A proposed classification system for opportunistic pathogens for improved healthcare infection prevention and control risk assessments

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Dear Editor,

Healthcare-associated infections (HCAIs) are a major challenge for healthcare systems. Many microorganisms responsible for HCAIs are considered to be opportunistic pathogens - defined as causing infection when outside of their normal ecological niche (1, 2). Such microorganisms can often be found in the physical hospital environment, where contamination can persist and contribute to transmission (3). In order to effectively target infection prevention and control (IPC) practice designed to mitigate environmental microbial contamination, a clear risk assessment framework is required to guide interventions. As there is great variation between infection rates caused by organisms which typically colonize humans and those found in the clinical environment, the classification of many such microbes as opportunistic pathogens does not support risk assessment development. Therefore, a more nuanced classification system is required to help establish the risks posed to patients.

Here, we propose a classification system for microorganisms originating from the hospital environment and associated with HCAI based on reported incidence in the scientific literature. Literature searches were conducted via PubMed (4) utilizing the search string ("*Species name*") AND (infections[MeSH]). Species were checked for synonyms through Taxonomy Browser (5) and where species names have been historically changed, the string was modified to ("*Species name*") OR ("*Species name synonym*") AND (infections[MeSH]). Only case reports, clinical studies, clinical trials and letters reporting infections in humans were included, and no time limitation was implemented.

Total academic reports for each search were enumerated and reporting incidences were classified (Table I). Searches were conducted for species typically regarded as opportunistic pathogens, species known to be detected in the clinical environment and species considered to be true pathogens in clinical practice for reference.

Table I: Summary of each reporting incidence categorization tier. Example organisms which group as either Very High, High, Moderate, Low or Very Low reporting incidence are listed. Organisms marked with ***** are human commensals which are regarded as true pathogens when outside of their normal human environment.

Total Reports Identified	Reporting Incidence Level	Species Examples
≥ 1000	**Very High**	*Staphylococcus aureus*, Escherichia coli*, Pseudomonas aeruginosa, Klebsiella pneumoniae*, Clostridioides difficile*, Enterococcus* spp**., Enterobacter* spp**., Staphylococcus epidermidis*
500 – 999	**High**	*Acinetobacter baumannii, Legionella pneumophila, Serratia marcescens, Proteus mirabilis*
100 – 499	**Moderate**	*Mycobacterium abscessus, Stenotrophomonas maltophilia, Burkholderia cepacia, Klebsiella oxytoca, Citrobacter freundii, Morganella morganii*
10 – 99	**Low**	*Staphylococcus haemolyticus, Micrococcus luteus, Rhizobium radiobacter, Pantoea agglomerans, Corynebacterium jeikeium, Pseudomonas putida, Pseudomonas stutzeri, Staphylococcus capitis*
≤ 9	**Very Low**	*Dermabacter hominis, Kocuria rhizophila, Acinetobacter johnsonii, Corynebacterium aurimucosum, Staphylococcus equorum, Brachybacterium muris*

The classification results show species which act as true pathogens are reported at a higher frequency to opportunists. *S. aureus, E. coli, P. aeruginosa, K. pneumoniae, C. difficile, Enterococcus* species, *Enterobacter* species and *S. epidermidis* all grouped as Very High reporting incidence. Other

HCAI-associated species were identified as having High (e.g. *S. marcescens, L. pneumophila* and *P. mirabilis*), Moderate (e.g. *M. abscessus*, *S. maltophilia, K. oxytoca*) and Low (e.g. Coagulase-Negative *Staphylococci* (CoNS) species and *C. jeikeium*) reporting incidence, with *C. jeikeium* often being associated with HCAI in immunocompromised patients (6).

In the examples listed, *Enterobacter* and *Enterococcus* species are included as genera instead of individual species as infections associated with them are often published in the literature at genus level only (for example as Vancomycin-Resistant *Enterococci*). CoNS are included here at species level, despite being historically reported simply as a grouping. The grouping of CoNS is classified as Very High reporting incidence in the proposed framework. As evidence has shown different species of CoNS are associated with different infection burdens (7), it is therefore more appropriate to classify their infection incidence rates at species level.

By determining the incidence of infections caused by opportunistic pathogens through reporting in the scientific literature, these microorganisms can be numerically compared and classified. When taken in conjunction with other factors contributing to IPC risk assessments (e.g. the severity of infection caused, the environmental loading of a species and the susceptibility of the surrounding patient population), the assigned classifications can contribute to an environmental IPC risk assessment framework. The use of such a framework would allow for more evidence-based and targeted IPC interventions relating to environmental microbial contamination.

There are some limitations when classifying species in this manner. As there is no central reporting framework for all HCAI-causative organisms, the incidence of scientific reports discussing each species are enumerated instead. However, scientific report incidences may not reflect to the true infection burden of each species, as publications may include multiple infections, outbreaks or discuss therapies for infections. Equally, the use of scientific reports allows the results to potentially be biased towards historically well-documented HCAI-associated microorganisms. Additionally, some species (e.g. individual CoNS species) may be under-reported due to issues with species-level identification

(8). Despite these limitations, this approach based on the quantitative measure of reporting incidence allows infection control teams to better categorize such microorganisms. This will support evidence-based infection control risk assessment development, improving patient safety within hospital spaces.

Competing Interests

None Declared.

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References

[1] Graeventiz AV. The role of opportunistic bacteria in human disease. Ann Rev Microbiol 1977;31:447-71. https://doi.org/10.1146/annurev.mi.31.100177.002311

[2] Brown SP, Cornforth DM, Mideo N. Evolution of virulence in opportunistic pathogens: generalism, plasticity, and control. Trends Microbiol 2012;20(7):336-42. https://doi.org/10.1016/j.tim.2012.04.005

[3] Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. Infect Control Hosp Epidemiol 2011;32(7):687-99. https://doi.org/10.1086/660363

[4] National Library of Medicine. PubMed, https://pubmed.ncbi.nlm.nih.gov/; 2020 [accessed 09/01/2023]

[5] Schoch CL et al. NCBI Taxonomy: a comprehensive update on curation, resources and tools. Database (Oxford). 2020: baaa062. PubMed: 32761142 PMC: PMC7408187.

[6] Pardo SMM, Patel RH, Ramsakal A, Greene, J. Disseminated Corynebacterium jeikeium Infection in Cancer Patients. Cureus 2020;12(6):e8764. https://doi.org/10.7759%2Fcureus.8764

[7] Hitzenbichler F, Simon M, Salzberger B, Hanses F. Clinical significance of coagulase-negative staphylococci other than S. epidermidis blood stream isolates at a tertiary care hospital. Infection 2017;45(2):179-86. https://doi.org/10.1007/s15010-016-0945-4

[8] Argemi X, Riegel P, Lavigne T, Lefebvre N, Grandpré N, Hansmann Y, et al. Implementation of Matrix-Assisted Laser Desorption Ionization- Time of Flight Mass Spectrometry in Routine Clinical Laboratories Improves Identification of Coagulase-Negative Staphylococci and Reveals the Pathogenic Role of Staphylococcus lugdunensis. J Clin Microbiol 2015;53(7):2030-6. https://doi.org/10.1128/jcm.00177-15