BMJ Open

Reduction in Percutaneous Coronary Intervention for Acute Coronary Syndromes during the COVID-19 outbreak in a non-overwhelmed European health care system: COVID ACS-PCI Experience in Ireland

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045590
Article Type:	Original research
Date Submitted by the Author:	06-Oct-2020
Complete List of Authors:	Connolly, Niall; Galway University Hospitals, Dept. of Cardiology Simpkin, Andrew; National University of Ireland Galway, School of Medicine Mylotte, Darren; Galway University Hospitals, Dept. of Cardiology Crowley, James; Galway University Hospitals, Dept. of Cardiology; National University of Ireland Galway, School of Medicine O'Connor, Stephen; St. James' Hospital, Dublin, Dept. of Cardiology AlHarbi, Khalid; St. James' Hospital, Dublin, Dept. of Cardiology Kiernan, Thomas; University of Limerick; University Hospital Limerick, Dept. of Cardiology Arockiam, Sacchin; University Hospital Limerick, Dept. of Cardiology Owens, Patrick; University Hospital Waterford, Dept. of Cardiology John, Amal; University Hospital Waterford, Dept. Of Cardiology Blake, Gavin; Mater Misericordiae University Hospital, Dept. of Cardiology Fitzgerald, Sean; Mater Misericordiae University Hospital, Dept. of Cardiology Cadogan, Diarmaid; Mater Misericordiae University Hospital, Dept. of Cardiology Rosseel, Liesbeth; Galway University Hospitals, Dept. of Cardiology
Keywords:	COVID-19, Ischaemic heart disease < CARDIOLOGY, Coronary intervention < CARDIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Reduction in Percutaneous Coronary Intervention for Acute Coronary Syndromes during the COVID-19 outbreak in a non-overwhelmed European health care system: COVID ACS-PCI Experience in Ireland

Niall P Connolly[1], Andrew J Simpkin[2], Darren Mylotte[1], James Crowley[1,2], Stephen O'Connor[3], Khalid AlHarbi[3], Thomas J Kiernan[4], Sacchin Arockiam[4], Patrick Owens[5], Amal John[5], Gavin J Blake[6], Sean Fitzgerald[6], Diarmaid Cadogan[6], Liesbeth Rosseel[1]

[1] Department of Cardiology, Galway University Hospital, Ireland

[2] School of Medicine, National University of Ireland Galway, Ireland

[3] Department of Cardiology, St James' Hospital, Dublin, Ireland

[4] Department of Cardiology, University Hospital Limerick, Ireland

[5] Department of Cardiology, University Hospital Waterford, Ireland

[6] Department of Cardiology, Mater Misericordiae University Hospital Dublin, Ireland

Word Count: 2251 (excluding figure legends and references)

Figures: 3

Tables: 2

Keywords: COVID-19, percutaneous coronary intervention, acute coronary syndrome, Ireland

Conflicts of interest: Darren Mylotte is a consultant for Medtronic, Boston Scientific, and Microport.

The other authors have no conflicts of interest to declare.

Corresponding Author:

Niall Connolly

Department of Cardiology

Galway University Hospital

Newcastle Road, Galway, Ireland

Mail: niallcon@gmail.com

ABSTRACT:

Aims

To evaluate temporal trends of acute coronary syndromes (ACS) treated via percutaneous coronary intervention (PCI) throughout the COVID-19 outbreak in a European healthcare system affected but not overwhelmed by COVID-19 related pathology.

Methods and Results

We performed a retrospective multicentre analysis of the rates of PCI for the treatment of ACS within the period two months pre and post the first confirmed COVID-19 case in Ireland, as well as comparing PCI for ST-Elevation Myocardial Infarction (STEMI) with the corresponding period in 2019. During the 2020-COVID period (29th February – 30th April 2020) there was a 24% decline in PCI for overall ACS (incidence rate ratio (IRR) 0.76; 95% confidence interval (CI) 0.65-0.88; P<0.001), including a 29% reduction in PCI for Non-ST Elevation-ACS (IRR 0.71; 95% CI 0.57-0.88; P=0.002) and an 18% reduction in PCI for STEMI (IRR 0.82; 95% CI 0.67-1.01; P=0.061), as compared to the 2020-PreCOVID period (January 1st - February 28th 2020). A 22% (IRR 0.78; 95% CI 0.65-0.93; P=0.005) reduction of PCI for STEMI was seen as compared with the 2019 reference period.

Conclusion

This study demonstrates a significant reduction in PCI procedures for the treatment of ACS since the COVID-19 outbreak in Ireland. The reasons for this decline are still unclear but patients need to be encouraged to seek medical attention when cardiac symptoms appear, in order to avoid incremental cardiac morbidity and mortality due to reduced rates of coronary revascularisation for the treatment of ACS.

Keywords: COVID-19, coronary intervention, ischaemic heart disease, public health

ARTICLE SUMMARY

Strengths and limitations of the study:

- This is a retrospective multicentre analysis of the temporal trends of acute coronary syndromes (ACS) treated via percutaneous coronary intervention (PCI) throughout the initial COVID-19 outbreak in Ireland.
- The participating centres account for 79.6% of all STEMI presentations in Ireland giving a very good representation of the overall national picture.
- The figures represent daily numbers of PCI procedures for the treatment of ACS, rather than hospital admission for PCI which could underestimate the true incidence of ACS presenting to hospitals due to alterations in clinical practice patterns, such as a potential for increased use of non-invasive strategies.
- The analysis was performed inter-year and intra-year thus allowing the assessment for confounding by seasonable variations in presentations with ACS.
- The overall impact on cardiovascular and mortality hard outcomes are not currently measurable within the remit of this study.

Text:

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic has brought many challenges for healthcare systems and has had a huge impact on social behaviour. To minimise the spread of infection social distancing measures and wide restrictions in the movement of people have been implemented. Intermittent deferral of non-urgent and elective care has been a central tenet to increase hospital capacity to deal with the surge in COVID-19 cases and to avoid unnecessary exposure of patients to a hospital environment where COVID-19 may be more prevalent.

Initial expectations would have been for an increase in acute coronary syndrome (ACS) presentations in line with existing evidence suggesting a link between respiratory infections and subsequent myocardial infarction[1,2]. However, first reports during the initial phase of the COVID-19 outbreak showed a decline in presentations of ST-elevation myocardial infarction (STEMI) and hospital admissions for ACS, even in geographies where the health care system was not overwhelmed by COVID-19 pathology[3-8]. As percutaneous coronary intervention (PCI) has a proven beneficial outcome in the management of ACS, there is a concern that a similar decline in PCI procedures during the COVID-19 pandemic could lead to incremental cardiac morbidity and mortality[9].

As opposed to the above-mentioned studies, that investigated rates of STEMI or ACS hospital admissions, we evaluated temporal trends in the rates of PCI procedures performed for the treatment of ACS during and before the COVID-19 outbreak. This study represents data from the Republic of Ireland, a European country where widespread social and lockdown measures were implemented during the first wave of the COVID-19 outbreak, and the healthcare system has been affected, but not overwhelmed by COVID-19 related pathology.

METHODS

In this multicentre retrospective registry, we examine the daily rates of PCI performed for the treatment of ACS during three different time periods in relation to the COVID-19 outbreak in Ireland. Participation was voluntary and data was anonymously collected by each participating centre in a dedicated electronic dataset. Cases were identified from cardiac catheterisation laboratory and hospital admission records and cross-referenced with patient electronic records to provide accurate descriptors of the indication for PCI. Variables were categorised according to the indication and timing of PCI. National data regarding the COVID-19 outbreak were collected from the official Department of Health resources[10]. Ethical approval for the study was gained from the National Research Ethics Committee (NREC) established for COVID-19 related research in Ireland.

Patient and Public Involvement

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

Study Population

The Health Service Executive (HSE) dedicated ACS Programme designates six primary PCI centres in Ireland[11]. In this study the data are collected from five primary PCI facilities (Galway University Hospitals, Mater Misericordiae University Hospital Dublin, St. James's Hospital Dublin, University Hospital Limerick and Waterford University Hospital). The five participating centres in this study account for 79.7% of STEMI presentations in Ireland based on the latest published national data[12]. This study does not include any private health care facilities which also treat non-ST elevation acute coronary syndromes (NSTE-ACS), but not STEMI cases.

Definitions

The daily rates of PCI procedures performed only for the treatment of ACS (ACS-PCI) during three delineated time periods were included in this study. The overall PCI group (´All ACS´) was dichotomised into two groups, as defined by the European Society of Cardiology guidelines: (1)

´STEMI´, and, (2) ´NSTE-ACS´, with the latter representing PCI performed for non-ST elevation myocardial Infarction (NSTEMI) and unstable angina (UA)[13,14]. Daily ACS-PCI rates were collected for three separate time periods: (1) the ´2020-COVID´ period, was set from the date of the first confirmed COVID-19 case in Ireland, February 29th 2020, until April 30th 2020 (62 days); (2) the ´2020-PreCovid´ including January 1st to February 28th 2020 (59 days); and, (3) the ´2019-Reference´ period covering January to April 2019 (120 days). Daily PCI rates for STEMI were collected for the ´2019-Reference´, ´2020-PreCOVID´and the ´2020-COVID´ periods, whilst data regarding PCI performed for the treatment of NSTE-ACS were collected for the ´2020-PreCOVID´ and ´2020-COVID´ periods.

