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Degree of host susceptibility in the initial disease outbreak influences subsequent epidemic spread

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Summary

1. Disease epidemics typically begin as an outbreak of a relatively small, spatially explicit population of infected individuals (focus), in which disease prevalence increases and rapidly spreads into the uninfected, at-risk population. Studies of epidemic spread typically address factors influencing disease spread through the at-risk population, but the initial outbreak may strongly influence spread of the subsequent epidemic.
2. We initiated wheat stripe rust *Puccinia striiformis* f. sp. *tritici* epidemics to assess the influence of the focus on final disease prevalence when the degree of disease susceptibility differed between the at-risk and focus populations.
3. When the focus/at-risk plantings consisted of partially genetic resistant and susceptible cultivars, final disease prevalence was statistically indistinguishable from epidemics produced by the focus cultivar in monoculture. In these experimental epidemics, disease prevalence was not influenced by the transition into an at-risk population that differed in disease susceptibility. Instead, the focus appeared to exert a dominant influence on the subsequent epidemic.
4. Final disease prevalence was not consistently attributable to either the focus or the at-risk population when focus/at-risk populations were planted in a factorial set-up with a mixture (~28% susceptible and 72% resistant) and susceptible individuals. In these experimental epidemics, spatial heterogeneity in disease susceptibility within the at-risk population appeared to counter the dominant influence of the focus.
5. Cessation of spore production from the focus (through fungicide/glyphosate application) after 1.3 generations of stripe rust spread did not reduce final disease prevalence, indicating that the focus influence on disease spread is established early in the epidemic.
6. *Synthesis and applications.* Our experiments indicated that outbreak conditions can be highly influential on epidemic spread, even when disease resistance in the at-risk population is greater than that of the focus. Disease control treatments administered shortly after the initial outbreak within the focus may either prevent an epidemic from occurring or reduce its severity.

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Keywords

disease epidemics; disease outbreak; disease spread; fat-tailed dispersal kernel; landscape epidemiology; long-distance dispersal; wheat stripe rust

Introduction

Epidemic disease spread is a spatio-temporal process that commonly begins with a spatially discrete group of infected individuals that form an outbreak focus (hereafter focus). Over time, disease prevalence increases within the focus and simultaneously spreads outward through an uninfected at-risk population, increasing in severity and expanse until the outbreak is classified as an epidemic. Most studies of epidemic spread are conducted on the at-risk population, with the aim of understanding the varied mechanisms by which disease prevalence, dispersal, host distribution, and landscape conditions interact (Aylor 2003; Eubank *et al.* 2004; Lloyd-Smith *et al.* 2005; Rohr *et al.* 2008; Balcan *et al.* 2009; Meentemeyer *et al.* 2011; Filipe *et al.* 2012). Epidemic spread is a complex process and there are many variables and landscape conditions that can suppress, reduce, or enhance disease spread in at-risk populations (reviewed by Ostfeld, Glass & Keesing 2005; Reisen 2010; Meentemeyer, Haas & Václavìk 2012; Burdon & Thrall 2013). Some of these landscape configurations, such as habitat heterogenity and dispersal corridors (Hess 1994; Plantegenest, Le May & Fabre 2007), represent universal landscape factors that influence organism movement and settlement (Gilbert-Norton *et al.* 2010; Prevedello & Vieira 2010).

The few attempts to model the influence of the focus on disease spread suggested that both epidemic severity and the rate of spread are related to characteristics and conditions of the initial outbreak (Zadoks & van den Bosch 1994; Xu & Ridout 1998; Dybiec, Kleczkowski & Gilligan 2009). Field studies investigating the contribution of the focus to epidemic severity are as rare as modelling studies, yet they too suggest a similar dominant influence of the focus on later epidemic severity (Mundt *et al.* 2009b,2012; Mundt & Sackett 2012; Estep, Sackett & Mundt 2014). Naturally occurring epidemics are, by necessity, studied through retrospectively calibrated models because the initial outbreak often eludes detection and the focus can only be unambiguously specified in the first disease generation (Kot, Lewis & van den Driessche 1996; Newman 2002; Eubank *et al.* 2004; Riley 2007; Meentemeyer *et al.* 2011). The empirical data used to populate these retrospective disease spread simulations are often collected after disease prevalence and expanse are substantial enough for the disease to be categorized as an epidemic (e.g. Dybiec, Kleczkowski & Gilligan 2009; Meentemeyer *et al.* 2011; Filipe *et al.* 2012; Mundt *et al.* 2013). In these situations, data gathered from naturally occurring epidemics are richest in mid-epidemic and limited to the later stages of epidemic spread, biasing research away from the influence of the focus. Experimental initiation of disease outbreaks would enable the study of epidemics from beginning to end, though for most diseases this is not ethically justifiable. Fortunately, crop pathogens provide the opportunity to initiate outbreaks and study pathogen spread with little or no risk to agricultural production or natural ecosystems.

