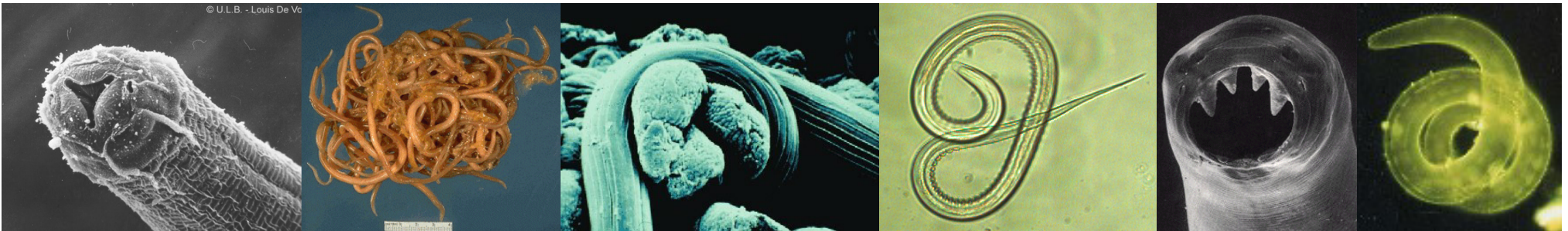


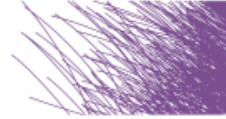
FACTORS PROMOTING ANTHELMINTIC RESISTANCE

European Medicines Agency

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- Contents
 - Important helminth parasites in livestock and horses
 - Prevalence of anthelmintic resistance
 - Factors promoting anthelmintic resistance
 - Sustainable use of anthelmintics



Cooperia spp.
Ostertagia ostertagi
Dictyocaulus viviparus
Fasciola hepatica



Nematodirus helvetianus
Teladorsagia circumcincta
Haemonchus contortus
Fasciola hepatica



Ascaris suum
Trichuris suis



Small strongyles
Parascaris equorum
Oxyuris equi



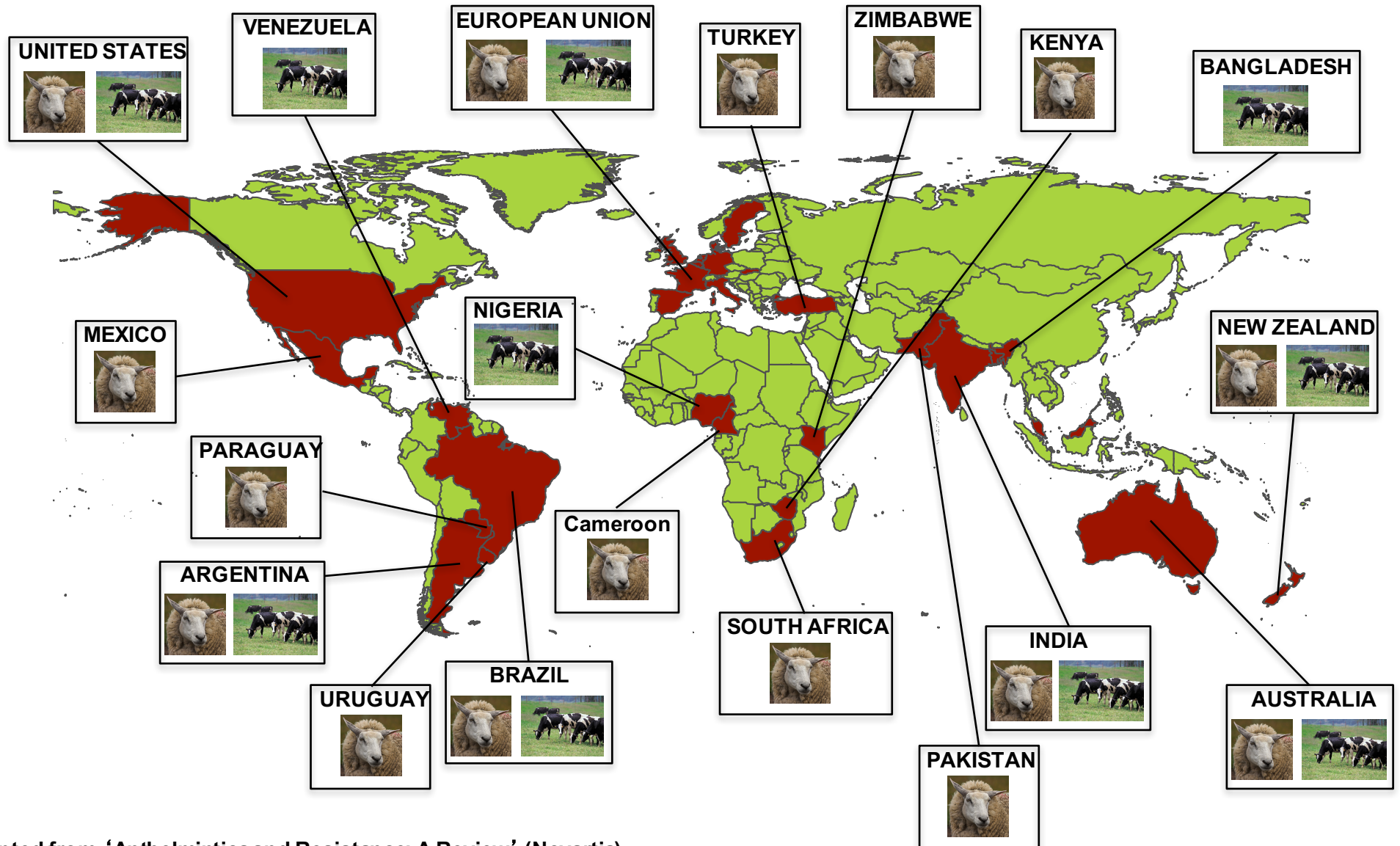
- Imidothiazoles (levamisole)
- Tetrahydropyrimidines (pyrantel)
- Benzimidazoles
- Macrocyclic lactones
- Amino-acetonitril derivatives (monepantel)
- Spiroindoles (derquantel)
- Phenol and salicylanilide derivatives (closantel, nitroxinil, oxyclosanide)

