Control strategies for a stochastic model of host-parasite interaction in a seasonal environment (DSABNS 2013, Lisbon)

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Talk based on a manuscript coauthored with M. López García

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Organization of the talk

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- A single host (lamb) that is born, parasite-free, at time $t = 0$.
- Over its lifetime, it is exposed to parasites (Nematodirus spp.) at times – Poisson process of rate $\lambda(t)$.
- At an exposure, the host acquires a single parasite, independently from one exposure to another.
- The number of parasites within the host may increase due to parasite reproduction – Poisson process of rate $\lambda_m^*(t)$ as the number of parasites in the host equals m.
- Natural mortality of the host – rate $\delta(t)$.
- Parasite-induced mortality of the host – rate $\delta_m^*(t)$ as there are m parasites within the host.

At age τ (1 year), the interest is in the number $M(\tau)$ of parasites acquired by the host up to time instant τ, when it has been moved to an *uninfected* area (clean pasture or with less concentration of infective larvae on herbage) at a certain age $t_0 < \tau$.

We may distinguish between:

- **free-living** interval $[0, t_0)$
- **isolated-living** interval $[t_0, \tau]$

In the **free-living** interval $[0, t_0)$, the dynamics of the process $\mathcal{X} = \{M(t) : 0 \leq t < t_0\}$ are given by

(i) $m \to m+1$ at rate $\lambda_m(t)$, for values $m = 0, 1, ..., M_0 - 1$;
(ii) $m \to -1$ at rate $\delta_m(t)$, for values $m = 0, 1, ..., M_0 - 1$;
(iii) $M_0 \to -1$ at rate $\delta_{M_0}(t) + \lambda_{M_0}(t)$.

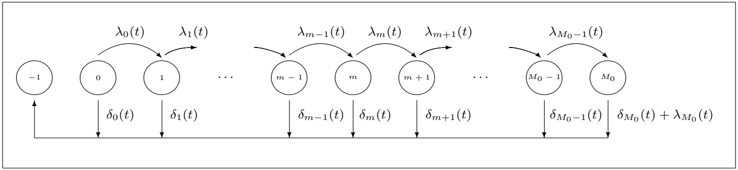

Figure: State space and transitions of the process $\mathcal{X}$.

In terms of $\pi_m(t) = P(M(t) = m | M(0) = 0)$ for $m \in \{-1\} \cup \mathcal{S}$,

$$\begin{aligned} \frac{d\pi_{-1}(t)}{dt} &= \sum_{m=0}^{M_0-1} \delta_m(t)\pi_m(t) + (\delta_{M_0}(t) + \lambda_{M_0}(t))\,\pi_{M_0}(t), \\ \frac{d\pi_m(t)}{dt} &= -(\lambda_m(t) + \delta_m(t))\,\pi_m(t) + (1 - 1_{0,m})\lambda_{m-1}(t)\pi_{m-1}(t), \;\; m \in \mathcal{S}, \end{aligned}$$

for $t < t_0$. Since $\pi_0(0) = 1$ and $\pi_{-1}(t) + \sum_{m=0}^{M_0} \pi_m(t) = 1$,

$$\begin{aligned} \pi_{-1}(t) &= 1 - \sum_{m=0}^{M_0} R_m(t) e^{-(\Lambda_m(t)+\Delta_m(t))}, \\ \pi_m(t) &= R_m(t) e^{-(\Lambda_m(t)+\Delta_m(t))}, \quad m \in \mathcal{S}, \end{aligned}$$

where $\Lambda_m(t) = \int_0^t \lambda_m(u)du$, $\Delta_m(t) = \int_0^t \delta_m(u)du$, $R_0(t) = 1$ and

$$R_m(t) = \int_0^t \lambda_{m-1}(u) R_{m-1}(u) e^{\tilde{\Lambda}_m(u)+\tilde{\Delta}_m(u)} du, \quad 1 \le m \le M_0,$$

with $\tilde{\Lambda}_m(t) = \Lambda_m(t) - \Lambda_{m-1}(t)$ and $\tilde{\Delta}_m(t) = \Delta_m(t) - \Delta_{m-1}(t)$.

