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Sébastien Picault, Pauline Ezanno, Sébastien Assié

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COMBINING EARLY HYPERTHERMIA DETECTION WITH METAPHYLAXIS FOR REDUCING ANTIBIOTICS USAGE IN NEWLY RECEIVED BEEF BULLS AT FATTENING OPERATIONS: A SIMULATION-BASED APPROACH

S. PICAULT*[1,2], P. EZANNO[1] AND S. ASSIÉ[1]

SUMMARY

Bovine Respiratory Disease (BRD) dramatically affects fattened young beef bull pens. How metaphylaxis and early detection help balance disease duration and antibiotics usage remains unclear. Our goal was to determine efficient control strategies, assessed on disease duration, antibiotics doses, and true positives, for various infection forces accounting for BRD pathogen diversity. A stochastic mechanistic individual-based model combined infectious processes, detection methods, and treatment protocols in a realistic simulated small-size pen. To enable veterinary experts to assess and revise model assumptions, a new artificial intelligence framework, EMULSION, was used to describe model features in an explicit and intelligible form. Parameters were calibrated from observed data. Overpassing on-farm reference scenario using boluses required to very early detect the first case while using longer hyperthermia for subsequent detections. Metaphylaxis was efficient only for high pathogen transmission. Besides concrete recommendations to farmers, EMULSION models could easily address other farming systems, treatments, and diseases.

INTRODUCTION

Young beef bulls entering fattening operations are highly susceptible to Bovine Respiratory Disease (BRD), which is difficult to prevent and control due to the multiple factors involved in their dynamics (Taylor et al., 2010). Indeed, the susceptibility of animals depends on their origin and distance travelled (Warriss et al., 1995; Sanderson et al., 2008). In addition, BRD is caused by multiple pathogens: most of the time, it results from a co-infection by viruses (e.g. the bovine respiratory syncytial virus) and bacteria (e.g. *Mannheimia haemolytica* or *Mycoplasma bovis*) (Assié et al., 2009). BRD can rapidly spread within pens, inducing high antibiotics usage to limit its impact on animal health and welfare, especially in high-risk cattle (Ives & Richeson, 2015). In a perspective of sustainable usage of antibiotics, it is still unclear how to resolve the balance between decreasing total disease duration and decreasing the number of antibiotics doses used at pen scale.

In France, feedlot management is based on extremely small pen size (typically 10 individuals), inducing a high stochasticity in infection dynamics (Assié et al., 2009). Such a pen size highly limits our ability to anticipate the possible consequences of pathogen presence at feedlot constitution. A first possible measure to prevent disease is arrival metaphylaxis, which consists in treating all animals in the pen after detecting first cases, the relevant threshold being a pending question (Edwards, 2010) as such a measure can lead to excessive usage of

* Sébastien Picault, Email: sebastien.picault@inra.fr
[1]BIOEPAR, INRA, Oniris, CS 40706, 44307, Nantes, France.
[2]Univ. Lille, CNRS, Centrale Lille, UMR 9189 - CRIStAL, Lille, France

antibiotics. Another option is to treat detected animals only, trying to detect them as early as possible while minimizing the number of false positive animals due to non-infectious hyperthermia (Lhermie et al., 2017). Currently in the field, detections rely on visual appraisal of clinical symptoms (White & Renter, 2009), sometimes conjugated with a search for hyperthermic animals (Schaefer et al., 2007), which is recommended twelve hours after the first detected case (Timsit et al., 2011). An alternative option to early detect new cases is to use reticulo-rumen boluses measuring hyperthermia and to use this information to trigger treatment against BRD spread. This has been proved useful compared to clinical sign detection alone (Timsit et al., 2011). However, early detection also can lead to false positives due to non-infectious hyperthermia episodes, thus also increasing antibiotics usage. Therefore, reasoning antibiotics usage in newly received beef bulls at fattening operations still is a crucial issue, which would beneficiate from resolving the balance between disease duration and antibiotics usage while prioritizing between metaphylaxis and early detection according to the epidemiological situation.

Our objective was to determine efficient control strategies mixing early detection and metaphylaxis, looking at various forces of infection to account for BRD pathogen diversity. Strategies were assessed based on the average individual disease duration at pen scale assumed as the main contribution to health and economic impact of BRD, antibiotics doses used, and strategy relevance as regards true positives.

MATERIALS AND METHODS

Modelling framework

A stochastic mechanistic individual-based model of a beef cattle pen combined infection processes, detection method, and treatment protocol. To ease integrating those aspects and endowing veterinary experts with a capability of assessing and revising model assumptions, parameters, and processes during the model design, a new generic modelling framework was used: EMULSION (Picault et al., 2017, 2018), based on recent artificial intelligence methods (Mathieu et al., 2018). In classical epidemiological models, model structure, assumptions, and parameter values are translated into simulation code, which makes them hardly revisable, and not understandable by epidemiologists. This hinders interdisciplinarity, but also makes modelling a long, one-way process where information can be lost or distorted throughout. EMULSION is designed to address this limitation and foster exchange loops between computer scientists, modellers, and epidemiologists. A Domain-Specific Language (DSL) allows the explicit and intelligible description of model components in a structured text file which can be read, commented, modified, and validated. Then, this model description is processed by a generic agent-based simulation engine where agents wrap several modelling paradigms (Individual-Based Models, Compartment-Based Models) and scales (individual, group, population, metapopulation) within a homogeneous architecture. For complex systems, a small software add-on can implement specific features not provided by the generic simulation engine. Besides, EMULSION fosters a decomposition of events and processes modelled. Processes are described as finite state machines, a formalism broadly used in computer science to represent states and transitions, and able to encompass flow diagrams more classically used in epidemiological modelling. State machines are able to incorporate individual conditions required to move between states, explicit state durations, and actions performed when entering, being in, or leaving a state. Hence, most model components are made explicit through the specification of the state machines associated with the relevant processes.