We used a virulent race of the wheat stripe rust pathogen *Puccinia striiformis* f. sp. *tritici* (to which all current commercial wheat cultivars are completely resistant) to induce disease outbreaks in fields planted with susceptible wheat *Triticum aestivum* L. cultivars that are no longer commercially grown. Wheat stripe rust is similar to other long-distance dispersed plant and animal (avian influenza, West Nile Virus) pathogens (Mundt *et al.* 2009a,b), in that it has a fat-tailed dispersal gradient and can produce an epidemic that spreads across regions and continents as an accelerating disease wave (Ferrandino 1993; Kot, Lewis & van den Driessche 1996; Frantzen & van den Bosch 2000, Mundt et al. 2009a). The wheat stripe rust pathosystem has some convenient qualities, aside from the low risk to production crops, which facilitate study over the entire epidemic life. First, experimental epidemics span 4 to 5 generations, which is comparable to the number of generations observed in naturally-occurring, continental-scale stripe rust epidemics (Shaner & Powelson 1971; Chen *et al.* 2002; Wan *et al.* 2004; Wellings 2007). Second, wheat stripe rust spread is well characterized by the inverse power law (Mundt 2009a). The exponent of a power law is unaffected by the scale used to measure the independent variable (distance in the case of pathogen dispersal), enabling the extrapolation of small-scale, experimental epidemics to much greater spatial scales (Gisiger 2001; Mundt 2009a).

To determine whether the focus exerts a dominant influence on epidemic outcome, we manipulated host susceptibility in the focus and the at-risk populations (the initially uninfected region outside of the outbreak focus) using a factorial planting design with experimentally planted plots. If the focus exerts a dominant effect on epidemic outcome, then we expect epidemics originating from foci with similar host susceptibilities to develop similarly, regardless of host susceptibility in the at-risk population. To further investigate the influence of the focus on epidemic severity, we halted spore production in the focus of some experimental plots after 1.3 generations of stripe rust build-up through direct application of a fungicide/herbicide spray. If cessation of spore production from the focus has no effect on final disease prevalence, then influence of the focus is established early in the epidemic. Conversely, if cessation of spore production from the focus generates differences in final disease prevalence, then the epidemic spreads through the dispersion of increasingly greater propagule numbers from the focus over the duration of the epidemic.

Materials and methods

STUDY SYSTEM

Wheat stripe rust is caused by an obligate parasitic fungus that requires high night-time relative humidity, mild temperatures, and healthy plants for infection, lesion growth, and sporulation (Chen 2005). Unlike some non-obligate fungal pathogens, which capitalize on weakened hosts, wheat stripe rust infection efficiency, spore production and lesion growth diminish with reductions in host plant vigour (Chen 2005). Our experimental fields are located on private property near Culver, Oregon, USA, an isolated agricultural district in arid central Oregon, where diel temperature fluctuations (~15–20° C) promote the overnight dew necessary for spore germination. Irrigation during the growing season encourages vigorous plant growth and the moisture required to sustain mini-epidemics for multiple generations in the arid climate. Low winter temperatures reduce the rust's overwintering

potential (Chen 2005) and geographic isolation from the region's major wheat-producing areas further decreases the chance of non-experimental stripe rust infections.

Fields were planted with a combination of three different winter wheat cultivars. Cultivar 'Jacmar' is completely susceptible (S) to wheat stripe rust race PST 5, and cultivar 'Faro' is partially resistant (PR). PST 5 causes 50–70% less disease on 'Faro' than it does on 'Jacmar' (Akanda & Mundt 1996; Brunet & Mundt 2000; Garrett & Mundt 2000). Cultivar 'Stephens', which is completely resistant to wheat stripe rust race PST 5 (Chen 2005), was planted between experimental plots to limit pathogen spread among plots with susceptible cultivars. Disease susceptibility was also manipulated through a mixture (Mix) planting of ~70% Stephens and 30% Jacmar. The mixture planting reduces population susceptibility by limiting the number of susceptible hosts whereas the Faro (PR) planting reduces disease susceptibility through genetic resistance shared by all individuals.

INOCULATION AND EXPERIMENTAL DESIGN

Experiments were planted in four different fields, two in the fall of 2011 and two in the fall of 2012, for the study of disease spread the following spring (hereafter we will refer to the years as 2012 and 2013, corresponding to the year disease data were collected). Experimental plots had the same basic design in both years: a rectangular plot with a 1.5-m strip in which the focus cultivar was planted (Fig. 1). Plots were oriented east–west to exploit the prevailing west north westerly winds (Van de Water *et al*. 2007) which favour an easterly spread of disease from the focus (planted in the west end of each plot (Mundt *et al.* 2009b). Plot dimensions were 13.7 × 73.2 m in 2012 and 7.6 × 42.7 m in 2013, and the distances between plots (buffers planted with the resistant Stephens cultivar) were a minimum of 19 m. Inoculation of a 1.5 × 1.5 m focus (within the focus strip) of each plot occurred in mid or late April. PST 5 spores were produced in growth chambers on susceptible wheat plants and applied to experimental foci as individual aliquots of a spore–talc mixture (0.42 g of spores to 3.2 g of talc). Inoculation took place on evenings with calm winds and inoculum was applied to moistened plants inside a PVC pipe frame covered with clear plastic film to prevent spore escape. To ensure high overnight relative humidity (which increases infection efficiency) and to confine spores to the outbreak focus, we covered the inoculation area immediately following spore introduction with black plastic film for ~13 hours (Sackett & Mundt 2005). One field in 2013 was dropped from study due to adverse conditions that resulted in low inoculation success.

