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Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England

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Abstract:	Background: Several countries affected by the COVID-19 epidemic have reported a substantial drop in the number of patients attending the emergency department with acute coronary syndromes (ACS), as well as a reduced number of cardiac procedures. Methods : Analysis of data on hospital admissions in England for acute coronary syndrome recorded in the Secondary Uses Service Admitted Patient Care (SUSAPC) database. Findings: Hospital admissions for ACS declined from early March 2020, falling from a 2019 baseline rate of about 3000 admissions per week to about 1700 per week by the end of March, a reduction of 46%. There were reductions in the numbers of admissions for all types of ACS, including both ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), but the relative and absolute reductions were larger for NSTEMI. There were larger falls in the number of admissions of older people,

those with a high burden of comorbidity, and in the London region. In parallel, there were reductions in the numbers of percutaneous coronary intervention (PCI) for both STEMI and NSTEMI, but the proportion of admitted patients who received PCI rose slightly, particularly on the day of admission among patients with NSTEMI. The median length of stay among patients with ACS halved from 4 to 2 days.
Interpretation: There has been a substantial reduction in the numbers of patients with myocardial infarction or other ACS who were admitted to hospital in England by early April. This is likely to have resulted in increases in out-of-hospital death and long-term complications of myocardial infarction, and missed opportunities to offer secondary prevention treatment for patients with coronary heart disease. Updated analyses will assess the full extent of the impact of COVID-19 on patients with ACS.

Manuscript

Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England

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Research in context

Evidence before the study: There have been reports of reductions in admissions for acute coronary syndrome and in primary percutaneous coronary intervention (PCI) procedures for acute myocardial infarction during the COVID-19 pandemic in several countries (e.g. Italy, Spain, Austria, and the US). These studies provided limited information, however, about the time course of the changes in admission rates, the impact on different types of ACS, the treatment of patients admitted with ACS, and the relevance of patient characteristics to the observed reductions.

Added value of the study: This study provides quantitative information about the time course of admission patterns and in-hospital management for acute coronary syndromes, including separately for ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), since the beginning of the pandemic period in England. It shows that there was a reduction of about one quarter in admissions for STEMI, and a reduction of about one half in admissions for NSTEMI since mid-February 2020. The declines in both STEMI and NSTEMI appear to have levelled off during April. The decline in admissions preceded the lockdown and was qualitatively similar throughout the country, with only minor variations in the magnitude of the changes in different demographic groups. The study also uncovered changes in the management of patients who were admitted with an acute MI during the pandemic period, with more patients receiving PCI on the day of admission, and a reduction in the median length of stay.

Implications of all the available evidence: Patients who do not go to hospital with an acute coronary syndrome, especially STEMI, where they can receive reperfusion therapy or other appropriate treatments, do not benefit from reperfusion therapy and are at increased risk of complications. The reasons for patients failing to attend emergency departments with acute coronary syndrome (and other urgent conditions) should be addressed urgently to avoid unnecessary deaths and disability.

ABSTRACT

Background: Several countries affected by the COVID-19 epidemic have reported a substantial drop in the number of patients attending the emergency department with acute coronary syndromes (ACS), as well as a reduced number of cardiac procedures.

Methods: Analysis of data on hospital admissions in England for acute coronary syndrome recorded in the Secondary Uses Service Admitted Patient Care (SUSAPC) database.

Findings: Hospital admissions for ACS declined from mid-February 2020, falling from a 2019 baseline rate of 3017 admissions per week to 1767 per week by the end of March, a reduction of 41% (95% CI 39%-44%), but without any further decline during April. There were reductions in the numbers of admissions for all types of ACS, including both ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), but the relative and absolute reductions were larger for NSTEMI. Admission rates for both STEMI and NSTEMI appeared to level off in April. Overall, there was a similar pattern of reduced admissions in different demographic groups, although there were slightly larger falls in those with a high burden of comorbidity, and in the London and East Midlands regions. In parallel, there were reductions in the numbers of percutaneous coronary intervention (PCI) procedures for both STEMI and NSTEMI, but the proportion of admitted patients who received PCI rose slightly, particularly on the day of admission among patients with NSTEMI. The median length of stay among patients with ACS halved from 4 to 2 days.

Interpretation: There has been a substantial reduction in the numbers of patients with myocardial infarction or other ACS who were admitted to hospital in England by early the end of April. This is likely to have resulted in increases in out-of-hospital death and long-term complications of myocardial infarction, and missed opportunities to offer secondary prevention treatment for patients with coronary heart disease. The full extent of the impact of COVID-19 on patients with ACS will continue to be assessed by updating these analyses.

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INTRODUCTION

Worldwide, the COVID-19 pandemic has resulted in substantial excess mortality arising directly from respiratory failure. In addition, it has necessitated major reorganisation of emergency care facilities to accommodate the additional workload anticipated with a rapid surge in critically ill patients with COVID-19. Cardiologists have reported substantial falls in the number of patients presenting with acute coronary syndromes (ACS), and in the numbers of emergency coronary procedures, in both Europe (1-4) and the US (5,6).

The first fatality for COVID-19 in the UK was reported on 5 March 2020. On 16 March, the Prime Minister of the United Kingdom urged the introduction of social distancing measures, and on 23 March he announced a nationwide 'lockdown'. The Health Protection (Coronavirus Restrictions) (England) Regulations 2020 which came into force on 26 March severely restricted movement among all citizens, although it still allowed people to leave their homes for essential reasons, including seeking healthcare. Analyses by Public Health England show that there has been about a 30% reduction in emergency ambulance calls for chest pain (7) and a greater than 50% reduction in emergency department attendances for myocardial ischaemia (8) in England, and surveys of cardiologists in the UK and elsewhere have suggested a substantial reduction in demand for coronary procedures (9). On 20 March, the British Cardiovascular Intervention Society issued guidance on measures to address the potential impact of COVID-19 on cardiology services (10).

In order to understand the scale, nature and duration of changes to admissions for different types of acute coronary syndrome (ACS), and to evaluate whether in-hospital management of these patients was also affected as a result of the pandemic, we sought data on all such admissions to National Health Service (NHS) acute hospital trusts in England from January 1, 2019. We used the Secondary Uses Service Admitted Patient Care (SUSAPC) database because it is updated more rapidly than the Hospital Episodes Statistics (HES) database. It is intended that analyses will be revised monthly and made available at https://www.ctsu.ox.ac.uk/research/covid-19-acute-coronary-syndromes in order to provide an updated summary of changes in such admissions as the response to the COVID-19 pandemic evolves over time.

METHODS

All episodes of care for patients admitted to acute NHS hospital trusts in England with ACS, defined using the International Classification of Diseases 10th revision (ICD-10) codes (11), from 1 January 2019 to 22 May 2020 were identified in the SUSAPC database (see Supplementary Methods). These admissions were classified as STEMI, NSTEMI, MI of unknown type, unstable angina or other acute ischaemic heart disease according to the recorded ICD-10 codes.

To prevent over-counting of ACS events, episodes of care for each person were linked into continuous single hospital admissions (spells) and spells linked between hospitals (superspells). Revascularisation procedures – percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery – undertaken during these admissions were identified from relevant Office of Population Censuses Surveys Classification of Surgical Operations and Procedures 4th revision (OPCS4) (12) codes (Supplementary Table 2). It is not possible to identify primary PCI in the SUSAPC data, so PCI on the day of admission was used as a surrogate for primary PCI among STEMI patients.

As a result of service reorganisation in response to COVID-19 (10), there may have been a reduction in the speed and completeness of clinical coding, which could result in artefactual reductions in ACS-related admissions (particularly in the most recent data). For each week after 17 February 2020, this was investigated by ascertaining the proportion of all SUSAPC records recorded in each week that contained no diagnostic ICD-10 codes, and an adjustment was made to the numbers of recorded admissions for ACS each week based on these proportions.

In all analyses of admission numbers, data are presented for 2019 as a median and interquartile range of the weekly recorded numbers. For 2020, a local polynomial regression (LOESS) smoothing function was fitted through the weekly numbers (using the 'loess' function in R with default settings). From 2020, the weekly adjusted numbers (indicating the number of admissions in the preceding 7 days) are also plotted along with their approximate standard errors (under the assumption that the count data follow a Poisson distribution). Percentage changes in weekly admissions were calculated by comparing the adjusted weekly admission number for the week commencing 23 March 2020, the first week following the 'lockdown', with the mean weekly number during 2019 and are presented with their 95% Confidence Intervals (CIs). The percentage changes in weekly admissions among particular subgroups were calculated similarly, with tests for heterogeneity across each subgroup presented. Monthly updates of the tables and figures are available online. Analyses were produced using R version 3.6.3.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication.

RESULTS

SUSAPC data were available from all 147 acute NHS hospital trusts in England.. The demographic characteristics of patients with ACS remained stable during 2019 (data not shown) but, as compared to earlier months, the patients admitted with ACS after February 2020 were younger and had fewer comorbid conditions (Table 1). In 2019, the average number of ACS admissions per week during February to April (3082 per week) was similar to the average number during the other months of the year (2994 per week).

After adjusting for the effects of incomplete coding of clinical data from trusts (see Supplementary appendix), there was a 41% (95% CI 39% - 44%) reduction in hospital admissions for ACS between mid-February and the end of March 2020 (Figure 1 and Table 2), with the 2019 baseline rate of 3017 admissions per week falling to 1767 per week, with no further decline during April in all ACS admissions combined (Figure 1).

Considered separately, there were reductions in the numbers of admissions for all acute MI, STEMI, and NSTEMI during this period (Figure 1 and Table 2), with a reduction of 37% (95% CI 33% - 40%; 2061 per week to 1299 per week) for all acute MI, 25% (95% CI 18% - 31%; 621 per week to 467 per week) for STEMI, and 44% (95% CI 39% - 48%; 1267 per week to 714 per week) for NSTEMI. The admission rate for both STEMI and NSTEMI levelled off during April (Figure 1).

The 25% reduction in admissions for STEMI was accompanied by a slight rise in the proportion of those admitted to hospital receiving PCI on the day of admission (Figure 2); as a consequence there was a reduction of 20% (95% CI 10 – 28%; 379 per week to 304 per week) in the absolute numbers of STEMI patients receiving PCI on the day of admission (Figure 3 and Table 2). The 44% reduction in NSTEMI admissions was accompanied by a slight increase in the proportion who received PCI at any time during the admission (Supplementary Figure 1, Table 2), which translated into a reduction of 38% (95% CI 30 – 45%; 384 per week to 238 per week) in the absolute numbers receiving PCI. For all types of ACS combined, there was a 60% (95% CI 54% - 66%; 429 per week to 170 per week) reduction in the absolute numbers of patients having angiography without revascularisation, and CABG surgery during the admission largely ceased (Figure 3 and Table 2).

By the end of April, the median length of stay among patients admitted with any ACS fell from 4 (interquartile range [IQR] 2 - 9) days to 2 (1 - 4) days (Supplementary Figure 2): for STEMI the reduction was from 3 (2 - 6) days to 2 (2 - 3) days, whilst for NSTEMI it was from 5 (3 - 11) days to 3 (2 - 4) days. There was no apparent change in in-hospital mortality among patients admitted with ACS (data not shown).

The relative reductions in weekly numbers of admissions for ACS were qualitatively similar in all of the subgroups studied, but they appeared slightly larger among those with higher (that is, a worse) Charlson comorbidity index and for those in the London and East Midlands regions (Supplementary Table 3 and Supplementary Figure 3).

DISCUSSION

Previous reports of reduced admission rates for ACS and the use of coronary procedures in various countries affected by the COVID-19 pandemic have indicated that the phenomenon is widespread. However, those reports have been limited in detail (1-6): in particular, only one study (6) reported the time course of the changes in admission rates, and there has been limited information about the relative impact on different types of ACS, the acute management of patients admitted with ACS, and the relevance of patient characteristics. By contrast, in the present study, unique access to rapidly available central NHS healthcare data has allowed us to produce near "real time" analyses based on all admissions for ACS in all 147 acute hospitals across England that can address all of these points and, in addition, will be able to follow the emerging trends over time as the response to COVID-19 evolves (eg, with easing of restrictions and any recurrent outbreaks of infection).

Our study has provided several key insights into the observed reduction in admissions for ACS. First, between the middle of February and the first week of April 2020, the number of ACS admissions fell by about a half, with the decline stabilising during April. It is of note that the decline appears to have commenced at least 2 weeks before the first UK death from COVID-19, and about a month before the UK Government implemented a 'lockdown'. This finding is consistent with a report based on US Kaiser Permanente Northern California, which indicated that the reduction in acute MI admissions preceded the 'shelter-in-place' order by about 2 weeks.(6)

By mid-February 2020, UK media were reporting the spread of coronavirus in China and (closer to home) in Northern Italy, and NHS hospitals had been told to prepare for a large influx of patients with COVID-19. As early as February 14th, it was noted that 'fear-inducing language' was breeding fear and panic (13). Taken together with survey data from Hong Kong that patients delayed seeking medical help due to a fear of acquiring COVID-19 (14), it seems likely that fear of contagion has been a major factor underlying the observed reduction in admissions for ACS in our study. In particular, the fact that the decline in admissions preceded the UK lockdown and, despite the lockdown, is now levelling off (7), suggests that environmental changes (eg reduced air pollution), reduced physical activity, or reduced stress due to lockdown are unlikely to be major contributors to the decline in ACS admissions in the current pandemic (15,16).