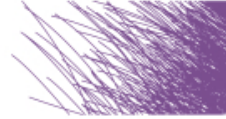
CRUCIAL TO MAINTAIN THE EFFECTIVENESS OF THESE DRUGS

- Limited introduction of new anthelmintics
- No real alternative control strategies

Anthelmintic resistance in animals

Host	Species	Benzimidazoles	Levamisole	Macrocytic lactones	Other
Cattle	<i>Cooperia spp.</i> <i>Haemonchus placei</i> <i>Ostertagia ostertagi</i> <i>Trichostrongylus axei</i>	X X X X	X X	X X X	
Sheep & Goats	<i>Haemonchus contortus</i> <i>Teladorsagia spp.</i> <i>Trichostrongylus spp.</i> <i>Nematodirus spp.</i>	X X X X	X X X	X X X	Monepantel Monepantel Monepantel
Horses	<i>Cyathostominae</i> <i>Parascaris equorum</i>	X		X	Pyrantel
Pigs	<i>Oesophagostomum spp.</i>	x	x	x	
Dogs	<i>Ancylostoma caninum</i>				Pyrantel





‘Drug resistance in nematodes: a paper tiger or a real problem ?’ (Waller, 1985)



Photos courtesy of Dr Neil Sargison (Edinburgh Vet School)

Case study of a cattle farm:

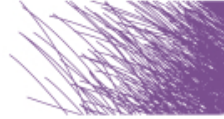
Ivermectin efficacy:

