Heuristic optimisation of the management strategy of a plant epidemic using sequential sensitivity analyses

<u>Short title</u>: Optimisation of plant disease management strategies

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Abstract

- Optimisation of management strategies of epidemics is often limited by constraints on experiments at large spatiotemporal scales. A promising approach consists in modelling the biological epidemic process and human interventions, which both impact disease spread. However, few methods enable the simultaneous optimisation of the numerous parameters of sophisticated control strategies. To do so, we propose a heuristic approach based on sequential use of sensitivity analysis. This work is motivated by sharka (caused by *Plum pox virus*), a vector-borne disease of prunus trees (especially apricot, peach and plum), and its management in orchards, mainly based on surveillance and tree removal.
- Our approach is based on three sensitivity analyses which respectively aim to: i) identify the key parameters of a spatiotemporal model simulating disease spread and control; ii) approach optimal values for the key parameters; iii) refine the optimisation.
- We highlight the importance of carefully designing the removal procedure, and propose improved strategies with regard to an economic criterion accounting for both the cost of the different control measures and the benefit generated by productive trees.
- We expect that our general approach will help policymakers to design sustainable and cost-effective strategies for the management of infectious diseases.

Keywords: cost-effectiveness, culling, PPV, roguing, SEIR, Sobol.

Introduction

Optimising large-scale disease management constitutes a major challenge. Faced with the urgent need to deal with emerging epidemics, one often relies on expert opinions to design management strategies for infectious diseases, but they are not necessarily based on quantitative data. Some specific control methods can be tested through field trials, but they constitute only part of a global management strategy, which must be assessed at large spatiotemporal scales. However, at such scales field trials are considerably limited by tractability issues arising from ethical, regulatory, or logistical constraints. Epidemiological models represent one promising approach to overcome these obstacles and to account for the numerous interactions between biological processes and human interventions that jointly impact disease spread. The key epidemiological parameters of these models constitute prime targets for control measures. As shown for plant viruses (Chan & Jeger, 1994; Jeger & Chan,

1995; Holt *et al.*, 1999; Rimbaud *et al.*, 2018a), plant fungi (Xu & Ridout, 1998; Papaïx *et al.*, 2014) and invasive plants (Coutts *et al.*, 2011), these parameters can be identified using global sensitivity analysis. By varying input parameters of a simulation model within their respective variation ranges, this statistical method allows the computation of 'sensitivity indices' which represent the influence of the variability of each input parameter on a given output variable (Saltelli *et al.*, 2008). The same approach may be used for simulation models that explicitly account for control actions and their potential interactions with epidemiological processes.

Some epidemiological models aim to assess the potential of different control actions in various epidemic scenarios (simulated using different combinations of epidemiological parameters). In this context, studies dealing with the management of perennial plant diseases have addressed management strategies based on roguing and possibly replanting (Parnell *et al.*, 2009; Parnell *et al.*, 2010; Filipe *et al.*, 2012; Sisterson & Stenger, 2013; Cunniffe *et al.*, 2014; Cunniffe *et al.*, 2015; Cunniffe *et al.*, 2016; Hyatt-Twynam *et al.*, 2017), planting with different densities (Chan & Jeger, 1994; Jeger & Chan, 1995; Cunniffe *et al.*, 2014; Cunniffe *et al.*, 2015), planting at distances that are isolated from contaminated areas (Chan & Jeger, 1994; Jeger & Chan, 1995; Filipe *et al.*, 2012), or spraying with insecticides (Filipe *et al.*, 2012). These studies proposed some optimal control parameters under various epidemiological scenarios, but mostly for one or two control parameters—the other parameters being fixed at their reference value.

An alternative approach is to use global sensitivity analysis to jointly explore numerous combinations of control parameters and identify a combination which maximise (or minimise) a criterion. In the present study, we perform a set of global sensitivity analyses of a model which jointly simulates an epidemic process and a flexible management (meta-)strategy. For this, we use Sobol's method, which is a reference method to compute sensitivity indices of model parameters and their interactions (Saltelli *et al.*, 2008). This method proved able to account for model stochasticity by replicating the simulations for all parameter combinations (e.g. Rimbaud *et al.*, 2018a).

The selection of a relevant criterion is a crucial task in an optimisation procedure. Epidemiological criteria that have been minimised for management optimisation include disease incidence (Xu & Ridout, 1998; Holt *et al.*, 1999), prevalence (Lurette *et al.*, 2009; Courcoul *et al.*, 2011), severity (Xu & Ridout, 1998), propagation rate (Coutts *et al.*, 2011; Filipe *et al.*, 2012), basic reproduction number (Chan & Jeger, 1994), proportion of infected plants

at the end of the simulation (Sisterson & Stenger, 2013), probability of pathogen establishment (Papaïx *et al.*, 2014), time until eradication (Jeger & Chan, 1995; Parnell *et al.*, 2009; Parnell *et al.*, 2010; Barclay & Vreysen, 2011; Courcoul *et al.*, 2011), or proportion/number of removed trees required to achieve eradication (Parnell *et al.*, 2009; Hyatt-Twynam *et al.*, 2017). Interestingly, the two last criteria aim to reduce the cost of the management strategy, which may be huge if disease eradication is intended. Nevertheless, to be feasible and sustainable, the choice of a management strategy must be guided by the balance between the costs induced by control actions and the economic benefits of the reduction of epidemic damage (Fraser *et al.*, 2004; Forster & Gilligan, 2007). Here, we solve this issue by proposing: i) an epidemiological criterion based on the number of productive hosts, and ii) an economic criterion based on the present value of the flow of benefits generated by productive hosts (i.e. harvest sales), minus the costs induced by different control actions.

Our approach is applied to sharka, the most damaging disease of prunus trees (Cambra *et al.*, 2006). Its causal agent, *Plum pox virus* (PPV, genus *Potyvirus*), is naturally transmitted by more than 20 aphid species in a non-persistent manner (Labonne *et al.*, 1995) and has spread worldwide due to human shipping and planting of infected material (Cambra *et al.*, 2006). Faced with the threat posed by sharka, various management strategies have been adopted in different countries (for a review, see Rimbaud *et al.*, 2015). In countries targeting disease limitation (e.g. France) or eradication (e.g. United States), a key element of the management strategy is the appropriate surveillance of nurseries and orchards, followed by tree removals. Surveillance methods rely on leaf sampling followed by serological or molecular diagnostics, or, alternatively, visual inspection of prunus trees to detect sharka symptoms (mostly on leaves and fruits). When infected trees are detected, they are culled to remove viral sources contributing to epidemics. Regardless of the surveillance method, the infection may be detected only several months or years after inoculation (Sutic, 1971; Quiot *et al.*, 1995). This delay hampers the detection of infected hosts and explains, combined with evidence of short-distance transmission of PPV (Dallot *et al.*, 2003; Gottwald *et al.*, 2013; Pleydell *et al.*, 2018), why non-symptomatic trees surrounding detected trees may need to be removed as well. In France, sharka management is compulsory and a national decree specifies the control actions mentioned above (JORF, 2011). In particular, this decree describes a complex procedure defining the frequency of visual inspections of orchards depending on

their distance to the nearest detected infection, the removal of whole orchards if their annual contamination rate exceeds a given threshold, and the conditions for replanting. Since this strategy is complex and based on expert opinions, it is crucial to conduct a cost-benefit analysis and identify potential improved management rules.

To identify improved alternatives to the current French management strategy, we propose a heuristic approach based on sequential sensitivity analyses of a stochastic spatiotemporal simulation model. This model simulates prunus cultivation in a real agricultural landscape (553 patches, representing a total area of 524 ha) with recurrent introductions of the pathogen through orchard plantings and its subsequent spread via aphid vectors, and its management with a flexible strategy. This strategy is defined by 24 parameters (14 for surveillance, 6 for removals and 4 for replanting restrictions; see Fig. 1 and Table 1 for details) and encompasses the management strategies of several countries, including France. Consequently, the identified strategies should be of interest for many countries targeting area-wide management of sharka and more generally perennial plant diseases.

Results

In a first step, we identified the most promising control measures to manage sharka, by ranking the control parameters by influence on both our epidemiological criterion (average number of fully productive trees per hectare and per year, μ_Y) and our economic criterion (average net present value over a period of 30 years, μ_{NPV}, measuring the discounted difference between benefits of fruit sales and costs generated by the management of all orchards of the landscape). In a second step, only the most influential control measures were retained and sensitivity analysis was used to approach an optimal combination of control parameters with regard to the economic criterion. In the last step, this optimisation was further refined using another sensitivity analysis. The identified management strategies were evaluated on simulated epidemics, in order to assess their epidemiological and economic performance relative to the current French strategy, as well as their robustness to stronger epidemics.

