

## **Title: Estimating the prevalence of hepatitis B and C in Denmark**

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### **Study Rationale**

The purpose of this study is to update the national estimates of the number of people living with chronic hepatitis C (HCV) and B (HBV) in Denmark. The most recent national HBV and HCV estimates in Denmark were based on data from 2007 [1][2]. For hepatitis C between 17.000 and 21.000 people in Denmark were estimated to have chronic infection and the vast majority (>80%) of those infected are either current (41%) or former (43%) injecting drug users [1]. The analysis of the 2007 data also found that less than half of the patients with chronic hepatitis C had been diagnosed and among these patients, one in three had attended specialised care [1].

The availability of simple, tolerable direct-acting antiviral (DAA) therapies with cure rates of >90% is one of the greatest clinical advances in the last decade. Currently, the list price of DAA therapies is very high and to ensure sound public health planning, it is of key importance that Denmark has up-to-date and valid estimates of the total number of people living with chronic hepatitis.

The new DAA therapies have made elimination of hepatitis C possible. This was listed as one of the goals of the 2030 Agenda for Sustainable Development (the Sustainable Development Goals, SDGs), adopted by the United Nation General Assembly in September 2015 [3]. Less than a year later the first Global Health Sector Strategy on Viral Hepatitis 2016-2021 was endorsed by the World Health Assembly [4] and in September 2016, the European Action Plan for the Health Sector Response to Viral Hepatitis in the 53 Member States of the WHO European Region was approved during the WHO Regional Committee meeting in Copenhagen [5]. Both the Global Health Sector Strategy and the European Action Plan recognises the need for robust national hepatitis strategic information systems and urges Member States to have sound estimates of national prevalence levels. Denmark has endorsed these international commitments and it is time to revise the national estimates of both HBV and HCV prevalence.

Compared to HCV, the situation regarding HBV is slightly different: The 2007 estimate was 10-16.000 chronic infections (0.24% of the adult populations) and  $\geq 90\%$  were born in high endemic regions. The number of people in Denmark infected with chronic HBV is steadily increasing due to immigration of people from endemic areas and Denmark is one of the few countries in the world who have not included HBV vaccination in the routine childhood vaccination programme meaning that there is an increased need for closely monitoring HBV in Denmark. For more than a decade, it

has been possible to treat (but not cure) chronic HBV infection. However, major advances in HBV research are also happening and it is hoped that a cure for this infection will be available in the coming decade. This treatment will likely be as costly as the DAA therapies for HCV and it is therefore also important for Denmark to have valid and up-to-date national estimates for the total number of people living with chronic HBV.

In the nearly ten years, since the collection of the data that was used to produce the most recent national estimates for the number of people infected with chronic hepatitis in Denmark, several important background factors affecting the transmission of viral hepatitis have changed significantly: The immigration to Denmark of people from areas where viral hepatitis is endemic has increased in the last ten years. And like in many other western European countries, data suggest that the number of people who use drugs intravenously in Denmark has declined in the last ten years [6]. Also, the screening of both HBV (among pregnant women) and HCV (among people who use drugs) in Denmark has increased. Therefore, there is an urgent need to revise the national estimates for HBV and HCV prevalence in Denmark.

**Study aims:**

To revise the national estimates of the number of people living in Denmark with chronic hepatitis B and C based on the most recently available data.

We aim to evaluate if Denmark has been successful in reducing the undiagnosed fraction of people with chronic hepatitis and to identify population groups and geographic areas where screening should be improved.

**Methods:**

We plan to repeat the methodology that was used for the 2007 national HCV prevalence estimates: A capture-recapture estimate based on multiple national registers using the Danish CPR-number as identifier [1]. However, we will also explore the methods used in other countries who have recently published revised national HCV prevalence estimates – for example the bayesian evidence synthesis approach used for England [7] and the modified version of the Workbook Method which has been applied in the Netherlands [8] to investigate if these might be applicable for Denmark. We will also look into the approaches used to estimate national HCV and HBV prevalence in the USA [9][10][11] and possibly other countries as well to ensure that we apply the most appropriate methodology for the data available in Denmark.

*Data sources*

We will use the following data sources and extract data from the start of the register and until 31.12.2016. We will only include people living in Denmark with a valid civil registration (CPR) number.

- The laboratory database (DANVIR) – data on all patients testing positive for antiHCV and/or HCV RNA as well as patients positive for HBsAg and/or HBV DNA and antiHBcIgM

- The clinical database (DANHEP) – data on all patients receiving specialised care for chronic viral hepatitis
- The communicable diseases register (Statens Serum Institut, SSI) – all notified cases of HBV and HCV infection, including both acute and chronic cases
- The Drug Treatment Register (SIB) – this database includes all patients treated for drug abuse in Denmark. This data will be used to estimate the proportion of drug users who have been tested for HCV and/or HBV
- The national hospital register (LPR) – all patients discharged with hepatitis related diagnoses (ICD10: B18.0, B18.1 or B18.2)
- The national register of births (MFR) – all births since 01.01.2005. This information will be used to estimate the proportion of the HBV population who is known.
- The Civil Register (CPR) – for all patients/CPR-numbers included in the data extracted from any of the above mentioned data sources, we want to have information on: vital status as of 31.12.2016 and migration status (measured by country of birth, nationality of the patient and their parents).

#### *Ethical approval*

This study will be done as a register-based study and there will be no prospective contact with individuals and no publication of data that can be linked to individuals. We will apply for approval from the data protection authority in “Region Syd” of Denmark and data will be stored and handled according to the national data protection act. As this is a register-based study, approval from the national committee on health research ethics (DNVK) is not needed.

#### **Planned outputs**

The results of this study will be published in minimum two separate scientific papers in international peer-reviewed journals. We will publish one paper with the HCV results (Stine Nielsen will be first author and Peer Brehm Christensen will be last author on this publication) and one paper with the HBV results (first and last authorship of this paper is not yet determined). On both papers we propose the co-authors mentioned in the beginning of this document and other members of DANHEP and DANVIR in acknowledgements

#### **Budget**

The costs of this study will include:

Extraction of data from the above mentioned sources	30,000 DKK
VIP salary	150,000 DKK
Travel, administration, data software etc.	30,000 DKK

Total 210,000 DKK

### *Time plan*

Data extraction and analysis should be done in first half of 2017. If possible, we hope to submit at least one manuscript in late 2017 or latest in the first part of 2018.

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