Model Framework to Derive Prevalence Estimates of Hepatitis Delta Based on Migration Patterns

MSR36

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Introduction:

Hepatitis delta (HDV) is a rare condition, affecting a subset of HBV+ patients. HDV is recognised as the most severe form of viral hepatitis-induced liver disease, with the most rapid progression to cirrhosis and hepatocellular carcinoma[1-2].

Until recently there have been no licenced treatments for HDV. The EMA recently approved the first treatment for this condition.

Despite its severity, the prevalence of HDV is largely unknown. There are several factors which contribute to this:

1. It is a sub-set of patients that have chronic HBV infection, and it is likely that a considerable number of these patients remain undiagnosed[3]
2. HDV diagnostics are not widely available and there is no standardization for HDV RNA assays, which are used for monitoring response to antiviral therapy[4]
3. Impact of HBV paediatric vaccination changes chronic HBV prevalence and thus will be expected to impact HDV prevalence[4]
4. Within the UK, HBV (and therefore HDV) risk factors are associated with migratory populations from countries where HBV is considered endemic by the WHO[5]

Key factors influencing the likely prevalence of HDV within the UK include country of birth, HBV status and HDV co-infection rate according to the country where the infection was likely to have occurred[10]. The objective of this research was to generate a scalable model framework to provide prevalence estimates for HDV infection for any given country, to guide local and national access discussions.

Methods:

The model was created combining 3 data sets: HBV prevalence, HDV co-infection & population data by country of birth, to calculate expected prevalence of HDV.

HBV prevalence: A systematic literature review was conducted for the prevalence of HBsAg+ by country, with a focus on collating data from observational studies.

Polaris Observatory[6] data were also added to the dataset created from the SLR. Where significant discrepancies were found, these instances were annotated and further investigated to ensure the latest most accurate data were selected and applied in the final model.

HDV co-infection: Two key papers formed the based for the co-infection estimates[7-8], although a systematic literature search was also conducted to uncover any data published more recently than the two key papers. Data representing co-infection within the wider HBsAg+ population were sought and applied.

Population data by country of birth: For the model architecture, generic tables were constructed to be populated with migration data specific to the country under study.

Data gaps: HBV prevalence & HDV co-infection data are incomplete (not all countries have data). Different methods were used to fill the data gaps:

1. No prevalence estimate available for a country - “nearest neighbour” methods applied to select for HBV & HDV values creating a mini-meta analysis.
2. Where migration data provide region of birth (no specific country) - prevalence estimate created based on countries with data in geographic region (two regional groupings were calculated based on ONS vs. WHO definitions).

Model outcome was assessed for sensitivity of data gap methodology at the national & sub-national level.

Results:

Using the United Kingdom as a pilot country to test the model, population migration data were available at national level for 60 individual countries of birth[9], but only available at aggregated ONS-defined groupings at sub-national level[9]. Of 60 named countries, HBV data was available for 56 / 60, HDV co-infection data was available for 38 / 60, 4 countries had no HBV or HDV data (HBV and HDV = 38, HBV only = 18, neither HBV or HDV = 4). When applied to the UK, HDV prevalence was calculated at: ~15,000 to ~18,000 (depending on data gap methodology). ONS method produced more granular, higher result compared with WHO method (18k vs 15k).

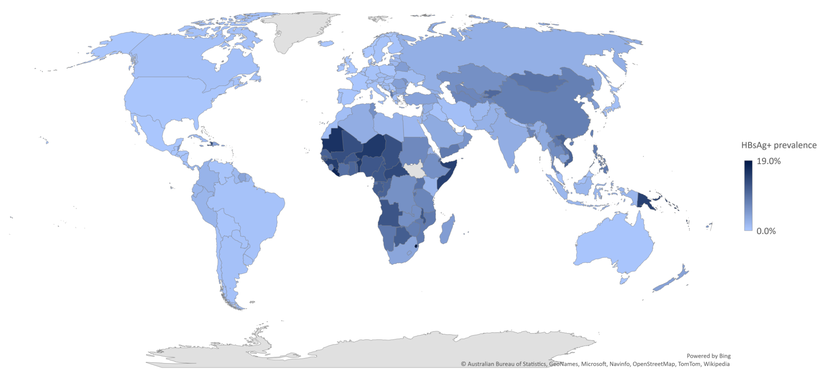


Figure 1: Geographic distribution of HBV HBsAg+ prevalence rates applied within the model

