

Risk of Pneumonia Hospitalization in the Danish population and COPD outpatients: The Impact of Social Distancing in connection to the COVID-19 pandemic- A Nationwide Cohort Study.

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Background

In December 2019 a new coronavirus, SARS-CoV-2, emerged in China.¹ The virus quickly spread globally and WHO declared it a pandemic on March 11th.² SARS-CoV-2 transmits by droplet and contact spread. Currently there is no approved vaccine or curative treatment, and containment of the pandemic relies on non-pharmaceutical measures. The general recommendations are self-isolation when symptomatic, hand hygiene, coughing etiquette, social distance of at least 1-2 m, use of face mask in certain situations and cleaning of contact surfaces^{3,4}. In addition to this some countries have, in response to community spread, implemented community-level social distancing in the form of closing public facilities. This is in accordance with recommendations from amongst other the European Center For Disease Prevention And Control (ECDC)⁵.

On February 27th the first case of COVID-19 in Denmark was reported. The following weeks we experienced a rapid increase in number of infected and by March 12th community-level social distancing was implemented to reduce and mitigate the infection. This included that all public personnel which did not carry critical functions were send home, schools and institutions were closed, bars, restaurants, fitness canters etc. were closed and an assembly ban of more than 10 people was introduced (for the full list of interventions see appendix)⁶. These measures worked,

Denmark “flattened the curve” and the first phase of reopening society began on April 15th.⁷ By mid to late May most schools and workplaces as well as several public facilities had been reopened⁸.

Several other respiratory pathogens, such as influenza and other coronaviruses, are transmitted by drop and contact spread as well. Studies have shown a decrease in the occurrence of influenza this season compared to previous influenza-seasons. This is suggested to be because of the non-pharmaceutical measures implemented during the COVID-19 pandemic.⁹⁻¹⁴ A Taiwan study showed not only a decrease in influenza but also enterovirus and pneumonia during the initial COVID-19 period.¹⁴ In Taiwan a lockdown was not necessary and promotion of social distancing was implemented weeks later than hand hygiene and mask wearing.¹⁴ In contrast an Australian study found that although there was a decrease in influenza and other respiratory viruses during COVID-19 this was not the case for the non-viral respiratory pathogens examined.¹²

Pneumonia continues to be a leading cause of hospitalization and mortality,¹⁵ and according to WHO lower respiratory infection is the fourth most common cause of death worldwide.¹⁶ Furthermore it has been proven that patients with COPD have a higher risk of pneumonia and mortality thereof.¹⁷ It is of great interest whether social distancing have affected the incidence of pneumonia hospitalization in the Danish population and amongst patients with COPD.

AIM

The purpose of this study is to investigate whether social distancing, implemented during COVID-19, impacted the risk of pneumonia hospitalization in the Danish population and COPD outpatients.

HYPOTHESIS

Social distancing* leads to decreased risk of pneumonia hospitalization in the Danish population and COPD outpatients.

* Social distancing here defined as the community level social distancing implemented in Denmark on March 12th which was upheld by law enforcement. For a detailed list of interventions see appendix.

DATA SOURCE

- 1) 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.
- 2) The Danish Register of Chronic Obstructive Pulmonary Disease (DrKOL): A nationwide database that contains information on the quality of treatment of all patients with COPD in Denmark (Lange P, Tøttenborg SS, Sorknæs AD, et al. Danish Register of chronic obstructive pulmonary disease. Clin Epidemiol 2016;8:673–8).

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 The entire Danish population and a subpopulation consisting of COPD outpatients.

Inclusion criteria

The Danish population:

- Danish citizens with permanent residence in Denmark
- Age >18 years

COPD subpopulation:

- COPD verified clinically by a specialist and by spirometry.
- Age >40 years

Exclusion criteria Diagnosis of influenza or COVID-19.

Endpoints Hospitalization with an ICD-10 diagnosis of pneumonia (ICD 10 J12-18).