In Ireland, phased containment and delay strategies were initiated on a national level in order to reduce the peak impact of the COVID-19 pandemic and slow the spread of the disease in the community. During the initial containment phase, all confirmed cases were isolated in COVID-19 designated hospitals (all participating hospitals), and there were local school/business closures where there had been contact with an infected patient. Measures steadily progressed in the delay phase with the closure of all schools from 12th March and a ban on mass gatherings, closure of all pubs/bars on 16th March, progressing to other non-essential services on 25th March and a full country-wide lockdown by 28th March (**Figure 1**). Importantly, these measures were enforced at a national level without regional variability and continued for the duration of the studies period.

Statistical analysis

The data collected are daily counts of ACS-PCI procedures across the five participating centres. Hence, a negative binomial model was used to compare the effect of the COVID-19 pandemic on the rate of daily interventions due to (1) STEMI, (2) NSTE-ACS and (3) all ACS, while allowing for over-dispersion in the daily rate of PCI procedures. Individual hospital was included as a random effect in all models, to account for clustering of data within settings. The '2020-COVID' times period is compared with the '2020-PreCOVID' and the '2019-Reference' periods and results are presented as

incidence rate ratios along with corresponding 95% confidence intervals and p-values. Values below 1.0 suggest a reduction in admissions during COVID-19. Continuous variables, such as the mean daily rate of PCI cases per hospital, are presented as a mean ± standard deviation (SD). All analyses were performed in R v3.6 (R Core Team, 2020).

RESULTS

After the first COVID-19 case was confirmed 29th of February 2020 in Ireland, the cumulative incidence of COVID-19 confirmed cases rose above 1,000 cases by March 23th and reaching 20,612 by April 30th with 1,232 COVID-19 related deaths at that moment (**Figure 1**)[10]. For an estimated 4.90 million inhabitants, intensive care bed capacity was expanded from 255 to 411 critical care beds within the Irish public health system, with additional surge capacity of up to a total of 800 beds[15]. The number of confirmed and suspected COVID-19 cases in critical care was 160 at its maximum on April 4th, 2020[10].

During January and February 2020, the two months preceding the first confirmed COVID-19 case, 490 ACS-PCI were performed for the treatment of all categories of ACS. This compares with a total of 387 ACS-PCI cases in the succeeding two months. The mean daily rates per centre of PCI for all ACS, STEMI and NSTE-ACS are outlined in **Table 1**.

Table 1. Mean and standard deviation of daily PCI procedures per centre for All ACS, NSTE-ACS and STEMI cases.

Period	Total	Daily mean per centre	±SD
All ACS			
2020-COVID[a]	387	1.25	1.34
2020-PreCOVID[b]	490	1.66	1.66

NSTE-ACS			
2020-COVID[a]	212	0.68	1.07
2020-PreCOVID[b]	288	0.98	1.29
STEMI			
2020-COVID[a]	175	0.56	0.77
2020-PreCOVID[b]	202	0.68	0.86
2019-Reference[c]	436	0.73	0.92

[a]2020-COVID is February 29th - April 30th, 2020 (62 days);

[b]2020-PreCOVID is January 1st - February 28th, 2020 (59 days);

[c]2019-Reference is January 1st - April 30th, 2019 (120 days).

During the '2020-COVID' period, there was a 24% reduction in PCI for the treatment of all ACS as compared to the '2020-PreCOVID' period (Incidence Rate Ratio[IRR] 0.76, 95% confidence interval (CI) 0.65-0.88; p<0.001) (**Table 2**).

Table 2. Comparison of PCI for the treatment of All ACS, NSTE-ACS and STEMI for the study period (2020-COVID) versus control period.

Period	Incidence rate ratio	95% Confidence Interval	P-Value
All ACS			
2020-COVID to 2020-PreCOVID	0.76	0.65 – 0.88	<0.001

NSTE-ACS			
2020-COVID to 2020-PreCOVID	0.71	0.57 – 0.88	0.002
STEMI			
2020-COVID to 2020-PreCOVID	0.82	0.67 – 1.01	0.061
2020-COVID to 2019-Reference	0.78	0.65 – 0.93	0.005

There was a corresponding 29% reduction in PCI for the treatment of NSTE-ACS (IRR 0.71, 95% CI 0.57-0.88; p=0.002) and an 18% reduction in PCI for STEMI (IRR 0.82, 95% CI 0.67-1.01; p=0.061), as compared to the '2020-PreCOVID' period (**Table 2**). During the '2020-COVID' period there was also a 22% reduction in PCI performed for the treatment of STEMI as compared to the '2019-Reference' period (IRR 0.78, 95% CI 0.65-0.93; p=0.005) (**Table 2**).

To assess confounding of the results by seasonal variability between the '2020-PreCOVID' and '2020-COVID' period (i.e. to verify whether admissions change naturally over time), we compared the overall STEMI rate in January/February 2019 with that of March/April 2019. There was no significant variability between both periods (IRR 1.05, 95% CI 0.87-1.27; p=0.583). Results were also reproducible year on year when we considered the STEMI PCI incidence in the period of March-April 2019 as compared to the corresponding ´2020-COVID' period, with a significant 24% lower PCI rate for STEMI in the '2020-COVID' period (IRR 0.76; 95% CI 0.62-0.92; p=0.006).

DISCUSSION

This study demonstrates a substantial reduction in PCI procedures performed for the treatment of all ACS, NSTE-ACS and STEMI during the initial stages of the COVID-19 pandemic in Ireland. During the two months since the first confirmed COVID-19 case, PCI rates for the treatment of all ACS, NSTE-ACS and STEMI dropped by 24%, 29% and 18%, respectively, with respect to the prior two months (**Figure 1**) (**Figure 2**). As compared to the 2019 reference period, there was a 22% reduction of PCI for STEMI during the '2020-COVID' period (**Figure 3**).

These data correspond with data from other countries detailing similar reductions in STEMI cases and ACS hospital admissions[3-8]. Unlike these studies, we highlight the impact of COVID-19 on the actual number of PCI procedures performed for the treatment of all ACS since the COVID-19 outbreak. This data is of particular relevance as it seems the pandemic affects both the number of patients presenting to hospital with ACS as well as the number of patients that undergo PCI as a treatment for ACS. Since coronary revascularisation has a proven survival benefit in the treatment of both STEMI and NSTE-ACS, this raises concern for incremental cardiac morbidity and mortality during the initial phases of the COVID-19 pandemic.

It is difficult to fully account for this sudden and significant drop in PCI performed for the treatment of ACS among these primary PCI centres. In Ireland, where the healthcare system was not overwhelmed by COVID-19 cases, the emergency departments and primary PCI facilities remained operational without any capacity limitation. It is also unlikely that the observed reduction in ACS treatments could be fully explained by changes in lifestyle or environmental factors, such as workplace stressors or exposure to air pollution, factors that have previously been associated with ACS.

It is quite likely that the true incidence of ACS in the population has remained largely unchanged during the COVID-19 pandemic, rather, that the proportion of patients presenting to the hospital has fallen. A major concern exists that a large proportion of ACS patients may not be presenting, or delaying their presentation, to health care facilities despite measures to preserve the function and capacity of emergency departments and acute cardiac facilities in Ireland. The Irish

Cardiac Society conducted a survey among cardiologists at the height of the pandemic, and reported that the reduction in ACS presentations to hospitals were attributed to: (1) people's fear of being exposed to COVID-19 within a healthcare facility (97%); (2) people not leaving their homes due to the government restrictions (41%); and, (3) people worried about putting a burden on the health services (41%)[16]. Fear for the healthcare environment as well as unawareness of the risk-mitigation efforts set up by the hospitals, were the overarching themes reported by patients in a series of semi-structured interviews performed during the pandemic in an American population[17]. Indeed, in relation to these latter assertions, cumulative incidence of PCI rates for ACS suggest further diverging of the curves the moment social distancing and lockdown measures were put in place, two weeks after the first confirmed COVID-19 case **(Figure 1)**.

Anecdotal evidence suggests that the reduction/delay in presenting to hospital with ACS during the COVID-19 era has resulted in an increase in the proportion of mechanical complications[18]. Given the reduction in acute coronary revascularisation observed in the current study and assuming the true incidence of ACS has not changed significantly, it is possible that we will yet see a future wave of new post myocardial infarction induced heart failure presentations or arrhythmias leading to further morbidity and mortality. It will take a significant period of time before the true measure of effect of this pandemic in a cardiovascular sense is known and we will need to monitor excess mortality figures to assess for this indirect impact caused by this pandemic.

Our study has limitations. First, we were only able to include five of six Primary PCI centres in Ireland. The participating centres however, account for more than three quarters of all STEMI presentations in Ireland. Herein, we present the daily numbers of PCI procedures for the treatment of ACS, rather than hospital admission for PCI. Using ACS-related PCI activity could underestimate the true incidence of ACS presenting to hospitals due to alterations in clinical practice patterns, such as an increased use of non-invasive strategies. However, our objective was to evaluate the patterns of invasive treatment of ACS during the COVID-19 pandemic. Further information on the number of ACS

presentations to the participating hospitals that were treated non-invasively are not available. Additional demographic, clinical, or mortality data on participating patients was not collected.

