INTRODUCTION

• Every hospital produces empirical antibiotic treatment guidelines. These indicate the agent that should be used for a specific condition until such time as an organism is isolated from a specimen (e.g. urine, blood). Such guidelines are largely didactic documents.

• Given the clear association between antibiotic use and the development of resistance within populations it is critical that a balance is struck between risking potentially ineffective, or unnecessarily broad, empirical treatment.

• The modern hospital has access to enormous amounts of information about each patient, including previous admissions, microbiology, diagnoses, electronic prescribing data and basic demographics.

• We hypothesised that this information could be used to generate an individualised antibiotic resistance risk assessment for individuals requiring antibiotics. This would direct prescribers to narrow spectrum agents for those at low risk of resistance, and restrict the use of broad agents to those at proven high risk.

• Such a system could be integrated into a hospital EPR system, seamlessly producing specific “intelligent” recommendations at the point of prescribing electronically.

• As a proof of principle we assessed the accuracy of a machine learning algorithm (MLA) trained in predicting antibiotic resistance in E. coli, pneumonias, and P. aeruginosa isolated from patients within 48 hours of admission.

• We calculated length of stay and mortality for patients treated with effective and ineffective initial therapy in order to guide the extent to which the MLA could accept the risk of ineffective empirical treatment.

RESULTS

Who is best at selecting appropriate empirical antibiotic therapy at admission? Medical staff or the machine learning algorithm?

• For every patient the MLA produces a number between 0 (susceptible) and 1 (resistant). This is determined by patient’s risk factors and what the MLA has learned from the test data regarding their influence on resistance.

• The “bravery” of the MLA’s choice of antibiotic can be varied by adjusting the threshold at which it labels a patient as likely to grow sensitive or resistant organisms.

• E.g. if the patient’s value was 0.4 and we set a threshold for predicting they had a resistant organism at 0.5, the MLA would consider the patient as likely to have a sensitive organism.

• Setting the “bravery threshold” too low means it will be likely to “over-treat” people with sensitive organisms, as it means it is likely to “under-treat” people with resistant organisms.

• Optimum reduction in over-prescribing with no significant rise in under-prescribing compared to medical staff is achieved with a threshold of around 0.35 (figure 3).

Does under-prescribing in the first 96 hours matter?

• Patients were prescribed a number of different antibiotics empirically at the point of admission. These were refined once culture and sensitivity information became available (figure 4).

• The level of risk one is willing to accept in this initial decision – whether that be as an individual prescriber or in designing a MLA – requires knowledge of the consequences of empirical under-prescribing.

• Length of stay and mortality rates were calculated for those patients who received effective and potentially ineffective initial treatment (figure 5).

• Ineffective therapy in the initial period before culture results was associated with an increased length of stay and death rate. However, this effect was probably confounded by the increased likelihood of older age and frailty in those patients at risk of resistant organisms.

• This is evidenced by the similar length of stay and death rates in people treated with piperacillin-tazobactam with organisms sensitive to this agent. Further work is needed to control for these factors.

DISCUSSION

• Medical staff selection of empirical antibiotics was appropriate approximately 55% of occasions. 33% of initiations were unnecessarily broad and 17% too narrow.

• A machine learning algorithm trained with data representing 2411 patient antibiotic initiations performed well when tested on the whole data set.

• A threshold of 0.35 produced no significant increase in under-prescribing decisions and increased appropriate treatment by 27%. Use of unnecessarily broad spectrum agents dropped by 44%.

• Outcome data indicated that ineffective initial treatment is potentially associated with adverse outcomes. However confounding factors which are themselves associated with an increased risk of resistant organisms would need to be controlled for prior to setting a “bravery level” for a MLA.

• There were a number of other limitations to this study. We restricted the data to emergency admissions, we were unaware of antibiotics that might have been prescribed on paper in A&E or by GPs, we restricted MLA training data to initiations with co-amoxiclav, piperacillin-tazobactam or carbapenems, a number of “one medium agents” may have been due to due to an allergy (the Trust’s current default being a carbapenem).

• The technique can be easily and quickly applied to data held by prescribers or in designing a MLA – requires knowledge of the consequences of empirical under-prescribing.

• Multiple winning teams competing in machine learning competitions [1].

• We compared the performance of medical staff and the trained algorithm in appropriate selection of co-amoxiclav, piperacillin-tazobactam and carbapenems therapy. This represented 2411 empirical antibiotic initiations.

CONCLUSIONS

• Machine learning techniques show considerable promise in the area of empirical antibiotic selection. They would allow more nuanced antibiotic selection, individualised according to the multiple risk factors of a specific patient.

• The technique can be easily and quickly applied to data held by different hospitals, creating a MLA suitable for each specific institution.

• Our study indicates that this could lead to reduced use of broad-spectrum agents. Improved antibiotic stewardship would likely lead to reduced patient complications (e.g. C. diff diarrhoea), costs, and a reduction in the later emergence of resistance.

• Further studies are needed in the following areas: replicating this proof of principle in different institutions, understanding the consequences of ineffective initial therapy so that an appropriate “bravery index” can be selected, and developing an MLA with a more comprehensive databases suitable for use in a clinical setting.

• Ultimately MLAs should sit behind hospital electronic prescribing systems, guiding appropriate antibiotic choice in line with a patient’s “real time” individual risk factor information.

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REFERENCES