A second novel finding in our analyses is the clear distinction between the reduction of about one quarter in STEMI admissions compared to the reduction of about one half in NSTEMI admissions. Our analyses in an unselected study population are based on much larger numbers of admissions than any previous study, some of which observed a smaller reduction for STEMI than for NSTEMI (Italy)(3) while others did not detect a difference in the reductions for different types of MI (in Austria and Northern California) (1,6). As STEMI is generally associated with severe and unremitting symptoms, patients may well be less reluctant to seek help irrespective of any fears they may have about attending a hospital, whilst those with NSTEMI may be able to tolerate less severe symptoms and so opt to remain at home.

Thirdly, we were able to document how the acute management of admitted patients changed during the pandemic period. In preparation for the COVID-19 pandemic, UK cardiology services were reorganised such that elective PCI and CABG would not be available routinely during the outbreak. Instead, it was recommended that, if current NSTEMI pathways could not be followed due to reduced intensive care unit capacity or other issues, PCI should be used in place of surgery and in-patient stays reduced to 36-48 hours (10). Consistent with these recommendations, our results show that patients admitted with NSTEMI were more likely to receive PCI whilst in hospital (often on the day of admission) and to have shorter hospital stays. However, as the numbers of patients admitted with both NSTEMI and STEMI were reduced, fewer ACS patients actually received PCI.

Finally, the large numbers of cases and the national coverage of the data, allowed us to show that the pattern of reduced admissions was qualitatively similar (albeit slightly different quantitatively) in a number of important demographic groups. For example, despite the greater risk with COVID-19 among older patients and those with comorbidities, there were similar reductions in the numbers of ACS cases admitted at younger ages and without comorbidities in whom the long-term benefits of cardiovascular interventions would typically be greater. Likewise, despite different COVID-19 admission rates across the UK during the early phase of the pandemic, there was little difference in the reduction in ACS admissions between different regions. This consistency suggests that the drivers of the observed fall in admissions are likely to be common – to a greater or lesser extent – to all patient groups.

Taken together, this substantial reduction in admissions for ACS during the pandemic is a serious concern since all patients with symptoms indicative of acute myocardial ischaemia would benefit from rapid in-hospital assessment (17,18), with the gain being greatest among those with STEMI. Among such patients, there is a substantial risk of out of hospital cardiac arrest (19), and the failure of patients with STEMI to be admitted to hospital in order to receive early reperfusion therapy and other appropriate treatments is likely to have resulted in avoidable deaths and complications, such as fatal arrhythmias (20) and disabling heart failure (21). Although no overall increase in mortality was observed among those patients who were admitted for ACS, a direct comparison between mortality rates before and after mid-March is likely to be confounded by differences in their underlying risk and by the duration of hospital stay. Moreover, it is not possible to assess directly the deaths and disability that are likely to have occurred among those patients with ACS who were not admitted to hospital and so did not receive treatment that is known to be effective.

What are the implications of our findings for the UK and other countries, including those in which the pandemic is only just starting, and how can they help inform preparations for any subsequent increases in infection rates when lockdown restrictions are relaxed? The findings confirm the general pattern reported from other countries. However, our demonstration of the qualitative similarity of the falls in ACS admission rates largely irrespective of age, sex, number of comorbidities and region suggest that the findings are likely to be generalisable to all patients who are having an acute MI, not just in the UK (e.g. in the event of recurrent outbreaks of infection) but also elsewhere in the world, unless appropriate measures are taken to avoid it recurring. If the reduction in hospital admissions is largely or wholly due to fear of coronavirus exposure, it seems likely the same phenomenon will be observed wherever there is a rapid increase in COVID-19 cases and public health messaging is not suitably nuanced. Regular updates of the present analyses will allow the success of interventions to reverse these adverse admission trends to be tracked, including during any future outbreak. More generally, it would be valuable to establish similar continuous analyses for other serious conditions in the UK, as well as elsewhere where centralised electronic health record data are available (such as China or Sweden, or in US health maintenance organizations), to monitor such trends to ensure that they reverse and do not recur during this pandemic (or, indeed, any subsequent ones).

Our study is subject to some limitations. SUSAPC data are timely but incomplete, with some trusts not having submitted any admissions data for the most recent week and, for a longer period, some trusts having recorded admissions without a diagnostic code. Such omissions will tend to exaggerate artefactually the depth of the decline in ACS admissions (particularly in the more recent weeks). We have addressed this issue by applying an adjustment (see Supplementary appendix), and validated our approach by showing that the adjusted results are consistent with unadjusted results for those Trusts that do report complete data frequently. This comparison suggests that our approach to adjustment is likely to be generalizable to the study of time trends for other serious conditions.

A further potential limitation is that the coding of STEMI and NSTEMI was inferred from ICD-10 codes, which may suffer from some inaccuracy. Our results provided a clear contrast between the rates of admission for, and management of, STEMI and NSTEMI that have been diagnosed and coded in much the same way throughout 2019 and into early 2020 versus after mid-March. Consequently, any bias in the comparison of the ACS rates due to misclassification of STEMI and NSTEMI is likely to be modest (other than due to late reporting in the most recent weeks) and, if removed, would yield even more striking differences between the rates for STEMI and NSTEMI. A further limitation is that the SUSAPC data do not allow assessments to be made of any delays in admissions from the onset of symptoms of ACS or of any impact on the rates of complications in the MI cases admitted.

Although there is now a national campaign to encourage all people experiencing symptoms of acute myocardial ischaemia to call an ambulance immediately, it has not addressed the public's fear that they might contract COVID-19 by going to hospital. In order address these concerns, all hospitals need to provide relatively clean areas for patients who do not have COVID-19 and the public needs to be made aware that this is the case. Otherwise, people may continue to be reluctant to call an ambulance, even if experiencing severe symptoms, resulting in unnecessary deaths and disability.

Author contributions and declaration of interests

All the authors contributed to study design, data interpretation and preparation of the report. Data were processed for analysis by DG, PC, SH, MB, CR. Statistical analysis was done by ES and RG. The first three authors made equal contributions, as did the last three authors.

BC is the Current President of the European Society of Cardiology (2018-20), a British Heart Foundation Chair-holder and the Lead of the Cardiovascular Theme of the Oxford NIHR Biomedical Research Centre. RC is a British Heart Foundation Chair-holder, and reports personal fees from UK Biobank, grants from Merck & Co, grants from Medicines Company (now Novartis), other from Pfizer, outside the submitted work; in addition, RC has a patent for a statin-related myopathy genetic test licensed to University of Oxford from Boston Heart Diagnostics (RC has waived any personal reward). MJL reports grants from Medical Research Council Population Health Research Unit, grants from Health Data Research UK, grants from National Institute for Health Research Oxford Biomedical Research Centre, during the conduct of the study; grants from Merck Sharp &

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FIGURE LEGENDS

Monthly updates of all Figures and Supplementary figures are available at https://www.ctsu.ox.ac.uk/research/covid-19-acute-coronary-syndromes

Figure 1: Weekly numbers of admissions with an acute coronary syndrome, by type
For weekly admissions in 2019, the boxplot shows the median and interquartile range (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartile, with any weekly counts beyond those ranges indicated by an 'x'. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the data points and standard errors plotted. The red lines/points represent unadjusted reported counts and the black lines/points represent the counts adjusted for incomplete coding. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction.

Figure 2: (a) Weekly numbers and (b) weekly proportions of admissions with an acute coronary syndrome that received PCI on the day of admission For weekly admissions in 2019, the boxplot shows the median and interquartile range (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartile, with any weekly counts beyond those ranges indicated by an 'x'. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the data points and standard errors plotted. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = Percutaneous coronary intervention.

Figure 3: Weekly numbers of admissions with an acute coronary syndrome that received a particular coronary procedure
For weekly admissions in 2019, the boxplots show the median and interquartile ranges (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartiles, with any weekly counts beyond those ranges indicated by an 'x'. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the data points and standard errors plotted. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; CABG = Coronary artery bypass graft; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = Percutaneous coronary intervention.

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***Table 1*: Characteristics over time of patients admitted to an English acute trust with a diagnosis of any acute coronary syndrome (Jan 2019 to April 2020)**

		Monthly average for 2019	2020			
			January	February	March	April
Gender	Female	4829 (37)	5126 (38)	4458 (36)	3585 (36)	2421 (34)
	Male	8244 (63)	8502 (62)	7821 (64)	6296 (64)	4628 (65)
Age group	<50	953 (7)	1051 (8)	945 (8)	748 (8)	610 (9)
	50-59	2082 (16)	2152 (16)	1986 (16)	1659 (17)	1286 (18)
	60-69	2723 (21)	2817 (21)	2528 (21)	2153 (22)	1580 (22)
	70-79	3353 (26)	3551 (26)	3143 (26)	2502 (25)	1733 (24)
	80+	3963 (30)	4058 (30)	3680 (30)	2826 (29)	1886 (27)
Ethnic group	White	10312 (79)	10665 (78)	9610 (78)	7678 (78)	5508 (78)
	Mixed	58 (0)	65 (0)	71 (1)	42 (0)	31 (0)
	Asian	956 (7)	998 (7)	882 (7)	669 (7)	438 (6)
	Black	196 (2)	203 (1)	175 (1)	146 (1)	114 (2)
	Other/Unknown	1552 (12)	1698 (12)	1544 (13)	1353 (14)	1004 (14)
Charlson Index	0	3933 (30)	4033 (30)	3616 (29)	3093 (31)	2383 (34)
	1	3591 (27)	3710 (27)	3452 (28)	2859 (29)	2039 (29)
	2	2180 (17)	2335 (17)	2084 (17)	1635 (17)	1107 (16)
	3+	3370 (26)	3551 (26)	3130 (25)	2301 (23)	1566 (22)
Region of acute admission	North East	705 (5)	700 (5)	690 (6)	550 (6)	420 (6)
	North West	2050 (16)	2200 (16)	1915 (16)	1605 (16)	1180 (17)
	Yorkshire & Humber	1510 (12)	1635 (12)	1435 (12)	1225 (12)	860 (12)
	East Midlands	1060 (8)	1115 (8)	1005 (8)	825 (8)	585 (8)
	West Midlands	1380 (11)	1395 (10)	1285 (10)	1030 (10)	810 (11)
	East of England	1380 (11)	1400 (10)	1375 (11)	1000 (10)	605 (9)
	London	1720 (13)	1800 (13)	1640 (13)	1235 (12)	900 (13)
	South East	1750 (13)	1850 (14)	1550 (13)	1295 (13)	935 (13)
	South West	1520 (12)	1535 (11)	1385 (11)	1125 (11)	795 (11)
Total		13074 (100)	13629 (100)	12282 (100)	9888 (100)	7095 (100)

The number of admissions shown are unadjusted for incomplete coding (see supplementary methods). Regional numbers are rounded to the nearest multiple of 5. Values shown are n (%). Percentage changes in admission rates for each subgroup are provided in Supplementary Table 3.

***Table 2*: Percent reduction in weekly acute coronary syndrome admissions across all English acute trusts, from the average number of weekly admissions seen in 2019 to the number of admissions in the week commencing 23 March 2020**

		Receiving particular coronary procedures				
	All admissions	With any PCI	With PCI on day of admission	With PCI after day of admission	With CABG	With angiography only
ACS						
2019 weekly average	3017	909	464	450	93	429
23-30 March 2020	1767	624	387	238	18	170
Percent reduction (95% CI)	41 (39, 44)	31 (26, 37)	17 (8, 25)	47 (40, 53)	81 (69, 88)	60 (54, 66)
Acute MI						
2019 weekly average	2061	834	453	386	80	306
23-30 March 2020	1299	587	375	211	16	137
Percent reduction (95% CI)	37 (33, 40)	30 (24, 35)	17 (8, 25)	45 (37, 52)	80 (67, 88)	55 (47, 62)
STEMI						
2019 weekly average	621	438	379	63	16	49
23-30 March 2020	467	340	304	37	4	33
Percent reduction (95% CI)	25 (18, 31)	22 (14, 30)	20 (10, 28)	41 (19, 58)	75 (33, 91)	33 (5, 52)
NSTEMI						
2019 weekly average	1267	384	67	317	63	245
23-30 March 2020	714	238	67	170	12	97
Percent reduction (95% CI)	44 (39, 48)	38 (30, 45)	0 (-27, 21)	46 (38, 54)	81 (66, 89)	60 (52, 68)

ACS=Acute coronary syndrome, MI=Myocardial infarction, PCI=Percutaneous Coronary Intervention, STEMI=ST elevation myocardial infarction, NSTEMI=Non ST elevation myocardial infarction

Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England

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Research in context

Evidence before the study: There have been reports of reductions in admissions for acute coronary syndrome and in primary percutaneous coronary intervention (PCI) procedures for acute myocardial infarction during the COVID-19 pandemic in several countries (e.g. ~~a number of countries~~Italy, Spain, Austria, and the US). These studies provided limited information, however, about the time course of the changes in admission rates, the impact on different types of ACS, the treatment of patients admitted with ACS, and the relevance of patient characteristics to the observed reductions.

