Towards sustainable gut worm and fluke control

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BE VERY CAREFUL THE
CAN OF WORMS YOU OPEN
ONCE THEY'RE OUT, IT'S ALMOST
IMPOSSIBLE TO GET THEM BACK IN
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Gastrointestinal nematodes (GIN) of cattle and their impact

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Which worms are we talking about here?

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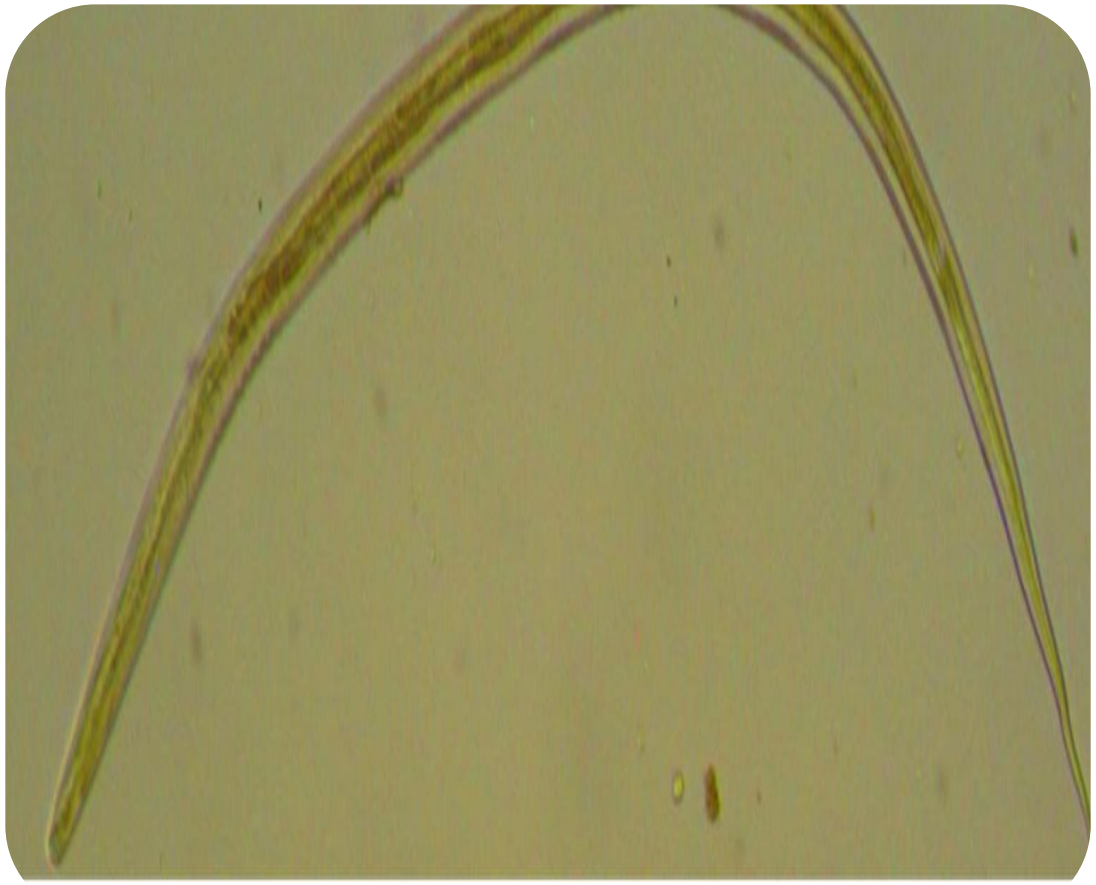
Ostertagia

- *Ostertagia ostertagi*
  - Small, slender red-brown worm
  - Inhabits the abomasum
  - The most pathogenic GIN of cattle
  - Females lay an average of 350 eggs per day[1]
  - Prepatent period is 21 days
  - Development from the egg to the infective stage takes under 7 days in optimal conditions
  - Approx 4% of developing larvae undergo hypobiosis (arrested development) – risk of type 2 disease[1]



. Verschave et al 2014 Int J Parasitol 44: 1091-1104

Cooperia

- *Cooperia oncophora*
  - Small reddish worms up to 10mm long
  - Inhabits the small intestine
  - The most prevalent parasite of cattle
  - Females very fecund, laying an average of 3000 eggs/day[2]
  - Pre-patent period is 15-18 days
  - Development from egg to infective stage takes 4 days in optimal conditions

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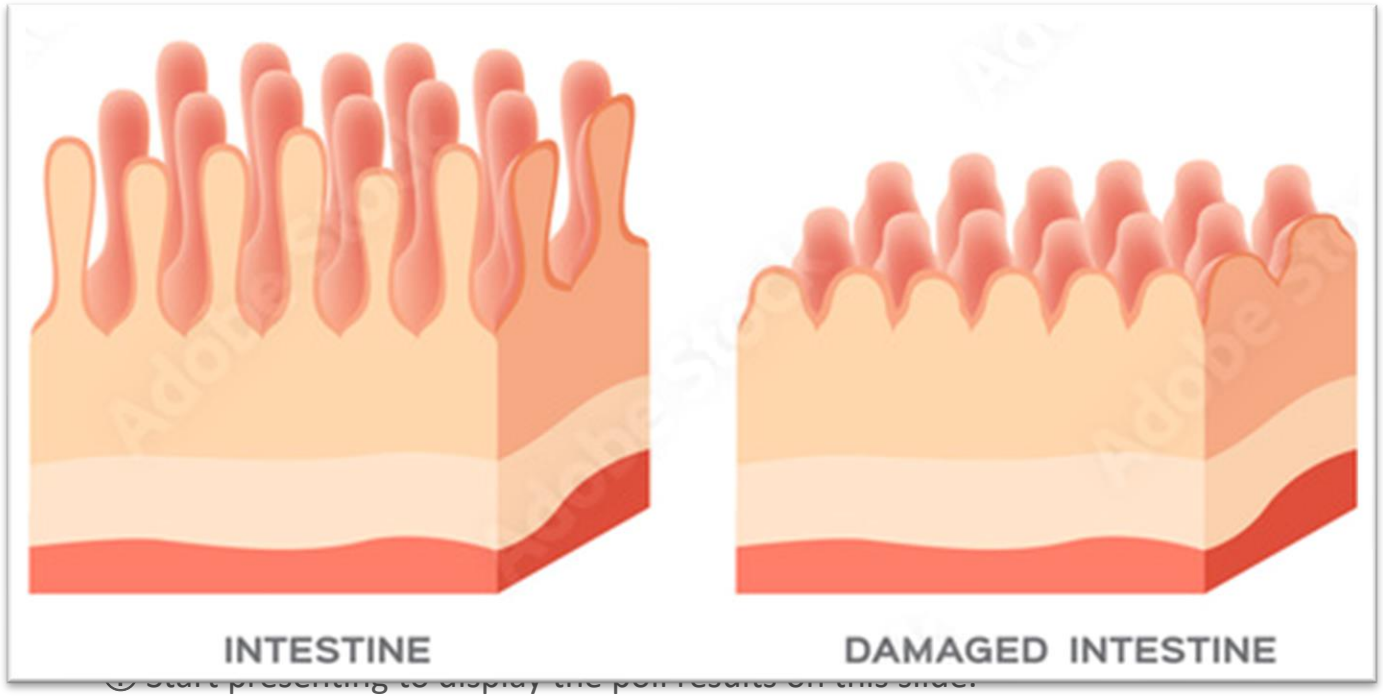
What damage can these worms do?



Adverse effects of a GIN burden

DIRECT

- Worms utilise host nutrients
- Tissue damage

INDIRECT

- Inflammation
- Immune response uses hosts protein

REDUCED FEED INTAKE

- Resulting from parasite-induced hormonal changes

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What is the infective stage of Ostertagia and Cooperia?

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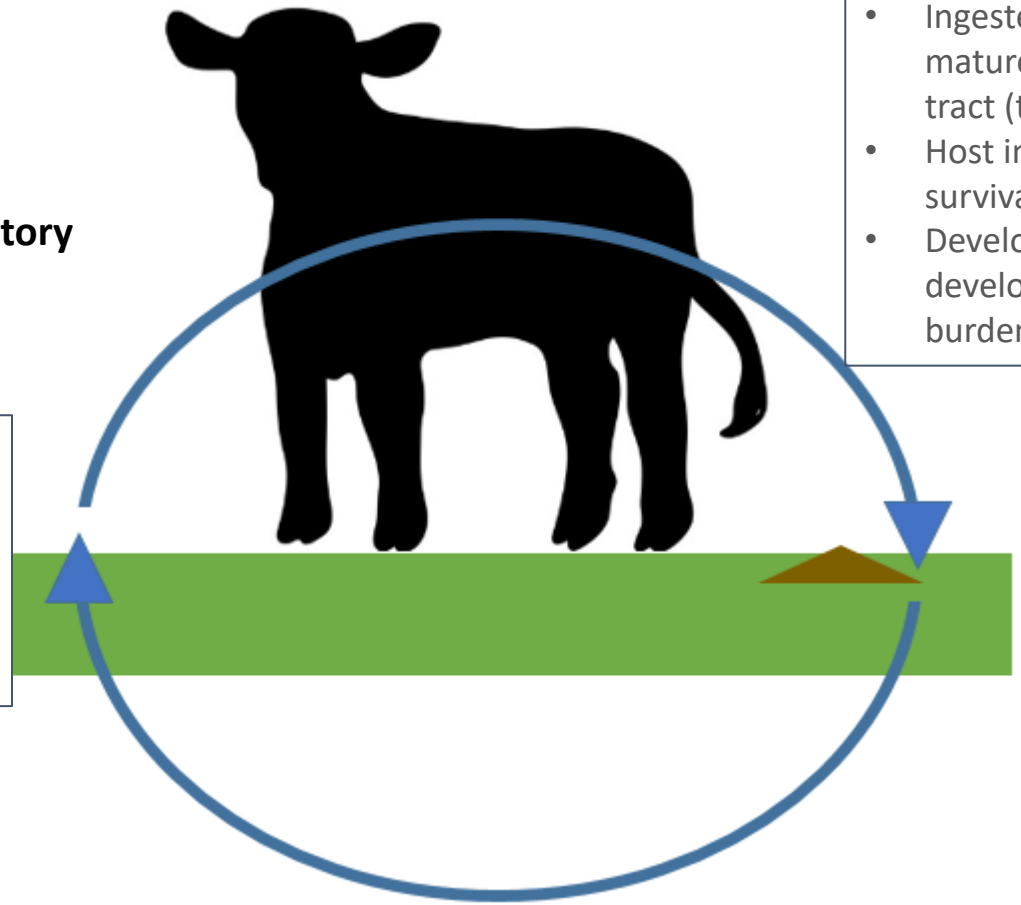
Lifecycle of cattle gastrointestinal nematodes (GIN)

Direct, non-migratory



Within the host:

- Ingested L3 larvae develop to sexually mature adults worms in the gastrointestinal tract (the pre-patent period)
- Host immunity inhibits development, survival and fecundity
- Developing larvae (EL4) can arrest their development – immunity, climate & worm burden are influencing factors

Free-living stages on pasture:

- Eggs hatch and develop to the L3 larvae the dung pat
- Warm (20-30^{o}C) wet weather favours development and survival
- No development below 5^{O}C

