Discussion

The objective of this study was to evaluate how bacteriophages influence total and resistant bacterial populations under antibiotic treatment using a mathematical model. The results support the hypothesis that bacteriophages reduce overall bacterial load, but do not completely support that phage-mediated transduction allows resistant bacteria to persist, as seen in figure 2 where all bacteria populations crash.

Deterministic simulations showed that phage treatment alone produced the most rapid decline in total bacterial populations, consistent with the current assumption that phage-resistance in bacteria is minimal. Antibiotic-only simulations showed strong selective pressure favoring resistant strands over susceptible ones due to early-on killing of susceptible bacteria. This pattern aligns with established evolutionary showing that antibiotic exposure accelerates resistance selection (Andersson & Hughes, 2010).

The combined phage-antibiotic treatment produced nonlinear oscillatory dynamics between phages and bacteria. This reflects early bacterial killing by antibiotics, reducing resources for the phages and causing their population to dip before experiencing a rebound due to the lack of antibiotics (due to antibiotic decay) to kill bacteria. Importantly, resistance was not eliminated in this combined scenario, indicating that increased bacterial suppression does not necessarily translate to resistance eradication.

The parameter sweep of initial phage concentrations revealed a nonlinear relationship between phage does and bacterial outcomes. Moderate phage levels minimized resistance while maintaining reduced total bacterial load. This finding suggests that maximizing phage concentration is not necessarily optimal, and that treatment intensity can influence evolutionary outcomes. Variability across

Monte Carlo trials demonstrated that identical initial conditions can lead to different outcomes, highlighting the importance of stochastic effects in microbial population dynamics.

Several limitations should be considered. In general, this model trades some biological accuracy in exchange for simplicity. An example of this is the assumption of homogeneous mixing of bacteria and phages, which neglects spatial structure present in real infections. Additionally, parameter values were selected from literature ranges rather than calibrated to a specific biological system, limiting quantitative predictive claims. Despite these constraints, the model captures key ecological and evolutionary processes.

Overall, this work contributes to the field by integrating antibiotic decay, phage predation, resistance persistence, and stochastic variability into a single framework. The results emphasize that phage therapy should be evaluated not only for bacterial clearance but also for its long-term evolutionary consequences.

Future Research

Future work should expand the model to incorporate spatial structure, such as biofilm formation, to better represent realistic infection dynamics. Including spatial dynamics would allow investigation of how localized phage amplification and antibiotic penetration influence resistance persistence in a living body rather than a two dimensional surface.

The model could also be refined by exploring the use of multiple different types of phages and antibiotics, which can further optimize treatment strategies and test the robustness of the model by verifying if it holds under various conditions.

Additional sensitivity analyses should be conducted to systematically identify which parameters most strongly influence resistant outcomes. This would improve model robustness and help determine which biological processes are most critical for therapeutic optimization.

Finally, the framework could be extended to explore timing strategies, including periodic antibiotic treatments. Optimizing treatment timing may prove more impactful than increasing dosage alone and could provide insights relevant to combination therapy design.

Advancing these directions will strengthen understanding of how ecological and evolutionary processes interact under combination antimicrobial therapies and may inform more resistance-aware treatment strategies.