Step 1: identifying the most promising control parameters

The first sensitivity analysis showed that the predicted economic impact strongly depends on the contamination threshold of the 'epicentre for removal' (χ_R, above which

orchards in the removal zone are culled; with a total sensitivity index (SI_{tot}) of 0.54; CI_{95}: 0.39-0.65) and the contamination threshold in orchards of the neighbourhood of a previously culled orchard (χ_n, above which replanting is forbidden; SI_{tot} of 0.36; CI_{95}: 0.25-0.45) (Fig. 2). These parameters were also the main contributors to model stochasticity (Fig. S1). Next came the radius of the removal zone (ζ_R, SI_{tot} of 0.15; CI_{95}: 0.08-0.20), then a Boolean variable indicating whether whole orchards are removed immediately or at the end of the year (Υ_R, SI_{tot} of 0.13, CI_{95}: 0.06-0.18), followed by the detection probability (ρ; SI_{tot} of 0.09; CI_{95}: 0.07-0.12) and the size of the removal epicentre–where the contamination rate is measured to assess if orchards in the removal zone must be culled–($r_{\zeta_{eR}}$; SI_{tot} of 0.09; CI_{95}: 0.05-0.12). The effect of all of these parameters seems to be mostly due to interactions with other parameters, since their total Sobol indices were much higher than their 1st-order indices. This probably explains why it was difficult to predict the net present value (NPV) from the values of ζ_R, Υ_R or $r_{\zeta_{eR}}$ only (Fig. 2, insets). The strong impact of removal and planting measures is likely due to excessive tree removals or orchard planting bans, when the respective contamination thresholds are low (below 5% for removals and below 10% for planting bans; Fig. 2, insets). However, for higher thresholds, μ_{NPV} remained stable, suggesting that these parameters no longer have an effect. This may be the sign of an absence (or rarity) of high contamination events in orchards or in removal epicentres (and thus of extremely rare planting bans or removal of whole zones). Finally, the quadratic effect of ρ reveals the existence of a trade-off between detection efficiency and the costs induced by orchard surveillance.

Interestingly, the 11 least influential parameters (5 epidemiological parameters and 6 control parameters) had very low total sensitivity indices (less than 0.03), which indicates a negligible effect of their variation on the mean output. Control actions governed by these parameters have little effect on the economic impact of epidemics, compared to the parameters discussed above. Similar conclusions emerged from the analysis of the epidemiological output of the model (Fig. S2). Consequently, the 6 least influential control parameters, governing the control measures with the highest degree of complexity (surveillance and planting ban reinforcement in locally highly contaminated areas), $r_{\chi_{y*}}$, η_{f*}, χ_O, $r_{\zeta_{eO}}$, η_{y*} and $\chi_{\bar{y}}$, were removed in the next step in order to simplify the model in the context of sharka management.

Step 2: approaching optimal values of control parameters

A second sensitivity analysis was performed on the control parameters only, except for the 6 parameters discarded in step 1. Optimal values of the 17 control parameters were approached either by using the parameter combination leading to the best μ_{NPV} ('best-value strategy'), or the combinations leading to the best percentile of μ_{NPV} ('best-percent strategy'). In both approaches, management is improved when detected trees are removed immediately (i.e. after an average of 10 days, rather than at the end of the year; see $\Upsilon_R{}^T$ in Fig. 3). The obtained values for the removal threshold (χ_R), and the radius of the removal zone (ζ_R) and its epicentre ($r_{\zeta_{eR}}$, where contamination rate is measured) were so high that no removal of whole orchards may occur in the associated simulations (see χ_R in Fig. 3 and all other parameters in Fig. S3). In addition, small values for these parameters (χ_R< 5%; ζ_R < 2 km; $r_{\zeta_{eR}}$ < 20%) were associated with the worst epidemics (last percentile of μ_{NPV}). These results suggest that in our model, removal of healthy hosts induces higher costs than the maintenance of undetected or latently infected hosts. With regard to observations, either the focal area matched approximately the security area (r_{ζ_f}, 'best-value strategy'), or the observation frequencies in these zones were the same (η_f and η_s, 'best-percent strategy'). This indicates that the distinction of two different zones may not be necessary. Thus the control actions governed by parameters χ_R, ζ_R, $r_{\zeta_{eR}}$, Υ_R, r_{ζ_f} and η_f were discarded in the next step.

Step 3: refining the optimisation

A third sensitivity analysis was performed on the 10 remaining control parameters to further refine their optimisation. In this analysis, variation ranges of the target parameters were restricted to the most probable optimal values (see ρ in Fig. 3 and all other parameters in Fig. S3). Then, the optimisation procedure was exactly the same as in step 2 (Fig. 3 and Fig. S4). The resulting 'best-value' and 'best-percent' strategies are significantly simpler than the current French strategy (Fig. 4). To summarise the best-value strategy, every time a symptomatic tree is detected in an orchard, this orchard is surveyed three times per year for the three following years (Table 2, reference epidemic context). Whole orchards are removed only if the proportion of living trees falls below χ_{SEHD}=0.66 (for profitability reasons, see Methods and Table S1), and in this case they can be replanted without delay. Nevertheless, replanting is forbidden within a radius of 2.8 km if the contamination rate of an orchard

exceeds 60% (i.e. in case of a massive introduction, in our simulations). In areas where no infected tree has been detected in the three previous years, orchards are surveyed once every four years. The detection probability is 36%, meaning that orchard are surveyed in approximately one every two rows under our assumptions.

Alternatively, in the best-percent strategy (Table 2), each time a symptomatic tree is detected, the orchard is surveyed once in the following year. Similar to the best-value strategy, whole orchards may only be removed for profitability reasons, and can be replanted without delay (except in the unlikely event of a contamination rate higher than 92% in an orchard within a radius of 962 m). In the first year after planting, young orchards are surveyed once. Older orchards in non-contaminated areas are routinely surveyed every four years. The detection probability is 60% (i.e. close to the reference value).

Simulation of the improved strategies

Repeated simulations of the identified improved strategies were carried out in order to compare their epidemiological (Y) and economic (NPV) outcomes with those obtained in disease-free and management-free scenarios, and with the reference management (i.e. the current strategy for managing sharka in France). Firstly, these simulations show that managing the disease is vital, since the median number of productive trees per hectare and per year is only 513 and is highly variable [2.5%; 97.5% quantiles: 462; 551] compared to the disease-free scenario (median number of 560 trees [551; 569]) (Fig. 5a). This results in a 59% decrease in the median NPV (6.03 million euros [-4.06; 13.0] in the absence of management, *vs* 14.6 million euros [13.5; 15.7] in the absence of disease), and possibly huge economic losses in the worst-case scenarios (Fig. 5b). It is interesting to note that, in our model, the reference strategy is very efficient with respect to the reduction of direct losses to sharka (median of 559 productive trees per ha and per year [550; 569]). Nevertheless, the costs associated to disease management considerably reduce the NPV (12.1 million euros [10.7; 13.4]). This NPV is 17% lower than in the disease-free scenario, but still much higher than in the absence of management. The improved best-value and best-percent strategies are nearly as efficient as the reference strategy with regard to the number of productive trees, but resulted in similar reduced costs, with a median NPV of 13.7 [12.2; 15.0] and 13.7 [11.7; 15.0] million euros, respectively. These management strategies are associated with slightly higher disease incidence and prevalence than for the current French strategy (Fig. S5, top line). This results

in more individual tree removal, but is overly compensated by the smaller number of observations in orchards (Fig. S6, top line). Consequently, both of these strategies are more cost-effective.

When tested in harsher epidemiological contexts with half expected duration of the latent period of the pathogen (θ_{exp}), the identified management strategies were still efficient with respect to both the epidemiological (Y) and economic (NPV) criteria (Fig. S7a,b). However, with doubled transmission coefficient (β), the improved management strategies (in particular the best-percent strategy) were not as efficient as the reference scenario (Fig. S7c,d). This resulted in higher levels of disease prevalence and incidence (Fig. S6, bottom line) and consequently more tree removals (Fig. S7, bottom line). In contrast, the reference management strategy was robust to the simulated changes in epidemic severity (Figs. S5, S6, S7). We re-ran the whole heuristic optimisation approach with shorter latent period or stronger transmission coefficient. The new identified strategies, indicated in Table 2, mainly differ from the previous ones by the increased surveillance frequency of contaminated and non-contaminated orchards, as well as by the introduction of a delay before orchard replanting. These new strategies satisfy both epidemiological and economic performance criteria (Figs. S8, S9).