A randomized block design with four replications was set up in each field with the following combinations of focus and at-risk populations: 1) susceptible focus and at-risk population (S-S), 2) partially resistant focus and at-risk population (PR-PR), 3) mixture focus and at-risk population (Mix-Mix), 4) partially resistant focus and susceptible at-risk population (PR-S), 5) susceptible focus and partially resistant at-risk population (S-PR), 6) mixture focus and susceptible at-risk population (Mix-S), and a 7) susceptible focus and mixture at-risk population (S-Mix).

In 2013, we included four additional all-susceptible plots to determine whether eliminating the production of spores from the focus in mid-epidemic impacts disease spread. We sprayed all plants in the inoculated focus with a combination of Stratego™ (trifloxystrobin +

propiconazole), a fungicide that arrests fungal lesion growth and spore production, and glyphosate, which initially reduces plant vigour and eventually leads to host death. After spray application, spore production ceases and plant vigour is reduced so that local infection within the focus cannot occur. Sprays occurred on 30 May, after ~1.3 generations of infectious spread (generation time calculated from local weather station data and Shrum's [1975] degree-day model).

DISEASE ASSESSMENT

Disease prevalence, as a percentage of the maximum number of lesions (~100 lesions/tiller), was assessed weekly throughout the infectious season in 1.5-m^2 quadrats located in the focus and at 3, 6, 12, 18, 24, 30, 36, 42, 48, 54, and 60 m (in 2012), and 1.5, 3, 6, 9, 12, 15, 18, 21, 24, 27, and 30 m (in 2013) from the focus centre. Plot lengths necessarily differed between 2012 and 2013 due to field size constraints and the necessity to maintain ample buffers between plots. Disease assessments began after the first appearance of rust lesions (mid-May) and ended in late June–early July of each study year (~4 generations of disease spread). Observer bias in disease prevalence estimates was reduced by cross-calibration and recording the mean disease prevalence value from observer pairs who were assigned to a single field for an entire growing season. In the mixture plots, only the susceptible cultivar could be infected, so we assessed disease prevalence as in the non-mixture treatments, but subsampled the number of susceptible and resistant tillers (these genotypes conspicuously differ in seed head morphology) to estimate stripe rust prevalence on the susceptible cultivar.

ANALYSIS

For each field, we plotted disease prevalence in the at-risk populations against distance from the focus. To evaluate epidemic outcome, we calculated the area under the disease gradient (AUDG) on the final assessment date (late June–early July) using the mid-point method (Madden, Hughes & van den Bosch 2007). Because we were interested in treatment effects on the at-risk population, we excluded disease prevalence in the focus from AUDG calculations. Preliminary analysis of AUDG-values within treatments and between years revealed no statistically significant interactions attributable to plot size differences (*P*-values generally > 0.20). Therefore, in subsequent statistical analyses we did not adjust for differences in plot size.

We subjected *ln*-transformed AUDG-values to an analysis of variance (ANOVA) using Proc GLM in SAS (SAS Institute 2008) to determine whether final disease prevalence in the at-risk populations differed among treatments. To ascertain whether there was a dominant effect of the focus on final disease prevalence in the at-risk population, we applied a separate GLM for each factorial combination of partially resistant/susceptible and mixture/susceptible plantings (Table 1). Planned comparisons of disease prevalence between treatment pairs were made using linear contrasts of least square means (Table 1).

A *t*-test on disease prevalence within the focus was used to determine whether the sprayed plots differed from the unsprayed plots on the spray application date. Since no statistically significant difference was found (mean spray prevalence = 6.6%, mean no-spray prevalence

= 6.3%, $T = 0.1291$, $P = 0.90$) there was no need to adjust for unequal initial disease prevalence in the two groups. We analysed AUDG-values (*ln*-transformed) with a *t*-test to determine whether spore cessation in the focus impacted final disease prevalence (27 June 2013) ~2.0 generations after spray application.

Results

EPIDEMIC PREVALENCE

Disease prevalence curves, after ~4 generations of epidemic spread, showed some consistent relationships within and between treatments in all study fields (Fig. 2). The focus appeared to exert a dominant influence on disease prevalence in the at-risk populations in factorial combinations of partial genetic resistance (PR) and susceptible (S) plantings. In these PR-S planting combinations, disease curves grouped according to the focus cultivar composition (*e.g.* disease curves from PR foci grouped together regardless of host susceptibility in the at-risk population) (Fig. 2a,c). At the end of the epidemic, disease prevalence in the foci followed the same pattern of grouping (PR foci grouped together as did S foci) (Fig 2a,c). In contrast, the focus did not appear to exert a consistently dominant influence on the at-risk population disease prevalence when the plantings were mixture (Mix) and susceptible (S). In these factorial plantings, combinations of non-matching foci and at-risk populations (Mix-S and S-Mix), produced epidemics with intermediate disease prevalence compared to plantings with matching foci and at-risk populations (Mix-Mix and S-S) (Fig. 2b,d). Final disease prevalence in the foci did not appear to form any clear patterns of association, with mixture foci either grouping with other mixture foci (Fig. 2d) or with susceptible foci (Fig. 2b).

