FACULTY OF VETERINARY MEDICINE
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DEPARTMENT VIROLOGY, IMMUNOLOGY AND PARASITOLOGY
RESEARCH GROUP PARASITOLOGY

TOWARDS DECISION SUPPORT FOR TREATMENT OF LUNGWORM INFECTIONS IN GRAZING CATTLE

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CONTENTS

- Epidemiology
- Pathology
- Effects on productivity
- Diagnosis
- Control
- Decision support

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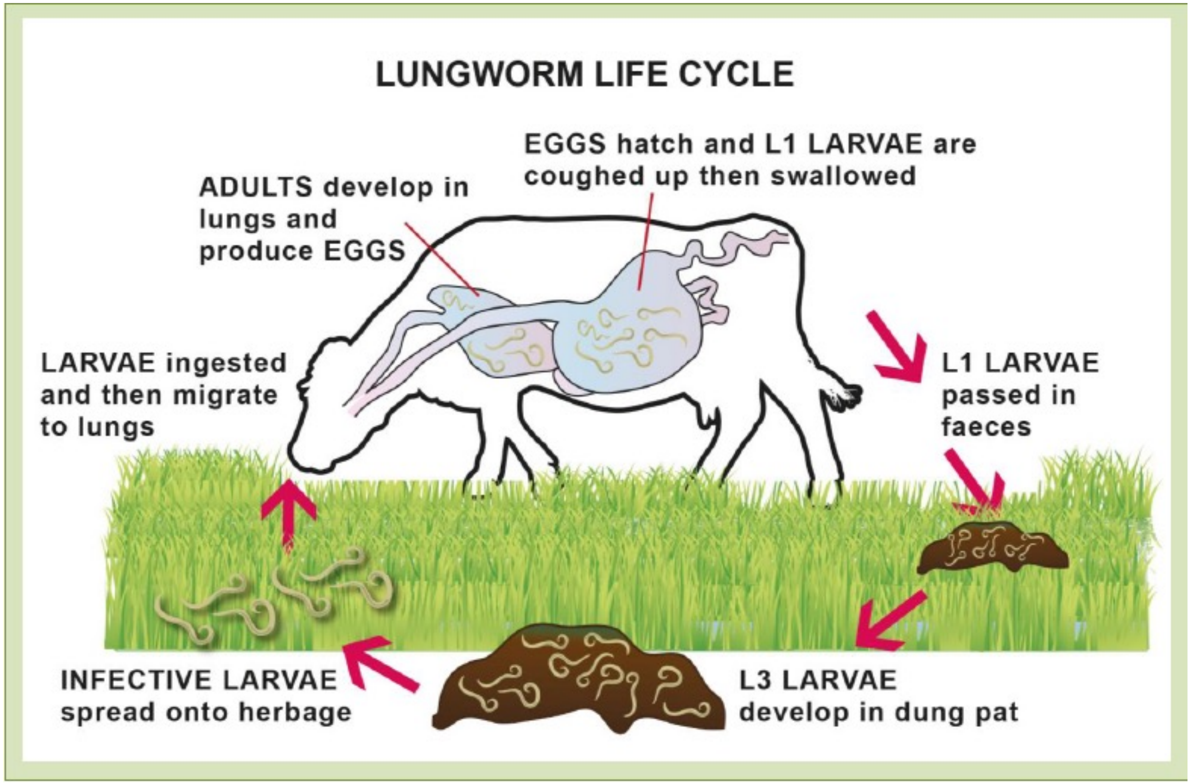
EPIDEMIOLOGY *DICTYOCAULUS VIVIPARUS*



Pre-patent period
3-4 weeks

Patent period
2-3 months

L1 -> L3: 1-4 weeks

http://www.cattleparasites.org.uk

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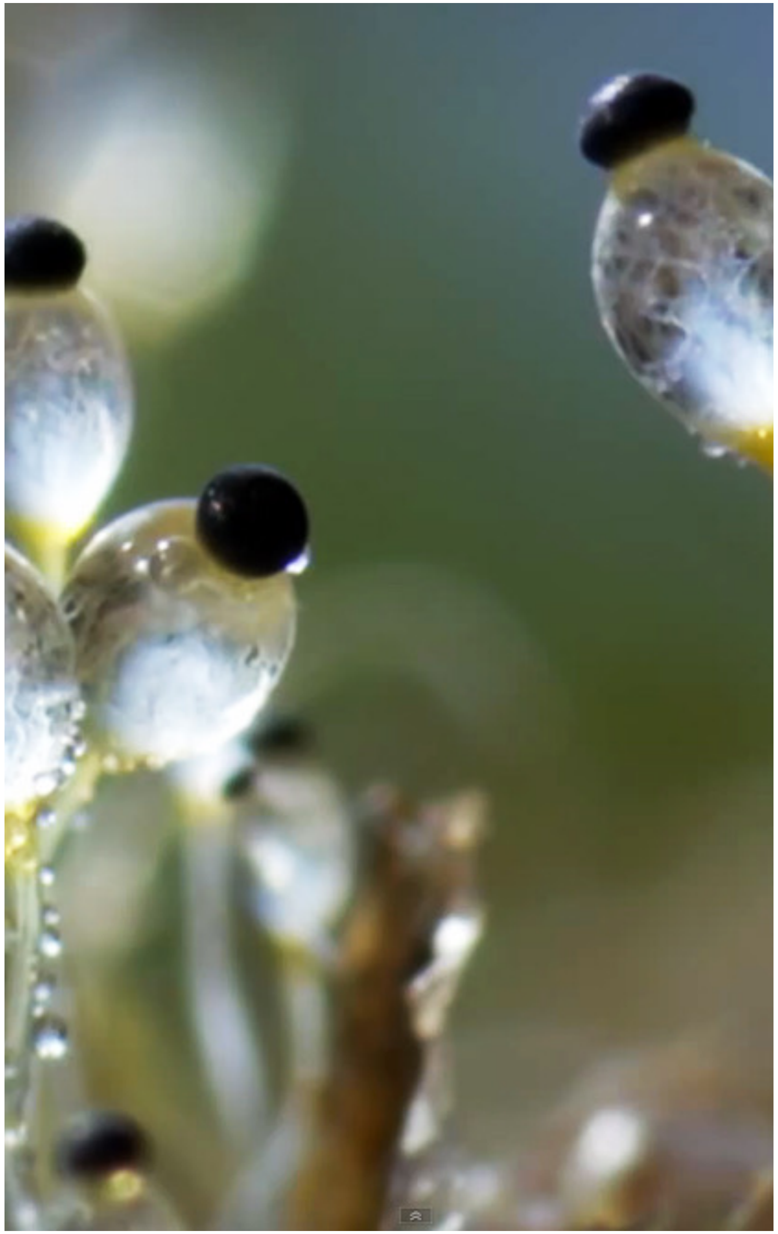