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with $\tilde{\Lambda}_m(t) = \Lambda_m(t) - \Lambda_{m-1}(t)$ and $\tilde{\Delta}_m(t) = \Delta_m(t) - \Delta_{m-1}(t)$.

In the **isolated-living** interval $[t_0, \tau]$, the dynamics are as follows:

- At time t_0, the host enters the uninfected area only if it is alive and infected.
  - (i) An eventual *intervention* is prescribed by a minimum number $m' \in \{1, 2, ..., M_0\}$ of parasites infecting the host.
  - (ii) With $P_{\geq m'}(t) = \sum_{m=m'}^{M_0} \pi_m(t)$, a natural *vaccination* strategy $\bar{\pi}$ is

$$\bar{\pi}_m = \begin{cases} 0, & \text{if } 1 \leq m \leq m' - 1, \\ P_{\geq m'}^{-1}(t_0)\pi_m(t_0), & \text{if } m' \leq m \leq M_0. \end{cases}$$

- Living under *noninfectious conditions* means:
  - The host undergoes a clinical treatment (anthelmintic) to decrease the parasite burden.
  - The reproduction of parasites within the host is stopped.
  - Mortality of parasites in the host – rate $\eta_m(t)$ when there are m parasites inside the host.
  - Natural and parasite-induced mortality of the host – rate $\delta'_m(t)$ as there are m parasites within the host.

For the process $\mathcal{Y} = \{M(t) : t_0 \leq t \leq \tau\}$,

(i) $m \to m-1$ at rate $\eta_m(t)$, for values $m = 1, ..., M_0$;

(ii) $m \to -1$ at rate $\delta'_m(t)$, for values $m \in \mathcal{S}$.

In terms of the probabilities $\pi_m(t_0; t) = P_{\bar{\pi}}(M(t) = m)$,

$$\begin{aligned} \frac{d\pi_{-1}(t_0;t)}{dt} &= \sum_{m=0}^{M_0} \delta_m(t)\pi_m(t_0;t), \\ \frac{d\pi_m(t_0;t)}{dt} &= -\left(\delta_m(t) + (1 - 1_{0,m})\eta_m(t)\right)\pi_m(t_0;t) \\ &\quad + (1 - 1_{m,M_0})\eta_{m+1}(t)\pi_{m+1}(t_0;t), \quad m \in \mathcal{S}. \end{aligned}$$

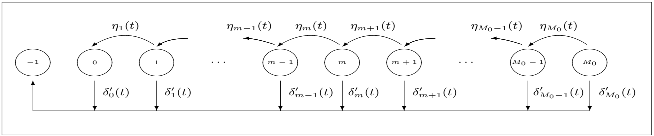


Figure: State space and transitions of the process $\mathcal{Y}$.

With initial conditions $\pi_m(t_0;t_0) = \bar{\pi}_m$ for $m \in \{1, 2, ..., M_0\}$, and $\pi_{-1}(t_0;t_0) = \pi_0(t_0;t_0) = 0$,

$$\begin{aligned}
\pi_{-1}(t_0;t) &= 1 - \sum_{m=0}^{M_0} \pi_m(t_0;t), \\
\pi_m(t_0;t) &= \left((1 - 1_{0,m})\bar{\pi}_m + (1 - 1_{m,M_0}) \sum_{j=0}^{M_0-1-m} \bar{\pi}_{m+1+j} \tilde{R}^j_{m+1}(t_0;t) \right) \\
&\quad \times e^{-(\Delta'_m(t_0;t) + H_m(t_0;t))}, \quad m \in \mathcal{S},
\end{aligned}$$

where $\Delta'_m(t_0;t) = \int_{t_0}^t \delta'_m(u)du$, $H_m(t_0;t) = \int_{t_0}^t \eta_m(u)du$,
$\tilde{\Delta}'_m(t_0;t) = \Delta'_m(t_0;t) - \Delta'_{m-1}(t_0;t)$,
$\tilde{H}_m(t_0;t) = H_m(t_0;t) - H_{m-1}(t_0;t)$.

