



Editorial

How much is enough? A bundled strategy for the control of multidrug-resistant gram-negative rod infections in the intensive care unit: Many questions, few answers



In this issue of the *International Journal of Infectious Diseases*, Frattari et al. admirably tackle the vexing problem of gram-negative multidrug-resistant organisms (GNMDRO) using an aggressive, multimodal approach in a small, nine-bed Italian intensive care unit (Frattari et al., 2019). Six-hundred sixty-eight patients were prospectively followed from January 2015 to May 2017, with at least one surveillance nasal/rectal isolate obtained from 399 patients. Multivariable analysis was employed. Impressive reductions in the prevalence of GNMDRO isolates were reported. The percentage of resistance for all GNMDROs fell from 91% to 13%, with significant reductions reported for *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. As the proportion of patients with infection and with gram-negative rod isolates was even across all study periods, the impact on healthcare-associated infection (HAI) rates was not significant, which is disappointing. No data were reported on the incidence of HAIs by other organisms.

Frattari et al. employed a broad, multimodal bundle for the reduction of GMDROs. The strategy included the implementation of an in-ward antimicrobial stewardship program to minimize antibiotic overuse, active detection and isolation of patients colonized or infected with multidrug-resistant pathogens, the use of procalcitonin assays for antimicrobial stewardship, reinforcement of existing procedures for infection prevention such as hand hygiene, appropriate use of gowns and gloves, update of local protocols for antimicrobial prophylaxis, and enhancing the local microbiology service to 24/7 functionality.

The extent to which HAIs can be prevented remains largely debatable. Several reviews suggest that up to 70% of HAIs are potentially preventable (Umscheid et al., 2011, Schreiber et al., 2018). With improvements in infection prevention and reductions in infection rates, the proportion of potentially preventable HAIs continues to decrease, resulting in an infection prevention law of diminishing returns (Schreiber et al., 2018). As the principle tenet of medicine is first do no harm, infection prevention programs should relentlessly pursue reliable, sustainable, and practical strategies for heightened patient safety (Bearman et al., 2019). In a published perspective, Edmond and Wenzel argue that horizontal infection prevention strategies should be the platform for all infection prevention programs (Wenzel and Edmond, 2010).

Horizontal infection prevention strategies target all pathogens transmitted by the same mechanism – contact. Common strategies include hand hygiene, use of central line checklists, safety bundles, and chlorhexidine patient bathing (Wenzel and Edmond, 2010). Frattari et al. employed both horizontal and vertical infection prevention strategies, specifically, active detection and isolation for GNMDROs.

Major barriers to improvements in infection prevention include failures of both practice standardization and implementation. A summary of process measures during clinical investigation trials, including the use of central line checklists and chlorhexidine-impregnated catheter dressings and chlorhexidine patient bathing, revealed variability in implementation even in motivated settings (Bearman et al., 2019). Fakhii et al. performed a survey of select key infection prevention practices across 71 US hospitals and similarly reported poor reliability with the implementation of various infection prevention measures including the use of urinary catheter electronic reminders to nurses, preoperative glucose monitoring, use of a central line checklist, and sedation vacation for ventilated patients (Fakhii et al., 2013).

This raises an important question. How much is enough? What elements of the bundles are most critical and with what degree of successful implementation? The multimodal interventions reported by Frattari et al. leave us with many unknowns. Compliance was reported for microbiological surveillance (64%), but data on other intervention components are lacking, including compliance with hand hygiene, use of central line checklists, and the proper use of gowns and gloves for isolated patients. More importantly, what were the specific interventions made by the single physician overseeing the antimicrobial stewardship program? The extent and mechanism by which the single physician antimicrobial stewardship oversight was able to monitor antimicrobial use remains unclear. The reported lack of impact on HAIs likely represents variability in implementation of infection prevention risk reduction practices such as hand hygiene and other best practice bundles. The reduction in GNMDRO isolates is thus almost certainly a reflection of aggressive antibiotic stewardship, overseen by one physician in a small intensive care unit.

Greater detail on specific infection prevention elements, including strategies for successful implementation, will lead to

broader adoption, possibly across diverse settings. Without a clear understanding of the mechanisms and policies employed for antimicrobial stewardship and without a clear understanding of the mechanism to promote, assess, and sustain compliance with infection prevention best practices, a recipe for broad implementation and reproducibility is lacking.

Infection prevention platforms should have two primary goals. The first is to prevent all HAIs across all pathogens. The second is an aggressive minimization of drug-resistant pathogens. The study by Frattari et al. is encouraging and most successfully tackles the latter on our path towards greater patient safety.

There is an urgent need for changing narratives in patient safety, one in which healthcare systems adopt more holistic and theory-based learning from high-risk industries, such as aviation, rather than relying on single, superficial, and siloed interventions (Pronovost et al., 2017). This includes standardization and broad implementation of safety practices as part of a multimodal approach to enhancing outcomes. Under this framework, a more detailed and specific understanding of the standardization, adoption, and impact of the bundle components reported by Frattari et al. would best guide implementation of some or all of the bundle elements across diverse settings, including low- and high-resource environments. These infection prevention safety bundles would ideally impact both infection rates and the prevalence of GNMDROs. This would be a significant leap forward in our infection prevention journey.

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Received 30 April 2019