Modeling the risk of inadvertent laboratory-origin outbreaks

Sandhya Dhawan[1], Wirichada Pan-gnum[1], C. Raina MacIntyre[2], Poh Lian Lim[3], Kazunobu Kojima[4], Stuart D. Blacksell[1,5]

1:Mahidol-Oxford Tropical Research Medicine Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand 2:Biosecurity Program, The Kirby Institute, UNSW Sydney, Australia 3:Asia Centre for Health Security, National University of Singapore, Singapore 4:Department of Epidemic and Pandemic Preparedness and Prevention, WHO, Geneva, Switzerland 5:Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom

sdhawan@tropmedres.ac sandhyadhawan1996@gmail.com

Introduction

Laboratory biosafety incidents pose significant challenges for public health and the wider community. Improved risk assessment and mitigation strategies are urgently needed. This study investigates biosafety incident data from 2000 - 2024, to identify recurring risk factors and epidemiological markers (1, 2). Our research offers a data-driven model to improve outbreak detection, bridge critical gaps in laboratory safety practices, and inform biosecurity policies (3).

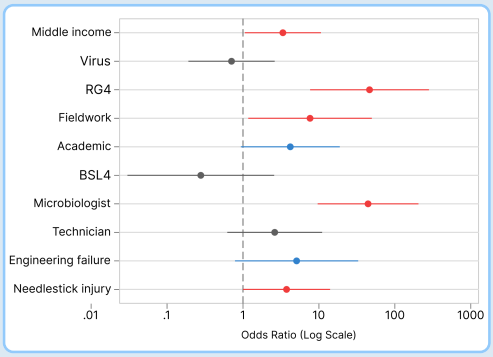

Figure 2. Forest plot of predictors associated with fatality outcome. Red = significant predictor; Blue = borderline significant predictor.

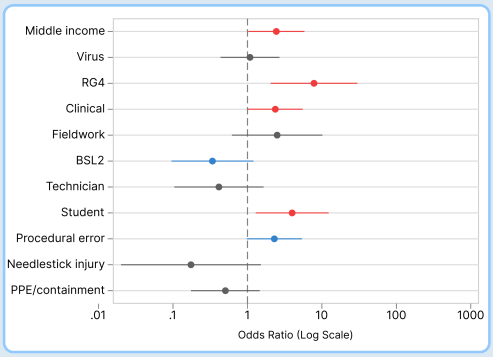

Figure 3. Forest plot of predictors associated with large outbreaks. Large outbreaks were classified as incidents with ≥5 cases. Red = significant predictor; Blue = borderline significant predictor.

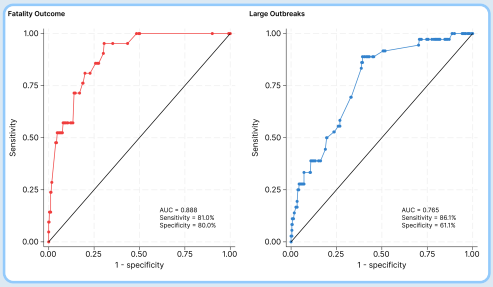

Figure 4. Reciever operating characteristic (ROC) curve analysis of fatalities and large outbreaks. The area under the curve (AUC), sensitivity, and specificity of each model is outlined.

Methods

A systematic review identified 487 biosafety incidents from 2000 - 2024 (Figure 1).

Logistic regression analysis was performed to find key risk factors. The odds ratios derived were used to develop a risk scoring model to distinguish large laboratory outbreaks (≥5 cases) and fatal outcomes. ROC analysis was conducted to evaluate the accuracy of the model.