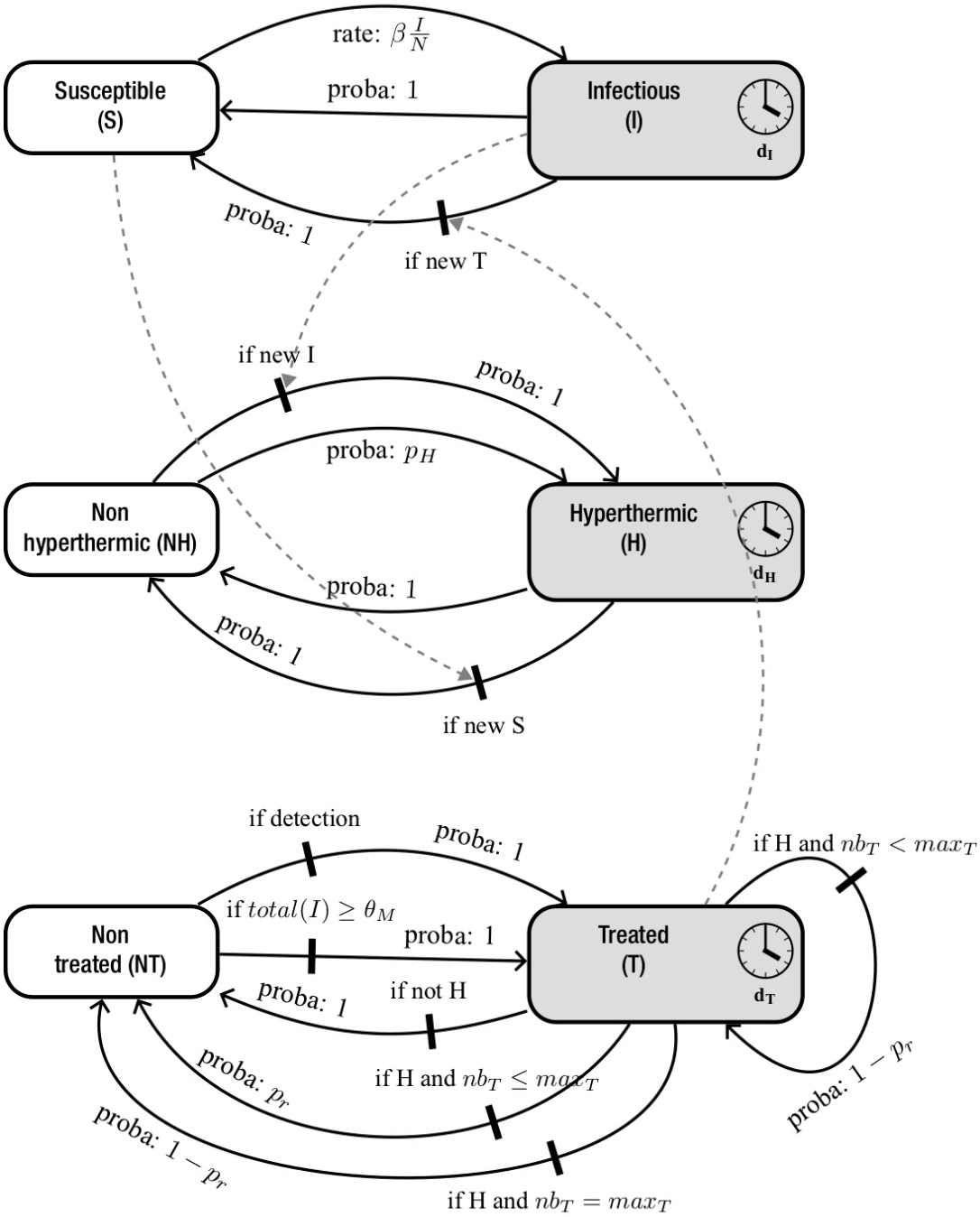

Fig. 1 Coupled processes in the BRD model, using a state machine formalism. Boxes: states possibly associated with a duration. Plain arrows: transitions between states (with a rate or probability and possibly a condition). Dashed arrows: how transitions in one process induce transitions in another process. Refer to Table 1 for parameter definition.

Model for Bovine Respiratory Disease (BRD)

The model was individual-based and stochastic to encompass the intrinsic variability of small pen size (10 individuals), and discrete-time with a time step of 12 hours corresponding to the delay between two successive visual appraisals at cattle feeding. A newly formed feedlot was considered having a fixed risk level (i.e. pathogens were brought in the pen by a given proportion $prev_0$ of infectious animals), for a given pathogen transmission rate within the pen.