Analysis of AUDG-values with GLMs and planned linear contrasts generally supported the qualitative patterns observed in disease curve groupings (Fig. 2). First, we found a statistically significant ($\alpha < 0.05$) difference in AUDG-values due to treatment and field, but no statistically significant treatment × field effect (Table 2). These results indicate that the field had an effect on epidemic prevalence but it did not statistically influence treatment effects associated with the partially resistant/susceptible and mixture/susceptible plantings. Second, GLMs indicated a statistically significant effect of the focus, but not the at-risk population, on AUDG-values when the partially resistant/susceptible factorial plantings were compared (Table 3). Planned comparisons of AUDG-values between factorial combinations of partially resistant/susceptible plantings generally agreed with the disease curves (Fig. 2a,c); plots containing a susceptible focus were statistically indistinguishable from each other but differed from treatments with a partially resistant focus (Table 4). There was, however, one planned treatment comparison that was not statistically significant at $\alpha < 0.05$. Comparison of the all partially resistant (PR-PR) to the susceptible focus and partially resistant at-risk population (S-PR) had a *P*-value of 0.078, suggesting that the two planting arrangements may not differ from each other (Table 4). Third, GLMs indicated that the mixture/susceptible plantings were not characterized by a dominant focus effect but rather an independent effect of both the focus and at-risk populations (Table 3). In the planned linear comparisons, AUDG-values did not consistently group according to the focus composition in the mixture/susceptible factorial plantings (Table 4). Non-matching plantings

of foci and at-risk populations (Mix-S and S-Mix) generally produced disease curves that were intermediate to the monoculture plantings (Mix-Mix and S-S) (Table 4). Last, AUDG-values statistically differed in pairwise comparisons between all three monoculture plantings (S-S, PR-PR, and Mix-Mix) (Table 4), indicating that each served as a suitable standard for statistical comparison between different planting combinations of foci and at-risk populations.

In the field, we observed that the completely resistant cultivar was often less vigorous in the mixture plantings than the susceptible cultivar. In the at-risk population mixture plantings, the relative reduction in plant vigour created within-plot patchiness and a non-continuous canopy of leaves that was atypical of our plantings with single cultivars. When these less vigorous plants were inspected closely, both within the at-risk population and the buffer areas, symptoms were consistent with take-all of wheat, a root disease caused by *Gaeumannomyces graminis* var. *tritici*, to which the stripe rust resistant cultivar (Stephens) appeared to be more susceptible than the other cultivars.

CESSATION OF SPORE PRODUCTION WITHIN THE FOCUS

Disease curves of sprayed and unsprayed plots did not appear to differ in overall shape (Fig. 3). After 2.0 additional generations of pathogen spread following the spray treatment, AUDG-values between the sprayed and no-spray plots did not statistically differ (mean *ln*-AUDG spray =3.73, mean ln-AUDG non-spray = 3.33, $T = 0.87$, d.f. = 6, $P = 0.42$), suggesting that the focus influence is established early in the epidemic progression.

Discussion

Understanding organism movement, settlement and reproduction is necessary to develop predictive models of infectious disease spread, biotic invasions, responses to anthropogenically driven landscape modifications, and species distribution shifts as a consequence of global climate change (Harvell *et al.* 2002; Nathan *et al.* 2008; Vos *et al.* 2008; Knowlton & Graham 2010, Filipe *et al.* 2012). Similar to functional connectivity and metapopulation dynamics (Revilla *et al.* 2004; Katul *et al.* 2005; Baguette & Van Dyck 2007, Hawkes 2009; Wotton & Kelly 2012), disease spread can be studied from a landscape perspective as it is a spatio-temporal process that can be impacted by landscape-level elements (Nathan *et al.* 2005,2008; Ostfeld, Glass & Keesing 2005; Soubeyrand *et al.* 2009; Meentemeyer, Haas & Václavìk 2012). Conditions within the focus have been hypothesized to influence the landscape-level dispersion of an epidemic (Zadoks & van den Bosch 1994; Xu & Ridout 1998) and our spray treatment results support this understudied aspect of disease epidemic spread. Furthermore, field experiments indicated that the influence of the focus remains detectable after several generations of pathogen reproduction and dispersal across the landscape, even when the focus (in our experiment 1.5×1.5 m) is < 1% of the total area of the at-risk population. The conditions during the initial outbreak, however small, can exert a large and persistent influence on the surrounding landscape.

By planting a susceptible focus and partially resistant at-risk population (S-PR) we created conditions analagous to a vaccination disease control strategy. By doing so, we could assess whether the disease prevalence would be reduced by the transition into a population with

greater genetic disease resistance. Epidemics in these partially resistant at-risk populations were statistically indistinguishable from the epidemics that were initiated and spread through plantings consisting entirely of the susceptible cultivar (Table 4), demonstrating the critical influence of the outbreak focus on epidemic outcome. Although this degree of focus influence is consistent with some modelling studies of epidemic spread (Zadoks & van den Bosch 1994; Xu & Ridout 1998; Dybiec, Kleczkowski & Gilligan 2009; Estep, Sackett & Mundt 2014), it is also counter to the prevailing view that epidemic severity is dominated by interactions within the at-risk population. Instead of the partial genetic resistance in the at-risk population decreasing disease prevalence as the pathogen spread from the foci with susceptible individuals (S-PR), the susceptible foci exerted a stronger influence on the final disease prevalence than the partially resistant at-risk population. When the plantings were reversed, so that the focus was partially resistant and the at-risk population was susceptible (PR-S), disease prevalence in the at-risk population was statistically indistinguishable from the epidemics produced in the partially resistant monocultures (Table 4). Our factorial plantings with susceptible and partially resistant cultivars indicate that epidemic severity can be dominated by the outbreak focus even when the at-risk population should, by disease ecology convention, facilitate or hinder spread through differences in genetic resistance.

