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Cohort profile: the Swedish Pancreatitis Cohort (SwePan)

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ABSTRACT

Purpose The Swedish Pancreatitis Cohort (SwePan) was designed to study long-term outcomes following an episode of acute pancreatitis. It can also be used to study various risk factors for developing acute pancreatitis.

Participants The SwePan is a register-based nationwide matched cohort. It includes all Swedish cases of acute pancreatitis during 1990–2019. It contains 95 632 individuals with acute pancreatitis and 952 783 pancreatitis-free individuals matched on sex, age and municipality of residence. Follow-up was censored at death, emigration or end of study (31 December 2019). The dataset includes comprehensive information based on several registries, and includes diagnoses, prescribed medications and socioeconomic factors both prior to inclusion and during follow-up.

Findings to date During the study period, the number of cases of acute pancreatitis in Sweden has more than doubled from 1977 cases in 1990 to 4264 cases in 2019. The median age of first episode of acute pancreatitis has increased from 58 years (IQR 44–73 years) in 1990 to 64 years (IQR 49–76 years) in 2019. Cases with acute pancreatitis were generally less healthy compared with the pancreatitis-free individuals (Charlson Comorbidity Index of 0 in 59.2% and 71.4%, respectively).

Future plans SwePan will be used to determine the incidence of acute pancreatitis in Sweden over time and assess long-term all-cause and cause-specific mortality after an episode of acute pancreatitis. Some examples of additional planned studies are (1) assessment of long-term risk of diabetes and (2) risk of malignancy in adjacent organs following acute pancreatitis and (3) assessment of risk factors for development of acute pancreatitis including various drugs.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The main strength of the Swedish Pancreatitis Cohort (SwePan) is the nationwide inclusion based on population-based registries which are centrally maintained.
⇒ The nationwide registries with validated high-quality data facilitate complete and long-term follow-up.
⇒ The population-based design of the study increases generalisability of future study findings to the general population.
⇒ There are no individual data on lifestyle factors including smoking habits, body mass index or dietary factors.
⇒ There might be variations in coding based on local clinical guidelines.

INTRODUCTION

The Swedish Pancreatitis Cohort (SwePan) was created with the purpose of studying aetiology and various outcomes in acute pancreatitis. Acute pancreatitis, inflammation of the pancreas, is one of the most common gastrointestinal diagnoses that require hospital admission.[1] Epidemiological studies show an increasing incidence of acute pancreatitis worldwide, with a current incidence estimate of 35–40 cases per 100 000 person-years in Sweden.[2–5] About 80% of cases are self-limiting and heal within 1–2 weeks, but the remaining cases suffer a severe disease with local complications such as pancreatic tissue necrosis, abscesses and/or multiple organ failure.[6] The mortality rate in the latter group is high, with estimates starting at 10%–15% and rising to as much as 35% when infectious complications are present.[7 8] The treatment is supportive with early fluid resuscitation, early enteral nutrition, antibiotics for infections and minimally invasive drainage of abscesses if needed.[6] The leading causes of acute pancreatitis are gallstone disease and alcohol abuse, but other less common causes such as drugs, hypertriglyceridaemia and endoscopic intervention also exist.[9 10]

Given the immense inflammatory process in acute pancreatitis, both locally in the pancreas and systemically, one can hypothesise that there may be various long-term health effects following an episode of acute pancreatitis. For example, population-based studies have found an increased risk of developing diabetes mellitus, a persistent increase in long-term mortality and reduced health-related quality of life after an episode of acute pancreatitis.[11–14]

The aim of this study is to describe the Swedish Pancreatitis Cohort (SwePan). The cohort was created with the intention to study various long-term outcomes following a first-time episode of acute pancreatitis. It is also

intended to be used to study different risk factors for developing acute pancreatitis.