EPIDEMIOLOGY

- **Rapid development of L1 to L3**
  - Humidity needed
  - Temperature dependent
    - > 37°C no development
    - 20 - 25 °C: 3 to 5 days
    - 10 - 15 °C: 14 days
    - 5 °C: 26 days
    - < 0°C: no development
  - Dispersal to neighboring fields through *Pilobolus*, rain, birds, insects, trampling…
- **Short survival time of L3**
  - Only weeks in summer
  - Poor survival of winter

EPIDEMIOLOGY

- **Rapid development of immunity**
  - Sufficient exposure needed
  - Affects parasite development, fecundity and survival
  - Immunity fades after 6-12 months in absence of re-infection
- **Hypobiosis**
  - Induced by cold stimulus or immunity
  - Hypobiotic larvae overwinter in the host, resume development next spring -> initial pasture contamination

EPIDEMIOLOGY

Infection pressure

McLeonard & van Dijk, 2017. In Practice 39:408-419

Host immunity

www.hobbyfarms.com

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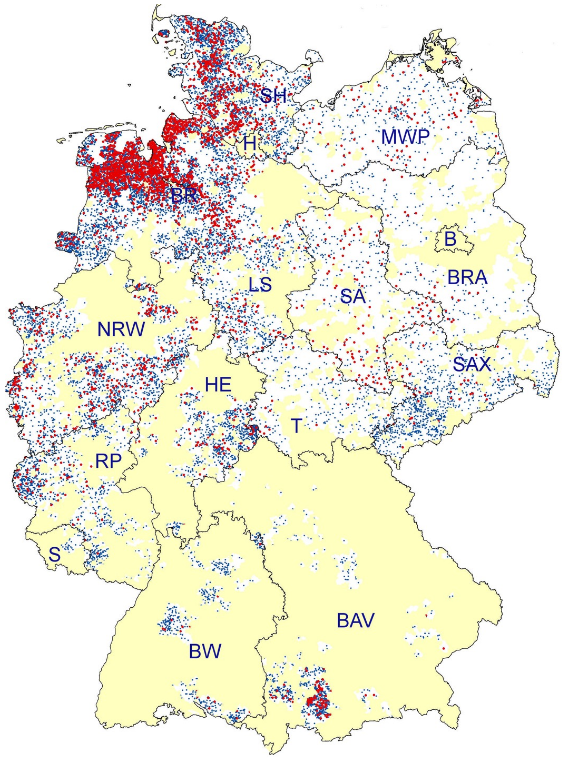
EPIDEMIOLOGY– PREVALENCE

- Worldwide
  - Europe: high prevalence in wet regions/years
    - Dairy cattle (bulk tank milk ELISA):
      - 9-21% (Belgium, Germany, Sweden)[1,2,3,4]
      - Switzerland 3%[5]
      - Ireland 63%[6]
      - Netherlands 2.6-63%[7]
    - Higher prevalence with individual faecal or serum samples[8,9,10]
    - UK: increasing incidence since 1990's[11]



Schunn et al., 2013. PLoS One 8, e74429

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[1]Bennema et al., 2009. Vet Parasitol 165, 51–57; [2]Klewer et al., 2012. Prev Vet Med 103, 243–245; [3]Schunn et al., 2013. PLoS One 8, e74429 ; [4]Höglund et al., 2010. Vet Parasitol 171, 293–299; [5]Frey et al., 2018. Vet Parasitol 250, 52–59; [6]Bloemhoff et al., 2015. Vet Parasitol 209, 108–116; [7]Ploeger et al., 2014. Vet Parasitol 199, 50-58; [8]Eysker et al., 1994. Vet Parasitol 53, 263-267 ; [9]Ploeger et al., 2012. Vet Parasitol 185, 335-338 ; [10]May et al., 2018. Parasit Vectors 11, 24; [11]McCarthy and van Dijk, 2020. Vet Rec 186, 642

