



Model development for the estimation of hepatitis delta prevalence in the general population

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Introduction

- Prevalence of hepatitis delta virus (HDV) infection is controversial
- Most prevalence data are based on patients with chronic hepatitis B in hospital clinics
- This risks over-estimation of prevalence due to the association of HDV infection with a more aggressive clinical course

Objectives

- Develop a model for extrapolating HDV prevalence in hospital referral clinics to the general population
- Apply model to estimate HDV prevalence in the EU

Data-driven model development

1. Literature search to identify all HDV prevalence studies in Europe from 1990 to 2025
2. Assumptions for Relative Risk of being HDV+ in a referred population versus the community was derived from studies documenting both populations
3. Assumptions for proportion of HBV carriers attending referral clinics was derived from literature and public health records
4. Assumptions (2) and (3) were applied to data generated in referral centres to calculate correction needed to estimate prevalence in general population
5. Application of model to each European country's data from referral populations
6. Validation of model by comparison of newly estimated versus previously reported HDV prevalence in general populations where available

Inputs to model

- RR of being HDV-RNA+ or Ab+ in general population derived from 4 studies comparing rates in referral clinics and community from Spain and UK.
- Proportion of HBsAg+ attending referral clinics estimated from studies of healthcare management cascade, physician surveys and public health databases in Austria, UK, France, Spain, Sweden.
- Uncertainty intervals constructed using a range of plausible alternative assumptions.

Model validation

- 7 countries identified with anti-HDV Ab prevalence based both on broad population and on referral clinic cohorts.
- Comparison of estimates from each population before and after correction of referral clinic estimate using the model showed stronger agreement after correction (figure below).

Final model assumptions

Assumptions in model (with plausibility ranges)

