

National direct acting antiviral utilisation for retreatment of hepatitis C virus due to reinfection or treatment failure in Australia

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Introduction

Population-level uptake of direct-acting antiviral (DAA) treatment for hepatitis C virus (HCV) infection, including retreatment, can be estimated through administrative pharmaceutical dispensation data. However, these data lack clinical detail do not capture the reasons for retreatment. We developed a machine learning model to classify retreatments as reinfection or treatment failure at a national level.

Methods

The Pharmaceutical Benefits Scheme (PBS) collects data of DAA dispensation from pharmacies throughout Australia. These administrative records provide individual-level data of prescribed medications, dates of prescription and dispensing, number of doses dispensed, patient's age, gender, residence area, and prescriber type. All instances of retreatment are collected by PBS but the reason for retreatment is not. Retreatment data from the REACH-C cohort (n=10,843 treated with DAAs; n=320 retreatments with known reason), were used to develop, develop a machine learning model to classify retreatments as reinfection or treatment failure using variables in REACH-C that were also available in PBS data. Nested cross validation was undertaken to assess model performance and optimize hyperparameters. The best performing model was selected by evaluating accuracy, precision, sensitivity, specificity and F1-Score performance metrics. The model was applied to PBS retreatment dispensation data, to identify treatment failure or reinfection. Confidence intervals (95%CI) for group sizes were computed by bootstrapping. The machine learning models were developed and implemented in Python. The code is available at https://github.com/joocarson/hcv_rt_classifier

Results

Average predictive accuracy, precision, sensitivity, specificity and F₁-Score for the model were 96.3%, 96.5%, 96.3%, 96.3% and 96.3%, respectively. Nationally, 95,272 individuals initiated DAAs, with treatment uptake declining from 32,454 in 2016 to 6,566 in 2021 (Figure 1). Of those treated, 6,980 (7%) were retreated. Model classified 51.8% (95%CI 46.7%, 53.6%; n=3,614) as reinfection and 48.2% (95%CI 46.4%, 53.3%; n=3,366) as treatment failure. Retreatment for reinfection increased steadily before, stabilising in 2021 (Figure 2). Retreatment for treatment failure increased in 2017 and 2019, then declined.

DAA regimens used for treatment and retreatment are displayed in Figure 3. Those retreated for reinfection (vs. treatment failure) were younger (35 vs 47-years), a higher proportion were male (87% vs. 76%) and higher proportion were retreated by general practitioners (54% vs 40%). Of individuals retreated for treatment failure, 52% had discontinued initial treatment

One percent (n=1035) of the total treated population received multiple retreatments. Among the 6,980 individuals retreated, the total number of retreatments was 8,196 (Figure 2).

The recently accepted paper can be accessed at: <https://doi.org/10.1016/j.jhep.2022.09.011>

Conclusion

Machine learning was used to classify retreatments for reinfection or treatment failure in national administrative data. Half of the estimated population with HCV initiated DAA treatment between 2016-2021. Seven percent were retreated and 1% received multiple retreatments. Retreatment for reinfection increased over time, reflecting increasing numbers of people at-risk for reinfection following cure. Retreatment for treatment failure increased when pangenotypic and salvage DAAs became available.

For further information about this study please contact Joanne Carson jcarson@kirby.unsw.edu.au

