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The impact of social distancing due to COVID-19 on admissions and mortality rates in patients with obstructive lung disease

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Background

Obstructive pulmonary disease is a broad term for diseases with airway obstruction limiting expiratory airflow[1]. These diseases include chronic obstructive pulmonary disease (COPD) and asthma, which are treated with inhalation drugs such as short-acting Beta agonists (SABA), long-acting Beta agonists (LABA), long-acting muscarinic antagonist (LAMA) and inhaled corticosteroids (ICS)[2]. LABA and LAMA have been shown to reduce COPD exacerbation while ICS have been shown to affect both COPD exacerbations and mortality rates of COPD patients. In COVID-19 patients, ICS has not been shown to have any effect on mortality[3]. COPD is the cause of 3300 deaths per year in Denmark and further a contributing factor in 2000 more deaths[4]. Severe acute exacerbation of COPD , is often caused by respiratory tract infections with virus or bacteria.[5]

In December 2019, a novel corona virus, Sars-CoV-2 was found in China and spread around the world with the first case being registered in Denmark on the 27th of February[6]. The general guidelines to the public were to ensure good hand hygiene, good coughing etiquette, avoiding physical contact and ensuring a distance of 2 meters to others[7]. As a response to the further spread of COVID-19 in the Danish society, the Danish government announced restrictions to ensure community-wide social distancing on March 11th, 2020[8]. These restrictions included closing of all higher education institutions, cultural institutions and government workplaces with non-essential functions from the 13th of March – later extending to schools and daycare. Furthermore, a ban on the assembly of more than 100 people was implemented which was subsequently reduced to just 10 people. A 4-stage reopening plan was created beginning on the 15th of April[9], but the full reopening was postponed due to an increase in the spread of COVID-19 in August.

In the monitoring of influenza virus in the period 2019/20 in Denmark, there was seen a decrease in the number of influenza cases when comparing to previous years[10]. It is therefore of great interest to see whether social distancing imposed to decrease the spread of the Sars-CoV-2 virus has led to fewer admissions and affected the mortality of obstructive lung disease patients in the same period.

Aim

The purpose of this study is to investigate whether social distancing measures, implemented in relation to COVID-19, influenced admissions and mortality rates in patients in the Danish population who use lung drugs to treat chronic obstructive lung disease.

Hypothesis

Social distancing measures, implemented due to COVID-19, lead to a decrease in admissions and mortality rates for patients using lung drugs against obstructive lung disease compared to prior to COVID-19.

Data sources

1. The National Prescription Registry (Lægemiddelregistret): Holds information on all prescriptions dispensed in Danish pharmacies since 2004 (coded according to the Anatomical Therapeutic Chemical (ATC) classification system)
2. The Danish Central Personal Registry (CPR registret): Holds information on citizens of Denmark including whether the citizen is living or not.
3. The Danish National Patient Registry (Landspatientregisteret, LPR3): Holds information on all admissions to Danish hospitals since 1977 and hospital outpatient specialist clinic visits since 1995.

Method

Study design

Retrospective cohort study

Study period

1. Period: January 1st, 2019 – June 21st, 2019
2. Period: January 1st, 2020 – June 21st, 2020

The intervention period being March 12th, 2020 – May 18th, 2020.

Study population

Case population: The entire Danish population receiving lung drugs (ATC CODE R01, R03, R05, R06, R07, H02, L04, B01 and J01)

The period of study will be defined from 1st of January 2018 to September 31st, 2020

Inclusion criteria

- Age >18

- De skal være 18 år eller derover i perioden fra 1.1.2018-udtrækstidspunktet

- Patients who have received lung drugs from January 2018 - September 31, 2020

Exclusion criteria

none

Primary Endpoint

The most frequent medical and surgical admissions:

Medical admission	**Code type**	**Code**
Infectious diseases	ICD-10	A00 - B99
Neoplasms	ICD-10	C00 - D48
Hematological disease	ICD-10	D50-D89
Endocrine, nutritional and metabolic disorders	ICD-10	E00-E90
Diseases of the nervous system	ICD-10	G00-G99
Diseases of the circulatory system	ICD-10	I00-I99
Diseases of the respiratory system	ICD-10	J00-J99
Diseases of the musculoskeletal system	ICD-10	M00-M99
Diseases of the genitourinary system	ICD-10	N00-N99
Diseases of the digestive system	ICD-10	K00-K93

Medical conditions requiring acute- or subacute surgery/ non-elective surgical procedures	**Code type**	**Code**
Fractures of the musculoskeletal system	(SKS) ICD-10	DS00 – DS99 + DT 00–DT14
Appendicitis	(SKS) ICD-10	DK35–DK38
Peptic ulcer	(SKS) ICD-10	DK25–DK29
Bile duct surgery	Danish Classification of Surgical Procedures (SKS)	KJK
Kidney stone surgery (ESWL not included)	Danish Classification of Surgical Procedures (SKS)	KKAE
Exploratory laparotomy	Danish Classification of Surgical Procedures (SKS)	KJAH00
Pancreatic surgery	Danish Classification of Surgical Procedures (SKS)	KJL

Secondary Endpoint

1. All-cause mortality
2. ICU admissions

Danish Classification of Surgical Procedures (SKS): NABE and NABB

Statistical analysis

Firstly, descriptive analysis, baseline tables and study flow charts will be made.

Continuous data will be compared using either non-parametric statistics or parametric statistics depending on the distribution. Categorical data will be analysed using chi-square and Fischer's exact test.

The primary analysis will examine the incidence rate of hospitalizations categorized by medical and surgical diagnoses from week 1 to 25 and compare 2019 and 2020 on a weekly basis. The incidence rate ratio of hospitalizations will be calculated from week 11 to 25 representing the period after implementation of social distancing.

The secondary analysis is a COX-regression model that will be used to evaluate the risk of hospitalization due to the 10 most frequent medical and surgical admissions comparing the intervention period with the previous year. The COX model will be adjusted for age, sex, FEV1%, Body Mass Index, smoking status and Charlson comorbidity index score.

Statistical analyses will be performed via "Forskermaskinen" using SAS 9.4.

Social perspective

In a social context, it is useful to understand whether measures such as social distancing that were implemented by the government to decrease the spread of COVID-19 have had a positive impact on the survival of patients with obstructive lung disease using lung medicine. This would

give an indication of whether these approaches also have secondary purposes and can be used to improve survival rates of patients using this type of medication.

Publication of results

The results of the study will be published whether they are positive, negative or inconclusive. Publication is planned in international peer-reviewed scientific journals. If publication in a scientific journal is not possible, the results of the study will be published in report format, which will be made available via the Internet.

Ethical statement/approval

The study has been approved by the Danish Data Protection Agency. In Denmark, retrospective use of register data does not require ethical approval or patient consent.

Name of institution responsible for data

Copenhagen Unit for Respiratory Epidemiology (CURE), Lungemedicinsk Afdeling

• Name of project manager

Pradeesh Sivapalan MD PhD

• Title of the project

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• End date of the project, if any

31st December 2024

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