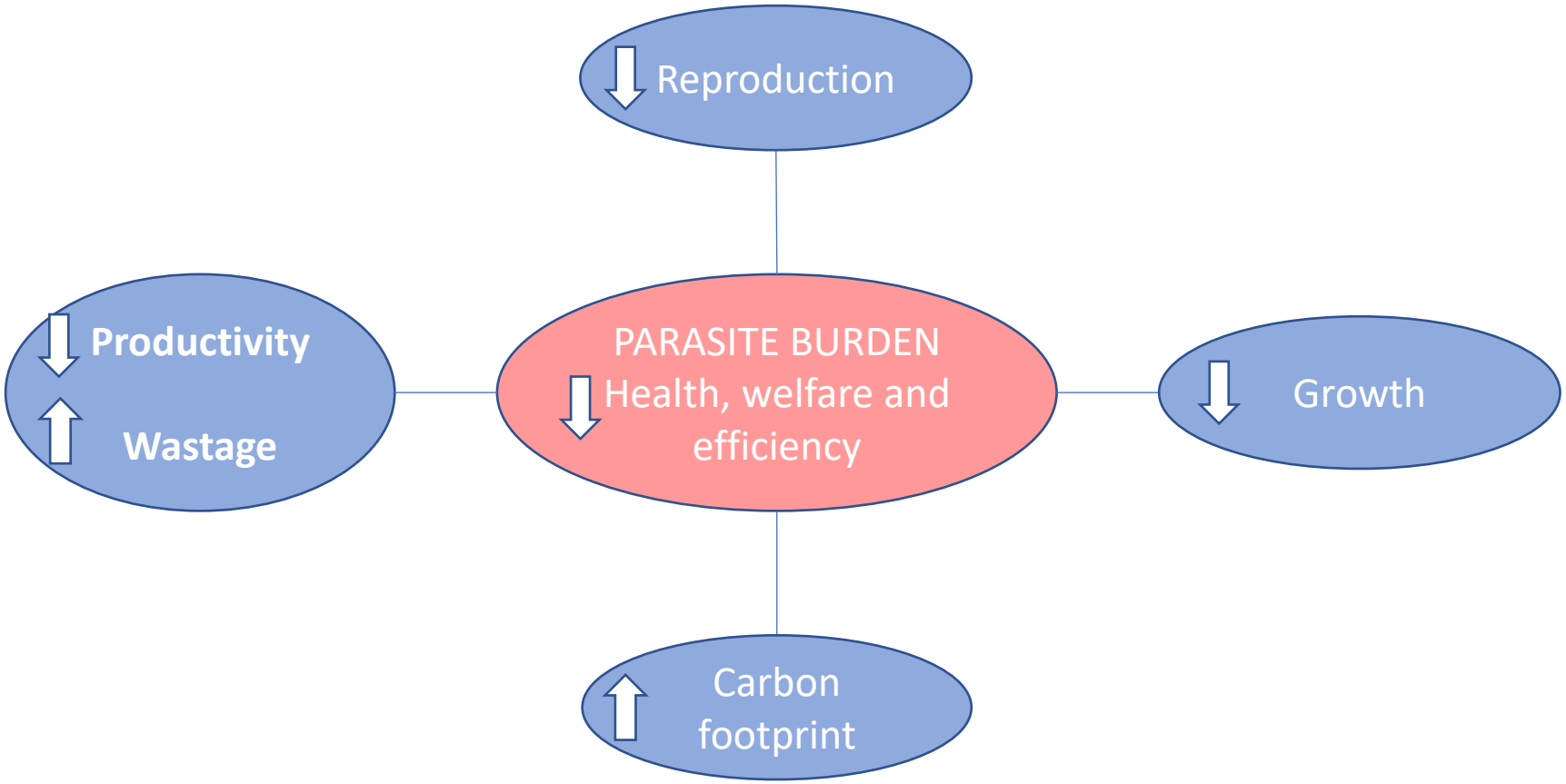
Risk of type 1 disease at pasture and type 2 disease – winter scours – if mass emergence during housing period

The outcome of a GIN burden at grass

Mixed worm infections within the abomasum and intestine
Risk is proportional to the pasture challenge

Clinical disease:
Typically occurs in non-immune youngstock
Watery diarrhoea; poor coat; anorexia; loss of body condition
Subclinical disease:
Impacts on growth & productivity without overt signs
Occurs in cattle of all ages

Why control GIN?



Developing sustainable control strategies

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Can you think of any control strategies other than anthelmintic treatments?

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Best Practice Worm Control

Best practices aim to protect herd health and productivity, whilst maintaining a long-term sustainable balance in parasite control on farms. When developing a best practice worming programme one must take into consideration the characteristics of the animal, the parasites, the environment, and the parasiticide.

There are three underlying principles:

✓the right pasture/grazing management

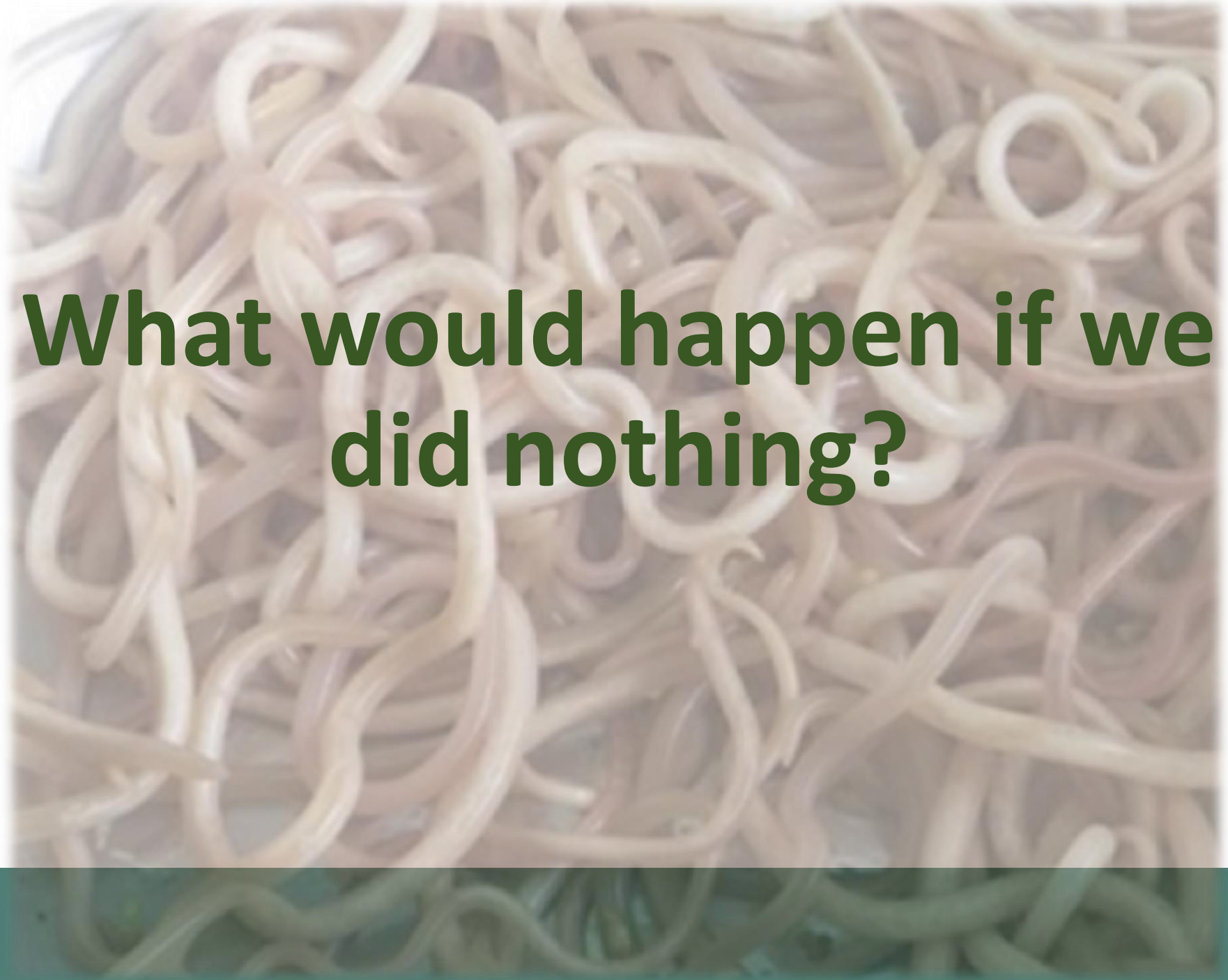
✓the optimisation of livestock immunity

✓the correct use of anti-parasitics

Pasture and Grazing Management

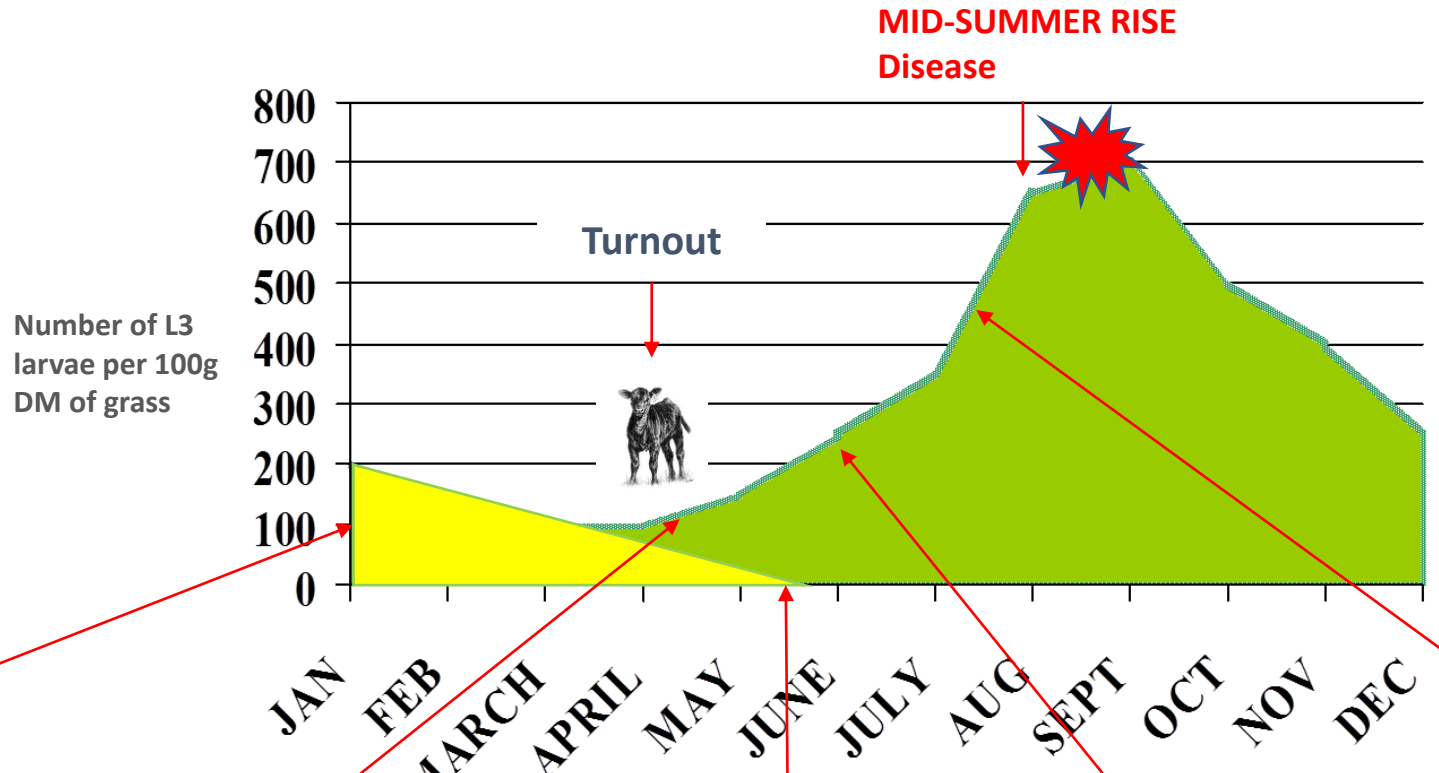
Pasture risk management

- An ongoing process, using grazing history and farm data and parasite forecasts to review and categorise pasture risk
- Allows planned grazing – prioritisation of ‘clean’, low risk pasture for high risk groups
- Consider the impact of climatic conditions and grazing practices on pasture challenge and worm burden



What would happen if we did nothing?