STATISTICAL ANALYSIS

For descriptive statistics, categorical variables will be presented as frequencies and proportions, and continuous variables as median values with interquartile ranges (IQRs).

Continuous variables will be compared using the appropriate parametric (e.g. T-test) or non-parametric tests (e.g. Mann-Whitney U-test). Unadjusted categorical analyses will be done using chi-square and Fisher's exact test, and time-to-event analyses will be displayed using Kaplan-Meier like graphs and corresponding log-rank test.

For the main analysis we will compare the incidence rate of pneumonia hospitalization on a weekly basis between 2019 and 2020 from week 1 to 25. Further the incidence rate ratio of pneumonia hospitalization will be calculated from week 11 to 25; the period after implementation of social distancing.

The secondary analysis is a cox proportional hazard model evaluating the risk of pneumonia hospitalization, counting death as competing risk, comparing the intervention period (March 12th 2020 – May 18th 2020) with the previous year. In the cox proportional model, we will adjust for age, sex (male vs. female), FEV1%, Body Mass Index, smoking status (smoker vs. non-smoker) and Charlson comorbidity index score.

The primary analysis will be performed in the population cohort and the COPD cohort. The secondary analysis will be performed in the COPD cohort.

Model control will be performed with key elements being test for proportionality of hazards, linearity of continuous variables and tests for possible interactions.

Statistical analyzes were performed using SAS 9.4 through Studio 3.71 (SAS Institute Inc., Cary, NC, USA).

ETHICAL STATEMENT

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.

References

1. WHO. Novel Coronavirus (2019-nCoV) Situation Report - 1. 21 January 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10_4: World Health Organization; 2020.
2. WHO. Coronavirus disease 2019 (COVID-19) Situation Report - 51. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf?sfvrsn=1ba62e57_10: World Health Organization; 2020.
3. Sundhedsstyrelsen. COVID-19: Forebyggelse af smittespredning. <https://www.sst.dk/-/media/Udgivelser/2020/Corona/Forebyggelse-af-smittespredning/Forebyggelse-af-smittespredning-publikation.ashx?la=da&hash=FD3E64042EEDB7A6C3305BD37A003B5B58B1BC79>: Sundhedsstyrelsen; 2020:15.
4. Cenciarelli O, Melidou A, Penttinen P. ECDC Technical Report: Guidelines for the use of non-pharmaceutical measures to delay and mitigate the impact of 2019-nCoV. February 2020 2020:10.
5. Adlhoch C, Baka A, Ciotti M, et al. ECDC Technical Report: Considerations relating to social distancing measures in response to COVID-19 - second update March 23 2020. <https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-social-distancing-measuresg-guide-second-update.pdf>: European Center for Disease Prevention and Control; 2020:12.
6. Sundhedsstyrelsen. COVID-19 i Danmark: Epidemiens første bølge. Status og strategi. Version 23. marts 2020. . In: Sundhedsstyrelsen, ed. 2.0 ed. <https://www.sst.dk/-/media/Udgivelser/2020/Corona/Status-og-strategi/COVID-19-i-Danmark-Epidemiens-foerste-boelge-Status-og-Strategi.ashx?la=da&hash=82C882C11953EE6C0B4FDFBBBA9DA763809158B5>: Sundhedsstyrelsen; 2020:37.
7. Sundhedsstyrelsen. COVID-19 i Danmark: Status - 7. epidemiuge. 15. april 2020. . In: Sundhedsstyrelsen, ed. <https://www.sst.dk/-/media/Udgivelser/2020/Corona/Status-og-strategi/COVID19-7-epidemiuge.ashx?la=da&hash=75500C3F2D990A479FA8BF6D5B7152E6014F4C95>: Sundhedsstyrelsen; 2020:55.
8. Politiske aftaler og initiativer - Faser i den kontrollerede genåbning af det danske samfund. <https://politi.dk/coronavirus-i-danmark/politiske-aftaler-og-initiativer>: Politi.dk; 2020.
9. Soo RJJ, Chiew CJ, Ma S, Pung R, Lee V. Decreased Influenza Incidence under COVID-19 Control Measures, Singapore. *Emerg Infect Dis*. Aug 2020;26(8):1933-1935.
10. Kuo SC, Shih SM, Chien LH, Hsiung CA. Collateral Benefit of COVID-19 Control Measures on Influenza Activity, Taiwan. *Emerg Infect Dis*. Aug 2020;26(8):1928-1930.
11. Suntronwong N, Thongpan I, Chuchaona W, et al. Impact of COVID-19 public health interventions on influenza incidence in Thailand. *Pathog Glob Health*. Jul 2020;114(5):225-227.
12. Marriott D, Beresford R, Mirdad F, et al. Concomitant marked decline in prevalence of SARS-CoV-2 and other respiratory viruses among symptomatic patients following public health interventions in Australia: data from St Vincent's Hospital and associated screening clinics, Sydney, NSW. *Clin Infect Dis*. Aug 25 2020.