In conclusion, we report a one quarter reduction in PCI for ACS during the COVID-19 pandemic in an affected, but not overwhelmed, European health-care system. Reasons for this reduction are numerous and varied. Clear public health messaging and measures are required to encourage patients to seek medical attention for non-COVID-19 related illness.

FUNDING STATEMENT

'This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors'.

AUTHOR CONTRIBUTIONS

- Niall P Connolly, Darren Mylotte, Liesbeth Rosseel; formed the concept, designed, wrote and revised the paper.
- Andrew J Simpkin; statistical analysis, graphics, critical revision of the paper for important intellectual content, final approval of the version to be published.
- James Crowley, Stephen O'Connor, Khalid AlHarbi, Thomas J Kiernan, Sacchin Arockiam, Patrick Owens, Amal John, Gavin J Blake, Sean Fitzgerald, Diarmaid Cadogan; data acquisition, critical revision of the paper for important intellectual content, final approval of the version to be published.
- All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Smeeth L, Thomas SL, Hall AJ et al. Risk of myocardial infarction and stroke after acute infection or vaccination. N Engl J Med 2004 Dec 16;351(25):2611-8. doi:10.1056/NEJMoa041747
2. Kwong, JC, Schwartz KL, Campitelli MA et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med 2018 Jan 25;378(4):345-353. doi:10.1056/nejmoa1702090
3. Garcia S, Albaghdadi MS, Meraj PM et al. Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States during COVID-19 Pandemic. J Am Coll Cardiol. 2020 Apr 9. pii: S0735-1097(20)34913-5. doi: 10.1016/j.jacc.2020.04.011.[Epub ahead of print]
4. De Filippo O, D'Ascenzo F, Angelini F et al. Reduced Rate of Hospital Admissions for ACS during COVID-19 Outbreak in Northern Italy. N Engl J Med. 2020 Apr 28. doi: 10.1056/NEJMc2009166.[Epub ahead of print]
5. Rodríguez-Leor O, Cid-Álvarez B, Ojeda S et al. Impacto de la pandemia de COVID-19 sobre la actividad asistencial en cardiología intervencionista en España. REC Interv Cardiol. 2020;2:82-89. doi:10.24875/RECIC.M20000120
6. Rangé G, Hakim R, Motreff P. Where have the STEMIs gone during COVID-19 lockdown? Eur Heart J Qual Care Clin Outcomes. 2020 Apr 29. pii: qcaa034. doi: 10.1093/ehjqcco/qcaa034.[Epub ahead of print]
7. De Rosa SC, Spaccarotella C, Basso C et al. Reduction of Hospitalizations for Myocardial Infarction in Italy in the COVID-19 Era. Eur Heart J. 2020 May 15;ehaa409. doi: 10.1093/eurheartj/ehaa409. Online ahead of print.
8. Metzler B, Siostrzonek P, Binder RK et al. Decline of Acute Coronary Syndrome Admissions in Austria Since the Outbreak of COVID-19: The Pandemic Response Causes Cardiac Collateral Damage. Eur Heart J. 2020 May 14;41(19):1852-1853. doi: 10.1093/eurheartj/ehaa314.

9. Neumann FJ, Sousa-Uva M, Ahlsson A et al; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019 Jan 7;40(2):87-165. doi: 10.1093/eurheartj/ehy394. PMID: 30165437.
10. Department of Health, Ireland. Latest updates on COVID-19 (Coronavirus). https://www.gov.ie/en/news/7e0924-latest-updates-on-covid-19-coronavirus/ (04 June 2020)
11. Health Service Executive, Ireland. National Clinical Programmes – Acute Coronary Syndrome. https://www.hse.ie/eng/about/who/cspd/ncps/acs/ (24 May 2020)
12. Health Service Executive, Ireland. Report of the National Clinical Programme for Acute Coronary Syndrome (ACS) on standardising treatment of patients with STEMI in 2016. https://www.hse.ie/eng/about/who/cspd/ncps/acs/resources/heart-attack-care-in-2016.pdf/ (4 June 2020)
13. Ibanez B, James S, Agewall S et al; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018 Jan 7;39(2):119-177. doi: 10.1093/eurheartj/ehx393. PMID: 28886621.
14. Roffi M, Patrono C, Collet JP et al; ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016 Jan 14;37(3):267-315. doi: 10.1093/eurheartj/ehv320. Epub 2015 Aug 29. PMID: 26320110.
15. Central Statistics Office, Ireland. Population and Labour Force Projections 2017 – 2051. https://www.cso.ie/en/releasesandpublications/ep/p-

plfp/populationandlabourforceprojections2017-2051/populationprojectionsresults/ (04 Jun 2020)

16. Irish Cardiac Society. Acute Coronary Syndromes activity during COVID-19 Irish Cardiac Society Survey, April 2020. Dublin: Irish Cardiac Society; 2020
17. Wong LE, Hawkins JE, Langness S et al. Where are all the patients? Addressing Covid-19 fear to encourage sick patients to seek emergency care. NEJM Catalyst Innovations in Care Delivery. 2020;1:3 doi: 10.1056/CAT.20.0193
18. Moroni F, Gramegna M, Ajello S et al. Collateral damage: medical care avoidance behavior among patients with acute coronary syndrome during the COVID-19 pandemic, JACC Case Reports (2020), doi: https:// doi.org/10.1016/j.jaccas.2020.04.010.

FIGURE LEGENDS

Figure 1. Panel A the cumulative incidence of PCI procedures for the treatment of All ACS is demonstrated during two months preceding (yellow) and succeeding (red) the first confirmed COVID-19 case in Ireland over time; **Panel B**, the daily new confirmed COVID-19 cases in Ireland with the orange line representing the locally smoothed trend; **Panel C,** The locally smoothed trend of COVID-19 daily new hospital and ICU admissions and confirmed/suspected deaths over time in Ireland; the orange dotted line in panel A, B and C represents the national closure of schools (13th March), the red dotted line represents the date of full lockdown implementation (28th March). (PCI, percutaneous coronary intervention; ACS, acute coronary syndrome; ICU, intensive care unit)

Figure 2. Cumulative incidence of PCI procedures for the treatment of NSTE-ACS and STEMI during the 2020-COVID period and the 2020-PreCOVID period. Panel A shows the overall cumulative incidence of PCI performed for the treatment of NSTE-ACS during 2020-PreCOVID (yellow) and 2020-COVID (red); In **Panel B** the overall cumulative incidence of PCI performed for the treatment of STEMI during the 2020-PreCOVID (yellow) and 2020-COVID periods (red) is shown; the orange dotted line in panel A and B represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction).

Figure 3. Cumulative incidence of PCI procedures for the treatment of STEMI comparing 2019 to 2020. The cumulative incidence of PCI procedures for the treatment of STEMI comparing January to April 2019 (yellow) to the same period in 2020 (red); the orange dotted line represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction)

DATA AVAILABILITY STATEMENT

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

Text Tables.

Table 1. Mean and standard deviation of daily PCI procedures per centre for All ACS, NSTE-ACS and STEMI cases.

Period	Total	Daily mean per centre	±SD
All ACS			
2020-COVID[a]	387	1.25	1.34
2020-PreCOVID[b]	490	1.66	1.66
NSTE-ACS			
2020-COVID[a]	212	0.68	1.07
2020-PreCOVID[b]	288	0.98	1.29
STEMI			
2020-COVID[a]	175	0.56	0.77
2020-PreCOVID[b]	202	0.68	0.86
2019-Reference[c]	436	0.73	0.92

[a]2020-COVID is February 29th - April 30th, 2020 (62 days);

[b]2020-PreCOVID is January 1st - February 28th, 2020 (59 days);

[c]2019-Reference is January 1st - April 30th, 2019 (120 days).

(PCI, percutaneous coronary intervention; ACS, Acute coronary syndrome; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation Myocardial Infarction)

Table 2. Comparison of PCI for the treatment of All ACS, NSTE-ACS and STEMI for the study period (2020-COVID) versus control period.

