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ORIGINAL RESEARCH

# The Copenhagen Primary Care Laboratory (CopLab) Database

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**Background:** The Copenhagen General Practice Laboratory (CGPL) was founded in 1922 to provide paraclinical analyses to the primary health-care sector in Copenhagen. At the end of 2015, CGPL was closed and the CopLab database was established to make CGPL data available for research.

**Methods:** We isolated tests performed at the CGPL with clinically relevant test results. The database was linked to national registers containing health, social, and demographic information. Results are presented with descriptive statistics showing counts, percentages, medians, and interquartile ranges (IQR).

**Results:** The CopLab database includes 1,373,643 unique individuals from primary care with test results from laboratory analyses of blood/urine/semen as well as cardiac and lung function tests collected by CGPL from greater Copenhagen from 2000 to 2015. The CopLab database holds nearly all test results requested by general practitioners throughout years 2000 to 2015 for residents in the greater Copenhagen area. The median age of the individuals was 51 years and 59.7% were females. Each individual has a median of 4 requisitions. More than 1 million participants are currently alive and living in Denmark and may be followed in national registries such as the Danish National Patient Registry, Laboratory Database, National Prescription Database etc.

**Keywords:** laboratory database, population-based cohort, register studies, clinical biochemistry, epidemiology

## Introduction

The Copenhagen General Practice Laboratory (CGPL) was established in 1922 to serve the general practitioners (GPs) in the Municipality of Copenhagen and the County of Copenhagen was included in the area served by CGPL in 1994. The laboratory provided primary care physicians with various paraclinical analyses. In total, CGPL assisted about 750 GPs and 300 private practicing specialists in the years 2000–2015. In 2001, the CPGL was the first laboratory in Denmark to become fully accredited by The Danish Accreditation Fund (DANAK).[1] Additionally, CGPL achieved being the first laboratory globally to attain full accreditation for cardiac, pulmonary, and other analyses. This accreditation, compliant with DANAK's 15,189 standard (previously known as International Organization for Standardization 17,025), represented the highest quality standards and assurance. Under this accreditation, stringent and well-defined criteria covered various aspects such as information management, patient data handling, data analytics, staff qualifications, procurement, IT management, staff education, and quality objectives at CGPL. Continuous oversight by DANAK staff guaranteed that CGPL consistently upheld the accreditation prerequisites.[2]

Upon its closure in late 2015, CGPL stood as one of Northern Europe's most extensive laboratories, with a workforce of 195 full-time employees. The core laboratory was the largest production area, where approximately 10 million analyses were carried out annually.[2] In addition to conducting a wide array of biochemical analyses, CGPL provided an extensive range of cardiac and clinical physiological tests, along with allergological, urine, and semen analyses. The CGPL facilitated blood sampling not only at its core laboratory, but also at its eight local branches, in doctors' consultation rooms and in patients' residences or nursing homes.[2]

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In 2008, researchers affiliated with The Research Unit for General Practice in Copenhagen initiated the CopDiff project using CGPL data as a pilot study. This endeavor served as basis for the establishment of the CopLab database following CGPL's closure.[2,3]

The primary objective was to construct a real-world evidence database rooted in high-quality clinical data sourced from primary care settings. Specifically, the CopLab database has the following goals: i) elucidate both established and new risk factors for diseases, ii) study the prevalence and incidence of various health conditions, and iii) investigate the etiology, prevention, and treatment modalities for diseases. All collected data are securely stored on a server hosted at the University of Copenhagen. Financial support for the CopLab database stems from collaborative projects and internal funding provided by the Department of Public Health, ensuring the sustained progress of this research initiative.[2] In the current paper, we present the content of the CopLab database including register linkage and compare the population in the database to the background population.

## Materials and Methods

The most frequent tests were performed at CGPL's own laboratory, while some more rare tests were sent for analysis by external providers. In such cases, CGPL served as an administrative unit of the tests, but often did not receive numeric test results. Documentation for the used methods is also lacking for these external tests and due to these limitations, we only present data for tests analysed at CGPL. Further, the presentation is limited to tests performed on individuals with a valid Personal Identification Number (PIN), test date and age range, and cancelled or failed tests have been omitted. Figure 1 gives an overview of the data selection.