What would happen if we did nothing?



Overwintered L3 larvae survive on the pasture from the previous year

Young, non-immune cattle initially become infected without showing signs of scouring

Overwintered L3 larvae on the pasture will die off by mid-June

Eggs shed onto pasture result in increased larval challenge

Cycles of reinfection and optimal climatic conditions lead to rapid increase in pasture contamination

Strategic control

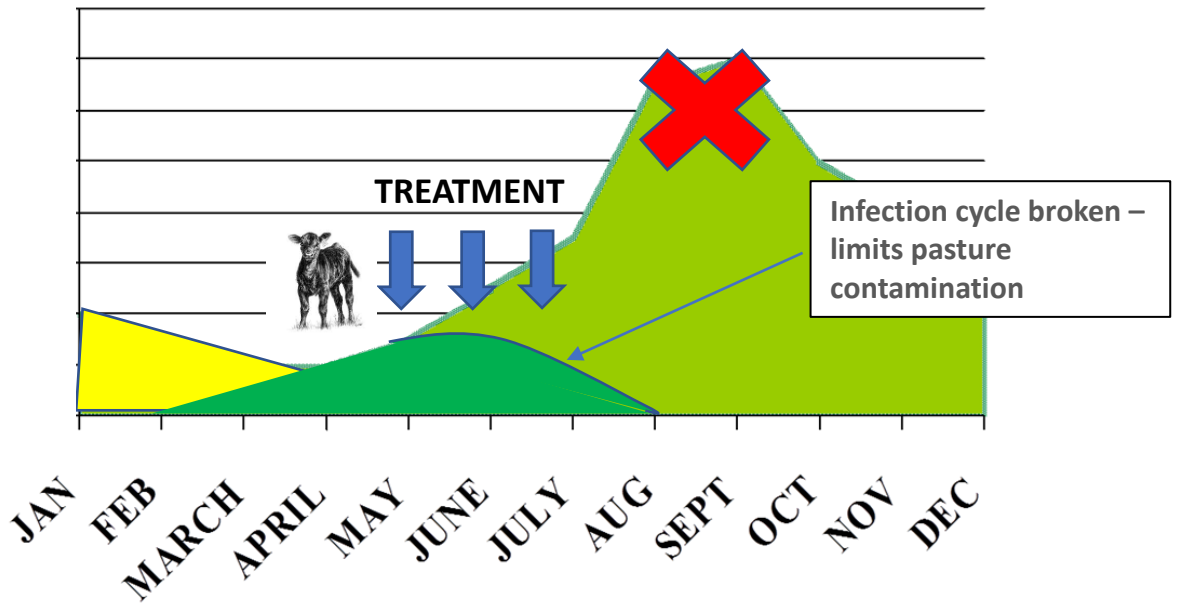
Timed treatment of groups of susceptible animals to prevent heavy worm burdens, reduce pasture contamination & disease

PROS

- Proven, reliable approach
- Season-long parasite control

CONS

- Requires repeated whole group treatment
- Preventative – treatments may not be needed



Can we adapt our approach to reduce reliance on anthelmintics and incorporate farm-level risk assessment to target treatments?

- Strategic worming with additional risk assessment to refine timing.
- Targeted selective treatment

Assessing Animal Risk and Optimising Immunity

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Why is Immunity important?

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Why is establishing immunity important?

The development of immunity is progressive.
When established, it helps in:*

- ✓ Reduction in size of the adult roundworm parasites
- ✓ Reduction in egg laying of female roundworm
- ✓ Reduction of inhibition of fourth stage larvae
- ✓ Reduction in the establishment of the larvae
- ✓ Expulsion of the adult worms

*Claerebout, E. et al. The immune response and the evaluation of acquired immunity against gastrointestinal nematodes in cattle: a review. Parasitology, 2000

Factors affecting development of immunity

GENETIC VARIATION
Three types of calf recognised[1]

SEX

HOST

NUTRITION

AGE[2]

IMMUNITY

DURATION AND LEVEL OF EXPOSURE

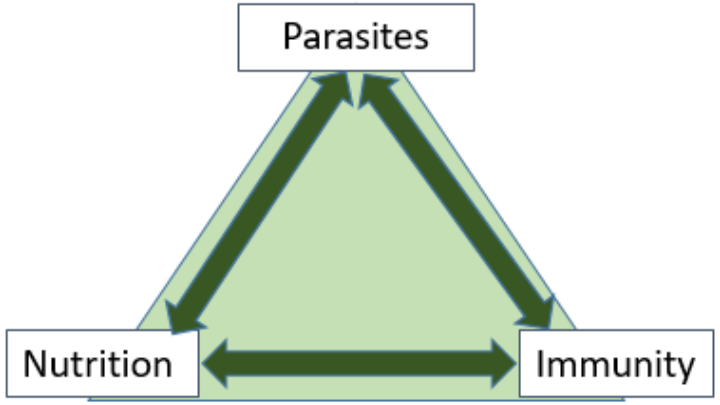
PARASITE SPECIES
C. oncophora< O. ostertagi

ANTHELMINTIC TREATMENTS

CLIMATIC CONDITIONS

GRAZING PRACTICES

FARMING SYSTEM
Suckled calves Vs weaned calves



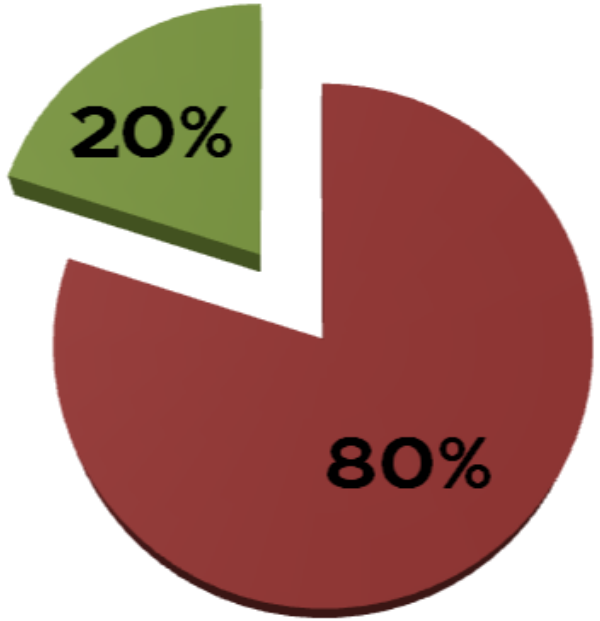
1. Gasbarre et al 2001 Vet Parasitol 98; 51-64
2. Kloosterman ey al 1991 39: 101-113

Animal risk assessment

Risk Factor	High	Medium	Low
Age/Grazing Season*	< 1 year First grazing season	1-2 years Second grazing season	>2 years Adult
Age at Turnout (Weaned calves)	< 6 months	6-8 months	>8 months
Weight gain 2 months post turnout (<2 yo)	<0.7kg/day	0.7-0.8kg/day	>0.8kg/day
Faecal Egg Count (epg) Weaned calves 2m post to	>200epg	50-200epg	<50epg
Bulk Milk O.ostertagi AB OD Ratio	>0.8	0.5-0.8	<0.5

*Suckled calves with their dams are low risk

Have you heard of the 80:20 Rule?



