Title

Using models to provide rapid programme support for California's efforts to suppress Huanglongbing disease of citrus

Journal

Philosophical Transactions of the Royal Society B Biological Sciences, 374(1776)

ISSN
0962-8436

Authors

McRoberts, Neil
Figuera, Sara Garcia
Olkowski, Sandra
et al.

Publication Date
2019-07-08

DOI
10.1098/rstb.2018.0281

PHILOSOPHICAL
TRANSACTIONS B

royalsocietypublishing.org/journal/rstb

Review

Cite this article: McRoberts N, Figuera SG, Olkowski S, McGuire B, Luo W, Posny D, Gottwald T. 2019 Using models to provide rapid programme support for California's efforts to suppress Huanglongbing disease of citrus. *Phil. Trans. R. Soc. B* **374**: 20180281. http://dx.doi.org/10.1098/rstb.2018.0281

Accepted: 1 March 2019

One contribution of 16 to a theme issue 'Modelling infectious disease outbreaks in humans, animals and plants: epidemic forecasting and control'.

Subject Areas:
plant science, health and disease and epidemiology

Keywords:
epidemiology, invasive species, Huanglongbing, regulatory response, modelling

Author for correspondence:
Neil McRoberts
e-mail: nmcroberts@ucdavis.edu

Electronic supplementary material is available online at https://dx.doi.org/10.6084/m9.figshare.c.4462784.

THE ROYAL SOCIETY
PUBLISHING

Using models to provide rapid programme support for California's efforts to suppress Huanglongbing disease of citrus

Neil McRoberts[1], Sara Garcia Figuera[1], Sandra Olkowski[1], Brianna McGuire[1], Weiqi Luo[2,3], Drew Posny[2,3] and Tim Gottwald[2]

[1]Plant Pathology, University of California, Davis, CA 95616, USA
[2]U.S. Department of Agriculture, Agricultural Research Service, Fort Pierce, FL 34945, USA
[3]Center for Integrated Pest Management, North Carolina State University, Raleigh, NC 27695, USA

NM, 0000-0001-6346-9461; TG, 0000-0003-0885-8004

We describe a series of operational questions posed during the state-wide response in California to the arrival of the invasive citrus disease Huanglongbing. The response is coordinated by an elected committee from the citrus industry and operates in collaboration with the California Department of Food and Agriculture, which gives it regulatory authority to enforce the removal of infected trees. The paper reviews how surveillance for disease and resource allocation between detection and delimitation have been addressed, based on epidemiological principles. In addition, we describe how epidemiological analyses have been used to support rule-making to enact costly but beneficial regulations and we highlight two recurring themes in the programme support work: (i) data are often insufficient for quantitative analyses of questions and (ii) modellers and decision-makers alike may be forced to accept the need to make decisions on the basis of simple or incomplete analyses that are subject to considerable uncertainty.

This article is part of the theme issue 'Modelling infectious disease outbreaks in humans, animals and plants: epidemic forecasting and control'. This theme issue is linked with the earlier issue 'Modelling infectious disease outbreaks in humans, animals and plants: approaches and important themes'.

1. Introduction

California, which has approximately 109 000 Ha (268 000 acres) of commercial citrus, is the most recent citrus-growing region to be threatened by Huanglongbing (HLB) [1,2]. HLB is associated with a non-reversible decline in tree vigour and fruit yield. Yield loss results from: reduced fruit number, size and mass; early fruit drop; failure to ripen; and unmarketable flavour. Citrus trees of all commercial species and varieties are susceptible and typically die less than 10 years after symptoms first become apparent.

HLB is associated with the Gram-negative fastidious bacteria *Candidatus* Liberibacter spp. which are vectored by two species of psyllids: the Asian citrus psyllid (ACP), *Diaphorina citri*, and the African citrus psyllid, *Trioza erytreae*. Of the two, ACP is of greater global concern and is the exclusive vector present in North, South and Central America, where it has spread '*Candidatus* Liberibacter asiaticus' (CLas) in most key citrus-growing areas.

In California, ACP was first detected in 2008 and CLas in 2012. A coordinated response to suppress ACP populations and limit the spread of HLB has been in place since shortly after ACP was first detected. The Citrus Pest and Disease Prevention Committee (CPDPC) was created in 2009, when the state legislature passed the purpose-written California Agriculture Bill AB-281, requiring the State Secretary of Food and Agriculture to establish a grower-funded programme for citrus pest and disease control, the California Citrus Pest and Disease Prevention Program (CPDPP). The CPDPC consists of 17 voting members (14 growers, two nursery tree producers and one public member), who make recommendations to the California Department of Food and Agriculture (CDFA) for the implementation of the CPDPP. Thus, the CPDPP operates under the regulatory jurisdiction of the CDFA. If a tree is confirmed by the approved regulatory diagnostic protocol—a quantitative polymerase chain reaction (qPCR)—to have CLas DNA present in its tissues, it must be destroyed. If tree owners in any context refuse to allow a qPCR-confirmed tree to be removed, CDFA staff have the legal authority to enforce removal and recover the costs from the owner; the cost of removing voluntarily surrendered infected trees is borne by the programme.

The CPDPC has relied, since its inception, on epidemiological modelling and analysis to support decision-making and to optimize resource allocation among different programme activities, but the scope of these analyses and their integration into the decision-making process have increased over time. The aim of this paper is to give an overview of the process of integration. Rather than focus on mathematical and statistical details, we provide an illustrative description of the practical use of epidemiological modelling to address a series of questions arising in sequence during the emerging HLB epidemic. We summarize the approach taken to address each question and the outcome in terms of the activity of the programme. Consequently, the paper consists of a series of vignettes, which are intended to have pedagogical value to researchers and decision-makers who might be faced with similar challenges in other contexts. Supplementary online material is used to provide details of analyses that cannot be accommodated within the main text of the paper.

In the order in which they appear, the examples we discuss can be considered under three headings. First, we discuss issues connected with disease surveillance and detection and the allocation of resources to that important task. Second, with a successful detection programme comes the issue of handling an increasing number of potentially exposed, but not yet confirmed, cases, and how modelling can be used to explore the adoption of alternative regulatory approaches, not based on confirmation. Finally, we discuss an example of the use of participatory risk modelling in which stakeholders have been asked to assist in evaluating the risk of inadvertent disease spread associated with transport of fruit for processing and packing.

2. Disease surveillance: finding the enemy

Surveillance for vector-borne diseases presents challenges over and above those of other infectious diseases because both vector populations and disease incidence must be monitored, with a sometimes uncertain relationship between the two, as observed in the dengue fever disease system [3,4]. Once vector populations are established in an area, early detection of disease becomes the critical factor in surveillance success; where ‘success’ can be evaluated, in part, as the ability of a surveillance system to detect unexpected increases in disease incidence with sufficient lead-time and spatial precision to guide targeted interventions [5,6].

There are several critical challenges to achieving this goal in the context of HLB. Surveillance efficiency is limited both by sampling errors associated with the localized nature of infections in tree canopies and by the relatively long and variable intrinsic incubation period, which greatly exceeds the latent period, and gives rise to asymptomatic infections that contribute to the spread of the pathogen [2], a phenomenon that has been described in both human and veterinary vector-borne disease systems [7,8]. The resulting diagnostic errors may cause erratic identification of individual infections and thus unreliable population-level estimates of disease. A related issue occurs when closely related pathogens cause bioassay cross-reactivity [9].

Understandably enough, decision-makers become unwilling to commit resources on the basis of information that is known to be error-prone. This tension between the reliability and accuracy of disease detection, and the need for action nevertheless, has been a significant factor in the activities of the CPDPC, and a common theme running through this review is that ‘Even when data are fluid, a decision must be made’ [10]. In a regulatory setting, the aim is often to provide a ‘good enough’ basis for decision-making in real time; gathering the information for complete understanding of the dynamics is a longer-term, academic pursuit, albeit a useful one, in future decision-making.