### Linkage to National Registers

The PIN allows for linkage with national registers at an individual level. At the moment, CopLab has been linked to several registers with information on health and sociodemographic factors and could potentially be linked with any other register or data source, which has a PIN after approval by relevant authorities and data owners.

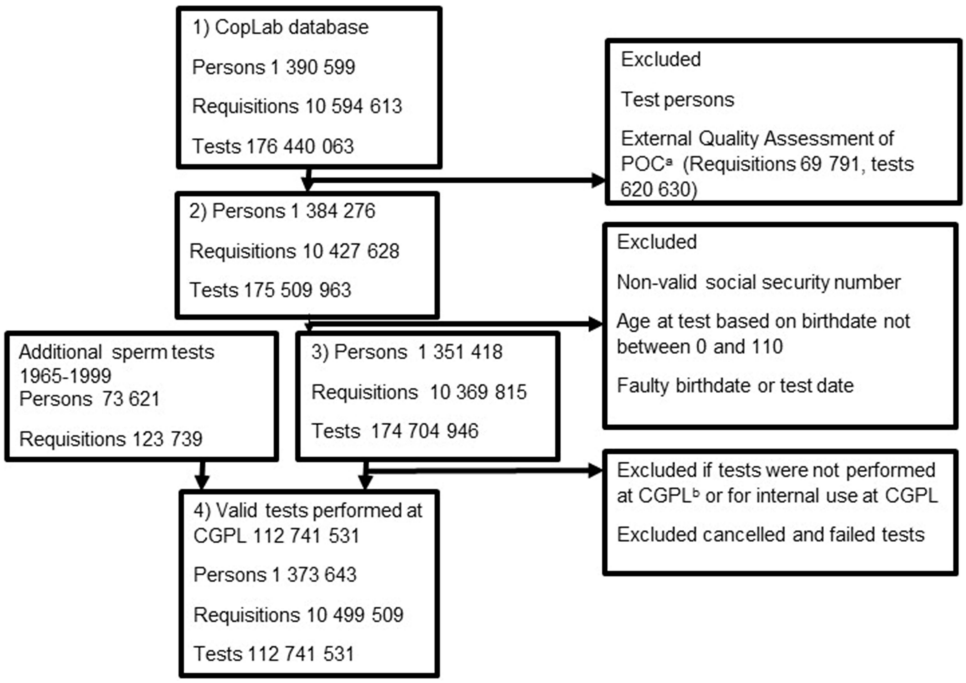


**Figure 1** Flowchart.
**Notes**: [a]Point of care tests. [b]Copenhagen General Practice Laboratory.

## Definition of the Background Population

The background population for CopLab is defined as individuals residing in the area served by CGPL between 2000 and 2015. The area served by CGPL remained the same throughout years 2000 through 2015, but in 2007, some municipalities were merged because of a reform of the structure of municipalities and regions. A list of municipalities defining the background population is described in Supplementary Table 1. Development in age distribution, gender, and use of GP and laboratory tests by calendar years are displayed in Supplementary Table 2.

For the comparison of the CopLab population with the background population that relies on register data, individuals who were not living in Denmark were excluded.

## Variables Used to Compare with the Background Population

Age and sex were available in the CopLab database and were retrieved from the population registry for the background population. Country of origin and marital status were derived from the population registry.[4] Based on country of origin, the population was grouped into Danish versus non-Danish (including descendants of migrants). Marital status was recorded as unmarried, married, divorced, and widowed. Few same-sex couples were grouped with the opposite sex counterparts for this analysis.

Household income data were sourced from income registers at Statistics Denmark and adjusted for inflation, aligning with the consumer price index in 2015.[5] The household income not only accounts for the total income of the household but also factors in the household's composition, including the number of adults and children. This approach measures the household's true purchasing power.

Educational attainment data was obtained from the education registry corresponding to the year of the test.[6] Following the guidelines of the International Standard Classification of Education (ISCED), the researchers categorized individuals into three distinct groups: Up to 10 years of education, 11–12 years of education, and 13 years and more of education.[6] For participants aged 24 or younger, the study also considered the educational levels of both parents. The individual was assigned the highest value among their own education, their father's, and their mother's education, ensuring a comprehensive evaluation of educational backgrounds in the analysis. The described method for measuring and grouping register variables was published in a study by Kaarhus et al.[7]

Results are presented using descriptive statistics showing count, percentages, medians, and interquartile ranges (IQR).