	Effic. D21
2006	73,0
2007	40,0
2008	0,0

Surviving species: *Cooperia oncophora*



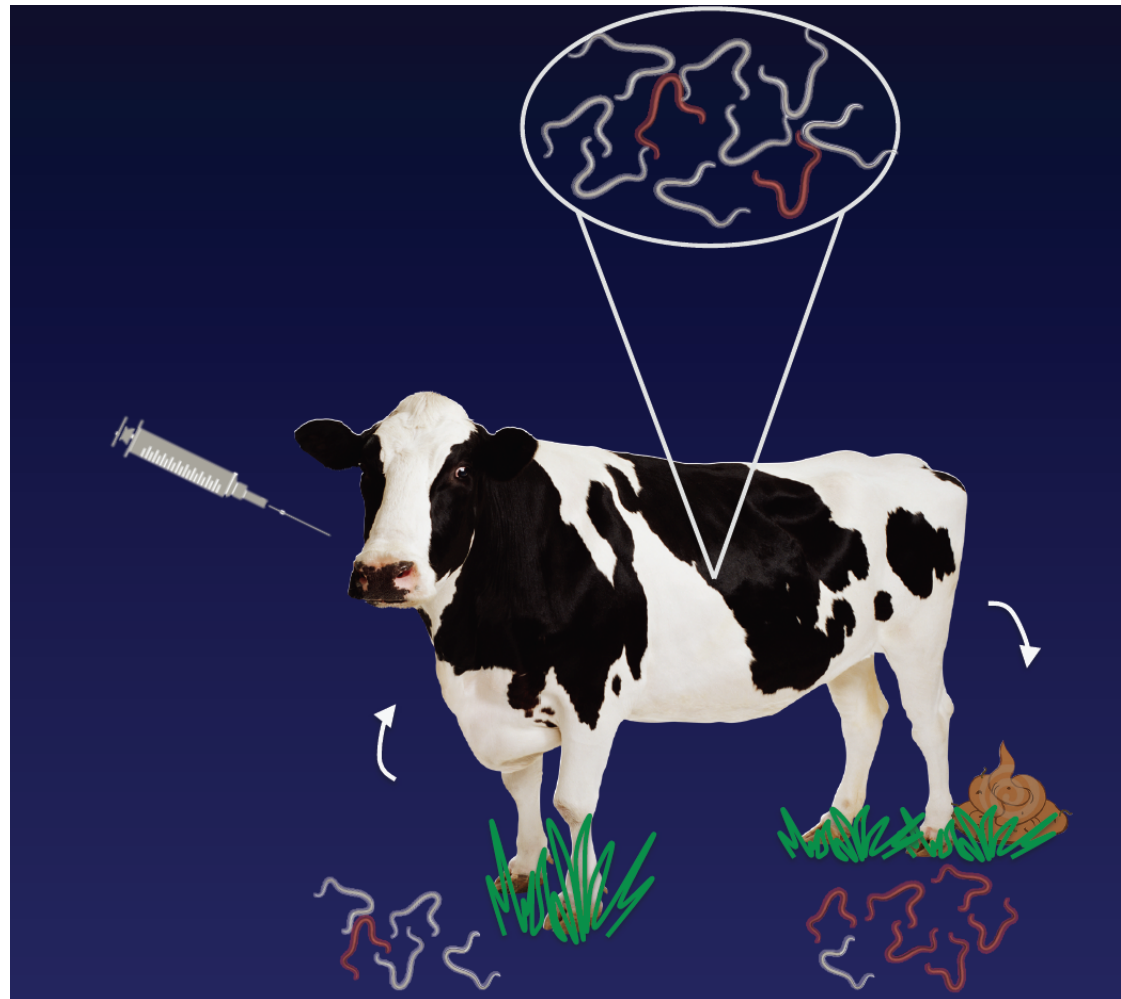
El-Abdellati et al., 2010. *Veterinary Parasitology* 171, 167-171



Reduced efficacy $\neq$ anthelmintic resistance

- Anthelmintic resistance
- Quality of the products
- Underdosing
- Drug formulation (injectable, oral, pour-on)
- Sensitivity of the detection technique
- ...