Added value of the study: This study provides quantitative information about ~~temporal changes~~the time course of ~~to~~ admission patterns and in-hospital management ~~in England~~ for acute coronary syndromes, including separately for ~~both~~ ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), since the beginning of the pandemic period in England. It shows that there was a reduction of about one quarter in admissions for STEMI, and a reduction of about one half in admissions for NSTEMI since mid-February 2020. The declines in both STEMI and NSTEMI appear to have levelled off during April. The decline in admissions preceded the lockdown and was qualitatively similar throughout the country, with only minor variations in the magnitude of the changes in different demographic groups. The study also uncovered changes in the management of patients who were admitted with an acute MI ~~altered~~ during the pandemic period, with more patients receiving PCI on the day of admission, and a reduction in the median length of stay. ~~It shows a rapid reduction of around 50% in acute coronary syndrome admissions, with the largest reductions observed among elderly patients, those with a high burden of comorbidity, and in the London region.~~

Implications of all the available evidence: Patients who do not go to hospital with an acute coronary syndrome, especially STEMI, where they can receive reperfusion therapy or other appropriate treatments, ~~are at increased risk of cardiac death~~do not benefit from reperfusion therapy and are at increased risk of ~~adverse long-term effects~~complications. The reasons for patients failing to attend emergency departments with acute coronary syndrome (and other urgent conditions) should be addressed urgently to avoid ~~further~~ unnecessary deaths and disability.

ABSTRACT

Background: Several countries affected by the COVID-19 epidemic have reported a substantial drop in the number of patients attending the emergency department with acute coronary syndromes (ACS), as well as a reduced number of cardiac procedures.

Methods: Analysis of data on hospital admissions in England for acute coronary syndrome recorded in the Secondary Uses Service Admitted Patient Care (SUSAPC) database.

Findings: Hospital admissions for ACS declined from ~~early March~~mid-February 2020, falling from a 2019 baseline rate of ~~about 3000~~ 3017 admissions per week to ~~about 1700~~ 17~~50~~67 per week by the end of March, a reduction of ~~46~~41% (95% CI 39%-~~ to ~~44%), but without any further decline ~~in the month of~~during April. ~~.~~There were reductions in the numbers of admissions for all types of ACS, including both ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), but the relative and absolute reductions were larger for NSTEMI. Admission rates for both STEMI and NSTEMI appeared to level off in April. Overall, there was a similar pattern of reduced admissions in different demographic groups, although there were slightly larger falls in those with a high burden of comorbidity, and in the London and East Midlands regions. ~~The percent reductions in ACS admission werere were larger in falls in the number of admissions of older people, those with a high burden of comorbidity, and in the those in the London and the East Midlands regionsregion.~~ In parallel, there were reductions in the numbers of percutaneous coronary intervention (PCI) procedures for both STEMI and NSTEMI, but the proportion of admitted patients who received PCI rose slightly, particularly on the day of admission among patients with NSTEMI. The median length of stay among patients with ACS halved from 4 to 2 days.

Interpretation: There has been a substantial reduction in the numbers of patients with myocardial infarction or other ACS who were admitted to hospital in England by early the end of April. This is likely to have resulted in increases in out-of-hospital death and long-term complications of myocardial infarction, and missed opportunities to offer secondary prevention treatment for patients with coronary heart disease. ~~Updated analyses will assess t~~The full extent of the impact of COVID-19 on patients with ACS will continue to be assessed by updating these analyses.

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INTRODUCTION

Worldwide, the COVID-19 pandemic has resulted in substantial excess ~~of~~ mortality arising directly from respiratory failure. In addition, it has necessitated major reorganisation of emergency care facilities to accommodate the additional workload ~~associated~~ anticipated with a rapid surge in critically ill patients with COVID-19. Cardiologists have reported substantial falls in the number of patients presenting with acute coronary syndromes (ACS), and in the numbers of emergency coronary procedures, ~~carried out~~ in both Europe (1-~~3~~4) and the US (~~4~~5,6).

The first fatality for COVID-19 in the UK was reported on 5 March 2020. On 16 March, the Prime Minister of the United Kingdom urged the introduction of social distancing measures, and on 23 March he announced a nationwide ‘lockdown’. The Health Protection (Coronavirus Restrictions) (England) Regulations 2020 which came into force on 26 March severely restricted movement among all citizens, although it still allowed people to leave their homes for essential reasons, including seeking healthcare. Analyses by Public Health England show that there has been about a 30% reduction in emergency ambulance calls for chest pain (~~5~~7) and a greater than 50% reduction in emergency department attendances for myocardial ischaemia (~~6~~8) in England, and surveys of cardiologists in the UK and elsewhere have suggested a substantial reduction in demand for coronary procedures (~~7~~9). On 20 March, the British Cardiovascular Intervention Society issued guidance on measures ~~to take~~ to address the potential impact of COVID-19 on cardiology services (~~8~~10).

In order to understand the scale, nature and duration of changes to admissions for different types of acute coronary syndrome (ACS), and to evaluate whether in-hospital management of these patients was also affected as a result of the pandemic, we sought data on all such admissions to National Health Service (NHS) acute hospital trusts in England from January 1, 2019. We used the Secondary Uses Service Admitted Patient Care (SUSAPC) database because it is updated more rapidly than the Hospital Episodes Statistics (HES) database. It is intended that analyses will be revised monthly and made available at https://www.ctsu.ox.ac.uk/research/covid-19-acute-coronary-syndromes in order to provide an updated summary of changes in such admissions as the response to the COVID-19 pandemic evolves over time.

METHODS

All episodes of care for patients admitted to acute NHS hospital trusts in England with ACS, defined using the International Classification of Diseases 10th revision (ICD-10) codes (11~~98~~), from 1 January 2019 to ~~27~~ 22 May~~April~~ 2020 were identified in the SUSAPC database (see Supplementary Methods). These admissions were classified as STEMI, NSTEMI, MI of unknown type, unstable angina or other acute ischaemic heart disease according to the recorded ICD-10 codes.

To prevent over-counting of ACS events, episodes of care for each person were linked into continuous single hospital admissions (spells) and spells linked between hospitals (superspells). Revascularisation procedures – percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery – undertaken during these admissions were identified from relevant Office of Population Censuses Surveys Classification of Surgical Operations and Procedures 4th revision (OPCS4) (12~~0~~) codes (Supplementary Table 2). It is not possible to identify primary PCI in the SUSAPC data, so PCI on the day of admission was used as a surrogate for primary PCI among STEMI patients. ~~Whilst most NHS hospital trusts submit SUSAPC data to NHS Digital on a monthly basis, a sensitivity analysis examined the effect in a smaller number of 'rapid response' trusts that report data more frequently.~~

As a result of service reorganisation in response to COVID-19 (10~~8~~), there may have been a reduction in the speed and completeness of clinical coding, which could result in artefactual reductions in ACS-related admissions (particularly in the most recent data). For each week after 17 February 2020, this was investigated by ascertaining the proportion of all SUSAPC records recorded in each week that contained no diagnostic ICD-10 codes, and~~. A~~ an adjustment was made to the numbers of recorded admissions for ACS each week based on these proportions~~, and an additional adjustment was made in the most recent week to account for reduced numbers of trusts submitting data after 31~~ 30 April~~March 2020 (see Supplementary methods)~~.

In all analyses of admission numbers, data are presented for 2019 as a median and interquartile range of the weekly recorded numbers. For 2020, a local polynomial regression (LOESS) smoothing function was fitted through the weekly numbers (using the '~~loess–~~loess' function in R with default settings). From ~~the week commencing 17 February~~ 2020, the weekly adjusted numbers (indicating the number of admissions in the preceding 7 days) are also plotted along with their approximate standard errors (under the assumption that the count data follow a Poisson distribution). Percentage changes in weekly admissions were calculated by comparing the adjusted weekly admission number for the week commencing 23 March 2020, the first week following the 'lockdown', with the mean weekly number during 2019 and are presented with their 95% Confidence Intervals (C~~i~~Is). The percentage changes in weekly admissions among particular subgroups were calculated similarly, with tests for heterogeneity across each subgroup presented. ~~Since data were available for the entire population of acute trusts in England, the recorded numbers of admissions in each week are not subject to sampling variation (hence, no confidence intervals were calculated or hypothesis-testing procedures used).~~ Monthly updates of the tables and figures are available online. Analyses were produced using R version 3.6.3.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication.

RESULTS

SUSAPC data were available from all 147 acute NHS hospital trusts in England~~, including 21 ('rapid response') trusts that provide weekly returns.~~. The demographic characteristics of patients with ACS remained stable during 2019 (data not shown) but, as compared to earlier months, the ~~after February 2020, the~~ patients admitted with ACS after February 2020 were younger and had fewer comorbid conditions (Table 1). In 2019, the average number of ACS admissions per week during February to April (3082 per week) was similar to the average number during the other months of the year (2994 per week).

After adjusting for the effects of ~~delayed submission~~incomplete coding of clinical data from trusts (see Supplementary appendix), there was a 4~~6~~1% (95% CI 39% -~~-to~~ 44%) reduction in hospital admissions for ACS ~~by~~ between mid-February and the end of March 2020 (Figure 1 and Table 2), with the 2019 baseline rate of ~~3053~~ 3017 admissions per week falling to ~~1649~~ 1767 per week,~~.~~ ~~Among the subset of 21 rapid response trusts, there was a similar 45% reduction in weekly admissions (692 admissions per week to 383 admissions per week) for ACS (Supplementary Figure 2). In both analyses, the available data from April indicated~~with no further decline during ~~that month~~April in all ACS admissions combined (Figure 1).

Considered separately, there were reductions in the numbers of admissions for all acute MI, STEMI, and NSTEMI during this period (Figure 1 and Table 2), with a reduction ~~in hospital admissions~~ of ~~42~~37% (95% CI 33% -~~-to~~ 40%; 20~~61~~75 per week to 12~~99~~05 per week) ~~in~~ for all acute MI, ~~26~~25% (95% CI 18% -~~-to~~- 31%; 621 per week to 4~~67~~58 per week) ~~in~~for STEMI~~ admissions~~, and 4~~4~~9% (95% CI 39% ~~to~~-- 48%; 12~~67~~79 per week to ~~714~~650 per week) ~~in~~ for NSTEMI~~ admissions~~. The admission rate for both STEMI and NSTEMI levelled off during April (Figure 1).

The 25% reduction in admissions for STEMI was accompanied by a slight rise in the proportion of those admitted to hospital receiving PCI ~~either~~ on the day of admission (Figure 2); as a consequence there was a reduction of 20% (95% CI 10 – 28%; 379 per week to 3~~41~~04 per week) in the absolute numbers of STEMI patients receiving PCI on the day of admission (Figure 3 and Table 2). T~~Since~~ the 44% reduction in NSTEMI admissions was accompanied by a slight increase in the proportion ~~of admitted patients~~ who received PCI at any time during the admission (Supplementary Figure ~~2~~1, Table 2), which translated into~~overall there was~~ a reduction of 38% (95% CI 30 – 45%; 38~~3~~4 per week to 2~~28~~38 per week) in the absolute numbers receiving PCI~~during the admission~~. ~~For NSTEMI, there was no change in the proportion receiving a PCI on the day of admission as compared to the 2019 average. There was a reduction of 1720% (95% CI 10% -to 28%); 379 379 per week to 341 304 per week) in the absolute numbers of STEMI patients receiving PCI on the day of admission (Figure 2 and Table 2), with a slight rise in the proportion of those admitted to hospital receiving PCI either on the day of admission or at any time (Supplementary Figures 3 and Supplementary Figure 24). For patients with NSTEMI, there was a reduction of 3238% (95% CI 30% -to 45%; 334 384 per week to 2328 per week) in the absolute numbers receiving PCI, but both the number and proportion of those admitted with NSTEMI who received PCI on the day of admission increased (Figures Figure 2 3and Supplementary Figure 3).~~ For all types of ACS combined, there was a ~~61~~60% (95% CI 54% ~~–~~-~~to~~ 66%; ~~414~~ 429 per week to ~~161~~ 170 per week) reduction in the absolute numbers of patients having angiography without revascularisation, and CABG surgery during the admission largely ceased (Figure ~~2~~ 3 and Table 2).