The functions $\tilde{R}^0_m(t_0;t)$ are evaluated from

$$\tilde{R}^0_m(t_0;t) \;=\; \int_{t_0}^{t} \eta_m(u) e^{-(\tilde{\Delta}'_m(t_0;u)+\tilde{H}_m(t_0;u))} du, \quad 1 \leq m \leq M_0.$$

For $1 \leq j \leq M_0 - m$ and $1 \leq m \leq M_0 - 1$, the functions $\tilde{R}^j_m(t_0;t)$ are specified by

$$\tilde{R}^j_m(t_0;t) \;=\; \int_{t_0}^{t} \eta_m(u) e^{-(\tilde{\Delta}'_m(t_0;u)+\tilde{H}_m(t_0;u))} \tilde{R}^{j-1}_{m+1}(t_0;u) du.$$

With no control strategy, the impact of the parasite load on the host will often result in significantly high values of the probability $\pi_{-1}(\tau)$ that the host does not survive to age τ, and small values of the probability $\pi_0(\tau)$ that the host is alive and parasite free.

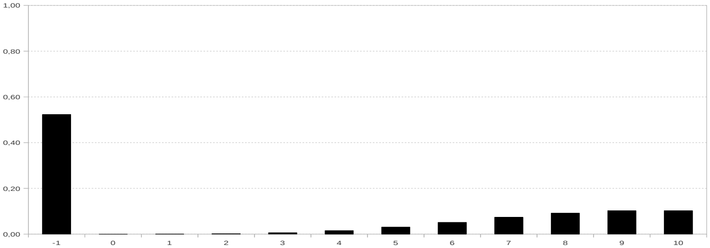


Figure: The mass function of $M(\tau)$ for $\tau = 1$ year under the assumption that the host is free living in the interval $[0, \tau]$. Critical parasite load $M_0 = 10$; combined rates $\lambda_m(t) = 20.0 \sin^2(4\pi t)$ and $\delta_m(t) = 0.2 + 0.1 \cos(2\pi t)$.

A control strategy is specified by

- An age t_0 or *vaccination instant*.
- A probability vector $\bar{\pi}$ defining the vaccination strategy, that is, a threshold $m' \in \{1, 2, ..., M_0\}$.

It is advisable to consider the age-dependent probability

$$P_{\geq m'}(t) \;=\; \sum_{m=m'}^{M_0} \pi_m(t)$$

and determine the set $I_{\geq m'}$ of *potential* vaccination instants $t \in (0, \tau)$ verifying

$$P_{\geq m'}(t) \;\geq\; p,$$

for a predetermined probability $p \in (0, 1)$, provided that $I_{\geq m'}$ is nonempty for the number m'.

- The set $I_{\geq m'}$ depends on p and m' (i.e., the vector $\bar{\pi}$ of initial probabilities at age t_0).
- Time instants $t \in (0, \tau) \setminus I_{\geq m'}$ can be termed *low-risk* vaccination instants and, consequently, they are not considered in subsequent arguments.

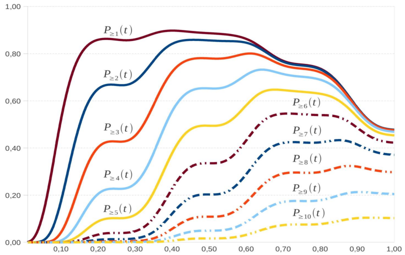


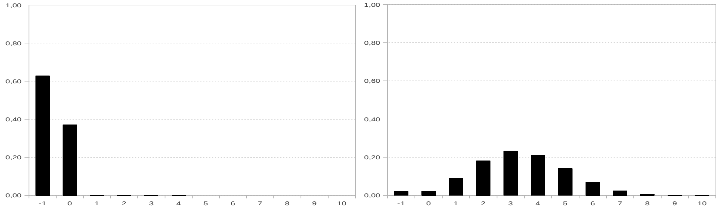
Figure: The age-dependent probability $P_{\geq m'}(t)$ as a function of $t \in (0, \tau)$ with $\tau = 1$ year, for $m' \in \{1, 2, ..., M_0\}$. Critical parasite load $M_0 = 10$; $\lambda_m(t) = 20.0 \sin^2(4\pi t)$, $\delta_m(t) = 0.2 + 0.1 \cos(2\pi t)$.

