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# Effect of Austrian COVID-19 lockdowns on acute myocardial infarction frequency and long-term mortality - a multicenter analysis

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## Abstract

**Objectives:** The aim of this study was to find out if the decrease in acute myocardial infarction (AMI) admissions during the first COVID-19 lockdowns (LD), that was described by previous studies, occurred equally in all LD periods (LD1, LD2, LD2021) which had identical restrictions. Further we wanted to analyze if the decrease of AMI admission had any association with the one-year mortality rate.

**Design & Setting:** This study is a prospective observational study of two centers that are participating in the Vienna STEMI network.

**Participants:** 1732 patients that presented with AMI according to the 4th universal definition of myocardial infarction in 2019, 2020 and the lockdown period of 2021 were included in our study. Patients with myocardial infarction with non-obstructive coronary arteries were excluded from our study.

**Main outcome measures:** The primary outcome of this study was the frequency of AMI during the LD periods and the all-cause and cardiac-cause one-year mortality rate of 2019 (pre-COVID) and 2020.

**Results:** Out of 1732 patients 70% (n=1205) were male and median age was 64 years. There was a decrease in AMI admissions of 55% in LD1, 28% in LD2 and 17% in LD2021 compared to 2019. There were no differences in all-cause one-year mortality between the year 2019 (11%; n=110) and 2020 (11%; n=79; p=0,92) or death by cardiac causes [10% (n=97) 2019 vs. 10% (n=71) 2020; p=0,983].

**Conclusion:** All LDs showed a decrease in AMI admissions, though not to the same extent, even though the regulatory measures were equal. Admission in a lockdown period was not associated with cardiac or all-cause one-year mortality rate in AMI patients. We suspect that other factors, in addition to fear of getting infected with COVID-19 in the hospital, have played a significant role in the decrease in AMI admissions during the LD periods.

**Strengths and limitations of this study**

- Prospective, multicenter study with large sample size
- First study to analyze the effect of the COVID-19 lockdowns on the long-term outcome of patients with acute myocardial infarction in a western population
- Contains data of only two major STEMI network centers in Vienna
- Observational study cannot be used to demonstrate causality

## Abbreviations

| | |
|---|---|
| COVID-19 | coronavirus disease 2019 |
| AMI | acute myocardial infarction |
| STEMI | ST-elevation myocardial infarction |
| NSTEMI | non-ST-elevation myocardial infarction |
| LD | lockdown |
| CPR | cardiopulmonary resuscitation |
| NTproBNP | N-terminal prohormone of brain natriuretic peptide |
| IQR | interquartile range |
| p | patients |
| w | weeks |
| p/w | patients per week |
| BMI | body mass index |
| MCI | myocardial infarction |
| BP | blood pressure |
| HR | heart rate |
| min | minutes |
| bpm | beats per minutes |
| ED | emergency department |

## Introduction

Since the worldwide outbreak of SARS-CoV-2 coronavirus disease-2019 (COVID-19) and the following strict government restrictions (so called lockdowns) many studies worldwide have reported a decrease in acute myocardial infarction (AMI) hospital admissions.(1-8) Some studies described a decrease in the admission rate of ST-elevation myocardial infarction (STEMI), (9-13) while others reported a decrease in non-ST-elevation myocardial infarction (NSTEMI) admissions. (14)

Literature on whether this decrease in AMI hospital admissions has any effect on the in-hospital outcome and mortality is still scarce and shows conflicting results. While some studies described an increase in in-hospital mortality in STEMI (3, 11) or NSTEMI patients (15) others did not find any changes of the in-hospital mortality in AMI patients during the COVID-19 pandemic. (7, 10)

In Austria three nationwide lockdowns (LD) with identical restrictions (closed schools, restaurants, hotels, non-essential businesses, shops and facilities) were implemented. The first lockdown started on the 16th of March 2020 and lasted till the 1st of May 2020. The second lockdown was from November 17th till December 6th, 2020. In 2021 an additional three-week nationwide strict lockdown was announced from 22nd of November 2021 till 11th of December 2021.

The aim of this study was to determine whether the widely described decrease in AMI during the COVID-19 lockdowns only occurred in the 1st or also in the 2nd and 3rd lockdowns which had identical contact restrictions as the initial one.

Further, we wanted to evaluate if there was an impact on long-term mortality in AMI patients.

## Methods

### *Study design*

In this prospective multicenter study data of all patients with AMI who had been admitted through the emergency departments in two major STEMI network centers were collected prospectively from 2019-2020 and the lockdown period of 2021. All patients were treated in the cardiac catheterization laboratory where the diagnosis acute coronary syndrome was confirmed. Diagnostic criteria of type 1 myocardial infarction according to the 4th universal definition of myocardial infarction(16) were applied. Patients with type 2-5 myocardial infarction and myocardial infarction with non-obstructive coronary arteries were excluded from our study.

The collected data included baseline characteristics such as age, sex, cardiovascular risk factors and comorbidities, blood parameters, duration of preclinical-symptomatic phase (onset of chest pain to hospital admission) and outcome parameters. Cardiogenic shock, cardiopulmonary resuscitation (CPR) and in-hospital death were defined as short-term outcome parameters.

To evaluate the long-term outcome one-year mortality data were provided by "Statistik Austria", an independent non-profit-making federal institution that supports scientific services.

The study was approved by the Ethics Committee of the City of Vienna (EK21-198-VK).

***Patient and Public Involvement***

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

***Statistical analysis***

Patients were split into three lockdown groups (LD 1, LD 2, LD 2021) according to their admission date. Data of all patients with AMI from 2019 were used as reference for the pre-COVID period.

Continuous variables were expressed either as a median and interquartile range (IQR) or as a mean and standard deviation (±SD) based on their distribution. For further comparison, the Student's t-test or univariate ANOVA were performed. Categorical variables were expressed as absolute numbers and percentage and compared with a $Chi^2$-test. Differences in baseline characteristics, cardiovascular risk factors, blood parameters and short-term outcome of each lockdown group were compared to the reference group of 2019.

To analyze the frequency of AMI, STEMI and NSTEMI hospital admissions during the lockdown periods the numbers of patients (p) were divided by the number of weeks (w) of each lockdown resulting in patients per week (p/w) and subsequently compared to the weekly average of admissions of 2019. Changes of the weekly hospital admission rates between 2019 and the lockdown periods were expressed in percentages.

Further, in order to take possible seasonal changes into account, the absolute numbers of admissions (patients) of each lockdown were compared to the equivalent time period of 2019.

The one-year mortality of 2019 and 2020 was calculated with the Kaplan-Meier estimate and compared using the log-rank test. To evaluate factors predictive for the patients one-year mortality a univariate regression model was performed. Variables that were significant in univariate analysis were included in a multiple regression model to search for independent predictors. To visualize the distribution of AMI admissions in 2020 compared with the incidence of the COVID-19 infections over time, we created a figure using the open data "COVID-19: Timeline of data on Covid19 cases per province" from the BMSGPK, "Österreichisches COVID-19 Open Data Informationsportal" (https://www.data.gv.at/covid-19) showing the 7-day incidence of COVID-19 and the AMI admissions in patients per month over the year 2020.

A (two sided) *p*-value of less than 0.05 was defined to be statistically significant. Data was managed using MS Excel 2016 (Microsoft, Redmond, CA). All statistical analyses were performed using SPSS statistics 27 (IBM Corporation, Somers, NY).

## Results

In total 1732 patients with AMI were included in our study of whom 60% (n=1032) had a STEMI and 40% (n=700) a NSTEMI.