COHORT DESCRIPTION

The SwePan is based on data from nationwide health registries in Sweden. A detailed description of the registries included in the cohort follows below. All Swedish citizens have a unique personal identity number assigned at birth, which allows direct linkage between the different registries.[15]

The Swedish Patient Register, first introduced in 1964, has complete national coverage of all inpatient care in Sweden since 1987. In 2001, the register was expanded to also include specialised outpatient care, that is, outpatient visits at hospitals but not in primary care. The accuracy of the International Classification of Diseases coding in the inpatient component of the Swedish Patient Register has been previously validated, with overall positive predictive values of 85%–95%.[16] The diagnosis of acute pancreatitis specifically has also been found to have high validity, with a positive predictive value of 83% for definitive disease and 98% for probable disease.[17] The Patient Register was also used to assess comorbidities using the Charlson Comorbidity Index, a well-validated index including chronic and severe diseases, at baseline.[18]

The Swedish Prescribed Drug Register holds a complete national coverage on all prescribed and dispensed drugs in Sweden since 1 July 2005. The register includes, among other, information on drug substances according to the Anatomical Therapeutic Chemical classification, the quantity of drug dispensed and date of expenditure. The register is nearly 100% complete and highly valid, since it is used for reimbursements, however, over the counter medications are not included in the register.[19 20]

The Swedish Cancer Register contains, since 1958, information on all diagnosed malignant tumours in Sweden. Each record includes, among other, information on the anatomic location and histological type of the tumour. The nationwide coverage has been estimated to be 96%–98%.[21 22]

The Cause of Death Register contains information on date of death for all deceased Swedish residents since 1952. Further, the register contains data regarding cause and contributing causes of death, whether an autopsy was conducted and if the patient had recently undergone surgery. The completeness and accuracy regarding date of death has been determined to be 100%.[23]

The Register of the Total Population was used to collect data on sex, year of birth, municipality of residence, country of birth and date of emigration. The register covers all Swedish residents since 1968.[24]

The Register on Participation in Education is a part of the longitudinal integrated database for health insurance and labour market studies. It was used to collect individual data on highest completed level of education, field of education and year of completion of education.[25]

Data are stored, managed and analysed on servers belonging to the local county, Region Sörmland, accessed through a virtual private network. Before delivery of data from the registers, all personal identification numbers were pseudonymised with a unique, arbitrary code number.

Following the implementation of the General Data Protection Regulation in the European Union during 2018, there has been an increased recognition and consideration for the integrity of the study participants in register-based research. The interpretation of the new regulation by the major record holding authorities in Sweden (The National Board of Health and Welfare) has led to new routines in the retrieval of register data for research purposes. Data which are not explicitly planned to be used in the foreseeable future are not handed out to researchers. A complete list of the data from the Swedish Patient Register and the Swedish Prescribed Drug Register in SwePan is presented in online supplemental table 1.

Patient and public involvement

Patients or the general public were not involved in the planning or design, recruitment or conduction of the study.

Participants

The exposed individuals included in the SwePan were selected based on a recorded diagnosis of acute pancreatitis between 1 January 1990 and 31 December 2019. The date of first recorded diagnosis of acute pancreatitis for each case was considered index date. Exclusions were made for individuals with (1) diagnosis of acute pancreatitis resulting in hospitalisation before 1 January 1990 or (2) diagnosis of chronic pancreatitis at any time before index date or (3) diagnosis of pancreatic cancer at any time before index date.

For each individual with acute pancreatitis, survivor sampling was used to randomly identify up to ten pancreatitis-free individuals (between 1 January 1990 and 31 December 2019) from the general population. The matching variables were sex, age and municipality of residence. The pancreatitis-free individuals could be matched to multiple cases with acute pancreatitis. Further exclusions were made for individuals with reused or erroneous personal identity number, and among the matched pancreatitis-free individuals due to occurrence of pancreatitis (acute or chronic) or pancreatic cancer before 1 January 1990.

