

# Atrial fibrillation burden during the coronavirus disease 2019 pandemic

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## Aims

The aim of this study is to determine the association between the coronavirus disease 2019 (COVID-19) pandemic and atrial fibrillation (AF) occurrence in individuals with cardiac implantable electronic devices (CIEDs).

## Method and results

Multi-centre, observational, cohort study over a 100-day period during the COVID-19 pandemic (COVID-19) in the USA. Remote monitoring was used to assess AF episodes in patients with a CIED (pacemaker or defibrillator; 20 centres, 13 states). For comparison, the identical 100-day period in 2019 was used (Control). The primary outcomes were the AF burden during the COVID-19 pandemic, and the association of the pandemic with AF occurrence, as compared with 1 year prior. The secondary outcome was the association of AF occurrence with per-state COVID-19 prevalence. During COVID-19, 10 346 CIEDs with an atrial lead were monitored. There were 16 570 AF episodes of  $\geq 6$  min transmitted (16 events per 1000 patient days) with a significant increase in proportion of patients with AF episodes in high COVID-19 prevalence states compared with low prevalence states [odds ratio 1.34, 95% confidence interval (CI) 1.21–1.48,  $P < 0.001$ ]. There were significantly more AF episodes during COVID-19 compared with Control [incident rate ratio (IRR) 1.33, 95% CI 1.25–1.40,  $P < 0.001$ ]. This relationship persisted for AF episodes  $\geq 1$  h (IRR 1.65, 95% CI 1.53–1.79,  $P < 0.001$ ) and  $\geq 6$  h (IRR 1.54, 95% CI 1.38–1.73,  $P < 0.001$ ).

## Conclusion

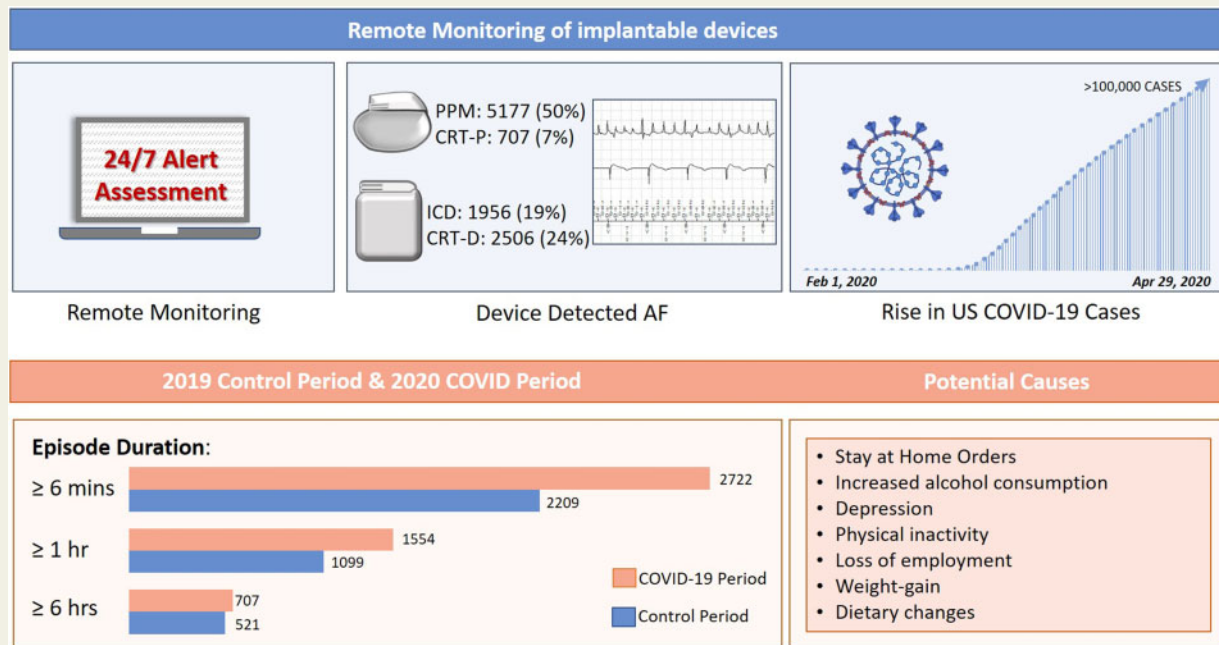
During the first 100 days of COVID-19, a 33% increase in AF episodes occurred with a 34% increase in the proportion of patients with AF episodes observed in states with higher COVID-19 prevalence. These findings suggest a possible association between pandemic-associated social disruptions and AF in patients with CIEDs.