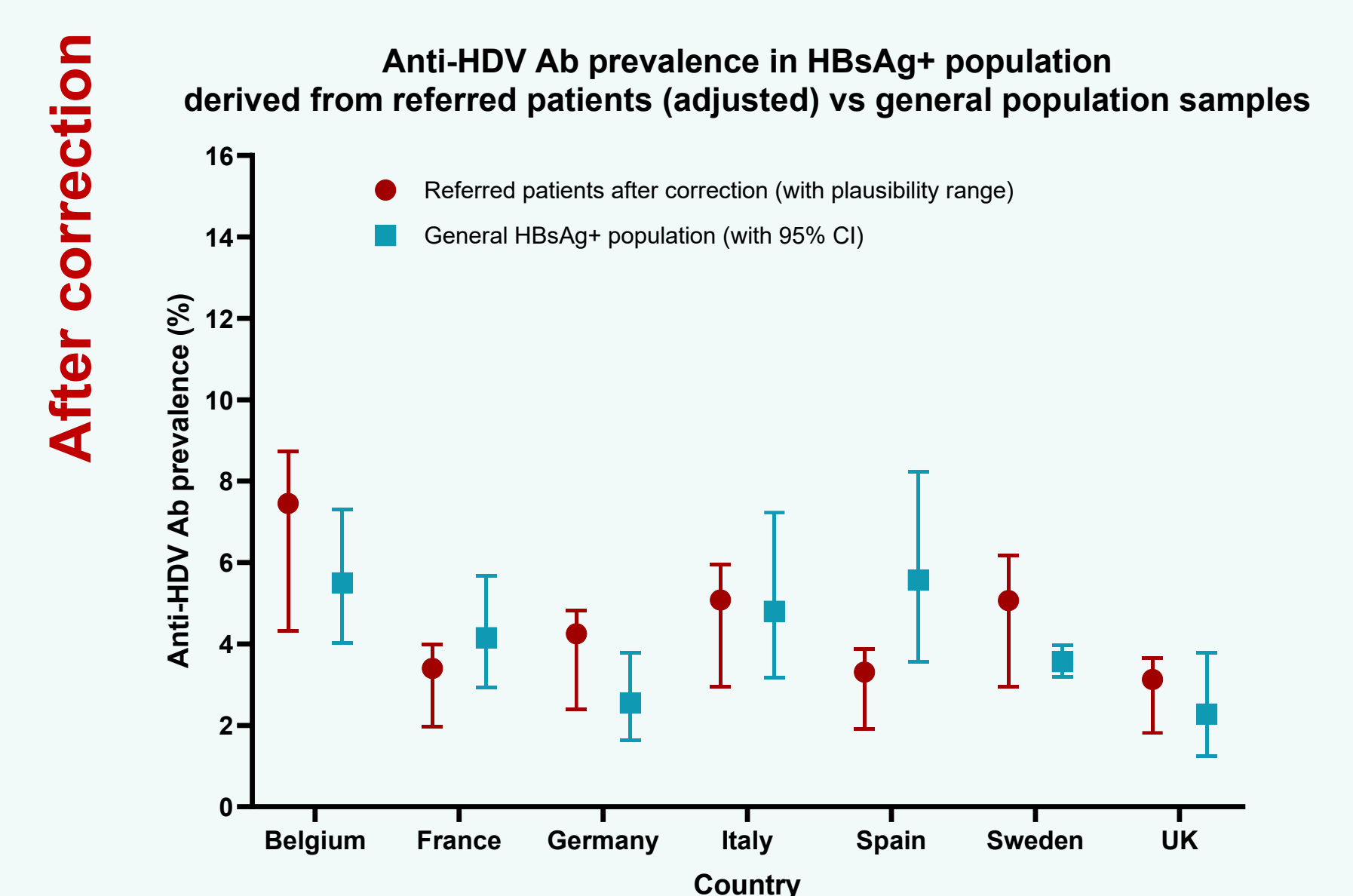
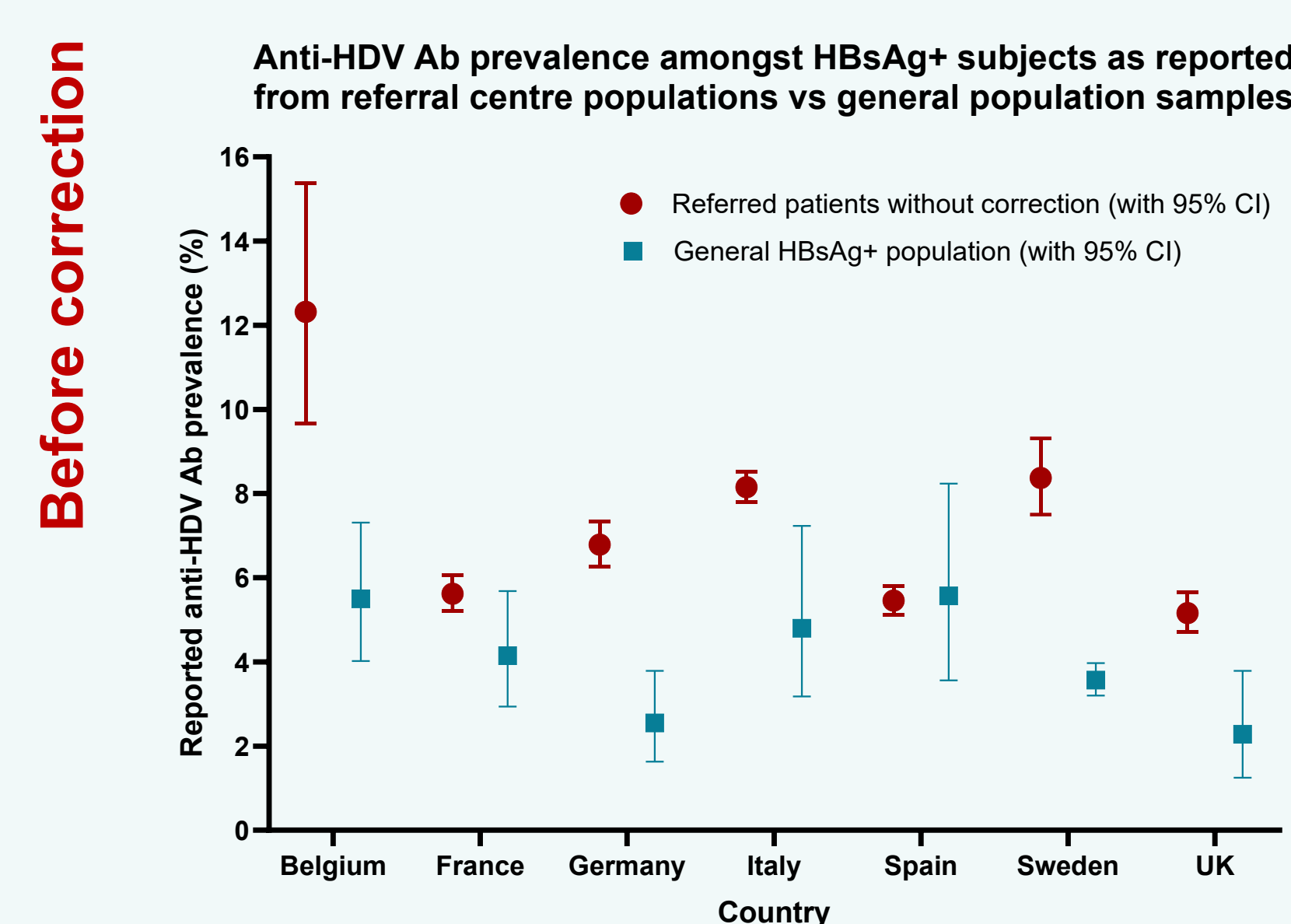
32% of HBsAg+ patients referred to hospital (20-50%)

0.42 relative risk of anti-HDV Ab+ in non-referred vs referred HBsAg+ patients (0.19-0.42)