Development of anthelmintic resistance



Refugia = proportion of helminth population that is not under selection pressure

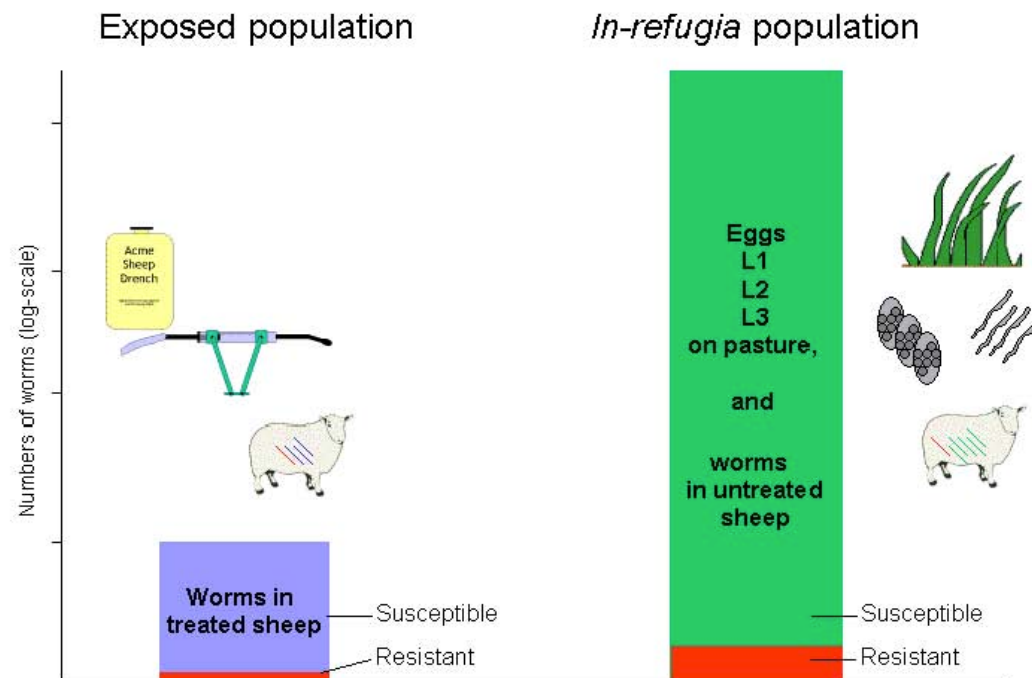


Fig 5.2 The exposed and in refugia worm populations

The worms inside the dosed sheep are exposed to the anthelmintic. Worms that are free-living on pasture, or are adults or immature in untreated sheep are in refugia. The in refugia population is typically 100 to 10,000 times larger than the exposed population and the relative sizes of these two populations influences how rapidly AR develops. There are resistant and susceptible worms in both populations but only the susceptible worms in the exposed population (in blue) are removed by treatment.

Factors promoting anthelmintic resistance

- Few published studies
 - Mostly observational studies
 - Few clinical studies
 - Systematic review and meta-analysis (sheep) :

Preventive Veterinary Medicine 117 (2014) 388–402



Contents lists available at [ScienceDirect](#)

Preventive Veterinary Medicine

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



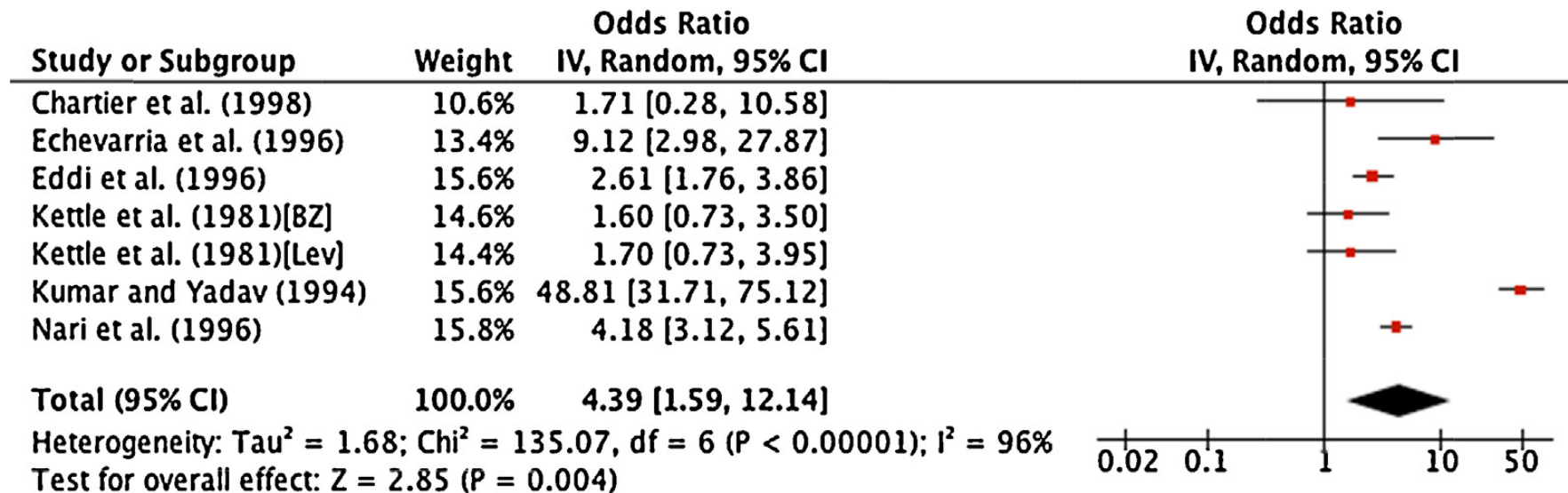
A systematic review and meta-analysis of factors associated with anthelmintic resistance in sheep