By the end of April, ~~T~~the median length of stay among patients admitted with any ACS fell from ~~a median of~~ 4 (interquartile range [IQR] 2 ~~–~~-~~to~~ ~~8~~9) days to 2 (1-~~to~~ ~~3~~4) days (Supplementary Figure ~~5~~2): for STEMI the reduction was from 3 (2-~~to~~ 6) days to 2 (~~1~~2-~~to~~ 3) days, whilst for NSTEMI ~~the reduction~~it was from 5 (3-~~to~~ ~~10~~11) days to ~~2~~ 3 (~~1~~2–~~to~~ 4) days. There was no apparent change in in-hospital mortality among patients ~~who were~~ admitted with ACS (data not shown).

The relative reductions in weekly numbers of admissions for ACS were qualitatively similar in all of the subgroups studied, but they appeared slightly ~~was bigger~~ larger among ~~older people and among~~ those with higher (that is, a worse) Charlson comorbidity index and for those in the London and East Midlands regions (Supplementary Table 3 and Supplementary Figure 3). ~~The relative and absolute reduction in weekly admissions for ACS was largest in the London region (Figure 4 and Supplementary Table 3).~~

DISCUSSION

Previous reports of reduced admission rates for ACS and the use of coronary procedures in various countries affected by the COVID-19 pandemic have indicated that the phenomenon is widespread. However, those reports have been limited in detail (1-6): in particular, only one study (6) ~~has~~ reported the time course of the changes in admission rates, and there has been limited information about the relative impact on different types of ACS, the acute management of patients admitted with ACS, and the relevance of patient characteristics. By contrast, in the present study, unique access to rapidly available central NHS healthcare data has allowed us to produce near “real time” analyses based on all admissions for ACS in all 147 acute hospitals across England that can address all of these points and, in addition, will be able to follow the emerging trends over time as the response to COVID-19 evolves (eg, with easing of restrictions and any recurrent outbreaks of infection).

Our study has provided several key insights into the observed reduction in admissions for ACS. First, between the middle of February and the first week of April 2020, the number of ACS admissions fell by about a half, with the decline stabilising during April. It is of note that the decline appears to have commenced at least 2 weeks before the first UK death from COVID-19, and about a month before the UK Government implemented a ‘lockdown’. This finding is consistent with a report based on US Kaiser Permanente Northern California, which indicated that the reduction in acute MI admissions preceded the ‘shelter-in-place’ order by about 2 weeks.(6)

By mid-February 2020, UK media were reporting the spread of coronavirus in China and (closer to home) in Northern Italy, and NHS hospitals had been told to prepare for a large influx of patients with COVID-19. As early as February 14th, it was noted that ‘fear-inducing language’ was breeding fear and panic (13). Taken together with survey data from Hong Kong that patients delayed seeking medical help due to a fear of acquiring COVID-19 (14), it seems likely that fear of contagion has been a major factor underlying the observed reduction in admissions for ACS in our study. In particular, the fact that the decline in admissions preceded the UK lockdown and, despite the lockdown, is now levelling off (7), suggests that environmental changes (eg reduced air pollution), ~~the adoption of healthy behaviours (eg increased exercise),~~ reduced physical activity, or reduced stress due to lockdown are unlikely to be major contributors to the decline in ACS admissions in the current pandemic (15,16).

~~Secondly~~A second novel finding in our analyses is the~~, we were able to demonstrate a~~ clear distinction between the reduction of~~patterns observed for STEMI admissions, which declined by~~ about one quarter in STEMI admissions compared to the reduction of about one half in~~, and for~~ NSTEMI admissions~~, which declined by about one half~~. Our analyses in an unselected study population are based on much larger numbers of admissions than any previous study, some of which observed a smaller reduction for STEMI than for NSTEMI (Italy)(3) while others did not detect a difference in the~~observed similar~~ reductions for ~~each~~different types of MI (in Austria and Northern California) (1,6). As STEMI is generally associated with severe and unremitting symptoms, patients may well be ~~more likely~~less reluctant to seek help irrespective of any fears they may have about attending a hospital, whilst those with NSTEMI may be able to tolerate less severe symptoms and so opt to remain at home.

Thirdly, we were able to document how the acute management of admitted patients changed during the pandemic period. In preparation for the COVID-19 pandemic, UK cardiology services were reorganised such that elective PCI and CABG would not be available routinely during the outbreak. Instead, it was recommended that, if current NSTEMI pathways could not be followed due to reduced intensive care unit capacity or other issues, PCI should be used in place of surgery and in-patient stays ~~should be~~ reduced to 36-48 hours (10~~7~~). Consistent with these recommendations, our results show that patients admitted with NSTEMI were more likely to receive PCI whilst in hospital (often on the day of admission) and to have shorter hospital stays. However, as the numbers of patients admitted with both NSTEMI and STEMI were reduced, fewer ACS patients actually received PCI.

Finally, the large numbers of cases and the national coverage of the data, allowed us to show that the pattern of reduced admissions was qualitatively similar (albeit slightly different quantitatively) in a number of important demographic groups. For example, despite the greater risk with COVID-19 among older patients and those with comorbidities, there were similar reductions in the numbers of ACS cases admitted at younger ages and without comorbidities in whom the long-term benefits of cardiovascular interventions would typically be greater. Likewise, despite different COVID-19 admission rates across the UK during the early phase of the pandemic, there was little difference in the reduction in ACS admissions between different regions. This consistency suggests that the ~~explanation~~drivers of ~~for~~ the observed fall in admissions ~~is~~are likely to be common – to a greater or lesser extent – to all patient groups.

Taken together, this~~ese~~ substantial reduction~~s~~ in admissions for ACS during the pandemic is a serious concern since all patients with symptoms indicative of acute myocardial ischaemia would benefit from rapid in-hospital assessment (1~~8~~7,1~~9~~8), with the gain being greatest among those with STEMI. Among such patients, there is a substantial risk of out of hospital cardiac arrest (~~20~~19), and the failure of patients with STEMI to be admitted to hospital in order to receive early reperfusion therapy and other appropriate treatments is likely to have resulted in avoidable deaths and complications, such as fatal arrhythmias (2~~1~~0) and disabling heart failure (2~~2~~1). Although no overall increase in mortality was observed among those patients who were admitted for ACS, a direct comparison between mortality rates before and after mid-March is likely to be confounded by differences in their underlying risk and by the duration of hospital stay. Moreover, it is not possible to assess directly the deaths and disability that are likely to have occurred among those patients with ACS who were not admitted to hospital~~,~~ and so did not receive treatment that is known to be effective~~, as a consequence of their response to the COVID pandemic~~.

What are the implications of our findings for the UK and other countries, including those in which the pandemic is only just starting, and how can they help inform preparations for any subsequent increases in infection rates when lockdown restrictions are relaxed? The findings ~~replicate~~confirm the general pattern ~~observed in less detail in~~ reporteds from other countries ~~during the COVID-19 outbreak~~. However, our demonstration of the qualitative similarity of the falls in ACS admission rates largely irrespective of age, sex, number of comorbidities and region suggest that the findings are likely to be generalisable to all patients who are having an acute MI, not just in the UK (e.g. in the event of recurrent ~~waves~~outbreaks -of ~~the pandemic~~infection) but also elsewhere in the world, unless appropriate measures are taken to avoid it recurring. If the reduction in hospital admissions is largely or wholly due to fear of coronavirus exposure, it seems likely the same phenomenon will be observed wherever there is a rapid increase in COVID-19 cases and public health messaging is not suitably nuanced. Regular updates of the present analyses will allow the success of interventions to reverse these adverse admission trends to be tracked, ~~and can be used as an early warning of a recurrence~~including during ~~in~~ any future outbreak. More generally, i~~I~~t would be valuable to establish similar continuous analyses for other serious conditions in the UK, as well as elsewhere where centralised electronic health record data are available (such as China or Sweden, or in US health maintenance organizations), to monitor ~~these~~such trends to ensure that they reverse and do not recur during ~~the next phase of~~ this pandemic (or, indeed, any subsequent ones).

Our study is subject to some limitations. SUSAPC data are timely but incomplete, with some trusts not having submitted any admissions data for the most recent week and, for a longer period, some trusts having~~e~~ recorded admissions without a diagnostic code. Such~~Both forms of~~ omissions will tend to ~~artefactually~~ exaggerate artefactually the depth of the decline in ACS admissions (particularly in the more recent weeks). We have addressed this issue by applying an adjustment (see Supplementary appendix), and validated our approach by showing that the adjusted results are consistent with unadjusted results for those Trusts that do report complete data frequently. This comparison suggests that our approach to adjustment is likely to be generalizable to the study of time trends for other serious conditions.

A further potential limitation is that the coding of STEMI and NSTEMI was inferred from ICD-10 codes, which may suffer from some inaccuracy. Our results provided a clear contrast between the rates of admission for, and management of, STEMI and NSTEMI that have been diagnosed and coded in much the same way throughout 2019 and into early 2020 versus after mid-March. Consequently, any bias in the comparison of the ACS rates due to misclassification of STEMI and NSTEMI is likely to be modest (other than due to late reporting in the most recent weeks) and, if removed, would yield even more striking differences between the rates for STEMI and NSTEMI. A further limitation is that the SUSAPC data do not allow assessments to be made of any delays in admissions from the onset of symptoms of ACS or of any impact on the rates of complications in the MI cases admitted.

Although there is now a national campaign to encourage all people experiencing symptoms of acute myocardial ischaemia to call an ambulance immediately, it has not addressed the public's fear that they might contract COVID-19 by going to hospital. In order address these concerns, all hospitals need to provide relatively clean areas for patients who do not have COVID-19 and the public needs to be made aware that this is the case. Otherwise, people may continue to be reluctant to call an ambulance, even if experiencing severe symptoms, resulting in unnecessary deaths and disability.

~~Between the middle of February and the first week of April 2020 the number of admissions for ACS in England fell by about a half, with a decline of about one quarter in STEMI admissions and of about one half in NSTEMI admissions. There were larger reductions in ACS admissions among the elderly and those with a higher burden of comorbidity and in London.~~

~~These changes are a serious concern since all patients with symptoms indicative of acute myocardial ischaemia would benefit from rapid in-hospital assessment (11,12), with the gain being greatest among those with STEMI. Among such patients, there is a substantial risk of out of hospital cardiac arrest (13), and the observed failure of patients with STEMI to be admitted to hospital for early reperfusion therapy and other appropriate treatment is likely to have resulted in otherwise avoidable deaths and complications, such as fatal arrhythmias (14) and heart failure (15).~~

~~In preparation for the COVID-19 pandemic, cardiology services were reorganised such that elective PCI and CABG would not be available during the emergency. It was recommended that, if current NSTEMI pathways could not be followed due to reduced intensive care unit capacity or other issues, PCI should be used in place of surgery and in-patient stays should be reduced to 36-48 hours (8). Consistent with the recommended changes, our results show that patients admitted with NSTEMI~~

~~were more likely to receive PCI whilst in hospital (often on the day of admission) and to have shorter stays in hospital. However, as there was a large reduction in the numbers of patients admitted with NSTEMI, far fewer actually received PCI.~~

~~No overall increase in mortality was observed among those patients who were admitted for ACS, but a direct comparison between mortality rates before and after mid-March is likely to be confounded by differences in their underlying risk (with, for example, a smaller proportion being aged over 70 or having pre-existing comorbidities; Table 1) and by the duration of hospital stay. Moreover, it is not possible to assess directly the deaths and disability that are likely to have occurred among patients with ACS who were not admitted to hospital, and did not receive treatment that is known to be effective, as a consequence of the response to the COVID pandemic.~~

~~The chief difficulty in these analyses is that some trusts have not submitted any admissions data for the most recent week and, for a longer period, some trusts have recorded admissions but not given a diagnostic code. Both forms of omission will artefactually exaggerate the depth of the decline in ACS admissions (particularly in the more recent weeks), so an adjustment was applied in order to make allowance for this phenomenon (see Supplementary appendix). These adjusted results are consistent with unadjusted results for those Trusts reporting data frequently; regularly updated analyses will help improve the adjusted analyses, and assess the full extent of the impact of the COVID-19 epidemic on patients with ACS. Limited detail about ACS admissions is available in the SUSAPC data, so these analyses are unable to report on complications of MI or delays in admissions from the onset of symptoms. The results provide a clear contrast between the rates of admission for, and management of, STEMI and NSTEMI that are likely to have been diagnosed and coded in much the same way throughout 2019 and into early 2020 versus after mid-March, and are consistent with findings from recent survey in Italy (16). Consequently, any bias in the rates of ACS due to misclassification of STEMI and NSTEMI is likely to be modest (other than due to late reporting in the most recent weeks) and, if removed, would yield even more striking differences between the rates for STEMI and NSTEMI.~~

~~It has been suggested (17,18) that this decline in admissions for ACS might be due, at least in part, to environmental or behavioural changes as a consequence of lockdowns. However, our analyses show that the sudden reduction in ACS admissions pre-dated the lockdown by about 3 weeks. Moreover, analyses of emergency attendances suggest that the numbers of patients who are presenting with ACS has increased during April despite the lockdown continuing (6). Consequently, the chief reason for this phenomenon seems likely to be that many patients with symptoms of ACS have not sought immediate medical help during the pandemic period.~~

~~There is evidence from Hong Kong that patients delay seeking medical help due to a fear of acquiring COVID-19, despite the fact that the immediate risks of CHD far exceed those of COVID-19 (19). So, although there is now a national campaign to encourage all people experiencing symptoms of acute myocardial ischaemia to call an ambulance immediately, it has not addressed the public's fear that they might contract COVID-19 by going to hospital. In order to provide reassurance on this point, it will be necessary to ensure that all hospitals provide relatively clean areas for patients who do not have COVID-19. Until this happens, people may continue to be reluctant to call an ambulance, even if experiencing severe symptoms, leading to unnecessary deaths and disability.~~

Author contributions and declaration of interests

All the authors contributed to study design, data interpretation and preparation of the report. Data were processed for analysis by DG, PC, SH, MB, CR. Statistical analysis was done by ES and RG. The first three authors made equal contributions, as did the last three authors.