For a fixed pair (m', p) resulting in the nonempty set $I_{\geq m'}$, the problem is to find the time instant $t_0 \in I_{\geq m'}$ that adequately balances the *effectiveness* and *cost of vaccination*:

- Effectiveness is measured in terms of the probability $\pi_0(t_0; \tau)$ that the host is alive and parasite free.
- We make the cost of vaccination depend on the probability $\pi_{-1}(t_0; \tau)$ that it does not survive at age τ.

Two *crude* criteria:

(i) Choose t_0 as the smallest time instant in $I_{\geq m'}$;
(ii) Choose t_0 as the highest time instant in $I_{\geq m'}$.



Criterion 1 **It minimizes the cost of vaccination, but it maintains a minimum level of effectiveness**. We translate the minimum level of effectiveness into a certain probability $p_1 \in (0,1)$, and determine the subset $J^1_{\geq m'}$ of potential vaccination instants $t \in I_{\geq m'}$ satisfying

$$\pi_0(t;\tau) \quad \geq \quad p_1.$$

Then, we suggest to choose the vaccination age t_0 verifying

$$\pi_{-1}(t_0;\tau) = \inf\{\pi_{-1}(t;\tau) : t \in J^1_{\geq m'}\}.$$

Criterion 2 **It maximizes the effectiveness, but it sets an upper bound to the cost of vaccination**. For a suitably chosen probability $p_2 \in (0,1)$, we first determine the subset $J^2_{\geq m'}$ of time instants $t \in I_{\geq m'}$ verifying

$$\pi_{-1}(t;\tau) \quad \leq \quad p_2,$$

and then select the vaccination age t_0 such that

$$\pi_0(t_0;\tau) = \sup\{\pi_0(t;\tau) : t \in J^2_{\geq m'}\}.$$

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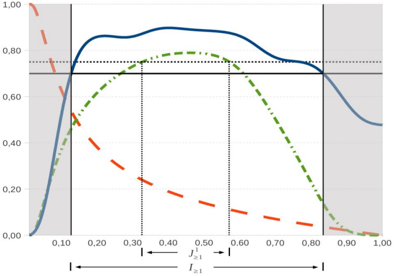

Figure: Applying **Criterion 1 (left)** with $p_1 = 0.75$ and **Criterion 2 (right)** with $p_2 = 0.25$ to a host-parasite model with critical parasite load $M_0 = 10$ and vaccination rule specified by $m' = 1$ and $p = 0.7$. *Solid*, *broken* and *dashed* lines correspond to the age-dependent probabilities $P_{\geq m'}(t)$, $\pi_{-1}(t;\tau)$ and $\pi_0(t;\tau)$, respectively, with $\tau = 1$ year.

The interest is in the parasite *Nematodirus* spp., with *Nematodirus battus*, *Nematodirus filicollis* and *Nematodirus spathiger* as main species.

- In nematodes, the sexes are separate, and the males are generally smaller that the females, which lay eggs or larvae.
- During development, a nematode moults at intervals, shedding its cuticle.
- In the complete life cycle of *Nematodirus* spp. there are four moults, the successive larval stages being designated L_1, L_2, L_3, L_4 and finally L_5, which is the immature adult.
- Infection in sheep only occurs by ingestion of the free-living L_3, with establishment proportions of L_3 in susceptible lambs ranging between 45% and 60%.

In practice, increments in the number of L_3 infective larvae on the small intestine are estimated by fixing the establishment proportion (55%) and incorporating specifications for the lamb growth pre-weaning and post-weaning.

Our starting point is Figure 2 of [Uriarte J, Llorente MM, Valderrábano J (2003), Seasonal changes of gastrointestinal nematode burden in sheep under an intensive grazing system, Veterinary Parasitology 118: 79-92] recording the number of L_3 infective larvae on herbage samples at weekly intervals from a fixed paddock of the farm. Results are expressed as infective larvae per kilogram of dry matter (L_3 kg^{-1} DM) after drying the herbage overnight at 60^o C.