With these challenges in mind, biological and operational factors should be considered when designing a fit-for-purpose surveillance strategy. Risk-based surveillance is a strategy that has been employed in diverse disease systems [11–13] to guide monitoring and control efforts and was the approach selected, soon after the inception of the CPDPP, to enable the programme to find and remove CLas-infected trees in California.

3. The primary surveillance tool: risk-based surveys for Asian citrus psyllid and Huanglongbing in California

The most important issue facing the CPDPC at the outset of the epidemic, and in continuing efforts to suppress HLB, has been to maximize the early detection of infected hosts and vectors across the state. The design of a suitable survey-sampling protocol was therefore the first analytical task faced by epidemiologists. Previous experience with HLB epidemics in China, Brazil and Florida, and knowledge of the local circumstances of citrus production in California, resulted in a risk-based survey (RBS) previously implemented in Florida being adapted for use in California as well as Texas and Arizona [14,15].

The risk model is, in effect, the summation of a series of individual risk factors to generate HLB/ACP risk scores for each relevant US section-township-range (STR) grid (i.e. 1 mile^2). The risk factors comprise a mixture of social, biophysical and environmental variables influencing HLB/ACP introduction and development within a landscape. Model components include human-mediated introduction risk from international travel, detected ACP density, Clas+ detections (trees and ACP), citrus nurseries, home improvement stores or other garden centres (which may serve as potential inoculum reservoirs), citrus transportation corridors, citrus packing houses, farmers’ markets, military bases and Native-American reservations (both of which are associated with lowered levels of census data), and weather suitability for ACP and HLB development. These factors were identified, via an informal Bayesian approach using an accumulation of scientific literature and expert knowledge about the epidemiology of HLB/ACP, as well as particulars of the local situation in California (see electronic supplementary material, figure S1) to generate risk maps optimized for resource allocation and sampling prioritization (figure 1). The risk score in each STR grid is normalized to the interval [0,1], and subsequently used as basemap for optimized resource allocation and sampling prioritization.

In contrast to risk-factor selection for RBS calculation, there were insufficient data, initially, to justify informative weights for risk factors in California; therefore, the original model was run with all risk factors at equal weighting. Since the initial run, the weights for the model parameters have been recalibrated and refined after each round of data collection to improve model predictive accuracy and reliability, and new risk scores will continue to be assigned to the STR grid as the HLB epidemic develops. Figure 1 shows a series of maps over time for the southern California region, with risk values indicated by colour scale from low (blue) to high (red). The initial detections of HLB in the Hacienda Heights and San Gabriel areas of greater Los Angeles, and subsequent clusters of infection in Los Angeles, Orange, Riverside and San Bernardino counties have all been within STR grid squares assigned high to very high risk status from the earliest rounds of risk calculation.

For operational purposes, the output from the RBS calculation is used in the next cycle (usually 2 or 3 cycles per year) of the survey to identify the STR squares to be surveyed, with selection being biased toward squares with highest risk values. However, a 5% proportion of low-risk squares can be included as a negative validation of the risk assignment. The exact number of squares to be sampled and the details of the sample are decided through deliberation between the risk modelling team and the resource managers working for CPDPC in the CDFA. The resource managers provide up-to-date information on human resource availability and other logistics in each cycle in an effort to maintain balance between survey coverage and sampling intensity according to the RBS model.

The RBS has provided the basic quantitative underpinning for the HLB management programme in California for the last 7 years, successfully identifying areas of high risk for HLB introduction and development, and directing programme resources to maximize detection. The RBS is intended to place the surveillance teams in the areas with the highest probability of infection. However, it is left to the regulatory agencies to determine sampling and assay protocols, which can strongly influence detection/confirmation. As of 15 January 2019, 1031 trees infected with CLas have been detected and confirmed in residential southern California by applying the RBS. It is worth noting the issues that have had to be resolved in making the process work; all of these have been operational rather than directly related to the risk modelling itself.

In order for the entire procedure to work, it is necessary for the field data collected in each survey cycle to be passed to the modelling team quickly enough for updated risk calculations to be used in resource allocation decisions. *It is hard to overstate how much preparatory work should be invested in data exchange protocols, particularly if different agencies are responsible for collecting data and providing risk calculation*. Some, but by no means all, of the issues that might need to be dealt with ahead of time include:

- having agreement to allow data collected for regulatory purposes to be passed to a third party for analysis;
- compliance with protection of identity laws, if the data contain information that allows individual properties to be identified;
- clear specification of which data are required for risk calculations;
- assignment of responsibilities for data exchange timeliness and quality assurance to specific individuals at the data-generating and data-receiving ends of the partnership;
- and regular oversight of the process by programme management to avoid delays at potential recurring bottlenecks in the data collection to risk calculation to resource deployment loop.

4. Re-evaluation of surveillance logistics: optimizing resource allocation to programme components

With the RBS established as the foundation of the programme, a further series of operational issues has arisen over time. The CPDPP annual budget, including all grower-generated, state and federal funding, is currently in the order of $40 M. While this appears a significant sum, translated into human activity, equipment, laboratory costs and other operating expenses, it is a modest budget with which to suppress the spread of HLB in a region as large and complex as California. The key issue facing decision-makers is essentially a classical economic problem of how to allocate scarce resources to optimize a desired outcome. Two related resource allocation questions, in particular, recently emerged as high priorities for decision-makers.

The first question concerns the allocation of sampling resources between delimiting surveys around new disease detections and continuing the RBS across the selected set of STR squares in each cycle of sampling. Until recently, the regulatory response called for the imposition of an 800 m quarantine zone around HLB detections. The delimitation sampling required to establish the size of the infection cluster, and therefore the location of the quarantine boundary, is considerable and entails moving survey staff from the RBS to the delimitation survey. The trade-off that results is between coverage of the wider area that needs to be sampled (via the RBS) on the one hand, and, on the other, the rate of detection and delimitation of infected areas along with the associated removal rate of inoculum from the epidemic. The question posed by the CPDPC to the epidemiology team has two parts:

A. Would a smaller delimitation radius around each new detection significantly reduce the detection efficiency of the delimitation surveys?
B. Is it possible to derive an estimate of the probability of HLB-infected trees in each STR square and the probability of detection by the RBS to gauge the benefit of moving resources from delimitation surveys to the RBS?

The epidemiology team has been able to provide answers to both questions.

(a) Part A: reducing delimitation radii

The history of positive detections in each infection cluster (where an infection cluster is defined as a distinct 800 m radius around one or more infected trees) was reconstructed