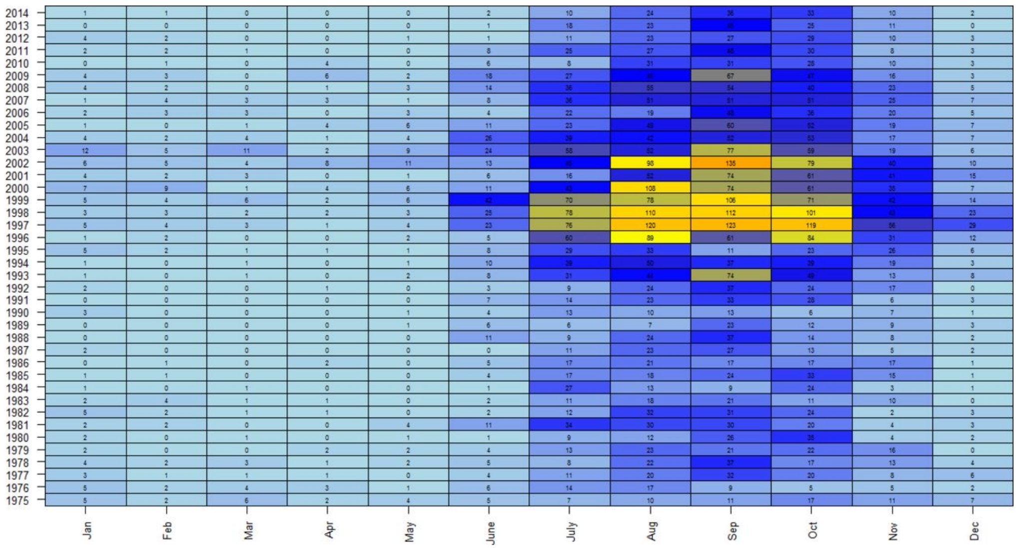
EPIDEMIOLOGY– PREVALENCE

- Worldwide
  - North America: reports of presence & outbreaks[1,2,3]
  - South America (Costa Rica, Colombia, Brazil, Argentina): reported outbreaks, low prevalence (?)[4-10]
  - Africa (Tanzania, Kenia, Ethiopia, Uganda, Ruanda): presence reported[11-13]
  - Asia (Malaysia): reported outbreaks, low prevalence[14]
  - Australia: presence reported[15]
  - New Zealand: widely present, limited clinical problems[16]

[1]Gupta & Gibbs, 1969. Can Vet J 10, 279-285; [2]Winters & Worley, 1975. Am J Vet Res 36, 327-329; [3]Lyons et al., 1981. J Am Vet Med Assoc 179, 456-457; [4]Jiménez et al., 2007. Vet Parasitol 148, 262-271; [5]Jiménez et al., 2008. Vet Parasitol 154, 294-299; [6]Chaparro et al., 2016. Parasite Epidemiol Control 14, 124-130; [7]Molento et al., 2006. Vet Parasitol 141, 373-376; [8]Henker et al., 2017. Acta Parasitol 62, 129-132; [9]Fiel et al., 2011. Parasitol Res 109, S105-S112; [10]de Macedo et al., 2021. Vet Parasitol Reg Stud Reports 26,100645; [11]Chartier C., 1990. Rev Elev Med Vet Pays Trop 43, 75-84; [11]Thamsborg et al., 1998. Trop Anim Health Prod 30, 93-96; [12] Fesseha & Mathewos, 2021. J Parasitol Res 6637718; [13]Lat-Lat et al., 2010. Trop Biomed 27, 236-40; [13]Smeal et al., 1977. Aust Vet J 53, 566-573; [14]Johnson et al., 2003. New Z Vet J 51, 93-98

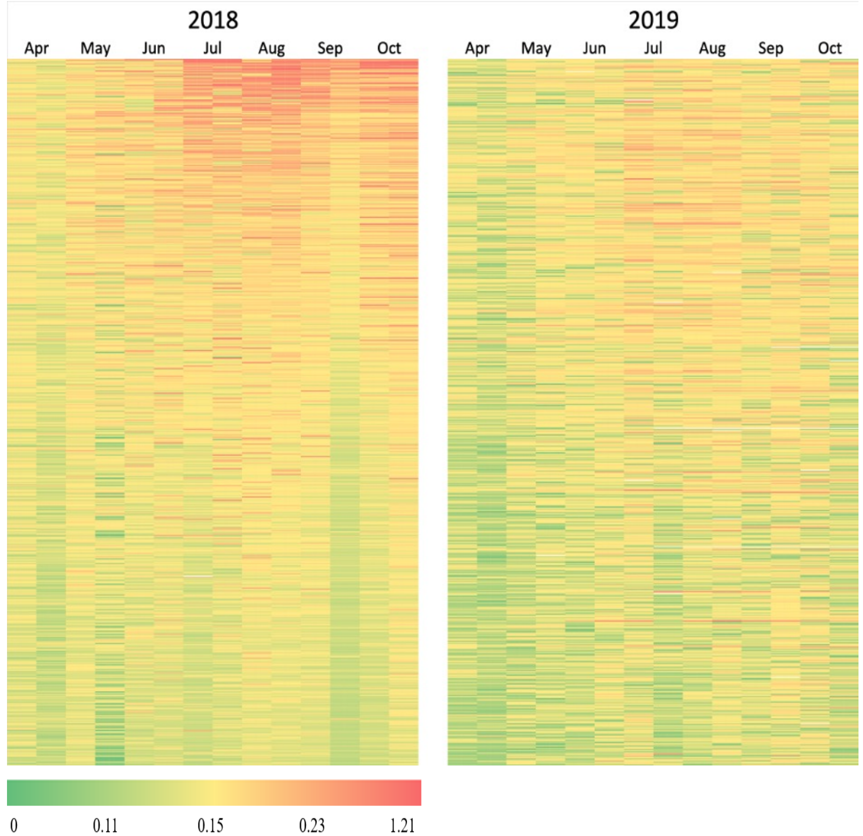
EPIDEMIOLOGY

Monthly distribution of lungworm cases in Great Britain 1975 to 2014 (rows).



