Development of an agent-based simulation of hepatitis C virus transmission dynamics in the Indian context

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Dedicated to:

Didabhai, my grandmother who passed away on the 7\textsuperscript{th} of July, 2019, with whose blessings I shall strive to make this world a healthier, happier and better place
Soham Das: Development of an agent-based simulation of hepatitis C virus transmission dynamics in the Indian context (under the guidance of Dr. Varun Ramamohan)

This thesis models the transmission of hepatitis C virus (HCV) in a high-risk population in the Indian state of Punjab and more specifically in the district of Ludhiana. The model once calibrated and validated is extended to the state of Punjab as a whole. Agent-based simulation has been used to model the transmission of the disease. This enabled modelling of the stochasticity of the transmission process and the individual heterogeneities. Each agent belonged to a family. Births and deaths were incorporated with daily rates resembling the age-wise population distribution as of 2011 and an average death rate for over the past fifty years.

This time of modelling can be verified by matching the HCV RNA (ribonucleic acid), HCV antibody and IDU (injecting drug user) prevalences in Ludhiana district as of 2014-15 (the latest data which is available from a comprehensive survey in the region). Also, the disease progression has been modelled using a discrete-time Markov model. This model has been frequently used in the progression of hepatitis C virus. Agent-based simulation enabled us to include an acute infection state in this model. We could also incorporate the relapse of disease once sustained virologic response (SVR) or cure was achieved. This in itself is a form of contribution to the disease progression modelling. The natural disease progression model was validated by observing the mean number of years lived by a person who dies of liver-related ailments due to HCV, since infection. In our model, this was found to be 30.75 years while the first paper on cost-effectiveness analysis of direct-acting antivirals in the Indian context found it to be 30.25 years (Aggarwal et al. 2017). This increase of six months can be attributed to the six months of acute infection stage in our model which was not present in the natural history model of Aggarwal et al. 2017.

The disease transmission takes place in four different representative environments, namely home, medical environment, social interaction environment and educational environment. These environments include different risk factors for HCV transmission such as unsafe medical procedures (unsafe blood transfusions, unsafe surgery, unsafe dental surgery and unsafe injection practices), unsafe sharing of contaminated needles and unprotected sex. Unsafe sharing of needles by IDUs was restricted to IDUs from the same cluster in the social interaction environment. Clustering was done by using distance-based k-means clustering. This was also true for influencing of non-IDUs into being IDUs. The cluster restriction was removed for interactions in the educational environment. The interactions between IDUs took place in groups of three. Treatment
using pegylated interferon and ribavirin was introduced for the last fifteen years of the burn-in period.

Once the model was run for a burn-in period of fifty years and the prevalences stabilized at the end of the burn-in period and the Markov model was validated. After that, two different regimes of directly-acting treatment were introduced for ten years. The effects of these regimes at different uptake rates on the HCV RNA prevalence, HCV antibody prevalence and IDU prevalence were noted. Of special interest was the active HCV infection represented by the HCV RNA prevalence. It was noted that when about 90% of the infected pool of patients were treated, the HCV RNA prevalence decreased a little over time for one regime of treatment while for the other regime, it still increased slightly over the years. This advocated the need for a public health awareness campaign for HCV to root out the disease at the transmission stage.

Sensitivity analysis with respect to percentage of unsafe medical professionals was done for the three prevalences. After this initial modelling was introduced, some parameters were re-calculated for the state of Punjab and the re-calibration of the model with respect to the prevalences in the Punjab context was started.
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