Variables and data management

The main variables included in SwePan from each register are presented in table 1. Due to the current Swedish legislation protecting the integrity of individuals in register data, the specific date of birth for each individual is replaced with data on year and month of birth only. To allow for time comparisons across the database, all individuals were assigned a date of birth of the 15th of their birth month. All individuals in the cohort were followed

Table 1 Main variables available from each registry respectively in the SwePan database

Register	Variables
The Patient Register	Diagnoses (ICD-codes), divided into main and supplementary for each hospital visit Interventions during hospital stay (Swedish version of NOMESCO Classification of Surgical Procedures 1.9) Date of admission and discharge
The Prescribed Drug Register	Drug type and intended route of administration (ATC-code) Size of dispensed prescription (strength, no of doses, defined daily doses) Prescription text/instructions (freely written by the prescribing healthcare professional)
The Cancer Register	Tumour diagnosis (ICD codes) Date of diagnosis Tumour, nodes and metastases (TNM) classification, incl basis for diagnosis (autopsy, histopathology, cytology, radiology, etc)
The Cause of Death Register	Age, place and date of death Underlying cause of death (ICD codes)
The Register of the Total Population	Country and place of birth Civil status and number and age of any children Household information (municipality of residence, no of residents in household, disposable income, etc)
The Register on Participation in Education	Highest formal education categorised into: ► Did not complete compulsory school. ► Completed compulsory school. ► <3 years high school ► Completed high school. ► ≤3 years university studies. ► >3 years university studies. ► Postgraduate degree.

ATC, Anatomical Therapeutic Chemical; ICD, International Classification of Diseases.

for as long as possible in the registers included in the study, that is, until death, emigration or end of study 31 December 2019.

STUDIES AND FINDINGS TO DATE

The final cohort consists of 95 632 individuals with acute pancreatitis and 952 783 matched pancreatitis-free individuals. The annual average number of pancreatitis-free individuals included for each individual with acute pancreatitis was high and stable over time. The final baseline characteristics of the study participants are presented in table 2. The median age of individuals with acute pancreatitis at inclusion was 62 years (IQR 47–75) and 52.4% were male. Individuals with acute pancreatitis were found to be less healthy at baseline compared with the pancreatitis-free individuals with a Charlson Comorbidity Index of 0 in 59.2% and 71.4%, respectively.

The annual number of cases of acute pancreatitis in Sweden increased to more than double of the initial during the study period (figure 1). There was an overrepresentation of men among included individuals with acute pancreatitis in the first years of the study period which decreased during the first decade and thereafter remained stable (figure 1). The median age of individuals with acute pancreatitis on inclusion in the cohort increased from 58 years (IQR 44–73 years) in 1990 to 64 years (IQR 49–76 years) in 2019 (figure 2).

The SwePan is an updated, elaborate version of a similar database which has been used to study for example the incidence of acute pancreatitis over time in Sweden and the association between acute pancreatitis and pancreatic cancer.[5 26] The current cohort can be used for long-term follow-up of patients with acute pancreatitis, assessing different complications, for example, cancer development or complications, such as diabetes. Data can also be used to investigate comorbidities, socioeconomic factors and causes of death. The cohort can also be used to investigate possible risk factors for development of acute pancreatitis, for example, drug exposure or previous diseases or surgeries.

STRENGTHS AND LIMITATIONS

The main strengths of the SwePan are the nationwide coverage of the registers used in the database and the high internal validity of the diagnoses included. Also, the large number of cases included in the cohort ensures the high estimate precision needed to study rare outcomes and risk factors of the disease.[27] Further, the population-based study design based on nationwide registries increases generalisability of the findings. Previously published cohorts lack either the size of SwePan or the comprehensive coverage of potential covariates, particularly the prescription of drugs.[28 29]