McCarthy and van Dijk, 2020. Vet Rec 186, 642

Distribution of the ODR values per sampling and farm in dairy farms in Belgium



Vanhecke et al., 2020. Vet Parasitol 288, 109280

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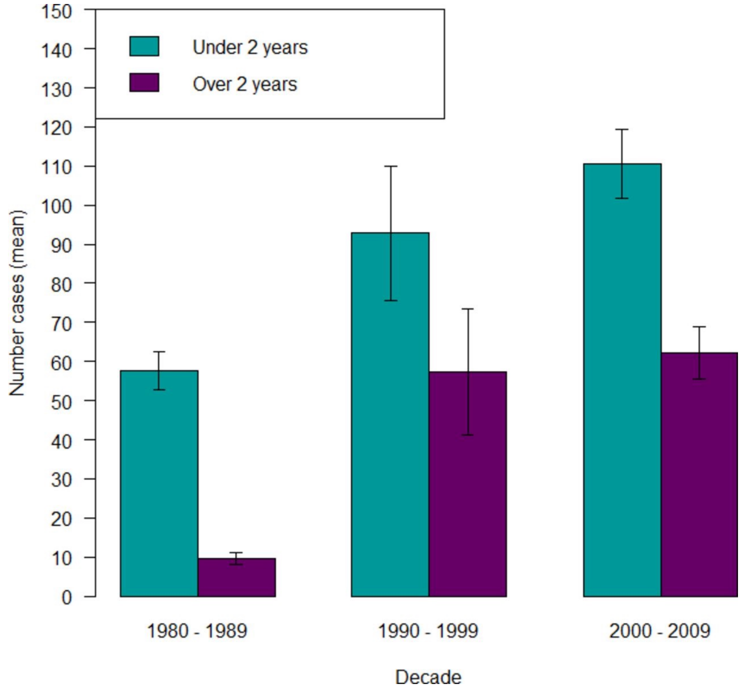
EPIDEMIOLOGY

- Different age classes
  - Grazing young stock most susceptible
  - Shift from young stock to adult cattle in Europe since 1990's[1,2]
  - Outbreak in adult dairy cattle in Brazil (Henker et al., 2016)[3]



McCarthy & Van Dijk, 2020. Vet Rec 186, 642

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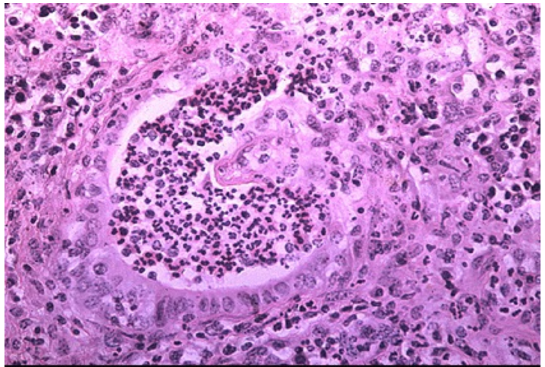
[1]Ploeger, 2002 Trends Parasitol 18, 329-332; [2]McCarthy & Van Dijk, 2020. Vet Rec.186, 642; [3]Henker et al., 2017. Acta Parasitol. 62, 129-132

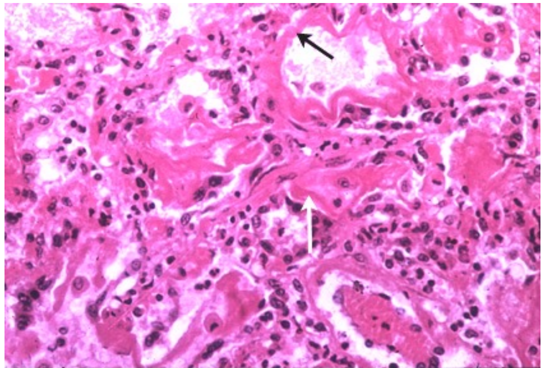
PARASITIC BRONCHITIS (HUSK)

- Pathology caused by L4 and adult worms
  - Inflammation
  - Obstruction of bronchioles (larvae, epithelial cells, eosinophils, mucus)
  - Alveolar emphysema -> interstitial emphysema
  - Hyperpnoea -> dyspnoea -> oedema -> hyaline membranes
  - Aspiration pneumonia (worms, eggs)

http://cal.vet.upenn.edu



Parasitic bronchitis - plug of eosinophils obstructing small bronchiole with collapse of surrounding alveoli



Hyaline membranes (black and white arrows) lining the epithelial surfaces of alveoli

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PARASITIC BRONCHITIS (HUSK)

- Clinical signs
  - Coughing
  - Hyperpnea -> dyspnoea
  - Nasal discharge
  - Mortality

- Post-patent phase
  - Recovery
  - Complications
    - Alveolar epithelisation
    - Secondary infections
    - Re-infection syndrome (heavy infection in immune animals)

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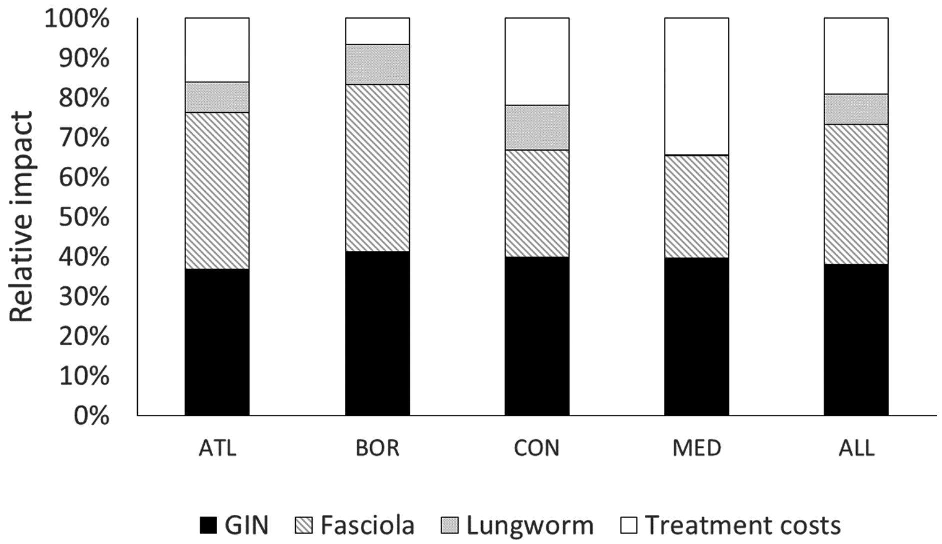
PRODUCTION LOSSES