### *Baseline Characteristics*

All baseline characteristics are shown in Table 1.

| | **All (n=1732)** | **2019 (n=962)** | **LD 1 (n=59)** | **LD 2 (n=40)** | **LD 2021 (n=46)** |
|---|---|---|---|---|---|
| Age (years) | 64 ± 13 | 64 ± 13 | 62 ± 12 | 61 ± 11 | 67 ± 11 |
| Male | 1205 (70%) | 692 (72%) | 43 (73%) | 29 (73%) | 28 (61%) |
| BMI | 27 ± 5 | 28 ± 5 | 28 ± 3 | 28 ± 6 | 27 ± 5 |
| Hypertension | 934 (54%) | 519 (54%) | 33 (56%) | 21 (53%) | 30 (65%) |
| Hyperlipidemia | 608 (35%) | 313 (33%) | 27 (46%) | 17 (43%) | 24 (52%) |
| Family history | 149 (9%) | 84 (9%) | 10 (17%) | 8 (20%) | 2 (4%) |
| Diabetes | 409 (24%) | 214 (22%) | 15 (25%) | 9 (23%) | 11 (24%) |
| Smoking | 735 (42%) | 382 (40%) | 29 (49%) | 20 (50%) | 17 (37%) |
| Atrial Fibrillation | 106 (6%) | 58 (6%) | 3 (5%) | 0 (0%) | 1 (2%) |
| Prior MCI | 350 (20%) | 172 (18%) | 18 (31%) | 7 (18%) | 13 (28%) |
| Systolic BP | 139 ± 29 | 139 ± 30 | 136 ± 28 | 140 ± 30 | 135 ± 31 |
| Diastolic BP | 81 ± 31 | 81 ± 27 | 79 ± 16 | 83 ± 22 | 77 ± 21 |
| HR (bpm) | 84 ± 34 | 83 ± 19 | 85 ± 18 | 85 ± 14 | 81 ± 17 |
| Creatine Kinase (U/l) | 179 [98-439] | 185 [98-475] | 167 [78-435] | 152 [104-268] | 183 [105-762] |
| Troponin T (ng/L) | 104 [32-556] | 116 [34-567] | 65 [26-497] | 63 [32-423] | 196 [35-879] |
| NTproBNP (pg/ml) | 470 [138-1900] | 425 [137-1896] | 386 [108-1021] | 623 [105-2645] | 552 [147-1331] |
| Creatinine (mg/dl) | 0,99 [0,82-1,19] | 0,99 [0,82-1,19] | 1,0 [0,8-1,18] | 1,1 [0,9-1,3] | 1,0 [0,8-1,2] |
| **Delay symptoms – ED** | | | | | |
| STEMI (min) | 486 ± 1004 | 555 ± 1209 | 368 ± 734 | 254 ± 305 | 520 ± 667 |
| NSTEMI (min) | 1861 ± 4112 | 1528 ± 3049 | 2157 ± 4190 | 2088 ± 2570 | 470 ± 283 |

**Table 1 – Baseline Characteristics**

***LD = lockdown; BMI = Body Mass Index; MCI = Myocardial infarction; BP = blood pressure; HR = heart rate; bpm = beats per minute; ED = emergency department; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction***

The median age was 64 ± 13 years and 70 % (n=1205) of all patients were male, 54 % (n=934) had hypertension, 35 % (n=608) hyperlipidemia, 24% (n=409) were diabetics, 42% (n=735) smokers and 9% (n=149) had a positive family history for cardiovascular disease.

The mean delay of onset of symptoms to admission to the emergency department was 486 ± 1004 minutes for STEMIs and 1861 ± 4112 minutes for NSTEMIs. Median Troponin T values at admission were 104 ng/L [IQR: 32-556] and median NTproBNP levels were 470 pg/ml [IQR: 138-1900] and there were no statistically significant differences between any of the collected laboratory parameters between the lockdown groups.

***Frequency of hospital admissions during the lockdown periods***

The frequency of overall AMI (with subgroups of STEMI and NSTEMI) admissions during the lockdown periods and the average of 2019 are shown in figure 1.

The frequency of AMI admissions decreased from a weekly average of 18,5 patients per week (p/w) in 2019 to 8,4 p/w in the first lockdown (-55%). In the second lockdown the admission rate of all AMI was 13,3 p/w (-28% from 2019 average). In the lockdown 2021 the AMI admission frequency decreased to 15,3 p/w (-17% from 2019 average).

The frequency of STEMI patients decreased by 51% from 10,7 p/w in 2019 to 5,3 p/w in the first lockdown. This decline in STEMI admissions was smaller in the second lockdown with 9,7 p/w which is a decrease of 9% as compared to the average of 2019. During the lockdown 2021 the STEMI admission frequency was 8,7 p/w (19% lower than 2019 average).

Moreover, NSTEMI admissions decreased substantially from 7,8 p/w in 2019 to 3,1 p/w in the first lockdown (60% decrease). The frequency of NSTEMI in the second lockdown was 3,7 p/w (53% lower than the 2019 average). In the lockdown 2021 the NSTEMI admissions decreased to 6,7 p/w (-14% compared to 2019 average).

Comparing each lockdown period to the same time period in 2019 the AMI admissions during the first lockdown dropped with 54% (127 patients 2019 vs. 59 patients 2020), the STEMI admissions decreased by 46% (69 patients 2019 vs. 37 patients 2020) and NSTEMI admissions by 62% (58 patients 2019 vs. 22 patients 2020).

In the second lockdown the AMI admissions were 17% reduced (48 patients 2019 vs. 40 patients 2020). There was no decrease in STEMI admissions (29 patients in 2019 and 2020), but the NSTEMI admissions in the second lockdown were 42% lower than in the equivalent time period of 2019 (19 patients 2019 vs. 11 patients 2020).

Looking at the last lockdown 2021 overall 12% fewer patients with AMI were admitted than in 2019 (52 patients 2019 vs. 46 patients 2021). While there was a 24% decrease in STEMI admissions (34 patients 2019 vs. 26 patients 2021), NSTEMI admissions increased by 11% (18 patients 2019 vs. 20 patients 2021).

The visualization of the distribution of AMI frequency (patients/month) in 2020 and the 7-day COVID-19 incidence rate showed that during the decrease of AMI admissions in spring 2020 (LD 1) the COVID-19 incidence was quite low. Interestingly, during the fall of 2020 (LD 2) the decrease of AMI admission was not as pronounced as in lockdown 1, but the COVID-19 incidence rate was clearly higher than in the first lockdown (Figure 2).

***In-hospital outcome***

Cardiogenic shock, CPR and in-hospital death were defined as short-term outcome parameters and are shown in Table 2. In total 5% (n=94) of all patients had a cardiogenic shock, CPR had to be performed on 5% (n=81) of the patients and overall, 3% (n=52) died in hospital. There were significant higher numbers of CPR admissions in the first lockdown (p=0,036) and in the lockdown 2021 (p=0,001) compared to the average number of 2019, but there were no significant differences in cardiogenic shock or in-hospital death between the groups (Table 2).

| | All (n=1732) | 2019 (n=962) | LD 1 (n=59) | LD 2 (n=40) | LD 2021 (n=46) | p-value* | p-value† | p-value‡ |
|---|---|---|---|---|---|---|---|---|
| Cardiogenic shock | 94 (5%) | 58 (6%) | 3 (5%) | 3 (8%) | 2 (4%) | 0,766 | 0,703 | 0,638 |
| CPR | 81 (5%) | 41 (4%) | 6 (10%) | 3 (8%) | 7 (15%) | 0,036 | 0,327 | 0,001 |
| In-hospital death | 52 (3%) | 29 (3%) | 0 (0%) | 1 (3%) | 3 (7%) | 0,176 | 0,852 | 0,185 |
| **One-year mortality** | | | | | | | | |
| All-cause mortality | 189 (11%) | 110 (11%) | 7 (12%) | 4 (10%) | - | 0,920 | 0,780 | - |
| Cardiac mortality | 168 (10%) | 97 (10%) | 6 (10%) | 4 (10%) | - | 0,983 | 0,986 | - |

**Table 2 – Short-term outcome parameters and one-year mortality**

***LD = lockdown; CPR = cardio-pulmonary resuscitation***

** denotes comparison between 2019 and LD 1*

*† denotes comparison between 2019 and LD 2*

*‡ denotes comparison between 2019 and LD 2021*

***One-year mortality***

One-year mortality data of 2019 and the lockdown periods of 2020 are shown in Table 2.

Overall, the one-year all-cause mortality rate for AMI patients was 11% (n=189) with no significant difference between STEMI (12%; n=117) and NSTEMI (11%; n=72) patients (p=0,506). In 2019 the all-cause one-year mortality rate was 11% (n=110) and in 2020 11% (n=79) with no significant difference between the pre-COVID year 2019 and the COVID year 2020 (p=0,736). Kaplan-Meier curves demonstrated similar mortality for both years as shown in figure 3.

Further, comparing the mortality rate of cardiac related death of 2019 (10%; n=97) with 2020 (10%; n=71) no significant difference could be found (p=0,851).

The comparison of the all-cause one-year mortality rate of lockdown 1 (12%; n=7) with the identical time period of 2019 (14%; n=18) also showed no significant difference (p=0,667). Looking at the second lockdown the mortality rate was 10% (n=4) as compared to 8% (n=4) of the identical time period of 2019 (p=0,787).