Discussion

Optimising management strategies of epidemics

In this article, we propose an innovative heuristic approach based on the sequential use of global sensitivity analysis of a simulation model to improve management strategies of plant disease epidemics. Following the identification of the most promising control measures (step 1), the exploration of parameter space, initially large (step 2) and then more restricted (step 3), enables a simplification of the strategy and the joint improvement of the control parameters by progressively approaching an optimal combination. One can note that further sensitivity analyses could be performed if more accuracy is required for some parameters. In contrast with previous studies focussing on a restricted number of control parameters (e.g. Parnell *et al.*, 2010; Cunniffe *et al.*, 2015; Hyatt-Twynam *et al.*, 2017), our approach includes a wide range of management strategies and enables to jointly improve the entire set of control parameters.

Accounting for the long-term costs and benefits of disease control is crucial to the design of feasible, durable, and cost-effective management strategies (Fraser *et al.*, 2004; Forster & Gilligan, 2007), which in turn, will increase the likelihood of adoption by growers. Some recent studies proposed approaches to prioritise surveillance or removal options under limited resources (Cunniffe *et al.*, 2016; Faulkner *et al.*, 2016). Other studies proposed optimised management of different perennial plant diseases using a composite criterion which includes the number of disease-induced deaths and removals of trees (i.e. proxies for intrinsic costs of the epidemic and the management, respectively) and the time to eradication (Cunniffe *et al.*, 2015), or accounting for the cost of observation of a single tree relative to the net profit generated by the cultivation of this tree (Cunniffe *et al.*, 2014). Here, we developed an economic criterion which explicitly accounts for the benefits generated by the cultivation of productive hosts (i.e fruit sales), and the costs induced by orchard cultivation plus different control actions comprising observations, removals, replantings and planting bans. By doing so, the different components of the management strategy can be optimised with explicit consideration of their cost relative to the benefit due to the reduction of epidemic damage. Although this criterion was specifically parameterised for peach orchards, it could easily be employed for other crops by reassessing the costs and benefits associated with their cultivation and disease management. Finally, we also used an epidemiological criterion to assess the epidemiological efficiency of the identified optimised strategies. This metric integrated the number of productive hosts across the whole landscape and the whole simulation period, and is therefore comparable to the 'healthy area duration' used in many epidemiological models (e.g. Lo Iacono *et al.*, 2013; Rimbaud *et al.*, 2018b; Papaïx *et al.*, early view).

Managing perennial plant epidemics and especially sharka

This work was motivated by the management of sharka, a viral disease of prunus trees against which a complex management strategy is currently applied in France. Once implemented in our simulation model, this strategy provided a particularly relevant reference point because it represents management strategies for numerous perennial plant diseases, based on surveillance, removals and replanting restrictions (Fig. 1). We note, however, that some control actions (for which we had no cost/benefit values) were not investigated in our model, like nursery protection measures or planting at different densities. In addition, vector

290 control by pesticides, shown to be efficient against some diseases like citrus huanglongbing
291 (Lee *et al.*, 2015), was not studied here because pesticides generally fail with non-persistent
292 viruses such as PPV (Perring *et al.*, 1999; Rimbaud *et al.*, 2015).

293 **Identifying promising control measures.** The first sensitivity analysis highlighted the
294 most influential control parameters on sharka epidemics in French peach orchards. These
295 were associated with the removal of orchards, the ban on plantings and the probability of
296 detection (Fig. 2). These elements highlight the importance of modelling studies designed to
297 optimise detection efficiency (e.g. using hierarchical sampling, Hughes *et al.*, 1997), and
298 removal actions (e.g. by identifying an optimal cull-radius, Parnell *et al.*, 2009; Parnell *et al.*,
299 2010; Cunniffe *et al.*, 2015; Cunniffe *et al.*, 2016).

300 Ranking model parameters by their influence on a given output variable also allows the
301 identification of weak contributors. Among the implemented control parameters, those
302 associated with the modification of surveillance in response to observed local prevalence had
303 a negligible impact on both epidemiological and economic outcomes (Fig. 2). Therefore, in the
304 scenarios we investigated, reinforcing surveillance in highly contaminated areas may not
305 result in improved management. Thus, the associated parameters could be discarded from
306 the modelled management strategy without altering its efficiency. It is important to note that
307 we assumed that each symptomatic tree had the same detection probability, regardless of its
308 age, cultivar and time elapsed since symptom expression. Nevertheless, field experience
309 shows that all these factors impact symptom expression and consequently visual detection.
310 Moreover, detection events were considered independent, which enabled an excellent global
311 detection rate after a few observation rounds. These elements could partly explain why
312 reinforcing surveillance in highly contaminated areas had a negligible impact.

313 In previous studies, the connectivity of the patch of first introduction was the most
314 influential epidemiological parameter on sharka spread in the absence of management
315 (Rimbaud *et al.*, 2018a). It is still the case here, in presence of management (Fig. 2, parameter
316 q_{κ}). This result suggests that reinforced baseline surveillance of highly connected patches
317 could be a promising control measure. This result also supports the need to match
318 management efforts with the risk index of different patches (Nelson *et al.*, 1994; Barnes *et al.*,
319 1999; Parnell *et al.*, 2014) or individual hosts (Hyatt-Twynam *et al.*, 2017) and to prioritise such
320 management under limited resources (Cunniffe *et al.*, 2016; Faulkner *et al.*, 2016). Favouring

321 the planting of resistant cultivars in patches with high risk indices could also be a promising
322 approach for disease management.

323 **Improving the management strategy.** Our results suggest that removing whole orchards
324 triggers higher costs than potential losses associated with maintaining cryptically infected
325 hosts. The identified improved strategies are thus based on a 'symptomatic hosts hunt' (Fig.
326 4). However, orchard surveillance to identify these symptomatic hosts also induces high costs.
327 Thus, in contaminated orchards, improved strategies relied either on few surveillance rounds
328 with a good probability of detection (close to the reference value), or a greater number of
329 surveillance rounds with a low probability of detection (half the reference value, which may
330 correspond to the orchard surveillance of every other row only, and was assumed here to
331 trigger smaller costs per surveillance round). Overall, while surveying an orchard more than
332 once a year multiplies the cost, it favours the detection of trees which may be cryptically
333 infected at the time of the first round of surveillance.

334 These surveillance procedures, and the absence of removal zones, make these strategies
335 simpler and less expensive than the current French management of sharka (Fig. 5).
336 Nevertheless, in the improved strategies, the basic frequency of orchard surveillance is
337 increased to once every four years (instead of once every six years for the reference
338 frequency). This indicates that better management should be obtained by more frequently
339 surveying all orchards in a region. Indeed, costs of management can be considerably
340 decreased by prompt implementation of control measures after new introductions (Cunniffe
341 *et al.*, 2016).

342 With respect to the improved strategies identified here, we note several assumptions
343 which may influence our recommendations. In particular, the ability to detect symptomatic
344 hosts may have been overestimated, as explained above. Consequently, in the field and under
345 certain conditions, it might still be interesting to rogue whole orchards (or even nearby
346 orchards if eradication is intended) in order to remove hardly detectable diseased trees.
347 Additionally, it may be interesting to investigate the potential of alternative detection
348 protocols, like serological or molecular methods, which are used for the management of
349 several perennial plant epidemics (including sharka) in the United States (Gougherty *et al.*,
350 2015). Such investigation could be performed with our model by changing the relationship
351 between the probability of detection and the cost of surveillance. Furthermore, we assumed

352 that all orchards had the same susceptibility to PPV. However, evidence suggests that young
353 plants may be more susceptible to viral infection than older ones (Astier *et al.*, 2007). Thus, in
354 our results, surveillance of young orchards was probably not as crucial as it should be.

355 Despite these considerations, the best-value and best-percent strategies deserve to be
356 investigated in order to improve cost-efficiency of sharka management. Globally, these
357 options are based on the simplification of surveillance and removal measures to reduce
358 management costs while maintaining good epidemiological performance. However, our
359 results show that these strategies may fail to control disease in harsh epidemic contexts. For
360 these situations, the flexibility of our approach allowed us to identify new strategies,
361 illustrating its general ability to find improved combinations of control parameters in a given
362 epidemic context.

363 Methods

364 Model description

365 **Model overview.** A stochastic, spatially-explicit, SEIR (susceptible-exposed-infectious-
366 removed) model was previously developed to simulate sharka epidemics in a cultivated
367 landscape (Pleydell *et al.*, 2018; Rimbaud *et al.*, 2018a). The model is orchard-based, with a
368 discrete time step of 1 week. Each host is in one of five different health states (Fig. 1a). The
369 epidemic process and the transitions between states are described in previous articles
370 (Pleydell *et al.*, 2018; Rimbaud *et al.*, 2018a), and summarised in Method S1. Briefly, healthy
371 trees (state S) become infected (state E) when successfully inoculated by infectious aphid
372 vectors. After a latent period, infected trees become infectious and symptomatic (state H),
373 from where they may be detected (state D) and subsequently culled (state R). It is assumed
374 that infectious trees are no longer productive, due to either diseased-induced reduction of
375 fruit yield, or a sales ban on fruit from symptomatic trees. However, the disease is not
376 supposed to affect host lifespan (no available data reported any increase in prunus mortality
377 due to PPV), thus hosts can move to state R only if removed. Due to orchard turnover
378 (independent from the disease), whole orchards can be replaced by trees in state S (or possibly
379 H). Table 1 summarises all the model parameters.

