# Prophylactic treatment for *Batrachochytrium dendrobatidis* increases infection loads in a field trial: A possible result of increased host survival

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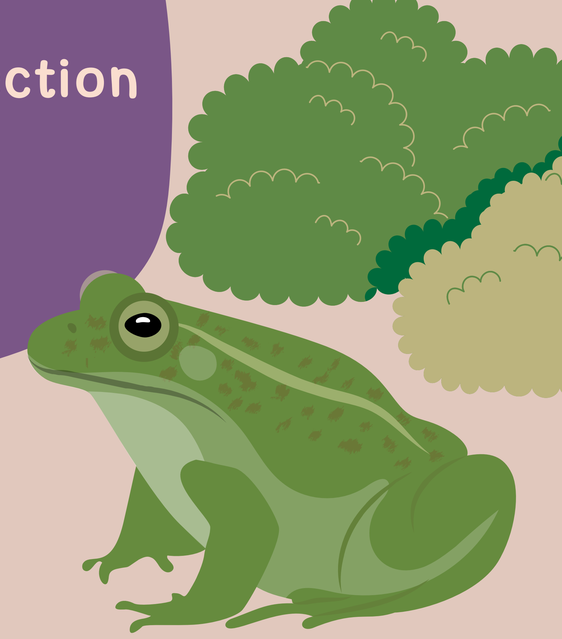


## Introduction

### Disease urgently requiring intervention

Chytridiomycosis, caused by the aquatic fungal pathogen Batrachochytrium dendrobatidis (Bd), has led to an unprecedented level of biodiversity loss attributable to a single pathogen [1] and disease interventions are urgently needed to prevent further losses.

### Promising, but imperfect, prophylactic treatment

Topical treatment with Bd-metabolites confers partial protection against the pathogen [2,3]. Treatment significantly reduces infection intensities when applied pre-pathogen exposure but does not completely block infection establishment or transmission. Partially protective treatments can confer population-level benefits, but may also backfire under certain circumstances [4].

## Objectives

1. **Determine how varying modes of treatment efficacy and levels of population coverage affect key epidemiological and conservation endpoints**

2. **Assess if partial protection from Bd-metabolite treatment is sufficient to reduce infection prevalence and intensities when administered in the field**

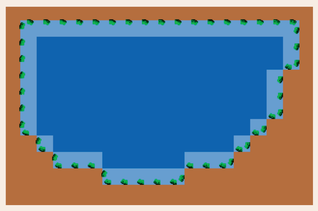
## Field Trial Methods

We conducted a Before-After Control-Impact experiment in which we administered the prophylactic treatment at the whole water body scale in replicated ponds in northern California following the breeding season. We measured infection prevalence and load among post-metamorphic frogs 1-2 months later to assess the effectiveness of treatment.

## Bd-amphibian-prophylaxis Model

In Netlogo 6.3.0, we built an agent-based eco-epidemiological model of our system and evaluated four mechanistic representations of imperfect immunity wherein Bd-metabolite treatment can alter:

1. probability of infection establishment
2. rate of pathogen clearance
3. rate of pathogen shedding
4. threshold of Bd-induced mortality



Mechanisms 1-3 are considered modes of resistance, while mechanism 4 is a mode of tolerance.

## Field Results

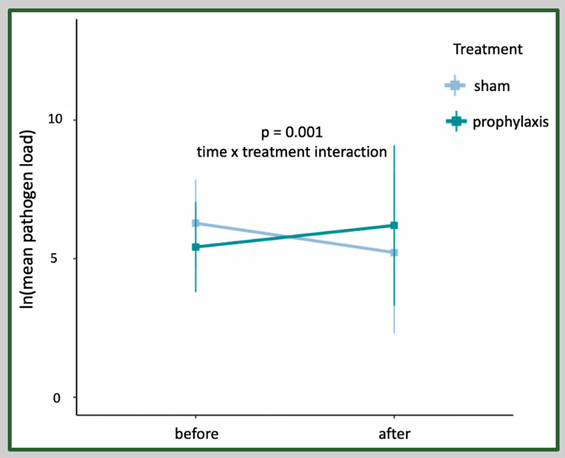



Figure 1. This interaction plot shows the change in Bd load before and after Bd metabolite addition. Ponds treated with Bd metabolites are represented in dark green and sham treated ponds are represented in light blue. There was a significant time by treatment interaction.