## Clinical TRIAL registration

Australian New Zealand Clinical Trial Registry: ACTRN12620000692932.

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## Graphical Abstract



## Keywords

Atrial fibrillation • Cardiac implantable electronic device • Pacemaker • Defibrillator • Coronavirus disease 2019 • Coronavirus

## What's new?

- During the first 100 days of coronavirus disease 2019 (COVID-19), there was a 33% increase in atrial fibrillation (AF) episodes in patients with cardiac implantable electronic devices.
- Compared with the same time 1-year earlier there was significantly more episodes during COVID-19.
- Patients in high COVID-19 states were more affected by AF than those in lower COVID-19 prevalent states.

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic has infected more than 7 million people and claimed over 200 000 lives in the USA as of early October 2020.<sup>1</sup> In addition, the pandemic has uniquely affected the daily lives of millions more, due to unprecedented unemployment figures, and the implementation of social distancing, enforced lockdowns, and work-from-home arrangements for many.

Historically, various significant world events, including natural disasters and the 2001 World Trade Center attack, have coincided with a substantial rise in ventricular arrhythmias<sup>2,3</sup>; however, the effects of such events on atrial arrhythmias are less clear. Atrial arrhythmias are

more likely to occur in the setting of various modifiable risk factors, inclusive of physical inactivity, weight gain, alcohol intake, and stress.<sup>4</sup> We hypothesized that the COVID-19 period would be associated with an increase in the burden of atrial fibrillation (AF), due to the effect of pandemic-related societal disruption on AF risk factors.

Device-detected AF is highly prevalent amongst patients with a cardiac implantable electronic device (CIED),<sup>5</sup> and infers a significant stroke risk.<sup>6</sup> Remote monitoring of CIEDs allows for the timely assessment of device-detected arrhythmic events. In the setting of social distancing, remote monitoring provides an opportunity to assess CIED arrhythmia episodes during the coronavirus pandemic without face-to-face patient–clinician contact. Here, we utilized remote monitoring technology to assess AF episodes in CIED patients during the early coronavirus pandemic, compared with the same time 1 year prior.

## Methods

### Study cohort and data source

This study is a multi-centre, observational cohort study, including all patients with a CIED with an atrial lead, receiving remote monitoring via PaceMate™, a vendor-neutral service providing remote monitoring to a broad outpatient demographic, inclusive of hospital-based and community-based device clinics, across multiple states in the USA.

Data were obtained from PaceMate LIVE™, a software system with automatic integration of all remote monitoring transmissions and alerts from multiple device vendor platforms, streamlined into a single user interface. Patients receiving remote monitoring during the 100 days following confirmation of the first COVID-19 case in the USA (COVID period: 21 January to 29 April 2020 inclusive) were identified. For comparison, the identical period in 2019 was utilized (Control Period: 21 January to 30 April 2019 inclusive). To account for the natural progression of AF episodes over time, a further comparison between the Control Period and a 100-day period in late 2019 (Pre-COVID Control Period: 12 September to 20 December inclusive, after exclusion of the Christmas period) was undertaken.

The authors assume responsibility for the accuracy and completeness of the data analysis. The study complies with the Declaration of Helsinki and was reviewed and approved by the Human Research Ethics Committees of the Royal Adelaide Hospital and the University of Adelaide, Adelaide, Australia. The study was registered with the Australia and New Zealand Clinical Trials Registry (ANZCTR12620000692932).