In some respect, the influence of the outbreak focus on epidemic spread resembles founder effects for wind dispersed propagules (*e.g.* spores and plumed seeds) and organisms (*e.g.* ballooning spiders); the conditions at the initial release point tend to make a defining contribution to the dispersal kernel (Nathan *et al.* 2002; Katul *et al.* 2005; Reynolds, Bohan & Bell 2007). Cessation of spores produced by the focus after ~1.3 generations of wheat stripe rust increase did not impact disease prevalence (Fig. 3), indicating that the dominant influence of the focus is established very early in the epidemic. Indeed, recent models of wheat stripe rust spread suggest that the focus exerts its greatest influence on the subsequent epidemic when the majority of spores produced from an infection remain local (Estep, Sackett & Mundt 2014). The focus appears to establish the initial landscape pattern of disease distribution with subsequent intensification being driven by local spore production and dispersion.

Spatial heterogeneity in disease resistance, represented in the current experiment by mixtures of susceptible and resistant plants, has the potential to slow, reduce, and localize disease occurrence in natural and human-impacted ecosystems (Mundt 2002; Ostfeld, Glass & Keesing 2005; Alonso, McKane & Pascual 2007; Real & Biek 2007; Laine *et al.* 2011; Meentemeyer, Haas & Václavìk 2012; Burton & Thrall 2013). In plant communities, the observation that disease occurrence is reduced with an increase in species diversity has been explained by the dilution effect, where disease prevalence is limited by the rarity of the susceptible host plant species (Rudolf & Antonovics 2005; Keesing, Holt & Ostfeld 2006). With spatially heterogeneous populations consisting of susceptible and resistant individuals (analogous to mixed-species communities), the all-mixture plots experienced reductions in wheat stripe rust prevalence when compared with all-susceptible and all-partially resistant plots (Table 4). In contrast to the dominant focus influence in the partially resistant/susceptible plantings, we found independent effects of both the focus and at-risk population on disease prevalence (Table 3). Furthermore, when the focus and at-risk population

plantings differed (Mix-S, S-Mix), the resulting epidemics in the at-risk population were intermediate to the all-susceptible and all-mixture treatments – an outcome we did not observe in the partial genetic resistance plantings (Fig. 2). Both of these results indicate that the mixture plantings introduced alternative sources of variation that resulted in disease prevalence fluctuations between fields and years.

Although the spatially heterogeneous distribution of completely susceptible and resistant individuals in the mixture plantings may have generated enough patchiness to account for the variable focus and at-risk population interactions, we suspect that vigour reductions in the resistant cultivar (through take all disease) further influenced disease prevalence. In a previous experiment, with similar factorial plantings of susceptible and mixture populations, there was a strong, dominant focus effect on disease prevalence in the at-risk population but no statistically significant at-risk population effect (Estep, Sackett & Mundt 2014). In that experiment, individuals in the mixture plantings were extremely vigorous and the mixture produced a continuous foliar canopy, essentially creating ideal conditions for epidemic stripe rust spread. In our present study, growing conditions were generally favourable for disease spread but the resistant genotypes seemed to be of below-average vigour, in all likelihood due to take-all disease. These less-vigorous, but resistant, individuals in the mixture reduced overall foliar density, creating canopy gaps that were not observed in the partially resistant/susceptible plantings and not all in the prior experiment with mixtures (Estep, Sackett & Mundt 2014). Discontinuity in canopy cover may have locally reduced infection rates on the susceptible plants by lowering the relative humidity (high relatively humidity encourages stripe rust infection and growth) and creating gaps over which the spread of spores was challenged. Our experiments with mixtures suggests that landscape and habitat heterogeneity is likely to generate an unpredictable epidemic progression (*e.g.* Alonso, McKane & Pascual 2007) and that spatial heterogeneity in the at-risk population can be strong enough to counter the dominant effect of the focus on later epidemic severity.

Experimental manipulation of host susceptibility within the focus and at-risk populations has provided strong evidence that conditions within the focus can be propagated across the landscape for the duration of a wheat stripe rust epidemic. Only in mixture plantings did we observe a statistically significant effect of the at-risk population on final epidemic prevalence, and it is likely that these independent focus and at-risk population effects were due to spatial heterogeneity arising from multiple sources. The overall result of our field experiments, i.e. a strong influence of host susceptibility in the outbreak focus established early in the course of an epidemic has two important implications for the management of disease outbreaks. First, implementation of eradication campaigns must be established very early if they are to be effective and efficient. This is best demonstrated by the results of our spray treatments, in which the cessation of spore production in the focus after 1.3 generations of spread had no discernible influence on epidemic development. Second, predictions of epidemic spread and implementation of disease interventions will be enhanced if the degree of host susceptibility in the outbreak focus is accounted for in predictive/retrospective models and disease control treatments.