In multivariate analysis we found a significant correlation between patients´ sex, cardiac arrest before admission and cardiogenic shock on admission with all cause one-year mortality. The admission during any of the lockdown periods in comparison to pre-COVID-19 era was not associated with any short- or long-term outcome. Results of multivariate testing are displayed in table 3.

| | Regression coefficient | OR (95% CI) | p-value |
|---|---|---|---|
| Female Sex | 0,38 | 1,46 (1,03-2,05) | **0,03** |
| Age | 0,01 | 1,01 (1,0-1,020) | 0,27 |
| Positive family history | -0,44 | 0,65 (0,32-1,31) | 0,22 |
| Cardiac arrest | 1,59 | 4,92 (2,85-8,50) | **<0,001** |
| Shock | 1,35 | 3,85 (2,32-6,38) | **<0,001** |

**Table 3 – Multivariate regression analysis for all cause one-year mortality**

***OR = Odds Ratio, CI = Confidence interval***

## Discussion

Our study confirmed the previously described trend of decreases in AMI admissions(1-8) during the first lockdowns at the beginning of the COVID-19 pandemic. This finding could later also be observed for both STEMI and NSTEMI in following lockdowns with identical restrictions as compared to the average admission frequency of 2019, although not to the same extent as in the initial lockdown.

Similar to findings of previous studies(1, 2) there were no differences in patient characteristics between the lockdown groups and the average patient population of the comparison year 2019 (Table 1).

Fear of getting infected with COVID-19 in the hospital has been discussed in multiple previous studies as a possible explanation for the AMI decrease during the first lockdowns. (2, 17, 18)

In our study the decrease in AMI admissions during the lockdown 2021 was the lowest of all lockdowns (-17% in LD 2021 vs. -55% in LD 1 and -28% in LD 2 from the average of 2019). During that period, 71% of the Austrian population had already received their first COVID-19 vaccination leading to the assumption that the general fear of getting infected with COVID-19 in the hospital was lower than in the first and second lockdowns where no vaccinations against the virus had been available. However, our study showed a decrease in AMI admissions in all lockdown periods which indicates that fear of getting infected with the virus in the hospital might not be the only explanation for the drop of AMI admissions.

A study from the Austrian Corona panel,(19) which questioned people about their risk assessment of COVID-19 showed that the fear of COVID-19 was similar in the first and second lockdown.(20)

However, the populations´ compliance to follow the government restrictions decreased after the first lockdown. Kittel et al. showed that in Austria ~90% of the people did not leave their home to visit friends or family members during the first lockdown, but this number decreased to ~41% during the second lockdown. (20)

In our opinion this may well imply that the observed decrease in AMI admissions in our study was not only due to fear of getting infected with COVID-19 in the hospital, but also to a reduction in actual AMI triggers due to the lockdown restrictions. A relationship between AMI frequency and work-related stress has been discussed in previous studies which described an increase in AMI admissions in the working population on Mondays[(21),](22), and an association between higher AMI risk and working overtime.(23) However, a higher risk of AMI on Mondays has also been described in elderly, retired patient populations leading to the assumption that other stress factors arising from life circumstances (e.g. requirements due to family roles) have an impact on the AMI admission rate.(24) Therefore, reduction of work-related stress and social requirements due to the lockdowns (home-office, contact restrictions) may also have contributed to the decrease in AMI admissions during the lockdown periods.

Taking into consideration that the one-year mortality of patients did not differ, regardless of admissions in COVID-19 period, in lockdown periods or before, we hypothesize that patients did not wait at home with ongoing AMI out of fear, but rather that the actual event rate decreased. Our data further supports this hypothesis since the intervals from pain onset to treatment did not differ.

Less exposure to external STEMI triggers such as ambient air pollution has also been discussed as a possible explanation for the decrease in AMI admission.(25) The pathophysiological pathways of acute and chronic effects of exposure to air pollution on the cardiovascular system have already been described elsewhere. (26) Many studies showed that the reduction of mobility during the COVID-19 lockdowns lead to a decrease of air pollution ($NO_2$, $PM_{2.5}$).(27-29) However, a study from Mohajeri et al. showed that the second lockdown in England had less mobility reduction resulting in higher $NO_2$ concentrations than the first lockdown.(30) Because in our study the decrease in AMI frequency was higher in the first than in the second lockdown (-55% vs. -28% compared to the average of 2019), we postulate that the higher mobility rate and the higher air pollution during the second lockdown might have had an impact on the frequency of AMI admissions.

Regarding in-hospital outcome our study showed no difference in in-hospital mortality during the lockdown periods. This is in line with findings of a meta-analysis from Rattka et al. who showed that even though some studies reported an increase of in-hospital mortality of STEMI patients during the pandemic(31, 32), on a more global scale the in-hospital mortality of the post-COVID-19 group is not significantly higher than before the pandemic.(33)

To our knowledge this is the first study that analyzed both the frequency of AMI in different and recent lockdown periods as well as the long-term mortality of a large cohort AMI patients during the COVID-19 pandemic in a western population.

We did not find any statistically significant differences in one-year mortality of AMI patients between the pre-COVID year 2019 and the COVID year 2020. Additionally, we analyzed the one-year mortality of lockdown 1 and lockdown 2 and compared it to the identical time period of 2019 which also showed no significant difference. Similar findings have been described by Phua et al. in a study from Singapore.(34)

This indicates that the decrease in AMI frequency did not affect the prognosis and long-term outcome of AMI patients.

Further, this finding strengthens our assumption that the decrease in AMI admissions was not (only) caused by patients presenting late to the hospital due to fear of getting infected with COVID-19, but rather that a general decrease of absolute AMI numbers had occurred, due to multiple reasons such as a reduction of social and work-related stress and environmental factors.

### Limitations

Our study has several limitations that need to be considered. First, it is an observational study and therefore cannot be used to demonstrate causality. Second, even though we described a decrease in AMI admissions to the hospital and the long-term outcome of those patients, we do not have data concerning out of hospital cardiac deaths caused by AMI not admitted to the hospitals. Third, our sample size only includes data from two major STEMI network centers and should therefore be considered as limited. Given the large overall sample size and the prospectively collected data of excellent quality we still consider our findings to add value to the discussion of the impact of COVID-19 and measures against it on patients with acute myocardial infarctions.

## Conclusion

We found a significant decrease in AMI admissions during the COVID-19 lockdown periods. The observed decrease seems to be due to multifactorial reasons and did not have any significant association with one-year mortality.

## Declarations

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**Competing interests:** All authors report no conflict of interest.

**Author contributions:** RM & AS planned the study, drafted the protocol, acquired and analyzed data, drafted the manuscript; DR & WS acquired data, drafted the protocol, revised the manuscript critically for important intellectual content; CW, GP, PS & GD made substantial contributions to conception, design, analysis and interpretation of data, revised the manuscript critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Ethics approval:** This study was approved by the Ethics Committee of the City of Vienna (EK21-198-VK).

**Data availability:** The data underlying this article will be shared on reasonable request to the corresponding author.

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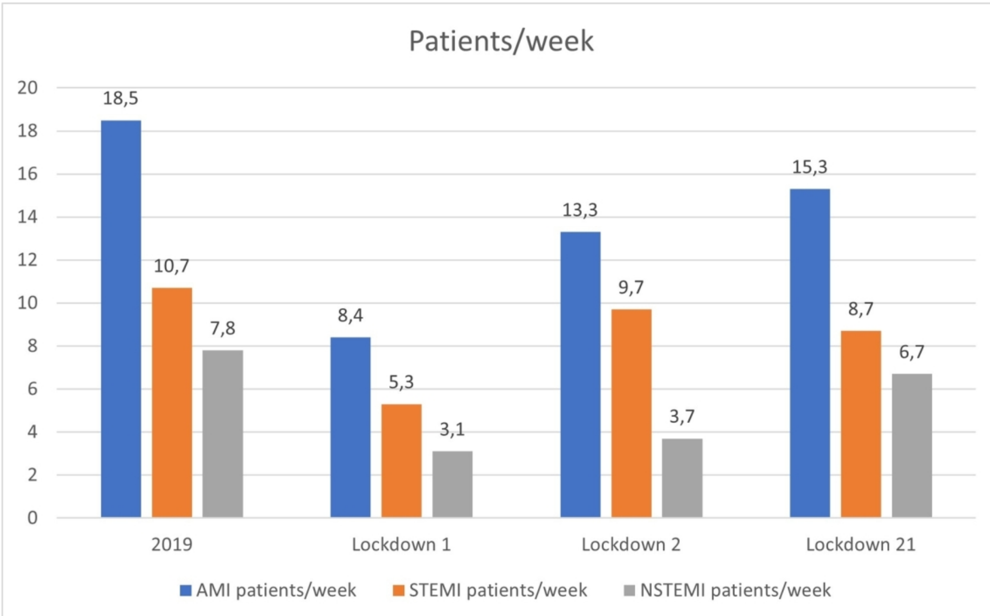
# Figure legends

