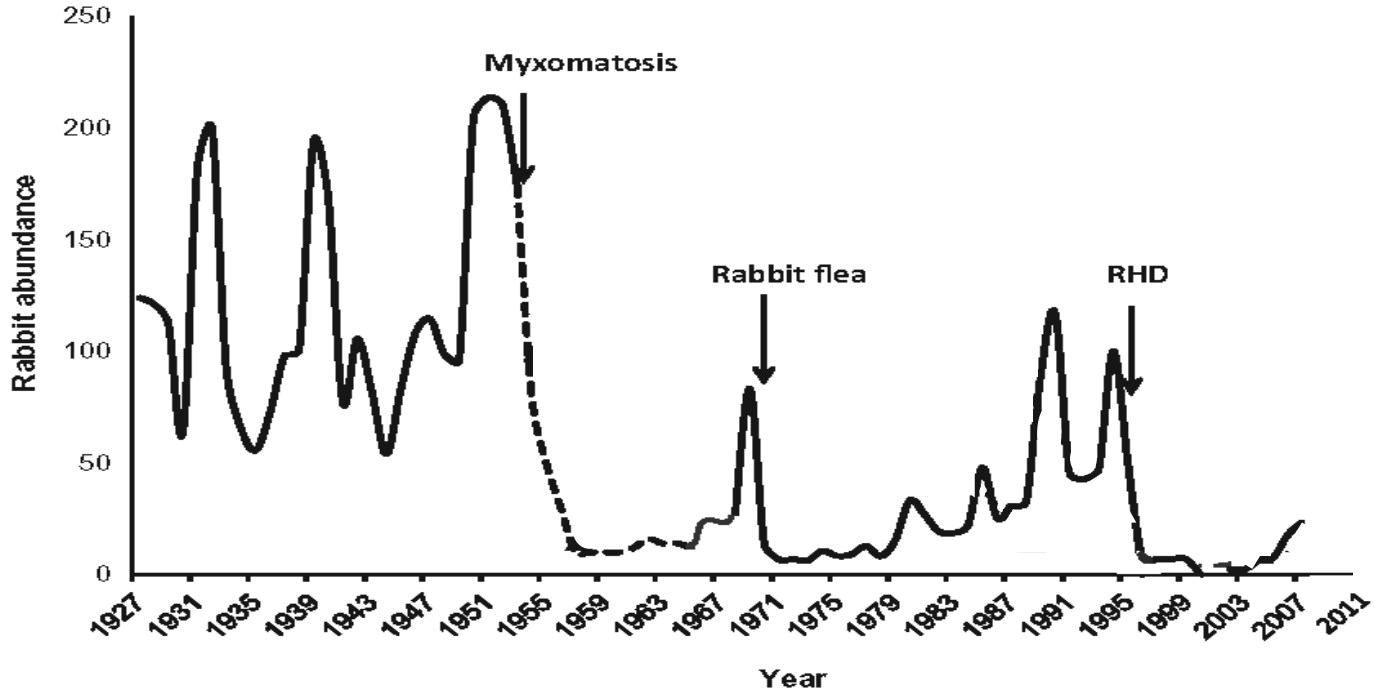
Download App and monitor

- **Rabbit abundance**
- **Rabbit control**
- **Rabbit disease**

If you find a dead rabbit:

- **Request a sampling kit!**
- **(or send me an email)**

Long term outlook?



- Biological control not a silver bullet, but a powerful tool in the arsenal
- Pipeline needed: new or improved controls needed on an ongoing basis (incl biological controls)
- Integrated pest management!
- Blue sky science? -> new revolutionary genetic control tools

Thank you!

CSIRO

Robyn Hall
Tegan King
Nina Huang
Ros Mourant
Mel Piper
Peter Kerr
June Liu
John Wright

NSW DPI

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