# Risk of major cardiovascular events according to educational level before and after the initial COVID-19 public lockdown: a nationwide study

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## ABSTRACT

**Background** During the COVID-19 pandemic, decreasing rates of hospitalisations for cardiovascular disease raised concerns for undertreatment, particularly for vulnerable groups. We investigated how the initial COVID-19 public lockdown, impacted the risk of being hospitalised with a major cardiovascular event (MCE: myocardial infarction/stroke/heart failure) according to educational level.

**Methods** We grouped all Danish residents according to educational attainment level (low, medium, high) and age (40–59, 60–69, ≥70 years). In each group, we calculated the age-standardised and sex standardised risk of MCE hospitalisation in the initial COVID-19 lockdown-period (13 March 2020–3 May 2020) and in the corresponding calendar period in 2019. We calculated age-standardised and sex-standardised risks to investigate whether the COVID-19 lockdown had a differential effect on MCE incidence according to educational level.

**Results** In the period in 2019, 2700 Danish residents were hospitalised with MCE, compared with only 2290 during the lockdown. During lockdown, the risk of hospitalisation for MCE decreased among residents aged ≥70 with low education (risk difference (RD) −46.2 (−73.2; −19.2) per 100,000) or medium education (RD −23.2 (−50.8; 4.3) per 100 000), but not among residents with high education (RD 5.1 (−32.3; 42.5), per 100 000). The risk of hospitalisation for MCE did not decrease significantly for the younger age groups.

**Conclusions** The COVID-19 lockdown is associated with a reduced incidence for MCE, especially among low educated, elderly residents. This raises concern for undertreatment that without clinical awareness and action may widen the educational gap in cardiovascular morbidity and mortality.

## INTRODUCTION

On the evening of 11 March 2020, the Danish government declared national lockdown, effective from 13 March, as a reaction to the global COVID-19 pandemic. The COVID-19 lockdown resulted in closing of schools, workplaces, daycares, restaurants and mandated physical distancing. Furthermore, the healthcare sector was reorganised to mitigate the COVID-19 pandemic. The reorganisation included cancellation of non-urgent surgery, hospital visits and postponement of scheduled appointments to the general practitioner. Residents were obligated to understand and adhere to the governmental recommendations and regulations regarding the COVID-19 lockdown and navigate accordingly in the reorganised healthcare system.[1] Navigating in a changing healthcare system requires adequate health literacy in order to for example, understand when a medical condition is urgent enough to seek care versus to wait at home.[2] Socioeconomic position is highly correlated with health literacy as residents with higher education more often comprehend and adhere to health recommendations.[3] Thus, residents with low educational levels may find the healthcare system particularly challenging to navigate in during the COVID-19 lockdown. These residents may refrain from seeking medical treatment out of precaution to avoid COVID-19, thereby ignoring or delaying getting medical treatment, even for serious illnesses. Studies from the USA, Italy and Austria have reported falling hospitalisation rates of stroke,[4] myocardial infarction (MI)[5] and acute coronary syndrome following the initial lockdowns.[6 7] However, it remains unknown whether the COVID-19 lockdown affected residents differently according to socioeconomic position. We investigated the impact of the initial national COVID-19 lockdown on the educational gradient in the incidence of getting hospitalised with a major cardiovascular event (MCE), including stroke, MI and heart failure (HF).

## METHODS

### Study design and population

We conducted a nationwide cohort study using national administrative Danish registers. All Danish residents are at birth or immigration assigned a personal identification number that allows researchers to link information from multiple registers.[8] We linked information on demographic variables on the entire Danish population from the Central Population Registry, information on educational status from the Student Register, and information on hospital admissions due to acute cardiovascular symptoms from the Danish National Patient Registry.

We defined the initial lockdown period (13 March 2020–3 May 2020) and a corresponding