**Figure 1** Admissions of acute myocardial infarctions (AMI), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) in 2019 and during the lockdown periods (patients/week)

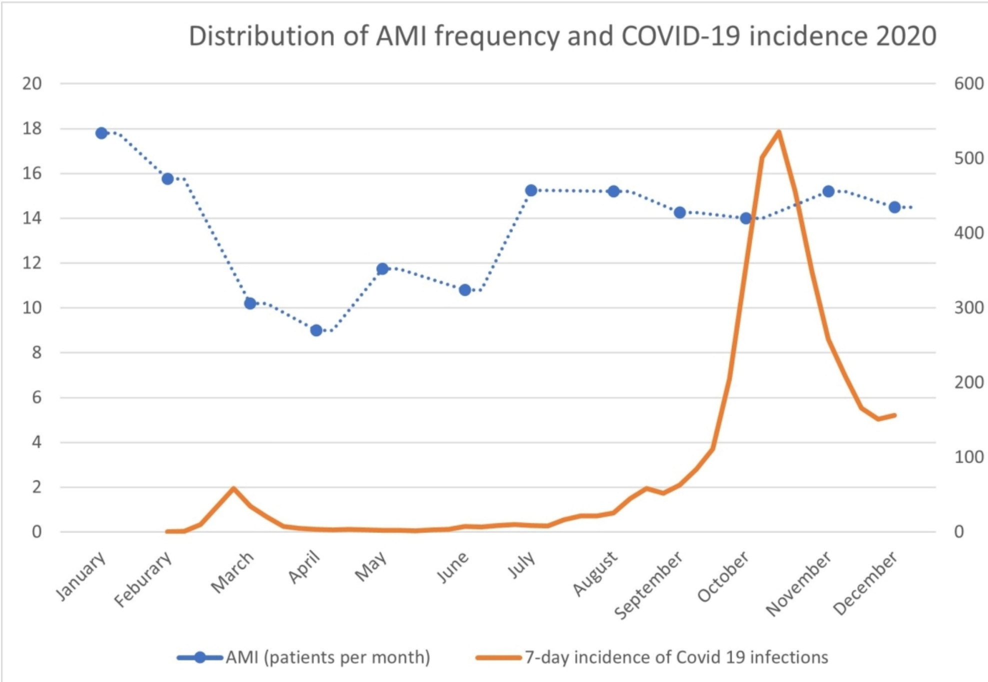
**Figure 2** Distribution of acute myocardial infarction (AMI) frequency (patients/month) and COVID-19 7-day incidence rate of 2020

**Figure 3** Kaplan-Meier analysis for all-cause one-year mortality in acute myocardial infarction (AMI) patients 2019 vs. 2020 (log rank: p=0,7)



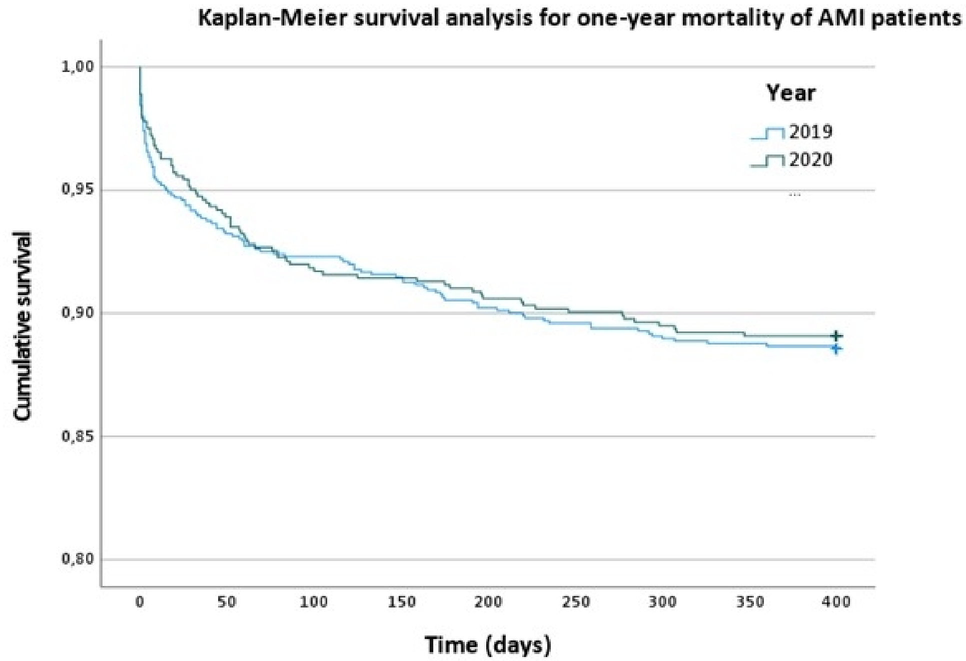

Admissions of acute myocardial infarctions (AMI), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) in 2019 and during the lockdown periods (patients/week)

153x95mm (300 x 300 DPI)




Distribution of acute myocardial infarction (AMI) frequency (patients/month) and COVID-19 7-day incidence rate of 2020

160x110mm (300 x 300 DPI)




Kaplan-Meier analysis for all-cause one-year mortality in acute myocardial infarction (AMI) patients 2019 vs. 2020 (log rank: p=0,7)

160x110mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract<br>(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(*b*) For matched studies, give matching criteria and number of exposed and unexposed | 5-6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 6 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 6-7 |
| Study size | 10 | Explain how the study size was arrived at | 5-6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 6-7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding<br>(*b*) Describe any methods used to examine subgroups and interactions<br>(*c*) Explain how missing data were addressed<br>(*d*) If applicable, explain how loss to follow-up was addressed<br>(*e*) Describe any sensitivity analyses | 6-7 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 8-9 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount) | 8-9 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 10-11 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 9-11 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 12-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

# Effect of Austrian COVID-19 lockdowns on acute myocardial infarction frequency and long-term mortality - a multicenter observational study



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SCHOLARONE™ Manuscripts

# Effect of Austrian COVID-19 lockdowns on acute myocardial infarction frequency and long-term mortality - a multicenter observational study

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## Abstract

**Objectives:** The aim of this study was to find out if the decrease in acute myocardial infarction (AMI) admissions during the first COVID-19 lockdowns (LD), that was described by previous studies, occurred equally in all LD periods (LD1, LD2, LD2021) which had identical restrictions. Further we wanted to analyze if the decrease of AMI admission had any association with the one-year mortality rate.

**Design & Setting:** This study is a prospective observational study of two centers that are participating in the Vienna STEMI network.

**Participants:** 1732 patients that presented with AMI according to the 4$^{th}$ universal definition of myocardial infarction in 2019, 2020 and the LD period of 2021 were included in our study. Patients with myocardial infarction with non-obstructive coronary arteries were excluded from our study.

**Main outcome measures:** The primary outcome of this study was the frequency of AMI during the LD periods and the all-cause and cardiac-cause one-year mortality rate of 2019 (pre-COVID) and 2020.

**Results:** Out of 1732 patients 70% (n=1205) were male and median age was 64 years. There was a decrease in AMI admissions of 55% in LD1, 28% in LD2 and 17% in LD2021 compared to 2019. There were no differences in all-cause one-year mortality between the year 2019 (11%; n=110) and 2020 (11%; n=79; p=0,92) or death by cardiac causes [10% (n=97) 2019 vs. 10% (n=71) 2020; p=0,983].

**Conclusion:** All LDs showed a decrease in AMI admissions, though not to the same extent, even though the regulatory measures were equal. Admission in a LD period was not associated with cardiac or all-cause one-year mortality rate in AMI patients in our study.