## Study design

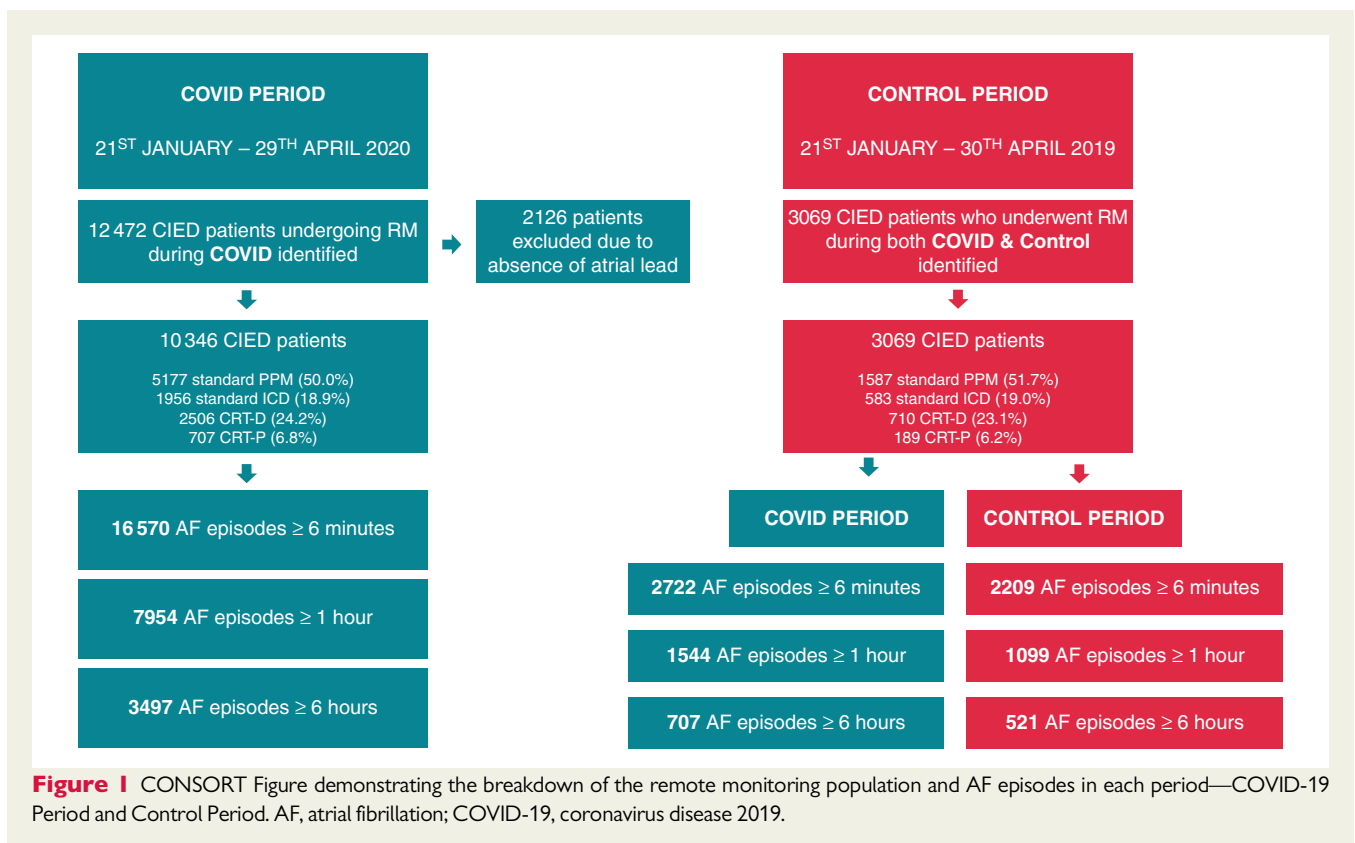
Analysis of the primary study cohort was designed to examine AF occurrence during the COVID-19 pandemic, and to compare AF occurrence between states according to COVID-19 prevalence. The primary cohort included all patients with a CIED [permanent pacemaker (PPM), cardiac resynchronization therapy pacemaker (CRT-P)], implantable cardioverter-defibrillator (ICD), or cardiac resynchronization therapy-defibrillator (CRT-D) *in situ* who received remote monitoring during the COVID-19 Period ( $n = 10\,346$ ; Figure 1). We excluded all patients without an atrial lead *in situ* and those patients programmed to a mode without atrial sensing and pacing, to aid accurate rhythm interpretation. The