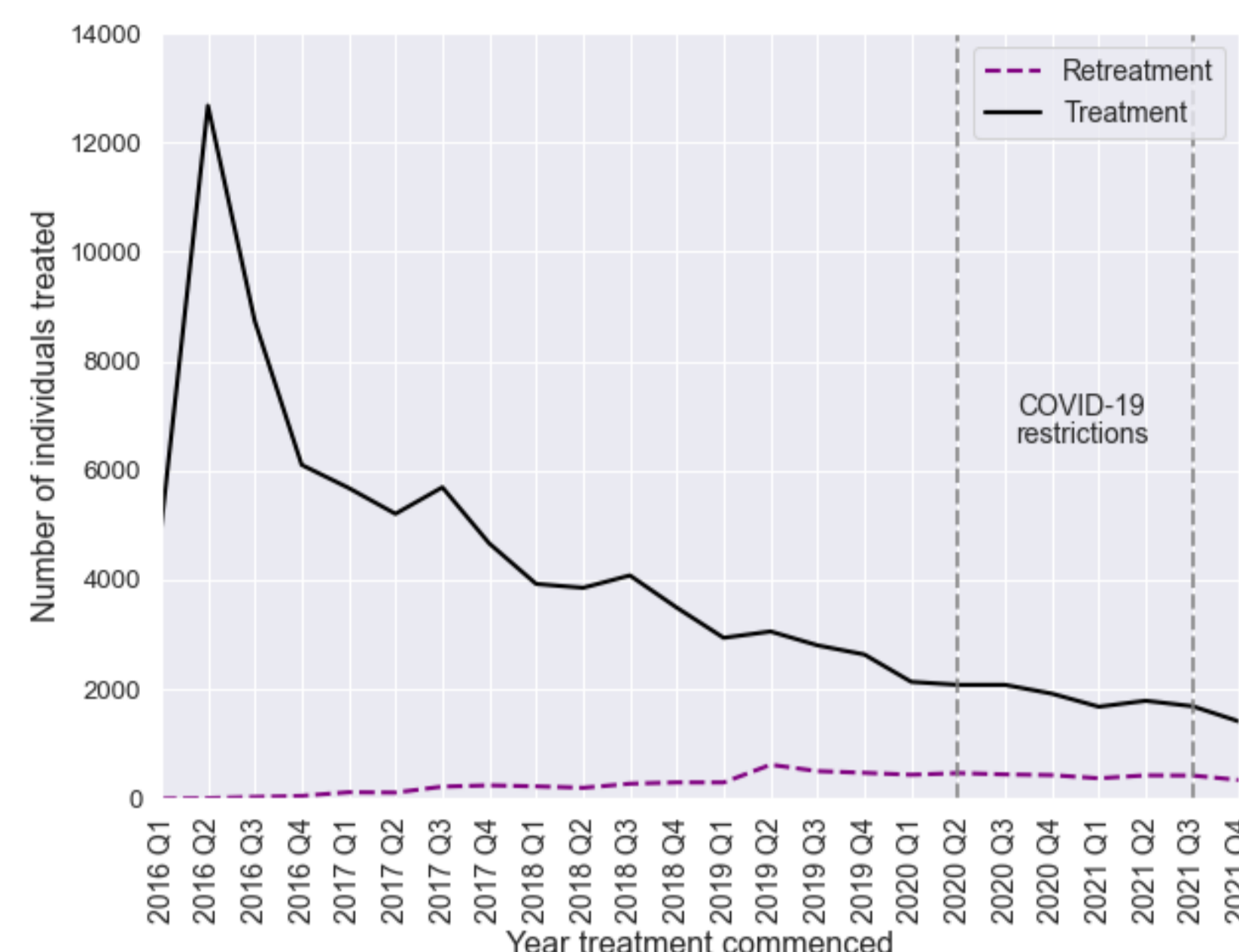


Figure 1. Number of individuals treated and retreated. Three-monthly number individuals receiving treatment for and retreatment for HCV

