Health outcomes and risk assessment in chronic liver disease (HERALD): a large Swedish research platform

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Background & Aims

The Nordic data landscape offers unique and internationally unmatched completeness of wide-ranging data with life-time follow-up of entire populations, creating a gold mind for real-world evidence (RWE) studies.

The 'HEalth outcomes and Risk Assessment in chronic Liver Disease' (HERALD) study is a multi-stakeholder Swedish research platform linking national and regional registries. The platform aims to investigate the epidemiology, resource-use, costs and risk factors of liver outcomes in patients with chronic liver diagnoses (CLD) or liver-related laboratory tests with a focus on non-alcoholic fatty liver disease (NAFLD). HERALD is a scalable research platform based on a public-private cooperation, planned to also include data from the Swedish National Diabetes Register and other Nordic countries during 2022, and is open to international collaboration.
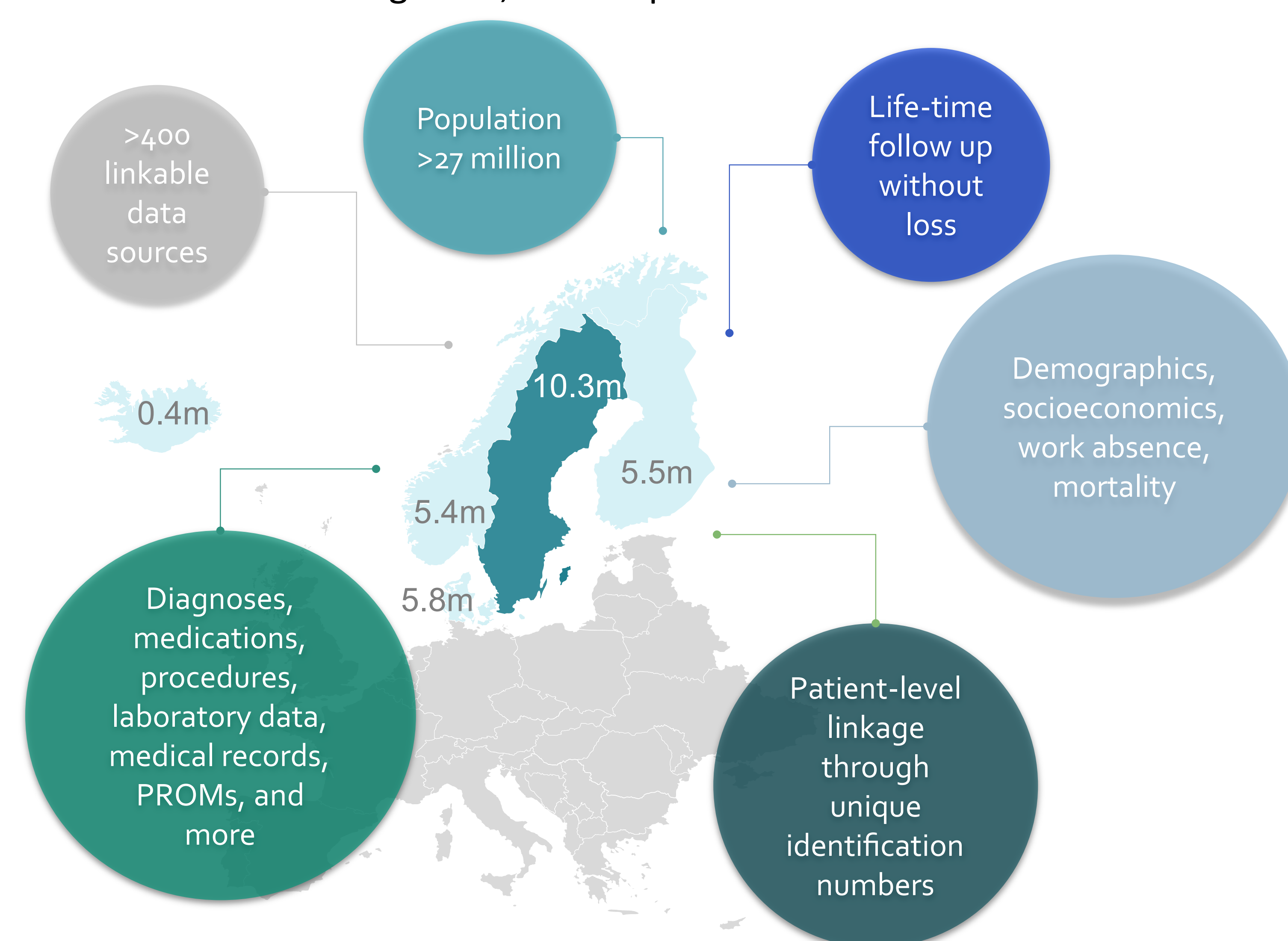