L.C. Falzon^{a,*}, T.J. O'Neill^b, P.I. Menzies^c, A.S. Peregrine^d, A. Jones-Bitton^c,
J. vanLeeuwen^e, A. Mederos^f

Factors promoting anthelmintic resistance

- **Introduction** of anthelmintic resistance (no quarantine treatment)
 - Suter et al., 2004, 2005
- **Frequent treatments***
 - Treatment interval close to pre-patent period

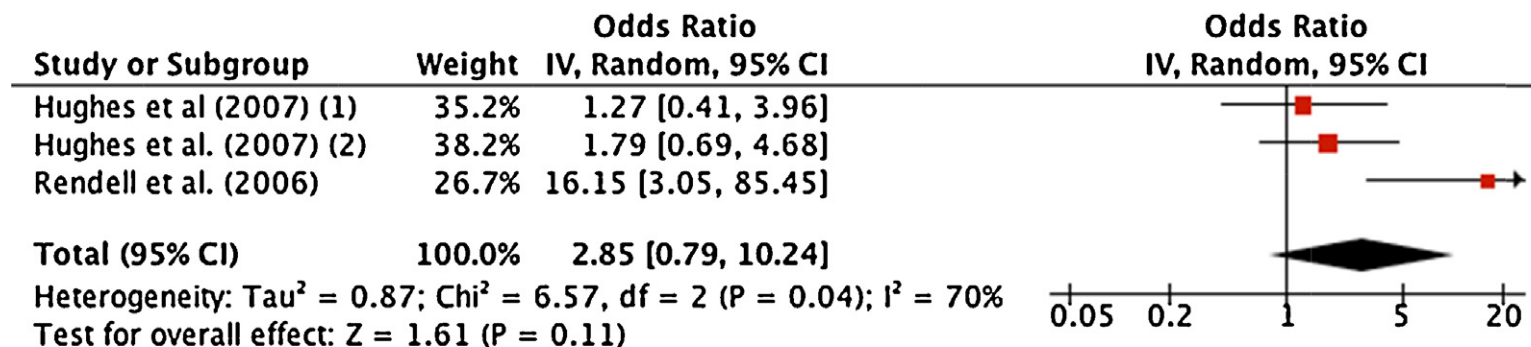


Falzon et al., 2014. Prev Vet Med 117(2):388-402 (sheep)

Suarez & Christel, 2014. Rev Bras Parasitol Vet 23(2):129-35 (cattle)

Factors promoting anthelmintic resistance

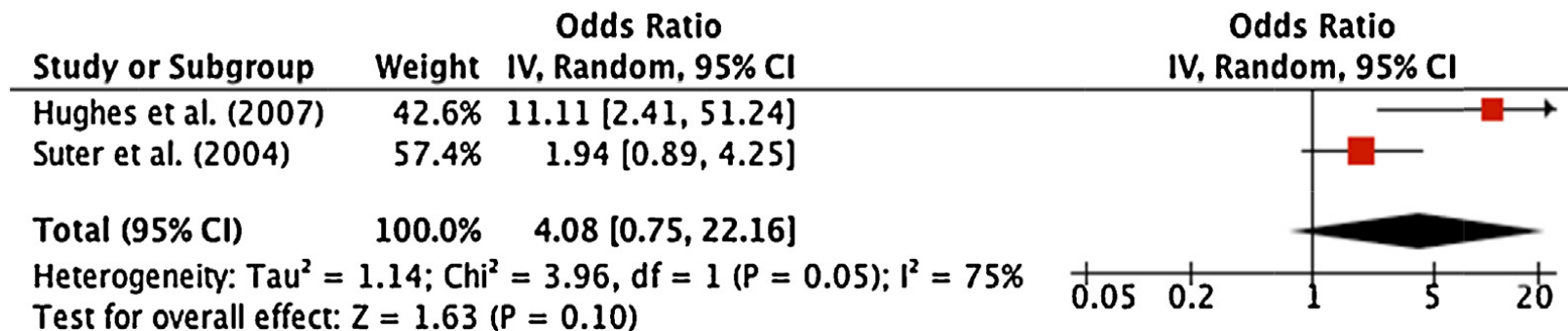
- **Long term** use of the same anthelmintic class vs. rotation?
 - Leignel et al., 2010
 - **Under-dosing**
 - No weighing prior to treatment
 - Treating goats with sheep dose
 - ‘Tailing off’ of long acting formulation (e.g. intraruminal bolus)^{NS}
- > Survival of worms with heterozygous resistance alleles.