- Clinical lungworm disease
  - Mortality
  - Reduced growth
  - Reduced milk production (€159-300/cow)[1,2]
- Subclinical lungworm infections
  - Increased ODR interquartile range: -0.3 to -0.5 kg/cow/day[3]
  - Positive vs neg bulk tank milk: -0.17 to -1.7 kg/cow/day[4,5]
  - Patent subclinical infection -1.6 kg/cow/day[5]
  - FGS calves: dose-dependent decrease in weight gain[6]



Annual cost (Europe) €139 million (€86-225 m)[7]

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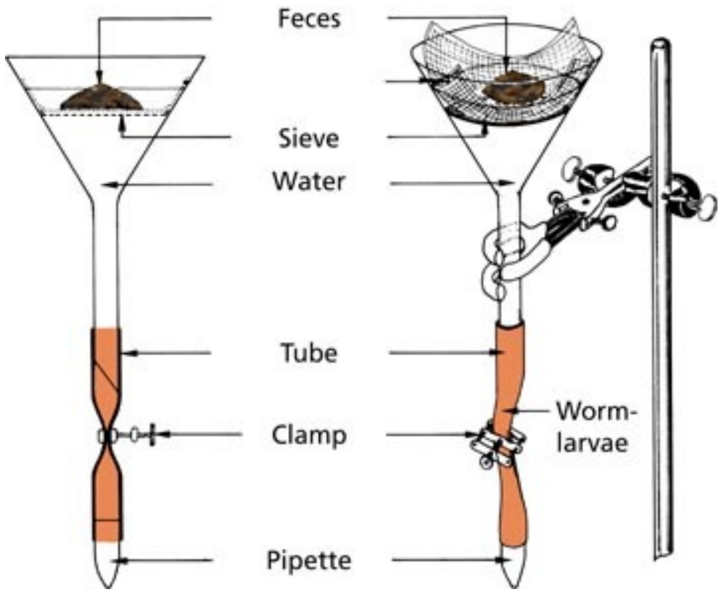
[1]Holzhauer et al., 2011. Vet Rec 169, 494; [2] Woolley, 1997 Cattle Pract 5, 315–318; [3]Charlier et al., 2016. Vet Parasitol 232, 36-42; [4]Dank et al., 2016. J Dairy Sci 98, 7741–7747; [5]May et al., 2018. Parasites Vectors 11:24; [6] Ploeger et al., 1990. Vet Parasitol.35, 307–322; [7]Charlier et al., 2020. Prev Vet Med 182, 105103

DIAGNOSIS



Mehlhorn, 2008.
https://doi.org/10.1007/978-3-540-48996-2_350

- Clinical signs
  - From 2-3 weeks pi[1,2]
- Farm history
- Detection of L1 in faecal samples (Baermann)
  - From 3-4 weeks pi[3]
  - High sensitivity in calves (30g)[3]
  - Multiple (9 heifers or 15 cows)[4] fresh samples, collected rectally
- Bronchoalveolar lavage
  - L1, eosinophils, Se 91%, Sp 85%[5]
- Autopsy
  - (pre-)adult worms in bronchi