Period	Incidence rate ratio	95% Confidence Interval	P-Value
All ACS			
2020-COVID to 2020-PreCOVID	0.76	0.65 – 0.88	<0.001
NSTE-ACS			
2020-COVID to 2020-PreCOVID	0.71	0.57 – 0.88	0.002
STEMI			
2020-COVID to 2020-PreCOVID	0.82	0.67 – 1.01	0.061
2020-COVID to 2019-Reference	0.78	0.65 – 0.93	0.005

(PCI, percutaneous coronary intervention; ACS, Acute coronary syndrome; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation Myocardial Infarction)

Figure 1. Panel A the cumulative incidence of PCI procedures for the treatment of All ACS is demonstrated during two months preceding (yellow) and succeeding (red) the first confirmed COVID-19 case in Ireland over time; Panel B, the daily new confirmed COVID-19 cases in Ireland with the orange line representing the locally smoothed trend; Panel C, The locally smoothed trend of COVID-19 daily new hospital and ICU admissions and confirmed/suspected deaths over time in Ireland; the orange dotted line in panel A, B and C represents the national closure of schools (13th March), the red dotted line represents the date of full lockdown implementation (28th March). (PCI, percutaneous coronary intervention; ACS, acute coronary syndrome; ICU, intensive care unit)

150x165mm (300 x 300 DPI)

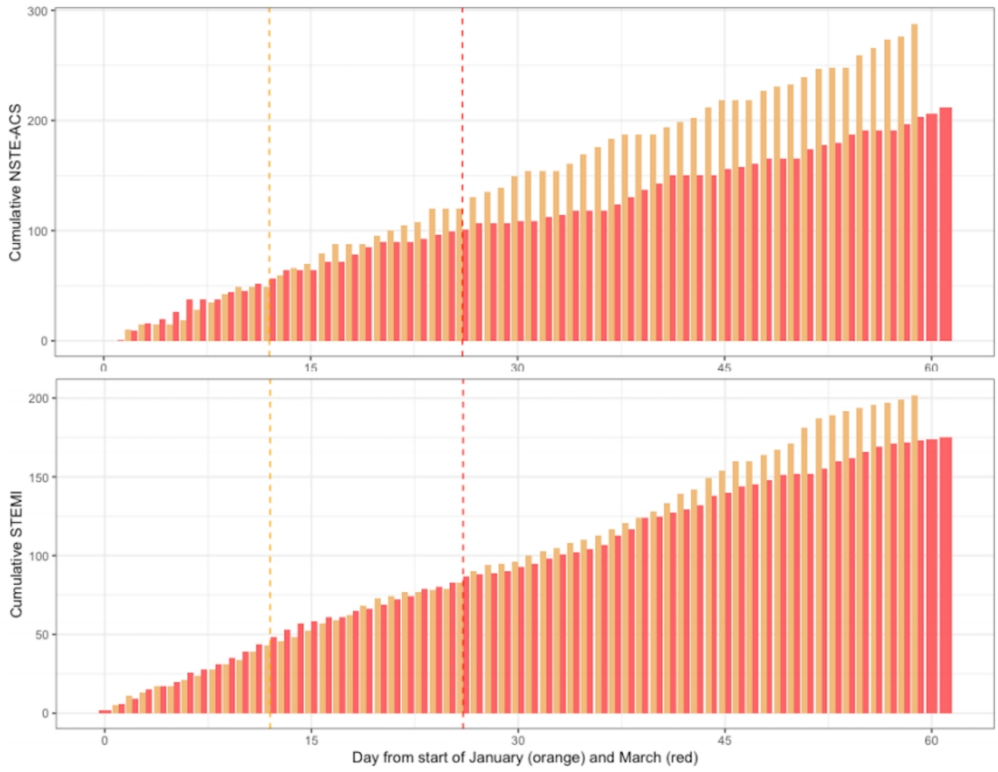

Figure 2. Cumulative incidence of PCI procedures for the treatment of NSTE-ACS and STEMI during the 2020-COVID period and the 2020-PreCOVID period. Panel A shows the overall cumulative incidence of PCI performed for the treatment of NSTE-ACS during 2020-PreCOVID (yellow) and 2020-COVID (red); In Panel B the overall cumulative incidence of PCI performed for the treatment of STEMI during the 2020-PreCOVID (yellow) and 2020-COVID periods (red) is shown; the orange dotted line in panel A and B represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction).

150x115mm (300 x 300 DPI)

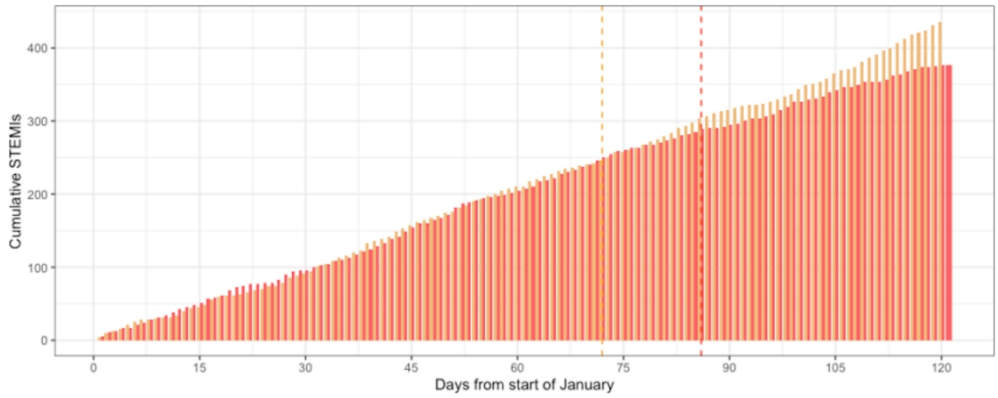

Figure 3. Cumulative incidence of PCI procedures for the treatment of STEMI comparing 2019 to 2020. The cumulative incidence of PCI procedures for the treatment of STEMI comparing January to April 2019 (yellow) to the same period in 2020 (red); the orange dotted line represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction)

150x60mm (300 x 300 DPI)

BMJ Open

Impact on Percutaneous Coronary Intervention for Acute Coronary Syndromes during the COVID-19 outbreak in a non-overwhelmed European health care system: COVID ACS-PCI Experience in Ireland

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-045590.R1
Article Type:	Original research
Date Submitted by the Author:	25-Feb-2021
Complete List of Authors:	Connolly, Niall; Galway University Hospitals, Dept. of Cardiology Simpkin, Andrew; National University of Ireland Galway, School of Medicine Mylotte, Darren; Galway University Hospitals, Dept. of Cardiology Crowley, James; Galway University Hospitals, Dept. of Cardiology; National University of Ireland Galway, School of Medicine O'Connor, Stephen; St. James' Hospital, Dublin, Dept. of Cardiology AlHarbi, Khalid; St. James' Hospital, Dublin, Dept. of Cardiology Kiernan, Thomas; University of Limerick; University Hospital Limerick, Dept. of Cardiology Arockiam, Sacchin; University Hospital Limerick, Dept. of Cardiology Owens, Patrick; University Hospital Waterford, Dept. of Cardiology John, Amal; University Hospital Waterford, Dept. Of Cardiology Blake, Gavin; Mater Misericordiae University Hospital, Dept. of Cardiology Fitzgerald, Sean; Mater Misericordiae University Hospital, Dept. of Cardiology Cadogan, Diarmaid; Mater Misericordiae University Hospital, Dept. of Cardiology Rosseel, Liesbeth; Galway University Hospitals, Dept. of Cardiology
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Infectious diseases
Keywords:	COVID-19, Ischaemic heart disease < CARDIOLOGY, Coronary intervention < CARDIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Impact on Percutaneous Coronary Intervention for Acute Coronary Syndromes during the COVID-19 outbreak in a non-overwhelmed European health care system: COVID ACS-PCI Experience in Ireland

Niall P Connolly[1], Andrew J Simpkin[2], Darren Mylotte[1], James Crowley[1,2], Stephen O'Connor[3], Khalid AlHarbi[3], Thomas J Kiernan[4], Sacchin Arockiam[4], Patrick Owens[5], Amal John[5], Gavin J Blake[6], Sean Fitzgerald[6], Diarmaid Cadogan[6], Liesbeth Rosseel[1]

[1] Department of Cardiology, Galway University Hospital, Ireland

[2] School of Medicine, National University of Ireland Galway, Ireland

[3] Department of Cardiology, St James' Hospital, Dublin, Ireland

[4] Department of Cardiology, University Hospital Limerick, Ireland

[5] Department of Cardiology, University Hospital Waterford, Ireland

[6] Department of Cardiology, Mater Misericordiae University Hospital Dublin, Ireland

Word Count: 2479 (excluding abstract, summary, figures, tables, legends and references)

Figures: 3

Tables: 2

Keywords: COVID-19, percutaneous coronary intervention, acute coronary syndrome, Ireland

Conflicts of interest: Darren Mylotte is a consultant for Medtronic, Boston Scientific, and Microport.

The other authors have no conflicts of interest to declare.

Corresponding Author:

Niall Connolly

Department of Cardiology

Galway University Hospital

Newcastle Road, Galway, Ireland

Mail: niallcon@gmail.com

ABSTRACT:

Aims

To evaluate temporal trends of acute coronary syndromes (ACS) treated via percutaneous coronary intervention (PCI) throughout the COVID-19 outbreak in a European healthcare system affected but not overwhelmed by COVID-19 related pathology.

Methods and Results

We performed a retrospective multicentre analysis of the rates of PCI for the treatment of ACS within the period two months pre and post the first confirmed COVID-19 case in Ireland, as well as comparing PCI for ST-Elevation Myocardial Infarction (STEMI) with the corresponding period in 2019. During the 2020-COVID period (29th February – 30th April 2020) there was a 24% decline in PCI for overall ACS (incidence rate ratio (IRR) 0.76; 95% confidence interval (CI) 0.65-0.88; P<0.001), including a 29% reduction in PCI for Non-ST Elevation-ACS (IRR 0.71; 95% CI 0.57-0.88; P=0.002) and an 18% reduction in PCI for STEMI (IRR 0.82; 95% CI 0.67-1.01; P=0.061), as compared to the 2020-PreCOVID period (January 1st - February 28th 2020). A 22% (IRR 0.78; 95% CI 0.65-0.93; P=0.005) reduction of PCI for STEMI was seen as compared with the 2019 reference period.

Conclusion

This study demonstrates a significant reduction in PCI procedures for the treatment of ACS since the COVID-19 outbreak in Ireland. The reasons for this decline are still unclear but patients need to be encouraged to seek medical attention when cardiac symptoms appear, in order to avoid incremental cardiac morbidity and mortality due to a reduction in coronary revascularisation for the treatment of ACS.