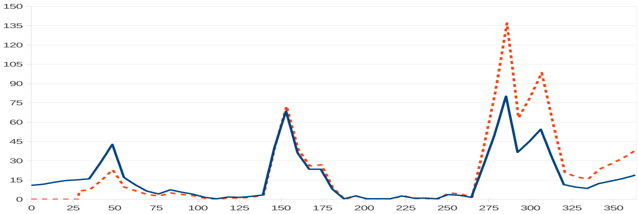

Figure: Numbers of L_3 infective larvae on pasture (*solid* line) and increments in the number of L_3 infective larvae on the small intestine (*dashed* line). Establishment proportion: 55%. Parasite: *Nematodirus* spp.

The efficacy of anthelmintics is measured in terms of reduction in faecal *eggs per gram (EPG)* percentages pre-treatment and post-treatment. *Points system*: 1 point is equivalent to the presence of 4000 worms, a total of 2 points in a young sheep is likely to be causing measurable losses of productivity, and clinical signs and deaths are unlikely unless the total exceeds 3 points.

Degree of infestation	Infection level m	Points system (farm)	Number of L_3 on small intestine	EPG value (laboratory)
Null	0	0	$[0, 1000)$	$[0, 50)$
Light	1	0	$[1000, 2000)$	$[50, 100)$
Light	2	0	$[2000, 3000)$	$[100, 150)$
Light	3	0	$[3000, 4000)$	$[150, 200)$
Moderate	4	1	$[4000, 5000)$	$[200, 250)$
Moderate	5	1	$[5000, 6000)$	$[250, 300)$
Moderate	6	1	$[6000, 7000)$	$[300, 350)$
Moderate	7	1	$[7000, 8000)$	$[350, 400)$
High	8	2	$[8000, 9000)$	$[400, 450)$
High	9	2	$[9000, 10000)$	$[450, 500)$
High	10	2	$[10000, 11000)$	$[500, 550)$
High	11	2	$[11000, 12000)$	$[550, 600)$
Heavy	-1	$\{3, 4, ...\}$	$[12000, \infty)$	$[600, \infty)$

In identifying age-dependent patterns, $M(t)$ records the level of infection at time t instead of number of parasites. Since infective larvae cannot reproduce directly within the host,

$$\lambda_m(t) = \lambda(t),$$

where $\lambda(t)$ is derived from empirical data and the previous Table by translating increments in the number of L_3 infective larvae into levels of infection:

- First, we specify the value $\lambda(n)$ at the nth day as
$$\frac{\lambda'(n) \times i(n) \times pr}{l},$$
where $\lambda'(n)$ is the number of L_3 infective larvae on pasture, $i(n)$ is the DM intake at the nth day, pr is the establishment proportion, and l is the interval length used to define levels m of infection in terms of infective larvae on pasture; i.e., $l = 1000$ for $m \in \mathcal{S}$.
- The age-dependent function $\lambda(t)$ is then defined to be a curve connecting the points $(n, \lambda(n))$ in order, by line segments.

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A reasonable assumption for the death rates of parasites is given by

$$\eta_m(t) = m\eta(t),$$

where $\eta(t)$ reflects the therapeutic efficacy of a concrete anthelmintic over time.

We use empirical data of Nasreen et al. (2007), where the efficacy of three anthelmintics against GI nematodes is investigated:

- Forty weaner sheep having naturally acquired infestation of GI nematodes were selected for the study, and randomly divided into four groups termed A, B, C and D, of ten animals each.
- Animals of groups B, C and D were orally administered ivermectin (0.2 mg kg^{-1} BW), fenbendazole (5.0 mg kg^{-1} BW) and albendazole (7.5 mg kg^{-1} BW), respectively, and animals of group A served as control.
- Faecal samples were collected at day 0 immediately before administering the drug, and thereafter on day 3, 7, 14, 21 and 28 (post-treatment), and EPG values of faecal samples were appropriately determined.

