

Assessing national direct acting antiviral utilization for retreatment of hepatitis C due to reinfection or virological failure in Australia

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Background: Data on HCV direct acting antiviral (DAA) therapy dispensation are reported through the Pharmaceutical Benefit Scheme (PBS), including retreatment dispensation. Retreatment reasons are important for evaluating HCV elimination, but not captured by PBS. We developed a machine learning model to classify PBS retreatments as virological failure (VF) or reinfection and assessed clinical characteristics of each group.

Methods: Retreatment data from REACH-C, a national cohort of people with HCV receiving DAA treatment (n=320 received retreatment with defined 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% (standard deviation 2.8%). Sensitivity, specificity, and F₁-Score were 96%, 95% and 96%, respectively. Of individuals initiating DAAs during 2016-2020, 6% were retreated (n=5269/88,790); model classified 52% (95%CI 48-57%; n=2751) as VF and 48% (95%CI 43-52%; n=2518) as reinfection. Of VF retreatments (male 76%; median age 48 [IQR 37-56], 2% HIV-coinfection), 54, 477, 474, 1041, and 661 individuals commenced in 2016, 2017, 2018, 2019 and 2020, respectively. Main prescribers were gastroenterologists (42%). Most common regimens were sofosbuvir/velpatasvir/voxilaprevir (34%), sofosbuvir/velpatasvir (30%) and glecaprevir/pibrentasvir (15%). Of reinfection retreatments (male 87%; median age 36 [IQR 28-44]; 3% HIV-coinfection), 6, 150, 472, 798, and 1092 individuals commenced in 2016, 2017, 2018, 2019, and 2020, respectively. Main prescribers were general practitioners (55%). Most common regimens were sofosbuvir/velpatasvir (55%), and glecaprevir/pibrentasvir (38%).

Conclusion: We used a novel methodology with high accuracy in retreatment classification. Higher VF retreatments in 2019 corresponded with PBS listing of salvage DAA regimens. Increasing reinfection retreatments likely reflects increasing reinfection incidence and/or improved post-treatment surveillance. These data provide important insight into HCV elimination progress.

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