Keywords: COVID-19, coronary intervention, ischaemic heart disease, public health

ARTICLE SUMMARY

Strengths and limitations of the study:

- This is a retrospective multicentre analysis of the temporal trends of acute coronary syndromes (ACS) treated via percutaneous coronary intervention (PCI) throughout the initial COVID-19 outbreak in Ireland.
- The participating centres account for 79.6% of all STEMI presentations in Ireland giving a very good representation of the overall national picture.
- The figures represent daily numbers of PCI procedures for the treatment of ACS, rather than hospital admission for PCI which could underestimate the true incidence of ACS presenting to hospitals due to alterations in clinical practice patterns, such as a potential for increased use of non-invasive strategies.
- The analysis was performed inter-year and intra-year thus allowing the assessment for confounding by seasonable variations in presentations with ACS.
- The overall impact on cardiovascular and mortality hard outcomes are not currently measurable within the remit of this study.
- Detailed demographic information including socio-economic status, age, gender and comorbidities was not available for analysis.

Text:

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic has brought many challenges for healthcare systems and has had a huge impact on social behaviour. To minimise the spread of infection social distancing measures and wide restrictions in the movement of people have been implemented. Intermittent deferral of non-urgent and elective care has been a central tenet to increase hospital capacity to deal with the surge in COVID-19 cases and to avoid unnecessary exposure of patients to a hospital environment where COVID-19 may be more prevalent.

Initial expectations would have been for an increase in acute coronary syndrome (ACS) presentations in line with existing evidence suggesting a link between respiratory infections and subsequent myocardial infarction[1,2]. However, first reports during the initial phase of the COVID-19 outbreak showed a decline in presentations of ST-elevation myocardial infarction (STEMI) and hospital admissions for ACS, even in geographies where the health care system was not overwhelmed by COVID-19 pathology[3-8]. As percutaneous coronary intervention (PCI) has a proven beneficial outcome in the management of ACS, there is a concern that a similar decline in PCI procedures during the COVID-19 pandemic could lead to incremental cardiac morbidity and mortality[9].

This study represents data from the Republic of Ireland, a European country where widespread social and lockdown measures were implemented during the first wave of the COVID-19 outbreak, and the healthcare system has been affected, but not overwhelmed by COVID-19 related pathology. Our goal is to evaluate temporal trends of acute coronary syndromes treated via percutaneous coronary intervention during and before the COVID-19 outbreak in a European healthcare system affected but not overwhelmed by COVID-19 related pathology.

METHODS

In this multicentre retrospective registry, we examine the daily rates of PCI performed for the treatment of ACS during three different time periods in relation to the COVID-19 outbreak in Ireland. Participation was voluntary and data was anonymously collected by each participating centre in a dedicated electronic dataset. Cases were identified by combining cardiac catheterisation laboratory records showing performed PCI and hospital admission records. The data was cross-referenced with patient's paper and electronic records to provide accurate descriptors of the indication for PCI based on ESC defined diagnoses. Variables were categorised according to the indication and timing of PCI. National data regarding the COVID-19 outbreak were collected from the official Department of Health resources[10]. Ethical approval for the study was gained from the National Research Ethics Committee (NREC) established for COVID-19 related research in Ireland.

Patient and Public Involvement

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

Study Population

The Health Service Executive (HSE) dedicated ACS Programme designates six primary PCI centres in Ireland[11]. In this study the data are collected from five primary PCI facilities (Galway University Hospitals, Mater Misericordiae University Hospital Dublin, St. James's Hospital Dublin, University Hospital Limerick and Waterford University Hospital). The five participating centres in this study account for 79.7% of all STEMI presentations in Ireland (est. population 4.90 million in 2020) based on the latest published national data[12,13]. This study does not include any private health care facilities which also treat non-ST elevation acute coronary syndromes (NSTE-ACS) during office hours, but not STEMI cases.

Definitions

The daily rates of PCI procedures performed only for the treatment of ACS (ACS-PCI) during three delineated time periods were included in this study. The overall PCI group (´All ACS´) was dichotomised into two groups, as defined by the European Society of Cardiology guidelines: (1) ´STEMI´, and, (2) ´NSTE-ACS´, with the latter representing PCI performed for both non-ST elevation myocardial Infarction (NSTEMI) and unstable angina (UA)[14,15]. Daily ACS-PCI rates were collected for three separate time periods: (1) the ´2020-COVID´ period, was set from the date of the first confirmed COVID-19 case in Ireland, February 29th 2020, until April 30th 2020 (62 days); (2) the ´2020-PreCovid´ including January 1st to February 28th 2020 (59 days); and, (3) the ´2019-Reference´ period covering January to April 2019 (120 days). Daily PCI rates for STEMI were collected for the ´2019-Reference´, ´2020-PreCOVID´and the ´2020-COVID´ periods, whilst data regarding PCI performed for the treatment of NSTE-ACS were collected for the ´2020-PreCOVID´ and ´2020-COVID´ periods.

In Ireland, phased containment and delay strategies were initiated on a national level in order to reduce the peak impact of the COVID-19 pandemic and slow the spread of the disease in the community. During the initial containment phase, all confirmed cases were isolated in COVID-19 designated hospitals (all participating hospitals), and there were local school/business closures where there had been contact with an infected patient. Measures steadily progressed in the delay phase with the closure of all schools from 13th March and a ban on mass gatherings, closure of all pubs/bars on 16th March, progressing to other non-essential services on 25th March and a full country-wide lockdown by 28th March (**Figure 1**). Importantly, these measures were enforced at a national level without regional variability and continued for the duration of the studied period.

Statistical analysis

The data collected are daily counts of ACS-PCI procedures across the five participating centres. Hence, a negative binomial model was used to compare the effect of the COVID-19 pandemic on the

rate of daily interventions due to (1) STEMI, (2) NSTE-ACS and (3) all ACS, while allowing for over-dispersion in the daily rate of PCI procedures. Individual hospital was included as a random effect in all models, to account for clustering of data within settings. The '2019-Reference' and the '2020-PreCOVID' periods are compared with the more recent '2020-COVID' time period. Results are presented as incidence rate ratios (IRR) along with corresponding 95% confidence intervals and p-values. The IRR represents the ratio of the current rate of PCI relative to the preceding rate. IRR values below 1.0 suggest a reduction in PCI over time, whereas values above 1.0 would suggest an increase in PCI. Continuous variables, such as the mean daily rate of PCI cases per hospital, are presented as a mean ± standard deviation (SD). All analyses were performed in R v3.6 (R Core Team, 2020).

RESULTS

After the first COVID-19 case was confirmed 29th of February 2020 in Ireland, the cumulative incidence of COVID-19 confirmed cases rose above 1,000 cases by March 23th and reaching 20,612 by April 30th with 1,232 COVID-19 related deaths at that moment (**Figure 1**)[10]. For an estimated 4.90 million inhabitants, intensive care bed capacity was expanded from 255 to 411 critical care beds within the Irish public health system, with additional surge capacity of up to a total of 800 beds[13]. The number of confirmed and suspected COVID-19 cases in critical care was 160 at its maximum on April 4th, 2020[10].

During January and February 2020, the two months preceding the first confirmed COVID-19 case, 490 ACS-PCI were performed for the treatment of all categories of ACS. This compares with a total of 387 ACS-PCI cases in the succeeding two months. The mean daily rates per centre of PCI for all ACS, STEMI and NSTE-ACS are outlined in **Table 1**.

Table 1. Mean and standard deviation of daily PCI procedures per centre for All ACS, NSTE-ACS and STEMI cases.

Period	Total	Daily mean per centre	±SD
All ACS			
2020-COVID[a]	387	1.25	1.34
2020-PreCOVID[b]	490	1.66	1.66
NSTE-ACS			
2020-COVID[a]	212	0.68	1.07
2020-PreCOVID[b]	288	0.98	1.29
STEMI			
2020-COVID[a]	175	0.56	0.77
2020-PreCOVID[b]	202	0.68	0.86
2019-Reference[c]	436	0.73	0.92
2019-Jan/Feb[d]	207	0.70	0.91
2019-Mar/Apr[e]	229	0.75	0.94

[a]2020-COVID is February 29th - April 30th, 2020 (62 days);

[b]2020-PreCOVID is January 1st - February 28th, 2020 (59 days);

[c]2019-Reference is January 1st - April 30th, 2019 (120 days);

[d]2019-Jan/Feb is January 1st - Feb 28th, 2019 (59 days);

[e]2019-Mar/Apr is March 1st - April 30th, 2019 (61 days).

.

During the '2020-COVID' period, there was a 24% reduction in PCI for the treatment of all ACS as compared to the '2020-PreCOVID' period (Incidence Rate Ratio[IRR] 0.76, 95% confidence interval (CI) 0.65-0.88; p<0.001) (**Table 2**).

Table 2. Comparison of PCI for the treatment of All ACS, NSTE-ACS and STEMI for the study period (2020-COVID) versus control period.