Table 2 Baseline characteristics of participants in the SwePan database

	Acute pancreatitis	Controls
No (n) of participants	95 632	952 783
Sex, n (%)		
Men	50 079 (52.4)	498 696 (52.3)
Women	45 553 (47.6)	454 087 (47.7)
Age (years) at cohort entry, n (%)		
<20	1749 (1.8)	17 486 (1.8)
20–39	13 813 (14.4)	138 116 (14.5)
40–49	11 785 (12.3)	117 824 (12.4)
50–59	15 422 (16.1)	154 129 (16.2)
60–69	17 606 (18.4)	175 893 (18.5)
70–79	18 361 (19.3)	183 361 (19.2)
≥80	16 896 (17.7)	165 974 (17.4)
Age, median (IQR)	62 (47–75)	62 (47–75)
Calendar period at cohort entry, n (%)		
1990–1994	11 463 (12.0)	14 278 (12.0)
1995–1999	13 725 (14.3)	136 810 (14.3)
2000–2004	14 683 (15.4)	146 234 (15.4)
2005–2009	15 634 (16.4)	155 817 (16.4)
2010–2014	19 246 (20.1)	191 600 (20.1)
2015–2019	20 881 (21.8)	208 044 (21.8)
Country of birth, n (%)		
Sweden	80 405 (84.1)	824 636 (86.6)
Outside Sweden	15 227 (15.9)	128 147 (13.4)
Charlson Comorbidity Index, n (%)		
0	56 646 (59.2)	679 814 (71.4)
1	16 929 (17.7)	135 596 (14.2)
≥2	22 057 (23.1)	137 373 (14.4)

The main limitations of the SwePan are lack of specific data on certain lifestyle factors, such as smoking status, body mass index and alcohol consumption. The registers on which the cohort is based do not include specific information regarding these factors. Thus, these potential confounders will need to be managed through surrogate markers such as socioeconomic status, education level, registered lifestyle-related diseases or prescribed drugs.

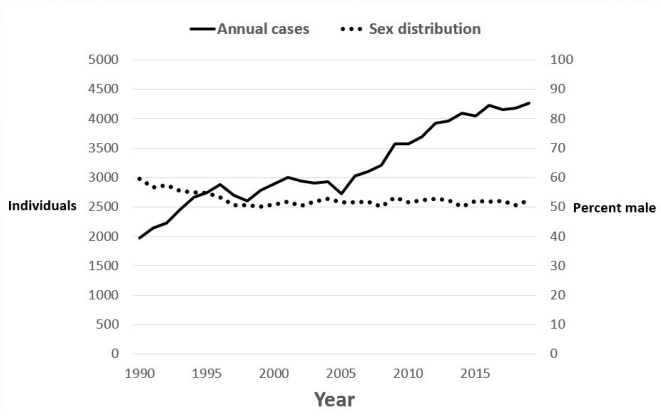

Figure 1 Annual number of included individuals with acute pancreatitis and their sex distribution in the SwePan during the study period.

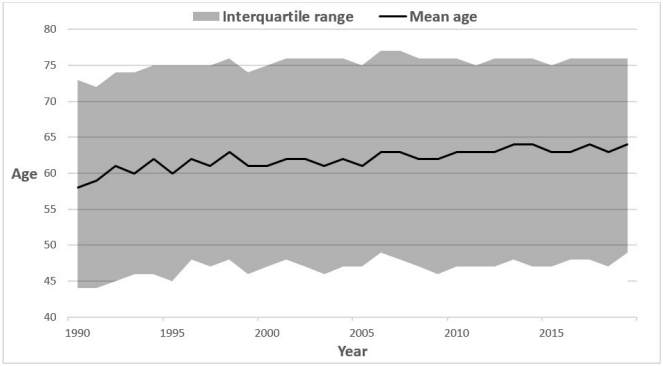

Figure 2 Median age and IQR at baseline of included individuals with acute pancreatitis in the SwePan during the study period.

Collaborators The authors are welcoming and encouraging research collaborations using the SwePan, and researchers interested in collaborating on the SwePan data are welcome to contact the research group.

Contributors DS, JM-O and OS-A handled the data collection. OS-A handled the ethical permissions. DS, BY and OS-A handled the data management, creation of working data sets and retrieval of presented descriptive data. DS drafted the manuscript. DS, JM-O, OS-A, BY, ML, MN and UA revised the manuscript for important intellectual content including interpretation of presented data and approval of final version. DS and JM-O were responsible for the final version of the manuscript. OS-A is guarantor of the study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethical permission for the cohort was granted by the Central Ethics Review Board in Stockholm, Sweden (permission registration numbers 2010/920-31/4 and 2015/0090-32).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. According to Swedish legislation, the research data need to be held by the authorities and are protected under statistical secrecy. The data are stored on servers of the regional authority and individual data cannot be shared with people who are not directly associated to the record-holding authority.

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