BRD spread was observed during the first 30 days, the period with the highest risk of occurrence. The model involved three coupled processes (Fig. 1), (1) to account for hyperthermia episodes which can be independent from infectious events (e.g. ruminal acidosis), (2) to reflect assumptions regarding infection spread, and (3) to represent the treatment protocol and its possible outcomes. Infection was assumed to induce hyperthermia, both ending with recovery. Most biological parameters were calibrated from available observed data, most taken from (Timsit et al., 2011). Others were set up according to realistic pen management, treatment protocol, and detection method (Table 1).

Hyperthermia: this first state machine was composed of two states, hyperthermic (H) and non-hyperthermic (NH) animals. NH became H with probability p_H due to non-infectious causes, and then stayed in H for a duration d_H drawn in a beta distribution calibrated from observed data, before returning to NH. The transitions from NH to H and then back to NH because of infection was totally driven by the infection process.

Infection process: two health states were considered, susceptible (S) and infectious (I) animals. New infections (transitions from S to I) occurred at rate $\beta I / N$, assuming a frequency-dependent force of infection, where β is the transmission rate, I the number of infectious animals, and N the total number of animals in the pen. When entering I state, two actions were triggered: (1) a delay before exhibiting observable clinical signs d_C was drawn from a beta distribution calibrated from observed data, (2) the animal change from NH to H state. Recovery (transition from I to S) occurred after duration d_I drawn from a Poisson distribution. When returning to S state, animals changed from H to NH. An example of how this process is described in EMULSION's DSL is shown on Fig. 2.

Detection: transitions from not treated (NT) to treated (T) state occurred either because of metaphylaxis, or because of animal detection. Metaphylaxis occurred when the number of detected animals from feedlot formation or from last metaphylaxis reached threshold θ_M (ranging from 1 to N=10). Two detection methods were assessed. A visual appraisal of clinical signs as made on farm was modelled, assuming depression was the most significant sign to calibrate the delay (d_C) between infection and sign occurrence. In the model, this detection mode could be used at any time for any animal, alone or combined with the alternative detection method. In the reference scenario, the detection of the first case by visual appraisal was followed by identifying all hyperthermic animals via rectal temperature measured at next feeding time 12h later. For the alternative detection method, animals were assumed to be equipped with intraruminal boluses to measure hyperthermia duration, and detected once hyperthermia reached a duration threshold (θ_1 for the first case; θ_{2+} for subsequent cases).

Treatment protocol: transitions from T to NT were driven by the treatment. Each treated animal received one antibiotics dose, effective after duration d_T. Animals hyperthermic after this duration were treated again (same duration), the number of treatments per episode being limited (max_T). Transitions from T to NT occurred in three cases: (1) recovery after d_T due to treatment with probability p_r, (2) end of infection while under treatment, (3) still hyperthermic but already treated max_T times (treatment failure).

Experiments

Combinations of disease detection methods and metaphylaxis policies were investigated, considering 11 scenarios for metaphylaxis, 4 for early detection of the first case, and 4 for early detection of subsequent cases (Table 1). Threshold duration longer than 48h were not tested since the delay between infectious hyperthermia and apparition of depression is 51h in average

(Timsit et al., 2011). Three values of the pathogen transmission rate were used to assess its impact on BRD spread and control. The combinations of those factors led to 561 scenarios, each stochastically replicated 500 times, over a 30-day time horizon (60 time steps).

```
# DESCRIPTION OF THE STATE MACHINES INVOLVED IN THE MODEL
state_machines:
  health_state:
    desc: 'Description of the infection process'
    states:
      - S:
          name: Susceptible
          desc: 'Not infected by BRD pathogens. S animals remain S
          until infected by I animals.'
      - I:
          name: Infectious
          desc: 'Infected and able to transmit pathogens. When
          becoming I, the animal also becomes hyperthermic (H). When
          becoming S again, the animal also returns to
          non-hyperthermic state (NH)'
          # infection duration
          duration: d_I  # drawn in a Poisson distribution defined
                         # later in EMULSION DSL file (not shown)
          on_enter:
            # define delay before clinical signs
            - action: define_clinical_sign_apparition
              d_params:
                delay: d_C # drawn in a Beta distribution defined
                           # later in EMULSION DSL file (not shown)
            # triggers transition NH -> H (infection-related hyperthermia)
            - become: hyperthermic
            # update hyperthermia duration to infection duration
            # to prevent early exit from H state before recovery
            - action: update_hyperthermia_duration
          on_exit:
            # triggers transition H -> NH (end of hyperthermia)
            - become: normal_temperature
    transitions:
      - from: S
        to: I
        rate: 'beta*I/N'
        desc: 'assuming frequency-dependant force of infection, beta
        being the pathogen transmission rate, defined later in
        EMULSION DSL file (not shown)'
      - from: I
        to: S
        proba: 1
        desc: 'a recovered animal returns to S state after its own
        duration d_I'
```

Fig. 2 Section of the model description file (EMULSION's DSL) which defines the "health_state" state machine, in charge of driving the infection process (35 lines, excluding comments, from a total of 516) . The specification of S and I states, with their description and possible durations or actions occurring when entering/leaving them, are followed by the transitions between states. The conversion of deterministic features (e.g. rates) into stochastic ones (e.g. probabilities) is automatically performed.