Period	Incidence rate ratio	95% Confidence Interval	P-Value
All ACS			
2020-COVID to 2020-PreCOVID	0.76	0.65 – 0.88	<0.001
NSTE-ACS			
2020-COVID to 2020-PreCOVID	0.71	0.57 – 0.88	0.002
STEMI			
2020-COVID to 2020-PreCOVID	0.82	0.67 – 1.01	0.061
2020-COVID to 2019-Reference	0.78	0.65 – 0.93	0.005
2019-Jan/Feb to 2019-Apr/May	1.05	0.87 – 1.27	0.583
2020-COVID to 2019-Apr/May	0.76	0.62 – 0.92	0.006

There was a corresponding 29% reduction in PCI for the treatment of NSTE-ACS (IRR 0.71, 95% CI 0.57-0.88; p=0.002) and an 18% reduction in PCI for STEMI (IRR 0.82, 95% CI 0.67-1.01; p=0.061), as

compared to the '2020-PreCOVID' period (**Table 2**). During the '2020-COVID' period there was also a 22% reduction in PCI performed for the treatment of STEMI as compared to the '2019-Reference' period (IRR 0.78, 95% CI 0.65-0.93; p=0.005) (**Table 2**).

To assess confounding of the results by seasonal variability between the '2020-PreCOVID' and '2020-COVID' period (i.e. to verify whether admissions change naturally over time), we compared the overall STEMI rate in January/February 2019 with that of March/April 2019. There was no significant variability between both periods (IRR 1.05, 95% CI 0.87-1.27; p=0.583) (**Table 2**). Results were also reproducible year on year when we considered the STEMI PCI incidence in the period of March-April 2019 as compared to the corresponding ´2020-COVID' period, with a significant 24% lower PCI rate for STEMI in the '2020-COVID' period (IRR 0.76; 95% CI 0.62-0.92; p=0.006) (**Table 2**).

DISCUSSION

This study demonstrates a substantial reduction in PCI procedures performed for the treatment of all ACS, NSTE-ACS and STEMI during the initial stages of the COVID-19 pandemic in Ireland. During the two months since the first confirmed COVID-19 case, PCI rates for the treatment of all ACS, NSTE-ACS and STEMI dropped by 24%, 29% and 18%, respectively, with respect to the prior two months (**Figure 1**) (**Figure 2**). As compared to the 2019 reference period, there was a 22% reduction of PCI for STEMI during the '2020-COVID' period (**Figure 3**).

These data correspond with data from other countries detailing similar reductions in STEMI cases and ACS hospital admissions[3-8]. Here we highlight the impact of COVID-19 on the actual number of PCI procedures performed for the treatment of all ACS since the COVID-19 outbreak. This data is of particular relevance as it seems the pandemic affects both the number of patients presenting to hospital with ACS as well as the number of patients that undergo PCI as a treatment for ACS. It has been shown in other jurisdictions that the hospital admission rate for ACS itself has declined and the reduction in admissions is also mirrored in a downward trend in PCI rates[16]. Since coronary

revascularisation has a proven survival benefit in the treatment of both STEMI and NSTE-ACS, this raises concern for incremental cardiac morbidity and mortality during the initial phases of the COVID-19 pandemic.

It is difficult to fully account for this sudden and significant drop in PCI performed for the treatment of ACS among these primary PCI centres. In Ireland, where the healthcare system was not overwhelmed by COVID-19 cases, the emergency departments and primary PCI facilities remained operational without any capacity limitation. Potential factors for an observed reduction in ACS treatments include changes in lifestyle or environmental factors, such as workplace stressors or exposure to air pollution. The link between environmental pollution and cardiovascular outcomes is long established with both short- and long-term exposures to pollutants such as $PM_{2.5}$ (fine particulate matter ≤2.5 μm in aerodynamic diameter), Nitrogen Dioxide and Ozone linked with ACS[17,18]. Indeed, there have been changes in air quality recorded during lockdowns for COVID-19, both in Ireland and abroad with Nitrogen Dioxide levels in Ireland well-below expected levels compared to previous years[19-21]. In contrast to findings in major industrial cities worldwide there was not a significant drop in $PM_{2.5}$ in Ireland[22]. However, it remains plausible that a rapid reduction in particulate and other environmental pollutants could contribute to a reduction in ACS incidence and mortality.

We must also consider the potential effect of physician selection of patients for intervention on PCI rates. A more conservative approach to patient selection could contribute to a fall in invasive intervention with more patients being managed non-invasively. Misconceptions in the required acuity of management of STEMI vs NSTE-ACS could also lead to differences in referral patterns from non-specialist centres. Assuming a tendency towards a more conservative approach to management of NSTE-ACS could explain why the drop in procedures was more exaggerated in this group. Indeed, a suggestion of a move to a lower risk profile of patient has been seen during the pandemic in other jurisdictions that have shown drops in PCI rates for STEMI and NSTE-ACS[23].

One of the major overriding concerns however is that the true incidence of ACS in the population has remained largely unchanged during the COVID-19 pandemic and that the proportion of patients presenting to the hospital appropriately has fallen. The worry here is that a large proportion of ACS patients may not be presenting, or delaying their presentation, to health care facilities despite measures to preserve the function and capacity of emergency departments and acute cardiac facilities in Ireland. The Irish Cardiac Society conducted a survey amongst cardiologists at the height of the pandemic and reported that the reduction in ACS presentations to hospitals were attributed to: (1) people's fear of being exposed to COVID-19 within a healthcare facility (97%); (2) people not leaving their homes due to the government restrictions (41%); and, (3) people worried about putting a burden on the health services (41%)[24]. Fear for the healthcare environment as well as unawareness of the risk-mitigation efforts set up by the hospitals, were the overarching themes reported by patients in a series of semi-structured interviews performed during the pandemic in an American population[25]. Indeed, in relation to these latter assertions, cumulative incidence of PCI rates for ACS suggests further diverging of the curves the moment social distancing and lockdown measures were put in place, two weeks after the first confirmed COVID-19 case **(Figure 1)**.

Anecdotal evidence suggests that the reduction/delay in presenting to hospital with ACS during the COVID-19 era has resulted in an increase in the proportion of mechanical complications[26]. Indeed, recent studies have documented both prolonged delays from symptom onset to first medical contact, increased door-to-balloon time and total ischaemia time for the reduced number of patients who do present to hospital[27,28].

Given the reduction in acute coronary revascularisation observed in the current study and assuming the true incidence of ACS has not changed significantly, it is possible that we will yet see a future wave of new post-myocardial infarction induced heart failure presentations and arrhythmias leading to further morbidity and mortality. It will take a significant period of time before the true measure of effect of this pandemic in a cardiovascular sense is known and we will need to monitor excess mortality figures to assess for this indirect impact caused by this pandemic.

Our study has limitations. First, we were only able to include five of six Primary PCI centres in Ireland. The participating centres however, account for more than three quarters of all STEMI presentations in Ireland. Herein, we present the daily numbers of PCI procedures for the treatment of ACS, rather than hospital admissions for PCI. Using ACS-related PCI activity could underestimate the true incidence of ACS presenting to hospitals due to alterations in clinical practice patterns, such as an increased use of non-invasive strategies. However, our objective was to evaluate the patterns of invasive treatment of ACS during the COVID-19 pandemic. Further information on the number of ACS presentations to the participating hospitals as well as referrals for intervention from district hospitals that were treated non-invasively were not available. Additional complete clinical and mortality data were not available for all centres participating and therefore were not analysed.

In conclusion, we report a one quarter reduction in PCI for ACS during the COVID-19 pandemic in an affected, but not overwhelmed, European health-care system. Reasons for this reduction are numerous and varied. Clear public health messaging and measures are required to encourage patients to seek medical attention for non-COVID-19 related illness.

FUNDING STATEMENT

'This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors'.

AUTHOR CONTRIBUTIONS

- Niall P Connolly, Darren Mylotte, Liesbeth Rosseel; formed the concept, designed, wrote and revised the paper.
- Andrew J Simpkin; statistical analysis, graphics, critical revision of the paper for important intellectual content, final approval of the version to be published.
- James Crowley, Stephen O'Connor, Khalid AlHarbi, Thomas J Kiernan, Sacchin Arockiam, Patrick Owens, Amal John, Gavin J Blake, Sean Fitzgerald, Diarmaid Cadogan; data acquisition, critical revision of the paper for important intellectual content, final approval of the version to be published.
- All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Smeeth L, Thomas SL, Hall AJ et al. Risk of myocardial infarction and stroke after acute infection or vaccination. N Engl J Med 2004 Dec 16;351(25):2611-8. doi:10.1056/NEJMoa041747
2. Kwong, JC, Schwartz KL, Campitelli MA et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med 2018 Jan 25;378(4):345-353. doi:10.1056/nejmoa1702090
3. Garcia S, Albaghdadi MS, Meraj PM et al. Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States during COVID-19 Pandemic. J Am Coll Cardiol. 2020 Apr 9. pii: S0735-1097(20)34913-5. doi: 10.1016/j.jacc.2020.04.011.[Epub ahead of print]
4. De Filippo O, D'Ascenzo F, Angelini F et al. Reduced Rate of Hospital Admissions for ACS during COVID-19 Outbreak in Northern Italy. N Engl J Med. 2020 Apr 28. doi: 10.1056/NEJMc2009166.[Epub ahead of print]
5. Rodríguez-Leor O, Cid-Álvarez B, Ojeda S et al. Impacto de la pandemia de COVID-19 sobre la actividad asistencial en cardiología intervencionista en España. Rec Interv Cardiol. 2020;2:82-89. doi:10.24875/RECIC.M20000120
6. Rangé G, Hakim R, Motreff P. Where have the STEMIs gone during COVID-19 lockdown? Eur Heart J Qual Care Clin Outcomes. 2020 Apr 29. pii: qcaa034. doi: 10.1093/ehjqcco/qcaa034.[Epub ahead of print]
7. De Rosa SC, Spaccarotella C, Basso C et al. Reduction of Hospitalizations for Myocardial Infarction in Italy in the COVID-19 Era. Eur Heart J. 2020 May 15;ehaa409. doi: 10.1093/eurheartj/ehaa409. Online ahead of print.
8. Metzler B, Siostrzonek P, Binder RK et al. Decline of Acute Coronary Syndrome Admissions in Austria Since the Outbreak of COVID-19: The Pandemic Response Causes Cardiac Collateral Damage. Eur Heart J. 2020 May 14;41(19):1852-1853. doi: 10.1093/eurheartj/ehaa314.

