Challenges in Forecasting Antimicrobial Resistance

Mamoon A. Aldeyab, William J. Lattyak

Author affiliations: University of Huddersfield, Huddersfield, UK (M.A. Aldeyab); Scientific Computing Associates Corp., River Forest, Illinois, USA (W.J. Lattyak)

DOI: https://doi.org/10.3201/eid2907.230489

To the Editor: We read with interest the article by Pei et al. (*1*), which discussed challenges in forecasting antimicrobial resistance (AMR) and emphasized the need for improved AMR predictive intelligence. We complement the authors on their findings and share our experience with a threshold-logistic modeling concept that we recently introduced to improve understanding of the relationship between antimicrobial drug use thresholds and incidence of resistant pathogens and a threshold transfer function model that can be used to project AMR prevalence (*2*,*3*).

AMR modeling and forecasting are challenging because of the evolutionary ability of pathogens to adapt to changing environmental conditions. To be useful, a model should address time-varying effects of explanatory variables on response function and changes in the structural relationship between predictor and target variables. Concepts such as threshold transfer function modeling that includes autoregressive moving average components can partially address those issues. Model recalibration is essential and dictated by breakdown in predictive ability. Model parameters can be reestimated after recording new observations. Model structure does not change, but parameter estimates are updated to reflect new information. If statistical significance of a parameter falls below a defined confidence level, model structure might need modification. In practice, model estimation and assessment can be automated. Forecasting model accuracy can also be automated by comparing ongoing performance to baseline accuracy. When model or predictive performance degradation is flagged, a more comprehensive model recalibration is dictated. The time between model calibrations is unknown and depends on the stability of identified relationships in the model and degree to which evolutionary changes in AMR are observed. Further real-world testing is required to determine other factors that can explain resistance and define thresholds, find optimal interventions to reduce antimicrobial drug use to identified thresholds, and assess feasibility of implementing those interventions in daily clinical practice.

References

1. Pei S, Blumberg S, Vega JC, Robin T, Zhang Y, Medford RJ, et al.; CDC MIND-Healthcare Program. Challenges in forecasting antimicrobial resistance. Emerg Infect Dis. 2023;29:679–85. https://doi.org/10.3201/eid2904.221552
2. Aldeyab MA, Bond SE, Conway BR, Lee-Milner J, Sarma JB, Lattyak WJ. Identifying antibiotic use targets for the management of antibiotic resistance using an extended-spectrum β-lactamase-producing *Escherichia coli* case: a threshold logistic modeling approach. Antibiotics (Basel). 2022;11:1116. https://doi.org/10.3390/antibiotics11081116
3. Aldeyab MA, Bond SE, Conway BR, Lee-Milner J, Sarma JB, Lattyak WJ. A threshold logistic modelling approach for identifying thresholds between antibiotic use and methicillin-resistant *Staphylococcus aureus* incidence rates in hospitals. Antibiotics (Basel). 2022;11:1250. https://doi.org/10.3390/antibiotics11091250

Address for correspondence: Mamoon A Aldeyab, Department of Pharmacy, School of Applied Sciences, University of Huddersfield, Huddersfield HD1 3DH, UK; email: m.aldeyab@hud.ac.uk

In Response: Real-time evaluation of predictive models for antimicrobial resistance (AMR) is critical for real-world applications, as indicated in our recently published article (*1*). Aldeyab and Lattyak introduced a threshold-logistic regression model that links antimicrobial drug use to AMR prevalence in hospital settings (*2*). The authors advocate implementing and testing this model in hospitals to assess operational utility. I agree that this is a practical starting point to challenge time-series model use for real-time AMR predictions. Most time-series models have been validated in retrospective analyses. Translational research is needed to promote the use of those models for real-world AMR control.

The authors mention several practical considerations when applying time-series models in real time, including stationarity of both predictor and target variables and criteria for model recalibration. Evaluating methods to address those issues is crucial to achieve desirable performance in hospital settings. In addition to those technical challenges, several broader questions remain regarding model design and utility. First, how much AMR prevalence variation can be explained by antimicrobial drug use? Are there other essential factors (e.g., community introduction) that should be included in the model? Second, how will healthcare providers and hospitals use AMR forecasts? What policies will be informed by forecasts, and what are the downstream effects? Answers to those questions will help determine the eventual real-world utility of predictive models.

Evaluating real-time AMR prediction is a complicated task. By drawing experience from computer vision (*3*) and forecasts for other infectious diseases (*4*–*6*), open-access challenges with transparent and fair evaluation methods run in a common task framework (*7*) can substantially stimulate the advance of predictive methods and might produce robust application models. Such collaborative efforts are needed to evaluate existing methods, identify difficulties and solutions, and push the operational use of AMR predictive models forward.

Acknowledgments

This work was supported by the US Centers for Disease Control and Prevention, grant nos. U01CK000592 and 75D30122C14289.

References

1. Pei S, Blumberg S, Vega JC, Robin T, Zhang Y, Medford RJ, et al.; CDC MIND-Healthcare Program. Challenges in forecasting antimicrobial resistance. Emerg Infect Dis. 2023;29:679–85. https://doi.org/10.3201/eid2904.221552
2. Aldeyab MA, Lattyak WJ. Challenges in forecasting antimicrobial resistance. Emerg Infect Dis. 2023 Jul [*date cited*]. https://doi.org/10.3201/eid2907.230489
3. Russakovsky O, Deng J, Su H, Krause J, Satheesh S, Ma S, et al. ImageNet large scale visual recognition challenge. Int J Comput Vis. 2015;115:211–52. https://doi.org/10.1007/s11263-015-0816-y
4. Cramer EY, Ray EL, Lopez VK, Bracher J, Brennen A, Castro Rivadeneira AJ, et al. Evaluation of individual and ensemble probabilistic forecasts of COVID-19 mortality in the United States. Proc Natl Acad Sci USA. 2022;119:e2113561119. https://doi.org/10.1073/pnas.2113561119
5. Reich NG, Brooks LC, Fox SJ, Kandula S, McGowan CJ, Moore E, et al. A collaborative multiyear, multimodel assessment of seasonal influenza forecasting in the United States. Proc Natl Acad Sci USA. 2019;116:3146–54. https://doi.org/10.1073/pnas.1812594116
6. Johansson MA, Apfeldorf KM, Dobson S, Devita J, Buczak AL, Baugher B, et al. An open challenge to advance probabilistic forecasting for dengue epidemics. Proc Natl Acad Sci USA. 2019;116:24268–74. https://doi.org/10.1073/pnas.1909865116
7. Donoho D. 50 years of data science. J Comput Graph Stat. 2017; 26:745–66. https://doi.org/10.1080/10618600.2017.1384734

Address for correspondence: Sen Pei, Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY 10032, USA; email: sp3449@cumc.columbia.edu

Sen Pei

Author affiliations: Columbia University, New York, New York, USA

DOI: https://doi.org/10.3201/eid2907.230617