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The age-dependent function $\eta(t)$ is defined as a curve connecting the points $(t_n, \eta(t_n))$ where instants t_n are given by t_0, $t_1 = t_0 + 3$, $t_2 = t_0 + 7$, $t_3 = t_0 + 14$, $t_4 = t_0 + 21$ and $t_5 = t_0 + 28$.
Values $\eta(t_n)$ with $n \in \{0, ..., 4\}$ are given by

$$\frac{1}{lev(t_n)} \times \frac{1}{t_{n+1} - t_n} \left(\frac{\lambda''(t_n)}{l'} \left(1 + \frac{\lambda''_A(t_{n+1}) - \lambda''_A(t_n)}{\lambda''_A(t_n)} \right) - \frac{\lambda''(t_{n+1})}{l'} \right),$$

where $\lambda''(t)$ and $lev(t)$ record the EPG value and the level of infection at time t, respectively, and l' is the interval length used in Table to define levels of infection in terms of EPG values. Since $l' = 50$ for levels $m \in \mathcal{S}$, $lev(t_n)$ is given by $[(l')^{-1}\lambda''(t_n)]$ where $[x]$ denotes integer part of x. EPG values in group A, denoted by $\lambda''_A(\cdot)$, allow us to estimate the effect of larvae established on the small intestine in the interval $(t_n, t_{n+1}]$.
It is assumed that $\eta(t) = 0$ if $t \geq t_5$ in order to reflect the end of the therapeutic period.

Natural and parasite-induced host mortality rates

$$\delta_m(t) \;=\; \delta'_m(t) = \delta(t), \quad m \in \mathcal{S}.$$

This implies that the parasite-induced death of the host is negligible, except as the total exceeds 3 points (i.e., $m = -1$). Then, with the specification $\delta(t) = e^{-10.0t}$ used in our examples, we notice that

- The probability of death of the young lamb in $(0, \tau)$ is negligible, but non-null.
- The conditional probability that the host death occurs within the first 24 hours, given that it dies in the interval $(0, \tau)$ with $\tau = 1$ year, is equal to 99.995%.

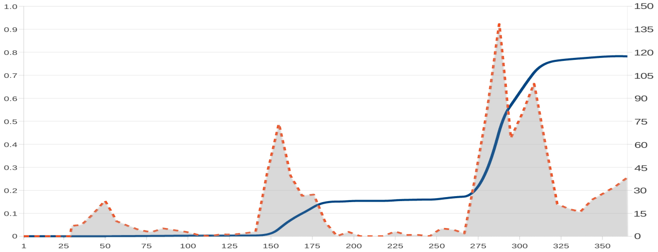


Figure: The age-dependent probability $P_{\geq 4}(t)$ (*solid* line) as a function of $t \in (0, \tau)$ with $\tau = 1$ year, and increments in the number of L_3 infective larvae of *Nematodirus* spp. on the small intestine (*shaded* area, *right* vertical axis).

Reasonable probabilities p such that $P_{\geq 4}(t) \geq p$ are, for example, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 0.7.

p	$I_{\geq 4}$	p_1	$J^{1,B}_{\geq 4}$	t_0^B	$J^{1,C}_{\geq 4}$	t_0^C	$J^{1,D}_{\geq 4}$	t_0^D
0.1	[170,365)	0.75	[170,295]	170	[170,317]	170	[170,311]	170
		0.70	[170,303]	170	[170,340]	170	[170,330]	170
		0.65	[170,308]	170	[170,343]	170	[170,341]	170
0.2	[274,365)	0.75	[274,295]	274	[274,317]	274	[274,311]	274
		0.70	[274,303]	274	[274,340]	274	[274,330]	274
		0.65	[274,308]	274	[274,343]	274	[274,341]	274
0.3	[281,365)	0.75	[281,295]	281	[281,317]	281	[281,311]	281
		0.70	[281,303]	281	[281,340]	281	[281,330]	281
		0.65	[281,308]	281	[281,343]	281	[281,341]	281
0.4	[286,365)	0.75	[286,295]	286	[286,317]	286	[286,311]	286
		0.70	[286,303]	286	[286,340]	286	[286,330]	286
		0.65	[286,308]	286	[286,343]	286	[286,341]	286
0.5	[290,365)	0.75	[290,295]	290	[290,317]	290	[290,311]	290
		0.70	[290,303]	290	[290,340]	290	[290,330]	290
		0.65	[290,308]	290	[290,343]	290	[290,341]	290
0.6	[298,365)	0.75	——	—	[298,317]	298	[298,311]	298
		0.70	[298,303]	298	[298,340]	298	[298,330]	298
		0.65	[298,308]	298	[298,343]	298	[298,341]	298
0.7	[308,365)	0.75	——	—	[308,317]	308	[308,311]	308
		0.70	——	—	[308,340]	308	[308,330]	308
		0.65	[308,308]	308	[308,343]	308	[308,341]	308