9. Neumann FJ, Sousa-Uva M, Ahlsson A et al; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019 Jan 7;40(2):87-165. doi: 10.1093/eurheartj/ehy394. PMID: 30165437.
10. Department of Health, Ireland. Latest updates on COVID-19 (Coronavirus). https://www.gov.ie/en/news/7e0924-latest-updates-on-covid-19-coronavirus/ (2021 Feb 1704 June 2020)
11. Health Service Executive, Ireland. National Clinical Programmes – Acute Coronary Syndrome. https://www.hse.ie/eng/about/who/cspd/ncps/acs/ (2021 Feb 1724 May 2020)
12. Health Service Executive, Ireland. Report of the National Clinical Programme for Acute Coronary Syndrome (ACS) on standardising treatment of patients with STEMI in 2016. https://www.hse.ie/eng/about/who/cspd/ncps/acs/resources/heart-attack-care-in-2016.pdf/ (4 June 20202021 Feb 17)
13. Central Statistics Office, Ireland. Population and Labour Force Projections 2017 – 2051. https://www.cso.ie/en/releasesandpublications/ep/p-plfp/populationandlabourforceprojections2017-2051/populationprojectionsresults/ (04 Jun 2020)
14. Ibanez B, James S, Agewall S et al; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018 Jan 7;39(2):119-177. doi: 10.1093/eurheartj/ehx393. PMID: 28886621.
15. Roffi M, Patrono C, Collet JP et al; ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016 Jan 14;37(3):267-315. doi: 10.1093/eurheartj/ehv320.

Epub 2015 Aug 29. PMID: 26320110.Central Statistics Office, Ireland. Population and Labour Force Projections 2017 – 2051. https://www.cso.ie/en/releasesandpublications/ep/p-plfp/populationandlabourforceprojections2017-2051/populationprojectionsresults/ (04 Jun 2020)

16. Moroni F, Gramegna M, Ajello S et al. Collateral damage: medical care avoidance behavior among patients with acute coronary syndrome during the COVID-19 pandemic, JACC Case Reports (2020), doi: https:// doi.org/10.1016/j.jaccas.2020.04.010.
17. Pope CA, Muhlestein JB, Anderson JL et al. Short-Term Exposure to Fine Particulate Matter Air Pollution Is Preferentially Associated With the Risk of ST-Segment Elevation Acute Coronary Events. J Am Heart Assoc. 2015 Dec 8;4(12):e002506. doi: 10.1161/JAHA.115.002506.
18. Rajagopalan S, Al-Kindi SG, Brook RD. Air Pollution and Cardiovascular Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018 Oct 23;72(17):2054-2070. doi: 10.1016/j.jacc.2018.07.099.
19. Environmental Protection Agency, Ireland. Recent trends in nitrogen dioxide (NO2) levels in air (Ireland). 2020 Dec 17. http://www.epa.ie/newsandevents/news/pressreleases2020/name,70312,en.html (2021 Feb 19)
20. Jephcote C, Hansell AL, Adams K et al. Changes in air quality during COVID-19 'lockdown' in the United Kingdom. Environ Pollut. 2021 Mar 1;272:116011. doi:10.1016/j.envpol.2020.116011. Epub 2020 Nov 20.
21. He, G., Pan, Y. & Tanaka, T. The short-term impacts of COVID-19 lockdown on urban air pollution in China. *Nat Sustain* 3, 1005–1011 (2020). https://doi.org/10.1038/s41893-020-0581-y

22. Environmental Protection Agency, Ireland. Recent trends in air pollution levels in Ireland. 2020 Apr 9. http://www.epa.ie/newsandevents/news/pressreleases2020/name,68631,en.html

23. Kwok CS, Gale CP, Curzen N et al. Impact of the COVID-19 Pandemic on Percutaneous Coronary Intervention in England: Insights From the British Cardiovascular Intervention Society PCI Database Cohort. Circ Cardiovasc Interv. 2020 Nov;13(11):e009654. doi: 10.1161/CIRCINTERVENTIONS.120.009654. Epub 2020 Nov 3.

24. Irish Cardiac Society. Acute Coronary Syndromes activity during COVID-19 Irish Cardiac Society Survey, April 2020. Dublin: Irish Cardiac Society; 2020

25. Wong LE, Hawkins JE, Langness S et al. Where are all the patients? Addressing Covid-19 fear to encourage sick patients to seek emergency care. NEJM Catalyst Innovations in Care Delivery. 2020;1:3 doi: 10.1056/CAT.20.0193

26. Mafham MM, Spata E, Goldacre R et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. Lancet. 2020 Aug 8;396(10248):381-389. doi: 10.1016/S0140-6736(20)31356-8. Epub 2020 Jul 14.

27. Perrin N, Iglesias JF, Rey F, Benzakour L, Cimci M, Noble S, Degrauwe S, Tessitore E, Mach F, Roffi M. Impact of the COVID-19 pandemic on acute coronary syndromes. Swiss Med Wkly. 2020 Dec 31;150:w20448. doi: 10.4414/smw.2020.20448.

28. De Luc, G, Verdoia M, Cercek M. et al. “Impact of COVID-19 Pandemic on Mechanical Reperfusion for Patients With STEMI.” *Journal of the American College of Cardiology* vol. 76,20 (2020): 2321-2330. doi:10.1016/j.jacc.2020.09.546

FIGURE LEGENDS

Figure 1. Panel A the cumulative incidence of PCI procedures for the treatment of All ACS is demonstrated during two months preceding (green) and succeeding (red) the first confirmed COVID-19 case in Ireland over time; **Panel B**, the daily new confirmed COVID-19 cases in Ireland with the orange line representing the locally smoothed trend; **Panel C,** The locally smoothed trend of COVID-19 daily new hospital and ICU admissions and confirmed/suspected deaths over time in Ireland; the orange dotted line in panel A, B and C represents the national closure of schools (13th March), the red dotted line represents the date of full lockdown implementation (28th March). (PCI, percutaneous coronary intervention; ACS, acute coronary syndrome; ICU, intensive care unit)

Figure 2. Cumulative incidence of PCI procedures for the treatment of NSTE-ACS and STEMI during the 2020-COVID period and the 2020-PreCOVID period. Panel A shows the overall cumulative incidence of PCI performed for the treatment of NSTE-ACS during 2020-PreCOVID (green) and 2020-COVID (red); In **Panel B** the overall cumulative incidence of PCI performed for the treatment of STEMI during the 2020-PreCOVID (green) and 2020-COVID periods (red) is shown; the orange dotted line in panel A and B represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction).

Figure 3. Cumulative incidence of PCI procedures for the treatment of STEMI comparing 2019 to 2020. The cumulative incidence of PCI procedures for the treatment of STEMI comparing January to April 2019 (green) to the same period in 2020 (red); the orange dotted line represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction)