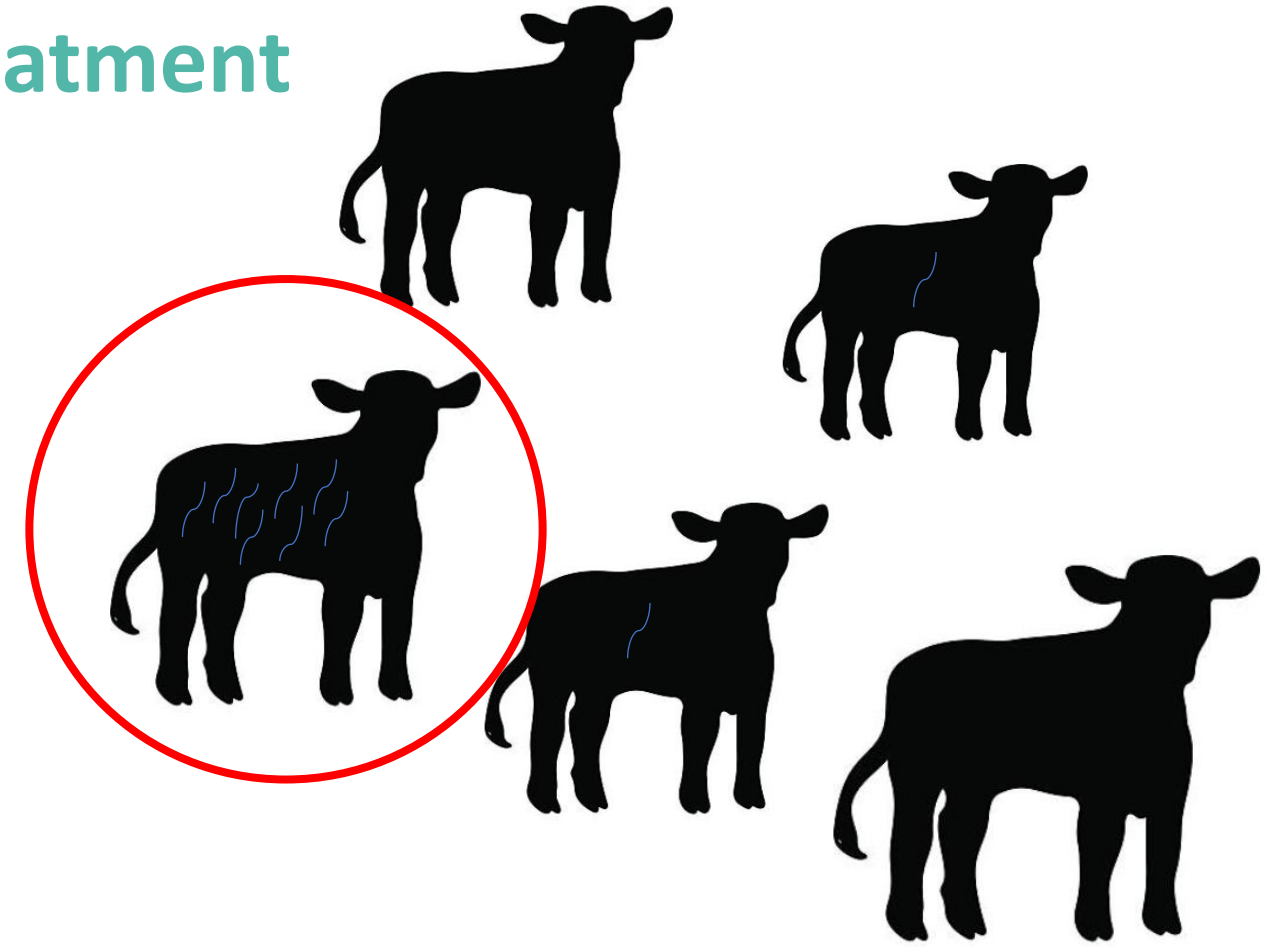
Assessing the risk to target treatment

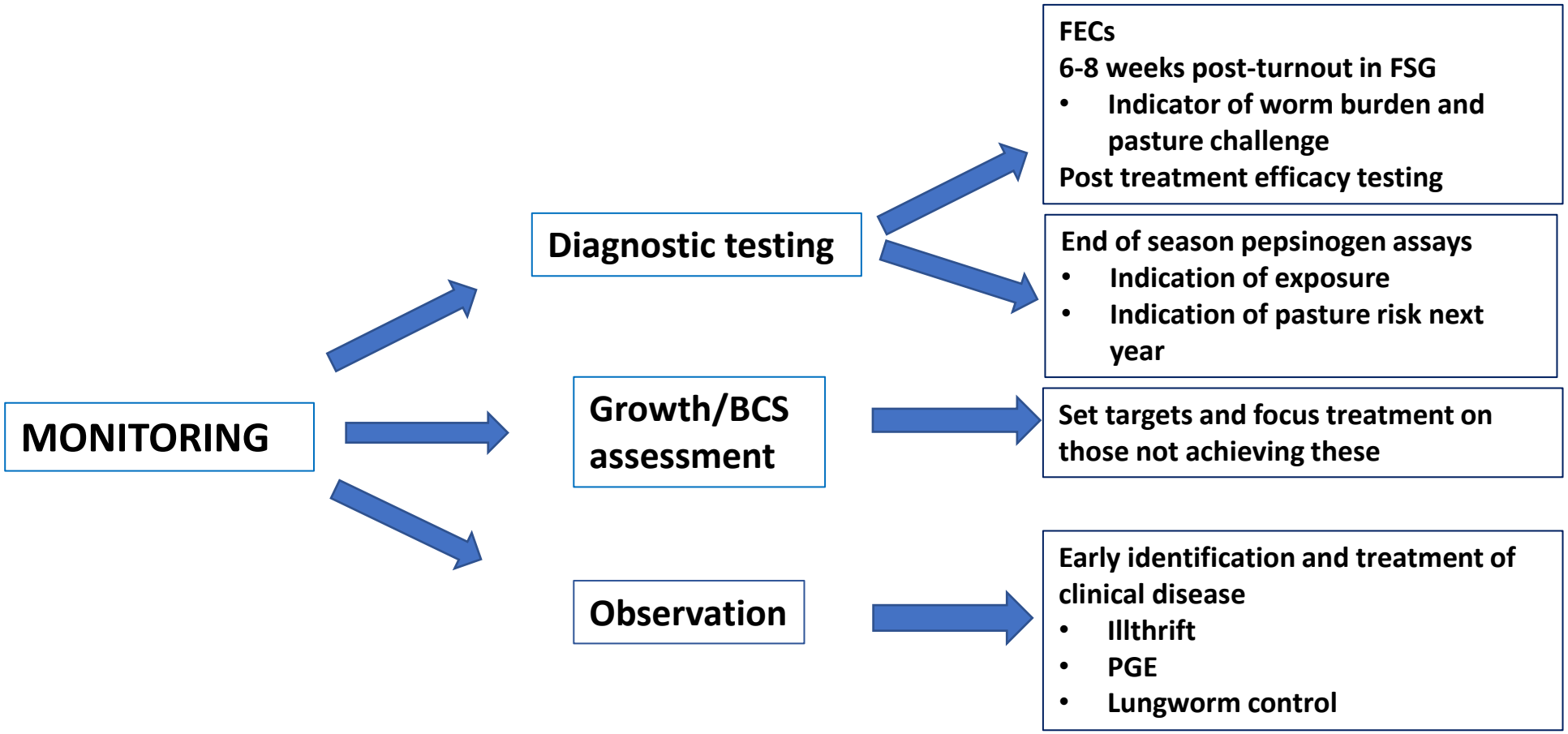
Overdispersion – the 80:20 rule

- GINs tend to be unevenly distributed among hosts, with few of the animals in a group carrying more of the parasites.

This distribution can be related to variation in:

- host exposure e.g. different grazing behaviors
- parasite establishment or survival eg resistance/resilience of the host




MONITORING
Diagnostic testing
FECs
6-8 weeks post-turnout in FSG
• Indicator of worm burden and pasture challenge
Post treatment efficacy testing
End of season pepsinogen assays
• Indication of exposure
• Indication of pasture risk next year
Growth/BCS assessment
Set targets and focus treatment on those not achieving these
Observation
Early identification and treatment of clinical disease
• Illthrift
• PGE
• Lungworm control

Using Appropriate Treatment

Anthelmintic resistance – a driver for change?

- Why?

Class	First released	First resistance
1-BZ	1961	1964
2-LV	1970	1979
3-ML	1981	1988

- How?

Reduce reliance on anthelmintics through integrated parasite control

Avoid risky practices:

- Frequent treatment
- Blanket treatment
- Whole group treat & move strategies

Implement a quarantine programme

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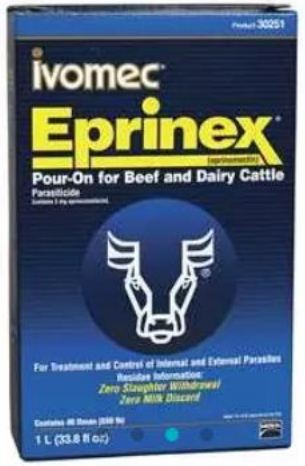
What do you and your customers think is important when selecting and administering an anthelmintic?



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Product selection and administration

Use the most appropriate product for the animals and the time of year – active ingredient, spectrum, persistency, route of administration, WD period

Administer it correctly - under-dosing compromises treatment efficacy and can select for resistance

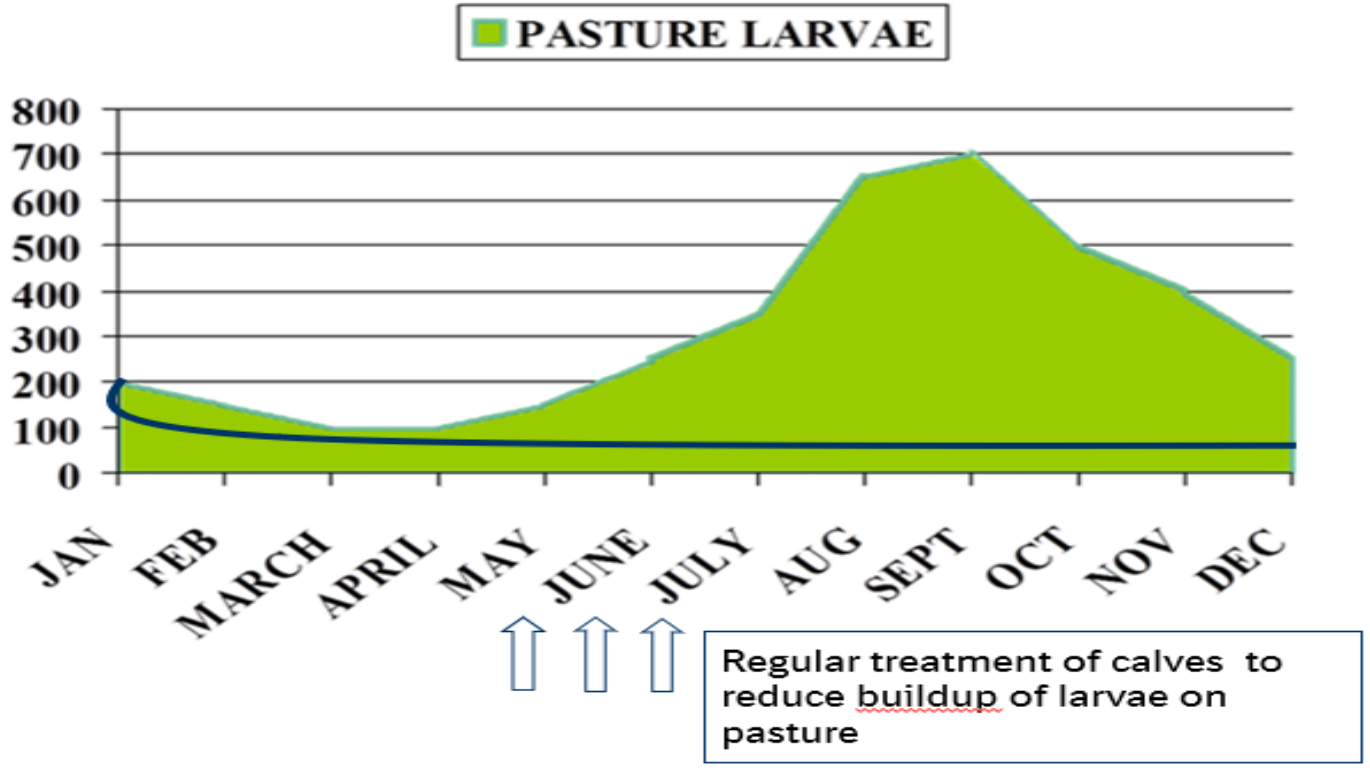
- Use an appropriate, well maintained and calibrated applicator
- Ensure that weight is accurately determined and the dose calculated correctly

Adopt the right treatment approach based on your needs

- **Strategic treatment** – plan the treatment of groups of animals based on previous experience/history to minimise worm burden, pasture contamination and disease (can be part of refugia strategy).
- **Targeted treatment (TT)** – treatment of groups of animals based on assessment of current parasite risk (e.g. treating at first grazing season when FEC indicates it) (can be part of refugia strategy).
- **Targeted selective treatment (TST)** – treatment of individuals or subgroups based on an assessment of current parasite risk (e.g. treating only poorer doing calves). Often discussed is leaving a small proportion of animals untreated (can be part of refugia strategy).
- **Therapeutic treatment** – treatment in response to clinical disease.