## Strengths and limitations of this study

- Prospective, multicenter study with large sample size
- First study to analyze the effect of the COVID-19 lockdowns on the long-term outcome of patients with acute myocardial infarction in a western population
- Contains data of only two major STEMI network centers in Vienna
- Observational study cannot be used to demonstrate causality

## Abbreviations

| | |
|---|---|
| COVID-19 | coronavirus disease 2019 |
| AMI | acute myocardial infarction |
| STEMI | ST-elevation myocardial infarction |
| NSTEMI | non-ST-elevation myocardial infarction |
| LD | lockdown |
| CPR | cardiopulmonary resuscitation |
| NTproBNP | N-terminal prohormone of brain natriuretic peptide |
| IQR | interquartile range |
| p | patients |
| w | weeks |
| p/w | patients per week |
| BMI | body mass index |
| MI | myocardial infarction |
| BP | blood pressure |
| HR | heart rate |
| min | minutes |
| bpm | beats per minutes |
| ED | emergency department |

## Introduction

Since the worldwide outbreak of SARS-CoV-2 coronavirus disease-2019 (COVID-19) and the following strict government restrictions (so called lockdowns) many studies worldwide have reported a decrease in acute myocardial infarction (AMI) hospital admissions.(1-8) Some studies described a decrease in the admission rate of ST-elevation myocardial infarction (STEMI), (9-13) while others reported a decrease in non-ST-elevation myocardial infarction (NSTEMI) admissions (14) and some observed a decrease in both STEMI and NSTEMI admissions.(1, 3, 5-7)

Literature on whether this decrease in AMI hospital admissions has any effect on the in-hospital outcome and mortality is still scarce and shows conflicting results. While some studies described an increase in in-hospital mortality in STEMI (3, 11) or NSTEMI patients (15) others did not find any changes of the in-hospital mortality in AMI patients during the COVID-19 pandemic.(7, 10)

In Austria three nationwide lockdowns (LD) with identical restrictions (closed schools, restaurants, hotels, non-essential businesses, shops and facilities) were implemented. The first LD started on the 16th of March 2020 and lasted until the 1st of May 2020. The second LD was from November 17th until December 6th, 2020. In 2021 an additional three-week nationwide strict LD was announced from 22nd of November 2021 till 11th of December 2021.

The aim of this study was to determine whether the widely described decrease in AMI during the COVID-19 LDs only occurred in the 1st or also in the 2nd and 3rd LDs which had identical contact restrictions as the initial one.

Further, we wanted to evaluate if there was an impact on long-term mortality in AMI patients.

## Methods

### *Study design*

In this prospective multicenter study data of all patients with AMI who had been admitted through the emergency departments in two major STEMI network centers were collected prospectively from 2019-2020 and the LD period of 2021. All patients were treated in the cardiac catheterization laboratory where the diagnosis acute coronary syndrome was confirmed. We did not include patients that were not admitted to the catheterization lab. Diagnostic criteria of type 1 myocardial infarction according to the 4$^{th}$ universal definition of myocardial infarction (16) were applied. Patients with type 2-5 myocardial infarction and myocardial infarction with non-obstructive coronary arteries were excluded from our study.

The collected data included baseline characteristics such as age, sex, cardiovascular risk factors and comorbidities, blood parameters, duration of preclinical-symptomatic phase (onset of chest pain to hospital admission) and outcome parameters. Cardiogenic shock, cardiopulmonary resuscitation (CPR) and in-hospital death were defined as short-term outcome parameters.

To evaluate the long-term outcome one-year mortality data were provided by "Statistik Austria", an independent non-profit-making federal institution that supports scientific services.

The study was approved by the Ethics Committee of the City of Vienna (EK21-198-VK).

***Patient and Public Involvement***

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

***Statistical analysis***

Patients were split into three LD groups (LD 1, LD 2, LD 2021) according to their admission date. Data of all patients with AMI from 2019 were used as reference for the pre-COVID period.

Continuous variables were expressed either as a median and interquartile range (IQR) or as a mean and standard deviation (±SD) based on their distribution. For further comparison, the Student's t-test or univariate ANOVA were performed. Categorical variables were expressed as absolute numbers and percentage and compared with a Chi$^2$-test. Differences in baseline characteristics, cardiovascular risk factors, blood parameters and short-term outcome of each LD group were compared to the reference group of 2019.

To analyze the frequency of AMI, STEMI and NSTEMI hospital admissions during the LD periods the numbers of patients (p) were divided by the number of weeks (w) of each LD resulting in patients per week (p/w) and subsequently compared to the weekly average of admissions of 2019. Changes of the weekly hospital admission rates between 2019 and the LD periods were expressed in percentages. Additionally, data of all unplanned hospital admissions of 2019, LD 1, LD 2 and LD 2021 were collected and the ratios of AMI admissions to all unplanned hospital admissions were calculated.

Further, in order to take possible seasonal changes into account, the absolute numbers of admissions (patients) of each LD were compared to the equivalent time period of 2019.

The one-year mortality of 2019 and 2020 was calculated with the Kaplan-Meier estimate and compared using the log-rank test. Further, the one-year mortality of AMI patients admitted during the LD periods was compared to the one-year mortality of all AMI patients of 2019 as well as to AMI patients of the equivalent time period of 2019. To evaluate factors predictive for the patients one-year mortality an univariate regression model was performed. Variables that were significant in univariate analysis were included in a multiple regression model to search for independent predictors. To visualize the distribution of AMI admissions in 2020 compared with the incidence of the COVID-19 infections over time, we created a figure using the open data “COVID-19: Timeline of data on Covid19 cases per province” from the BMSGPK, “Österreichisches COVID-19 Open Data Informationsportal” (https://www.data.gv.at/covid-19) showing the 7-day incidence of COVID-19 and the AMI admissions in patients per month over the year 2020.

A (two sided) *p*-value of less than 0.05 was defined to be statistically significant. Data was managed using MS Excel 2016 (Microsoft, Redmond, CA). All statistical analyses were performed using SPSS statistics 27 (IBM Corporation, Somers, NY).

## Results

In total 1732 patients with AMI were included in our study of whom 60% (n=1032) had a STEMI and 40% (n=700) a NSTEMI.

### *Baseline Characteristics*

All baseline characteristics are shown in Table 1.

| | All (n=1732) | 2019 (n=962) | LD 1 (n=59) | LD 2 (n=40) | LD 2021 (n=46) |
|---|---|---|---|---|---|
| Age (years) | 64 ± 13 | 64 ± 13 | 62 ± 12 | 61 ± 11 | 67 ± 11 |
| Male | 1205 (70%) | 692 (72%) | 43 (73%) | 29 (73%) | 28 (61%) |
| BMI | 27 ± 5 | 28 ± 5 | 28 ± 3 | 28 ± 6 | 27 ± 5 |
| Hypertension | 934 (54%) | 519 (54%) | 33 (56%) | 21 (53%) | 30 (65%) |
| Hyperlipidemia | 608 (35%) | 313 (33%) | 27 (46%) | 17 (43%) | 24 (52%) |
| Family history | 149 (9%) | 84 (9%) | 10 (17%) | 8 (20%) | 2 (4%) |
| Diabetes | 409 (24%) | 214 (22%) | 15 (25%) | 9 (23%) | 11 (24%) |
| Smoking | 735 (42%) | 382 (40%) | 29 (49%) | 20 (50%) | 17 (37%) |
| Atrial Fibrillation | 106 (6%) | 58 (6%) | 3 (5%) | 0 (0%) | 1 (2%) |
| Prior MI | 350 (20%) | 172 (18%) | 18 (31%) | 7 (18%) | 13 (28%) |
| Systolic BP | 139 ± 29 | 139 ± 30 | 136 ± 28 | 140 ± 30 | 135 ± 31 |
| Diastolic BP | 81 ± 31 | 81 ± 27 | 79 ± 16 | 83 ± 22 | 77 ± 21 |
| HR (bpm) | 84 ± 34 | 83 ± 19 | 85 ± 18 | 85 ± 14 | 81 ± 17 |
| Creatine Kinase (U/l) | 179 [98-439] | 185 [98-475] | 167 [78-435] | 152 [104-268] | 183 [105-762] |
| Troponin T (ng/L) | 104 [32-556] | 116 [34-567] | 65 [26-497] | 63 [32-423] | 196 [35-879] |
| NTproBNP (pg/ml) | 470 [138-1900] | 425 [137-1896] | 386 [108-1021] | 623 [105-2645] | 552 [147-1331] |
| Creatinine (mg/dl) | 0,99 [0,82-1,19] | 0,99 [0,82-1,19] | 1,0 [0,8-1,18] | 1,1 [0,9-1,3] | 1,0 [0,8-1,2] |
| **Delay symptoms – ED** | | | | | |
| STEMI (min) | 145 [75-420] | 130 [70-450] | 108 [64-283] | 122 [78-331] | 213 [133-767] |
| NSTEMI (min) | 445 [146-1513] | 460 [146-1406] | 320 [92-2561] | 1198 [625-2348] | 411 [243-726] |

**Table 1 – Baseline Characteristics**

***LD = lockdown; BMI = Body Mass Index; MI = Myocardial infarction; BP = blood pressure; HR = heart rate; bpm = beats per minute; ED = emergency department; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction***

The median age was 64 ± 13 years and 70 % (n=1205) of all patients were male, 54 % (n=934) had hypertension, 35 % (n=608) hyperlipidemia, 24% (n=409) were diabetics, 42% (n=735) smokers and 9% (n=149) had a positive family history for cardiovascular disease.