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**Table 1** Baseline characteristics of the population during the initial COVID-19 lockdown (13 March 2020–3 May 2020) and the corresponding calendar period in the year before (13 March 2019–3 May 2019) by educational level

| | | | Educational level | | |
|---|---|---|---|---|---|
| Year | Variable | Level | Low | Medium | High |
| 2019 | Total | N | 652 965 | 1 331 524 | 772 198 |
| | Major cardiovascular events | N (%) | 993 (0.2) | 1225 (0.1) | 482 (0.1) |
| | Age | Median (IQR) | 64 (53–74) | 57 (49–68) | 55 (47–66) |
| | Men | N (%) | 292 036 (44.7) | 701 757 (52.7) | 320 514 (41.5) |
| | Living alone | N (%) | 280 905 (43.0) | 404 188 (30.4) | 215 418 (27.9) |
| | Income (EUR) | Median (IQR) | 26 700(22 100–35,300) | 35 000(27 000–44 800) | 43 200(33 700–56 100) |
| | Ethnicity | Danish | 585 818 (89.7) | 1 215 450 (91.3) | 694 054 (89.9) |
| | | Immigrants | 64 725 (9.9) | 112 142 (8.4) | 75 001 (9.7) |
| | | Descendants | 2422 (0.4) | 3932 (0.3) | 3143 (0.4) |
| | Diabetes | N (%) | 71 743 (11.0) | 91 647 (6.9) | 31 242 (4.0) |
| | Chronic obstructive lung disease | N (%) | 31 290 (4.8) | 29 517 (2.2) | 8843 (1.1) |
| | Hypertension | N (%) | 143 386 (22.0) | 203 039 (15.2) | 79 232 (10.3) |
| | Atrial fibrillation | N (%) | 32 164 (4.9) | 44 410 (3.3) | 21 551 (2.8) |
| | Peripheral artery disease | N (%) | 22 991 (3.5) | 29 349 (2.2) | 10 191 (1.3) |
| | Ischaemic heart disease | N (%) | 35 225 (5.4) | 50 335 (3.8) | 21 443 (2.8) |
| | Chronic kidney disease | N (%) | 8559 (1.3) | 10 345 (0.8) | 3881 (0.5) |
| 2020 | Total | N | 645 355 | 1 345 043 | 792 208 |
| | Major cardiovascular events | N (%) | 767 (0.1) | 1098 (0.1) | 425 (0.1) |
| | Age | Median (IQR) | 64(53, 75) | 57(49, 68) | 55(47, 66) |
| | Men | N (%) | 290 783 (45.1) | 708 522 (52.7) | 327 469 (41.3) |
| | Living alone | N (%) | 280 449 (43.5) | 412 421 (30.7) | 221 876 (28.0) |
| | Income (EUR) | Median (IQR) | 26 800 (22 200–35 400) | 35 000 (27 100–44 800) | 43 100 (33 700–55 800) |
| | Ethnicity | Danish | 576 097 (89.3) | 1 227 319 (91.2) | 711 590 (89.8) |
| | | Immigrants | 66 534 (10.3) | 113 304 (8.4) | 77 121 (9.7) |
| | | Descendants | 2724 (0.4) | 4420 (0.3) | 3497 (0.4) |
| | Diabetes | N (%) | 74 689 (11.6) | 98 372 (7.3) | 34 218 (4.3) |
| | Chronic obstructive lung disease | N (%) | 31 792 (4.9) | 30 790 (2.3) | 9257 (1.2) |
| | Hypertension | N (%) | 139 386 (21.6) | 204 784 (15.2) | 80 253 (10.1) |
| | Atrial fibrillation | N (%) | 34 096 (5.3) | 48 653 (3.6) | 23 705 (3.0) |
| | Peripheral artery disease | N (%) | 23 851 (3.7) | 31 628 (2.4) | 11 180 (1.4) |
| | Ischaemic heart disease | N (%) | 36 081 (5.6) | 52 666 (3.9) | 22 526 (2.8) |
| | Chronic kidney disease | N (%) | 8423 (1.3) | 10 451 (0.8) | 3946 (0.5) |

calendar in the year before, where no lockdown had occurred (13 March 2019–3 May 2019). All Danish residents aged 40–90 years, alive at the beginning of the periods, without any previous hospitalisation for an MCE, or missing information on educational level were included in the study. This left us with a total of 2 756 687 and 2 782 606 Danish residents in the non-lockdown and lockdown period, respectively (online supplemental figure S1).

## Major cardiovascular event

We defined a MCE as an overnight hospital admission of HF (International Classification of Diseases, 10th revision (ICD-10): I50.0-I50.9, I110, II30, II32), stroke (ICD:10: I60, I61, I63, I64, G458, G459) or MI (ICD-10 I200, I210A, I211A, I214, I210B, I211B, I219) as primary diagnosis. This definition of HF, stroke and MI has been validated to have high positive predictive values in Danish registers.[9 10]

## Educational level

We used individual educational level as an indicator of socioeconomic position. We obtained information on the highest attained educational level from the national student register and classified education according to International Standard Classification of Education (ISCED-11)[11] into three educational levels: Low (ISCED-11: 0–2: early childhood education/primary education/lower secondary education), medium (ISCED-11: 3–5: upper secondary education/postsecondary non tertiary education/short-cycle tertiary education) and high (ISCED-11: 6–8: bachelors/masters/doctoral or equivalent).