380 A management strategy, based on orchard surveillance and tree removal, is applied
381 after a_m=6 years of epidemic during 30 years, which is twice the mean lifespan of the hosts

382 and consequently a reasonable duration in which to assess the efficiency of a management
383 strategy. The reference management strategy is based on the French management of sharka
384 in prunus orchards (JORF, 2011). Nevertheless, our model allows a multitude of variations on
385 each control measure, which makes it possible to include some aspects of sharka management
386 in other countries (e.g. removal radius around detected trees, as done in the United States,
387 Gottwald *et al.*, 2013).

388 **Orchard surveillance.** All orchards in a region are effectively surveyed for disease at least
389 once every $1/\eta_0$ years, and at each survey symptomatic hosts (state H) are independently
390 detected with probability ρ. Detected trees trigger the definition of two nested zones around
391 their orchard: a security zone whose radius is ζ_s, and a focal zone whose radius is ζ_f (Fig. 1b).
392 Within security and focal zones, orchards are surveyed η_s and η_f times per year, respectively,
393 during γ_o years. Furthermore, in the focal zone the surveillance frequency is changed to η_{f*} if
394 the contamination rate of the epicentre exceeds a threshold value χ_o (see Method S2 for
395 calculation of the contamination rate). The 'observation epicentre', whose radius is ζ_{eO},
396 corresponds to a fraction of the focal area where the contamination rate (noted q_{eO}) is
397 calculated. Additionally, young orchards are surveyed η_Y times per year during γ_Y years, but
398 this frequency is changed to γ_{Y*} if the contamination rate of the environment around the patch
399 to be planted exceeds a threshold value χ_{y*} (Fig. 1c). The environment is a zone around the
400 patch to be planted; its radius is ζ_{eO} (i.e. the same as the observation epicentre).

401 When an orchard falls simultaneously within several surveillance zones, the maximal
402 surveillance frequency is applied. The observation dates are drawn from a uniform distribution
403 between the 92th and the 207th day of the year, i.e. the earliest and the latest observation
404 dates in the database collected in southeastern France, respectively. If the cultivar produces
405 flowers with petals (on which symptoms may be observed), the observation period is
406 extended from the 59th to the 207th day (Fig. S10).

407 **Removals and replantings.** Detected trees are removed individually and are not
408 supposed to be replanted, because it would lead to orchard desynchronization in terms of
409 phenology and fruit maturation. Moreover, if contamination rate q_{eR} in the 'removal
410 epicentre' (defined by a radius ζ_{eR}) exceeds a threshold value χ_R, all orchards inside the
411 removal zone (whose radius distance is ζ_R) are removed as well (Fig. 1d). Two Boolean
412 variables, Y_R^T and Y_R, indicate whether individual detected trees or whole orchards,
413 respectively, are to be removed after a mean delay of δ, or at the end of the year. To avoid

excessive fragmentation of orchards due to individual removals, orchards are totally removed if the proportion of living trees (i.e. trees in all health states except R) falls below χ_{SEHD}, which is a threshold for economic profitability (see details in Table S1).

Orchards can be replanted after a delay of γ_S years. However, planting is forbidden if the contamination rate of the environment exceeds a threshold value $\chi_{\bar{y}}$, or if an orchard located at a distance below ζ_n has a contamination rate above a threshold value χ_n (Fig. 1c).

Output variables. The model generates two output variables. The epidemiological output, noted Y, is the mean equivalent number of fully productive trees per hectare per year, from the first (a_m=6) to the last (a_f=35) year of management. In this criterion, fully described in (Rimbaud *et al.*, 2018a), mature trees count for 1 whereas diseased and newly planted trees count for 0.

The economic output (used as an optimisation criterion in our approach based on sensitivity analyses) is based on the net present value (in euros) of prunus cultivation over the same time period (years 6 to 35). Considering the whole landscape as a single 'farm' with all the benefits and costs associated with prunus cultivation and sharka management, the gross margin, noted GM_a, of this farm can be calculated for year a (a=a_m,..., a_f) as the benefit generated by fruit production and sale (p), minus fixed cultivation costs (c_F), orchard planting cost (c_S), orchard observation cost (c_O), and the cost of removal of a tree (c_R^T) or a whole orchard (c_R). Reference values for these economic parameters were estimated (Table S1) based on expert opinions, as well as data on French peach production (Agreste, 2013, 2014, 2015), selling price (FranceAgriMer, 2015), and consumer price index (INSEE, 2015). The cost of one orchard observation is described by a simple linear function of the detection probability: $c_O = 40 + 182 \times \rho$, to account for the effect of partial observation of orchards (e.g. surveillance of every other row only), which reduces both the probability of detection and the cost of observation. Thus, GM_a is calculated as follows:

$$GM_a = \sum_{i=1}^{I} \left\{ y_{i,a}.p.\frac{S_{i,a}+E_{i,a}}{N_{i,a}}.A_i - c_F.A_i - \mathbb{I}_{i,a}^{R}.c_R.A_i - \mathbb{I}_{i,a}^{S}.c_S.A_i - c_R^T.R_{i,a}^{+} - c_o.O_{i,a}.A_i \right\},$$

with, for orchard i in {1, … , I} during year a:

$y_{i,a}$ the relative age-dependent fruit yield of the hosts in S and E states;

A_i the orchard area (ha);

$\frac{S_{i,a}+E_{i,a}}{N_{i,a}}$ the proportion of the orchard that produces fruits;

$O_{i,a}$ the number of observations;

$R^{+}_{i,a}$ the number of newly (individually) removed trees due to PPV detection;

$\mathbb{I}^{R}_{i,a}$ a Boolean which equals 1 if the orchard is removed, and 0 otherwise;

$\mathbb{I}^{S}_{i,a}$ a Boolean which equals 1 if the orchard is planted, and 0 otherwise.

Using a discount rate τ_a=4% (Quinet, 2013), the net present value (NPV) for the landscape from a_m to a_f is:

$$NPV = \sum_{a=a_m}^{a_f} \frac{GM_a}{(1+\tau_a)^{(a-a_m)}}.$$

Management improvement through sequential sensitivity analyses

Improvement of the management strategy was performed using three sensitivity analyses. For these analyses, we used Sobol's method, which consists of: i) defining the target parameters, their respective variation ranges and probability distributions (uniform, in this work); ii) generating a design to explore the parameter space; iii) running simulations; and iv) computing Sobol's sensitivity indices which quantify the influence of the variation of each target parameter on the output variable (Saltelli *et al.*, 2008). The 1st-order sensitivity index of a parameter, noted SI_1, measures the main effect of this parameter whereas the total sensitivity index, noted SI_{tot}, accounts for its interactions with other parameters. These indices are bounded by 0 and 1, thus a total index close to 0 means that the parameter has a negligible effect on the output variable.

Sobol's method requires that exploration of the parameter space be performed using independent distributions to sample the target parameters. Thus, since the focal zone, the epicentre for observation and the epicentre for removal are nested in the security zone, the focal zone and the removal zone, respectively, these zones were re-parameterised using the following area ratios:

$r_{\zeta_f} = \frac{\pi \times \zeta_f^2}{\pi \times \zeta_s^2} = \left(\frac{\zeta_f}{\zeta_s}\right)^2$, $r_{\zeta_{eO}} = \left(\frac{\zeta_{eO}}{\zeta_f}\right)^2$, and $r_{\zeta_{eR}} = \left(\frac{\zeta_{eR}}{\zeta_R}\right)^2$.

In addition, the contamination threshold, above which the observation frequency in young orchards is modified, was re-parameterised using its ratio relative to the contamination threshold above which replanting is forbidden: $r_{\chi_{y*}} = \frac{\chi_{y*}}{\chi_{\bar{y}}}$.

Step 1: assessing the relative influence of model parameters. The 23 control parameters defined in the implemented management strategy were targeted in this first step,

473 in addition to 6 parameters associated with the main epidemiological processes (introduction:
474 q_κ, Φ, and p_{MI}; dispersal: W_{exp}; transmission coefficient: β; and latent period duration: θ_{exp}).
475 Except for q_κ and p_{MI}, variation ranges were defined as the 99% credibility intervals of the
476 parameter estimates provided by a Bayesian inference model applied to PPV-M epidemics in
477 southeastern France (Pleydell *et al.*, 2018). In contrast, variation ranges of q_κ, p_{MI} and the 23
478 control parameters were defined as their respective domain of definition, possibly restricted
479 using expert opinions when this domain was infinite (Table 1).