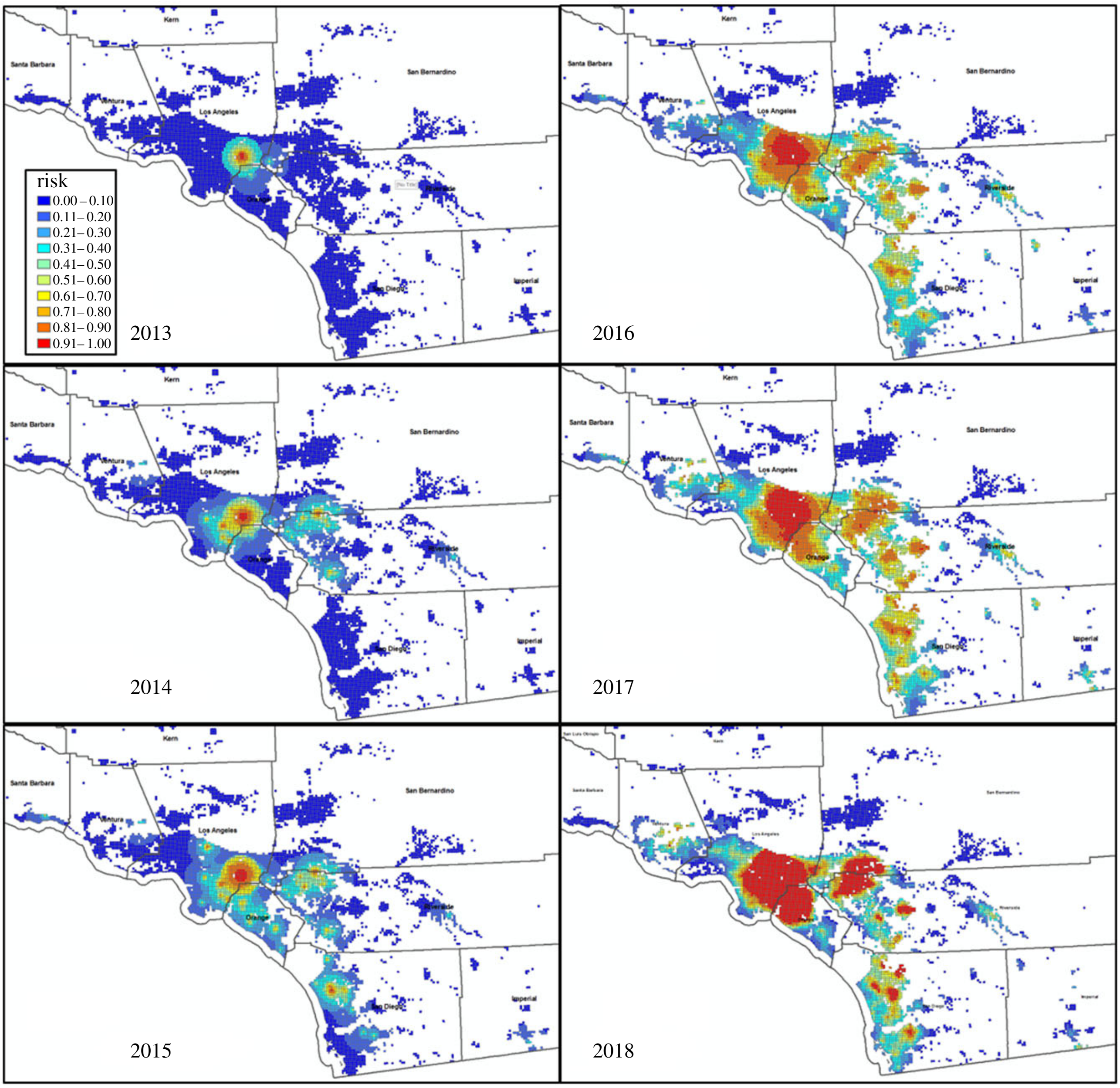


Figure 1. A progression of RBS risk maps for the HLB epidemic in southern California over the period 2013–2018. (Online version in colour.)

from the database maintained by CDFA. Samples both of confirmed CLas positive trees and of ACP were used to reconstruct the detection timeline within each cluster. By expressing the cumulative distribution of detections as a function of distance from the initial detection, it was possible to show in simulated data-resampling experiments that reducing the radius of the delimitation survey from 800 to 400 m would result in the detection of greater than 90% of the CLas-positives detected by the larger radius. For some of the clusters, the sampling effort required to sample the smaller area would be only 25% of that needed for the larger area. Figure 2 shows the temporal reconstruction of detections in one disease cluster and the summarized outcome of the data-resampling experiments used to simulate disease detection efficiency with reduced delimitation radii. The findings were reported to the Science sub-committee of the CPDPC in July 2018 and the CPDPC voted to reduce the delimitation survey radius to 450 m at its July meeting; 450 m was chosen rather than 400 m in an attempt to add additional assurance of disease detection and control.

(b) Part B: estimating state-wide disease incidence

The resources released by reducing the area of delimitation surveys should be available for disease surveillance in the RBS. An operational question for decision-makers, however, was what difference the extra resources might make to disease detection. To answer that question, it was necessary to provide estimates of the probability of infected trees in each STR grid square, as a basis for estimating detection rates. Through RBS deployment and data collection, the number of samples and the number of HLB detections are recorded each survey cycle, and estimates of the number of residential citrus trees are updated for each STR. In STR grids where sufficient information is available (i.e. more than 1% survey coverage occurs), predictions can be made on HLB incidence based on the data collected and the detection accuracy, with the underlying assumption that infected trees are homogeneously distributed. Figure 3 summarizes the statistical approach for estimating the probable HLB incidence range for each STR in California, and provides a snapshot of predicted incidence ranges for southern California using qPCR as the detection technique,

