BAYESIAN NETWORK INFORMED ANTIMICROBIAL STEWARDSHIP IN THE SAFE-ICU INITIATIVE

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Background. The 2014 WHO report on Antimicrobial Resistance (AMR) warned that the world is poised to enter the post-antibiotic era (WHO, 2014) because of steadily growing resistance in organisms. AMR infections kill at least 23,000 of at least 2 million lives affected each year in the US alone (CDC, 2013) with much higher rates in developing countries (Laxminarayan & Heymann, 2012). Recognizing this as an imminent threat, antimicrobial stewardship programs have been launched with the aim to measure, monitor and improve antibiotic use. Intensive Care Units (ICUs) are high-risk breeding-grounds of AMR due to the prevalence of healthcare associated infections and higher antibiotic usage. Primarily aimed at surveillance, stewardship programs have an untapped potential of being informed by machine learning insights on a rolling basis. In 2015, we launched the Sepsis Advanced Forecasting Engine for ICUs (SAFE-ICU) initiative pediatric patients at a large tertiary care hospital in New Delhi, India. In-house developed pipelines and software for warehousing and integrating data across measurements such as continuous vitals, medications and laboratory investigations including culture-sensitivity (C/S) profiles were deployed enabling us to learn from data. The phenomenon of cross-resistance is well known reflected as correlations in C/S profiles, yet these are not actionable because of confounding effects. Bayesian Networks (BNs) are highly suited to model this problem of modeling complex datasets with a joint probabilistic model and the ability to interactively update beliefs by setting evidences as these are observed. However, rigorous BN learning, inference and cross-validation is often inaccessible to clinicians. We addressed the dual problem of learning AMR decisions from data and deploying interactive interfaces through an open source application.

Cohort. The SAFE-ICU has warehoused more than 3,00,000 patient hours of data since 2014 integrated with treatments and investigations. Culture sensitivity tests on 4577 samples were ordered in this period and 552 cultures were positive for organisms.

Methods and Results. An open-source web-application and dashboard, *AMR_Steward* (*http://doi.org/10.5281/zenodo.1255584*) was created using Shiny and R through *wiseR,* an in-house developed software. *wiseR* (manuscript in communication) democratizes the use of Bayesian Networks by domain experts such as clinicians and computational biologists while allowing sophisticated model ensembling and statistical evaluation through bootstraps, confidence intervals and policy learning. The structure of the bacterial species and antibiotics network was learnt from the data using a score-based hill climbing algorithm, bootstrap evaluations (500 times) and model averaging through features built into wiseR. Approximate Inference with confidence intervals and Exact Inference were done revealing comparable results. Known patterns such as the rising threat of resistant acinetobacter species and terminal nodes formed by antibiotics known for resistance in the directed hierarchy were obvious. Importantly, other actionable insights such as Cefotaxime being a critical branch-point for taking decisions were infered. Setting the evidence of resistance to Cefotaxime and its immediate children (Amoxicillin + Clavulanic acid and Ceftazidime), Chloramphenicol was the only grandchild with a distinct mechanism of action. However, only 11% of culture isolates were tested for chloramphenicol sensitivity. When tested, these the organism had the highest probability (60%) of being sensitive to Chloramphenicol among all other antimicrobials, thus indicating that it may be an under-tested and under used option (perhaps due to side-effects) at our site. wiseR also has functionality to deploy customized dashboards without revealing sensitive data, thus enabling sharing of insights in the community.

References

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