

The impact of social distancing on hospital admissions for severe acute exacerbation of chronic obstructive pulmonary disease (COPD) and mortality in patients with severe and very severe COPD

Participants

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Background

Chronic Obstructive Pulmonary Disease (COPD) is an almost exclusively preventable disease that causes approx. 5% of all deaths in the world [1]. Tobacco smoking is the main cause of COPD [2]. One of the most feared complications to COPD is the acute exacerbation of COPD (AECOPD), and a focused area within treatment and research in COPD is to limit the incidence of this complication that leads to increased mortality, hospitalizations, anxiety, shortness of breath, depression, as well as severe side effects of treatment [3,4].

Globally, there are no systematic data on the effect of social distancing on the risk of hospitalization-requiring AECOPD, i.e. severe AECOPD (s-AECOPD).

Social distancing was introduced globally in winter-spring 2020 in almost all countries to limit the ongoing COVID-19 pandemic, and in Denmark it was introduced from midnight on March 12, 2020.

Social distancing in Denmark

The Danish government started on March 12 to introduce a number of initiatives to combat COVID-19 infection in society [5]. On March 13, all pupils and students in every public upper secondary and higher education program were sent home, as well as all civil employees who did not perform critical functions. In addition, all indoor public cultural institutions, libraries, leisure facilities and the like were closed from the same day, and a ban was introduced on gatherings over 100 persons as well as Denmark's borders were closed down. On March 16, all schools and day care centers were closed. On March 18, further measures were introduced, and social distancing was fully implemented [6]. These involved an assembly ban against assemblies larger than 10 persons and that all restaurants, cafés, nightclubs, bars, gyms and malls etc. should be closed.

Due to the low basic reproduction number, the Danish government announced phase one of the reopening of the Danish society on April 6 [7], which meant that day care institutions, primary school from 0th-5th grade and upper secondary education for graduating students could be opened from April 15. Furthermore, a number of self-employed businesses such as hairdressers, dentists, private hospitals/clinics, psychologists etc. could open from April 20 [7].

On May 8, phase two of the reopening started, where i.a. all shops, malls and outdoor sports could reopen [7]. Moreover, restaurants, cafés, bars and the entire primary school could open from May 18, as well as cultural institutions from May 21. In addition, all youth and adult education and public research activities with a requirement for physical presence reopened on May 27 [7].

The Danish authorities have introduced laws and with this legal authority, the police have enforced these interventions, incl. injunctions and, in certain cases, fines and temporary restraining orders [8].

It is well known that s-AECOPD are often caused by either viral or bacterial infection. Since viruses other than SARS-CoV-2, as well as bacteria, are also dependent on well-functioning transmission routes, it must be assumed that the incidence of infections with viruses and bacteria in general will fall during a social distancing intervention. As s-AECOPD are most often caused by such infections, it is conceivable that the incidence of hospitalization-requiring s-AECOPD will also fall during a social distancing intervention.

Hypothesis

A "Social distancing intervention", as the one introduced in Denmark on March 12, 2020, will lead to reduced risk of hospitalization-requiring s-AECOPD and mortality in outpatients with severe and very severe COPD.

Methods

Study design: Observational cohort study.

Study population: Danish patients with COPD registered in the Danish Register for Chronic Obstructive Pulmonary Disease (DrCOPD). DrCOPD is a nationwide database that contains information on the quality of treatment of all patients with COPD in Denmark. Patients from here are linked via the social security number (CPR-no.) with the Danish National Patient Register (DNPR), which contains information on all admissions to Danish hospitals and outpatient clinic visits with diagnosis codes according to the International Classification of Diseases, 10th revision (ICD-10) from 1994). Patients are also linked with The Danish National Health Service Prescription Database (DNHSPD) contains information on all dispensed prescriptions (coded according to the Anatomical Therapeutic Chemical (ATC) classification system).

Study period: March 12, 2020 – June 25, 2020 compared to March 12, 2019 – June 25, 2019. In addition: January 1, 2020 – March 11, 2020 compared to January 1, 2019 – March 11, 2019.

Inclusion criteria:

- Diagnosed COPD [*spirometry verified and evaluated by pulmonary specialist*]
- Affiliated with a specialist pulmonary outpatient clinic
- Age \geq 40 years

Exclusion criteria:

- Confirmed COVID-19 infection

Outcomes:

- Admissions for s-AECOPD or mortality

Statistical analyzes:

Statistical analyzes are performed using SAS 9.4 with databases through the Danish Health Data Authority. For data, categorical variables are presented as frequencies and proportions, and continuous variables as median values and interquartile ranges (IQRs). A p-value of <0.05 is considered statistically significant. Comparisons are made with t-test if they are normally distributed, otherwise non-parametric tests are used such as Wilcoxon or Mann-Whitney. Survival analysis will be done with Cox proportional hazards model.

Approval

Approval is being sought from The Danish Data Protection Agency. According to Danish legislation, informed consent or approval from ethics committee are not required for register-based studies.

References

1. World Health Organization. *Chronic obstructive pulmonary disease fact sheet*. Available from: [http://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](http://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)) (visited 29/05-2020).
2. Alberg, A.J., et al., *Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines*. Chest, 2013. **143**(5 Suppl): p. e1S-e29S.
3. Wang, Q. and J. Bourbeau, *Outcomes and health-related quality of life following hospitalization for an acute exacerbation of COPD*. *Respirology*, 2005. **10**(3): p. 334-40.
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5. <https://nyheder.tv2.dk/samfund/2020-03-11-danmark-lukker-ned-her-er-regeringens-nye-tiltag> (visited 24/05-2020)
6. <https://www.tv2east.dk/sjaelland-og-oerne/statsministeren-paa-pressemoede-vi-forlaenger-nedlukning> (visited 29/05-2020)
7. <https://politi.dk/coronavirus-i-danmark/kontrolleret-genaabning-af-danmark> (visited 29/05-2020)
8. <https://politi.dk/coronavirus-i-danmark/forlaengelse-af-tiltag-mod-covid-19-i-danmark> (visited 29/05-2020)

Appendix

Diagnosis codes - ICD8 and IC10 – Comorbidities:	
Myocardial infarction	ICD10 I21-I22; ICD8: 410
Atrial fibrillation	ICD10: I48; ICD8: 427.93–427.94
Heart failure	ICD10: I110, I42, I50, J81; ICD8: 425, 428

Hypertension	ICD10: I10–I15; ICD8: 400–404
Peripheral vascular diseases	ICD10: I700, I702, I709, I739; ICD8: 444.00, 444.40-444.44, 444.48, 444.49, 444.90, 445.00, 445.08, 445.09, 445.90
Cerebrovascular diseases	ICD10: I60–I64, G458, G459; ICD8: 430–438
Renal failure	ICD10: I120, I131, I132, E102, E112, E132, E142, N02-N08, N11, N14, N158, N159, N160, N162-N164, N168, N18, N19, N26, Z992; ICD-8: 249.02, 250.02, 582, 583, 584, 590.09, 593.20
Asthma	ICD10: J45; ICD8: 493