The mean delay of onset of symptoms to admission to the emergency department was 145 [IQR: 75-420] minutes for STEMIs and 445 [IQR: 146-1513] minutes for NSTEMIs. Median Troponin T values at admission were 104 ng/L [IQR: 32-556] and median NTproBNP levels were 470 pg/ml [IQR: 138-1900] and there were no statistically significant differences between any of the collected laboratory parameters between the LD groups.

***Frequency of hospital admissions during the LD periods***

The frequency of overall AMI (with subgroups of STEMI and NSTEMI) admissions during the LD periods and the average of 2019 are shown in figure 1.

The frequency of AMI admissions decreased from a weekly average of 18,5 patients per week (p/w) in 2019 to 8,4 p/w in the first LD (-55%). In the second LD the admission rate of all AMI was 13,3 p/w (-28% from 2019 average). Further, an increase of AMI admissions was observed in the no LD periods after LD 1 (12,2 p/w) and LD 2 (16,3 p/w) as shown in supplementary figure 1.

In the LD 2021 the AMI admission frequency decreased to 15,3 p/w (-17% from 2019 average).

The frequency of STEMI patients decreased by 51% from 10,7 p/w in 2019 to 5,3 p/w in the first LD. This decline in STEMI admissions was smaller in the second LD with 9,7 p/w which is a decrease of 9% as compared to the average of 2019. During the LD 2021 the STEMI admission frequency was 8,7 p/w (19% lower than 2019 average).

Moreover, NSTEMI admissions decreased substantially from 7,8 p/w in 2019 to 3,1 p/w in the first LD (60% decrease). The frequency of NSTEMI in the second LD was 3,7 p/w (53% lower than the 2019 average). In the LD 2021 the NSTEMI admissions decreased to 6,7 p/w (-14% compared to 2019 average).

Comparing each LD period to the same time period in 2019 the AMI admissions during the first LD dropped with 54% (127 patients 2019 vs. 59 patients 2020), the STEMI admissions decreased by 46%

(69 patients 2019 vs. 37 patients 2020) and NSTEMI admissions by 62% (58 patients 2019 vs. 22 patients 2020).

In the second LD the AMI admissions were 17% reduced (48 patients 2019 vs. 40 patients 2020). There was no decrease in STEMI admissions (29 patients in 2019 and 2020), but the NSTEMI admissions in the second LD were 42% lower than in the equivalent time period of 2019 (19 patients 2019 vs. 11 patients 2020).

Looking at the last LD 2021 overall 12% fewer patients with AMI were admitted than in 2019 (52 patients 2019 vs. 46 patients 2021). While there was a 24% decrease in STEMI admissions (34 patients 2019 vs. 26 patients 2021), NSTEMI admissions increased by 11% (18 patients 2019 vs. 20 patients 2021).

The visualization of the distribution of AMI frequency (patients/month) in 2020 and the 7-day COVID-19 incidence rate showed that during the decrease of AMI admissions in spring 2020 (LD 1) the COVID-19 incidence was quite low. Interestingly, during the fall of 2020 (LD 2) the decrease of AMI admission was not as pronounced as in LD 1, but the COVID-19 incidence rate was clearly higher than in the first LD (Figure 2). The ratios of AMI admissions to all unplanned hospital admissions are presented in supplementary table 1.

***In-hospital outcome***

Cardiogenic shock, CPR and in-hospital death were defined as short-term outcome parameters and are shown in Table 2. In total 5% (n=94) of all patients had a cardiogenic shock, CPR had to be performed on 5% (n=81) of the patients and overall, 3% (n=52) died in hospital. There were significant higher numbers of CPR admissions in the first LD (p=0,036) and in the LD 2021 (p=0,001) compared to the average number of 2019, but there were no significant differences in cardiogenic shock or in-hospital death between the groups (Table 2).

| | All (n=1732) | 2019 (n=962) | LD 1 (n=59) | LD 2 (n=40) | LD 2021 (n=46) | p-value* | p-value† | p-value‡ |
|---|---|---|---|---|---|---|---|---|
| Cardiogenic shock | 94 (5%) | 58 (6%) | 3 (5%) | 3 (8%) | 2 (4%) | 0,766 | 0,703 | 0,638 |
| CPR | 81 (5%) | 41 (4%) | 6 (10%) | 3 (8%) | 7 (15%) | 0,036 | 0,327 | 0,001 |
| In-hospital death | 52 (3%) | 29 (3%) | 0 (0%) | 1 (3%) | 3 (7%) | 0,176 | 0,852 | 0,185 |
| **One-year mortality** | | | | | | | | |
| All-cause mortality | 189 (11%) | 110 (11%) | 7 (12%) | 4 (10%) | - | 0,920 | 0,780 | - |
| Cardiac mortality | 168 (10%) | 97 (10%) | 6 (10%) | 4 (10%) | - | 0,983 | 0,986 | - |

**Table 2 – Short-term outcome parameters and one-year mortality**

***LD = lockdown; CPR = cardio-pulmonary resuscitation***

** denotes comparison between 2019 and LD 1*

*† denotes comparison between 2019 and LD 2*

*‡ denotes comparison between 2019 and LD 2021*

### *One-year mortality*

One-year mortality data of 2019 and the LD periods of 2020 are shown in Table 2.

Overall, the one-year all-cause mortality rate for AMI patients was 11% (n=189) with no significant difference between STEMI (12%; n=117) and NSTEMI (11%; n=72) patients (p=0,506). In 2019 the all-cause one-year mortality rate was 11% (n=110) and in 2020 11% (n=79) with no significant difference between the pre-COVID year 2019 and the COVID year 2020 (p=0,736). Kaplan-Meier curves demonstrated similar mortality for both years as shown in figure 3.

Further, comparing the mortality rate of cardiac related death of 2019 (10%; n=97) with 2020 (10%; n=71) no significant difference could be found (p=0,851).

The comparison of the all-cause one-year mortality rate of LD 1 (12%; n=7) with the identical time period of 2019 (14%; n=18) also showed no significant difference (p=0,667). Looking at the second LD the mortality rate was 10% (n=4) as compared to 8% (n=4) of the identical time period of 2019 (p=0,787).

In multivariate analysis we found a significant correlation between patients´ sex, cardiac arrest before admission and cardiogenic shock on admission with all cause one-year mortality. The admission during any of the LD periods in comparison to pre-COVID-19 era was not associated with any short- or long-term outcome. Results of multivariate testing are displayed in table 3.

| | **Regression coefficient** | **OR (95% CI)** | **p-value** |
|---|---|---|---|
| Female Sex | 0,38 | 1,46 (1,03-2,05) | **0,03** |
| Age | 0,01 | 1,01 (1,0-1,020) | 0,27 |
| Positive family history | -0,44 | 0,65 (0,32-1,31) | 0,22 |
| Cardiac arrest | 1,59 | 4,92 (2,85-8,50) | **<0,001** |
| Shock | 1,35 | 3,85 (2,32-6,38) | **<0,001** |

**Table 3 – Multivariate regression analysis for all cause one-year mortality**

***OR = Odds Ratio, CI = Confidence interval***

## Discussion

Our study confirmed the previously described trend of decreases in AMI admissions (1-8) during the first LDs at the beginning of the COVID-19 pandemic. This finding could later also be observed for both STEMI and NSTEMI in following LDs with identical restrictions as compared to the average admission frequency of 2019, although not to the same extent as in the initial LD.

Similar to findings of previous studies (1, 2) there were no differences in patient characteristics between the LD groups and the average patient population of the comparison year 2019 (Table 1).