## Statistical analysis

We summarised characteristics of the study populations on 13 March 2020 and 13 March 2019, respectively, with frequencies for categorical variables, and with medians and IQRs for continuous variables.

To describe the trends in first time admission with MCE, we estimated the expected daily rate during 13 March–3 May by the average daily rate observed in the period from 1 January to 12 March for each educational level separately. We then compared the observed daily rate after March 13th against the estimated rate. We performed this analysis for both 2020 and 2019 to compare with a year without lockdown.

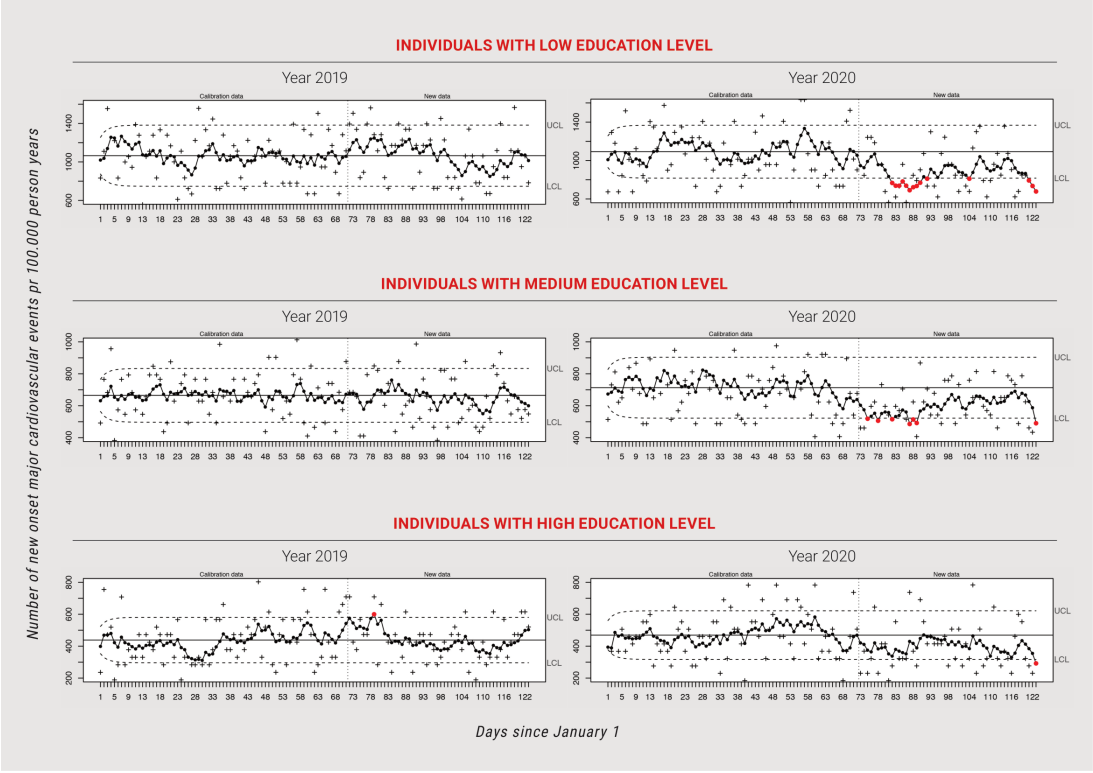


**Figure 1** Changes in incidence rates of being hospitalised with major cardiovascular events when comparing 1 January–12 March (calibration data) to after 12 March (new data). The dashed vertical line at day 71 separates the two time periods. The black plus signs are the RAW data of daily incidence rate. The black dots are the moving average of the daily incidence rates. UCL and LCL is the UCL and LCL predicted in the calibration data. Red dots indicate that the moving average of the daily incidence rates are outside the predicted CI. LCL, lower confidence level; UCL, upper confidence level.

