Indirect impacts of the coronavirus pandemic on non-COVID outcomes and health inequalities: An international comparison of the UK and Denmark using the OpenSAFELY platform and National Registry Data

Analysis plan

This study forms part of the COVID-Collateral protocol, this analysis plan is specifically for the deprivation and migration status analysis.

Introduction

- Diversion of healthcare resources to pandemic management has negatively affected non-COVID-related healthcare provision, including prevention activities, potentially creating or worsening physical and mental health (1).
- While the UK has experienced one of the worst COVID-19 outbreaks in Europe, several Scandinavian countries have experienced better COVID-19 outcomes and faster healthcare system recovery (2).
- We do not know which aspects of the pandemic are driving non-COVID health consequences. Comparing countries with different pandemic curves where different measures have been taken at different times will allow us to gain insight into which components, if any, drive between-country differences. This will help inform policy for any future infectious disease outbreaks in the UK.
- While the direct effects of the COVID-19 pandemic have been found to disproportionately affect older people, minority ethnic groups, and deprived populations, inequalities in the indirect effects of the pandemic have yet to be fully explored (3–5).
- The aim of this study is to determine the impact of the pandemic on differences in deprivation and hospitalisations and mortality for non-COVID conditions in Denmark and England between March 2018 and December 2022.

Methods

Data Sources

England

Primary care records managed by the GP software provider, TPP were linked to ONS death data through OpenSAFELY, a data analytics platform created by our team on behalf of NHS England to address urgent COVID-19 research questions (https://opensafely.org). OpenSAFELY provides a secure software interface allowing the analysis of pseudonymized

primary care patient records from England in near real-time within the EHR vendor's highly secure data centre, avoiding the need for large volumes of potentially disclosive pseudonymized patient data to be transferred off-site. This, in addition to other technical and organisational controls, minimises any risk of re-identification. Similarly pseudonymized datasets from other data providers are securely provided to the EHR vendor and linked to the primary care data. The dataset analysed within OpenSAFELY is based on 24 million people currently registered with GP surgeries using TPP SystmOne software. **It includes pseudonymized data such as coded diagnoses, medications and physiological parameters. No free text data are included**. Further details on our information governance can be found on page X, under information governance and ethics.

Denmark

The tax-supported health care system in Denmark ensures unfettered access to medical care for all residents (approximately 5.9 million individuals). All Danes are assigned a unique personal identification number (the CPR-number) at birth or immigration, which makes it possible to link individual information between relevant registries: the Danish National Patient Registry, containing all inpatient discharge diagnoses from all hospitals since 1977 and from emergency room and outpatient specialist clinic contacts since 1995; to the Danish Civil Registration System, including vital status and date of death for the entire Danish population; and socioeconomic registries maintained by Statistics Denmark, including data on family and household socioeconomics, country of origin, educational level, employment status, and income.

Study design and population

In England the study population will be adults (males and females, age 18 years and above) registered in a TPP general practice, in Denmark the study population will be all adults. The study period will be 1st March 2018 and 31st December 2022. People can enter the study at any time point during follow-up as counts of outcomes will be measured monthly.

For both countries:

- Inclusion criteria: Adults age 18 and over prior to study entry.
- Exclusion criteria: missing age, sex or deprivation information, household size >15 or household size missing.
- Follow-up: Followed until death or the end of the study period, whichever is soonest.

In England there will be an additional inclusion criteria requiring people to have been registered with their GP for at least 3 months prior to study entry. They will be followed up as detailed above or additionally until they deregister with their GP.

Subgroup inclusion criteria

- The inclusion and exclusion criteria above will generate a general population study population. For disease specific outcomes there will be two disease study populations required:
    - Diabetes: People with a primary care SNOMED CT code (England) or an inpatient or outpatient hospital record ICD-10 diagnosis (Denmark) for type 1 or type 2 diabetes at any time prior to the start of follow-up, followed from the study start or the first diabetes code, whichever is latest.
    - Respiratory disease: there will be two groups: 1) people with asthma defined as having a primary care SNOMED CT code for asthma or an inpatient or outpatient hospital record ICD-10 diagnosis (Denmark) in the previous 3 years, followed from the study start or the first asthma code, whichever is latest. 2) people with chronic obstructive pulmonary disease (COPD) defined as those age >40 with a primary care SNOMED CT code (England) or an inpatient or outpatient hospital record ICD-10 diagnosis (Denmark) for COPD followed from study start or first COPD code, whichever is latest.

Study measures

Exposures

- Introduction of population-wide restrictions: UK - 23rd March 2020, Denmark - 13th March 2020.
- Migration status:
    - England: Based on SNOMED codes relating to being born outside of the UK, a visa status indicating migration and first/main language not English (Pathak et al, 2021).
    - Denmark: Based on country of birth.
- Deprivation:
    - UK: deprivation quintiles based on the index of multiple deprivation as of 1st February 2020.
    - Denmark: have the following measures: Family income, years of schooling, employment status, marital status and foreign-born. Five categories of household income will be used initially.