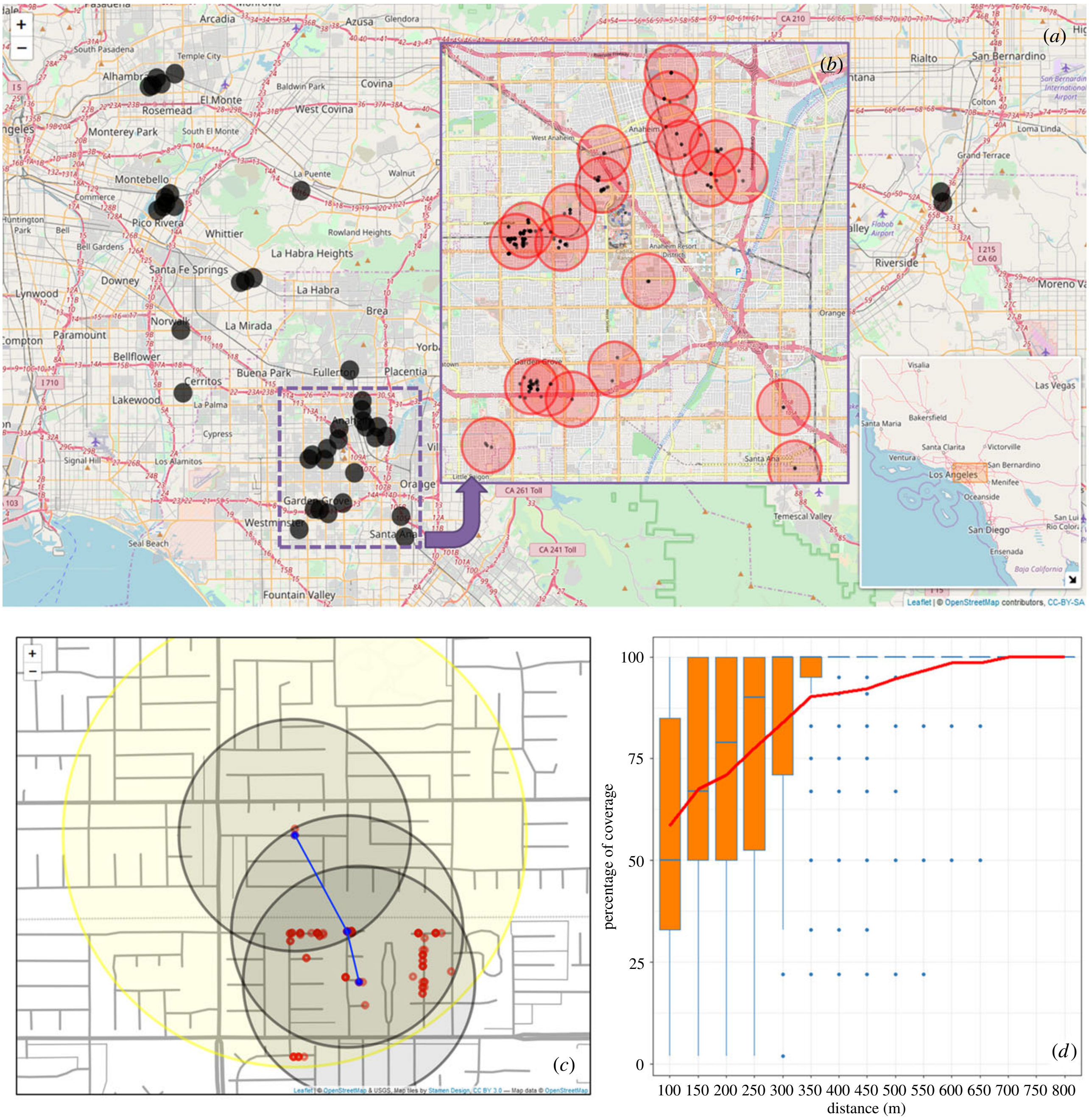
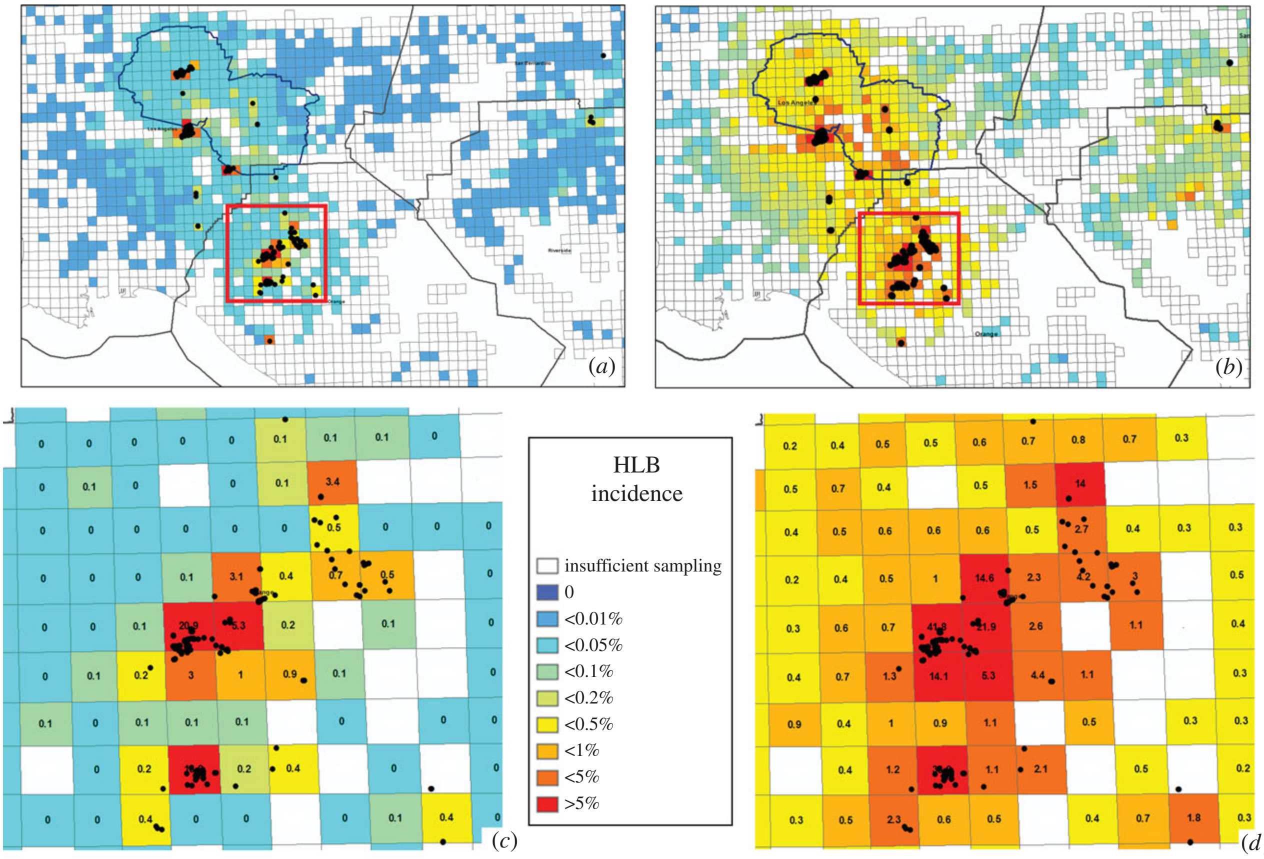


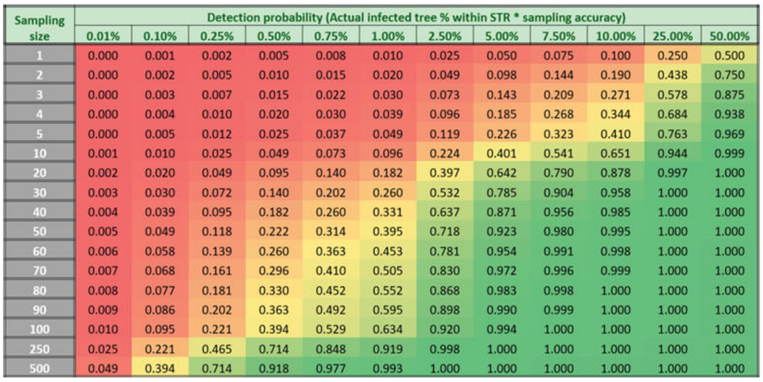
Figure 2. (*a*) Spatio-temporal cluster analysis identified 41 HLB clusters in southern California when using an 800 m delimitation distance. (*b*) High-resolution inset image of HLB clusters in Orange County. (*c*) Reconstructed timeline of HLB-positive tree detections in one infection cluster in Anaheim, CA. The large, yellow circle identifies the original 800 m delimitation survey; the smaller, black circles demonstrate a 400 m delimitation survey, starting with the initial find and iteratively capturing all confirmed CLas+ trees. (*d*) Summary results for data resampling simulation experiments showing the cumulative percentage of detections achieved by delimitation surveys of different radii using all known detection data from California from the period 2012 to December 2017. The simulations indicate that greater than 90% of all known positive trees would have been detected by delimitation surveys of 400 m radius; the eradication programme operated with a radius of 800 m during this period. (Online version in colour.)

with a realized detection accuracy of 25%. This is the assumed detection efficacy of the sampling protocol for individual trees, based on independent experiments (T Gottwald 2018, unpublished data, see the electronic supplementary material).

5. Exploring the feasibility of changing regulatory policy: defining exposure to the pathogen—the first step to changing the process of mandatory tree removal

The second major question posed by CPDPC follows from the two-part first question. One of the main uses of human resources in the delimitation surveys is in collecting plant and ACP samples for diagnostic laboratory tests. Trees inside 800 m quarantine areas that initially produce negative qPCR test results are added to a watch list and resampled at regular intervals to determine whether they have become CLas+. As the number of detections grows, and new quarantine areas are declared, the number of trees on the watch list grows with the area under quarantine. It is estimated that garden citrus trees compose approximately one-quarter to one-third of all citrus in the state. In southern California, 40 to 50% of properties have a citrus tree of some kind, with the median number of trees per property estimated at just over two trees; the watch list of potentially infected trees in urban gardens is now in the tens of thousands.