Separately for groups defined by education (low, medium, high) and age (40–59, 60–69,>70 years), we calculated age-specific (rounded to nearest integer) and sex-specific risks of the outcome events (MCE, MI, stroke, HF, death) in the 50-day long periods before and after 13 March in 2020 and in 2019, respectively. We report the group-specific average 50-day risks standardised to the age and sex distribution of the low education groups on 13 March 2020 with 95% CIs. We further report differences between the standardised risks in 2019 and 2020, and changes in the educational gradient (low educated subtracted by high educated) with 95% CIs (online supplemental figure S2). We tested if the declines and changes in the educational gradient were significant by performing all-pairwise comparisons and using a single step max-t test approach to adjust the p values for the multiple comparisons.[12] We subdivided the composite measure of MCE into: MI, stroke and HF and also analysed all-cause mortality. The level of statistical significance was set at 5%. All analyses were carried out using R.[13]

## RESULTS

The study populations during the initial COVID-19 lockdown and in the corresponding period the year before had similar distributions of sex, age and comorbidities according to educational level (table 1). The incidence rate of hospitalisation with MCE was lower during the initial COVID-19 lockdown than in the months preceding the lockdown, in particularly for the low and medium educated. A similar pattern did not apply in 2019 (figure 1, online supplemental figure S3).

We observed, both during the lockdown-period and in the corresponding period the year before, an educational gradient in the 50-day risk of being hospitalised with a MCE. This educational gradient was similar in 2015–2018 (online supplemental figure S4). In all age categories (40–59, 60–69, ≥70), the low educated had highest risk, followed by the medium and then the high educated category, and the steepest decline in absolute risk occurred among residents above 70 years of age (figure 2). Among residents above the age of 70, the 50-day risk decreased by −46.2 (95% CI −73.2 to −19.2) per 100 000 persons for low educated residents, compared with a decrease of −23.2 (95% CI −50.8 to 4.3) and a slight increase of 5.1.6 (95% CI −32.3 to 42.5) per 100 000 for residents with medium and high education, respectively (table 2). The educational gradient in risk of hospitalisation of MCE decreased during the lockdown, compared with 2019 for residents aged 70 years or older (Difference: 51.3 (−106.4; 3.7)), but less for residents aged 40–59 (−10.6 (−45.8; 25.0)) or aged 60–69 (−2.7 (−22.3; 16.9)) (table 2). The risk of all-cause mortality did not change markedly between 2019 and 2020, and the educational gradient in all-cause mortality likewise remained unchanged (online supplemental figure S5).

Among residents 70 years or older, for all included subtypes of MCE, the risk of hospitalisation declined most for residents with low education, whereas for residents with high education no change in risk of hospitalisation with MI, stroke or HF was observed (figure 3). Same pattern was not as clear in age group 40–59 (online supplemental figure S6) and age group 60–69 (online supplemental figure S7).

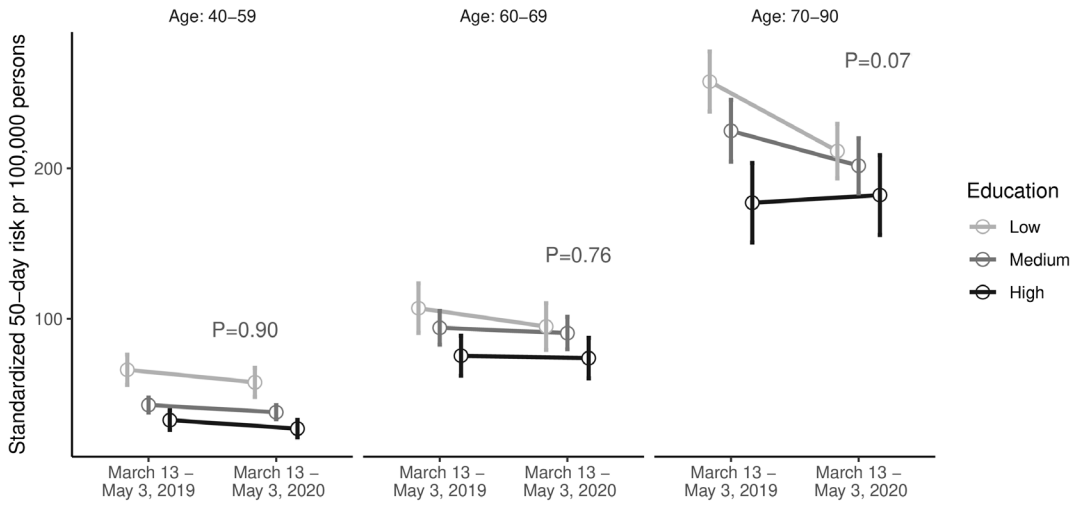


**Figure 2** Absolute risk of being hospitalised with MCE standardised to the distribution of age and sex among the low educated in 2020, during the initial COVID-19 lockdown (13 March–3 May, 2020), compared with the corresponding calendar period in the year before (13 March–3 May, 2019). P values refer to single step max-t-test of changes in the educational gradient between low and high educated being equal. MCE, major cardiovascular event.