Table 1. Parameters of the BRD model. Values in bold define reference scenarios

Parameter	Definition (with unit)	Source	Value
N	Feedlot size (animals)	pen management	10
$prev_0$	Initial prevalence (proportion)	expert	0.1
d_I	Duration of infection in each animal (h)	expert	~ Poisson(120)
d_C	Delay between infection and apparition of clinical signs (h)	data	~ Beta(1.08, 1.69) * 111 + 12 [average: 55.3]
d_H	Duration of a non-infectious hyperthermia episode (h)	data	~ Beta(1.33, 13.2) * 257 + 6 [average: 29.5]
p_H	Probability that a non-infectious hyperthermia episode appears (per hour)	expert	0.05/24
d_T	Duration of one treatment (h)	protocol	48
p_r	Probability to recover when treated (per treatment)	protocol	0.95
max_T	Maximum of nb_T, the number of consecutive treatments for the same episode (doses)	protocol	2
θ_M	Number of detected cases above which a metaphylaxis is triggered (animals)	scenario	**[1, *N*], never**
θ_1	Bolus-measured hyperthermia duration above which the first case is detected (h)	scenario	12, 24, 36, 48, **R**
θ_{2+}	Bolus-measured hyperthermia duration above which subsequent cases are detected (h)	scenario	12, 24, 36, 48, **R**
β	Pathogen transmission rate (h^{-1})	scenario	0.005, 0.01, 0.02

RESULTS

As expected, very early metaphylaxis ($\theta_M \leq 2$) contributed to reduce infection duration, especially with a high pathogen transmission rate (Fig. 3A). Interestingly, metaphylaxis mainly reduced prediction dispersion, contributing to a less risky health management of the pen. Late metaphylaxis ($\theta_M \geq 3$) was not more effective than no metaphylaxis. Combined with bolus detection, early metaphylaxis slightly decreased infection duration, but at the expense of many antibiotics doses (Fig. 3B) because of false positives. Such results are consistent with observations (Timsit et al., 2011). Bolus false-positives were amplified very quickly by successive metaphylaxis episodes. Without metaphylaxis, early detecting and treating BRD using boluses generally reduced infection duration compared to the reference scenario (Fig. 3A, θ_M = "never"), but also increased antibiotics doses (Fig. 3B, θ_M = "never"), highlighting a balance between improving animal health and reducing antibiotics usage. To assess bolus usage added-value, we searched for efficient combinations in experiments without metaphylaxis.