480 Simulations were performed for 310,155 different parameter combinations generated
481 with Sobol sequences (Sobol, 1976). To account for stochasticity, each combination was
482 replicated 30 times (this number was found to be largely sufficient to generate robust
483 estimates of the mean and standard deviation associated with each combination; Fig. S11).
484 Then, the indices were calculated as in (Rimbaud *et al.*, 2018a) on the standardised means and
485 standard deviations of the epidemiological (μ_Y and σ_Y) and economic (μ_{NPV} and σ_{NPV}) criteria.

486 **Step 2: approaching optimal values of the most influential parameters.** In the second
487 step, only the most influential control parameters (i.e. those with the highest SI_{tot}) identified
488 in the first step were retained. The 17 remaining parameters were varied within the same
489 variation ranges as previously (Table 1), using 310,156 different parameter combinations and
490 30 stochastic replicates. In this sensitivity analysis, the 6 epidemiological parameters were not
491 targeted, but for each simulation they were drawn from uniform distributions using the same
492 bounds as in the previous step, in order to optimise the management strategy for variable
493 epidemics.

494 A heuristic joint optimisation of the 17 control parameters was obtained by isolating the
495 parameter combination associated with the highest μ_{NPV} ('best-value strategy'). Additionally,
496 a marginal optimisation of the same parameters was achieved using the mode of the
497 distribution of each parameter within the combinations associated with the best 1% values of
498 μ_{NPV} ('best-percent strategy'). A similar approach allowed identification of the parameters
499 associated with the worst 1% values of μ_{NPV}. It is important to note that the first method
500 accounted for possible interactions between parameters, since a whole parameter
501 combination was retained.

502 **Step 3: refining the optimisation.** Based on the results of the previous step, six control
503 parameters were found unnecessary (see Results section), one control parameter was

504 improved with certainty, and the estimated values of the 10 remaining control parameters
505 were still imprecise. These 10 parameters were further improved using a dedicated sensitivity
506 analysis and variation ranges restricted to the most probable optimal values (Table 1). This
507 sensitivity analysis was performed as in previous steps, using 310,152 different parameter
508 combinations and 30 replicates.

509 **Simulation of the improved management strategies**

510 To test the performance of the identified management strategies, 10,000 simulation
511 replicates were performed with parameters corresponding to different scenarios: (A)
512 "Disease-free" (PPV is not introduced in the landscape); (B) "Management-free" (PPV is
513 introduced and not managed); (C) "Reference management" (PPV is introduced and managed
514 according to the current French strategy, defined in (JORF, 2011)); (D) "best-value strategy";
515 and (E) "best-percent strategy". In scenarios B to E, the six epidemiological parameters were
516 varied inside their respective specific ranges (Table 1). The impact of the epidemic was
517 assessed by the distribution of the epidemiological criterion (Y), the economic criterion (NPV),
518 as well as the dynamics of annual prevalence and incidence, and the dynamics of observations
519 and removals. Furthermore, similar simulations were performed using doubled values for the
520 pathogen transmission coefficient (β) and halved values for the latent period duration (θ_{exp}),
521 in order to test the robustness of the identified management strategies to harsher epidemic
522 contexts.

523 **Computing tools**

524 The model was written in R and C languages. Sobol's sequences and Sobol's indices were
525 respectively generated and calculated using the packages *fOptions*, v3010.83 (Wuertz *et al.*,
526 2017) and *sensitivity*, v1.11 (Pujol *et al.*, 2017) of the R software, v3.0.3 (R Core Team, 2012).
527 A simulation takes approximately 8 seconds with a regular desktop (Intel® Core™ i7-4600M).

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Author Contributions

Designed research: LR, SD, EJ, SS, GT. Performed research: LR. Analysed data: LR, SD, CB, ST, EJ, SS, GT. Wrote the paper: LR, EJ, SS, GT. Secured funding for project's execution: SD, EJ, SS, GT.

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Table 1. Parameters of the model: description, reference values for sharka epidemics in French peach orchards, and variation ranges in the sensitivity analyses. The first sensitivity analysis (step 1) targeted 23 control parameters and 6 epidemiological parameters to assess their relative influence on model outputs. In the second step, only the 17 most influential control parameters (bounds in bold) were kept and improved. In the third step, 6 unnecessary parameters were removed, 1 parameter was fixed, and the remaining 10 parameters (in bold) were further improved.

Parameter and description		Reference value	Steps 1 and 2		Step 3	
			Min	Max	Min	Max
Temporal and landscape parameters						
a_0	First year of epidemic	1	-	-	-	-
a_m	First year of management	6	-	-	-	-
a_f	Last year of simulation	35	-	-	-	-
ψ	Expected orchard duration (years)	15 [a]	-	-	-	-
Epidemiological parameters						
q_κ	Quantile of the connectivity of the patch of first introduction	0.50	0.00 [b]	1.00 [b]	-	-
ϕ	Probability of introduction at planting	0.007 [a]	0.0046 [a]	0.0107 [a]	-	-
p_{MI}	Relative probability of massive introduction	0 [a]	0.00 [a]	0.10 [a]	-	-
W_{exp}	Expected value of the dispersal weighting variable	0.486 [c]	0.469 [c]	0.504 [c]	-	-
W_{var}	Variance of the dispersal weighting variable	0.0434 [c]	-	-	-	-
β	Transmission coefficient	1.32 [c]	1.25 [c]	1.39 [c]	-	-
θ_{exp}	Expected duration of the latent period (years)	1.92 [c]	1.71 [c]	2.14 [c]	-	-
θ_{var}	Variance of the latent period duration (years)	0.44 [c]	-	-	-	-
Surveillance parameters						
$\boldsymbol{\rho}$	Probability of detection of a symptomatic tree	0.66 [c]	**0 [b]**	**0.66 [h]**	**0.2**	**0.66**
γ_o	Duration of observation zones (years)	3 [d]	**0 [b]**	**10 [i]**	**0**	**10**
γ_Y	Duration of young orchards (years)	3 [d]	**0 [b]**	**10 [i]**	**0**	**3**
ζ_s	Radius-distance of security zones (m)	2,500 [d]	**0 [b]**	**5,800 [j]**	**0**	**1,000**
r_{ζ_f}	Ratio of the focal area over the security area	0.36 [d]	**0 [b]**	**1 [b]**	-	-

$r_{\zeta_{eO}}$	Ratio of the observation epicentre area over the focal area	0.14 [d]	0 [b]	1 [b]	-	-
$1/\eta_0$	Maximal period between 2 observations (year)	6 [d]	**1 [b]**	**15 [k]**	**1**	**15**
η_s	Observation frequency in security zones (year^{-1})	1 [d]	**0 [b]**	**8 [l]**	**0**	**4**
η_f	Observation frequency in focal zones (year^{-1})	2 [d]	**0 [b]**	**8 [l]**	-	-
η_{f*}	Modified observation frequency in focal zones (year^{-1})	3 [d]	0 [b]	8 [l]	-	-
η_y	Observation frequency in young orchards (year^{-1})	2 [d]	**0 [b]**	**8 [l]**	**0**	**2**
η_{y*}	Modified observation frequency in young orchards (year^{-1})	3 [d]	0 [b]	8 [l]	-	-
χ_o	Contamination threshold in the observation epicentre, above which the observation frequency in focal zone is modified	0.02 [d]	0 [b]	1 [b]	-	-
$r_{\chi_{y*}}$	Ratio (over $\chi_{\bar{y}}$) of the contamination threshold in the environment, above which the observation frequency in young orchards is modified	0.50 [d]	0 [b]	1 [b]	-	-
Removal parameters						
δ	Mean delay before removal of a detected tree (days)	10 [d]	-	-	-	-
$\gamma_R{}^T$	(Boolean) Individual trees are removed: 0: after a mean delay δ 1: at the end of the year	0 [d]	**0 [b,m]**	**1 [b,m]**	0	
γ_R	(Boolean) Whole orchards are removed: 0: after a mean delay δ 1: at the end of the year	1 [d]	**0 [b,m]**	**1 [b,m]**	-	-
ζ_R	Radius-distance of the removal zone (m)	0 [d]	**0 [b]**	**5,800 [j]**	-	-
$r_{\zeta_{eR}}$	Ratio of the removal epicentre area over the removal area	0 [d]	**0 [b]**	**1 [b]**	-	-
χ_R	Contamination threshold in the removal epicentre, above which orchards inside the removal zone are removed	0.10 [d]	**0 [b]**	**0.34 [n]**	-	-
Replanting parameters						
γ_S	Delay before replanting of a removed orchard (years)	0 [d]	**0 [b]**	**10 [i]**	**0**	**7**
ζ_n	Radius-distance of the neighbourhood (m)	200 [d]	**0 [b]**	**5,475 [j]**	**0**	**5,475**
$\chi_{\bar{y}}$	Contamination threshold in the environment around young orchards, above which the planting of orchards is forbidden	0.02 [d]	0 [b]	1 [b]	-	-
χ_n	Contamination threshold in the neighbourhood, above which the planting of orchards is forbidden	0.05 [d]	**0 [b]**	**1 [b]**	**0.2**	**1**