p	$I_{\geq 4}$	p_2	$J^{2,B}_{\geq 4}$	t^B_0	$J^{2,C}_{\geq 4}$	t^C_0	$J^{2,D}_{\geq 4}$	t^D_0
0.1	[170,365)	0.25	[170,365)	170	[170,365)	170	[170,365)	170
		0.20	[170,365)	170	[170,365)	170	[170,365)	170
		0.15	[170,360]	170	[170,360]	170	[170,360]	170
0.2	[274,365)	0.25	[274,365)	274	[274,365)	274	[274,365)	274
		0.20	[274,365)	274	[274,365)	274	[274,365)	274
		0.15	[274,360]	274	[274,360]	274	[274,360]	274
0.3	[281,365)	0.25	[281,365)	281	[281,365)	281	[281,365)	281
		0.20	[281,365)	281	[281,365)	281	[281,365)	281
		0.15	[281,360]	281	[281,360]	281	[281,360]	281
0.4	[286,365)	0.25	[286,365)	286	[286,365)	286	[286,365)	286
		0.20	[286,365)	286	[286,365)	286	[286,365)	286
		0.15	[286,360]	286	[286,360]	286	[286,360]	286
0.5	[290,365)	0.25	[290,365)	290	[290,365)	290	[290,365)	290
		0.20	[290,365)	290	[290,365)	290	[290,365)	290
		0.15	[290,360]	290	[290,360]	290	[290,360]	290
0.6	[298,365)	0.25	[298,365)	298	[298,365)	298	[298,365)	298
		0.20	[298,365)	298	[298,365)	298	[298,365)	298
		0.15	[298,360]	298	[298,360]	298	[298,360]	298
0.7	[308,365)	0.25	[308,365)	308	[308,365)	308	[308,365)	308
		0.20	[308,365)	308	[308,365)	308	[308,365)	308
		0.15	[308,360]	308	[308,360]	308	[308,360]	308

t_0	Treatment	$\pi_{-1}(t_0;\tau)$	$\sum_{m=0}^{3}\pi_m(t_0;\tau)$
170	B	0.09516	0.89296
	C (fenbendazole)	0.09516	0.90104
	D	0.09516	0.89999
274	B	0.09517	0.87534
	C	0.09517	0.89480
	D	0.09517	0.89218
281	B	0.09521	0.85437
	C	0.09521	0.88681
	D	0.09521	0.88230
286	B	0.09540	0.82248
	C	0.09540	0.87372
	D	0.09540	0.86636
290	B	0.09592	0.78717
	C	0.09592	0.85808
	D	0.09592	0.84758
298	B	0.09763	0.73694
	C	0.09763	0.83380
	D	0.09763	0.81895
308	B	0.10415	0.65801
	C	0.10415	0.79063
	D	0.10415	0.76935

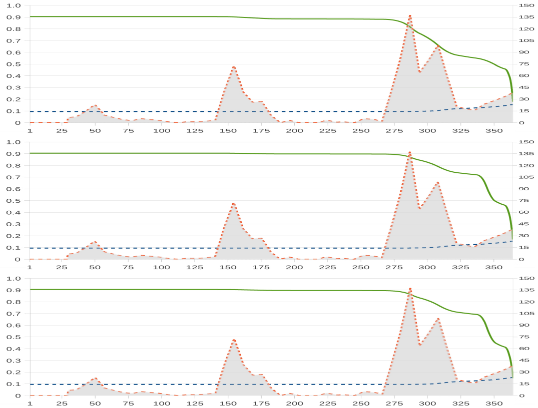


Figure: The age-dependent probabilities $\pi_{-1}(t_0;\tau)$ (*broken* line) and $\sum_{m=0}^{3} \pi_m(t_0;\tau)$ (*solid* line) as a function of the vaccination instant t_0 for $\tau = 1$ year, and increments in the number of L_3 infective larvae on the small intestine (*shaded* area, *right* vertical axis). Althelmintic treatments B, C and D (*from top to bottom*). Parasite: *Nematodirus* spp.