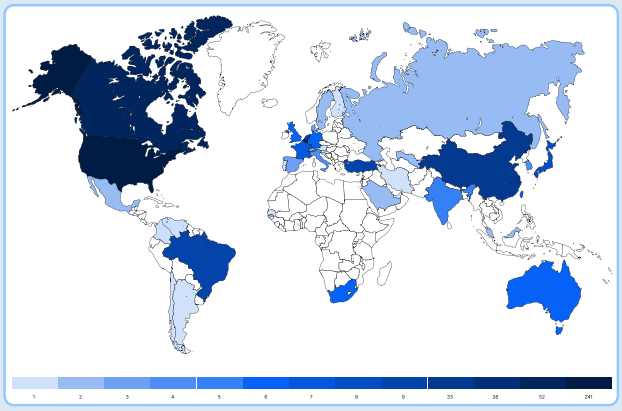

Figure 1. Geographical distribution of biosafety incidents from 2000 - 2024. 481 incidents identified via systematic review were included in the map. Incidents where the country of origin was unknown are not shown. The number of incidents is outlined in the colour-graded scale shown.

Results

Logistic regression analysis of the biosafety incidents reported from 2000 - 2024 (Figure 1) identified five significant risk predictors associated with fatalities (Figure 2) and four associated with large outbreaks (Figure 3). Risk scoring models were developed to identify the likelihood of both outcomes. These models showed moderate to strong predictive ability (AUC: 0.88 for death, 0.77 for large outbreaks; Figure 4), though accuracy was limited by overlapping variables, low precision, and wide confidence intervals.

Main Findings

~45x
Higher fatality risk associated with **Microbiologists** (OR=44.4, p<0.001) and **RG4 pathogens** (OR=46.4, p<0.001)

~8x
Higher fatality risk associated with **Fieldwork-acquired infections** (OR=7.6, p=0.033)

~3x
Higher fatality risk associated with **Needlestick injuries** (OR=3.8, p=0.050) and **Middle Income countries** (OR=3.4, p=0.040)

~8x
Higher risk of a large outbreak associated with **RG4 pathogens** (OR=7.8, p=0.003)

~4x
Higher risk of a large outbreak associated with **Students** (OR=4.0, p=0.016)

~2x
Higher risk of a large outbreak occurring in **Clinical labs** (OR=2.4, p=0.047) and **Middle Income countries** (OR=2.4, p=0.046)

Discussion

Our study highlights high-risk personnel groups, activities and regions requiring specialised training and focused biosafety support. These significant predictors can inform and strengthen risk assessments across laboratories. The risk models developed were highly sensitive but not specific, limiting their practical application (Figure 4). Further studies using factor analysis of mixed data (FAMD), and machine learning techniques can be conducted to calibrate and improve overall model performance. The epidemiological indicators from this study can contribute to risk management frameworks for distinguishing laboratory-origin outbreaks from natural ones, and guide targeted interventions and risk mitigation strategies for biosafety incidents (3, 4).

References

1. Blacksell SD, Dhawan S, Kusumoto M, Le KK, Summermatter K, O'Keefe J, Kozlovac JP, Almuhairi SS, Sendow I, Scheel CM, Ahumibe A, Masuku ZM, Bennett AM, Kojima K, Harper DR, Hamilton K. Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review. Lancet Microbe. 2024 Feb;5(2):e194-e202.
2. Dhawan S, Muluneh AG, Pan-gnum W, Summermatter K, MacIntyre CR, Blacksell SD. (In press). Systematic Review of Laboratory-Acquired Infections in Research and Clinical Laboratories Worldwide: Risk Factors and Mitigation Strategies. Lancet Microbe. 2025.
3. Raina MacIntyre C, Engells TE, Scotch M, et al. Converging and emerging threats to health security. Environ Syst Decis 2018; 38(2): 198-207.
4. Zhang P, MacIntyre CR, Chen X, Chughtai AA. Application of the Modified Grunow-Finke Risk Assessment Tool to the Sverdlovsk Anthrax Outbreak of 1979. Mil Med. 2025 Jan 16;190(1-2):e59-e66. doi: 10.1093/milmed/usae289. PMID: 38870034.