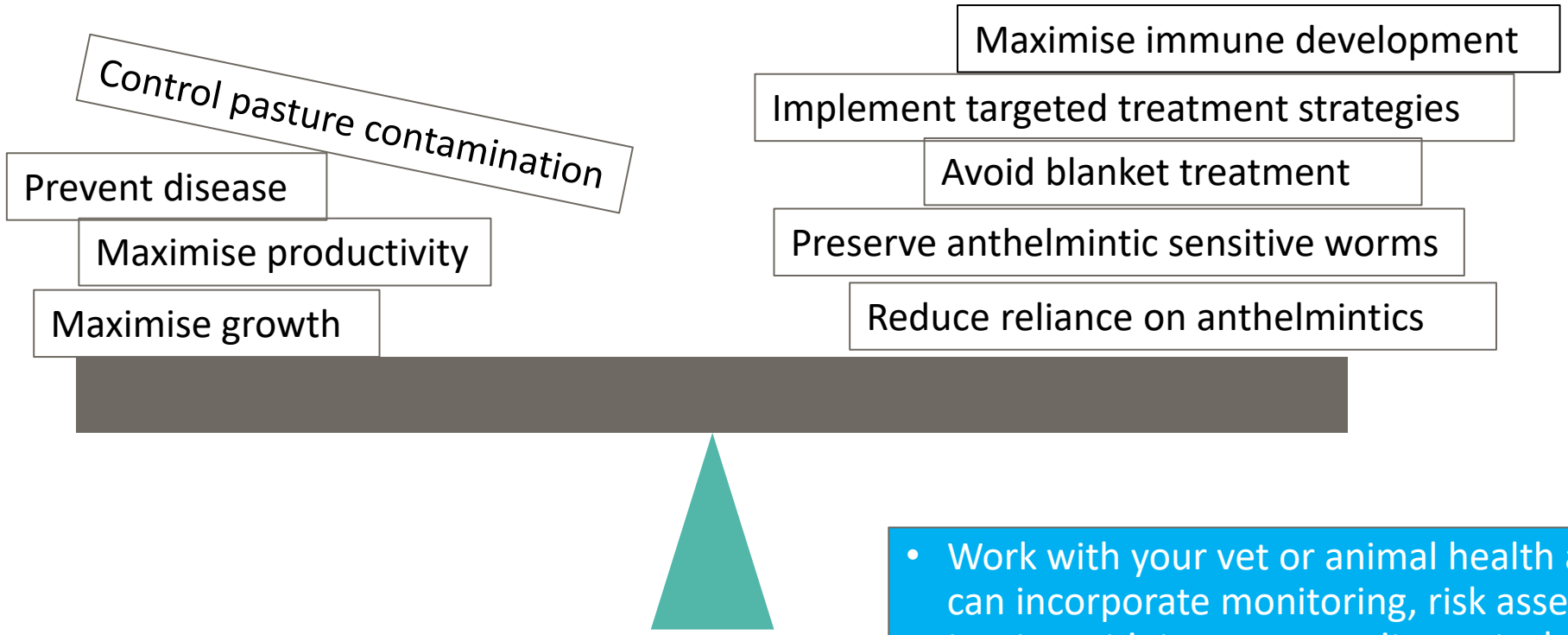
Broad Spectrum Anthelmintics

Group 1 (BZ)	Group 2 (LV)	Group 3 (ML)
Benzimidazoles	Levamisoles	Macrocyclic-lactones
White drenches	Yellow drenches	Clear drenches



The right product at the right time to the right animals, which are then turned to the right grazing!

Aligning the objectives for sustainable control



- Work with your vet or animal health advisor to determine how you can incorporate monitoring, risk assessment and targeted treatment into your parasite control plan
- Small changes can have a big impact on the long term sustainability of parasite control – where will you start?

Fluke

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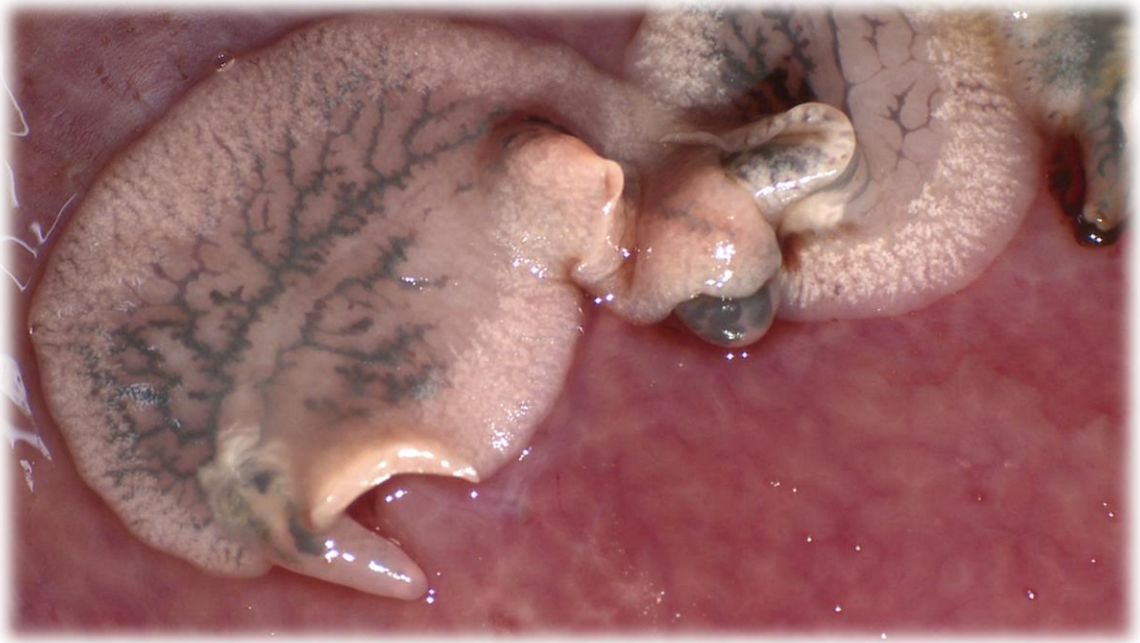
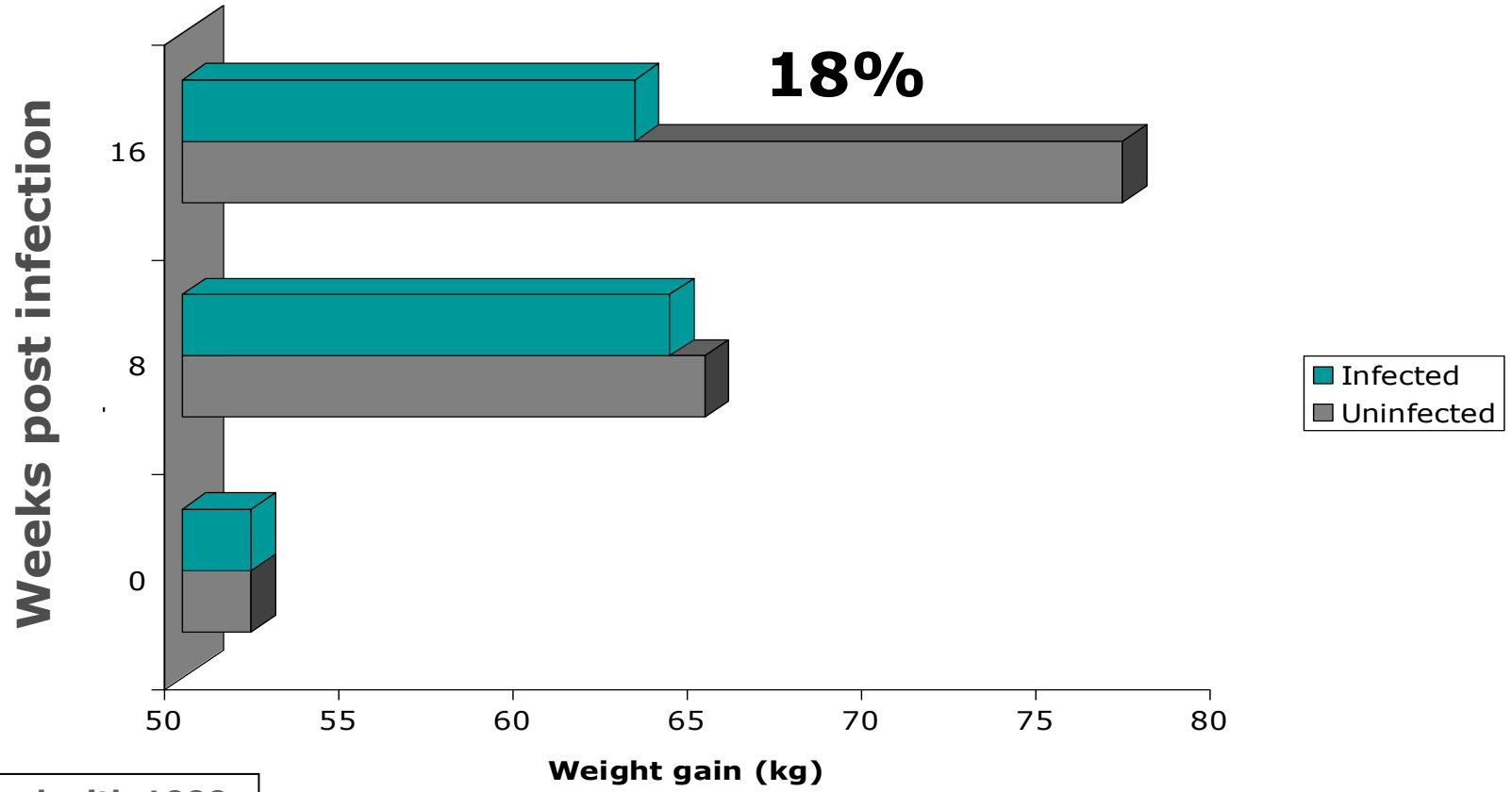
Liver fluke in the UK

- *Fasciola hepatica*
- Can infect all grazing livestock with significant impact on health, welfare and productivity
- Herd prevalence across UK
  - 88% in Wales[1]
  - 77.5% in England[1]
  - 73.4% in Scotland[1]
  - 61-65% in Northern Ireland[2]
- A significant cost to the livestock industry:
  - Annual direct cost approx. €120M to UK producers[3]



1. Howell et al., (2015) Epidemiology and impact of *Fasciola hepatica* in high-yielding dairy herds. Prev Vet Med 121: 41-48
2. Byrne et al ., (2016) Liver fluke infection in cattle in Northern Ireland: a large-scale epidemiological investigation utilising surveillance data. Parasites & Vectors 9: 209-222
3. Charlier et al (2020) Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. Prev Vet Med 102: 105103

Impact of liver fluke on weight gain



Infected with 1000 metacercariae

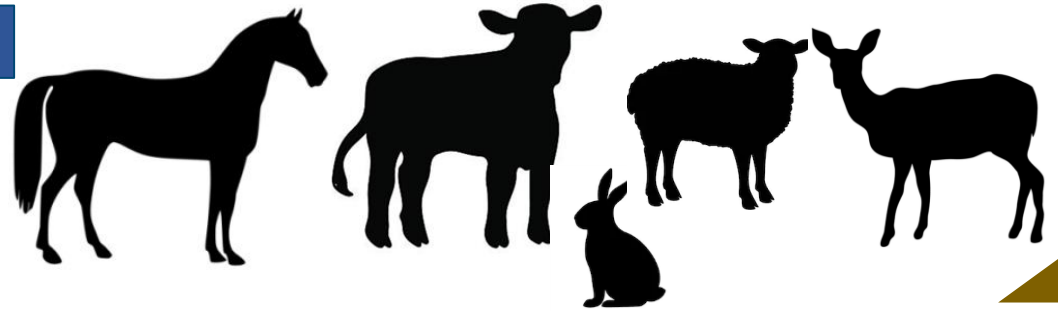
Adult fluke have the greatest impact on cattle weight gain

Reid *et al*, Vet Rec 1972

Fasciola hepatica – The Lifecycle

Excysts, penetrates gut and migrates through the peritoneal cavity to liver, burrowing through the tissue to the bile ducts. Develops to egg-laying adult

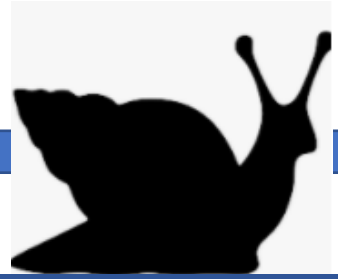
Metacercaria ingested from pasture



Eggs shed in faeces of infected host from 10-12 weeks post infection (prepatent period)