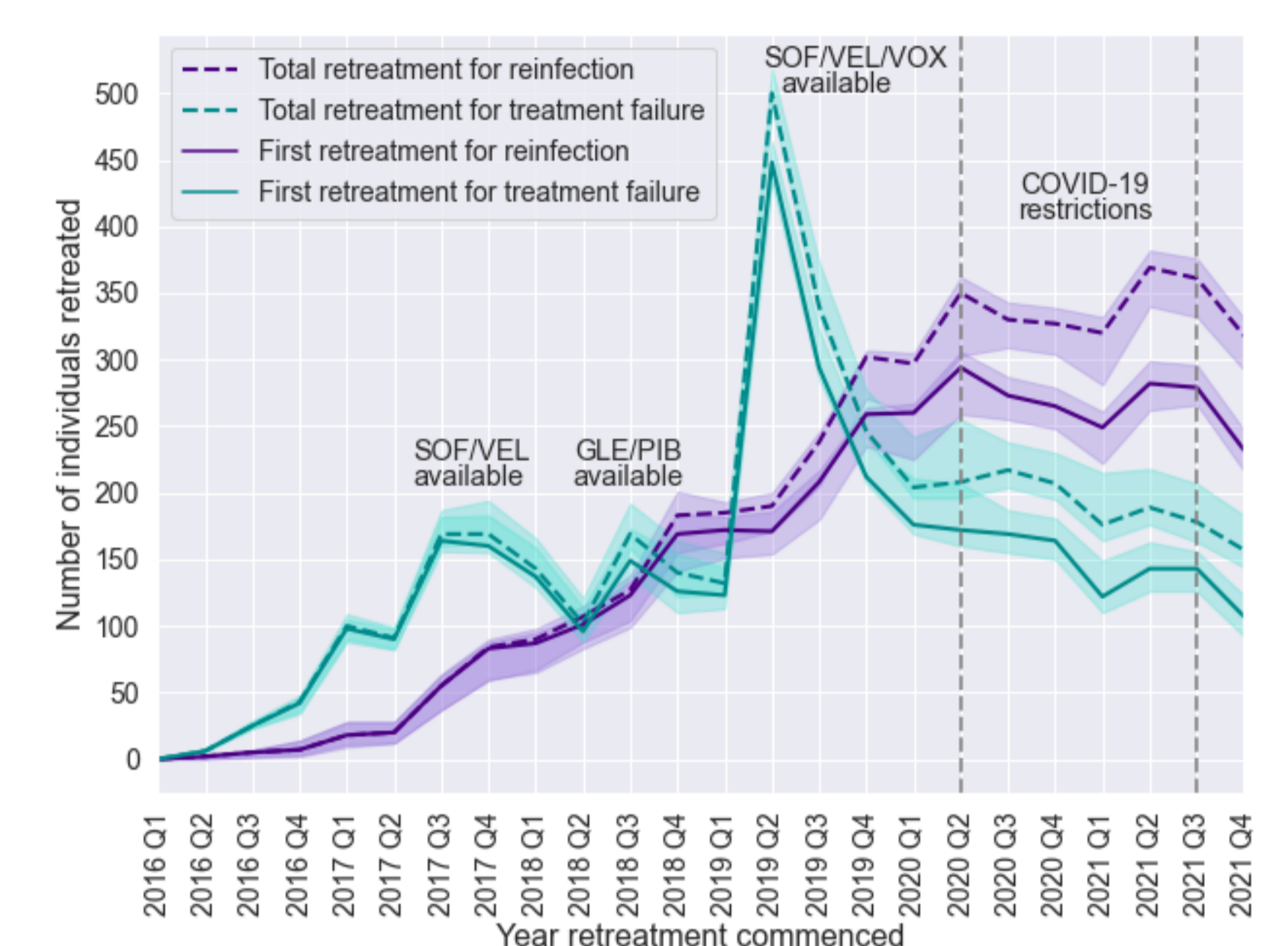


Figure 2. Number of individuals retreated for HCV reinfection and treatment failure. Three-monthly number individuals receiving first retreatment for HCV reinfection and treatment failure with 95% confidence intervals