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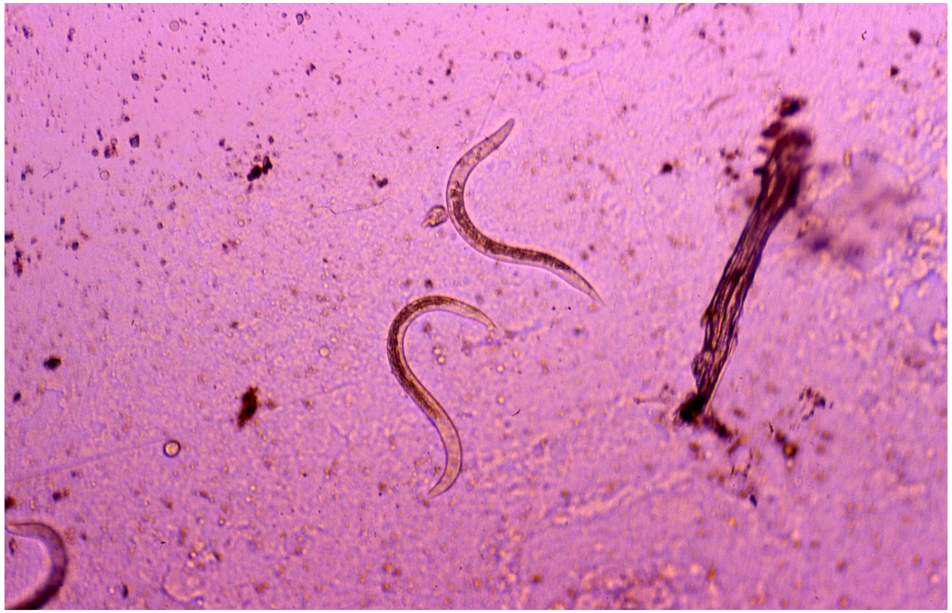
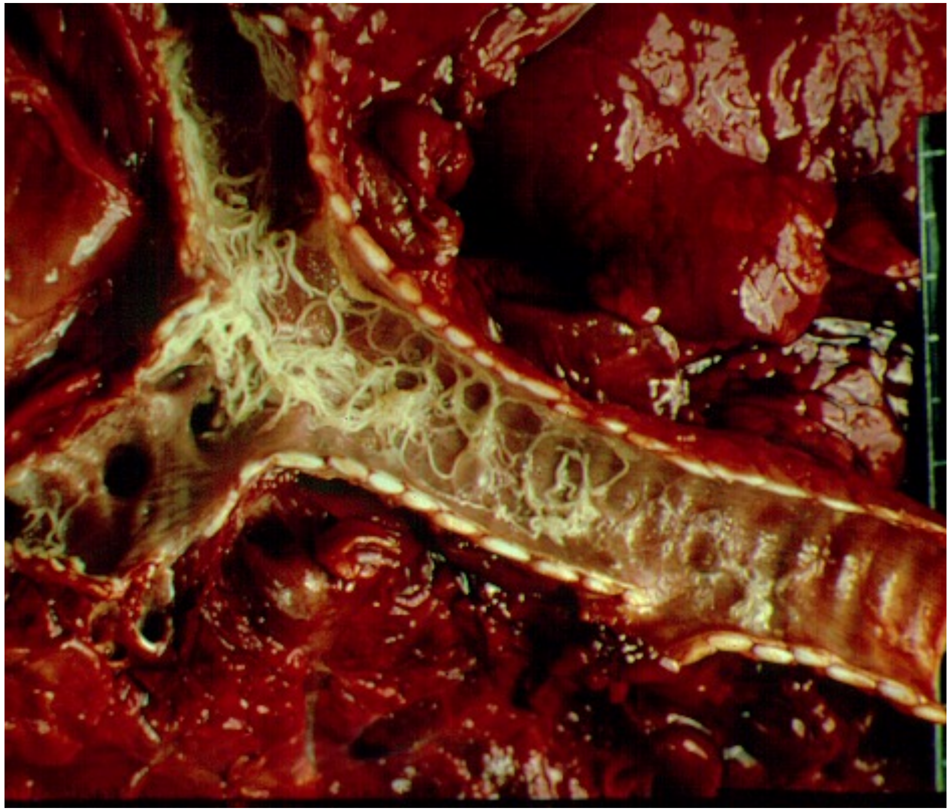
[1]Michel & McKenzie, 1965. Res Vet Sci 6, 344–395; [2]Boon et al., 1984. Vet Parasitol 16, 261–272; [3]Eysker, 1997. Vet Parasitol 69, 89-93; [4]Ploeger et al., 2012. Vet Parasitol 184, 168–179; [5]Lurier et al., 2018. Prev Vet Med 154, 124– 131

DIAGNOSIS





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DIAGNOSIS

- Detection of antibodies (serum, milk)
  - Individual serum or milk samples:
    - From 21-28 days (serum) or 30-46 days (milk) until 123-146 days p.i. (milk)[1,2,3]
    - Individual serum samples from ≥ 6 heifers or ≥ 10 cows[4]
    - High Se 98% and Sp 98%[3] (serum)
  - Bulk tank milk samples:
    - At least 20-30% of the herd seropositive[1,3]
    - Low Se (50-83%)[4,5,6], especially when within-herd prevalence < 10% (Se 36%)[5]
    - Shorter and lower antibody response after re-infection[7]

[1]Fiedor et al., 2009. Vet Parasitol 166, 255– 261; [2]Strube et al., 2017. Vet. Parasitol. 242, 47– 53; [3]Goździk et al., 2012. Res Vet Sci 93, 813–818; [4]Ploeger et al., 2012. Vet Parasitol 184, 168–179; [5]Ploeger et al., 2014. Vet Parasitol 199, 50-58; [6]Charlier et al., 2016. Vet Parasitol 232, 36-42; [7]Strube et al., 2017. Vet Parasitol 242, 47-53.

CONTROL

- Vaccination
  - Vaccine available in some countries
  - Living, irradiated L3
  - Two oral immunisations prior to turnout on infected pasture (booster infection required)
  - Don’t combine with anthelmintic treatment
  - Solid protection for a full grazing season
  - Disadvantages: short shelf life (not user-friendly), no sterile immunity, no life-long protection

CONTROL

- Biosecurity and management: avoid risk factors
  - Frequent purchase of animals, introduction of lungworm-naïve animals in an infected herd or infected animals into a naïve herd[1-4]
  - Not mowing or resting pasture (6 weeks) prior to cattle grazing[4,5,7]
  - Long grazing season[5,6]
  - Mixed grazing of different ages[5]
  - Over-treating young grazing stock[7]
  - (Semi)permanent water bodies[8]

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[1]Eysker et al., 1994. Vet Parasitol 53, 263-267; [2]Holzhauer et al., 2003. Tijdschr Diergeneeskd 128, 174-178; [3]Ploeger et al., 2012. Vet Parasitol 184, 168–179; [4]Charlier et al., 2016. Vet Parasitol 233, 36-42; [5]Schnieder et al., 1993. Vet Parasitol 47, 289-300; [6]Höglund et al., 2004. Vet Parasitol 125, 343-352; [7]Bloemhoff et al., 2015. Vet Parasitol 209, 108-116; [8]Schunn et al., 2013. PLoS One 8, e74429

CONTROL

- Anthelmintic treatment
  - Levamisole, benzimidazoles: no persistent efficacy
  - Macrocyclic lactones (ML): persistent efficacy 4-6 weeks
  - Long-acting ML: persistent efficacy 84-150 days
  - Anthelmintic boli: persistent efficacy 130-140 days
  - Mainly therapeutic treatment after diagnosis of parasitic bronchitis[1,2]
  - Difficult to determine the optimal time and frequency of preventive or metaphylactic treatment[3]

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[1]Eysker *et al.*, 1994. Vet Parasitol 53, 263-267; [2]Vercruysse and Claerebout, 2001. Vet Parasitol 98, 195-214; [3]Ploeger & Holzhauer 2012. Vet Parasitol 185, 335-338.

TOWARDS TREATMENT DECISION SUPPORT?