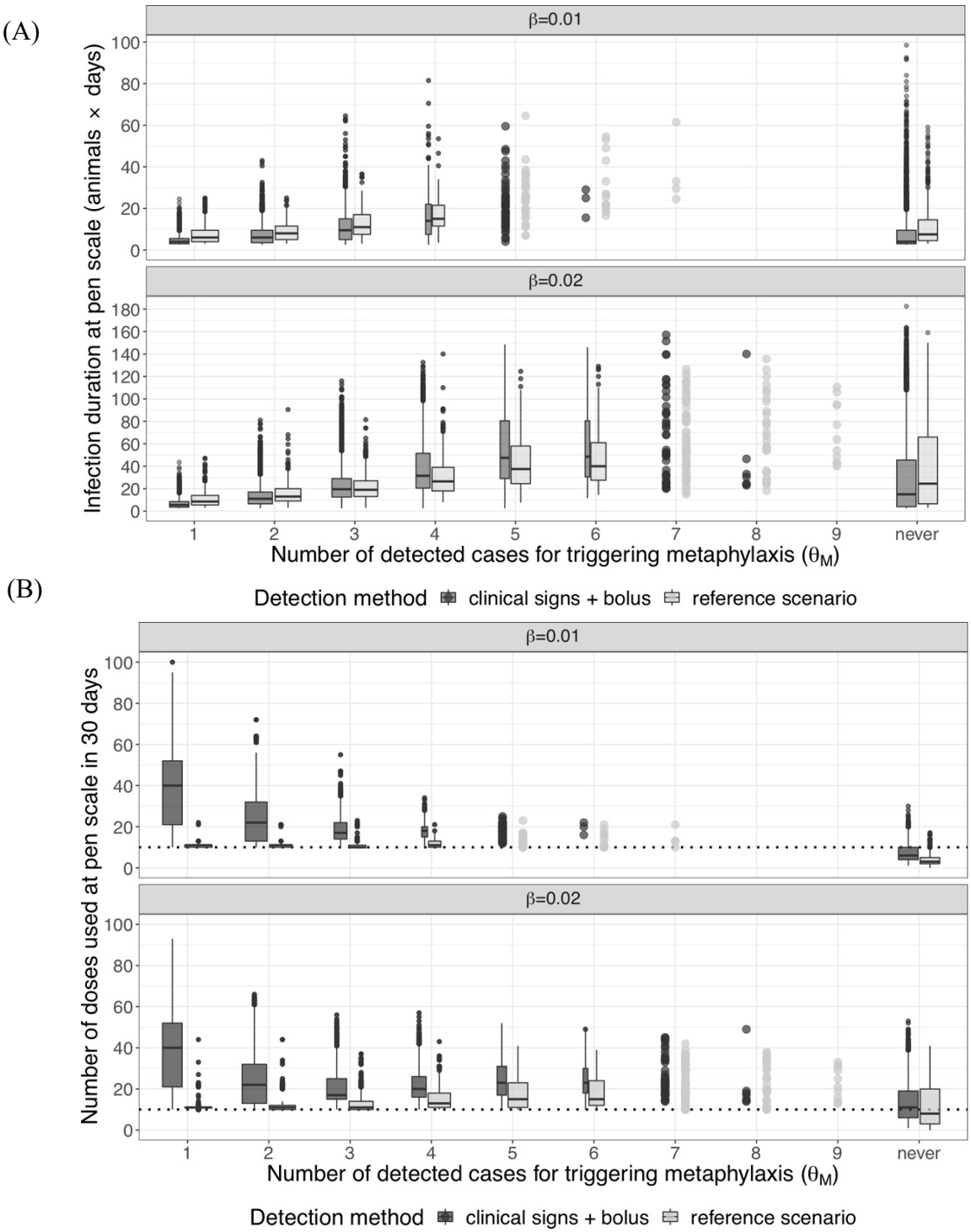

Fig. 3 Infection duration in animal-days (A) and antibiotics usage in 30 days (B) at pen scale depending on pathogen transmission (β), metaphylaxis (threshold θ_M, considering only repetitions where it occurred, vs. not used), and detection (with (dark) or without (light) bolus, aggregated over all values of θ_1 and θ_{2+}). Boxplots show percentiles 25, 50 and 75 of durations (with whiskers extending up to 1.5 times the inter-quartile range), their width varying with the proportion of repetitions where metaphylaxis was triggered (below 10% dots are used). Results for $\beta = 0.005$ (not shown) and 0.01 were qualitatively similar. The dotted line in panel B represents one dose per animal.

Unexpectedly, the proportion of false positives (treated while healthy) detected using boluses decreased mainly with higher values of θ_{2+}, i.e. detecting secondary cases when hyperthermia was long enough (Fig. 4). Indeed, it is usually assumed that - once a first case is detected - vigilance increases to quickly identify other infected animals. In the reference scenario representing on-farm practices, the visual appraisal of the first case was quickly followed by the identification of hyperthermic animals 12h later. The counterintuitive prediction made here could not be observed in previous field studies (Timsit et al., 2011), since a single threshold was evaluated ($\theta_1 = \theta_{2+}$). More in line with expectations, bolus usage was more efficient with low values of θ_1, i.e. very early detecting the first case (Fig. 5).

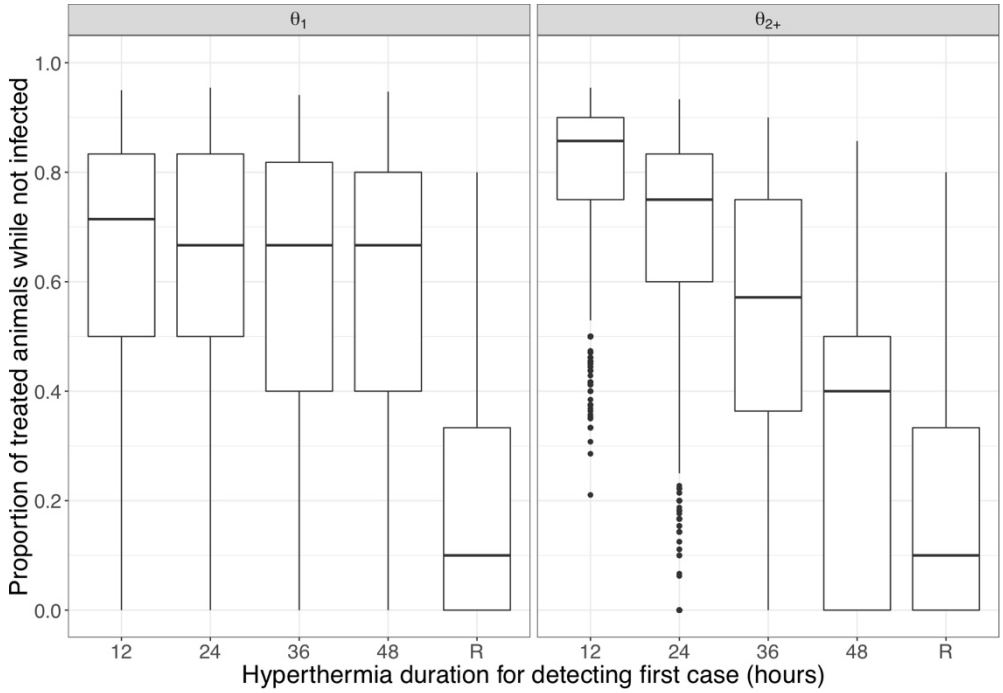

Fig. 4 Impact of hyperthermia duration thresholds and detection method on the proportion of unnecessary treatments ("R": reference scenario; $\beta = 0.01$; θ_M = "never")

The balance between dose and infection duration reduction can be adjust according to the priorities of farmers or public health decision-makers. For a given transmission rate, a combination of early first detection with longer hyperthermia for subsequent cases can be find which overpasses the reference scenario in terms of infection duration while using lower or similar antibiotics doses. For instance, with moderate pathogen transmission ($\beta = 0.01$), the reference scenario induces the use of 3 doses with an infection duration per animal of 3.5 days. Bolus detection with θ_1 = 12h and θ_{2+}= 48h (Fig. 5, black lozenge) reduced infection duration of 1.5 days at the expense of 1 additional dose. A later first detection (e.g. θ_1 = 48h: Fig. 5, light grey lozenge) required also an additional dose but was not as efficient for reducing infection duration (0.5 day gained). A shorter threshold for detecting subsequent cases (e.g. θ_{2+}= 48h: Fig. 5, black triangle) led to gain one more day in infection reduction but at the expense of another antibiotics dose. Other threshold combinations appeared less cost-effective.