BC is the Current President of the European Society of Cardiology (2018-20), a British Heart Foundation Chair-holder and the Lead of the Cardiovascular Theme of the Oxford NIHR Biomedical Research Centre. RC is a British Heart Foundation Chair-holder, and reports personal fees from UK Biobank, grants from Merck & Co, grants from Medicines Company (now Novartis), other from Pfizer, outside the submitted work; in addition, RC has a patent for a statin-related myopathy genetic test licensed to University of Oxford from Boston Heart Diagnostics (RC has waived any personal reward). MJL reports grants from Medical Research Council Population Health Research Unit, grants from Health Data Research UK, grants from National Institute for Health Research Oxford Biomedical Research Centre, during the conduct of the study; grants from Merck Sharp & Dohme, grants from The Medicines Company, grants from Boehringer Ingelheim, grants from UK Biobank outside the submitted work. MMM reports grants from Medco/Novartis, outside the submitted work. JE and CB report grants from Boehringer Ingelheim, outside the submitted work. ES, RG, DG, PC, MB, SH, RR, CPG, MAM, JED, MAdeB, TFL, TD, and EJAM have nothing to disclose.

FIGURE LEGENDS

Monthly updates of all Figures and Supplementary figures are available at https://www.ctsu.ox.ac.uk/research/covid-19-acute-coronary-syndromes

Figure 1: Weekly numbers of admissions with an acute coronary syndrome, by type

For weekly admissions in 2019, the boxplot shows the median and interquartile range (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartile, with any weekly counts beyond those ranges indicated by an ‘x’. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the ~~adjusted~~ data points and standard errors ~~after 23 February also~~ plotted. The red lines/points represent unadjusted reported counts and the black lines/points represent the counts adjusted for incomplete coding. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction.

~~Symbols and conventions as for Figure 1.~~

Figure 2: (a) Weekly numbers and (b) weekly proportions of admissions with an acute coronary syndrome that received PCI on the day of admission ~~Figure 3: Weekly number of admissions with an acute coronary syndrome, by age, sex, Charlson index, ethnicity and region~~

For weekly admissions in 2019, the boxplot shows the median and interquartile range (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartile, with any weekly counts beyond those ranges indicated by an ‘x’. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the data points and standard errors plotted. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = Percutaneous coronary intervention.

Figure 3: Weekly numbers of admissions with an acute coronary syndrome that received a particular coronary procedure

For weekly admissions in 2019, the boxplots show~~s~~ the median and interquartile ranges (IQR), with the whiskers extending (up to) 1.5 times the IQR above the upper quartile and below the lower quartiles, with any weekly counts beyond those ranges indicated by an ‘x’. For 2020, a LOESS smoothing spline is fitted through the weekly reported counts, with the data points and standard errors plotted. The date of the UK COVID-19 lockdown (23 March 2020) is shown with a vertical dotted line. ACS = acute coronary syndrome; CABG = Coronary artery bypass graft; MI=myocardial infarction; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = Percutaneous coronary intervention.

~~Symbols and conventions as for Figure 1.~~

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***Table 1*: Characteristics over time of patients admitted to an English acute trust with a diagnosis of any acute coronary syndrome (Jan 2019 to ~~April~~ April 2020)**

		Monthly average for 2019		2020							
				January		February		March		April	
Gender	Female	4829	(37)	5126	(38)	4458	(36)	3585	(36)	2421	(34)
	Male	8244	(63)	8502	(62)	7821	(64)	6296	(64)	4628	(65)
Age group	<50	953	(7)	1051	(8)	945	(8)	748	(8)	610	(9)
	50-59	2082	(16)	2152	(16)	1986	(16)	1659	(17)	1286	(18)
	60-69	2723	(21)	2817	(21)	2528	(21)	2153	(22)	1580	(22)
	70-79	3353	(26)	3551	(26)	3143	(26)	2502	(25)	1733	(24)
	80+	3963	(30)	4058	(30)	3680	(30)	2826	(29)	1886	(27)
Ethnic group	White	10312	(79)	10665	(78)	9610	(78)	7678	(78)	5508	(78)
	Mixed	58	(0)	65	(0)	71	(1)	42	(0)	31	(0)
	Asian	956	(7)	998	(7)	882	(7)	669	(7)	438	(6)
	Black	196	(2)	203	(1)	175	(1)	146	(1)	114	(2)
	Other/Unknown	1552	(12)	1698	(12)	1544	(13)	1353	(14)	1004	(14)
Charlson Index	0	3933	(30)	4033	(30)	3616	(29)	3093	(31)	2383	(34)
	1	3591	(27)	3710	(27)	3452	(28)	2859	(29)	2039	(29)
	2	2180	(17)	2335	(17)	2084	(17)	1635	(17)	1107	(16)
	3+	3370	(26)	3551	(26)	3130	(25)	2301	(23)	1566	(22)
Region of acute admission	North East	705	(5)	700	(5)	690	(6)	550	(6)	420	(6)
	North West	2050	(16)	2200	(16)	1915	(16)	1605	(16)	1180	(17)
	Yorkshire & Humber	1510	(12)	1635	(12)	1435	(12)	1225	(12)	860	(12)
	East Midlands	1060	(8)	1115	(8)	1005	(8)	825	(8)	585	(8)
	West Midlands	1380	(11)	1395	(10)	1285	(10)	1030	(10)	810	(11)
	East of England	1380	(11)	1400	(10)	1375	(11)	1000	(10)	605	(9)
	London	1720	(13)	1800	(13)	1640	(13)	1235	(12)	900	(13)
	South East	1750	(13)	1850	(14)	1550	(13)	1295	(13)	935	(13)
	South West	1520	(12)	1535	(11)	1385	(11)	1125	(11)	795	(11)
Total		13074	(100)	13629	(100)	12282	(100)	9888	(100)	7095	(100)

The number of admissions shown are unadjusted for incomplete coding ~~and delayed reporting~~ (see supplementary methods). ~~The number of hospital trusts contributing data for April is limited.~~ Regional numbers are rounded to the nearest multiple of 5. Values shown are n (%). Percentage changes in admission rates for each subgroup are provided in Supplementary Table 3.

Table 2: **Percent reduction in weekly acute coronary syndrome admissions across all English acute trusts, from the average number of weekly admissions seen in 2019 to the number of admissions in the week commencing 23 March 2020**

	All admissions	Receiving particular coronary procedures: With any PCI	With PCI on day of admission	With PCI after day of admission	With CABG	With angiography only
ACS						
2019 weekly average	3017~~3053~~	909~~848~~	464~~469~~	450~~382~~	93~~56~~	429~~414~~
23-30 March 2020	1767~~1649~~	624~~623~~	387~~406~~	238~~217~~	18~~8~~	170~~161~~
Percent reduction (95% CI)	41 (39, 44)~~46~~	31 (26, 37)~~27~~	17 (8, 25)~~14~~	47 (40, 53)~~43~~	81 (69, 88)~~86~~	60 (54, 66)~~61~~
Acute MI						
2019 weekly average	2061~~2075~~	834~~779~~	453~~457~~	386~~325~~	80~~49~~	306~~293~~
23-30 March 2020	1299~~1205~~	587~~586~~	375~~392~~	211~~193~~	16~~8~~	137~~127~~
Percent reduction (95% CI)	37 (33, 40)~~42~~	30 (24, 35)~~25~~	17 (8, 25)~~14~~	45 (37, 52)~~41~~	80 (67, 88)~~84~~	55 (47, 62)~~57~~
STEMI						
2019 weekly average	621~~621~~	438~~433~~	379~~379~~	63~~57~~	16~~11~~	49~~49~~
23-30 March 2020	467~~458~~	340~~349~~	304~~314~~	37~~35~~	4~~2~~	33~~32~~
Percent reduction (95% CI)	25 (18, 31)~~26~~	22 (14, 30)~~19~~	20 (10, 28)~~17~~	41 (19, 58)~~39~~	75 (33, 91)~~80~~	33 (5, 52)~~35~~
NSTEMI						
2019 weekly average	1267~~1279~~	384~~334~~	67~~71~~	317~~263~~	63~~36~~	245~~233~~
23-30 March 2020	714~~650~~	238~~228~~	67~~73~~	170~~154~~	12~~6~~	97~~89~~
Percent reduction (95% CI)	44 (39, 48)~~49~~	38 (30, 45)~~32~~	0 (-27, 21)~~-3~~	46 (38, 54)~~41~~	81 (66, 89)~~84~~	60 (52, 68)~~62~~

ACS=Acute coronary syndrome, MI=Myocardial infarction, PCI=Percutaneous Coronary Intervention, STEMI=ST elevation myocardial infarction, NSTEMI=Non ST elevation myocardial infarction