- Associations with (future) infection levels
  - Previous exposure (antibody levels)?
  - Risk factors?
  - Weather conditions?



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TOWARDS TREATMENT DECISION SUPPORT?

Bulk tank milk

MSP ELISA (ODR)

Questionnaire survey

Risk factors

Association with farmer-reported outbreaks?

Prediction of lungworm outbreaks?

Association with production losses?

Prediction of production losses?

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TOWARDS TREATMENT DECISION SUPPORT?

+

Higher risk for farmer-reported outbreak (2018-2019):

- ODR > 0.41 once (OR 2.0-3.4) or twice consecutively (OR 5.5-6.4)
- ODR > 0.41 in August (OR 3.7-4.2) or October (OR 2.7-2.6)
- Frequent purchase of animals: OR 2.0 (NS)
- Proportion of grazing season covered by anthelmintics: OR 2.8 (NS)

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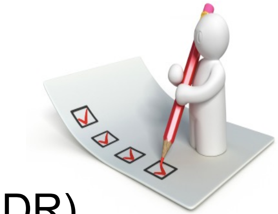
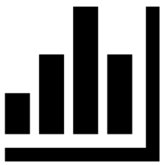
Vanhecke et al., 2020. Vet Parasitol 288, 109280

TOWARDS TREATMENT DECISION SUPPORT?



MSP ELISA (ODR)



+ Milk production data

Risk factors

- Purchase of new animals (OR 2.7)
- >50% of first grazing season covered by anthelmintics (OR 3.9)
- Mowing pastures (OR 0.57)

Milk production losses

- T-test between farms above and below threshold
  - ODR > 0.41 once: - 0.17 to -0.70 kg/cow/d (NS)
  - ODR > 0.41 twice: - 0.58 (NS) to -1.74 kg/cow/day
- Linear mixed effects model (2019)
  - ODR > 0.41 once: - 0.48 kg/cow/d (NS)
  - ODR > 0.41 twice: -1.34 kg/cow/d
- No association between ODR in Aug, Sept or Oct and milk yield

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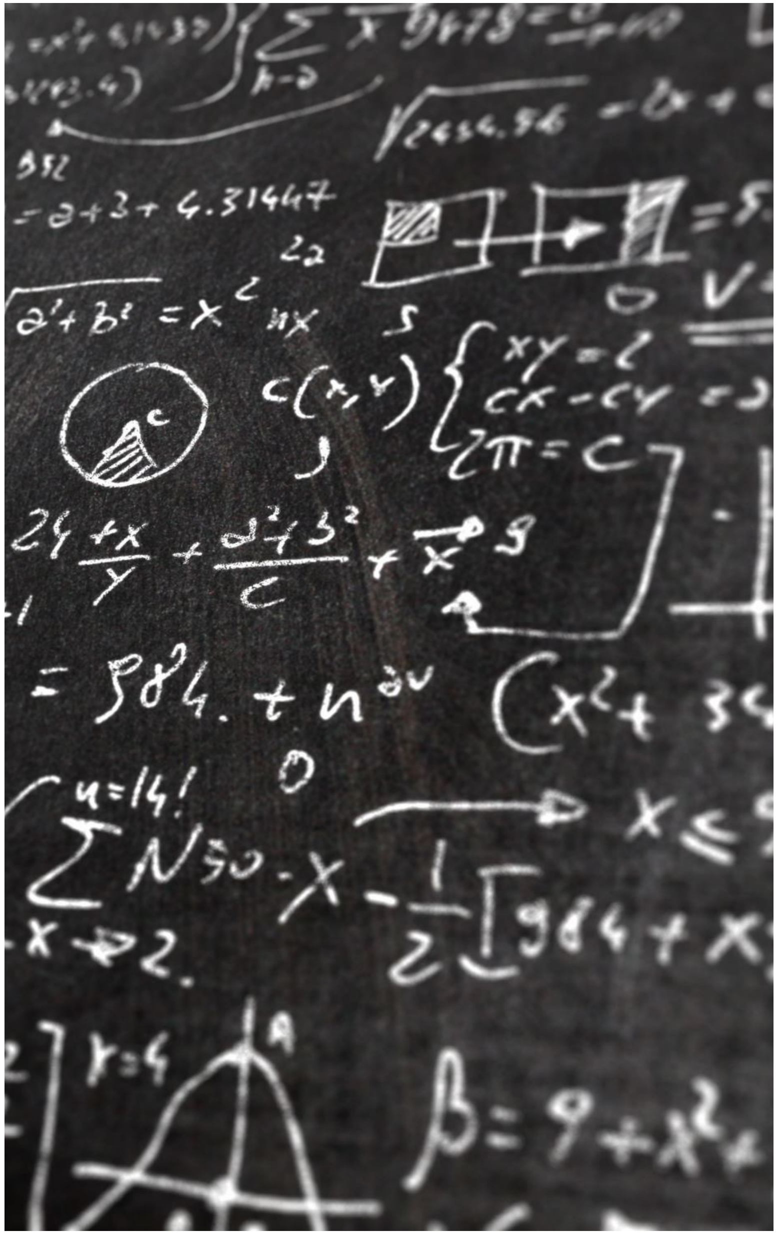
Vanhecke et al., 2021. Vet Parasitol 292, 109414



TOWARDS TREATMENT DECISION SUPPORT?

- Substantial, but variable and not always significant, reduced milk yield in farms with one or at least two consecutive BTM samples > 0.41 ODR
- Repeated monitoring is necessary to identify herds at risk for lungworm-associated production losses.
- A cut-off of 0.41 ODR could be a possible threshold for production limiting infections.
- **BUT**
  - Confirmation needed in different conditions (year, weather, management)
  - Mitigating parasite-associated production losses does not always improve economic performance[1]

Van der Voort et al., 2016. Animal 10, 274-282

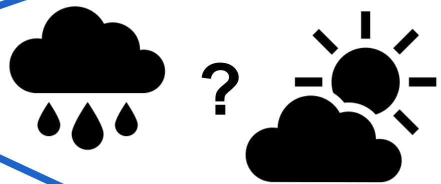
TOWARDS TREATMENT DECISION SUPPORT?