Economic parameters						
y	Relative age-dependent yield of hosts in S or E states	0.00 until 2 years [a] 0.50 at 3 years [a] 0.65 at 4 years [a] 0.85 at 5 years [a] 1.00 from 6 to 15 years [a] 0.80 from 16 years [a]	-	-	-	-
c_S	Planting cost of one orchard (€.ha^{-1})	14,000 [a]	-	-	-	-
c_R	Removal cost of one orchard (€.ha^{-1})	1,000 [a]	-	-	-	-
$c_R{}^T$	Removal cost of one individual tree (€)	15 [a]	-	-	-	-
c_F	Yearly fixed cost associated with prunus cultivation (€.ha^{-1})	13,600 [e]	-	-	-	-
c_O	Cost of one observation (€.ha^{-1})	160 [a,f]	-	-	-	-
p	Maximal yearly benefit generated by fruit harvest (€.ha^{-1})	37,250 [e]	-	-	-	-
τ_a	Discount rate	0.04 [g]	-	-	-	-
χ_{SEHD}	Minimum proportion of living trees, below which the orchard is not profitable and thus removed	0.66 [e]	-	-	-	-

[a] estimated through expert opinion.

[b] domain of definition.

[c] estimated in (Pleydell *et al.*, 2018).

[d] fixed by (JORF, 2011). With regard to ζ_R and $r_{\zeta_{eR}}$, when fixed at 0, the removal zone or the removal epicentre correspond to the contaminated orchard only.

[e] estimated from the economic analysis of prunus cultivation (Table S1).

[f] with ρ=0.66.

[g] (Quinet, 2013).

[h] we assumed that the detection probability could not go further because of technical limitations.

[i] these durations aim at detecting latent infections, and 10 years is well beyond the expected duration of the latent period (θ_{exp}).

[j] 5,800 m is the maximal distance between the centroids of 2 orchards in the landscape; 5,475 m is the maximal distance between the closest points of 2 orchards.

[k] 15 years is the expected duration (ψ) of an orchard.

[l] given the time window to survey prunus leaves in orchards, 8 observations/year is equivalent to 1 observation/fortnight. We supposed that higher observation frequencies were not economically viable (Table S1), which has been confirmed by the results of the sensitivity analyses.

[m] either 0 or 1 (Boolean variable).

[n] the management process of the model does not change any more for χ_R above 0.34, since any orchard with a proportion below χ_{SEHD}=0.66 of living trees is removed for profitability reasons (Table S1).

Table 2. Summary of the economically improved management strategies in different epidemic contexts. Values of the control parameters estimated using the combination leading to the best value (1), or the best percentile (1%) of μ_{NPV}, and outputs of 10,000 simulations, in the reference epidemic context or in harsh epidemic contexts (halved values for the expected duration of the latent period, θ_{exp}; or doubled values for the transmission coefficient, β).

	Epidemic context:	**Reference**		**Shorter latency**		**Stronger transmission**	
	Management strategy:	1	1%	1	1%	1	1%
Parameters							
ρ	Detection prob.	0.36	0.60	0.57	0.62	0.47	0.61
ζ_s	Radius-dist. of security zones (m) [a]	61	54	54	60	27	45
ζ_n	Radius-dist. of neighbourhood (m)	2787	962	4579	856	4157	814
χ_n	Neighbourhood conta. thres. above which orchard planting is forbidden	0.60	0.92	0.70	0.92	0.73	0.93
$1/\eta_0$	Maximal period between 2 obs. (years)	4	4	4	3	1	2
η_s	Obs. freq. in security zones (year^{-1})	3	1	2	2	7	2
η_y	Obs. freq. in young orchards (year^{-1})	-	1	1	-	-	1
γ_o	Duration of obs. zones (years)	3	1	1	1	1	1
γ_y	Duration of young orchards (years)	-	1	1	-	-	1
γ_S	Delay before replanting (years)	0	0	1	1	3	1
Median output of 10,000 replicates							
Y	Nb. of productive hosts (trees.ha^{-1}.year^{-1})	559	558	559	558	559	558
NPV	Net present value (million euros)	13.7	13.7	13.7	13.6	12.7	13.1

[a] when ζ_s is so small, the security zone corresponds to the contaminated orchard.

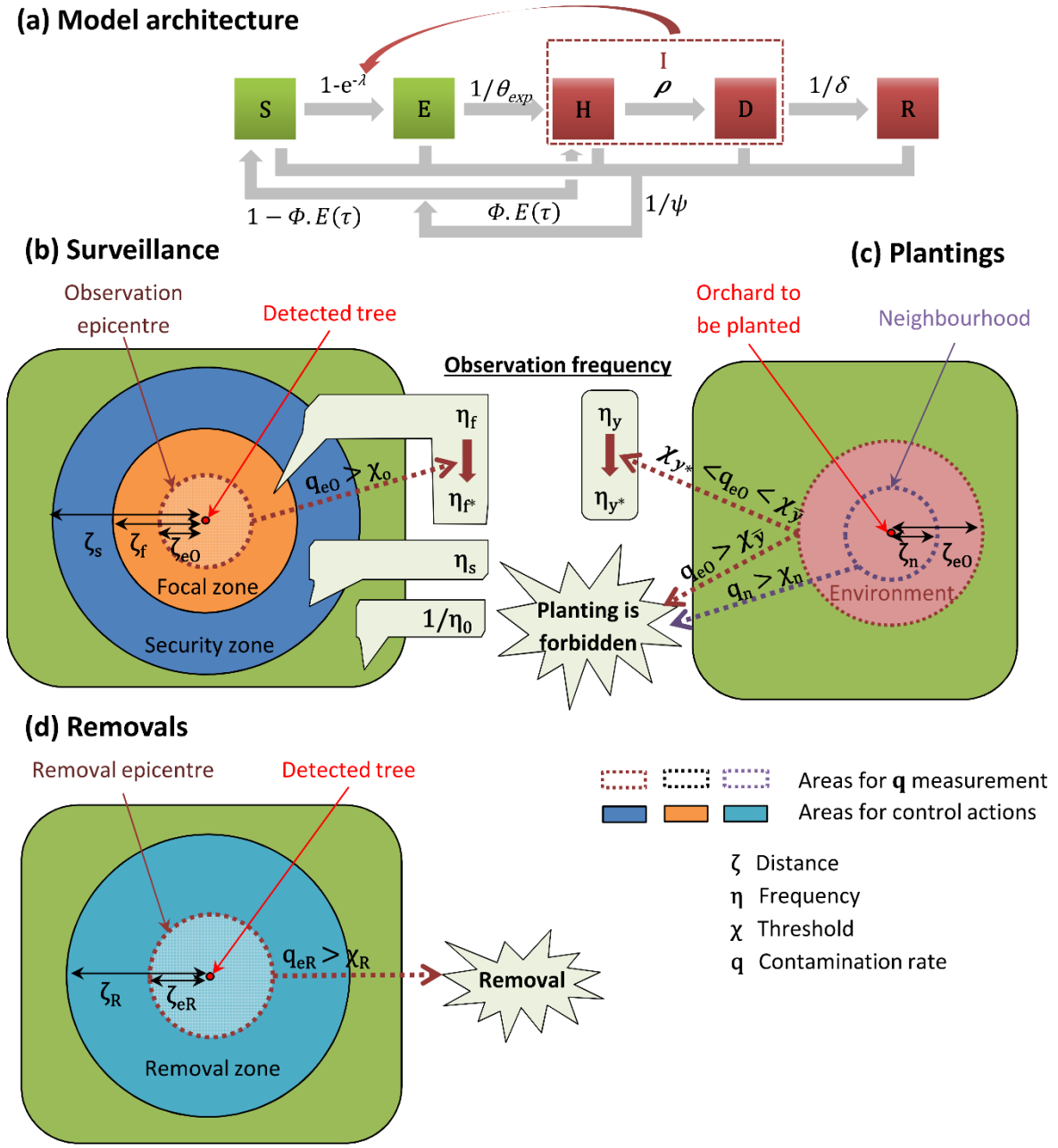

Fig. 1 Schematic representation of the spatiotemporal stochastic model simulating sharka spread and its management. (a) Flow diagram of the SEHDR architecture. S: susceptible (i.e. healthy); E: exposed (i.e. infected but neither infectious nor diseased); I: infectious and symptomatic; H: hidden (i.e. not detected); D: detected; R: removed. Productive and non-productive (diseased) hosts are in green and red, respectively. Healthy hosts incur the infectious potential (λ) applied by infectious hosts at various distances. Infected hosts become infectious after a mean latent period θ_{exp}. Symptomatic hosts can be detected with probability ρ, and next removed after a mean delay δ. Regardless of their sanitary state, hosts can be removed due to orchard turnover (with mean orchard lifespan ψ). Each orchard planting has a mean risk of introduction (ϕ) of infectious trees (whose mean proportion is $E(\tau)$ in the orchard). (b) Orchard surveillance, depending on their location relative to previously infected

trees and contamination rate of the epicentre. (c) Planting restrictions and surveillance for young orchards, depending on the contamination rates of the environment and neighbourhood. (d) Removal of orchards depending on the contamination rate of the epicentre. In the French strategy to manage sharka, the removal zone and its epicentre correspond to the orchard only (i.e. $\zeta_{eR} = \zeta_R = 0$). All model parameters are defined in Table 1.