Figure

Figure 1

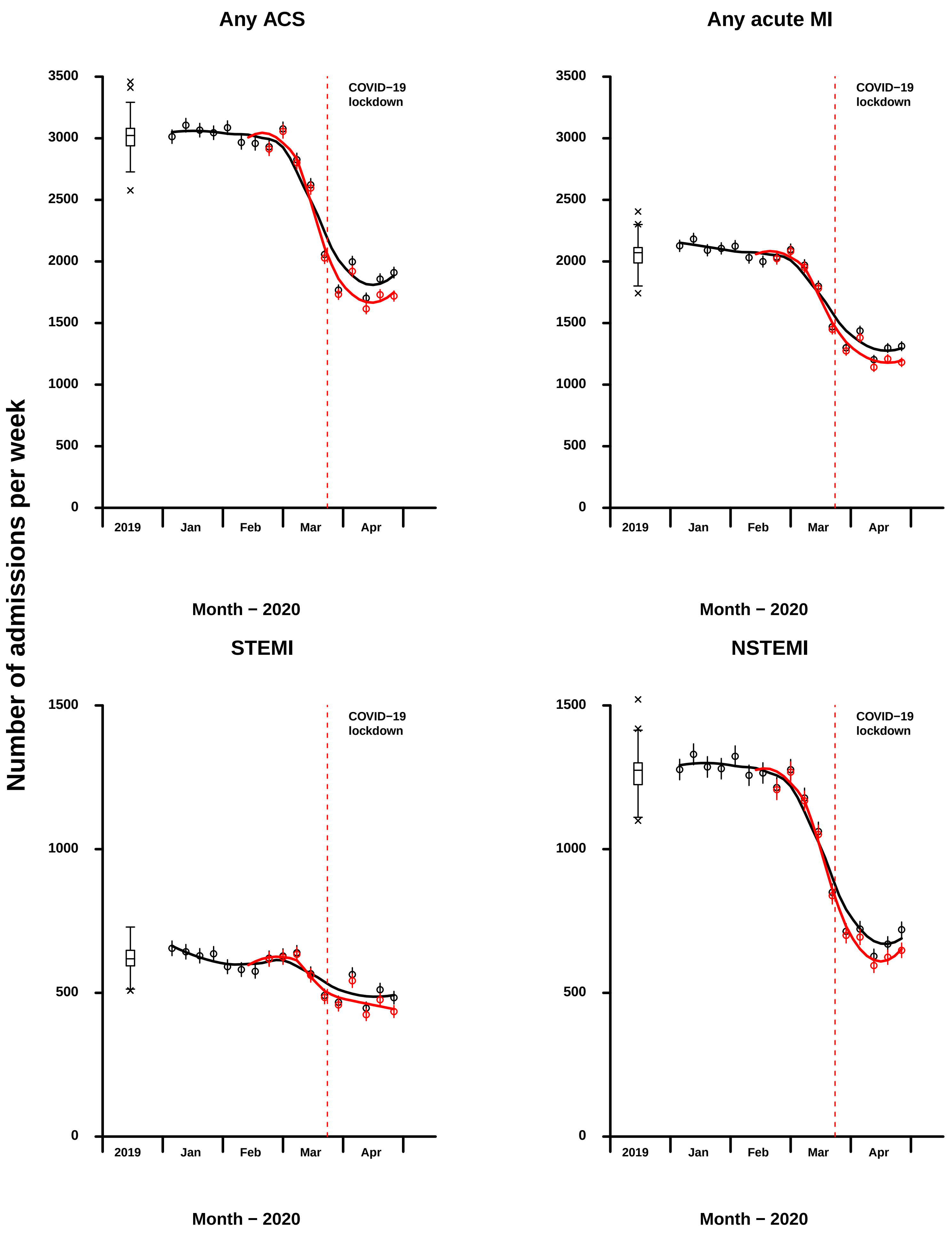


Figure 2

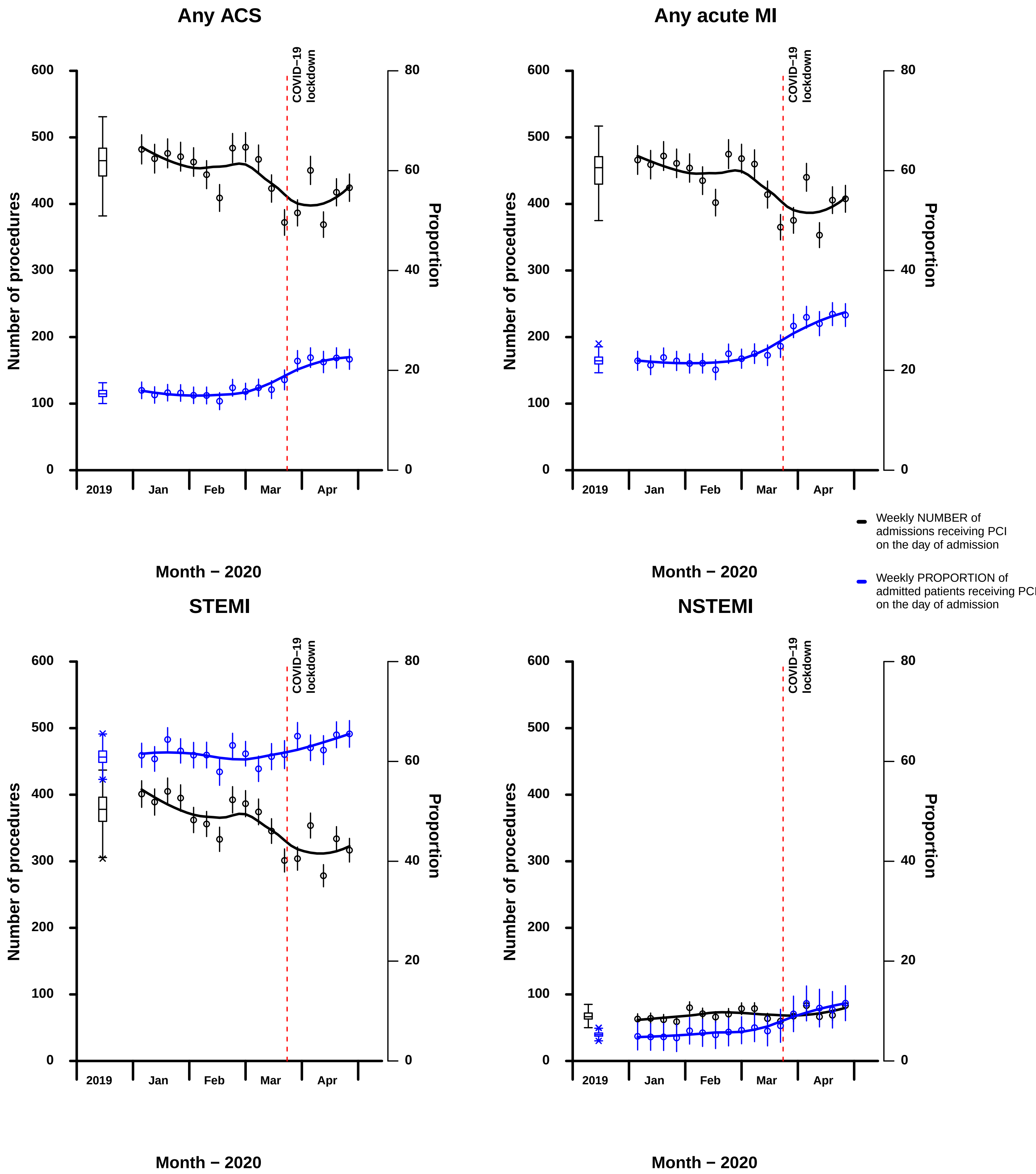
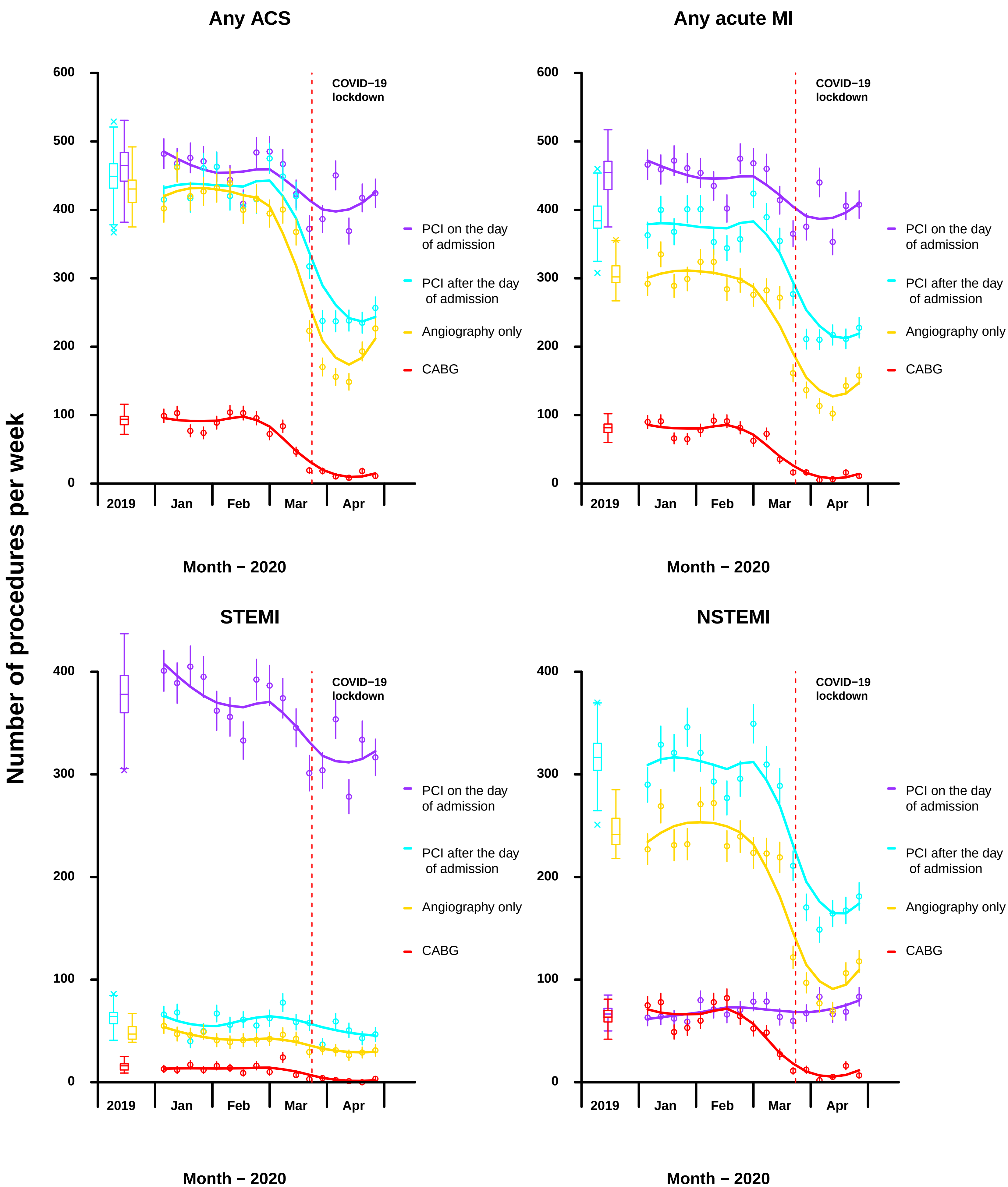

Any ACS
Any acute MI
STEMI
NSTEMI
Number of procedures
Proportion
COVID−19 lockdown
2019
Jan
Feb
Mar
Apr
Month − 2020
Weekly NUMBER of admissions receiving PCI on the day of admission
Weekly PROPORTION of admitted patients receiving PCI on the day of admission

Figure 3



Any ACS
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PCI on the day of admission
PCI after the day of admission
Angiography only
CABG
2019
Jan
Feb
Mar
Apr
Month − 2020
0
100
200
300
400
500
600

Responses to editorial and reviewers' comments

THELANCET-D-20-10305, Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England

Please note: Revised responses for the current version of the manuscript (R3) are shown as highlighted text.

Editorial points - IMPORTANT

The following points list items that must be included before a manuscript can be considered further. Addressing them at this stage reduces the risk of errors and delays later.

Journals differ in requirements for revisions, so please read the requests below carefully and consult me or http://www.thelancet.com/lancet/information-for-authors for further details or clarification if needed.

Additional tips on artwork are available at http://www.thelancet.com/pb/assets/raw/Lancet/authors/artwork-guidelines.pdf

If your manuscript is a RCT, Formatting guidelines are available at http://www.thelancet.com/pb/assets/raw/Lancet/authors/Rctguidelines.pdf

Please note that not every point below will be relevant to your manuscript.

1. Please indicate after each of the reviewers' points the text changes which have been made (if any) and the line number on the revised manuscript at which your change can be found. [Line numbers can be added to your word document using the 'page layout' tab. Please select continuous numbers.]

Response: done.

2. When interpreting editorial points made by reviewers, please remember we will edit the final manuscript if accepted.

Response: noted.

3. Please indicate any authors who are full professors.

Response: done.

4. Please list the highest degree for each author (one degree only, please).

Response: done

5. Please check that all author name spellings and affiliations are correct.

Response: done

6. For randomised trials please follow the CONSORT reporting guidelines (http://www.consort-statement.org) and CONSORT for abstracts (http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(07)61835-2/fulltext), and include a CONSORT checklist with your resubmission.

Response: not applicable since the study was not a randomised trial.

7. Please ensure that the title of the paper is non-declamatory (ie, it describes the aim of study rather

than the findings) and that it includes a description of the study type (eg, a randomised controlled trial).

Response: done.

8. Please limit the summary to pre-defined primary endpoints and safety endpoints.

Response: done

9. For RCTs, please state the trial registration number.

Response: not applicable.

10. At the end of the methods section please state the role of the funder in: data collection, analysis, interpretation, writing of the manuscript and the decision to submit. Please also state which author(s) had access to all the data, and which author(s) were responsible for the decision to submit the manuscript etc.

Response: done.

11. Please explain any deviations from the protocol.

Response: There was no formal protocol for this study. The study was performed by designing the required format of the download from SUSAPC data, and then analysing those data.

12. Please report all outcomes specified in the protocol.

Response: not applicable.

13. If any exploratory outcomes are reported that were not pre-specified, please make it clear that these analyses were post-hoc.

Response: not applicable.

14. Please use rINNs for drug names. For genes and proteins, authors can use their preferred terminology so long as it is in current use by the community, but should provide the preferred human name from Uniprot (http://www.uniprot.org/uniprot/) for proteins and HUGO (http://www.genenames.org) for genes at first use to assist non-specialists.

Response: not applicable.

15. For drug studies, please ensure that details of doses, route of delivery, and schedule are included.

Response: not applicable.

16. For the main outcome measures, please include a result for each group, plus a point estimate (eg, RR, HR) with a measure of precision (eg, 95% CI) for the absolute difference between groups, in both the Summary and the main Results section of the paper.

Response: done.

17. p-values should be exact, but no longer than 4 decimal places (eg p<0.0001). Two decimals are acceptable in tables for non-significant p-values

Response: done.

18. Please provide absolute numbers to accompany all percentages. Percentages should be rounded to whole numbers unless the study population is very large (>10 000 individuals).

Response: done.

19. Please give 95% confidence intervals for hazard ratios/odds ratios.

Response: done.

20. For means, please provide standard deviation (or error, as appropriate).

Response: done.

21. Please provide interquartile ranges for medians.

Response: done

22. Please provide numbers at risk for Kaplan-Meier plots and ensure that plots include a measure of effect (eg, log-rank p); estimates should be reported with 95% CIs.

Response: not applicable.

23. Please ensure that the Discussion contains a section on limitations of the study.

Response: done.

24. Please provide the text, tables, and figures in an editable format. See link above this list for details of acceptable formats for figure files.

Response: done

25. Our production system is not compatible with Endnotes. Please convert to normal text.

Response: done.

26. If accepted, only 5-6 non-text items (figures, tables, or panels) can be accommodated in the print edition; additional material can be provided in a web appendix. Please indicate which items can go in a web appendix.

Response: done.

27. Please provide a research in context panel with 3 parts: Evidence before this study (which includes a description of how you searched for evidence and how you assessed the quality of that evidence); Added value of the study; and Implications of all the available evidence.

Response: done.