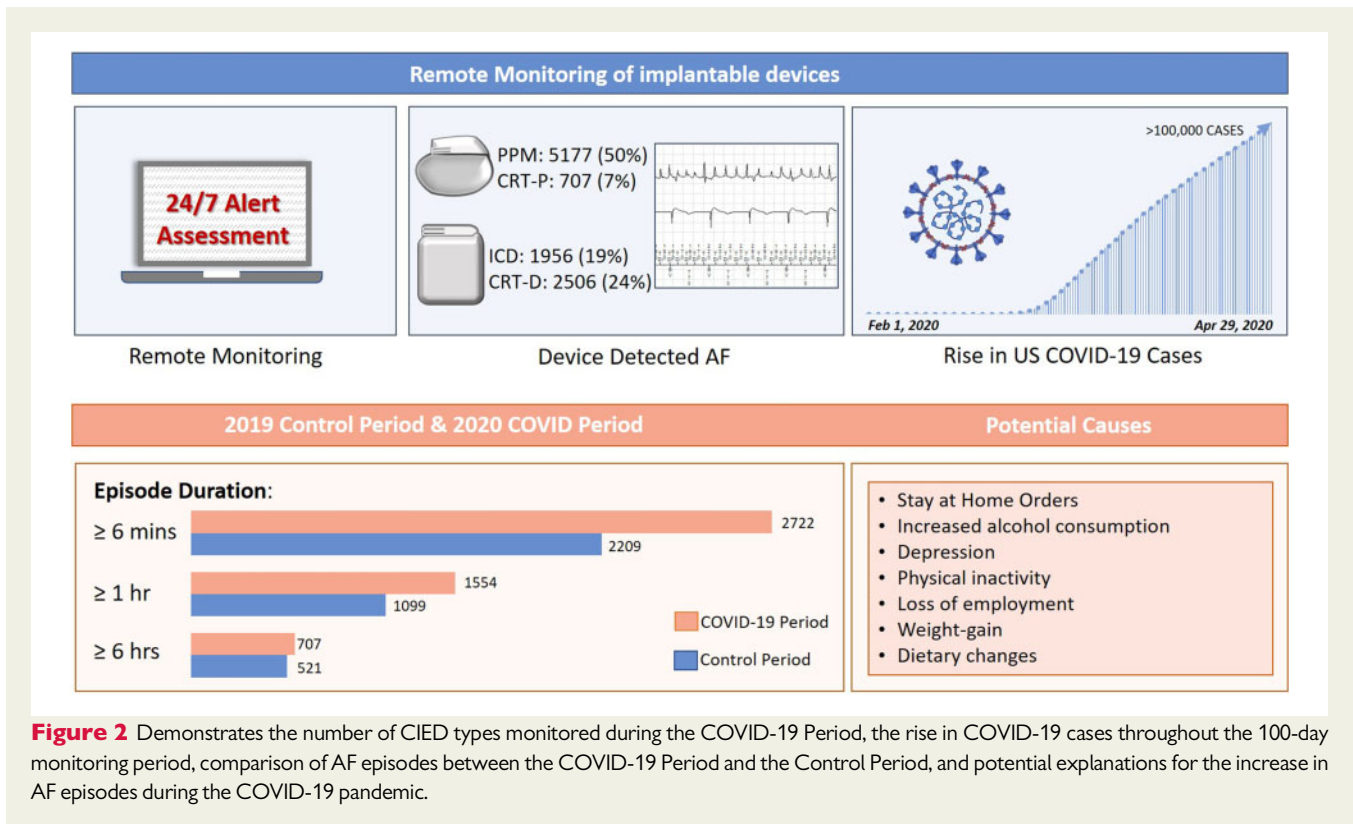
quantity and duration of AF episodes was determined across all monitoring sites and divided into respective states and correlated with per-state COVID-19 prevalence.