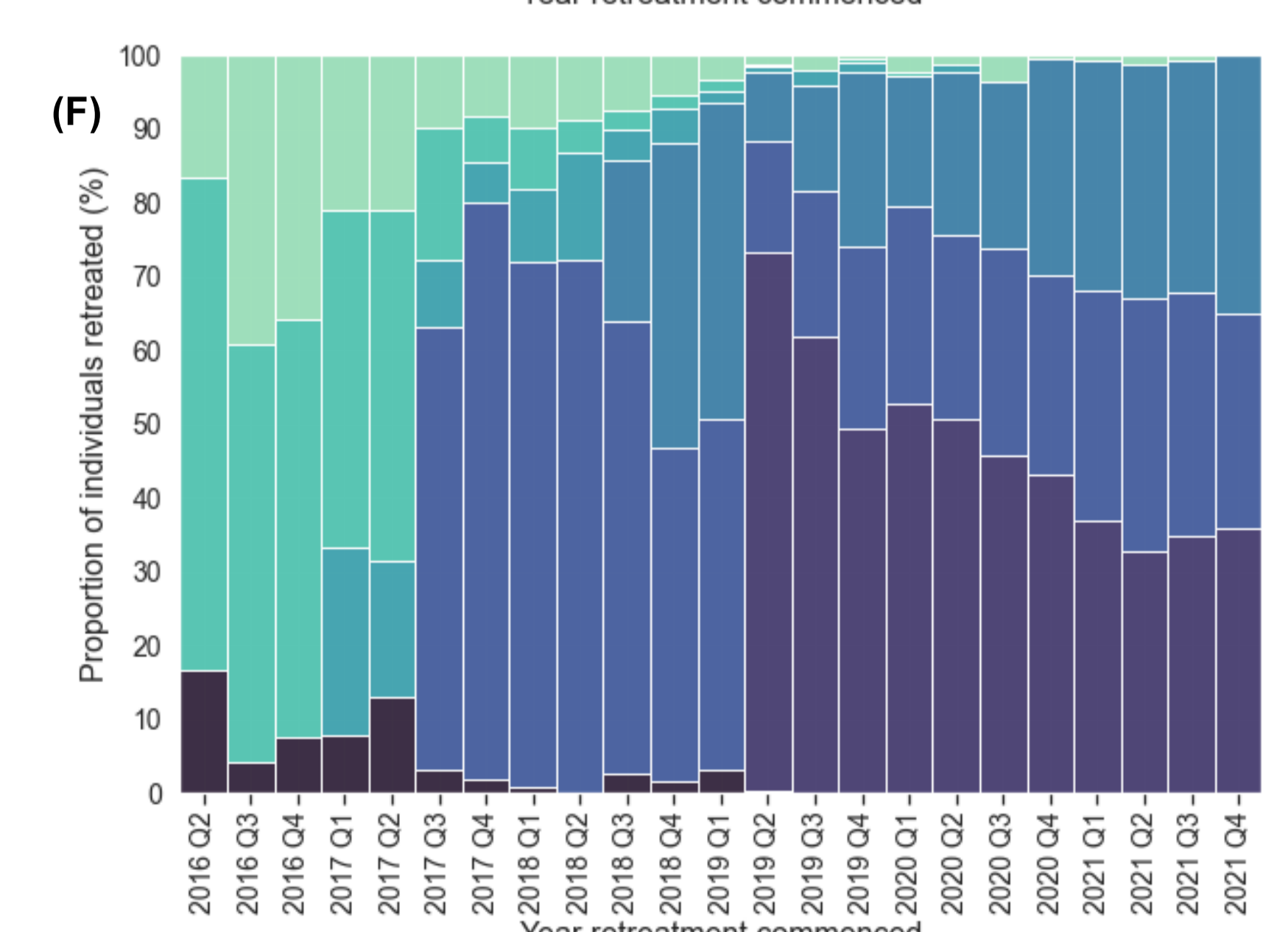
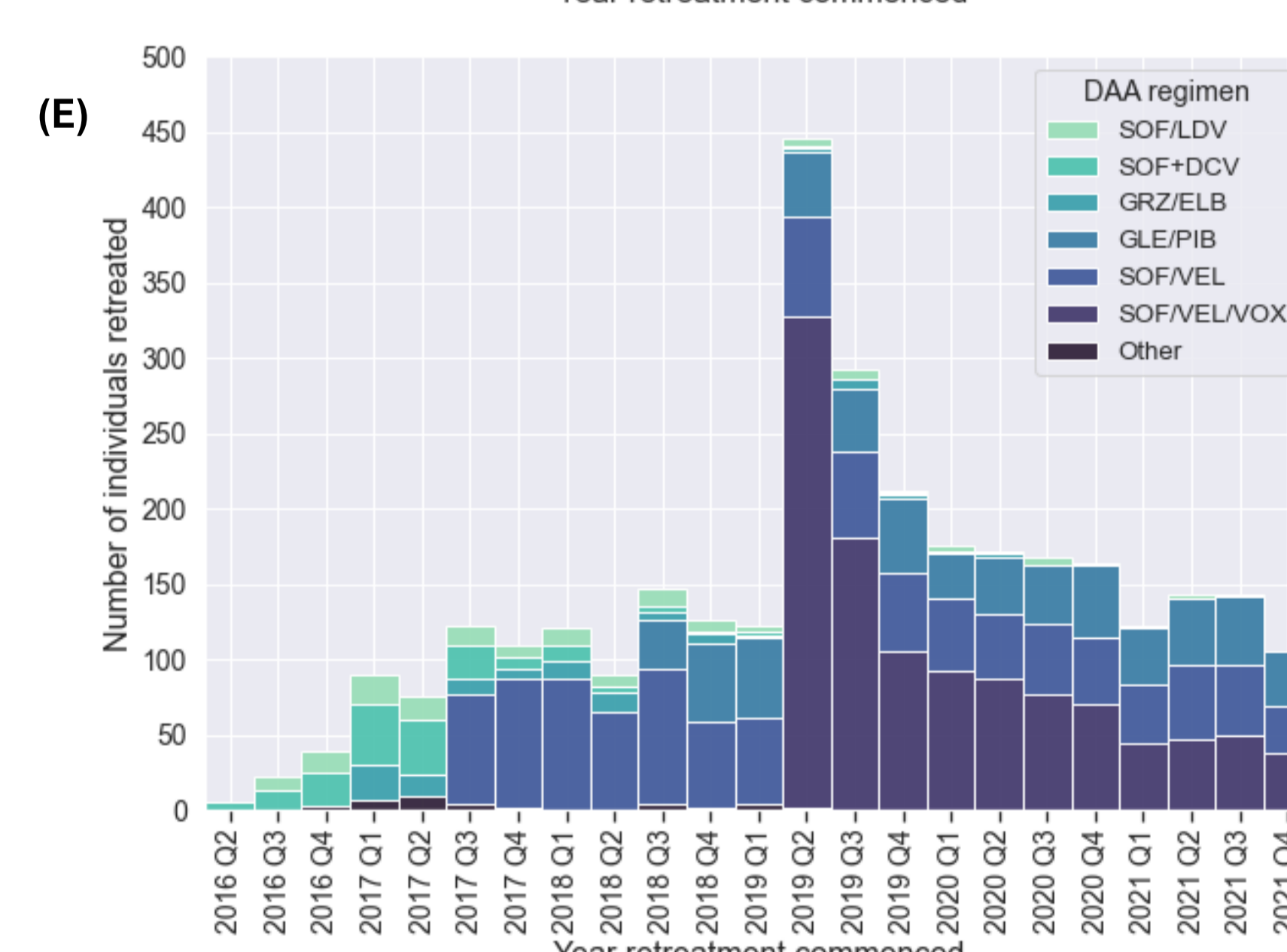
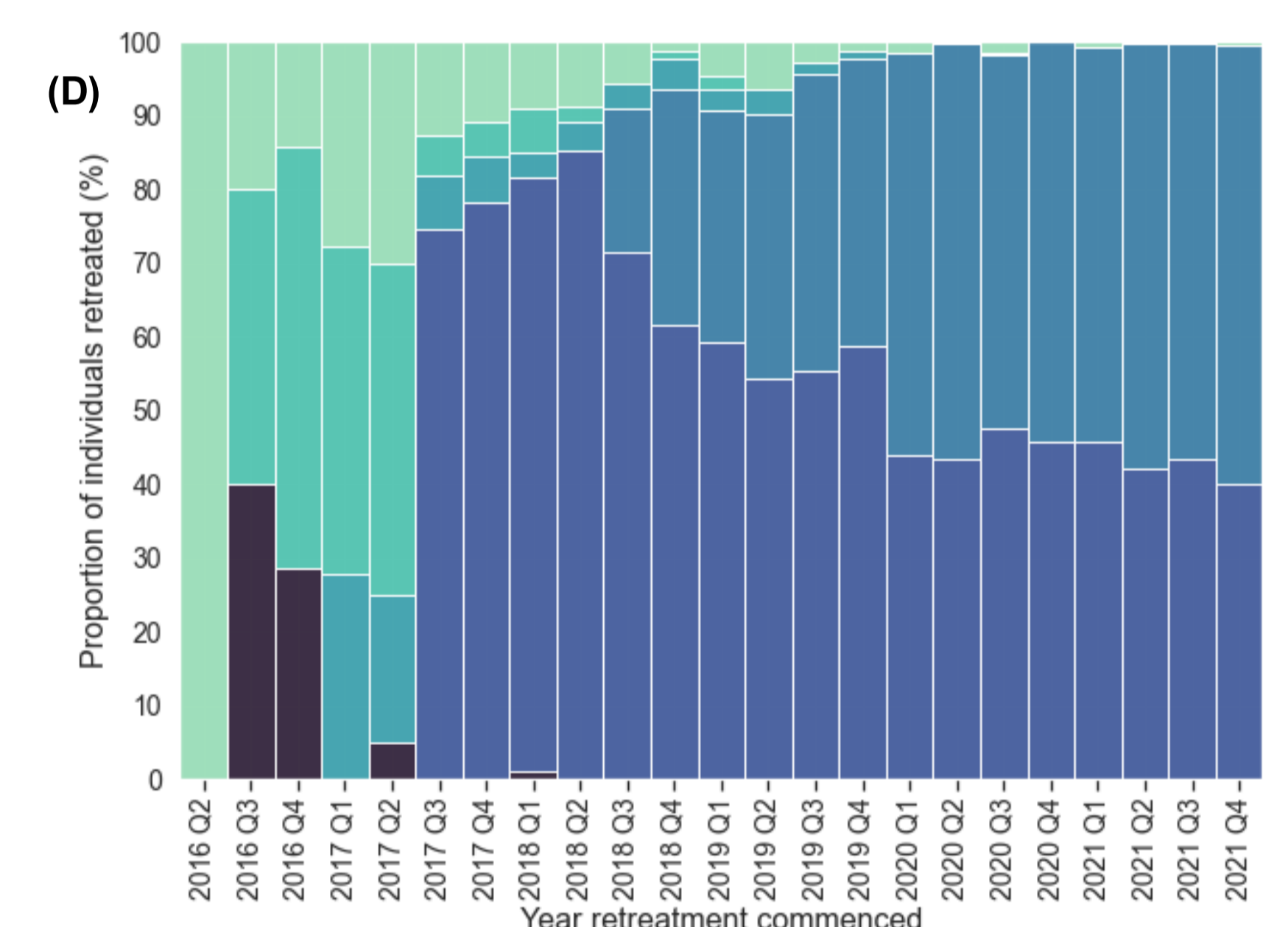