# Results

From the 1,373,643 unique individuals, a total of 10,499,509 requisitions and 112,741,531 tests exist in the CopLab database. Of these requisitions, 86% were requested by a GP. The annual number of requisitions increased during 2000–2015 from 3.3 million in 2000 to 7.9 million in 2015.

Table 1 demonstrates the number of unique individual requisitions and test results for subgroups of clinical biochemistry and for other tests. Every individual has a median of 4 requisitions (IQR: 2; 9) in the database. In each requisition, one or more tests have been requested. By far, clinical biochemistry constitutes most of the tests.

The frequency of a selection of biochemical tests and their distribution in relation to reference limits is shown in Supplementary Table 3. The selected tests are partly the most frequent tests and partly rarer tests assessed by the authors to be of clinical interest. Information concerning all biochemical tests in the CopLab database and their distribution in age and sex groups are publicly available at an aggregate level. Figure 2 presents an overview of existing register linkages. At the end of the current register-update in 2021 more than a million participants are still alive and can be followed in future updates of the registers.

Figure 2 presents an overview of registers linked to the CopLab database. All registers have an overlap in time with the CopLab database and are continuously being updated. The health registers include The National Laboratory database (2013-),[8] the Danish National Patient Registry (1978-),[9] The Danish National Health Service Register (1990-),[10] The Danish National Prescription Registry (1995-),[11] the Danish Cancer Registry (1943-),[12] The Danish Medical Birth Registry (1997-), and The Danish Psychiatric Central Register (1968-).[13] Demographic registers include The Danish Register of Causes of Death (1968-)[14] Registry of Migrations (1968-)

**Table 1** Number of Tests, Requisitions, and Unique Individuals by Test Group

| Tests by Test Group | Number of Tests | Number of Requisitions (% from GP) | Number of Unique Persons |
|---|---|---|---|
| **Clinical biochemistry (number of different IUPAC[a] codes)** | | | |
| Haematology (32) | 46,049,982 | 5,234,173 (87.20%) | 1,133,114 |
| Organ markers (17) | 17,502,552 | 5,718,958 (88.29%) | 1,085,083 |
| Endocrinology (19) | 8,025,696 | 4,201,236 (85.95) | 1,016,059 |
| Metabolism (17) | 18,513,782 | 4,844,049 (91.98) | 966,981 |
| Immunology and inflammation (17) | 5,154,639 | 3,501,060 (86.92%) | 960,145 |
| Fluid and electrolyte balance (2) | 7,902,597 | 3990,776 (92.02%) | 893,189 |
| Trace elements and vitamins (1) | 1,708,356 | 1,708,356 (92.28%) | 631,395 |
| Infection (11) | 1,276,921 | 626,000 (88.72%) | 388,830 |
| Urine tests (11) | 2,031,433 | 707,187 (87.88%) | 253,897 |
| Allergy (143) | 1,293,268 | 267,155 (62.83%) | 211,528 |
| Tumor markers (3) | 470,127 | 463,709 (89.66%) | 180,038 |
| Coagulation (2) | 1,165,630 | 1,150,006 (81.12%) | 149,211 |
| Pharmacology (4) | 106,721 | 105,280 (73.20%) | 24,894 |
| Acid-base balance of oxygen (1) | 384 | 384 (64.84%) | 245 |
| **Other tests** | | | |
| 12 lead resting ECG | | 1,022,842 | 463,576 |
| Exercise ECG | | 29,133 | 24,120 |
| Allergy skin test | | 95,554 | 85,044 |
| 24 hour blood pressure monitoring[b] | | 8577 | 7795 |
| Echocardiography | | 35,056 | 30,153 |
| Distal blood pressure[c] | | 28,582 | 24,484 |
| Lung function tests | | 26,614 | 23,599 |
| Blood in faeces[d] | | 51,019 | 42,839 |
| Helicobacter Pylori breath test[e] | | 93,228 | 69,191 |
| Semen analyses[f] | | 148,838 | 88,625 |