## DISCUSSION

In this study, we observed that the initial Danish national COVID-19 lockdown is likely to have expanded the educational gap in cardiovascular disease, as the incidence of hospitalisation with a MCE declined most among residents with low education compared with medium and highly educated residents. Further, our results showed that this wider educational gap affected people aged 70 years and above more than younger individuals, possibly because of their higher baseline risks of hospitalisations. Our finding regarding the educational gradient in the risk of hospitalisation with a MCE has been well-documented in previous studies.[14] The increased risk among lower educational groups can in part be explained by a higher burden of well-established risk factors, such as hypercholesterolaemia, hypertension, diabetes other comorbidities and smoking.[15]

Our finding of a decline in hospital admissions of MCE following the COVID-19 pandemic supports studies from the USA, Italy and Austria, reporting decreasing rates of stroke,[4] MI[5] and acute coronary syndrome.[6 7] Additionally, in the US declines in prescriptions rates of cardiometabolic therapies were observed following the pandemic, possible reflecting reduced contact with the prescribing clinicians.[16] During our lockdown period only 417 Danish residents died after being diagnosed with COVID-19, and no excess mortality has been reported.[17] Thus, compared with the previous reports of declining rates of cardiovascular disease, competing risk from COVID-19 mortality does not constitute a major concern.

### Clinical implications

Cardiovascular diseases, including stroke, are among the leading causes of death worldwide,[18] as well as in Denmark.[19] We can only speculate on the causal mechanisms driving the decline in incidence of hospitalisation with MCE and why residents with low educational levels, in particular among the elderly, experience a steeper decline. The explanation is probably multifactorial and complex and may be explained by changes in patient behaviour, reallocation of hospital resources and changes in disease burden.[20] Patients may delay or ignore seeking medical treatment or entirely not react on symptoms of MCE.[21] Neglecting to react to symptoms of a MCE, such as symptomatic HF, MI or stroke may lead to delayed diagnosis, and as a result poorer outcomes.[22] The healthcare sector was reorganised to mitigate the COVID-19 pandemic, which included cancellation of non-urgent surgery, hospital visits and postponement of scheduled appointments to the general practitioner. This too may explain the decline as fewer patients, despite in need, may have been referred to hospital treatment. All-cause mortality did

**Table 2** Absolute risk and RD of incident major cardiovascular event per 100 000 persons during the initial COVID-19 lockdown (13 March 2020–3 May 2020) and in the corresponding calendar period the year before (13 March 2019–3 May 2019) according to educational level

| | Age: 40–59 | | | Age: 60–69 | | | Age: 70–90 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Absolute risk* | | | Absolute risk* | | | Absolute risk* | | |
| Educational level | 2019 | 2020 | RD | 2019 | 2020 | RD | 2019 | 2020 | RD |
| Low | 66.1 | 57.7 | −8.4 (−22.3; 5.6) | 107.5 | 94.9 | −12.2 (−34.9; 10.5) | 257.6 | 211.4 | −46.2 (−73.2; −19.2) |
| Medium | 42.7 | 37.9 | −4.9 (−11.6; 1.9) | 94.0 | 90.5 | −3.5 (−19.1; 12.0) | 224.9 | 201.7 | −23.2 (−50.8; 4.3) |
| High | 32.7 | 27.0 | −5.7 (−14.4; 3.1) | 75.4 | 73.8 | −1.6 (−20.5; 14.3) | 177.1 | 182.2 | 5.1 (−32.3; 42.5) |
| Difference in educational gradient (RD low-RD high) | | | −2.7 (−22.3; 16.9) | | | −10.6 (−45.8; 25.0) | | | −51.3 (−106.4; 3.7) |

*Absolute risks were standardised to the distribution of age and sex among the low educated in 2020.
RD, risk difference.