Minimum 4-6 months for completion of cycle

Shedding of cercariae onto pasture commences after 4-7 weeks



Infection of *Galba truncatula* intermediate host – clonal amplification and maturation

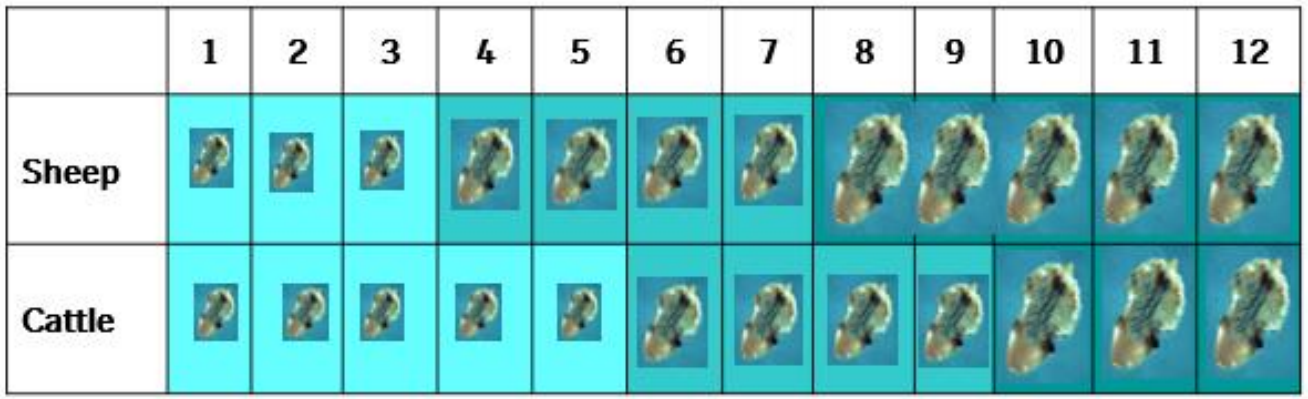
Embryonation and hatching of egg to release miracidium – 8-12 days

Maturation within the definitive host

- Pre-patent period of 10-12 weeks
  - Immature fluke penetrate liver after 1 week
  - Immature/Late Immature/Adult

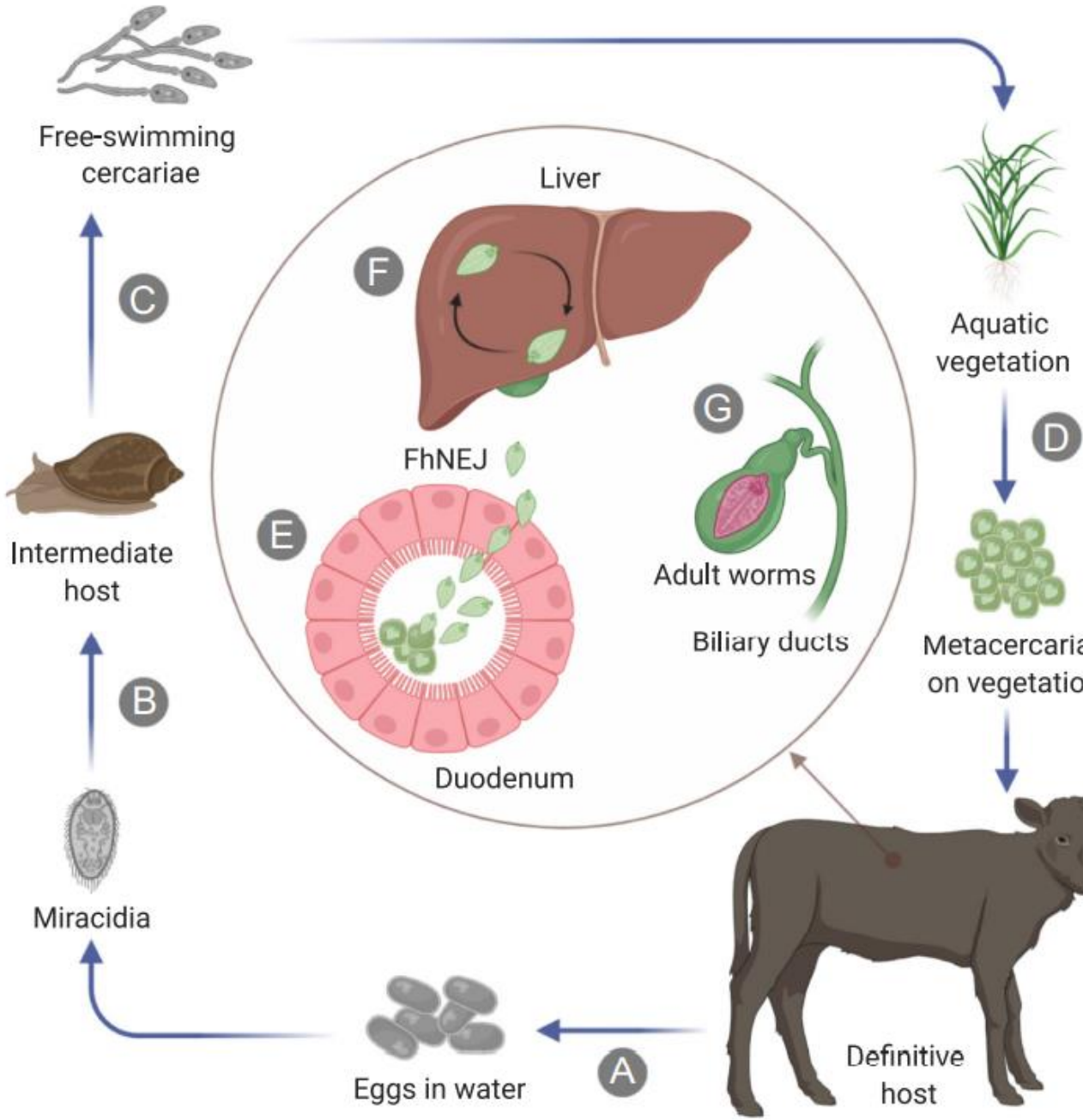
- High fecundity – up to 25,000 eggs per day[1]

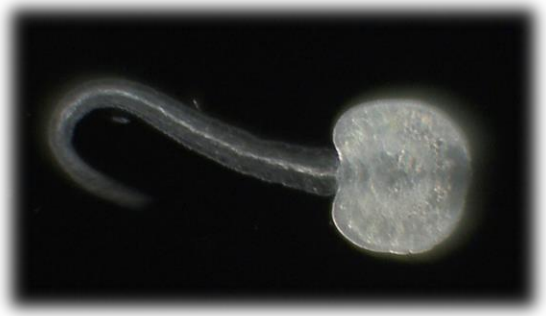
- Hermaphtoditic - self-fertilisation can take place, but evidence that this is rare in the field (<2% of fertilisation events[2])



1. Walker et al., (2006) Stage-specific differences in fecundity over the life-cycle of two characterized isolated of the liver , *Fasciola hepatica.* Parasitology 133: 209-216
2. Beesley et al., (2017) *Fasciola hepatica* demonstrates high levels of genetic diversity, a lack of population structure and high gene flow:possible implications for drug resistance. Int J Parasitol 47:11-20

Development [illegible] *ba truncatula*





a – infection with a
of >3000

- metacercariae

1. Hodgkinson e
varia

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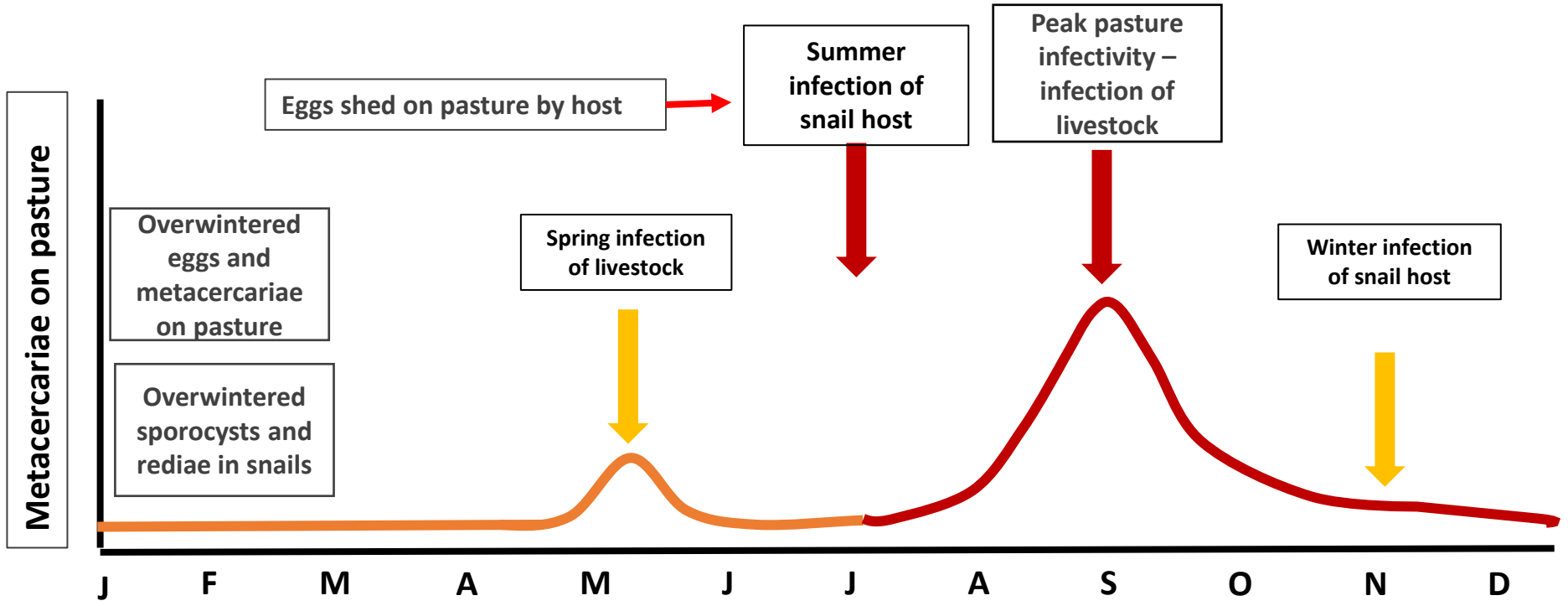
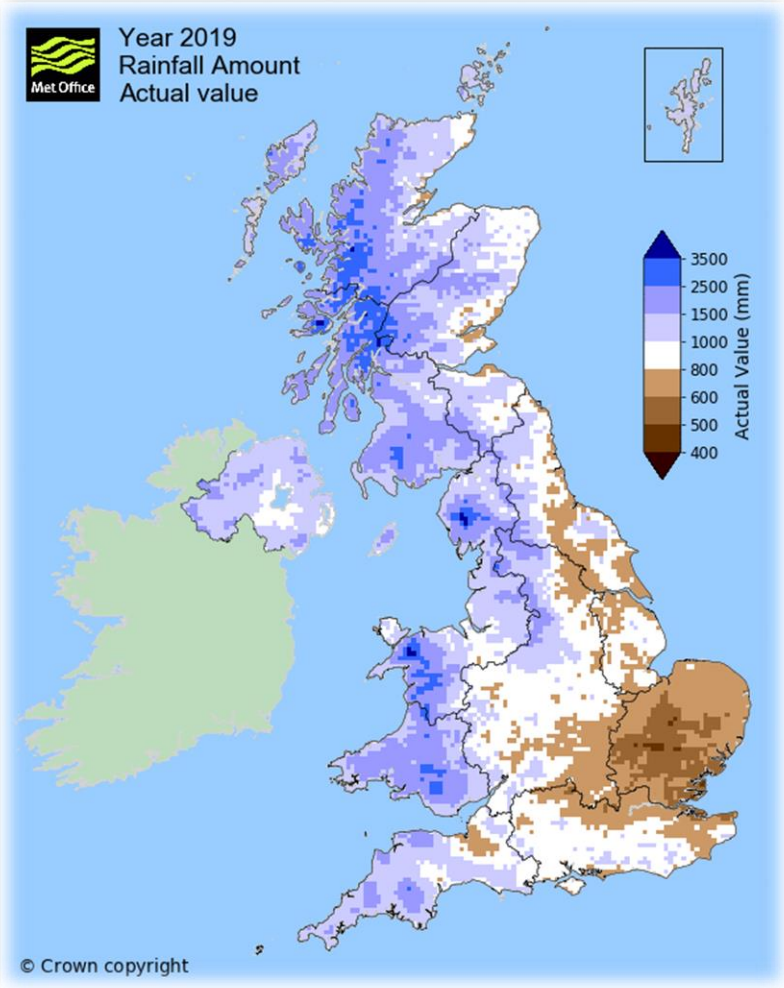
Seasonality of pasture challenge in the UK