MSP ELISA (ODR)

- Threshold?
- Frequency?

+

Risk factors



Prediction of lungworm outbreaks?

Assessment of production losses?

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TOWARDS TREATMENT DECISION SUPPORT?

- Associations meteorological data vs. ODR (2018)
- Random effects models: random intercept and random slope model $Y = mx + b$
- Variables: mean of 14 days, different lags between measurement of meteo data and ODR
  - ODR
  - Temperature 2 m (min., max., mean.)
  - Temperature 1 cm deep (min., max., mean.)
  - Temperature 1-2 m deep (min., max., mean.)
  - Precipitation
  - Evapotranspiration
  - Solar radiation
  - Number of warm days (> 8°C)
  - Number of hot days (> 20°C)
  - Number of rainy days (> 2mm)

(Temperature 2 m, Temperature 1 cm deep, Temperature 1-2 m deep: Moderate correlation (R> 0.6))

parasit'Xpert

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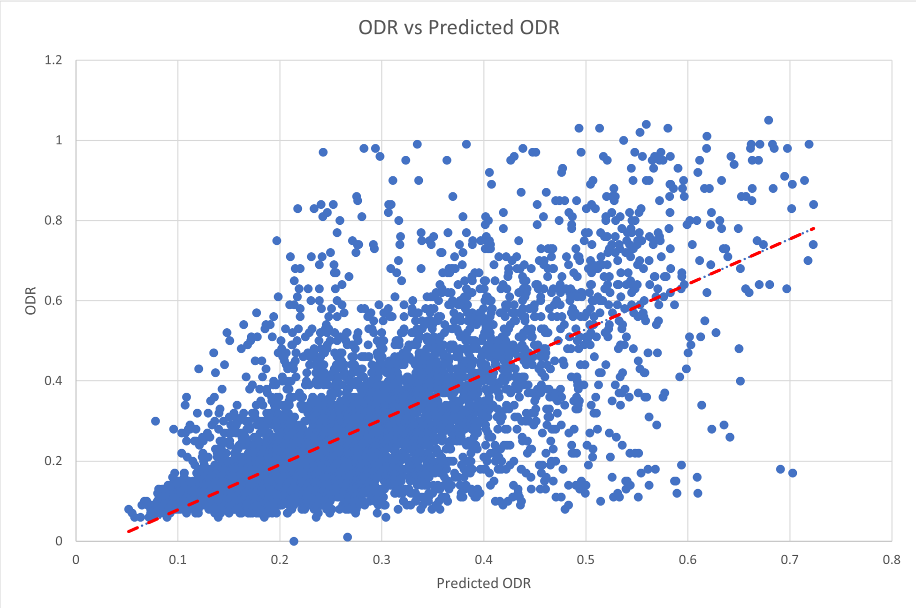
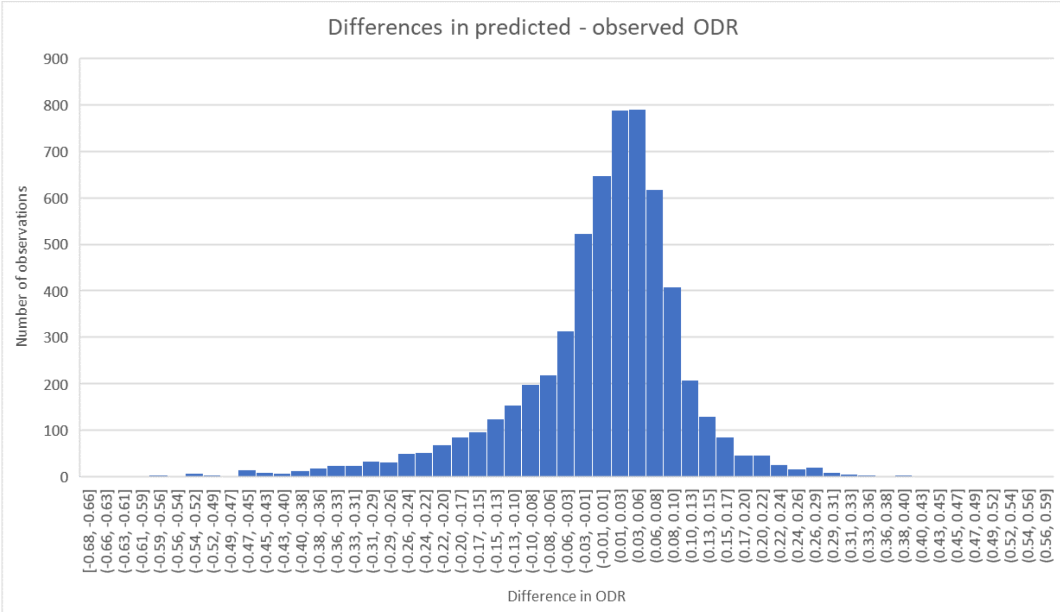
TOWARDS TREATMENT DECISION SUPPORT?

ODR ~ Month + Evap + Hot + Rain + Temp





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Vanhecke et al., 2021. *28th* WAAVP Conference, Dublin, O-4020; Vanhecke et al., 2022. Int J Parasitol, under review

TOWARDS TREATMENT DECISION SUPPORT?

- Improve association model
- Validate association model
  - Internal validation (bootstrap)
  - External validation
- Build prediction model
- Validate prediction model
  - Internal validation (bootstrap)
  - External validation

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