Outcomes

- Hospital admissions (all types - elective and emergency) with primary reason for admission ICD-10 code related to four disease areas: diabetes, respiratory disease, cardiovascular disease (CVD) and mental health as detailed below.
- Deaths with underlying cause ICD-10 code related to the same four disease areas as detailed below.
- Four disease areas:
    - Diabetes outcomes in people with type 1 and type 2 diabetes:
        - Type 1 diabetes
        - Type 2 diabetes

        - Diabetic ketoacidosis
    - Respiratory disease outcomes:
        - Asthma exacerbation in patients with asthma
        - COPD exacerbation in people with COPD
    - CVD outcomes in the general population:
        - Myocardial infarction
        - Stroke
        - Heart failure
        - Venous thromboembolism
    - Mental health one combined outcome in the general population:
        - any of the following: depression, anxiety, severe mental illness, self harm (fatal and non-fatal), eating disorder, obsessive compulsive disorder and suicide (available in England only) (fatal self harm and suicide for death outcome only)

Demographic variables

- Age, categorised in 20 year bands,
- Sex,
- Urban/rural location
- Household size (since we use this for inclusion/exclusion)

Statistical analysis

Each month (March 2018 to December 2021, inclusive), the inclusion criteria will be assessed and the denominator adult population who meet the inclusion criteria will be extracted. This will assume that a person is eligible in the denominator for the whole month if they are eligible on the 1st of the month. Each outcome will be analysed separately in the relevant study population (diabetes, respiratory disease, or general population). Outcomes will be counted once each month, but people can appear in multiple months if they have repeated records of the outcome.

The monthly percentage for each outcome will be determined. We will plot the monthly percentage and the percentage change (first derivative) by deprivation and migration status.

To estimate the absolute impact of the pandemic on each outcome, we will use Poisson regression to estimate the average count of each outcome, by deprivation and migration status, pre-pandemic (pre March 2020) and during the pandemic (Post March 2020). We will account for autocorrelation by including first-order lagged residuals. We will use the predictions from the Poisson model to generate rate differences in the number of each monthly outcome, stratified by IMD and migration status. We will model the crude and then age and sex adjusted counts. After initial review of the data we may explore factors, such as COVID-19 rates, to further understand any differences seen.

Skeleton tables

Table 1: Summary of English and Danish study designs

	England	Denmark
Study population	Adults age 18 and over, registered at GP for at least 3 months prior to study entry.	
Exclusion criteria	Missing age, sex, or deprivation information, household size >15 or household size missing.	
Cohort entry	Latest of being registered with their GP for 3 months or 1st March 2018.	
Cohort exit	Earliest of death, deregistering with their GP or end of study period.	
Subpopulations		
Diabetes cohort	People with a primary care SNOMED CT code for type 1 or type 2 diabetes followed from the study start or the first diabetes code, whichever is latest.	
Respiratory cohorts	There will be two groups: 1) people with asthma defined as having a primary care SNOMED CT code for asthma in the previous 3 years, from the study start or the first asthma code, whichever is latest. 2) people with chronic obstructive pulmonary disease (COPD) defined as those age >40 with a primary care SNOMED CT code for COPD followed from study start or first COPD code, whichever is latest.	

Exposures		
Deprivation measurement	Deprivation quintiles based on the index of multiple deprivation as of 1st February 2020	
Migration status measurement	Based on SNOMED codes relating to being born outside of the UK, a visa status indicating migration and first/main language not English (Pathak et al, 2021).	
Outcomes		
Hospital admissions	Hospital admissions with primary reason ICD-10 code for admission related to four disease areas: diabetes, respiratory disease, cardiovascular disease (CVD) and mental health.	
Death	Deaths registered with ONS with underlying cause ICD-10 code related to four disease areas: diabetes, respiratory disease, CVD and mental health.	

Table 2: Characteristics of cohorts as of 1st March 2020

		England	Denmark
N			
Age category	18 - 40 years		
	41 - 60 years		
	61 - 80 years		
	>80 years		

Sex	Male		
Urban-rural classification	Rural		
	Urban		
Deprivation: IMD (England)/Income(Denmark)	1 (most deprived)		
	2		
	3		
	4		
	5 (least deprived)		
Migration status			
Diagnosis of diabetes	Type 1 diabetes mellitus		
	Type 2 diabetes mellitus		
Diagnosis of Asthma			
Diagnosis of COPD			

Graphs with percentage of admissions/deaths each month by deprivation/migration status

Supplementary data: Table of monthly percentage of outcomes.

References