13. Cowling BJ, Ali ST, Ng TWY, et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. *Lancet Public Health*. May 2020;5(5):e279-e288.
14. Chiu NC, Chi H, Tai YL, et al. Impact of Wearing Masks, Hand Hygiene, and Social Distancing on Influenza, Enterovirus, and All-Cause Pneumonia During the Coronavirus Pandemic: Retrospective National Epidemiological Surveillance Study. *J Med Internet Res*. Aug 20 2020;22(8):e21257.
15. Sogaard M, Nielsen RB, Schonheyder HC, Norgaard M, Thomsen RW. Nationwide trends in pneumonia hospitalization rates and mortality, Denmark 1997-2011. *Respir Med*. Aug 2014;108(8):1214-1222.
16. WHO. Top 10 global causes of deaths. <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death> World Health Organization; 2016.
17. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. *Chest*. Oct 2005;128(4):2005-2011.

Kathrine Breikarstein

Appendix

Community-level social distancing interventions implemented on March 12th 2020. From the Danish Health Authority status rapport COVID-19 in Denmark: The epidemics first wave. Status and strategy. Version March 23th 2020.

- Closure of all public schools, day cares, secondary and higher educations and encouragement for private institutions to do the same.
- Sending home all public servants, who do not perform critical functions, and encouraging private employers to ensure as many people as possible work from home or in other ways stay at home.
- Prohibition to visit hospitals and nursing homes with few exceptions.
- Closure of all indoor cultural institutions, libraries, leisure activities etc. and encouragement for private institutions to do the same.
- Closure of night clubs, bars, restaurants and cafés etc.
- Closure of shopping centers, covered arcades etc. where a larger number of people is moving indoor.
- Closure of indoor sports facilities, including fitness centers and solariums.
- Prohibition to hold and participate in indoor or outdoor activities, arrangements, events etc. with more than 10 people. Except for funerals.
- Encouragement to limited use of public transport and to spread over as much time as possible ie. avoiding rush hour as much as possible.
- Requirements to stores, supermarkets of among other things ensuring 4m² floorspace per customer, setting up information material on recommendations for behavior, including ensuring distance between customers and good hygiene, ensuring access to water and soap and/or rubbing alcohol.
- Temporary prohibition against liberal professions, where close contact with costumers are unavoidable, such as hairdressers, tattoo artists, masseurs etc.
- Strong appeal to people who return to Denmark from abroad to stay home for 14 days.
- Extension of border control to include all of Denmark's borders in order to refuse entry to Denmark for third-country nationals and EU citizens, who do not already have legal residence in Denmark and who do not have a recognizable purpose.
- Restriction of rights in the field of health and the elderly in connection with dealing with the COVID-19 epidemic in relation to ensuring the necessary priorities.