**Notes**: [a]International Union Of Pure And Applied Chemistry. [b]Available from January 2010 through March 2013. Results are expressed as mmHg systolic and diastolic blood pressure. [c]Results available from February 2000 through March 2013. Approximately 97% of the results are expressed as mmHg and a percentage of the arm blood pressure. [d]Results available from February 2000 through December 2015. Each requisition includes guaiac fecal occult blood test results from faecal samples collected at three different days. Approximately 10% of the results are positive for blood. [e]Results are expressed as positive (25,5%) or negative (74,5%). [f]Semen analyses collected between 1965 and 2015.

and The Population Register (1986-) and the Death registry (1968-) all derived from The Danish Civil Registration System.[5] Social registries include The Income Registry (1987-), Registry of the Workforce (1990-),[5] and The Education Registry (1981-).[6]

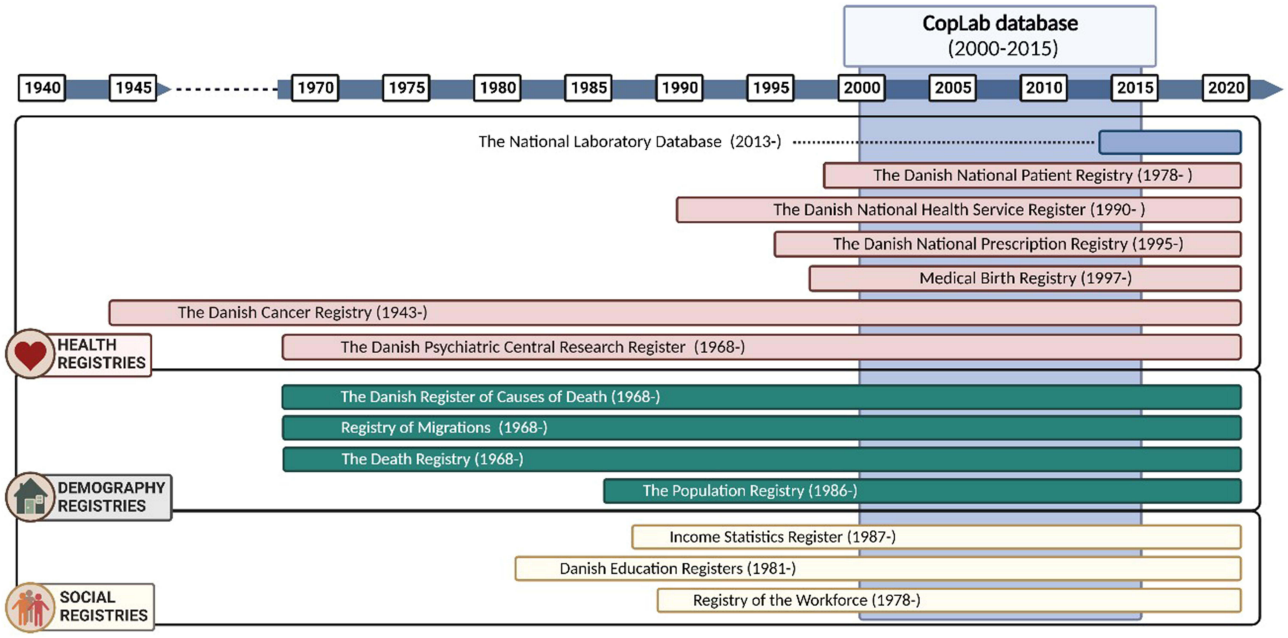


**Figure 2** Overview of registers linked to the CopLab database. Created with Biorender.com.

## Comparing the CopLab Population to the Background Population

Table 2 depicts sociodemographic characteristics of the CopLab population in 2006 and the background population in 2006. If an individual had more than one test in 2006, the first was selected. The CopLab population had more women (59.7%) compared to the background population (51.3%) and the CopLab population was older (median 51 years) compared to the background population (median 37 years). The CopLab population was also characterized by a lower proportion of never married individuals, reflecting their higher age. The proportion with low or unknown education was