Figure 1. Key features of the Nordic data landscape

Methods

By 2022, the CLD cohort will consist of all patients ≥ 18 years with ≥ 1 CLD diagnosis (ICD-10) in Swedish specialist care, or primary care from the capital region (Stockholm). A partially overlapping cohort will consist of patients with laboratory tests (AST, ALT and platelets) in all care settings in Stockholm, with no requirement on CLD diagnosis. Using both cohorts, prevalence, risk factors and resource use can be analyzed in patients with both manifested CLD and patients with potentially undiagnosed liver disease in a broad, unselected, health care seeking population, using for example the non-invasive Fibrosis-4 (Fib-4) score.

Both cohorts will be linked with longitudinal data on diagnoses, comorbidities, healthcare utilization, prescribed medicines, mortality, work absence, socioeconomic status and demographics.

Table 1. Examples of CLD included in the HERALD research platform

Examples of chronic liver diseases		
Alcohol-related liver disease	Gaucher disease	Primary Biliary Cholangitis
Alpha-1 Antitrypsin Deficiency	Hemochromatosis	Primary Sclerosing Cholangitis
Autoimmune Hepatitis	Hepatocellular carcinoma (HCC)	Toxic liver disease (DILI)
Budd-Chiari Syndrome	Non-Alcoholic Fatty Liver Disease	Viral Hepatitis
Cirrhosis	Non-Alcoholic Steatohepatitis	Wilson Disease