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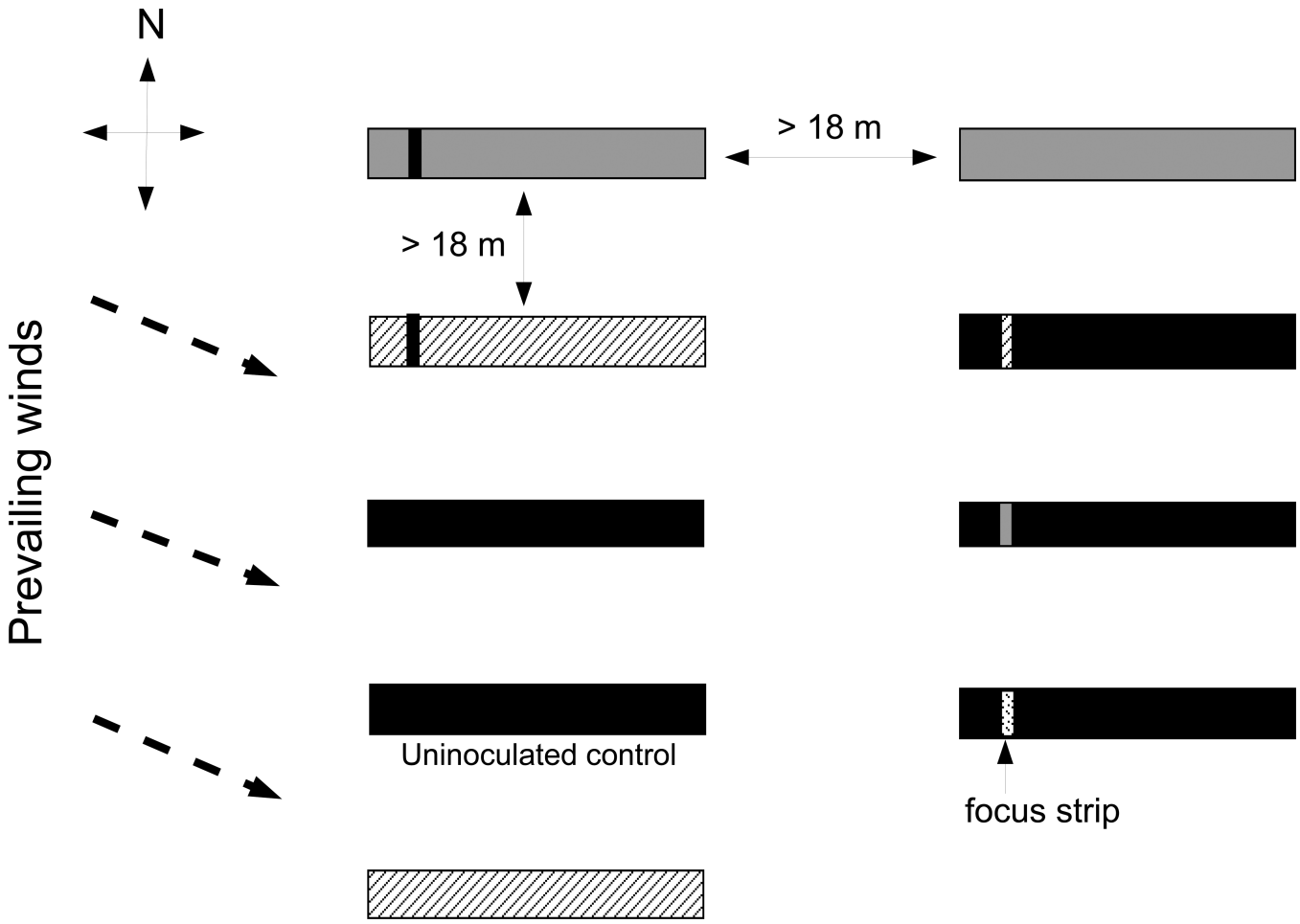

Fig. 1.

Mock schematic of experimental plots showing one complete block containing all combinations of outbreak foci and at-risk populations. Black areas are susceptible (S), grey areas are partially resistant (PR), hatched areas are mixture (M) and white areas are resistant buffers.