**Table 2** Characteristics of the CopLab Population and the Background Population in 2006[a]

| | CopLab Population 2006 (N=326,543) | Background Population 2006 (N=1,102,811) |
|---|---|---|
| **Sex**, number and % | | |
| Women | 194,874 (59.7%) | 565,239 (51.3%) |
| **Age distribution**, number and % | | |
| 0–17 | 16,189 (5.0%) | 222,308 (20.2%) |
| 18–29 | 42,971 (13.2%) | 188,338 (17.1%) |
| 30–49 | 95,817 (29.3%) | 340,022 (30.8%) |
| 50–69 | 105,004 (32.2%) | 239,545 (21.7%) |
| 70–89 | 62,031 (19.0%) | 104,641 (9.5%) |
| 90+ | 4531 (1.4%) | 7957 (0.7%) |
| Age median (IQR[b]) | 51 (34, 66) | 37 (22, 55) |

(*Continued*)

**Table 2** (Continued).

| | CopLab Population 2006 (N=326,543) | Background Population 2006 (N=1,102,811) |
|---|---|---|
| **Country of origin**, number and % | | |
| Danish | 50,098 (15.3%) | 930,507 (84.4%) |
| **Marital status**, number and % | | |
| Married | 147,188 (45.1%) | 379,024 (34.4%) |
| Never married | 99,819 (30.6%) | 557,521 (50.6%) |
| Divorced | 42,754 (13.1%) | 104,558 (9.5%) |
| Widowed | 33,810 (10.4%) | 61,708 (5.6%) |
| No information | 2972 (0.9%) | 0 |
| **Household equivalized income in Euro**[c] | | |
| Median (IQR) | 28,806.9 (20,715.3, 39,789.0) | 29,337.9 (20,793.8, 39,451.6) |
| No information | 7257 (2.2%) | 24,139 (2.2%) |
| **Education** number and % | | |
| Low | 76,263 (23.4%) | 208,528 (18.9%) |
| Medium | 121,747 (37.3%) | 414,975 (37.6%) |
| High | 102,724 (31.5%) | 420,921 (38.2%) |
| No information | 25,809 (7.9%) | 58,387 (5.3%) |

**Notes**: [a]Information on country of origin, marital status, and income was retrieved from national registers. The CopLab population was restricted to those with at least one occurrence in the population registry. Missing data is omitted, [b]Inter Quartile Range, [c]Based on family disposable income.

higher compared with the background population, while the distributions of family equalized income and proportion with Danish origin were similar.

## What Has Been Found?

Before the CopDiff and CopLab databases were established, limited data extracts from CGPL were documented in separate studies.[15–18] The CopDiff Database has been documented in nine publications primarily focusing on hematological cancer.[3,19–25] To date, more than 40 publications have been based on CopLab data in the following areas:

### Endocrinology

In a series of publications, we have scrutinized subclinical hypothyroidism in primary care. Among 929,684 primary care patients, the number of patients treated with levothyroxine increased annually and at the same time, the median value of thyroid stimulating hormone (TSH) of the last measurement before starting treatment decreased. There was an increase in the number and proportion of patients with treatment initiation with normal TSH and the likelihood of initiating treatment was 8% higher for individuals with short and medium education compared to individuals with longer education. At TSH <5 mIU/L,[26] the likelihood of starting treatment was between 22% and 53% higher for citizens with long education compared to citizens with short and medium education indicating societal instead of medical factors for treatment initiation.[26–28] In diabetes, we have analysed the validity of HbA1c in primary care and the potential influence of concomitant anaemia and chronic kidney disease.[29] In a primary health-care population suspected of heart failure, we have shown that brain natriuretic peptide in plasma is a valid predictor of all-cause mortality.[30]

### Cancer

In particular, haematological neoplasms have been the interest in many studies. We have provided risk estimates for the subsequent risk of haematological malignancies and death when eosinophilia is observed in routine blood samples and show that eosinophilia may also act as a biomarker for solid tumour development.[22] We also studied the risk of lymphoma and solid cancer in patients with rheumatoid arthritis[20] and in another study found that thrombocytosis was a strong predictor of late diagnosis and high mortality of gynaecological cancer.[19] We have evaluated the prevalence and clinical significance of neutropenia discovered in routine complete blood cell counts – alone or in conjunction with other cytopenias[23,31] and have shown that anaemia is present years before diagnosis of myelodysplastic syndromes among primary care patients.[24] Lately, our data have been used to show that abnormal eosinophil count in chronic lymphatic leukaemia (CLL) diagnosis is associated with shorter treatment-free survival[32] and that machine learning has the potential to recognize recently diagnosed CLL patients who are highly susceptible to infections.[33] For solid tumours, we have shown that the presence of cancer heightened the risk of developing new-onset type 2 diabetes, which, in turn, was linked to elevated overall mortality rates.[34]

