NATIONAL DIRECT ACTING ANTIVIRAL UTILIZATION FOR RETREATMENT OF HEPATITIS C VIRUS DUE TO REINFECTION OR VIROLOGICAL FAILURE IN AUSTRALIA

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Background:
Half of the 188,000 Australians with hepatitis C virus (HCV) infection in 2015 have received direct acting antiviral (DAA) treatment, including a high proportion of people who inject drugs (PWID). DAA dispensations are reported through the Pharmaceutical Benefit Scheme (PBS), including retreatment. Retreatment reasons are important for evaluating HCV elimination, but not captured by PBS. We developed a machine learning model to classify DAA retreatments as reinfection or virological failure (VF).

Methods: Retreatment data from REACH-C, a national cohort of people receiving DAAs (n=10,843 treated; n=320 retreated with known reason), were used to train a Random Forest machine learning model. Nested cross-validation was undertaken to assess model performance and optimize hyperparameters. The model was applied to PBS retreatment data to identify VF or reinfection. Confidence intervals (95%CI) for group sizes were computed by bootstrapping.

Results:
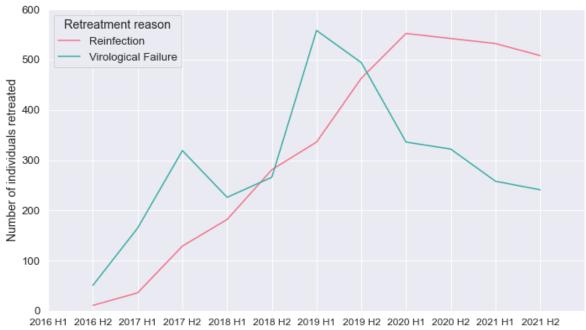Average predictive accuracy of the model was 96.3% (standard deviation 2.7%). Average sensitivity, specificity, and F_1-Score were 95.4%, 95.4% and 96.3%, respectively. Of individuals initiating DAAs 2016-2021, 7% were retreated (n=6,808/95,274); model classified 47.5% (95%CI 45.9-50.6%; n=3,236) as VF and 52.5% (95%CI 49.4-54.1%; n=3,572) as reinfection. Reinfection retreatment increased from 11 in 2016 to 1,040 in 2021. VF retreatment increased from 51 in 2016 to 1,055 in 2019, then declined to 499 in 2021 **(Figure)**. Reinfection retreatment (male 87%, median age 35-years [IQR 28-43], HIV coinfection 2%), was mostly prescribed by general practitioners (48%). Most common regimens were sofosbuvir/velpatasvir (52%) and glecaprevir/pibrentasvir (39%). VF retreatment (male 76%; median age 47-years [IQR 37-55], HIV coinfection 2%) was mostly prescribed by gastroenterologists (43%). Most common regimens were sofosbuvir/velpatasvir/voxilaprevir (35%) and sofosbuvir/velpatasvir (30%).

Conclusion:
We used a novel methodology with high accuracy in retreatment classification. Higher VF retreatment corresponds with access to salvage DAAs. Increasing reinfection retreatment reflects increasing reinfection incidence among PWID and/or improved post-treatment surveillance.

Figure. DAA retreatment for HCV reinfection and virological failure in Australia (n=6,808)