Distributions of antibiotics doses (Fig. 6, left) and infection duration (Fig. 6, right) confirmed that bolus strategies based on a quick detection of first case and later detection of subsequent cases were efficient compared to visual appraisal. Antibiotics doses induced by bolus detection with θ_{2+} = 48h were similar to those required in the reference scenario. Infection durations were also reduced by early detection based on boluses. Doses and durations

associated to several values of θ_1 for a given value of θ_{2+} were closely distributed, which suggests that the main effect of small values of θ_1 consisted in reducing rare but extreme values in doses and infection duration: detecting infection early, even with a higher risk of false positives, is better than delaying detection of the first case with the risk of a broader spread, as long as the detection of subsequent cases is less subject to false positives.

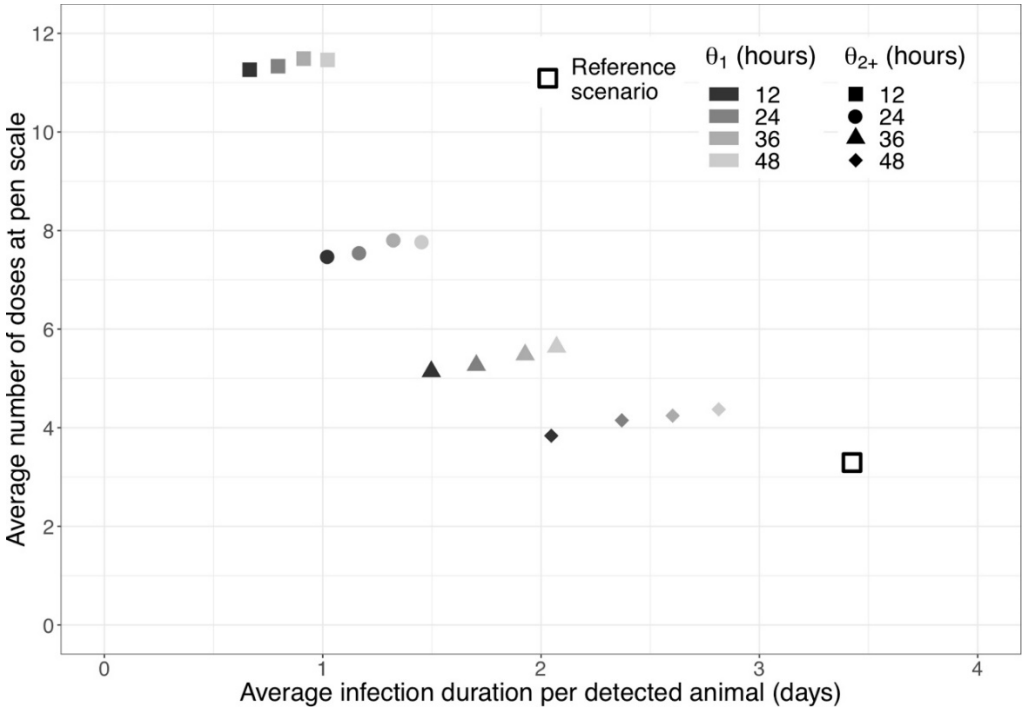

Fig. 5 Balance between infection duration (x axis) and antibiotics doses (y axis), depending on detection method (θ_M = "never", β = 0.01)