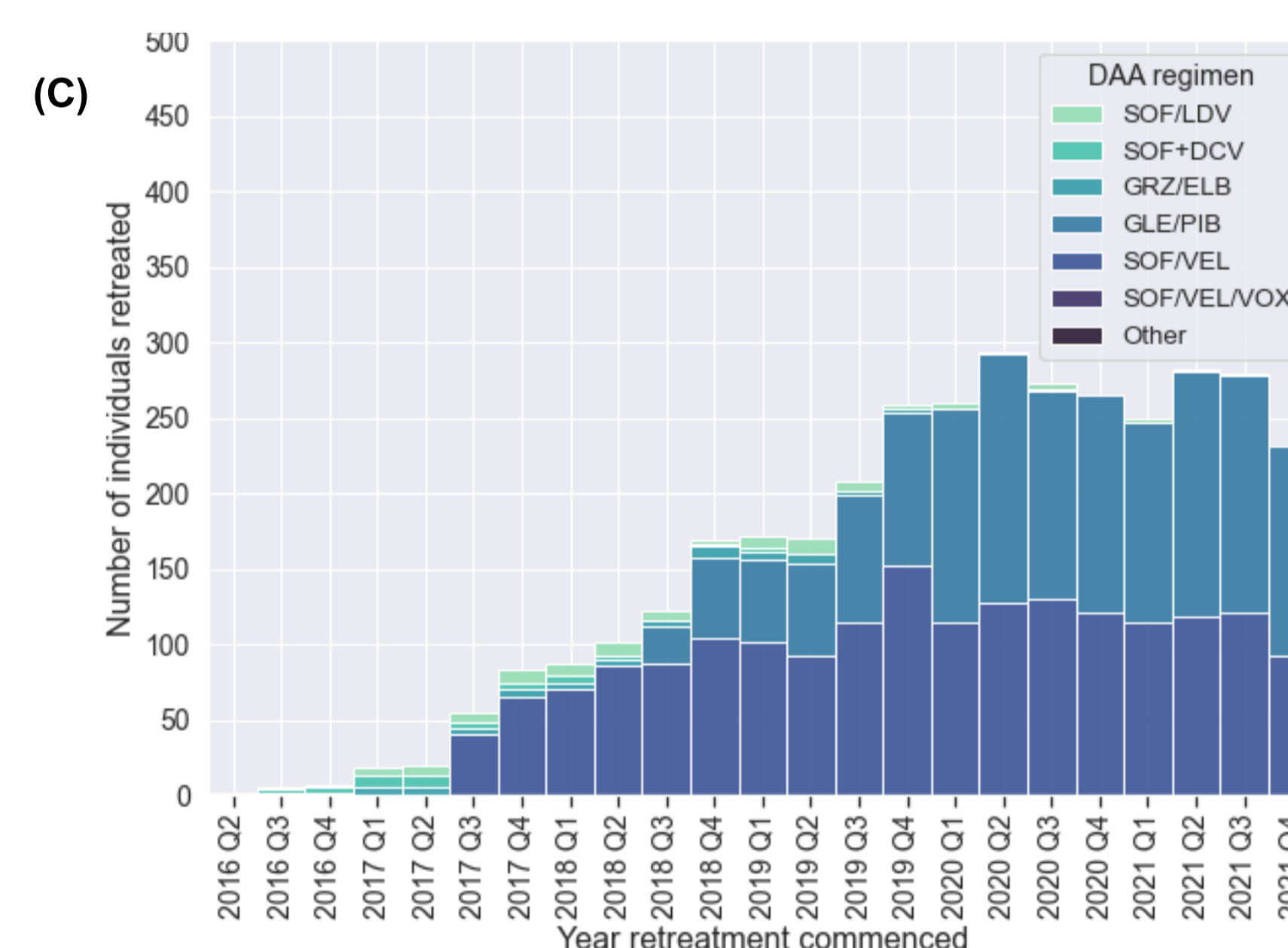
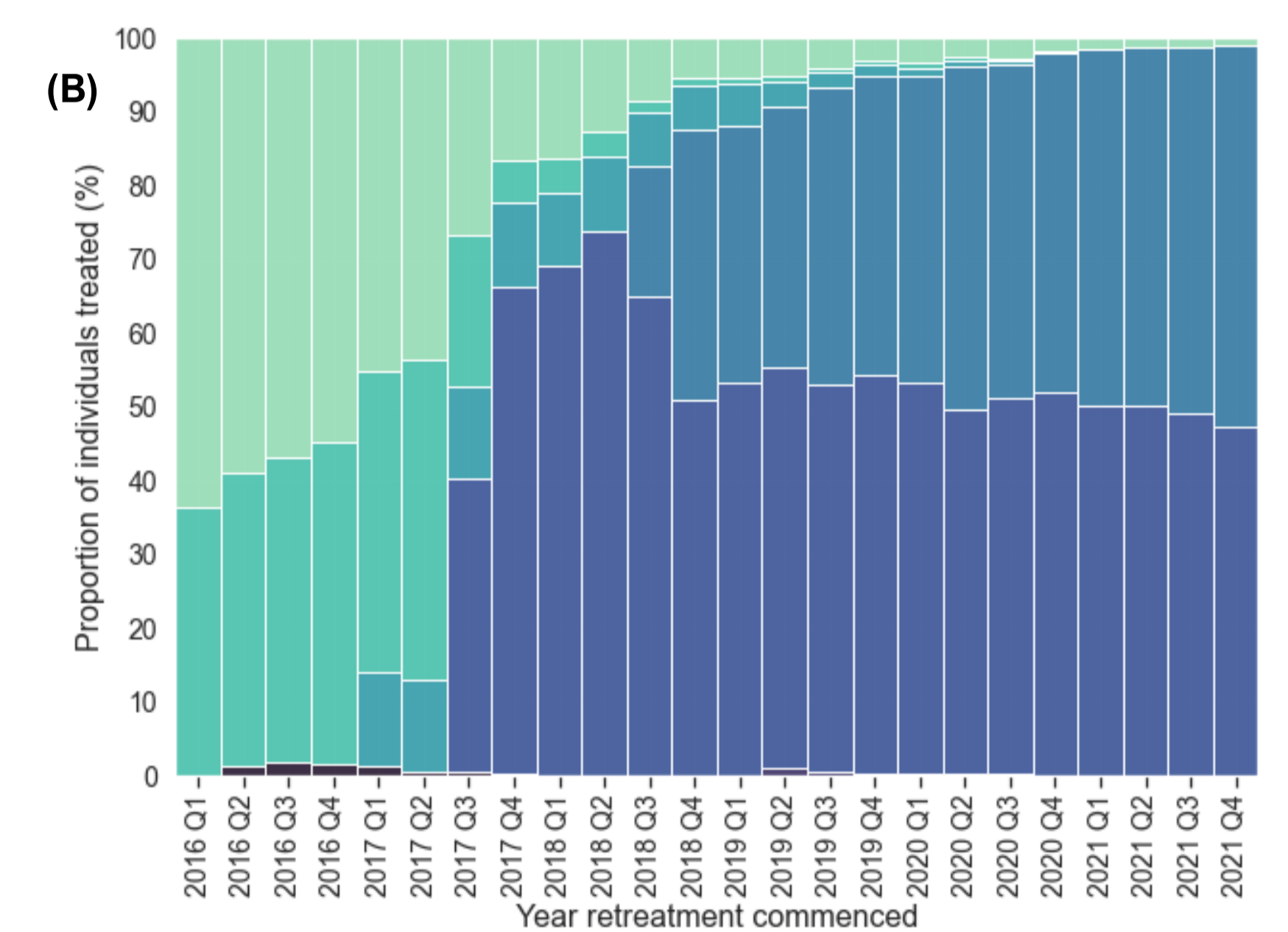
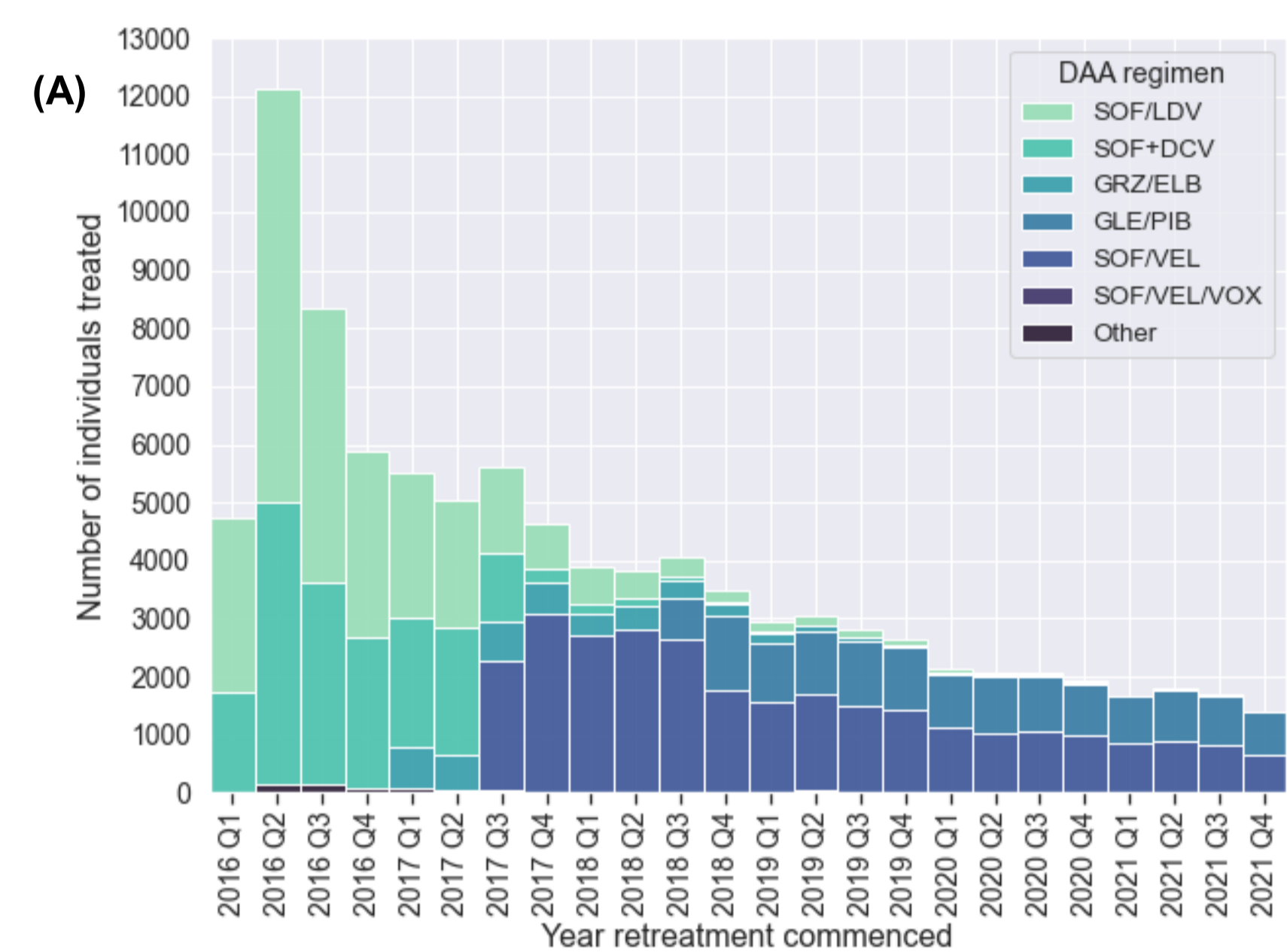


Figure 3. DAA regimens used for treatment and retreatment. The number (A) and proportion (B) of individuals treated for HCV infection (n=95,272), the number (C) and proportion (D) individuals retreated for reinfection (n=3,614) and the number (E) and (F) proportion of individuals retreated for treatment failure (n=3,366)