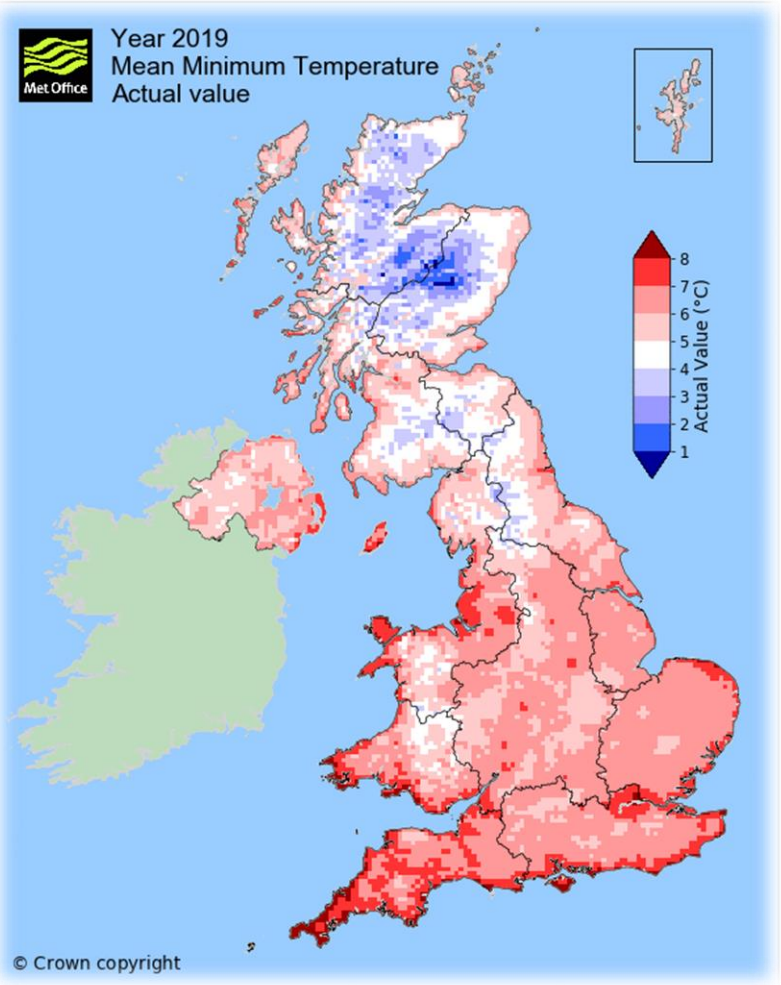


Seasonal pasture risk is rainfall & temperature dependent

- Require a minimum of 3 months favourable (moisture and temperature) climatic conditions for completion of fluke development within *G. truncatula*
- Longer periods of favourable conditions result loss of defined risk period and prolongation of challenge

The UK fluke landscape





https://www.metoffice.gov.uk/research/climate/maps-and-data/uk-actual-and-anomaly-maps

Clinical Effects - Acute Fasciolosis

- Typically seen in sheep in late summer/autumn
- 6-8 weeks after ingestion of high numbers of metacercariae (>1000)
- Clinical signs include, anaemia, weightloss and sudden death

THE ROT IN SHEEP, OR THE LIFE-HISTORY OF THE LIVER-FLUKE

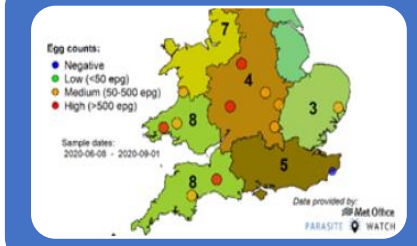
THE winter of 1879-80 was marked by a widely-spread outbreak of the liver-rot amongst our sheep. The losses during that winter were estimated at three million sheep, or about one-tenth of the total number in the United Kingdom, and during the following winter the losses were equally severe. It had long been known that the disease was due to the presence in large numbers of a parasite called the liver-fluke (*Fasciola hepatica*) in the liver of the affected animals, and that the parasite invaded sheep or sometimes other animals allowed to feed on wet pastures, and especially on flooded ground. But

Thomas. Nature, October 19 1882 607

Chronic Fasciolosis

- Seen in cattle and sheep
- 4+ months after ingestion of moderate numbers of metacercariae
- Clinical signs include, anaemia, weightloss, submandibular oedema, and liver damage (fibrosis)
- Sub-clinical disease results in reduced milk yield, poor fertility, poor growth rates

Principles of fluke control



Quantify seasonal risk

- Regional fluke forecasts
- Monitoring e.g. sentinel testing to determine farm level risk

Assess and manage exposure

- Identify snail habitats on farm and reduce if possible
- Avoid high risk pasture at high risk periods
- Take measures to reduce egg shed on to pasture

Strategic/Targeted treatment at key risk periods

- Acute disease in sheep
- Clinical and subclinical chronic fluke infections
- Quarantine protocols

Key treatment considerations

The parasite

- Impact
- Resistance
- Stages present

Risk

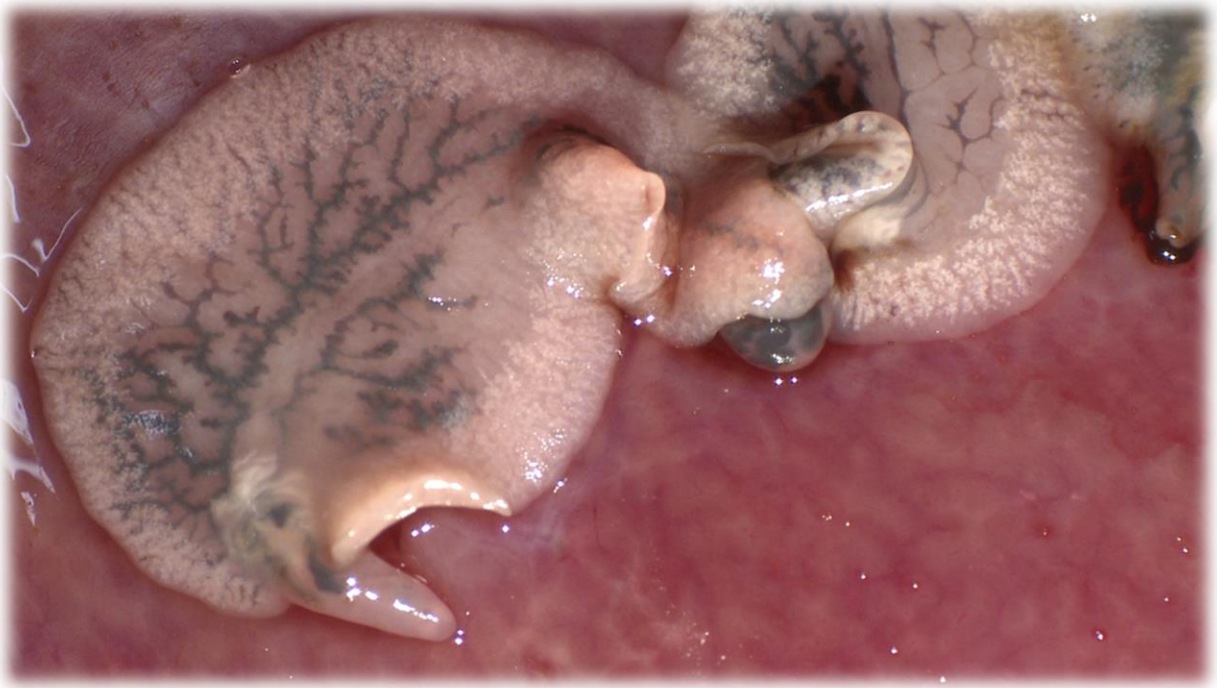
- Farm history
- Seasonal forecast
- Diagnostic test results

Product features

- Spectrum
- Meat/**milk** withhold
- Mode of administration

Practicality

- Farming system
- Handling facilities



UK treatment options – 6 actives

Active (and formulation)	Stage of liver fluke			Cattle	Sheep
	Immature	Late immature	Adult		
Triclabendazole (Oral drench)	+	+	+	+	+
Triclabendazole (Pour-on)	-	+	+	+	_
Nitroxynil (Injection)	-	+	+	+	+
Closantel (Injection)	-	+	+	+	+
Closantel (Pour-on)	-	+	+	+	_
Closantel (Oral drench)	-	+	+	-	+
Clorsulon (Injection)	-	-	+	+	_
Oxyclozanide (Oral drench)	-	-	+	+	+
Albendazole (oral drench)	-	-	+	+	+

List includes single active and combination products
Refer to SPC for specific product information

UK treatment options – 6 actives

Active (and formulation)	Stage of liver fluke			Cattle (Meat WD)	Sheep (Meat WD)	Dairy use
	Immature	Late immature	Adult			
Triclabendazole (Oral drench)	+	+	+	+ (52d)	+ (56d)	(45d +48hrs 50d)
Triclabendazole (Pour-on)	-	+	+	+ (143d)	–	
Nitroxynil (Injection)	-	+	+	+ (60d)	+ (49d/60d)	
Closantel (Injection)	-	+	+	+ (49d)	+ (28d)	
Closantel (Pour-on)	-	+	+	+ (58d)	–	
Closantel (Oral drench)	-	+	+	-	+ (42d)	
Clorsulon (Injection)	-	-	+	+ (66d)	–	(60d)
Oxyclozanide (Oral drench)	-	-	+	+ (13d)	+ (14d)	(108 hrs)
Albendazole (oral drench)	-	-	+	+ (14d)	+ (3-5d)	(72hrs)