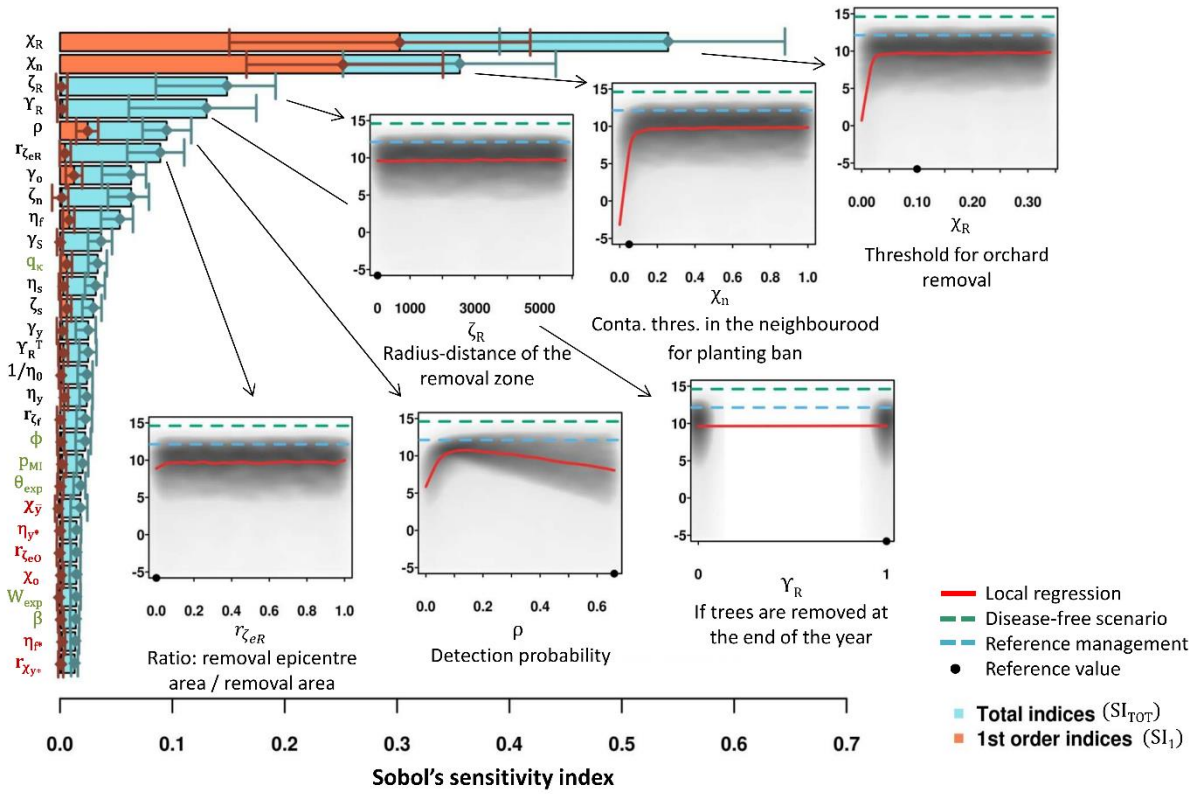

Fig. 2 Step 1: Sobol's sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the mean output of the stochastic replicates (μ_{NPV}, average net present value). $\sum SI_1 = 0.64$. Parameters in black are kept in step 2; parameters in red are removed; parameters in green are the epidemiological parameters. Insets: value of the output variable (μ_{NPV}, in million €) obtained with the different values of the six most influential parameters (grey colouration: density). All model parameters are defined in Table 1.

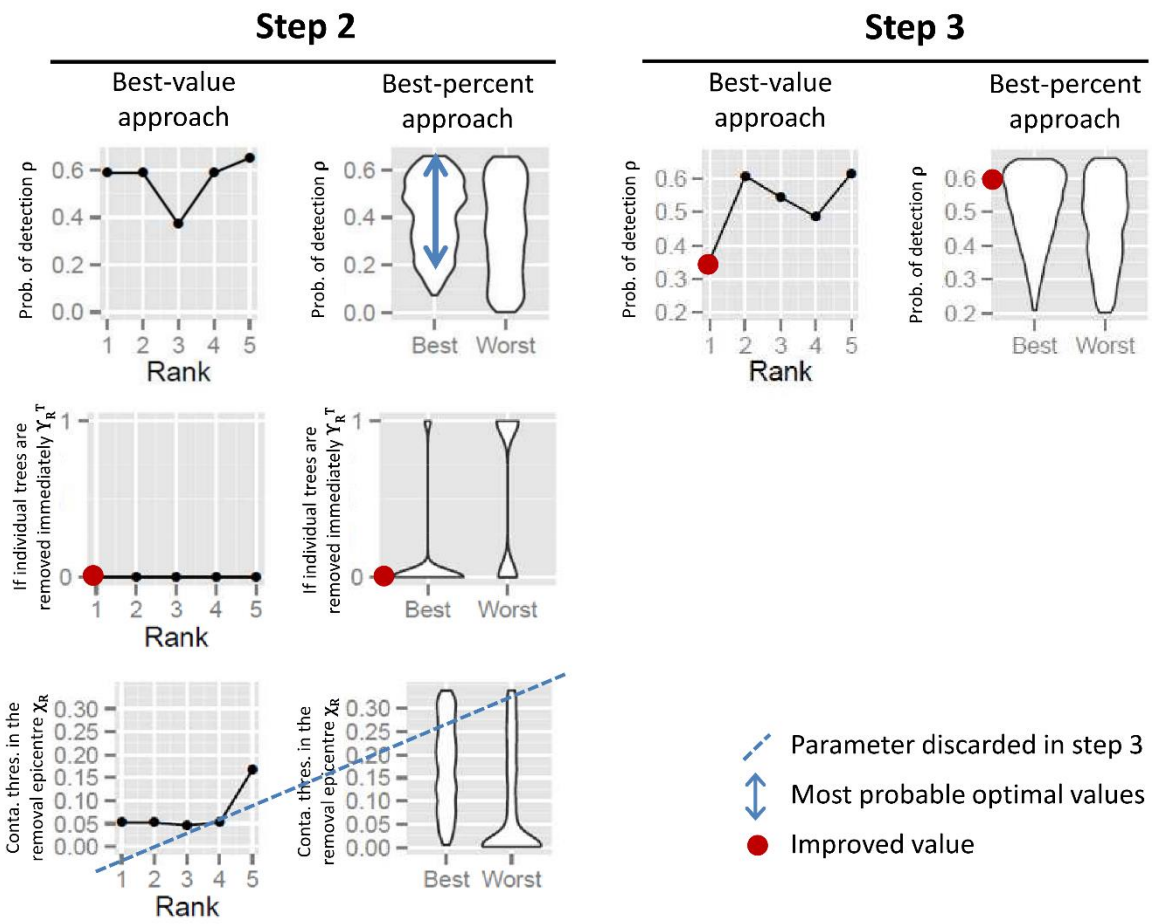

Fig. 3 Heuristic optimisation of control parameters through sequential sensitivity analyses: example on three parameters. The improved combination of control parameters is approached by isolating the combination associated with the highest value of μ_{NPV}, or using the mode of the distribution of each parameter within the combinations associated with the best percentile of μ_{NPV}. In step 2, an improved value (red circle) is found for Y_R^T, and χ_R can be removed from further analyses (dashed blue line: improved values for removal parameters are so high that removals may never occur). The improvement of ρ is refined in step 3, using a restricted variation range (blue arrows). See the results with all control parameters in Figs. S10 and S11.