Fear of getting infected with COVID-19 in the hospital has been discussed in multiple previous studies as a possible explanation for the AMI decrease during the first LDs.(2, 17, 18)

In our study the decrease in AMI admissions during the LD 2021 was the lowest of all LDs (-17% in LD 2021 vs. -55% in LD 1 and -28% in LD 2 from the average of 2019). During that period, 71% of the Austrian population had already received their first COVID-19 vaccination leading to the assumption that the general fear of getting infected with COVID-19 in the hospital was lower than in the first and second LDs where no vaccinations against the virus had been available. However, our study showed a decrease in AMI admissions in all LD periods which indicates that fear of getting infected with the virus in the hospital might not be the only explanation for the drop of AMI admissions. To take possible differences in the frequency of all unplanned hospital admissions into account we calculated ratios of AMI admissions to all unplanned hospital admissions. Interestingly, though we observed a decrease in all unplanned hospital admissions during the LD periods, a relative reduction of AMI admissions was found especially in LD 1 which strengthens our hypothesis of a true reduction of AMI admission during the LD periods.

A study from the Austrian Corona panel, (19) which questioned people about their risk assessment of COVID-19 showed that the fear of COVID-19 was similar in the first and second LD.(20)

However, the populations´ compliance to follow the government restrictions decreased after the first LD. Kittel et al. showed that in Austria ~90% of the people did not leave their home to visit friends or family members during the first LD, but this number decreased to ~41% during the second LD.(20)

In our opinion this may well imply that the observed decrease in AMI admissions in our study was not only due to fear of getting infected with COVID-19 in the hospital, but also to a reduction in actual AMI triggers due to the LD restrictions. A relationship between AMI frequency and work-related stress has been discussed in previous studies which described an increase in AMI admissions in the working population on Mondays (21),(22), and an association between higher AMI risk and working overtime.(23) However, a higher risk of AMI on Mondays has also been described in elderly, retired patient populations leading to the assumption that other stress factors arising from life circumstances (e.g. requirements due to family roles) have an impact on the AMI admission rate.(24) Therefore, reduction of work-related stress and social requirements due to the LDs (home-office, contact restrictions) may also have contributed to the decrease in AMI admissions during the LD periods.

Taking into consideration that the one-year mortality of patients did not differ, regardless of admissions in COVID-19 period, in LD periods or before, we hypothesize that patients did not wait at home with ongoing AMI out of fear, but rather that the actual event rate decreased. Our data further supports this hypothesis since the intervals from pain onset to treatment did not differ.

Less exposure to external STEMI triggers such as ambient air pollution has also been discussed as a possible explanation for the decrease in AMI admission.(25) The pathophysiological pathways of acute and chronic effects of exposure to air pollution on the cardiovascular system have already been described elsewhere. (26) Many studies showed that the reduction of mobility during the COVID-19 LDs lead to a decrease of air pollution ($NO_2$, $PM_{2.5}$).(27-29) However, a study from Mohajeri et al. showed that the second LD in England had less mobility reduction resulting in higher $NO_2$ concentrations than the first LD.(30) The mobility in Austria was reduced by 72% in the first LD, however, the reduction was only 47% in the 2nd LD and 30% in LD 2021 as compared to 2019. (31, 32)

Because in our study the decrease in AMI frequency was higher in the first than in the second LD (-55% vs. -28% compared to the average of 2019), we postulate that the higher mobility rate and the higher air pollution during the second LD might have had an impact on the frequency of AMI admissions. We further observed a return to higher AMI frequencies in the no LD periods after LD 1 and LD 2 (Supplementary Figure 1) which further strengthens our hypothesis that the observed decrease of AMI admissions during LD periods might have been due to reduced exposure to factors triggering AMI.

Regarding in-hospital outcome our study showed no difference in in-hospital mortality during the LD periods. This is in line with findings of a meta-analysis from Rattka et al. who showed that even though some studies reported an increase of in-hospital mortality of STEMI patients during the pandemic(33, 34), on a more global scale the in-hospital mortality of the post-COVID-19 group is not significantly higher than before the pandemic.(35)

To our knowledge this is the first study that analyzed both the frequency of AMI in different and recent LD periods as well as the long-term mortality of a large cohort AMI patients during the COVID-19 pandemic in a western population.

We did not find any statistically significant differences in one-year mortality of AMI patients between the pre-COVID year 2019 and the COVID year 2020. Additionally, we analyzed the one-year mortality of LD 1 and LD 2 and compared it to the identical time period of 2019 which also showed no significant difference. Similar findings have been described by Phua et al. in a study from Singapore.(36)

This indicates that the decrease in AMI frequency did not affect the prognosis and long-term outcome of AMI patients.

Further, this finding strengthens our assumption that the decrease in AMI admissions was not (only) caused by patients presenting late to the hospital due to fear of getting infected with COVID-19, but rather that a general decrease of absolute AMI numbers had occurred, due to multiple reasons such as a reduction of social and work-related stress and environmental factors.

**Limitations**

Our study has several limitations that need to be considered. First, it is an observational study and therefore cannot be used to demonstrate causality. Second, even though we described a decrease in AMI admissions to the hospital and the long-term outcome of those patients, we do not have data concerning out of hospital cardiac deaths caused by AMI not admitted to the hospitals. Third, our sample size only includes data from two major STEMI network centers and should therefore be considered as limited. Given the large overall sample size and the prospectively collected data of excellent quality we still consider our findings to add value to the discussion of the impact of COVID-19 and measures against it on patients with AMIs.

## Conclusion

We observed a decrease in AMI admissions during all COVID-19 LD periods, though not to the same extent, even though the regulatory measures were equal. The observed decrease might have been due to multifactorial reasons and admission during LD periods was not associated with increased one-year mortality in our study. Further studies are needed to evaluate the underlying causes for the observed decreases of AMI admissions during the COVID-19 LD periods.

## Declarations

**Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Competing interests:** All authors report no conflict of interest.

**Author contributions:** RM & AS planned the study, drafted the protocol, acquired and analyzed data, drafted the manuscript; DR & WS acquired data, drafted the protocol, revised the manuscript critically for important intellectual content; CW, GP, PS & GD made substantial contributions to conception, design, analysis and interpretation of data, revised the manuscript critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Ethics approval:** This study was approved by the Ethics Committee of the City of Vienna (EK21-198-VK).

**Data availability:** The data underlying this article will be shared on reasonable request to the corresponding author.

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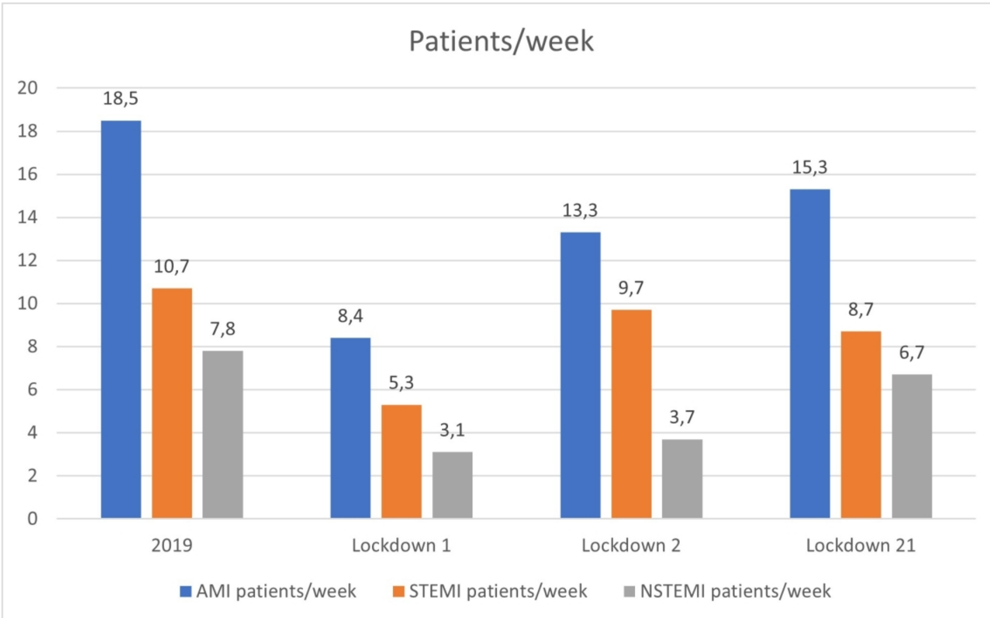
# Figure legends

**Figure 1** Admissions of acute myocardial infarctions (AMI), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) in 2019 and during the lockdown periods (patients/week)