Analysis of the secondary study cohort was designed to determine the association between the pandemic and AF occurrence, by assessment of AF episodes during COVID-19 in comparison with the same time period 1 year prior. The secondary cohort included all patients with a CIED (PPM, CRT-P, ICD, or CRT-D) *in situ* who received remote monitoring during both the COVID-19 Period and the Control Period ( $n = 3069$ ; Figure 1), allowing for a paired analysis with direct comparison. PaceMate™ had provided a remote monitoring service since 2017 with gradual expansion since, leading to a progressive increase in the number of CIED patients undergoing PaceMate™ remote monitoring over this time. As a result, the number of patients included in the secondary cohort, who underwent remote monitoring during both the COVID-19 Period and the Control Period (in early 2019), was fewer than the number of patients who were included in the primary cohort.

Analysis of the tertiary study cohort was designed to account for the natural progression of AF episodes over time. The tertiary cohort included all patients with a CIED (PPM, CRT-P, ICD, or CRT-D) *in situ* who received remote monitoring during both the Control Period and the Pre-COVID Control Period ( $n = 3359$ ), prior to the pandemic (12 September to 20 December 2019 inclusive, after exclusion of the Christmas period), allowing for a paired analysis with direct comparison.

All transmitted AF episodes were identified. Episode classification occurred according to the arrhythmia adjudication algorithms of each pacemaker or defibrillator model, combined with programmed arrhythmia detection thresholds at the treating physician's discretion. All transmissions were received and adjudicated by cardiac device specialists certified by the International Board of Heart Rhythm Examiners.





## COVID infection prevalence

COVID-19 prevalence per state was obtained via data from the US Centres for disease control and prevention website.<sup>1</sup> Infections per state as at 29 April (end of COVID-19 study monitoring period) were recorded. For the purposes of our analysis, states were classified as either high-COVID-prevalent ( $\geq 10\,000$  confirmed COVID cases) or low-COVID-prevalent ( $< 10\,000$  confirmed COVID cases).

## Study outcomes

The primary outcomes of the study were AF occurrence in CIED patients during the COVID-19 pandemic, and the impact of the pandemic on AF episodes, as determined by comparison with the same time period 1 year prior. The secondary outcome was the association of AF with prevalence of COVID-19 infection per state.

## Atrial fibrillation episode duration

Previous studies have demonstrated device-detected AF episodes  $\geq 6$  min have a high positive predictive value,<sup>7</sup> and an associated increase in the risk of ischaemic stroke and systemic embolism.<sup>7</sup> Therefore, in the current study, AF episodes were categorized in a binary fashion according to duration. To mitigate the inclusion of false-positive AF transmissions, episodes  $\geq 6$  min duration were deemed significant, with episodes  $< 6$  min deemed insignificant.

To further extrapolate the association of the pandemic with AF occurrence, based on current understanding of device-detected AF episodes, and the increase in stroke risk with longer episode durations,<sup>5,6</sup> we additionally evaluated the following AF episode durations:  $\geq 1$  and  $\geq 6$  h.