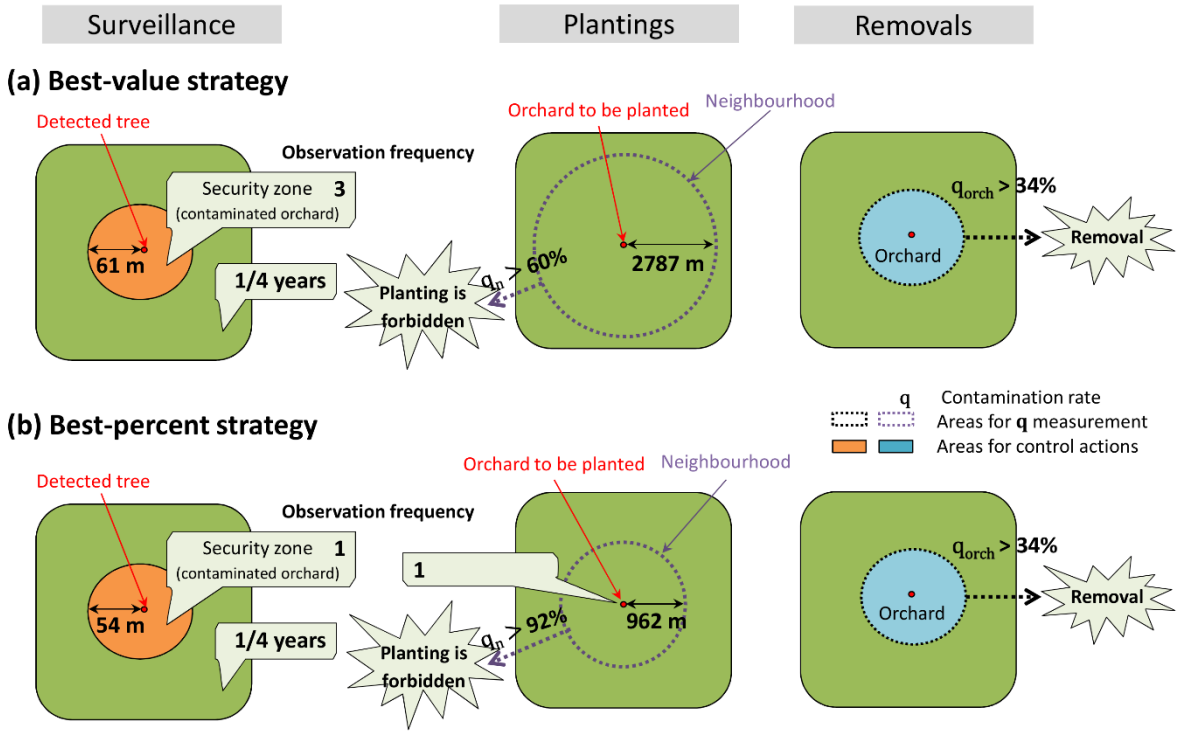

Fig. 4 Improved management strategies. Surveillance, plantings and removals according to the combination of control parameters associated with the best value (a) or the best percentile (b) of μ_{NPV}. Given its radius, the security zone may consist of the contaminated orchard only. Whole orchards may only be removed if the proportion of remaining trees falls below a profitability threshold (χ_{SEHD}=0.66).

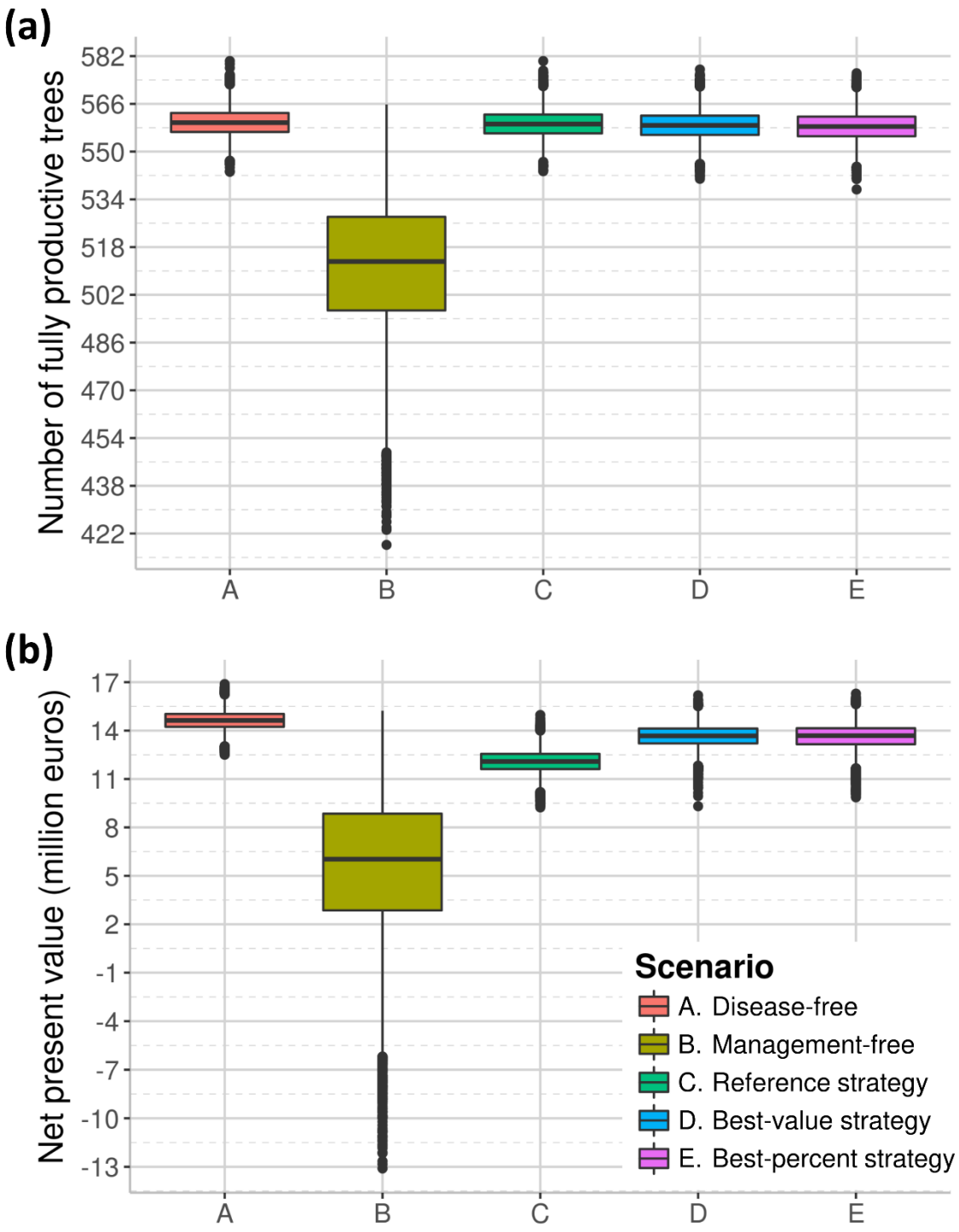

Fig. 5 Distribution of Y (equivalent number of fully productive trees per hectare and per year, a), and NPV (net present value of all orchards of the landscape, b) after 30 years of management. Different scenarios are simulated: absence of disease, absence of management, disease managed with the reference strategy (French management in orchards), or with economically improved management strategies identified through two different methods (combination associated with the best value or the best percentile of μ_{NPV}).

Supporting information

The following supporting information is available for this article:

Fig. S1. Step 1: Sobol's sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the standard deviation of the stochastic replicates.

Fig. S2. Step 1: Sobol's sensitivity indices of the 23 control parameters and 6 epidemiological parameters on the mean epidemiological output of the stochastic replicates.

Fig. S3. Step 2: Five best values, and distributions of the best and worst percentiles of each parameter with regard to the mean economic criterion in the second sensitivity analysis.

Fig. S4. Step 3: Five best values, and distribution of the best and worst percentiles of each parameter with regard to the mean economic criterion in the third sensitivity analysis.

Fig. S5. Distribution of Y and NPV after 30 years of management in harsher epidemic contexts.

Fig. S6. Dynamics of annual prevalence and incidence under different management strategies and epidemic contexts.

Fig. S7. Dynamics of observations, tree and orchard removals under different management strategies and epidemic contexts.

Fig. S8. Distribution of Y and NPV after 30 years of management in harsh epidemic contexts, with strategies specifically improved in these contexts.

Fig. S9. Dynamics of annual prevalence and incidence under management strategies specifically improved in harsh epidemic contexts.

Fig. S10. Distribution of the observation dates, depending on the observed plant organ.

Fig. S11. Convergence of the mean and standard deviation of NPV with the number of replicates.

Table S1. Economic analysis of prunus cultivation in France.

Method S1. Description of the epidemic model.

Method S2. Calculation of the contamination rate.