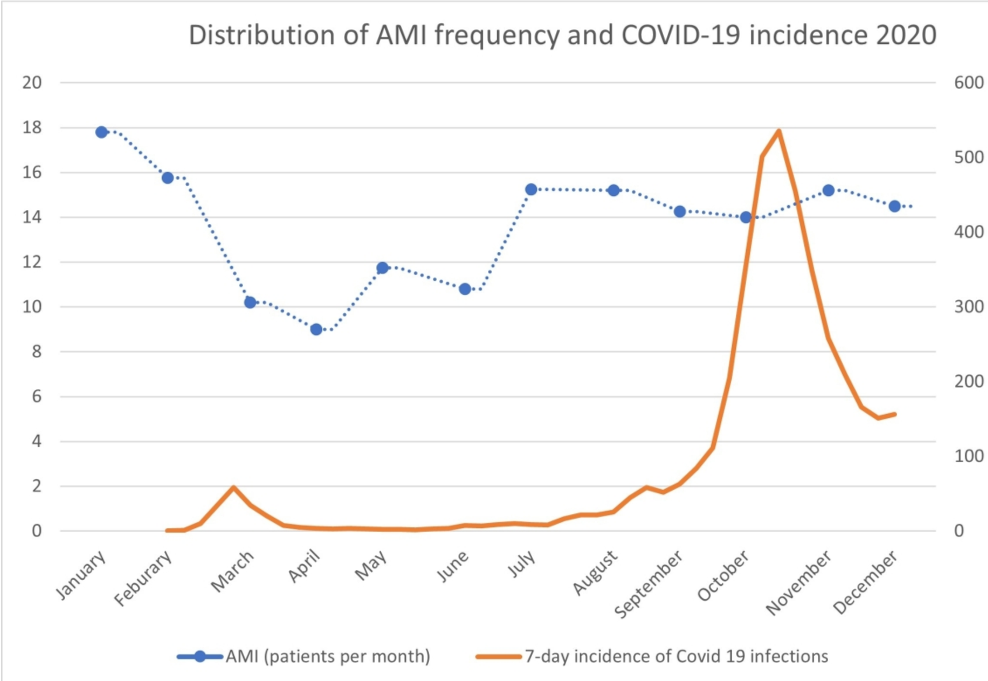
**Figure 2** Distribution of acute myocardial infarction (AMI) frequency (patients/month) and COVID-19 7-day incidence rate of 2020

**Figure 3** Kaplan-Meier analysis for all-cause one-year mortality in acute myocardial infarction (AMI) patients 2019 vs. 2020 (log rank: p=0,7)



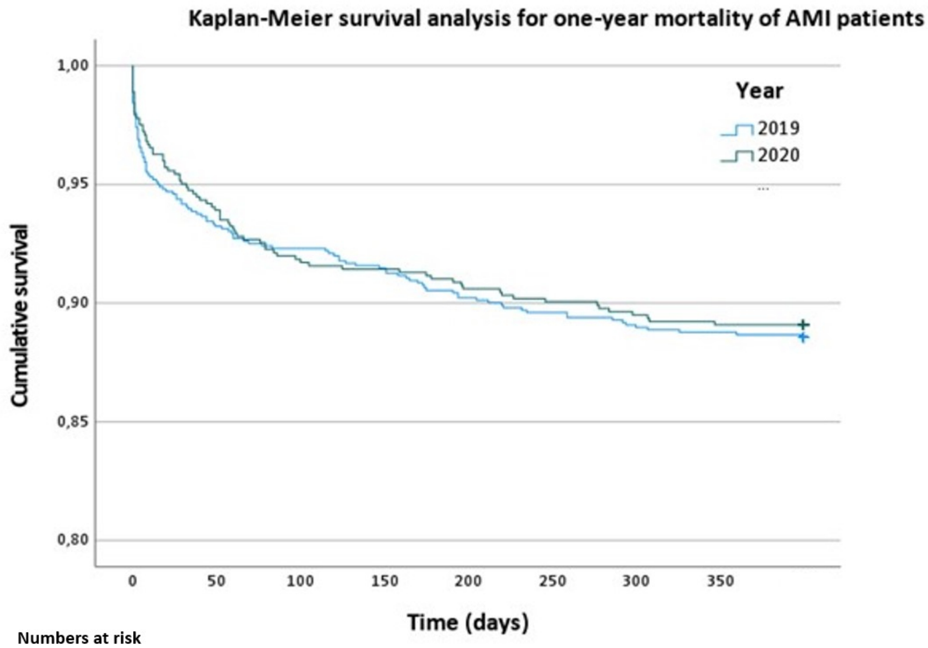

Admissions of acute myocardial infarctions (AMI), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) in 2019 and during the lockdown periods (patients/week)

154x95mm (330 x 330 DPI)




Distribution of acute myocardial infarction (AMI) frequency (patients/month) and COVID-19 7-day incidence rate of 2020

160x110mm (330 x 330 DPI)




Numbers at risk

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **2019** | 962 | 897 | 888 | 880 | 868 | 862 | 857 | 854 |
| **2020** | 724 | 680 | 665 | 662 | 656 | 652 | 648 | 645 |

Figure 3

199x142mm (144 x 144 DPI)

# Supplementary material

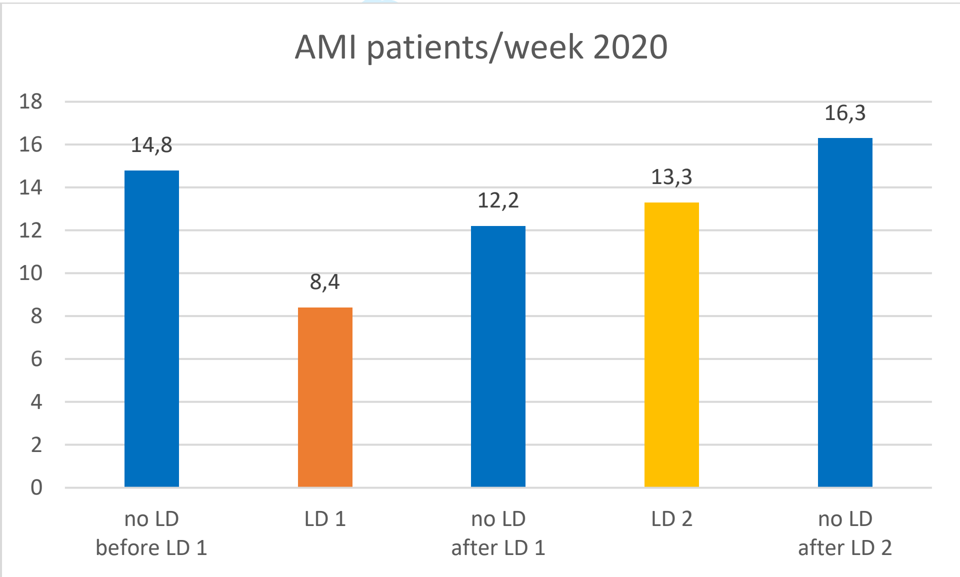
**Supplementary Table 1 – Ratio of AMI admissions/unplanned hospital admissions**

| | 2019 | LD 1 | LD 2 | LD 2021 |
|---|---|---|---|---|
| All admissions (patients/week) | 401,9 | 278,9 | 378,9 | 439,3 |
| AMI admissions (patients/week) | 18,5 | 8,4 | 13,3 | 15,3 |
| AMI/all admissions (%) | 5 | 3 | 4 | 4 |

All unplanned hospital admissions presented as weekly ratios, AMI admissions presented as weekly ratios and ratio of AMI/all admissions during 2019 and the LD periods

*AMI=acute myocardial infarction, LD=lockdown*

**Supplementary Figure 1 – AMI admissions of 2020 categorized into LD and no LD periods**




*LD = lockdown; data presented in patients per week; no LD before LD 1 = January 1st, 2020 – start LD 1; no LD after LD 1 = end of LD 1 – beginning of LD 2; no LD after LD 2 = period after LD 2*

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

| | Item No | Recommendation | Page No |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract<br>(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 5 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(*b*) For matched studies, give matching criteria and number of exposed and unexposed | 5-6 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 6 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 6-7 |
| Study size | 10 | Explain how the study size was arrived at | 5-6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 6-7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding<br>(*b*) Describe any methods used to examine subgroups and interactions<br>(*c*) Explain how missing data were addressed<br>(*d*) If applicable, explain how loss to follow-up was addressed<br>(*e*) Describe any sensitivity analyses | 6-7 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 8-9 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount) | 8-9 |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | 10-11 |

| | | | |
|---|---|---|---|
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(*b*) Report category boundaries when continuous variables were categorized<br>(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 9-11 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 12-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.