28. At the end of the manuscript, please summarise the contribution of each author to the work.

Response: done

29. At the end of the manuscript please summarise the declaration of interests for each author.

Response: done

30. If you have not yet done so, please return all signed authorship statements and conflict of interest forms. We also require signed statements from any named person in the acknowledgements saying that they agree to be acknowledged.

Response: done.

31. For any personal communication, please provide a letter showing that the person agrees to their name being used.

Response: not applicable.

32. As corresponding author, please confirm that all authors have seen and approved of the final text.

Response: I confirm that all authors have seen and approved the final text.

33. If your author line includes a study group, collaborators' names and affiliations may be listed at the end of the paper or in the appendix. Additionally, if you wish the names of collaborators within a study group to appear on PubMed, please upload with your revision a list of names of all study group members presented as a two-column table in Word. First and middle names or initials should be placed in the first column, and surnames in the second column. Names should be ordered as you wish them to appear on PubMed. The table will not be included in the paper itself - it's simply used to make sure that PubMed adds the names correctly.

Response: not applicable.

34. Please note our guideline length for research articles is 3500 words and 30 references. For RCTs, the text can be expanded to 4500 words.

Response: noted (and our paper is comfortably within this limit).

35. From July 1, 2018, all submitted reports of clinical trials must contain a data sharing statement, to be included at the end of the manuscript or in an appendix (please provide as a separate pdf). Data sharing statements must indicate:
*Whether data collected for the study, including individual participant data and a data dictionary defining each field in the set, will be made available to others;
*What data will be made available (deidentified participant data, participant data with identifiers, data dictionary, or other specified data set);
*Whether additional, related documents will be available (eg, study protocol, statistical analysis plan, informed consent form);
*When these data will be available (beginning and end date, or "with publication", as applicable);
*Where the data will be made available (including complete URLs or email addresses if relevant);
*By what access criteria data will be shared (including with whom, for what types of analyses, by what mechanism - eg, with or without investigator support, after approval of a proposal, with a signed data access agreement - or any additional restrictions).

Clinical trials that begin enrolling participants on or after Jan 1, 2019, must include a data sharing plan in the trial's registration. If the data sharing plan changes after registration, this should be reflected in the statement submitted and published, and updated in the registry record. For reports of research other than clinical trials, data sharing statements are encouraged but not required. Mendeley Data (https://data.mendeley.com) is a secure online repository for research data, permitting archiving of any file type and assigning a permanent and unique digital object identifier (DOI) so that the files can be easily referenced. If authors wish to share their supporting data, and have not already made alternative arrangements, a Mendeley DOI can be referred to in the data sharing statement.

Response: not applicable.

COMMENTS TO THE AUTHOR:

Reviewer #1: The authors reported the impact of COVID-19 pandemic on ACS admission rates and management strategy. This is an important clinical question. Numerous accounts on social media and peer communications have already suggested the reduction in ACS, AMI admissions and PPCI number. This is also backed up by preliminary reports in Europe (Austria, Italy) and the USA as cited by the authors. Using nationwide data of NHS in England, the authors were able to perform a robust analysis on ACS admissions and care. I would like to congratulate the authors for the analysis and their attempt to try to overcome the difficulty of analyzing large data pool with unreported and missing data. Another strength of the study is that the authors not only reported the decline in ACS admission rates but they also looked into the subgroup and details of management strategy.

The results are important and strengthened our impression that patients may be scared to go to hospital even they have ischemic symptoms. Together with the report of marked increase in out-of-hospital cardiac arrest in Italy, the death toll of COVID-19 far exceeds its direct effect.

Response: We thank the reviewer for their supportive comments.

I have a few comments for the authors to address.

Major comment

1. For retrospective analysis of healthcare database, we used diagnostic codes to identify patients with ACS and AMI etc. As such, we solely depend on various sites/trusts to self-report AMI diagnosis instead of strict AMI diagnostic criteria (such as 4th universal definition of MI). This may sometimes cause mis-diagnosis, under-diagnosis or over-diagnosis. How can you minimize bias on this issue?

Response: We have added some new text in the Discussion (lines 282-288; page 10 paragraph 2) to address this point. The analyses are based on ACS diagnoses made by clinicians in each hospital Trust, which were then recorded in the Secondary Uses Service Admitted Patient Care (SUSAPC) data using ICD-10 codes to distinguish between STEMI and NSTEMI. As would be anticipated if NSTEMI and STEMI were being coded accurately, our results show the clinically-expected differences between the relative rates of admission for, and the management of, STEMI and NSTEMI. Since NSTEMI and STEMI are likely to have been diagnosed and coded in much the same way throughout 2019 and into early 2020 versus after mid-March, any bias in the rates of ACS due to misclassification of STEMI and NSTEMI is likely to be modest. If any such bias was to be removed, moreover, we would expect to see even more striking differences between the rates for STEMI and NSTEMI.

2. Besides, AMI can be classified into Type I and Type II MI or even just myocardial injury. Type I and II MI have different causes and implications and treatment strategy. Type II MI tends to occur in

older people with multiple co-morbidities (eg an elderly with multiple co-morbidities suffering from sepsis and mild troponin elevation), aggressive medical treatment and intervention may not be the best treatment. As your analysis showed that the major decline in ACS is for older patients with co-morbidities and proportion of PCI increased instead, do you think the main reason for decline in ACS admission is due to reduction in Type II MI? Do you think segregate type I and type II MI is meaningful?

Response: We thank the reviewer for the suggestion. ICD-10 was updated to include a code for type II MI, but having checked our data, we can confirm that there were no records of type II MIs.

Minor comment
3. ACS/AMI admissions started to decline in mid February while the first COVID death was in March and lockdown in late March? How do you explain this? Is it due to increase in public awareness early in February and fear to go to hospital?

Response: We have now added a new paragraph in the Discussion to address this point (pages 7-8, lines 208-17). In our opinion, the available data suggest that fear of contagion is likely to be the most important reason for the observation that the decline precedes the lockdown. (Similar findings were reported in the recent publication of data from Kaiser Permanente Northern California [reference 6 in the text].)

4. There seems to be an increase in AMI in second week of April (particularly in adjusted data and data from rapid response trusts). How do you explain this?

Response: We have taken the opportunity to update the analyses with new data that became available since the paper was reviewed, and they now include data up to the end of April 2020. The revised data are more complete than those originally submitted, and now suggest that a nadir was reached around the first week of April and that ACS admission rates (particularly NSTEMI) may now have levelled off. This may suggest that public concerns about the risks of acquiring coronavirus have diminished given the falling infection and death rates, but regular updates of the analyses will in due course track any increase in admission rates.

Reviewer #2: THELANCET-D-20-10305 Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England

Statistical review

Comments for the Authors

The authors provide a well written study on a very topical and under analysed feature of the COVID-19 pandemic, and report clear and useful findings. The statistical methods are appropriate for the objectives, and are expertly applied, and the figures and tables with supporting data are very clear, and the extensive supplementary methods and findings very useful. There are some presentational issues to address, as follows:

Response: We thank the statistical reviewer for their supportive comments.

Major

1. The authors take a very simple 'headline' view on reporting the numbers - e.g. in the Abstract, we are told 'there was a 46% reduction in hospital admissions for ACS, with the baseline rate of about 3000 admissions falling to about 1700 per week' and sometimes not quantifying it at all - just 'There were reductions in the numbers for all types of ACS, including both ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI)' and 'There were larger falls in the number of admissions of older people, those with a high burden of comorbidity, and in the London region' - and so on.

Response: Done: numerical detail, with 95% confidence intervals, is now provided in a new Table 2 and Supplementary Table 3.

a. And when these broad statements are quantified later in the text, they are all point estimates, with no indication of precision (e.g. 95% uncertainty or confidence intervals) - e.g. Lines 152 - 153 '… with a reduction of 26% in STEMI admissions, and of 49% in NSTEMI admissions'? Then Line 154 'There was a reduction of about 17% …', then Line 156 '… reduction of 32%', then line 159 'reduction of 61%' - and so on.

Response: Revised. We have now modified the paper to include standard error bars around the weekly numbers and around the relative reductions in admissions, by assuming that numbers of admissions in our data follow a Poisson distribution. Throughout the text we now provide 95% confidence intervals, also based on the Poisson distribution.

b. The exception is the plots, which just for the baseline 2019 period appear to give 95% confidence intervals.

Response: Revised. Although they previously showed SD bars rather than confidence intervals, we have now replaced the 2019 numbers with boxplots to show the *distribution* of weekly reported cases in 2019.

c. Although just giving the point estimates - and avoiding almost completely giving P-values (except for the trend tests) - makes for an uncluttered read, on the other hand it is important to understand that there is a range of information being portrayed here, with different denominators and event rates - so e.g. when the authors say that London had 'larger falls' - is this just compared with non-London sites, or can we see whether London's fall is greater than several individual regions, and not just chance?

Response: Revised. The new Table 2 and Supplementary Table 3 now give the population changes to the nearest percent together with 95% confidence intervals.

2. The authors carefully explain the potential pitfalls of using routine 'NHS management' data, and how most recent data might be influenced by reporting timelines and missing codes, and generally this is persuasive. However, couple of points:

a. In the supplementary methods, lines 74-76, despite several attempts, I couldn't understand the rationale for the adjustment 'assuming this proportion of activity was missing for 5 days of this week' - could the authors just try to provide the missing link here to explain the reas0ning behind the 5-day assumption?

Response: The explanation was that, since 30 March was a Monday and the 31 March was a Tuesday, the adjusted proportion had to be applied to 5 out of 7 days of the week commencing on 30 March. However, in the updated manuscript, we have included data to the end of April, so this adjustment is no longer required.

b. And it would seem that what the authors are doing with these adjustments is taking out any temporal artefacts (the speed at which the complete data is reported) and quality aspects (the lack of codes, and any other completeness and accuracy issue). So, would it be possible to conduct the exact same exercise on say the 2019 data, recreating the data feeds at precisely the same time as that received in 2020 for the 2019 data, and the fast forwarding to e.g. May or June 2019 when all the data had been verified and corrected - and see then empirically what the adjustments had to be? Or are these historic data cuts not available?

Response: The real-time contemporary feeds of 2019 data are not readily available and, in any case, we would suggest that the timeliness, completeness and accuracy of the 2019 data could not justifiably be generalised to the 2020 data. However, one of the key strengths of this study is that the findings can be updated dynamically; as further data accrue, the regularly updated analyses will correct any minor inaccuracies owing to incomplete data entry from recent weeks.

Minor

3. Page 2 line 50 (and elsewhere) - the authors indicate that by not seeking medical help at the hospital 'they … are at increased risk of cardiac death and adverse long-term effects' - but could they actually quantify this from what is known from overall event rates for relevant bad outcomes over a sensible time frame e.g. a year?

Response: We do not believe that we can do this reliably based on the current analyses, for two main reasons: First, much of the information required to model the excess burden resulting from failing to go to hospital, or arriving late, are not available within the SUSAPC data (eg time from symptoms to PCI for STEMI). Secondly, long-term impact depends on how rapidly cardiological services are restored to normal, as this will determine the prognosis of patients who experience repeat events. Analyses of excess mortality due to these observed reductions in urgent admission and treatment for ACS are likely to become available from analyses of other databases (although these may well be confounded by mis-attribution of causes of death) which would provide complementary information to that provided by our study.

4. And is it possible that the issues around the longer-term adverse events may be over stated if there is an upswing in people that have had ACS and survived then present for treatment at a delay after the fears around the pandemic subside. Of course, that delay may make such treatments less effective, but not necessarily totally ineffective?

Response: The reviewer is correct (highlighting the difficulties of such modelling).

5. This report is for England, and the authors promise to update it as more data becomes available (which will presumably also have to be adjusted at the edges of the time series) - that is useful - but is there corresponding analyses available for Scotland & Wales & NI - or are the data not available in an amenable format?

Response: We will be regularly updating our analyses using the NHS Digital data in order to follow the emerging trends over time for England as the response to COVID-19 evolves. We have expanded our discussion (see page 9, lines 258-73) of how these findings are informative for other healthcare systems, and to emphasise the value of using centralised electronic health record data where they are available (e.g. not just in the devolved nations, but also in China, Sweden and in US health maintenance organizations) to monitor such trends to ensure that they reverse and do not recur during this pandemic.

6. The authors explain the spells and superspells clearly - but is it possible that the changes in demand and workflows caused by the COVID-19 pandemic also might have changed the quality (completeness and accuracy) of documenting & recording the dates of admission, discharge and transfers - and so changed the reliability of identifying accurately the spells and super-spells? If so, what impact might that have had on the findings?

Response: The chief problem is likely to be data coming late from Trusts, or partial completion of spell data (most importantly missing diagnostic codes). The adjustments that we have made in the analysis account for both delays in submission and incomplete coding. It is also worth noting that aggregation of spells into superspells decreases the total number of admissions by only 4%, so any inaccuracies around dates would have negligible impact.

