Summary ODD:

A summarized model description, following the ODD (Overview, Design concepts, Details) protocol (Grimm et al. 2006, 2010, 2020) is provided. The full model code is available at https://github.com/vanhasseltlab/PolyMicro-ABM-Virulence without restrictions.

The overall purpose of our model is to provide an improved understanding of ecological dynamics within polymicrobial infections which may support development of improved treatment strategies using antimicrobials and anti-virulence compounds. Specifically, we assessed (i) how bacterial virulence factors targeting neutrophil function influence the survival and community composition of a dual-species infection and (ii) the effect of bacterial virulence targeting neutrophil function on the treatment outcome of a dual-species infection. **To consider our model realistic enough for its purpose, we use the following patterns:** 1) bacterial dynamics and antimicrobial treatment based on pharmacodynamic equations assuming capacity-limited bacterial growth with sigmoidal drug effect inhibiting the bacterial replication rate 2) neutrophil dynamics based on previously developed model.

The model includes the following entities: bacterial agents, neutrophil agents, patches on grid with environment shared by all agents present on this grid, collectives of agents representing bacterial species subpopulations. **They are characterized by the following state variables:** 1) bacterial agents of one species collective differ from agents belonging to another bacterial species in their virulence characteristics, specifically the virulence strength parameters v_c, v_r and v_s which are constant over time; 2) neutrophil agents have a state variable tracking their age and the number of bacteria they have phagocytosed in their lifetime. **As for the spatial and temporal resolution:** The model is simulated at a 5 minute time step for up to 24 hours. The spatial extent of the model are 100 patches on a toroidal grid. Each patch represents an infection volume which can harbor approximately 50 bacterial agents and one neutrophil agent in average when at capacity.

The most important processes of the model, which are repeated every time step, every agent is activated in random order and will execute its actions in a set order. The type of actions an agent performs is determined by the type of agent. Bacterial agents can 1) move, 2) replicate or die from natural causes or as a result of drug treatment. Neutrophil agents can 1) move, 2) phagocytose bacteria and 3) die by natural clearance or as a result of pathogen-induced apoptosis. The action-specific probabilities P_net, P_phag and P_death determine whether each action takes place. At the end of every timestep, neutrophil agents for the next timestep are recruited to the grid and the time variable is advanced. The presence of bacteria possessing phagocytosis-inhibiting virulence factors v_c and v_s affect the probability of phagocytosis P_phag, whereas the presence of recruitment-inhibiting

virulence factors v_r affects the number of neutrophils recruited at the end of the timestep.

The most important design concepts of the model are the way we incorporate virulence factors, in particular their rule-based description which does not make assumptions about their effect on global dynamics. Thereby we let the population dynamics emerge from their interplay with other virulence strategies.