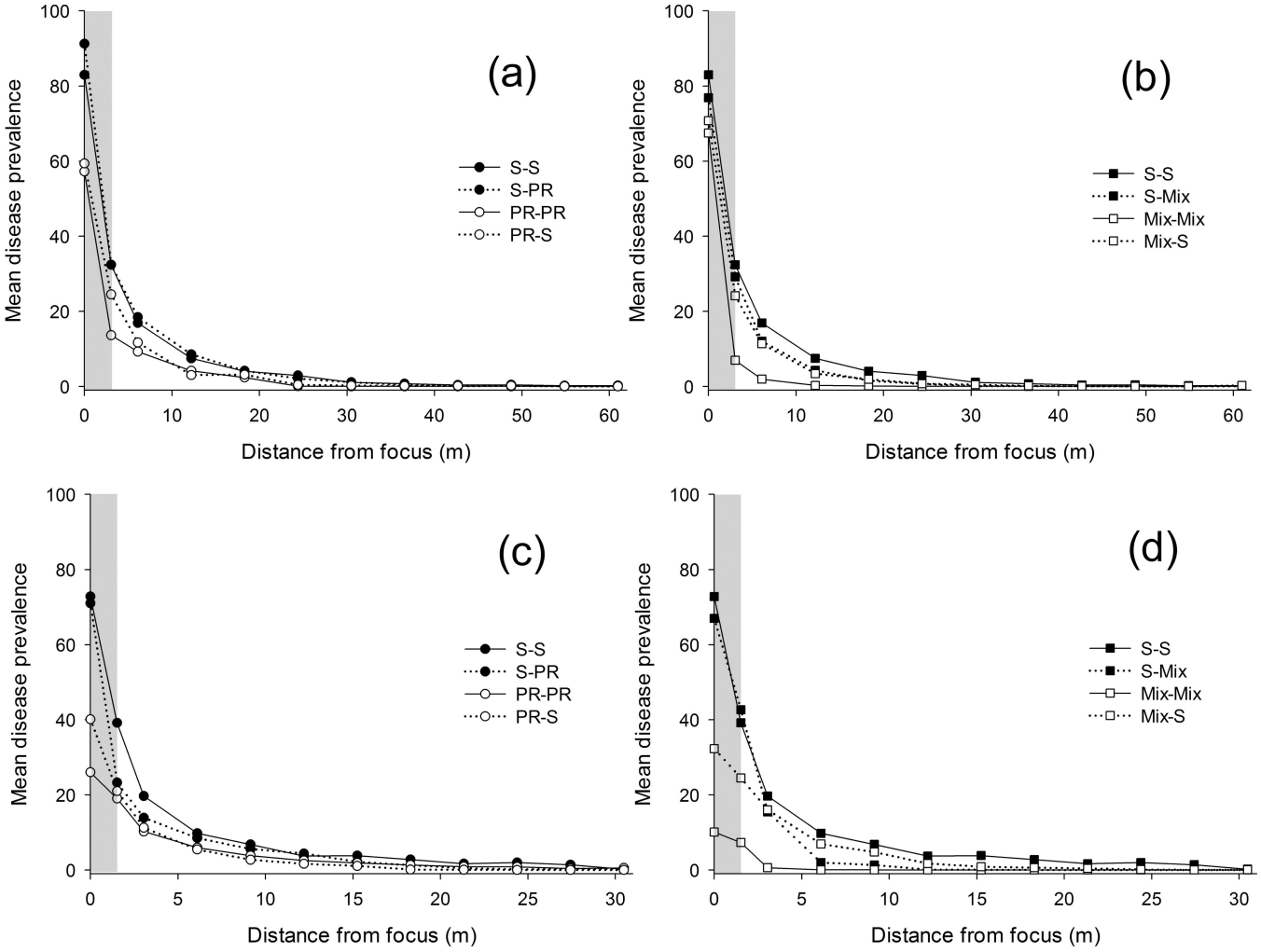

Fig. 2.

Mean disease prevalence with distance from the outbreak focus (disease gradient curves) in the at-risk population grouped by year and pre-planned comparisons: (a) 2012 PR-S combinations, (b) 2012 Mix-S combinations, (c) = 2013 PR-S combinations, (d) = 2013 Mix-S combinations. The outbreak focus disease prevalence (region in grey) was excluded from the area under the disease gradient (AUDG) calculations while the remaining area (in white) was included.