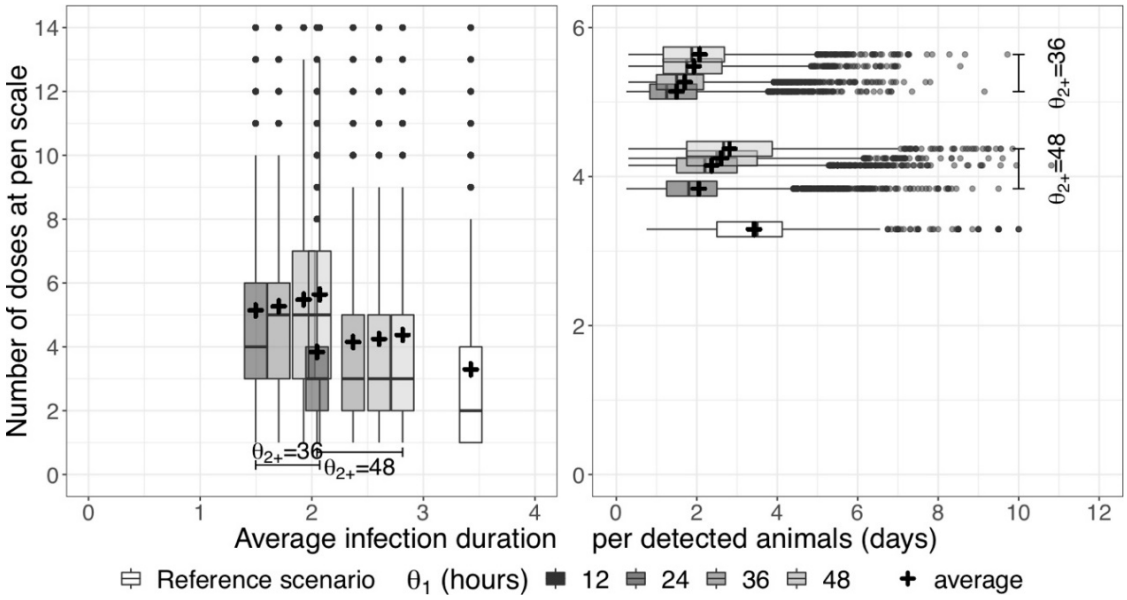

Fig. 6 Distribution of doses at pen scale (left) and infection durations (right) for the most efficient bolus-based detection strategies, compared to reference scenario (β = 0.01, θ_M = "never"). The horizontal (resp. vertical) position of each boxplot is the average individual disease duration (resp. number of doses) in corresponding simulations.

Results obtained with other values of pathogen transmission (β = 0.005 and 0.02) led to similar qualitative results. Bolus detection efficiency favoured high values of θ_{2+} combined with low values of θ_1 (Fig. 7). However, the choice of relevant values for hyperthermia thresholds θ_1 and θ_{2+} appeared to be dependent on transmission rate. At low values (Fig. 7, left), infection duration could easily be reduced by early detection, but keeping doses low required a precise tuning of θ_{2+} which mainly drove this output. Conversely, higher values (Fig. 7, right) required doses always above the feedlot size, which also corresponded to the level obtained with the reference scenario when using metaphylaxis (Fig. 3B). The interplay between the two thresholds was more complex, possibly leading to situations worse than the reference scenario regarding infection duration (Fig. 7, light grey lozenge). Because antibiotics doses are more numerous than for a low transmission rate, the decision of favouring the reduction of infection duration had a moderate relative cost in terms of dose number increase.

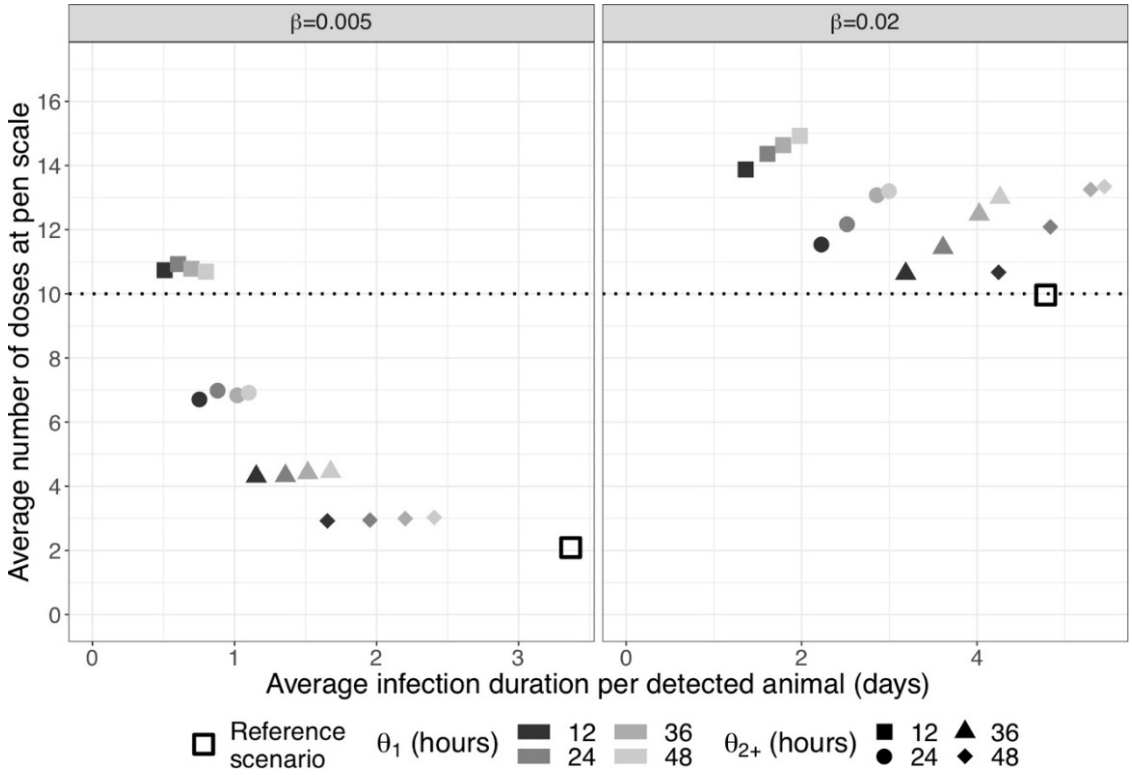

Fig. 7 Impact of the pathogen transmission rate on the balance between shortening infection duration and reducing antibiotics doses, depending on detection method (θ_M = "never")

DISCUSSION

We showed that early detection based on individual monitoring (here, the use of intraruminal boluses for detecting hyperthermia) could be used to reduce infection duration at a moderate cost compared to visually detectable clinical signs. The only way to overpass the reference scenario using boluses was to combine detection of short hyperthermia as first case with longer hyperthermia for subsequent cases, the difference in durations reducing with the force of infection. Other bolus usage also reduced disease duration but with more antibiotics doses used.

