MACHINE LEARNING MODEL TO PREDICT RESPONSE TO SHORT DURATION DIRECT-ACTING ANTIVIRAL THERAPY FOR HEPATITIS C VIRUS INFECTION

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Background:
Despite increasing use of pangenotypic direct-acting antivirals (DAA) to treat hepatitis C virus (HCV) in Australia (8-12 week durations), national discontinuation rates continue to rise. Shortening treatment duration could reduce costs and optimize adherence, particularly among key populations (people who inject drugs, people in prison). This analysis aimed to develop a machine learning model to predict response to short duration DAA treatment.

Methods:
Data from clinical trials evaluating response to short duration DAAs (4-6 weeks), and data of individuals discontinuing standard duration DAAs were collated. An XGBoost machine learning model was developed using baseline demographic, clinical and laboratory data. Nested cross-validation was undertaken to assess model performance and optimize hyperparameters. Treatment failures were weighted to adjust for imbalanced data.

Results:
Of 208 individuals receiving short duration DAAs (median age 45 years; 95% male; 33% HIV, 44% injecting drug use [IDU] past month; 13% ≤4 weeks treatment; 46% sofosbuvir-velpatasvir; 27% glecaprevir-pibrentasvir), 48 (23%) treatment failures were identified. Comparing cured vs. failures, 42% vs. 36% had acute HCV (<6 months), median HCV RNA was 5.9 vs. 6.5 log10 IU/mL and median liver stiffness was 5.9 vs 7.1 kPa. Overall accuracy of the model was 84% (standard deviation [s.d.] 6%). Model sensitivity for HCV cure was high (92%; s.d. 5%), but specificity was lower (60%; s.d. 26%). Factors with the greatest impact on short duration outcome were DAA regimen, treatment duration, baseline HCV RNA, and aspartate aminotransferase (AST). No impact of current injecting drug use or acute infection were apparent.

Conclusions:
Although limited by sample size, these findings suggest there is potential to identify individuals with high probability of HCV cure with short duration DAAs. A larger more diverse sample is being sought to improve model stability and predictive capability, externally validate clinical utility, and design a clinical prediction tool.