For the Fib-4 cohort, longitudinal data of other laboratory values, spanning over ten years, are extracted from electronic health records (EHR) and for a subset of these, data on transient elastography (FibroScan) are extracted. This enables calculation of other risk scores, such as AST/ALT (AAR), AST to Platelet Ratio Index (APRI), FibroScan-AST (FAST) and NAFLD fibrosis score (NFS). High-risk subgroups and costs will be compared with matched controls from the general population.
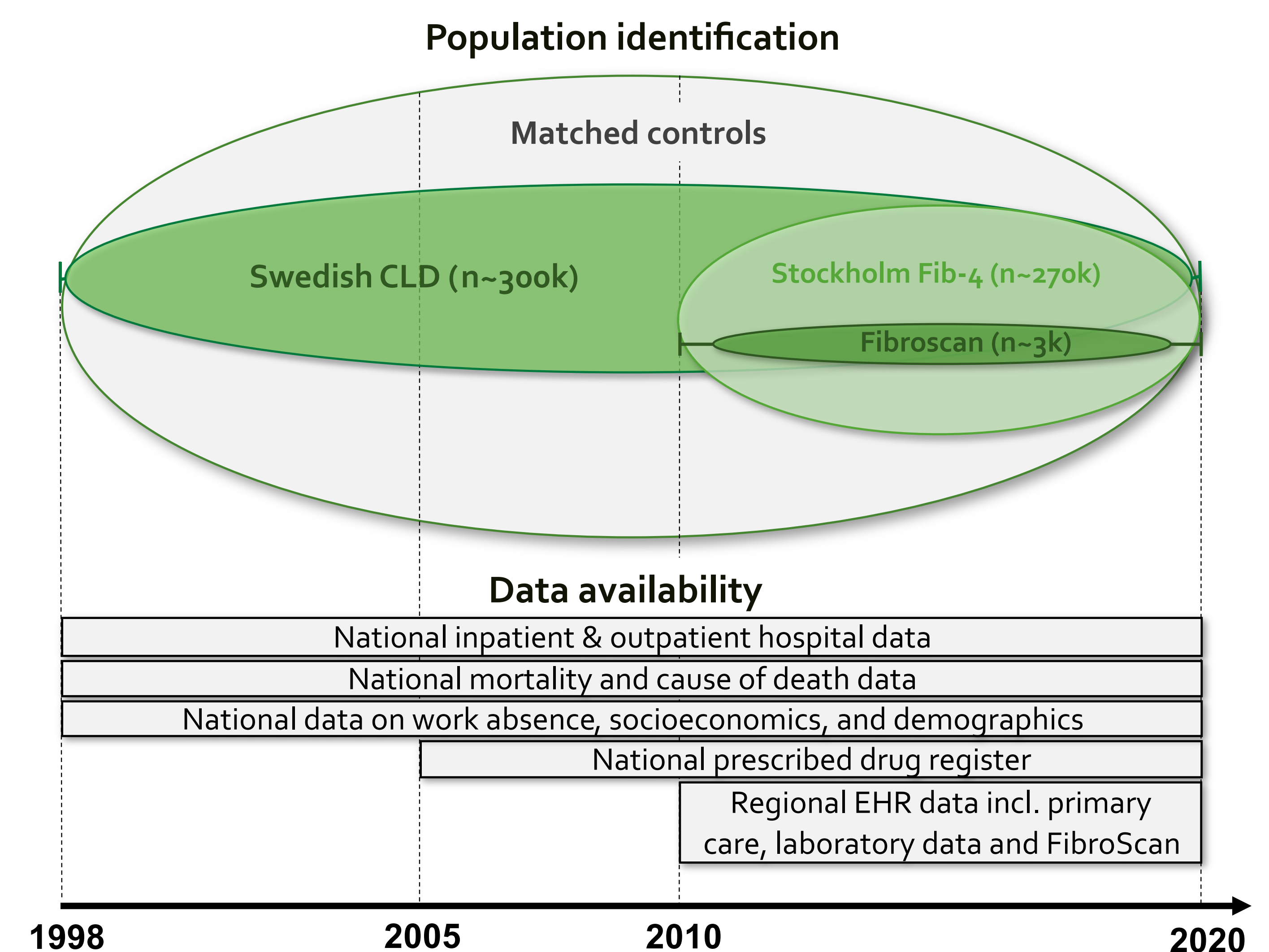

Figure 2. Population identification and data availability in HERALD

Results

A feasibility study was completed in 2020 and ethical approval for HERALD was granted in August 2020, with additional approvals in 2021. Table 2 presents the number of patients for selected diagnoses in the CLD cohort between 2001 and 2019 in Sweden. In total, approximately 200,000 to 300,000 patients with CLD are expected, partly overlapping with the ~270,000 patients expected in the Fib-4 cohort.

Table 2. Examples of patient numbers in the Swedish CLD cohort, 2001-2019

Disease	Number of patients
Non-Alcoholic Fatty Liver Disease (NAFLD)	16,285*
Chronic Hepatitis C virus (HCV)	53,602
Autoimmune Hepatitis (AIH)	5,337
Primary biliary cholangitis (PBC)	5,247

*with at least 46,122 patient years of follow-up

Conclusion

This scalable research platform is the result of a multi-stakeholder collaboration. HERALD will be the largest data collection to date to estimate a contemporary prevalence of liver disease, as well as the risk for advanced fibrosis in a broad, unselected population of healthcare-seeking individuals in Sweden, with and without recorded liver diagnoses.

Furthermore, HERALD will utilize clinical and non-clinical information to characterize patients with different risk profiles and to estimate long-term societal burden associated with severe liver outcomes in clinical practice over a 20-year period.