0.17 relative risk of HDV-RNA+ in non-referred vs referred patients

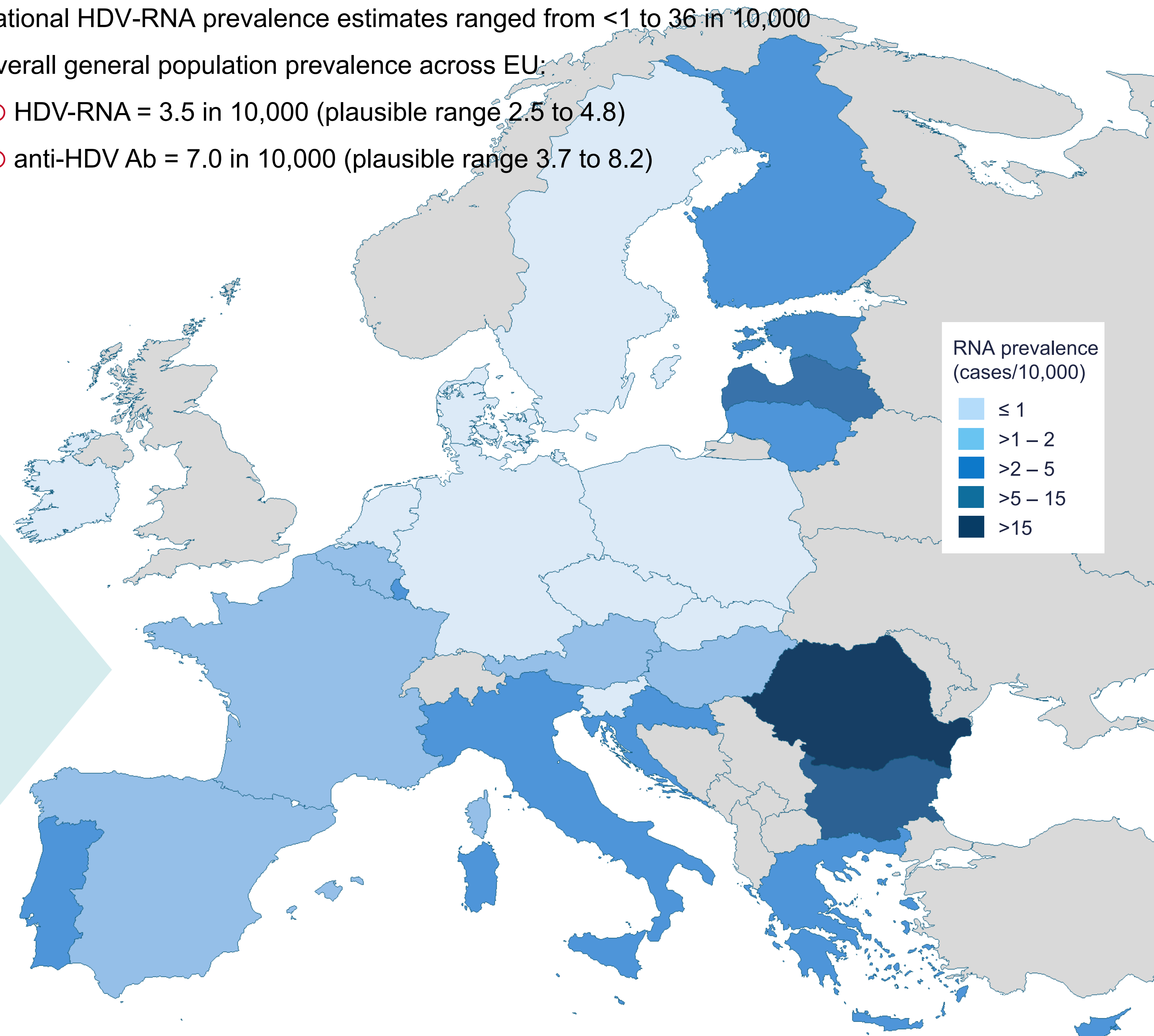
67% of patients HDV-RNA+ amongst anti-HDV Ab+ in hospital population

40% of patients HDV-RNA+ amongst anti-HDV Ab+ in general HBsAg+ population



Model application and results

- 75 estimates of HDV prevalence from EU countries identified; 80% based on referral clinic cohorts
 - Referral clinic-based estimates corrected for selection bias using model
- Total estimated patients with current HDV infection in the EU is 157,000, range 112,000 - 216,000
- National HDV-RNA prevalence estimates ranged from <1 to 36 in 10,000
- Overall general population prevalence across EU:
 - HDV-RNA = 3.5 in 10,000 (plausible range 2.5 to 4.8)
 - anti-HDV Ab = 7.0 in 10,000 (plausible range 3.7 to 8.2)



Anti-HDV Ab data on referred HBV+ populations

HDV-RNA data on referred HBV+ populations

Incorporate mean proportion of anti-HDV Ab+ with detectable RNA

Incorporate assumptions on

- Proportion of HBsAg+ referred to hospital
- RR of HDV-RNA or Ab in non-referred patients

Anti-HDV Ab and HDV-RNA in overall HBsAg+ population

Factor in national prevalence of HBsAg

Anti-HDV Ab and HDV-RNA prevalence in general population

Summary of procedure for extrapolating from referral clinic populations – performed for each EU country – to estimate general population prevalence

Conclusion and limitations

- Adjusted anti-HDV Ab prevalences estimated from referral clinic cohorts approached those of the available general population cohorts
- Uncertainty intervals around estimates remain wide due to scarcity of some data and likely national differences
- Model could be applied with refinements for local referral systems