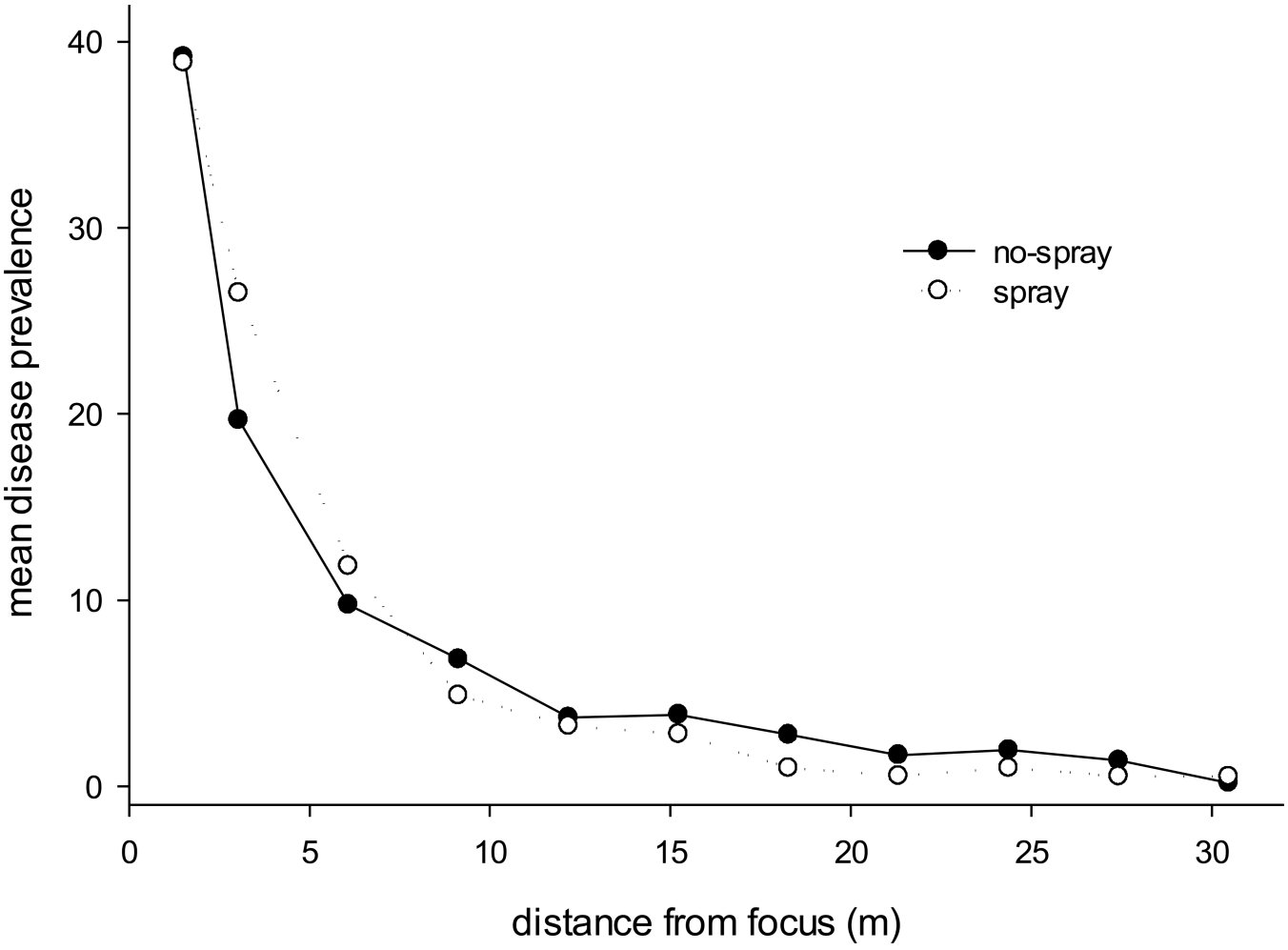

Fig. 3.

Final mean disease prevalence for spray (focus spore production arrested) and no-spray susceptible monoculture plots after ~1.3 generations of initial spread from the outbreak focus in the at-risk population.

Table 1

List of treatments, treatment codes and planned comparisons for the influence of the outbreak focus on epidemic prevalence

Treatment	Code	Outbreak Focus	At-risk population	Planned comparisons
1	S-S	Susceptible	Susceptible	1 vs 2, 1 vs 3
2	PR-PR	Partial Resistance	Partial Resistance	*Treatments should statistically differ in disease prevalence as suitable standards for comparison of factorial combinations*
3	Mix-Mix	Mixture	Mixture	
4	PR-S	Partial Resistance	Susceptible	1 vs 4, 2 vs 4, 1 vs 5, 2 vs 5
5	S-PR	Susceptible	Partial Resistance	*Full factorial test to determine whether the outbreak focus drives disease prevalence*
6	Mix-S	Mixture	Susceptible	1 vs 6, 3 vs 6, 1 vs 7, 3 vs 7
7	S-Mix	Susceptible	Mixture	*Full factorial test to determine whether the outbreak focus drives disease prevalence*

Table 2

GLM results, degrees of freedom (*d.f.*), F-statistic (*F*), and probability value (*P*) for treatment, field and treatment × field effects

Source of variation	*d.f.*	*F*	*P*
Treatment	6	2.71	0.023
Field	2	9.13	0.004
Treatment × Field	12	0.46	0.93

Table 3

GLM results, degrees of freedom (*d.f.*), F-statistic (*F*), and probability value (*P*) for susceptible–partial resistance factorial combinations and mixture–susceptible factorial combinations (S = susceptible, PR = partially resistant, Mix = mixture)

Source of Variation S-PR	***d.f.***	***F***	***P***
Model	11	2.83	*0.01*
Field	2	8.78	*0.0009*
Outbreak Focus	1	8.55	*0.006*
At-risk population (Population)	1	0.81	0.38
Field×Focus×Population	2	0.77	0.47
Focus×Population	1	0.07	0.79
Field×Focus	2	0.58	0.57
Field×Population	2	0.05	0.95
Source of Variation S-Mix			
Model	11	4.99	*0.0002*
Field	2	4.04	*0.027*
Outbreak Focus	1	11.73	*0.002*
At-risk population (Population)	1	25.11	*<0.0001*
Field×Focus×Population	2	1.29	0.29
Focus×Population	1	2.46	0.13
Field×Focus	2	1.26	0.30
Field×Population	2	0.63	0.54

Table 4

Linear contrast results of pre-planned treatment comparisons listed in order of outbreak focus-at risk population *vs* outbreak focus-at risk population (S = susceptible, PR = partially resistant, Mix = mixture)

Treatment	Treatment	*P*
S-S	PR-PR	*0.013*
S-S	Mix-Mix	*<0.001*
S-S	PR-S	*0.047*
S-S	S-PR	0.440
PR-PR	PR-S	0.694
PR-PR	S-PR	**0.078**
S-S	Mix-S	0.164
S-S	S-Mix	*0.014*
Mix-Mix	Mix-S	*<0.001*
Mix-Mix	S-Mix	*0.001*

* *P*-values < 0.05 are in italics, *P*-values < 0.10 are in bold