Sampling size	Detection probability (Actual infected tree % within STR * sampling accuracy)											
	0.01%	0.10%	0.25%	0.50%	0.75%	1.00%	2.50%	5.00%	7.50%	10.00%	25.00%	50.00%
1	0.000	0.001	0.002	0.005	0.008	0.010	0.025	0.050	0.075	0.100	0.250	0.500
2	0.000	0.002	0.005	0.010	0.015	0.020	0.049	0.098	0.144	0.190	0.438	0.750
3	0.000	0.003	0.007	0.015	0.022	0.030	0.073	0.143	0.209	0.271	0.578	0.875
4	0.000	0.004	0.010	0.020	0.030	0.039	0.096	0.185	0.268	0.344	0.684	0.938
5	0.000	0.005	0.012	0.025	0.037	0.049	0.119	0.226	0.323	0.410	0.763	0.969
10	0.001	0.010	0.025	0.049	0.073	0.096	0.224	0.401	0.541	0.651	0.944	0.999
20	0.002	0.020	0.049	0.095	0.140	0.182	0.397	0.642	0.790	0.878	0.997	1.000
30	0.003	0.030	0.072	0.140	0.202	0.260	0.532	0.785	0.904	0.958	1.000	1.000
40	0.004	0.039	0.095	0.182	0.260	0.331	0.637	0.871	0.956	0.985	1.000	1.000
50	0.005	0.049	0.118	0.222	0.314	0.395	0.718	0.923	0.980	0.995	1.000	1.000
60	0.006	0.058	0.139	0.260	0.363	0.453	0.781	0.954	0.991	0.998	1.000	1.000
70	0.007	0.068	0.161	0.296	0.410	0.505	0.830	0.972	0.996	0.999	1.000	1.000
80	0.008	0.077	0.181	0.330	0.452	0.552	0.868	0.983	0.998	1.000	1.000	1.000
90	0.009	0.086	0.202	0.363	0.492	0.595	0.898	0.990	0.999	1.000	1.000	1.000
100	0.010	0.095	0.221	0.394	0.529	0.634	0.920	0.994	1.000	1.000	1.000	1.000
250	0.025	0.221	0.465	0.714	0.848	0.919	0.998	1.000	1.000	1.000	1.000	1.000
500	0.049	0.394	0.714	0.918	0.977	0.993	1.000	1.000	1.000	1.000	1.000	1.000

(e)

statistical approach to estimate HLB incidence

observed event: number of HLB+ trees detected in each STR

1. Using binomial theory, estimate the chance of the observed event under different incidence scenarios and the accuracy of the detection technique implemented to construct the potential HLB incidence range.
2. Adjust incidence range based on available information: STR risk and sampling density; STRs with less than 1% sampling coverage are not considered (insufficient information).

(*f*)

Figure 3. Estimated minimum (*a*) and maximum (*b*) HLB incidence for each STR in southern California. (*c,d*) Higher resolution of estimated incidence range for Orange County subregion with detections from the RBS identified (dots). (*e*) Sampling efficacy table predicting the probability of finding at least one CLas+ tree given the sampling effort and detection probability, using the binomial theory. (*f*) Summary of the statistical methodology for estimating HLB incidence ranges for each STR using the RBS, and subsequent data collection via survey deployment. (Online version in colour.)

The rate of growth in the size of the watch list derives from the way State Agriculture Code is interpreted for regulatory purposes. The state's right to take action against noxious organisms is established by this code, which is itself drawn from federal statute. The definition of 'infected' that it uses is based on that established by the United States Department of Agriculture, Animal and Plant Health Inspection Service, Plant Protection and Quarantine (USDA-APHIS-PPQ, 'PPQ' for brevity) under its mandate as the national plant protection organization. Regulatory authority established by PPQ is always based on *direct* confirmation of the presence of the quarantine organism. In the case of HLB, this means that the definition of 'infected' is based on confirmation of the presence of pathogen DNA by qPCR. Because of the high probability of false negatives, caused by the variable interval between initial infection and the time when CLas becomes widespread in a tree, increase in the number of trees on the watch list for re-testing is essential to allow useful state removal activities, compliant with the strictest interpretation of the Code.

Despite the interpretation that has historically been used, however, the actual wording of the California Agriculture Code offers a potential solution to the problem of the growing watch list. The relevant section of the code (article 4, §5762) states:

> Any pest with respect to which an eradication area has been proclaimed, and any stages of the pest, its hosts and carriers, and any premises, plants, and things infested or infected ***or exposed to*** infestation or infection with such pest or its hosts or carriers, within such area, are public nuisances, which are subject to all laws and remedies which relate to the prevention and abatement of public nuisances.

Thus, state law in California allows the state regulatory agency (i.e. CDFA) to take action against noxious organisms, or locations that may harbour them, when they have been *exposed to* infestation or infection. It seems safely arguable that 'exposure' concerns possibility rather than confirmed fact.

Hypothetically, this interpretation allows a solution to the resource limitation issue by reducing the need for a re-testing programme on an ever-increasing number of trees. If a definition of '*exposed to*' could be made along these lines, trees within an exposure radius around confirmed positive detections could be removed (i.e. culled) without testing, freeing up resources to allocate to the RBS or establishing new delimitation surveys. There are also added potential benefits of removing undetected sources of inoculum from the epidemic and reducing the host density in high-risk areas. The question posed by the CPDPC to the epidemiology team was whether a suitable definition of exposure could be derived from the available data in California. The question was similar to that which underpinned the Asiatic citrus canker eradication programmes in Florida and Brazil [16,17].

The initial analysis of this problem was similar to that used in Part A of the earlier question. Data from the time-course of infections were used to characterize each infection cluster according to the cumulative proportion of known positives occurring with time and distance from the first detection. These analyses revealed that while some clusters were relatively dense—having large numbers of infected trees in close physical proximity, and consequently confirmed to be infected over a short time from the start of sampling—other clusters were more diffuse, with infected trees that were more widely spaced, and which consequently took longer to be detected. Since culling is itself resource-intensive, it is only likely to be feasible for dense clusters, where the total number of trees inside the exposure radius will be relatively small. This sets a useful constraint for the rule-making process to turn the definition of exposure into operational phytosanitary activities, but it leaves the issue of the definition of exposure, *per se*, unanswered.

Ideally, a definition of exposure used in rule-making would be based on definitions in published peer-reviewed analyses. Such definitions do exist (e.g. [18]), but key data on ACP numbers needed to adapt the definitions for urban California are lacking. This is because once a region is considered to be 'generally infested' with psyllids, no further estimates of vector population density tend to be made.

However, as already noted, there are accurate records of verified infected hosts. This allows the possibility of exploiting the fact that the vector and host dynamics are coupled, to use the infected tree data as a proxy for the missing psyllid data, and to construct the definition of exposure primarily from the disease incidence data, knowing that pathogen spread is essentially impossible without the involvement of the vector. The basic concept is well known in the analysis of population time-series data [19,20]. The implicit involvement of the vector in disease spread allows the time-series of disease detections to be expressed in terms of its own history alone, even though the underlying process, in which the vector exposes the trees to infection, involves coupled dynamics between two populations. In other words, precisely because the system has a biological interdependence between vectors and diseased hosts, we can express exposure in terms of the outcome of that interaction, even when the outcome is characterized by the numbers of infected hosts alone.

6. Using the new definition of exposure: a second step in changing the process of mandatory tree removal

Despite lacking primary data on vector populations, the modelling team can yet use details of observed psyllid behaviour to draw up guidelines for tree removal and managing watch lists.

Figure 4 shows the distribution of density of HLB infections around 659 known infected trees in southern California, when a radius of 170 m around the infected trees is considered. To give an illustrative example to aid interpretation, approximately 70 of the infected trees had no other infected trees (indicated by 0 on the horizontal axis) within 170 m. Bars toward the left end of the figure represent conditions of relatively sparse infection, while those toward the right hand end are characteristic of denser infection clusters. Clusters toward the right-hand end of the scale would be more likely targets for a removal policy based on exposure than those toward the left.

The substitution of 'exposed' for 'infected' and the use of cluster observation data to determine the likelihood of exposure potentially allow a shift from a strategy of spot-removal of individual trees, verified as infected, to a strategy of clearing dense clusters of trees, known to be exposed and therefore almost inevitably infected. However, such a shift might trigger legal challenges to the authority of the tree removal programme. A citrus canker eradication programme in Florida that used a comparable approach was successfully challenged in class actions brought by homeowners [16].

A hypothetical example of how this process could, nevertheless, be made operational is given in the supplementary material. The issue of whether the approach could be feasible is under active discussion by the CPDPC with advice from CDFA staff and the modelling team.