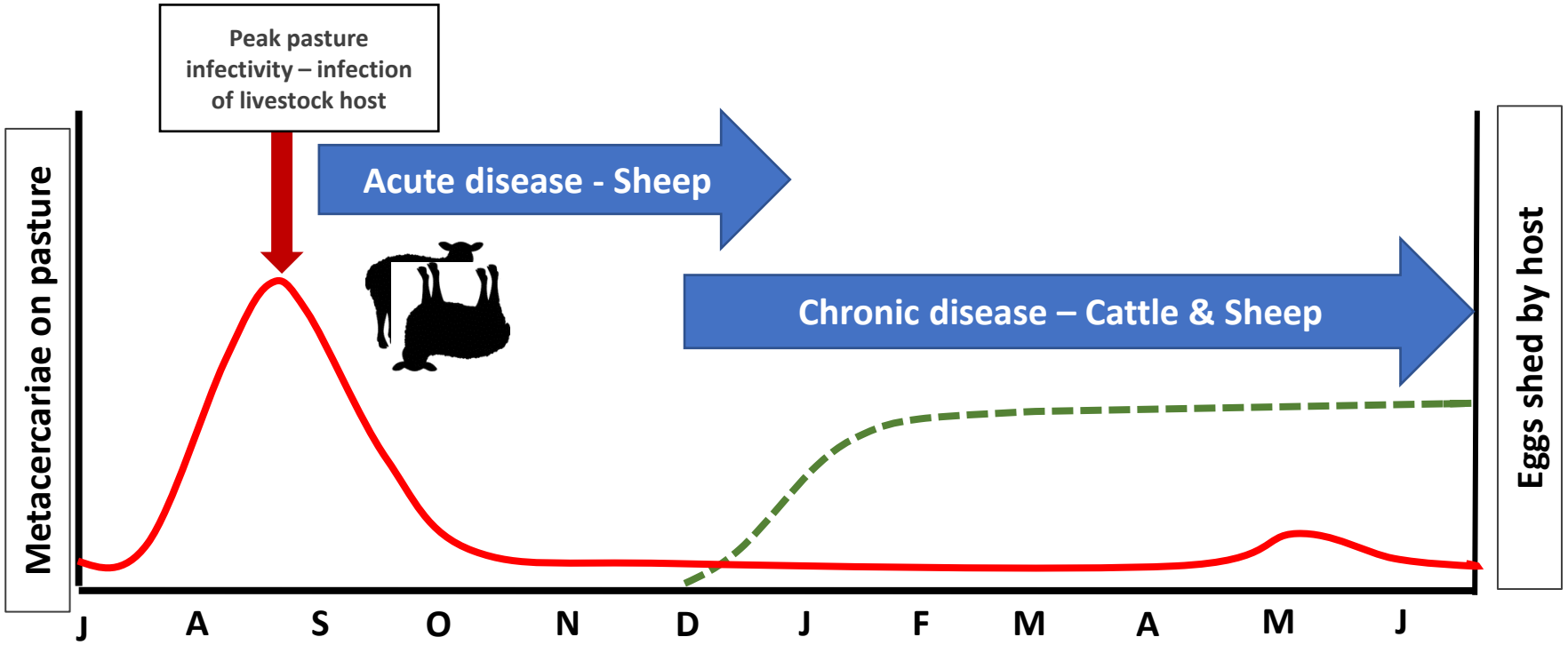
List includes single active and combination products
Withdrawal periods relate to reference products -
Refer to SPC for specific product information

Flukicide resistance

- Flukicide resistance is a growing concern
- Resistance to triclabendazole in fluke carried by both sheep and cattle
  - 21/26 sheep farms positive on FECRT
  - Reductions ranging from 0%-89%[1]
- Triclabendazole is only active available to treat acute fasciolosis in sheep
- Risk of emergence of resistance to other actives
  - Cross resistance?

1. Kamaludeen et al., (2019) Lack of efficacy of triclabendazole against Fasciola hepatica is present on sheep farms in three regions of England, and Wales. Vet Rec doi:10.1136/vr.105209

General seasonality of fluke infection and disease



Use seasonal forecasts and monitoring data to implement treatment targeted at:

- Preventing acute fasciolosis – Sheep (TBZ)
- Preventing clinical and subclinical chronic disease
- Breaking the infection cycle by preventing egg shed onto pasture

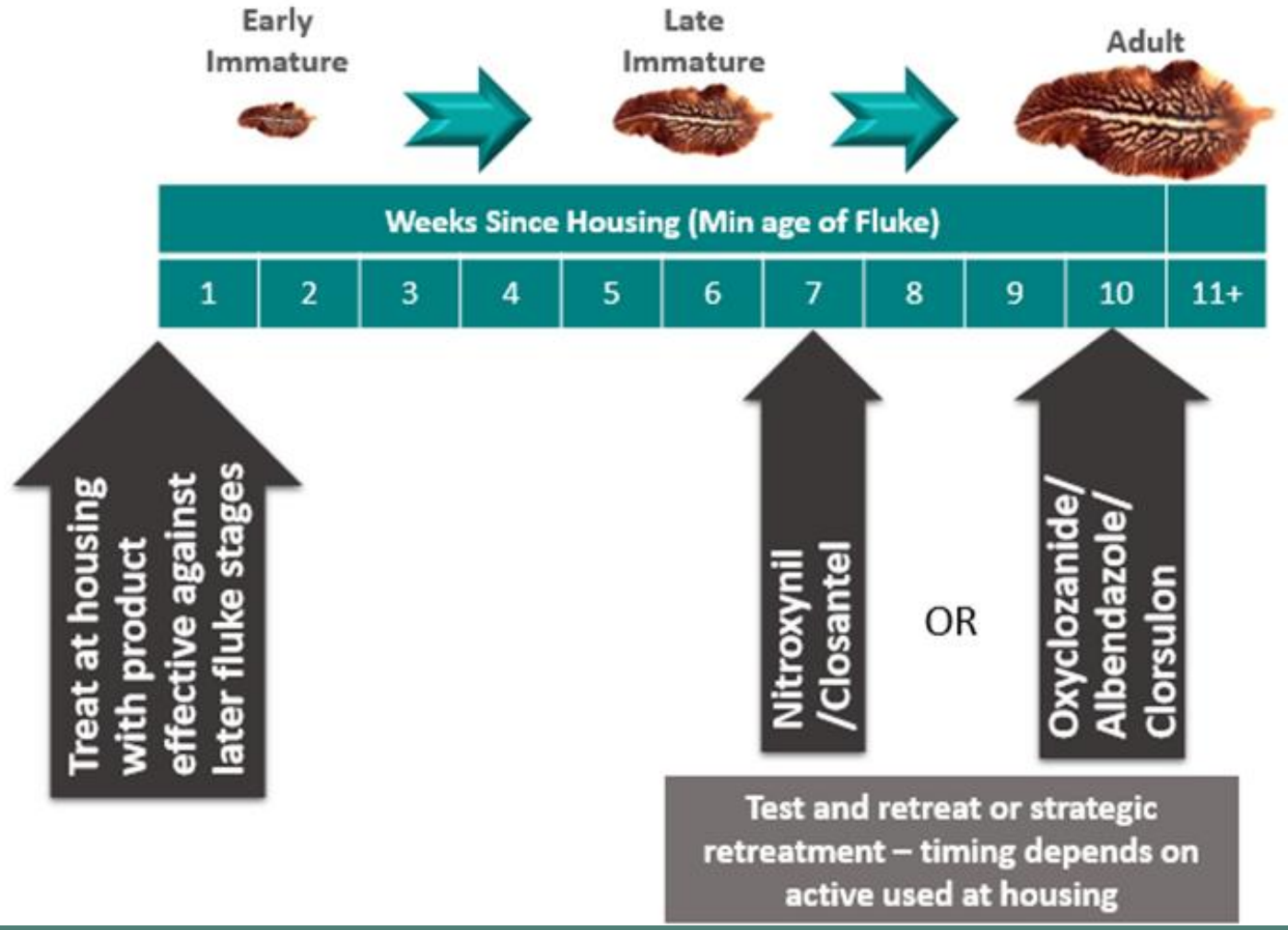
Breaking the cycle – Winter treatment of cattle

Remove fluke to maximise health and productivity and growth over the housing period

→

Ensure cattle remain free of fluke and do not shed eggs on to pasture in spring

Treatment at housing: Managing the risk for the housing period and beyond…



Quarantine treatments

- Objectives are to manage risk of introduction of (resistant) fluke and prevent disease/production loss in the brought in stock

- **Assess the risk:**
- **Are there potential mud snail habitats on the farm?**
- **Is *Fasciola hepatica* already present on the farm?**
- **Is resistant *Fasciola hepatica* already present on the farm?**

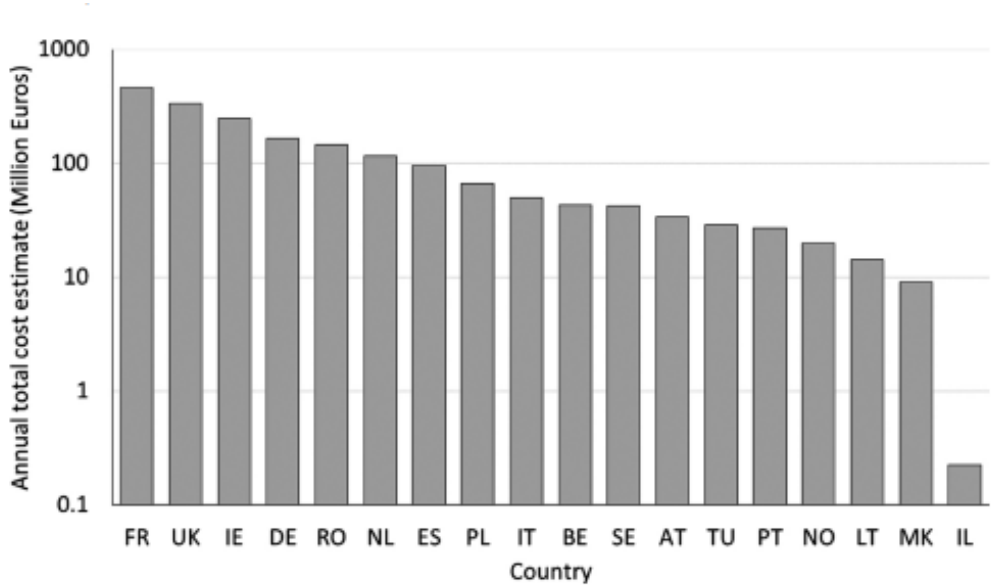
- **Treatment programme typically involves treatment with TBZ followed by sequential treatments with Nitroxynil/Closantel**
- **Follow up diagnostics**
- **Housing, then turnout onto quarantine paddock or ground free of snail habitats**

Conclusions

- Parasites pose a major cost to the livestock to livestock industries around the world
- In the UK liver fluke contributes the greatest single component of this cost
- Effective control relies on an understanding of the parasites complex lifecycle
- Treatment options are limited and have defined therapeutic profiles
- Factors such as emerging resistance and the impact of climate change on epidemiology

Need for further research to develop novel approaches to diagnosis, treatment & control

Estimated total annual cost of helminth infections on ruminant livestock production in 18 European and neighbour countries[1]



1. Charlier et al (2020) Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. Prev Vet Med 102: 105103

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Boehringer Ingelheim

Thank you

Additional resources:

https://www.liverpool.ac.uk/infection-and-global-health/research/liver-fluke/

https://www.moredun.org.uk/research/diseases/liver-fluke

SCOPS
Sustainable Control of Parasites

COWS
Control Of Worms Sustainably
Promoting sustainable control of cattle parasite