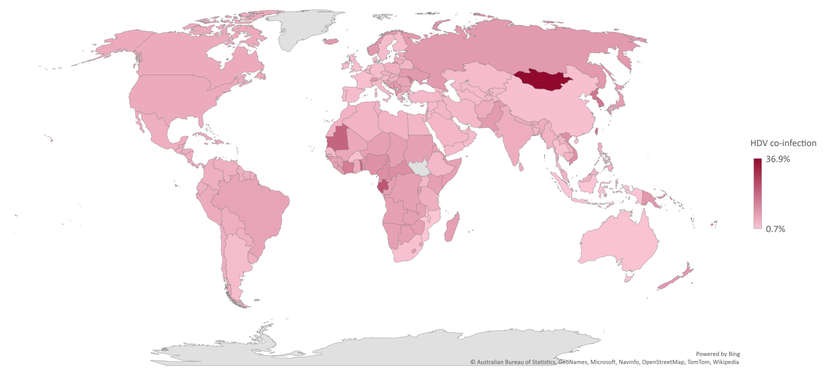


Figure 2: Geographic distribution of HDV+ co-infection prevalence in HBV+ population applied within the model

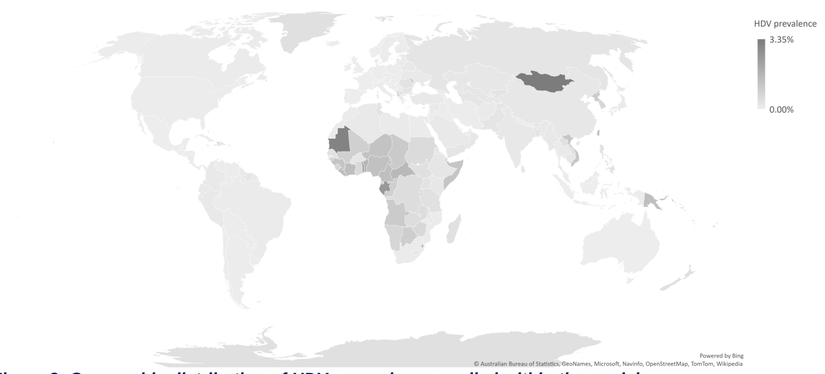
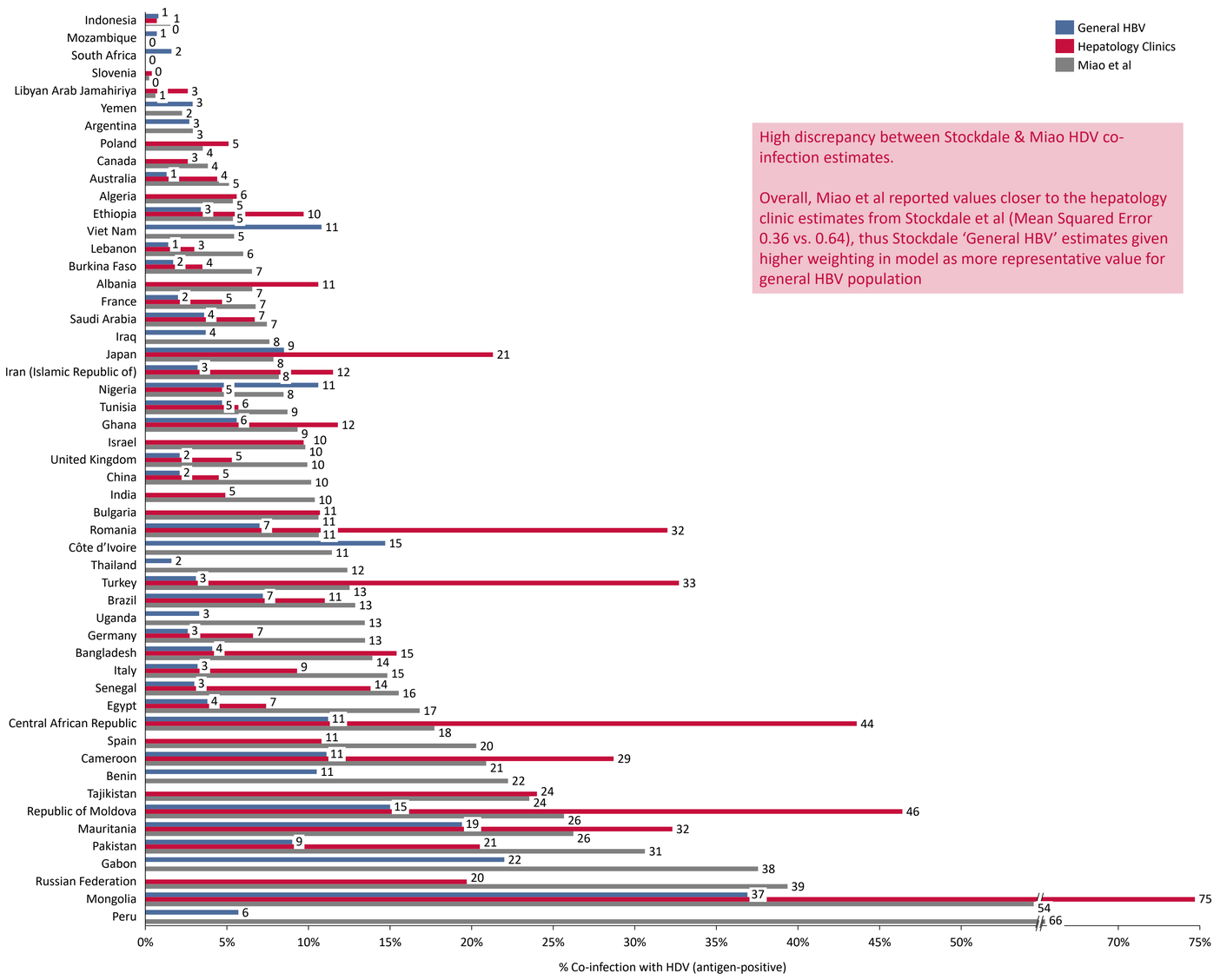


Figure 3: Geographic distribution of HDV+ prevalence applied within the model

Figure 4: Comparison Stockdale vs. Miao HDV+ co-infection rates in different select populations



High discrepancy between Stockdale & Miao HDV co-infection estimates.

Overall, Miao et al reported values closer to the hepatology clinic estimates from Stockdale et al (Mean Squared Error 0.36 vs. 0.64), thus Stockdale ‘General HBV’ estimates given higher weighting in model as more representative value for general HBV population

Conclusions:

The model is sensitive to variation in availability of migration data in terms of prevalence estimates, i.e., regardless of gaps in prevalence data by country of birth, the quality and granularity of the migration data for the country under study has a significant impact on the overall calculated prevalence estimate. Best utility for the model would be to generate ranges output estimates as a basis for establishing disease burden. The model framework appears to cope with scaling for both additional countries and subnational drill-down, with minimal adaptation providing a flexible tool for rapid evaluation and exploration of prevalence estimates. Consideration should be given to differences in migration population data at the national vs. the sub-national level, as there can be differences in data reporting & reconciliation. The model framework can easily be extended and updated to incorporate new data when available, providing a framework for consistent prevalence estimates for regional application which align with overall national estimates.

Other considerations for validation of HDV prevalence should include population migration patterns (not only net migration but also movement within a given country as this will affect where patients are likely to access care), excess mortality, clinical events and chronicity of disease (e.g., not all HDV antigen positive patients will become chronic HDV sufferers).

References:

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