While homeowners with citrus trees on their properties have in the past in Florida [16] mounted determined resistance to unwelcome phytosanitary regulation, and might do so again in the future in California, such a response is a typical example of the conflict between private utility and public welfare in disease management; there are obvious parallels with the desire to opt out of public vaccination programmes for communicable diseases. In forcing a choice between private benefits and a wider public good such conflicts have similarities to many of the choices faced by commercial California growers, who are regularly forced to resolve trade-off problems in the course of the HLB epidemic in California.

7. Participatory analysis of the risk of disease spread and associated quarantine policy

One of the most problematic aspects of a disease like HLB is that it forces growers and regulators to make inter-temporal trade-off choices between current and expected future benefits; that is, it requires incurring immediate costs to protect against possible, larger, future losses. The removal of infected but fruit-bearing trees is one such trade-off [21]; imposing quarantines and requiring mitigation measures on fruit transport is another.

When citrus fruit is harvested, it is loaded in bulk on trailers for transportation to packing houses, where it is cleaned

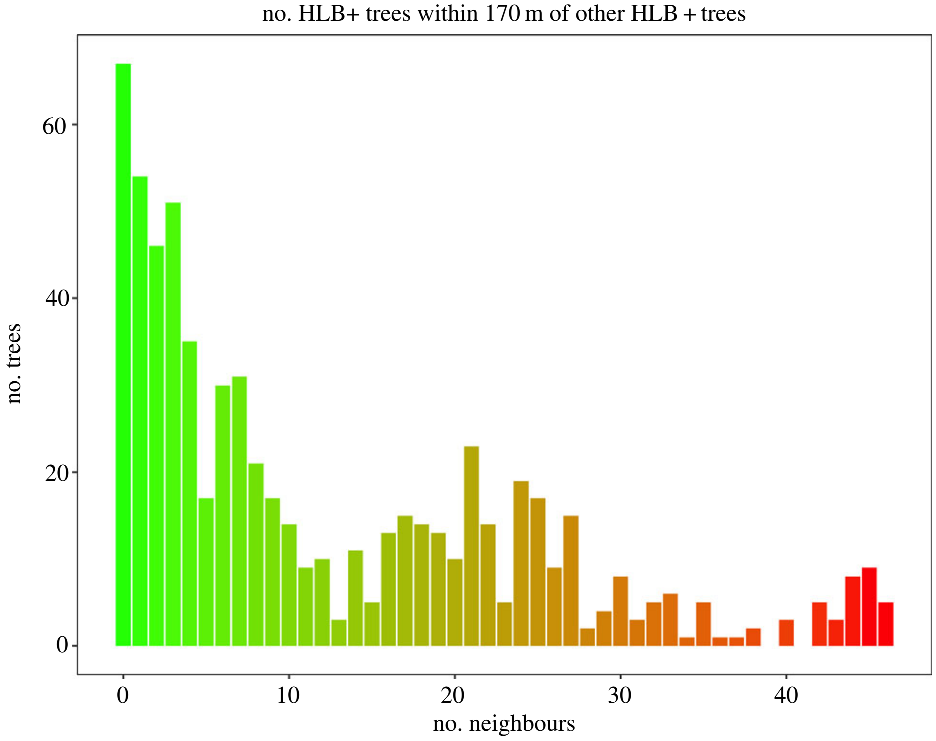


Figure 4. The distribution of density of infected citrus trees within 170 m of newly detected, infected trees. Note that many newly detected trees have no, or few, other infected trees within 170 m at the time of detection, but several have in the order of 20–30 infected close neighbours, and there is a set of trees that have 40 or more infected neighbours. (Online version in colour.)

and packaged for sale. A few packing houses handle the majority of the state's production, meaning that fruit can travel hundreds of kilometres to be processed. The risk of spread of ACP along with bulk citrus loads has been known about for several years, and has been quantified based on observations collected in Florida [15,22]. During the period 2014–2017, the whole of southern California was under quarantine for ACP while only selected areas of northern California, associated with isolated psyllid detections, were quarantined. The incidence of psyllid detections in northern California increased steadily during that period and there were calls from the industry for a state-wide quarantine to be declared and for within-state mitigations associated with fruit movement to be stopped, on the basis that the existing regulations were costly and failing to prevent incursion of the vector into the northern region.

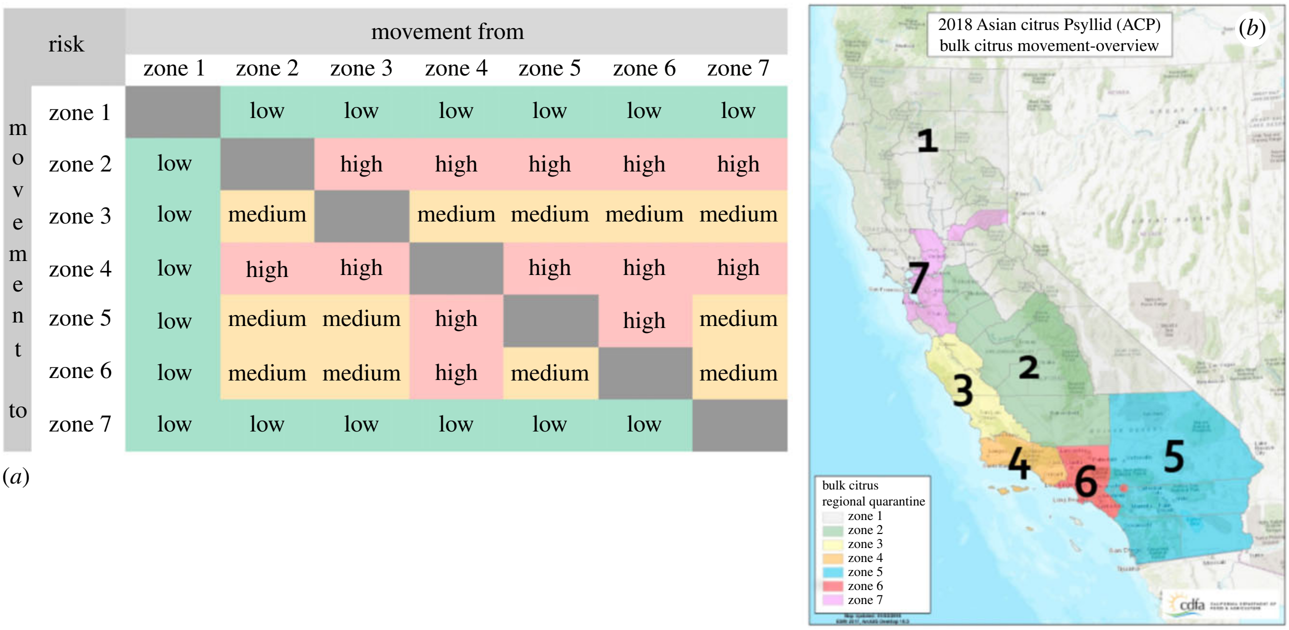
Prioritizing long-term viability for the industry as a whole, over maximizing immediate profitability for individual growers and packers, the epidemiology team argued against setting a single state-wide quarantine. We used the relationship between the presence of transportation routes and the risk of ACP and HLB presence estimated in Florida to illustrate the association between ACP detections in northern California and major fruit transport routes. A briefing paper was produced which recommended that the state be subdivided into more zones, and mandatory covering of bulk citrus loads to be initiated, along with mitigation steps such as treatment of orchards with insecticide and fruit cleaning to remove leaves, stems and insects, prior to road transport of bulk citrus. CPDPC voted to request the necessary rule-making, and CDFA used emergency rule-making provisions to pass the new regulations, which came into effect in January 2018. Figure 5 shows the locations of the seven zones demarcated by CDFA and the initial risk matrix produced by the epidemiology team for fruit movement between pairs of zones.