**Frogs from ponds treated with Bd metabolites had significantly higher Bd loads after treatment than ponds treated with sham treatment.**

## Key Model Results

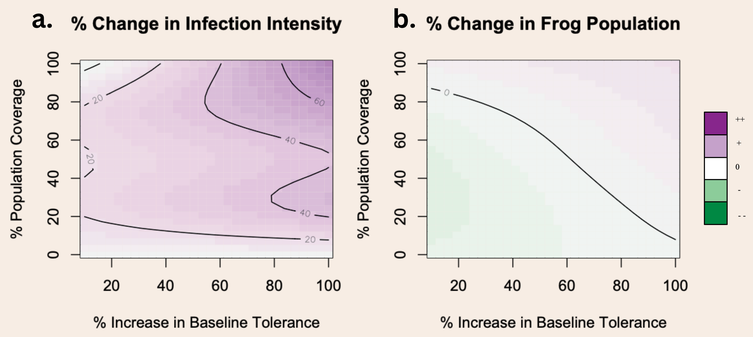



Figure 2. Modeled changes in a) infection intensity and b) final frog population as treatment increases host tolerance (i.e. host's ability to survive high infection burdens) and population coverage. Deeper green shades represent reductions and deeper purples represent increases compared to populations without treatment. Contour lines define increments of 20% change.

**Infection loads increase with increasing levels of host tolerance. Across the four types of treatment efficacy we modeled, boosted tolerance is most consistent with our field results.**

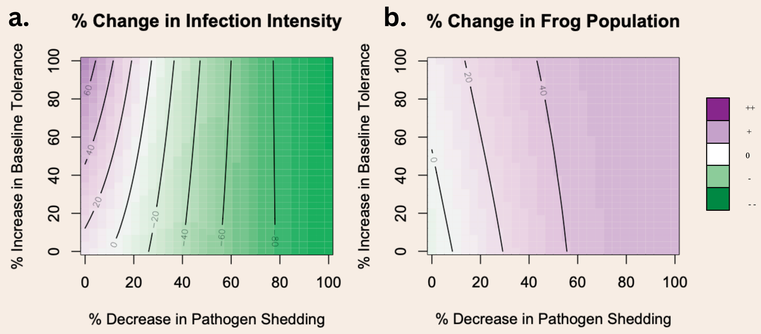



Figure 3. Modeled changes in a) infection intensity and b) final frog population as treatment boosts both resistance (by decreasing pathogen shedding) and host tolerance in a population where 75% of hosts are treated. Deeper green shades represent reductions and deeper purples represent increases compared to populations without treatment. Contour lines define increments of 20% change.

**Results from our model show that the impact of tolerance on increasing infection intensities can be counteracted by the addition of a resistance mechanism.**

## Alternative scenario investigated but inconsistent with field results

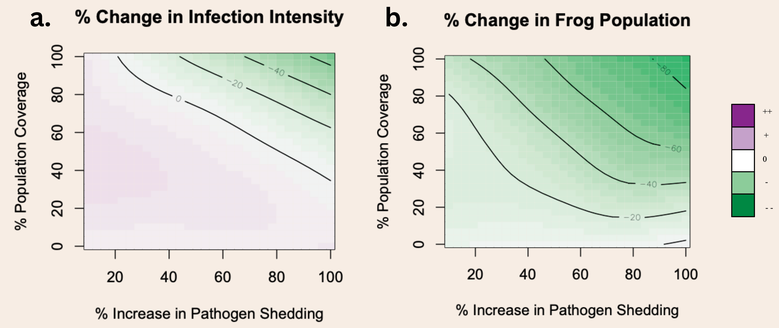



Figure 2. Modeled changes in a) infection intensity and b) final frog population of an alternative scenario wherein treatment backfires and increases disease transmission (i.e., pathogen shedding) across increasing levels of population coverages. Deeper green shades represent reductions and deeper purples represent increases compared to populations without treatment. Contour lines define increments of 20% change.

## Main Conclusions

- **Counter to previous lab findings, Bd infection intensity significantly increased (p = 0.001) after ponds were treated with Bd-metabolites (Figure 1).** We found no change in infection prevalence.

- **Model scenarios in which the prophylaxis boosts tolerance (i.e. increases a host's ability to survive high infection burdens) were most consistent with our field results (Figure 2) given that none of the modes of resistance increased infection loads.**

- While it may be positive that frogs are less likely to succumb to Bd-induced mortality, it can be problematic at the population-level if longer infection durations increase onward transmission, thereby increasing risk of infection to untreated sympatric amphibians. Additionally, increasing tolerance was not effective at increasing frog population size.

- When a treatment at least moderately increases resistance (with or without increasing tolerance), infection intensities decrease and frog population sizes increase (Figure 3). This suggests that Bd metabolite prophylaxis has a much stronger effect on increasing tolerance relative to its effect on increasing resistance.

- To investigate the hypothetical possibility that an environmental interaction caused the treatment to be harmful when applied in the field, we tested scenarios in which treatment increased disease susceptibility (Figure 4). However, under our model parameterization, these scenarios led to population die-offs and subsequently lower infection intensities of surviving frogs, thus inconsistent with our field observations.

- **Our findings underline the importance of accounting for how different mechanisms of individual-level protection can scale up to counterintuitive and potentially harmful population-level outcomes.**

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