Metaphylaxis was less cost-efficient, especially for moderate pathogen transmission. When applied after a few cases detected by the appraisal of clinical signs followed by rectal

temperatures, metaphylaxis allowed to control BRD with nearly constant doses (pen size). Yet, such values can be overpassed by bolus-based detection for low or moderate pathogen transmissions, making metaphylaxis an interesting method at higher transmission rates. No situation was found where combining metaphylaxis with early detection was proved efficient. At such a small pen size, metaphylaxis dramatically increased antibiotics doses with a small proportion of truly infected among treated animals, due to non-infectious hyperthermia. The interest of metaphylaxis for larger populations, and the possibility to integrate finer-grained information in the triggering strategy (e.g. infection speed) is an interesting perspective.

Using EMULSION significantly speeds up model design, implementation, and testing, the BRD model development having required about 3 man-months, while developing, discussing, and revising individual-based models usually takes 1-2 years. Model integration into EMULSION required a small code add-on (160 lines in Python, excluding comments) for features specific to BRD. Thanks to the user-friendly language dedicated to epidemiological models, all assumptions and the model structure were kept intelligible in a short (516 lines) structured text file, which fostered constant interactions between scientists of complementary disciplines (epidemiological modelling, cattle medicine, computer science).

In addition to providing concrete recommendations to veterinarians and farmers, our approach could easily be adapted to other farming systems, other treatment protocols, and other diseases, due to the facility to change model assumptions using EMULSION. Interesting perspectives could be addressed such as the impact on disease management of a diversity of BRD pathogens co-circulating within the same population, or of a heterogeneity in animal susceptibility as related to risk factors associated to feedlot constitution.

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REFERENCES

Assié, S., Seegers, H., Makoschey, B., Désiré-Bousquié, L., and Bareille, N. (2009). Exposure to pathogens and incidence of respiratory disease in young bulls on their arrival at fattening operations in France. Vet. Rec. 165, 195–199

Edwards, T.A. (2010). Control Methods for Bovine Respiratory Disease for Feedlot Cattle. Vet. Clin. North Am. Food Anim. Pract. 26, 273–284

Ives, S.E. and Richeson, J.T. (2015). Use of Antimicrobial Metaphylaxis for the Control of Bovine Respiratory Disease in High-Risk Cattle. Vet. Clin. North Am. Food Anim. Pract. 31, 341–350

Lhermie, G., Toutain, P.-L., El Garch, F., Bousquet-Mélou, A., and Assié, S. (2017). Implementing Precision Antimicrobial Therapy for the Treatment of Bovine Respiratory Disease: Current Limitations and Perspectives. Front. Vet. Sci. 4

Mathieu, P., Morvan, G., and Picault, S. (2018). Multi-level agent-based simulations: Four design patterns. Simul. Model. Pract. Theory 83, 51–64

Picault, S., Huang, Y.-L., Sicard, V., and Ezanno, P. (2017). Enhancing Sustainability of Complex Epidemiological Models through a Generic Multilevel Agent-based Approach. In, Proceedings of the 26th International Joint Conference on Artificial Intelligence (IJCAI'2017). AAAI, Melbourne, Australia

Picault, S., Huang, Y.-L., Sicard, V., Hoch, T., Vergu, E., Beaudeau, F., and Ezanno, P. (2018). A generic multi-level stochastic modelling framework in computational epidemiology. bioRxiv 491605

Sanderson, M.W., Dargatz, D.A., and Wagner, B.A. (2008). Risk factors for initial respiratory disease in United States' feedlots based on producer-collected daily morbidity counts. Can. Vet. J. Rev. Veterinaire Can. 49, 373–378

Schaefer, A.L., Cook, N.J., Church, J.S., Basarab, J., Perry, B., Miller, C., and Tong, A.K.W. (2007). The use of infrared thermography as an early indicator of bovine respiratory disease complex in calves. Res. Vet. Sci. 83, 376–384

Taylor, J.D., Fulton, R.W., Lehenbauer, T.W., Step, D.L., and Confer, A.W. (2010). The epidemiology of bovine respiratory disease: What is the evidence for predisposing factors? Can. Vet. J. Rev. Veterinaire Can. 51, 1095–1102

Timsit, E., Assié, S., Quiniou, R., Seegers, H., and Bareille, N. (2011). Early detection of bovine respiratory disease in young bulls using reticulo-rumen temperature boluses. Vet. J. 190, 136–142

Warriss, P.D., Brown, S.N., Knowles, T.G., Kestin, S.C., Edwards, J.E., Dolan, S.K., and Phillips, A.J. (1995). Effects on cattle of transport by road for up to 15 hours. Vet. Rec. 136, 319–323

White, B.J. and Renter, D.G. (2009). Bayesian Estimation of the Performance of Using Clinical Observations and Harvest Lung Lesions for Diagnosing Bovine Respiratory Disease in Post-weaned Beef Calves. J. Vet. Diagn. Invest. 21, 446–453