Advancing risk assessment: mechanistic dose-response modelling of *Listeria monocytogenes* infection in human populations

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The utility of characterizing the effects of strain variation and individual/subgroup susceptibility on dose-response outcomes has motivated the search for new approaches beyond the popular use of the exponential dose-response model for listeriosis. While descriptive models can account for such variation, they have limited power to extrapolate beyond the details of particular outbreaks. By contrast, this study exhibits dose-response relationships from a mechanistic basis, quantifying key biological factors involved in pathogen-host dynamics. An efficient computational algorithm and geometric interpretation of the infection pathway are developed to connect dose-response relationships with the underlying bistable dynamics of the model. Relying on in vitro experiments as well as outbreak data, we estimate plausible parameters for the human context. Despite the presence of uncertainty in such parameters, sensitivity analysis reveals that the host response is most influenced by the pathogen-immune system interaction. In particular, we show how variation in this interaction across a subgroup of the population dictates the shape of dose-response curves. Finally, in terms of future experimentation, our model results provide guidelines and highlight vital aspects of the interplay between immune cells and particular strains of *Listeria monocytogenes* that should be examined.

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References

[1] Rahman, A., Munther, D., Fazil, A., Smith, B. and Wu, J., 2018. Advancing risk assessment: mechanistic dose-response modelling of Listeria monocytogenes infection in human populations. Royal Society open science, 5(8), p.180343.