7. Line 126 - useful to give more details on the parameters for the LOESS smoothing spline, plus methodological reference (the authors just later state on line 133 they used R 3.6.3)?

Response: Done. Detail added about the LOESS smoothing spline to the methods (lines 138-149 page 5 paragraph 4).

8. Line 144 - whereas later the authors use 'trend' in an appropriate statistical sense (i.e. in a test of trend) stating '… there was a slight trend among admitted patients towards younger age and fewer comorbid conditions' doesn't seem an appropriate use of the word - are they describing a difference that might have arisen by chance given the sample sizes?

Response: This has now been reworded (page 7 lines 186-9) as follows: 'The relative reductions in weekly numbers of admissions for ACS were qualitatively similar in all of the subgroups studied, but they appeared slightly larger among those with higher (that is, a worse) Charlson comorbidity index and for those in the London and East Midlands regions (Supplementary Table 3 and Supplementary Figure 3).'

9. Lines 167-170 - and when the authors present the statistically significant test for trends (older age, Charlson comorbidity index) useful to give the estimated slope of the change e.g. for 10 years, or for a suitable number of units of the CCI? And perhaps quantify London vs. not-London?

Response: Based on the updated analyses, a test for heterogeneity has been used, so this has been reworded (see page 7, lines 186-189). New Table 2 and Supplementary table 3 provide the exact population values.

10. Line 205 'However, our analyses show that the sudden reduction in ACS admissions pre-dated the lockdown by about 3 weeks' and then Line 210 'Consequently the chief reason for this phenomenon seems likely to be that many patients with symptoms of ACS have not sought immediate medical help during the pandemic period' - but do the authors have any references for patient attitudes on fear of pandemic and avoiding hospital appointments e.g. for perhaps routine clinics; or perhaps increased consults / contacts by phone with GP etc - that would have coincided with this 3-week timeline?

Response: Reference 14 provides evidence from Hong Kong that fear of acquiring COVID-19 was a major factor in delays seeking medical assistance, but we are not aware of any published study for the UK (although there have been media reports of the same phenomenon).

11. Figure 1 - could the authors provide a bit more background on how these numbers (don't add up) e.g. >3000 ACS, ~2100 Any acute MI, ~600 STEMI, ~1300 NSTEMI?

Response: Done. The Supplementary Methods did provide a reference to coding of unstable angina and other IHD, but we have now also included an explanatory sentence at the end of paragraph 1 of the Methods (Lines 122-124; page 5).

12. Lines 40-42 and Lines 45-46 - the authors explain their hierarchical assignment of both type of ACS and procedures, so that any event is only assigned once. Did they consider a sensitivity analysis at the other extreme, assigning any mention of a type or procedure to count - just in case there might have been a differential pre and peri-pandemic recording of the important codes?

Response: We were unable to examine this possibility because the structure of the data provided by NHS Digital is of a single row per spell or superspell, with the hierarchy for both ACS and procedures applied at the point of data extraction.

Reviewer #3: The study is well conducted and leverages the Secondary Uses Service Admitted Patient Care (SUSAPC) dataset to give a national perspective on ACS trends during the COVID-19 pandemic. This is made possible due to a centralized health care system in England.

Response**:** We thank the statistical reviewer for their supportive comments.

The study shows a 46% decrease in ACS admissions with a more marked decrease in NSTEMI admissions compared with STEMI which is notable and worthy of further explanation.

Acute Coronary Syndrome especially myocardial infarction is known to have a seasonality associated with it - 10-20% difference between summer and winter months. I could not find a suitable reference from NHS data, but it is likely that is the case in England. The study could be strengthened if the comparison week to week was against weekly admissions in the last say 5 years. However, given that there is a clear drop in admissions it is likely not needed to prove the point. I would however put this in the limitation and say that it is acceptable by comparing mean admissions annually in literature to that in Feb-Apr and noting the absence of a large difference.

Response: We have only been provided with access to data for 2019 and 2020 by NHS Digital. As the reviewer states, the magnitude of this observed reduction in ACS admission rate far exceeds that which could be explained by chance. In order to address the reviewer's comment about seasonal variability, we have revised the main figures so that the distribution of weekly numbers during 2019 is illustrated by a boxplot (i.e. the median, the interquartile range (IQR), 1.5 times above the IQR above and below the quartiles, and any weekly outliers). In addition, we found that the weekly admissions rates for February to April 2019 were very similar to the average weekly admission rates during the rest of 2019 and this has been added to the results (line 158-160 page 5).

An important feature of the study is the attention to detail for the possibility of system wide under-coding of ACS due to incomplete claims, and additionally the adjustments made for lower number of centers reporting in the later time period, which both appear sound. However, it would be helpful if the adjusted curves for admissions similar to Supplementary Figure 1 are also shown in the main Figure 1, as they are the true estimates. Of note the adjustment has been shown in Supplementary Figure 1 only for overall ACS and not by ACS type.

Response: Done. We have revised Figure 1 so that it includes each of the 4 conditions with unadjusted and adjusted values.

Line 151-152 mentions that PCI numbers on the day of admission decreased 17%. I felt it was important to note that PCI on subsequent days markedly decreased, showing either expeditious work up and management to minimize LOS, or that these patients were sicker needing PCI sooner.

Response: Text revised. We have modified the Results section (pages 6, lines 171-174) to explain these results more carefully. The 17% reduction refers to PCI on the day of admission for STEMI only. As shown in Figure 3, there were very few PCIs performed for STEMI after the day of admission, and these declined only slightly.

Showing weekly numbers for PCI and CABG by ACS type is not easily interpretable in itself without the context of proportion. It is preferable that the proportion of PCI for all ACS and by ACS type is in the main paper. Also providing just the N without the proportion, and mentioning 'reduction of about 17% in the numbers of STEMI patients receiving PCI', may be misinterpreted as a reduction in PCI being offered.

Response: Done. We have now added a main Figure 2 showing the proportions receiving PCI on the day of admission.

Figure 3 could be moved to supplement to make room. The result is of the older age group which is there in the text.

Response: Done. We have now moved the subgroup figure to the web appendix.

Figure 1 could be condensed by showing multiple ACS types in the same graph.

Response: Done. Figure 1 now includes both adjusted and unadjusted plots (as suggested by this reviewer) for each type of ACS.

Line 205-211 I felt the arguments suggested as to why the phenomenon of decreased ACS is due to not seeking care are hypothesis generating, and may be helpful to not completely rule out the role of decreased activity leading to decreased ACS. We know from other data sources like fitbit and device data that response to people to lockdowns may vary and not be an instant response.

Line 209 - ACS increasing in second half of April could mean that stress levels are rising due to extended lockdown.

Response: In the revised Discussion (see page 8, lines 213-7), we have expanded the rationale for hypothesising that changes in activity or in stress levels are unlikely to explain these trends:

'In particular, the fact that the decline in admissions preceded the UK lockdown and, despite the lockdown, is now levelling off (7), suggests that environmental changes (eg reduced air pollution), reduced physical activity, or reduced stress due to lockdown are unlikely to be major contributors to the decline in ACS admissions in the current pandemic (15,16).'

Overall, given the nature of the pandemic and the need to disseminate findings quickly I do not feel that these changes are mission critical to the paper. The deaths due to non-COVID causes may never be apparent. US reports suggest that total deaths occurring are higher than that explained by COVID alone. Thus, there is grave concern of patients not seeking necessary care and that is the main message of the paper.

Response: We agree with the reviewer that the findings require urgent and prominent publication so that this potentially life-threatening issue is addressed rapidly.

Reviewer #4:

Major comments.
1. From a clinical and public health perspective the topic is timely and addresses a major issue: How SARS-CoV-2 has an impact on health care of patients beyond Covid-19
2. Study design is appropriate to address the topic.
3. Data are of good quality and seem to be reliable despite limitations which are adequately addressed in the discussion section. Data analyses are profound and clear.
4. The manuscript is well written and of adequate length.
5. It is of general interest because of importance of the Topic and the large number of patients affected in every Country and Region addressing potentially life-threatening Events.
6. There are two important new findings reported:
a) Decline of admission due to acute coronary syndromes started before the lockdown indicating a major impact of additional factors
b) Admission numbers increase in the second half of April despite the lockdown continuing.

Response: We thank this reviewer for their supportive comments, and note that our updated analyses provide further evidence to support the reviewers comment in 6(b).

However, new aspects reported are mostly of regional interest (England) and general impact of the manuscript would increase substantially by including two aspects :
1. Data on complications in these patients as presumed by the authors and
2. Data/Parameters on delayed admission of patients even in STEMI

Response: We have modified the Discussion (lines 288-290; page 10) to point out that SUSAPC data are either not available, or are insufficiently granular, to address these important points.

Minor comments: data on specific regions in England don't add to the overall findings and can be skipped or summarized in the text

Response: Done. The figure describing regional variation has now been moved to the webappendix. Note, however, that the consistency of the findings in different geographic regions supports the hypothesis that the observed patterns are driven by a common issue across the country.

Reviewer #5:

Reviewer Blind Comments to Author
The manuscript entiteled „Impact of the COVID-19 pandemic on admission rates for, and management of, acute coronary syndromes in England" is interesting, but several limitations have to be addressed.
During the last weeks (starting at the begin of April 2020) in several cardiolovascular media, such as tctmd.org, New England Journal of Medicine European Heart Journal, JACC and also a huge number of national and international newspapers the observed decline in admission rates of ACS patients was published. The extent of decline of ACS-numbers was amazing comparable in all of the publications. This observation was reported consistently in several central european countries, as well as China and USA.
So, as in the present manuscript in the first sentence of the abstract is written „Several countries affected by COVID-19 epidemic have reported a substantial drop in the number of patients attending the emergency department with acutte coronary syndromes" this manuscript do not add some relevant new or additional knowledge.

Response: We regret that we did not make it clearer that this work does contribute additional knowledge. In response to these comments, we have modified the Discussion extensively in order to clarify the way in which these analyses and the findings are novel (see, in particular lines 199-243):

· This is the first such analysis to involve updates of the hospitalisation data which track not only the time-course of this large and rapid fall in admissions for acute coronary syndromes (showing, for example, that it predates the lockdown in the UK) but also of the levelling off now under way, as well as future trends that will illustrate the impact of national and local interventions on admissions for acute coronary syndromes and help identifying strategies to prevent the reoccurrence of this phenomenon should there be a second wave of the pandemic.

· Our report is the first to document changes in admission rates reliably for different types of acute coronary syndrome, demonstrating a much larger reduction in NSTEMI than in STEMI. In addition, it is the first to provide evidence about the impact on their acute management (in particular, those STEMI patients who were admitted continued to receive urgent PCI whereas those with NSTEMI were much more likely to receive revascularisation treatment than normal).

· These are the first such analyses from all acute hospital providers across a complete country (England), so avoiding potential selection biases of previous analyses based on particular hospitals or area, or surveys rather than systematic data collection. The scale and scope of the data also allow assessment of the impact in different circumstance (see below).

· As indicated above, these analyses provide the first available information about the impact of the response to COVID-19 on admissions among different types of patient (e.g. only slightly higher in the elderly and those with comorbidities) and in different parts of the country (e.g. only slightly higher rates regions with large numbers of COVID-19 cases).

Even more because the presented findings are descriptive and lack of any scientific explanation.

Response: We have now substantially revised the Discussion (as described in the previous response) in order provide an explanation for our findings and the evidence to support it, as well as ways to mitigate these adverse trends (which will be monitored by our ongoing analyses that will be made available on a regular basis).

The relatively high number of patients, arround 3000/week, is notably and has more of statistical impact, compared to some previous reports. Nevertheless, there is absolutely no novelty in the data of this manuscript.
Also no control group (from the same time frame the year before) of this study is shown,

Response: The variability in the weekly admission numbers in 2019 is now shown by the boxplots of the 2019 weekly data in each figure, from which it can be seen that there are not marked seasonal fluctuations. In addition, the average weekly numbers of ACS admissions during February to April 2019 is now provided in the results (line 159-160; page 6)

so for me The LANCET seems not to be the proper journal for such a retrospective observational study, just showing the decline in the rate of ACS patients. No further correlation was shown with any gradual increase of public restrictions ordered by the UK government.

Response: We have shown clearly both that the reduction in admissions for ACS preceded the lockdown and, having incorporated a fresh download of data for the present revision, there is a levelling off despite a continuing lockdown.

The shortening of the median length of stay from 4 to 2 days also simply is an observation, most likely caused by the fear of the doctors to expose the patients to some COVID-positve people or to have same free beds for coming COVID-patients.

Response: We agree; this reduction in hospital stay is in accordance with instructions issued prior to the pandemic for managing such patients.

Despite the interesting finding, I do not think that this data are worth to be published in The LANCET, maily because of the lack of novelty.

Response: As described in response to the reviewer's first point, the Discussion has been modified extensively in order to explain the ways in which these analyses and the findings are novel, and how they can be used to inform strategies for addressing these observed reductions in patients with ACS seeking urgent assessment and effective treatment.

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Web Appendix

2020-05-29 Online appendix.pdf