## Discussion

The CopLab database contains complete data from July 2000 through 2015; data before 2000 was not included because it was not fully electronically recorded and due to lack of documentation. The CopLab database ends in 2015, but national register data with similar content make it possible to extend follow-up for the included individuals indefinitely. During the years 2000 through 2015 individuals had to live in Greater Copenhagen to be eligible for inclusion. Fortunately, most cohort members lived in the area for a long time (median 10 years) and can all be followed in registers even if they moved to other parts of Denmark thereafter. This makes it possible to document this issue and take it into consideration in studies. Also, the CopLab database contains only tests performed on primary care patients. Hospitals had their own laboratories serving in- and outclinic patients. In both CopLab and nationwide registries important information for epidemiological research such as life style factors is missing. Any existing data source like survey data, which contains a PIN may be linked to CopLab data upon approval from data owners and authorities, and there are ongoing efforts to enrich the cohort with such data for future projects.

The tests in CopLab were requested with an indication, but the database seldom contains this information. For some epidemiological studies, this presents a statistical challenge and appropriate methods should be used in the analyses to account for this. If the aim is to investigate the level of a biomarker in a group of patients, some may not have a test in the CopLab database. An analysis on the complete cases alone will most likely be biased and methods for dealing with missing data, such as imputation or weighting, should be employed instead.

We found that the number of tests per person increased between 2000 and 2015. Other studies from primary health-care databases have found similar trends.[35,36] In the case of the CopLab database, the increase cannot be fully explained by population aging or a growing background population, but may be attributed to several factors. The introduction of electronic ordering devices at the GP's office including the use of panels of tests promotes the ordering of a broad range of automated routine laboratory tests.[37,38] Furthermore, a drastic increase in specific tests contributes to the observed annual increase in number of tests per person. An example of this is the number of vitamin D measurements analyzed at CGPL, which grew exponentially between 2000 and 2010, and 14% of all request of blood samples received at CPGL between 2004 and 2010 included vitamin D.[15,39] For HbA1c new guidelines introduced by the World Health Organization and the Danish Health Authorities in 2011–2012, stated that HbA1c should be used, not only for screening and monitoring but also as a diagnostic tool. This caused a steep increase in the usage of HbA1c in these years, followed by a stabilization.[37]

## Conclusion

Health data are an expanding resource of key knowledge with the potential to improve public health and develop tailored health solutions for the benefit of individual patients and society. Nordic countries have some of the finest and most comprehensive health data assets in the world. Combined with new real-world data, these register data can be used in the development of personalized medicine and innovative solutions with public health in focus. However, this requires that data is accessible to students, researchers, and health-care professionals.

The CopLab data holds the potential to unveil significant physiological and pathophysiological relationships for a wide range of medical conditions. Its extensive collection of clinical and administrative variables has been rigorously validated, establishing a cutting-edge database infrastructure. This robust foundation enables accurate interpretation of the database content, facilitating meaningful insights into various medical scenarios.[2]

## How Can I Get Hold of the Data?

Information on how to access data from the CopLab cohort is provided by the steering group upon request in e-mail to christen.andersen@sund.ku.dk. Data are stored at a server at University of Copenhagen. Research projects may be carried out using the facilities of The Public Health Database at the Department of Public Health, University of Copenhagen, following national and local restrictions on data access and processing.

Information concerning all biochemical tests in CopLab and their distribution in age and sex groups are publicly available in a database of aggregated data on the CopLab webpage https://shiny.sund.ku.dk/CopLab/database-overview/.[40]

## Abbreviations

CGPL, Copenhagen General Practice Laboratory; GP, general practitioner; DANAK, The Danish Accreditation Fund; PIN, Personal Identification Number; DKK, Danish crowns; ISCED, International Standard Classification of Education; TSH, thyroid stimulating hormone; CLL, chronic lymphatic leukaemia.

## Ethics

The study is approved by the Danish Data Protection Agency and registered in the data processing inventory of University of Copenhagen (514-0460/20-3000). Danish law does not require informed consent for registry studies using administrative data.

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## Disclosure

The authors report no conflicts of interest in this work.

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