Some work in progress

The host is living under noninfectious conditions only for a concrete interval of length τ_0 (anthelmintic):

- A first **free-living** interval $[0, t_0)$
- A **isolated-living** interval $[t_0, t_0 + \tau_0)$
- A second **free-living** interval $[t_0 + \tau_0, \tau]$

For empirical data in Nasreen et al. (2007), the therapeutic period has length $\tau_0 = 28$ days.

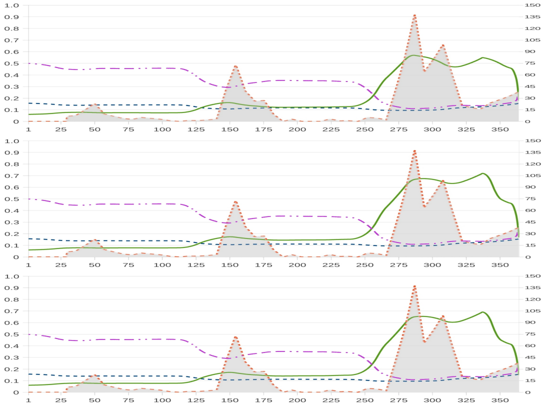


Figure: The age-dependent probabilities $\pi_{-1}(t_0;\tau)$, $\sum_{m=8}^{11}\pi_m(t_0;\tau)+\pi_{-1}(t_0;\tau)$ and $\sum_{m=0}^{3}\pi_m(t_0;\tau)$ versus t_0 for $\tau=1$ year, and increments in the number of L_3 infective larvae on the small intestine (*shaded* area). Althelmintic treatments B, C and D (*from top to bottom*) and setstocking. Parasite: *Nematodirus* spp.

Some work in progress

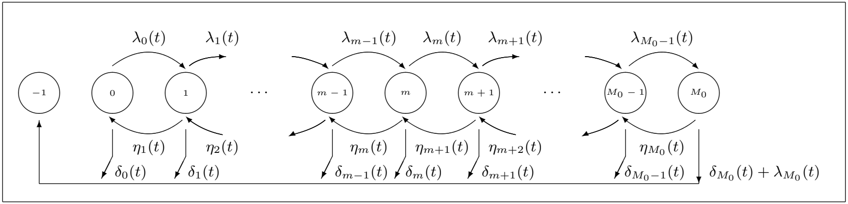
The isolated-living interval $[t_0, t_0 + \tau_0)$ becomes an intermediate interval in

> *Boa ME, Thamsborg SM, Kassuku AA, Bøgh HO (2001), Comparison of worn control strategies in grazing sheep in Denmark, Acta Veterinaria Scandinavica* **42**, *57-69,*

where grazing strategies are related to

- TS: strategic treatment and setstocking
- TM: strategic treatment and move to clean pasture
- US: no treatment and setstocking
- UM: no treatment and move to clean pasture

Regarding the age-dependent assumptions in the intermediate interval,



To solve the system of differential equations $\frac{d}{dt}\mathbf{\Pi}(t) = \mathbf{B}(t)\mathbf{\Pi}(t)$, we use **time-dependent splitting methods**, which are based on an appropriate decomposition of the tridiagonal matrix $\mathbf{B}(t)$ into two bi-diagonal matrices $\mathbf{B}(t) = \mathbf{U}(t) + \mathbf{V}(t)$.

The talk is based on

1. "Control strategies for a stochastic model of host-parasite interaction in a seasonal environment", by A Gómez-Corral, M López García, under evaluation.
2. "On the use of grazing management strategies for the control of gastrointestinal nematodes in sheep", by A Gómez-Corral, M López García, in preparation.

Thank you for your attention!