When the resulting bulk citrus movement regulations were initially implemented, CPDPC approved a uniform requirement for mitigation measures before fruit could be moved between zones. With the basic policy in place, there has been a steady demand from some groups of growers to make the regulations more responsive to perceived local risk levels and to institute flexible mitigation requirements for different zones.

In response to these mitigation requests, CPDPC asked the epidemiology group to re-evaluate the risk of moving bulk citrus between the regional quarantine zones and to provide evidence upon which any potential changes to the regulations could be based. The epidemiology group developed a pilot qualitative risk model, using the federal framework for pest risk analysis as a guide.

The analysis of the risk posed by fruit transport highlights the recurring theme of the need to deal with a 'fluid' situation, in terms of the features of analyses needed for rapid programme support, but also how the behaviour of decision-makers can contribute to the fluidity. On the first point, as with the starting situation for the RBS, the information required for a quantitative analysis of the risk of fruit transport was mostly unavailable. In both cases (which are typical of situations where empirical data are absent or inadequate for quantitative analysis), qualitative models built from expert knowledge were used as substitutes. This is accepted as an inevitable next-best option in many regulatory contexts [23] since 'a decision must be made'.

With respect to human behaviour, the objective for the analysis changed, iteratively, as decision-makers were exposed to the results of the work and their opinions changed accordingly. The initial balance of opinion in favour of removing internal state quarantines changed to acceptance of the need for increased quarantine zoning of the state when the evidence from Florida was presented to CPDPC; the acceptance of the quarantine zones and the accompanying uniform requirement



risk		movement from						
		zone 1	zone 2	zone 3	zone 4	zone 5	zone 6	zone 7
movement to	zone 1		low	low	low	low	low	low
	zone 2	low		high	high	high	high	high
	zone 3	low	medium		medium	medium	medium	medium
	zone 4	low	high	high		high	high	high
	zone 5	low	medium	medium	high		high	medium
	zone 6	low	medium	medium	high	medium		medium
	zone 7	low	low	low	low	low	low	

Figure 5. (*a*) Risk matrix for HLB associated with bulk fruit transport between different pairs of quarantine zone within California, depending on risk of infection in the zone of origin and magnitude of potential impact in the zone of destination. (*b*) Map of California showing the quarantine zone boundaries. The majority of commercial production is located in zone 2. All known HLB cases have been in zone 6. Note that zone 6 is discontinuous, with a small subsection (Riverside) encircled by zone 5. (Online version in colour.)

for mitigation of the risk of transport of ACP with fruit movement gave way to requests for a more nuanced policy based on a risk evaluation, once the cost and inconvenience of the initial regulations were experienced; the finding of the risk evaluation—that nearly all possible pairs of zones of consequence to the citrus industry were at high risk (because either the source had elevated risk status, or the potential impact in the destination zone was high, or both)—was questioned by some members of the CPDPC. This resulted in the current situation, in which the modelling team is facilitating an industry working group to evaluate the risk analysis, to adapt the model if necessary and to generate recommendations of further changes to the regulations for consideration by CPDPC.

8. Discussion

In a recent analysis of the role of human behaviour in the efficacy of disease control in agriculture, McQuaid *et al*. [24] noted:

> The success or failure of a disease control strategy can be significantly affected by the behaviour of individual agents involved, influencing the effectiveness of disease control, its cost and sustainability. This behaviour has rarely been considered in agricultural systems, where there is significant opportunity for impact.

The analyses described by McQuaid *et al*. [24] and the work described in this paper can be thought of as representing contrasting alternatives, lying towards opposite ends of a continuum of approaches, for dealing with the complexity of human behaviour in disease dynamics. The approach taken by McQuaid *et al*. [24] to address the need they identify can be characterized as strategic and external to the problem at hand. The modellers summarize the system, including human behaviour, in a mathematical framework aimed at broad understanding of the factors that determine the dynamics, and provide valuable strategic suggestions about potential interventions from the viewpoint of external observation. In contrast, the approach adopted in our efforts to support the CPDPC in California can be characterized as tactical and internal to the problem. The modellers analyse individual questions that arise from operational activities and deal with the human behavioural component of the dynamics through direct interaction with the decision-makers in the system of interest.

The strategic/external perspective has had considerable success in identifying guiding principles of disease management in botanical epidemiology [25–28], public health [29–31] and veterinary epidemiology [32,33]. The general principles of intervention that such strategic modelling approaches have yielded provide a useful framework for decision-makers in rapidly developing, invasive epidemics, such as the HLB problem in California, but do not often provide detailed information that can resolve operational questions. As McQuaid *et al*. [24] point out, variation in the behaviour of those responding to a disease outbreak further complicates the situation facing decision-makers attempting to manage regional resources. Here again, as with strategic modelling of disease dynamics, analyses that provide useful general insights into behaviour under risky conditions across a population [24,34,35] are less likely to be applicable to help decision-makers dealing with specific tactical decisions, with imperfect information, under time pressure.

In contrast to the clarity often available in the results of strategic modelling work, the type of analysis conducted in close programme support inevitably inherits much of the uncertainty that makes decision-making in these circumstances difficult in the first place. Rather than a unified analysis of the entire problem posed by the epidemic, what develops in such circumstances is a set of more-or-less distinct analyses, each focused on a particular issue. However, the questions addressed in the current support work are typical of those encountered in the response to invasive diseases. It is vital that we recognize the broad issues that the California HLB epidemic, and the response to it, share with comparable outbreaks and develop the methodology needed to include these general features in strategic epidemiological models, for the benefit of future decision-makers facing the same challenges. Good progress in this kind of integrative work has already been made [21,24,36–40]. A significant challenge faced by epidemiology is to integrate the valuable insights these analyses provide with close programme support work of the type described here.

Data accessibility. This article has no additional data.

Competing interests. We declare we have no competing interests.

Funding. The work described in this paper was supported by the Citrus Pest and Disease Prevention Committee, the Citrus Research Board, and the HLB Multi-Agency Coordination (HLB MAC).

Acknowledgements. The authors are grateful to members of the CPDPC and numerous citrus growers in California for their cooperation and willingness to discuss problematic issues in the management of the HLB epidemic, and CDFA staff for data collection and data sharing.