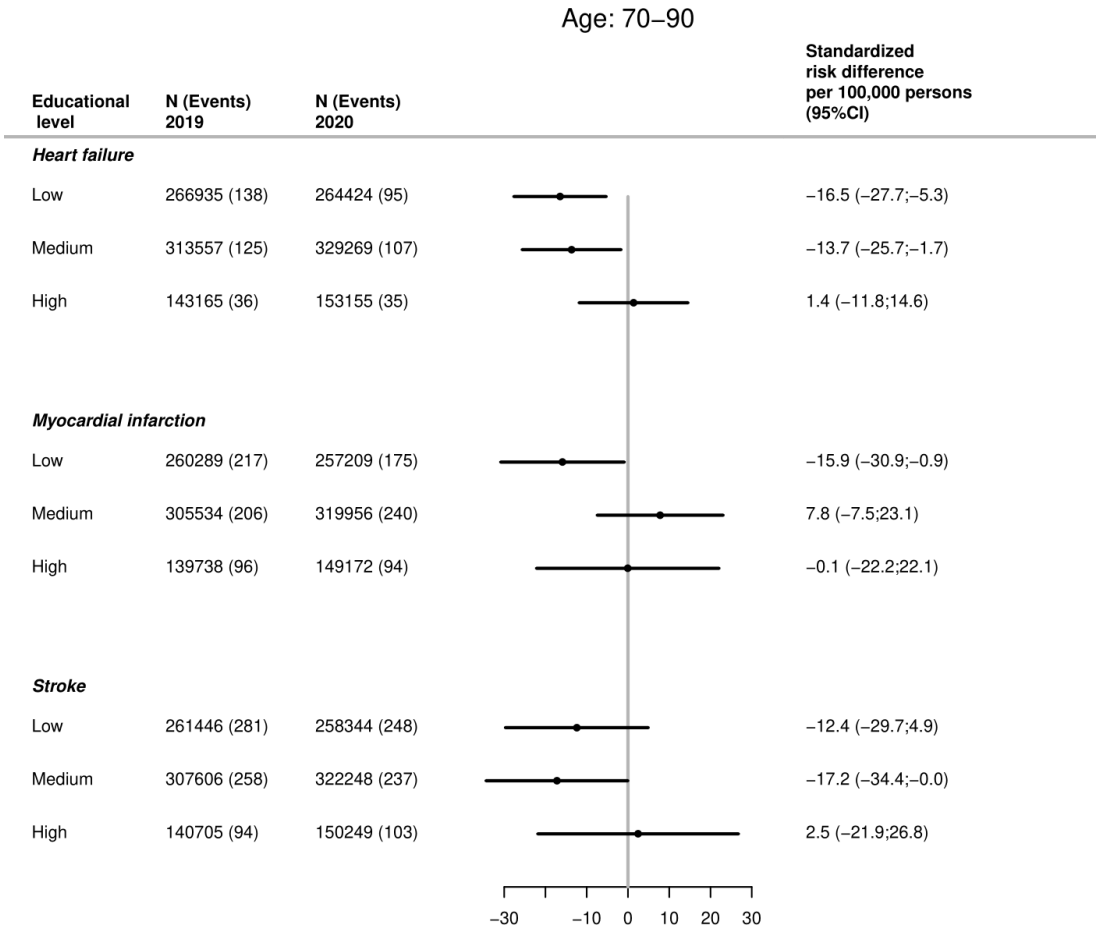


**Figure 3** Risk difference among residents aged 70 or older in 50-day risk of MCE during the initial COVID-19 lockdown period (13 March 2020–3 May 2020), compared with the corresponding calendar period in the year before (13 March2019–3 May 2019). The risks were standardised to the distribution of age and sex among the low educated in 2020. MCE, major cardiovascular event.

not change during the initial lockdown, as well as no change of the educational gradient in mortality, which imply that the decrease in MCE hospitalisations did not cause the low educated to experience a dramatically excess mortality.

Lower levels of health literacy may explain why patients with low educational levels, especially among the elderly, experience a larger drop in hospitalisation with MCE, as it is more challenging for these residents to navigate during circumstances with changing health information and a reorganised healthcare system.[1] This raises concern that the steeper decline in hospitalisation with MCE among low educated residents will widen the educational gap in cardiovascular morbidity and mortality in near future, as a consequence of undertreatment during the initial lockdown.