DATA AVAILABILITY STATEMENT

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

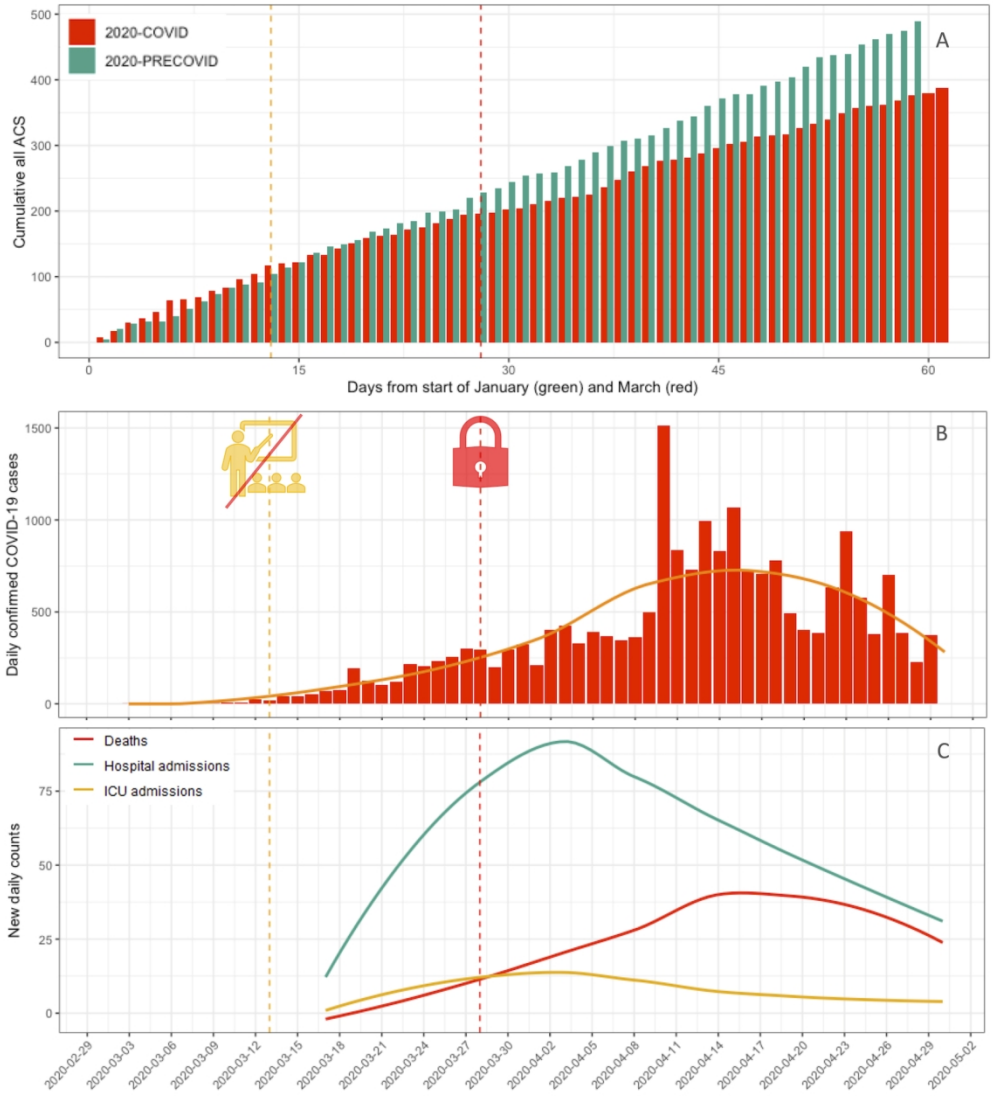

Figure 1. Panel A the cumulative incidence of PCI procedures for the treatment of All ACS is demonstrated during two months preceding (green) and succeeding (red) the first confirmed COVID-19 case in Ireland over time; Panel B, the daily new confirmed COVID-19 cases in Ireland with the orange line representing the locally smoothed trend; Panel C, The locally smoothed trend of COVID-19 daily new hospital and ICU admissions and confirmed/suspected deaths over time in Ireland; the orange dotted line in panel A, B and C represents the national closure of schools (13th March), the red dotted line represents the date of full lockdown implementation (28th March). (PCI, percutaneous coronary intervention; ACS, acute coronary syndrome; ICU, intensive care unit)

150x166mm (300 x 300 DPI)

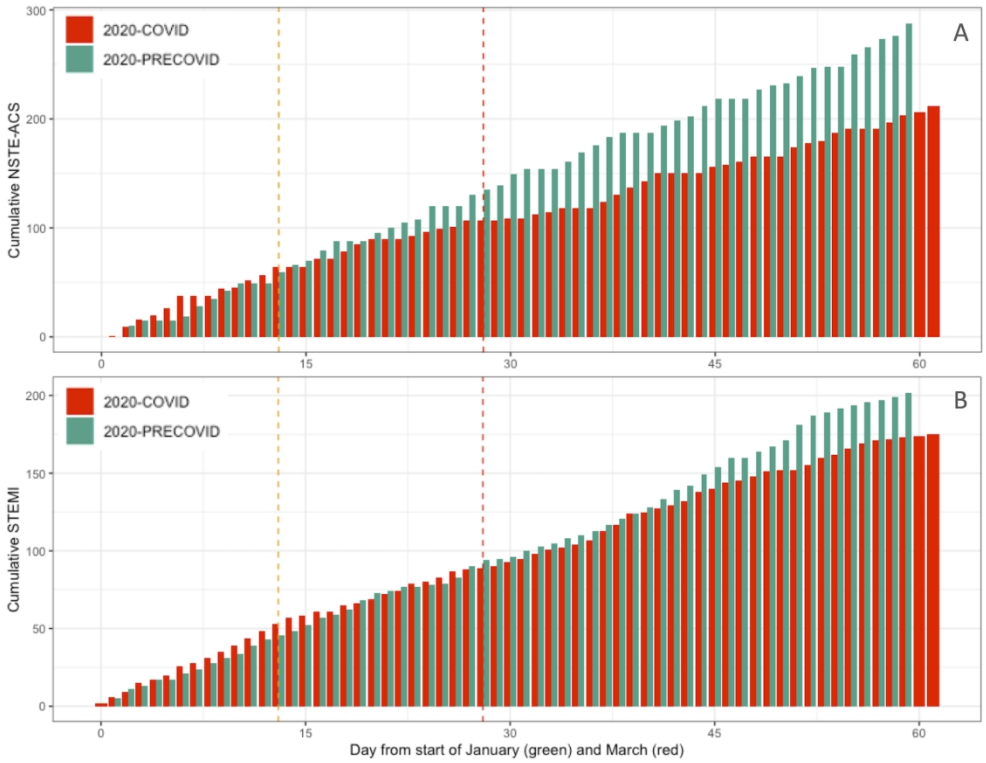

Figure 2. Cumulative incidence of PCI procedures for the treatment of NSTE-ACS and STEMI during the 2020-COVID period and the 2020-PreCOVID period. Panel A shows the overall cumulative incidence of PCI performed for the treatment of NSTE-ACS during 2020-PreCOVID (green) and 2020-COVID (red); In Panel B the overall cumulative incidence of PCI performed for the treatment of STEMI during the 2020-PreCOVID (green) and 2020-COVID periods (red) is shown; the orange dotted line in panel A and B represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction).

150x117mm (300 x 300 DPI)

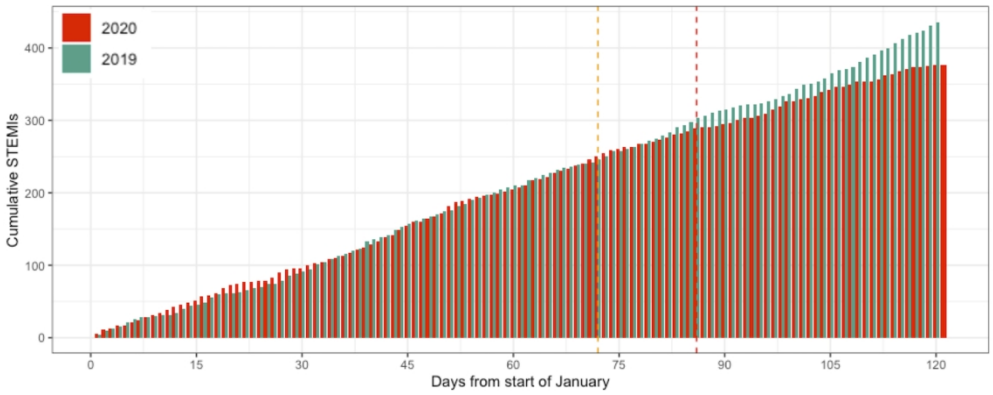

Figure 3. Cumulative incidence of PCI procedures for the treatment of STEMI comparing 2019 to 2020. The cumulative incidence of PCI procedures for the treatment of STEMI comparing January to April 2019 (green) to the same period in 2020 (red); the orange dotted line represents the national closure of schools, the red dotted line represents the date of full lockdown implementation. (PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction)

150x61mm (300 x 300 DPI)

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

	Item No	Recommendation	Page No	Relevant text from Manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Title
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	3	Introduction – Final summarizing sentence
Methods				
Study design	4	Present key elements of study design early in the paper	5-7	Methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6	Methods – Study Population, Definitions
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5,6	Methods – Study Population, Definitions
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed		Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7	Methods – Definitions, Statistical Analysis
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6	Methods –Definitions
Bias	9	Describe any efforts to address potential sources of bias	6,7	Methods – Statistical Analysis
Study size	10	Explain how the study size was arrived at		Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Not applicable
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6,7	Methods – Statistical Analysis
		(*b*) Describe any methods used to examine subgroups and interactions	6,7	Methods – Statistical Analysis
		(*c*) Explain how missing data were addressed	13	See limitations
		(*d*) If applicable, explain how loss to follow-up was addressed		Not Applicable

		(*e*) Describe any sensitivity analyses		
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		Not applicable
		(b) Give reasons for non-participation at each stage		Not applicable
		(c) Consider use of a flow diagram		Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13	See limitations, limited data set without demographic, social information
		(b) Indicate number of participants with missing data for each variable of interest		See limitations, limited data set without demographic, social information
		(c) Summarise follow-up time (eg, average and total amount)	5,6	Methods – Study Population, Definitions
Outcome data	15*	Report numbers of outcome events or summary measures over time	7-10	Results
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-10	Results
		(*b*) Report category boundaries when continuous variables were categorized		Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-10	Results
Discussion				
Key results	18	Summarise key results with reference to study objectives	10-13	Discussion
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13	See limitations
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-13	Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-13	Discussion and Conclusion
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if	14	Funding Statement

	applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

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