References

1. Bové JM. 2006 Huanglongbing: a destructive, newly-emerging, century-old disease of citrus. *J. Plant Pathol.* **88**, 7–37. (doi:10.4454/jpp.v88i1.828)
2. Gottwald TR. 2010 Current epidemiological understanding of citrus Huanglongbing. *Annu. Rev. Phytopathol.* **48**, 119–139. (doi:10.1146/annurev-phyto-073009-114418)
3. Bowman LR, Runge-Ranzinger S, McCall PJ. 2014 Assessing the relationship between vector indices and dengue transmission: a systematic review of the evidence. *PLoS Negl. Trop. Dis.* **8**, e2848. (doi:10.1371/journal.pntd.0002848)
4. Cromwell EA, Stoddard ST, Barker CM, Van Rie A, Messer WB, Meshnick SR, Morrison AC, Scott TW. 2017 The relationship between entomological indicators of *Aedes aegypti* abundance and dengue virus infection. *PLoS Negl. Trop. Dis.* **11**, e0005429. (doi:10.1371/journal.pntd.0005429)
5. Lemon SM, Hamburg MA, Sparling PF, Choffnes ER, Mack AL. 2007 *Global infectious disease surveillance and detection: assessing the challenges*. Washington, DC: National Academies Press.
6. German RR, Lee LM, Horan J, Milstein R, Pertowski C, Waller M. 2001 Updated guidelines for evaluating public health surveillance systems. *MMWR Recomm. Rep.* **50**, 1–35.
7. ten Bosch QA *et al.* 2018 Contributions from the silent majority dominate dengue virus transmission. *PLoS Pathog.* **14**, e1006965. (doi:10.1371/journal.ppat.1006965)
8. Singh OP, Hasker E, Sacks D, Boelaert M, Sundar S. 2014 Asymptomatic *Leishmania* infection: a new challenge for *Leishmania* control. *Clin. Infect. Dis.* **58**, 1424–1429. (doi:10.1093/cid/ciu102)
9. Kucharski A, Riley S. 2017 Reducing uncertainty about flavivirus infections. *Lancet Infect. Dis.* **17**, 13–15. (doi:10.1016/S1473-3099(16)30524-2)
10. Berger PH, Brown LG. 2012 Even when data are fluid a decision must be made. *Phytopathology* **102**, 163. (doi:10.1094/PHYTO-102-7-S4.146)
11. Barker CM, Reisen WK, Kramer VL. 2008 California state mosquito-borne virus surveillance and response plan: a retrospective evaluation using conditional simulations. *Am. J. Trop. Med. Hyg.* **68**, 508–518. (doi:10.4269/ajtmh.2003.68.508)
12. Anyamba A *et al.* 2009 Prediction of a Rift Valley fever outbreak. *Proc. Natl Acad. Sci. USA* **106**, 955–959. (doi:10.1073/pnas.0806490106)
13. VanderWaal K, Enns EA, Picasso C, Alvarez J, Perez A, Fernandez F, Gil A, Craft M, Wells S. 2017 Optimal surveillance strategies for bovine tuberculosis in a low-prevalence country. *Sci. Rep.* **7**, 4140. (doi:10.1038/s41598-017-04466-2)
14. Gottwald TR, Luo W, McRoberts N. 2013 *Risk-Based Residential HLB/ACP Survey for California, Texas, and Arizona*. Plant Management Network, American Phytopathological Society. See http://www.plantmanagementnetwork.org/edcenter/seminars/Outreach/Citrus/HLB/.
15. Gottwald TR, Luo W, McRoberts N. 2014 Risk-based residential HLB/ACP survey for California, Texas, and Arizona. *Citrograph Mag.* **2014**, 54–58.
16. Gottwald TR, Graham JH, Schubert TS. 2002 Citrus canker: the pathogen and its impact. *Plant Health Progress* **3**, 1. (doi:10.1094/PHP-2002-0812-01-RV)
17. Gottwald TR, Bassanezi RB, Amorim L, Bergamin-Filho A. 2007 Spatial pattern analysis of citrus canker-infected plantings in São Paulo, Brazil, and augmentation of infection elicited by the Asian leafminer. *Phytopathology* **97**, 674–683. (doi:10.1094/PHYTO-97-6-0674)
18. Parry M, Gibson GJ, Parnell S, Gottwald TR, Irey MS, Gast TC, Gilligan GA. 2014 Bayesian inference for an emerging arboreal epidemic in the presence of control. *Proc. Natl Acad. Sci. USA* **111**, 6258–6262. (doi:10.1073/pnas.1310997111)
19. Royama T. 1984 *Analytical population dynamics*. London, UK: Chapman and Hall.
20. Turchin P. 2003 *Complex population dynamics*. Princeton, NJ: Princeton University Press.
21. Craig AP, Cunniffe NJ, Parry M, Laranjeira FF, Gilligan CA. 2018 Grower and regulator conflict in management of citrus disease Huanglongbing in Brazil: a modelling study. *J. Appl. Ecol.* **55**, 1956–1965. (doi:10.1111/1365-2664.13122)
22. Halbert SE, Keremane ML, Ramadugu C, Brodie MW, Webb SE, Lee RF. 2010 Trailers transporting oranges to processing plants move Asian citrus psyllids. *Florida Entomol.* **93**, 33–38. (doi:10.1653/024.093.0104)
23. Devorshak C. 2012 *Plant pest risk analysis : concepts and application*. Wallingford, UK: CABI.
24. McQuaid CF, Gilligan CA, van den Bosch F. 2017 Considering behaviour to ensure the success of a disease control strategy. *R. Soc. Open Sci.* **4**, 170721. (doi:10.1098/rsos.170721)
25. Vanderplank JE. 1963 *Plant diseases: epidemics and control*. Cambridge, MA: Academic Press.
26. Jeger MJ. 2004 Analysis of disease progress as a basis for evaluating disease management practices. *Annu. Rev. Phytopathol.* **42**, 61–82. (doi:10.1146/annurev.phyto.42.040803.140427)
27. Jeger MJ, Holt J, Van Den Bosch F, Madden LV. 2004 Epidemiology of insect transmitted plant viruses: modelling disease dynamics and control interventions. *Physiol. Entomol.* **29**, 291–304. (doi:10.1111/j.0307-6962.2004.00394.x)
28. van den Bosch F, van den Berg FN, McRoberts N, Madden LV. 2008 The basic reproduction number of plant pathogens: matrix approaches to complex dynamics. *Phytopathology* **98**, 239–249. (doi:10.1094/PHYTO-98-2-0239)
29. Kermack WO, McKendrick AG. 1927 A contribution to the mathematical theory of epidemics. *Proc. R. Soc. Lond. A* **115**, 700–721. (doi:10.1098/rspa.1927.0118)
30. Anderson RM, May RM. 1985 Vaccination and herd immunity to infectious diseases. *Nature* **318**, 323–329. (doi:10.1038/318323a0)
31. Phong VVL, Kumar P, Ruiz MO. 2018 Stochastic lattice-based modelling of malaria dynamics. *Malar. J.* **17**, 250. (doi:10.1186/s12936-018-2397-z)
32. O'Farrell H, Gourley SA. 2014 Modelling the dynamics of bluetongue disease and the effect of seasonality. *Bull. Math. Biol.* **76**, 1981–2009. (doi:10.1007/s11538-014-9989-8)
33. Brooks-Pollock E, Wood JLN. 2015 Eliminating bovine tuberculosis in cattle and badgers: insight from a dynamic model. *Proc. R. Soc. B* **282**, 20150374. (doi:10.1098/rspb.2015.0374)
34. McRoberts N, Hall C, Madden LV, Hughes G. 2011 Perceptions of disease risk: from social construction of subjective judgments to rational decision making. *Phytopathology* **101**, 654–665. (doi:10.1094/PHYTO-04-10-0126)
35. Babcock BA. 2015 Using cumulative prospect theory to explain anomalous crop insurance coverage choice. *Am. J. Agric. Econ.* **97**, 1371–1384. (doi:10.1093/ajae/aav032)
36. Parnell S, Gottwald TR, Cunniffe NJ, Chavez VF, van den Bosch F. 2015 Early detection surveillance for an emerging plant pathogen: a rule of thumb to predict prevalence at first discovery. *Proc. R. Soc. B* **282**, 20151478. (doi:10.1098/rspb.2015.1478)

37. Cunniffe NJ, Cobb RC, Meentemeyer RK, Rizzo DM, Gilligan CA. 2016 Modelling when, where and how to manage a forest epidemic, motivated by sudden oak death in California. *Proc. Natl Acad. Sci. USA* **113**, 5640–5645. (doi:10.1073/pnas.1602153113)
38. Thompson RN, Gilligan CA, Cunniffe NJ. 2016 Detecting presymptomatic infection is necessary to forecast major epidemics in the earliest stages of infectious disease outbreaks. *PLoS Comput. Biol.* **12**, e1004836. (doi:10.1371/journal.pcbi.1004836)
39. Thompson RN, Cobb RC, Gilligan CA, Cunniffe NJ. 2016 Management of invading pathogens should be informed by epidemiology rather than administrative boundaries. *Ecol. Modell* **32**, 28–32. (doi:10.1016/j.ecolmodel.2015.12.014)
40. Adrakey HK, Streftaris G, Cunniffe NJ, Gottwald TR, Gilligan CA, Gibson GJ. 2017 Evidence-based controls for epidemics using spatio-temporal stochastic models in a Bayesian framework. *J. R. Soc. Interface* **14**, 20170386. (doi:10.1098/rsif.2017.0386)