Another explanation might be that the decrease in hospitalisation with MCE may be due to an actual decrease in disease burden. The global influenza activity was lower than expected at that time of year,[23] and this may have caused a decrease in MCE.[24] Further, the initial COVID-19 lockdown forced many workplaces to close temporarily or to reorganise their employees to work from home. This may have reduced work related stress that might decrease the risk of cardiovascular diseases.[25] On the other hand, the COVID-19 lockdown also resulted in job layoffs and thereby increased financial strain that increases cardiovascular events.[26] Therefore, it is unsettled whether the lockdown led to increase or decrease stress levels in the population, and further the stress impact is likely to vary according to educational level.[27] However, this would affect the working populations and not the elderly retired residents, and thus, do not support our observation of the decline in educational gradient being among the residents 70 years and above.

## Methodological considerations

A major strength of this study is the large national sample size that covers all Danish residents and the ability to link high quality individual level information on educational level[28] and hospital visits.[29] Data up to 3 May are the major strength, as the non-COVID related activity in the healthcare system was resumed 18 April, and thereby expected to gradually increase from thereon, and hopefully the most severely ill patients were given first priority, and thereby treated first. Thereby the period in our study covers the strictest lockdown, in which the patients' right to assessment and treatment within 30 days was periodically suspended. Further, the population coverage and completeness of the Danish register data reduces the risk of selection bias due to non-participation from low educational groups.[30] Another major strength is the use of the identical period in 2019 as comparison to the lockdown period with further possibilities to check if the social gradient was parallel in the preceding years from 2015. Thereby, we could determine changes in risk in educational groups that must have been caused by the COVID-19 lockdown, and not by low educational level in general being a risk factor of MCE. Although, socioeconomic differences in risk of MCE may

change over time, we found these differences to be relatively constant in the years leading up to the COVID-19 lockdown (online supplemental figure S4). We, therefore, expected that these differences would be parallel between 2019 and 2020 if no lockdown had occurred. Further, due to the low number of residents infected with COVID-19 in Denmark during the first wave of the pandemic, it was possible for us to calculate a relatively unbiased estimate of a public lockdown as a mitigation act.

Our results might not be generalisable to different healthcare systems, as Denmark is one of the most economically equal countries in the world[31] and provides free and equal access to healthcare. Shortly following the lockdown, the Danish government negotiated elaborate economic-relief packages with labour unions and employer organisations to reduce financial anxiety and social inequality. Therefore, our estimate of the effect of the initial COVID-19 lockdown on the educational gradient in incidence of MCE are probably conservative and expected to be larger in countries with greater economic disparities.

A limitation of this study is that we are not able to determine what is causing the decrease in hospitalisation with a MCE. Future studies are needed to investigate how the healthcare seeking behaviour, and particularly, among residents with low education and elderly, was affected by the COVID-19 lockdown. Further, we only had real time data on all-cause mortality, as the Danish Cause of Death register are updated on a yearly basis, and we were, therefore, not able to investigate if the cardiovascular mortality increased. Future studies are needed to determine whether the decline in hospitalisation with MCE will result in higher cardiovascular mortality rates in near future.

## CONCLUSION

The risk of hospitalisation with a MCE declined during the initial national COVID-19 lockdown of Denmark, particularly for low educated residents. The educational gradient in hospitalisation declined most in the elder residents, aged 70 years and above. These results raise concern for possible undertreatment and thereby poor prognosis of MCE for this vulnerable group. Increased awareness from physicians and healthcare planners is warranted to ensure that future lockdowns does not cause the educational gap in cardiovascular mortality to increase.

### What is already known on this subject

- The COVID-19 pandemic led many countries to execute national lockdowns to avoid spreading of disease. During COVID-19 lockdowns, many countries have reported declining rates of hospitalisations for stroke, myocardial infarction and heart failure, which has raised concerns for undertreatment. However, it is unknown whether national lockdowns have impacted residents differently according to educational level.

### What this study adds

- In this nationwide cohort study, we found that the initial Danish public lockdown caused a greater decline in the risk of being hospitalised with stroke, myocardial infarction and heart failure among low educated elderly residents, compared with high educated elderly residents.
- Policy-makers and clinicians should consider and address that public lockdowns may cause undertreatment of cardiovascular diseases among low educated residents.

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**Correction notice** This article has been corrected since it first published online. A sentence in the Methods section of the Abstract has been corrected. In addition, the penultimate author's middle name has been included.

**Contributors** JA, KS-L, TG and MS contributed to the conception, design and analysis of the work. JA drafted the manuscript. All authors contributed to the acquisition or interpretation of data for the work, revised the manuscript and gave final approval.

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