(1) Moxidectin injection
 (2) Macrocyclic lactone capsules

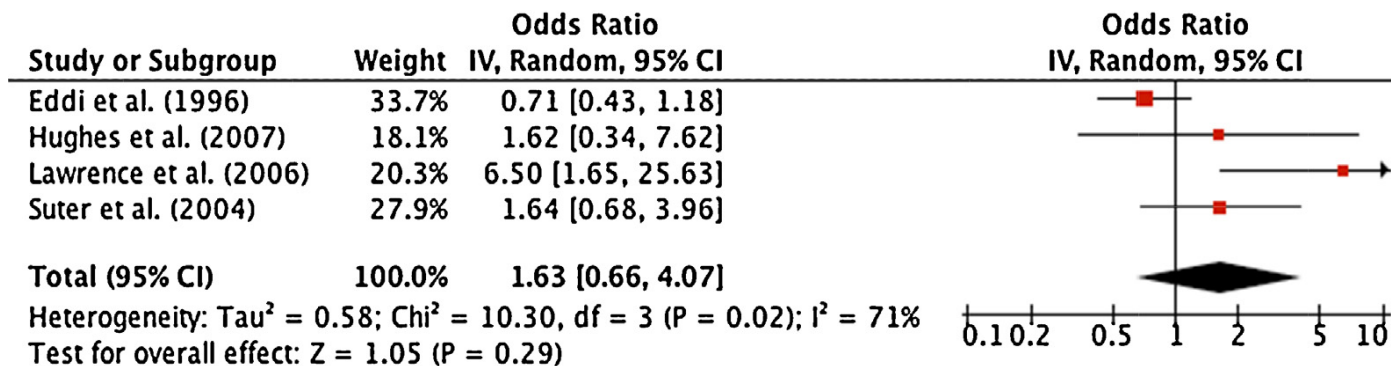
Factors promoting anthelmintic resistance

- Lack of efficacy **testing**
- Treatment when environmental **refugia** is low
 - Treating ewes at lambing (*Haemonchus contortus*)
 - Treating during draught period
 - Treat and move to clean pasture ('Dose and move', 'Drench-and-shift') ^{NS}

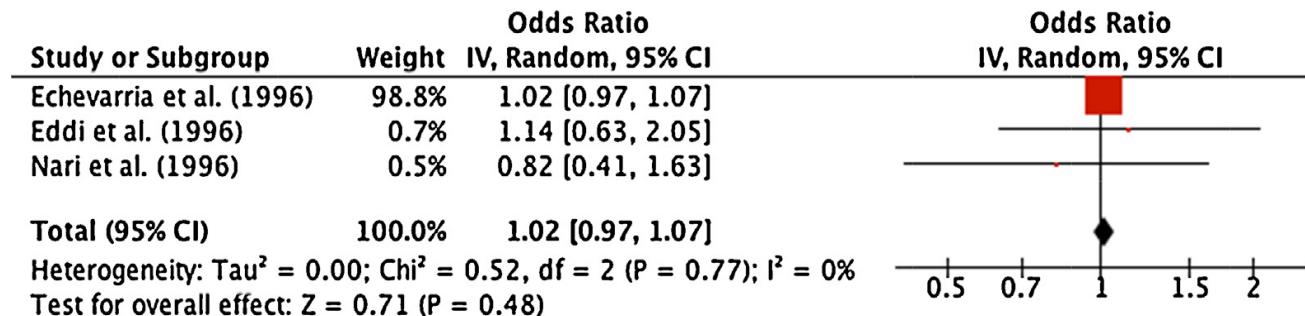


Factors promoting anthelmintic resistance

- Mixed-species grazing? ^{NS}
 - Protective or risk factor?



- Flock/herd size? ^{NS}



Sustainable use of anthelmintics

- Avoid risk factors mentioned above
 - SCOPS (www.scops.org.uk)
- Reduced number of treatments ('targeted treatments')
 - Monitoring infection levels (FEC, pepsinogen, antibodies)
 - Monitoring production (weight, milk)
- Treatment of individual animals ('targeted strategic treatments')
 - Monitoring infection levels (FEC, milk antibodies)
 - Monitoring production (weight, milk)
- Combination anthelmintics?
- Development of alternative control methods
 - Vaccines
 - Anthelmintic plant components (condensed tannins)
- Development of economic farm system models with integrated worm control (e.g. ParaCalc®)

Solution = integrated parasite control