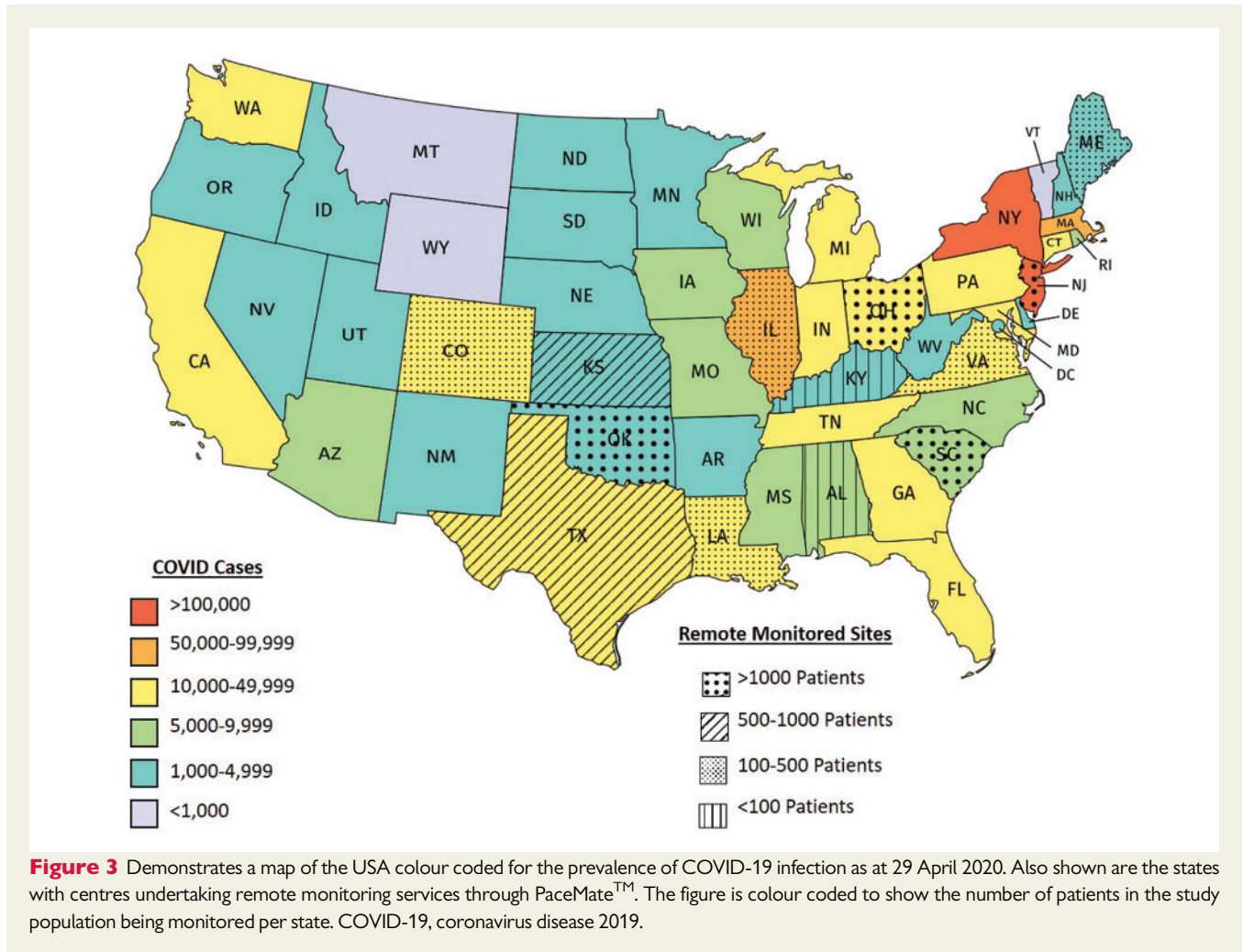
## Statistical analysis

The summary statistics are presented as frequencies and percentages, and continuous variables as mean [standard deviation (SD)] or median [interquartile range (IQR)]. Paired data regarding AF episodes in patients undergoing monitoring during both the COVID-19 Period and Control Periods were analysed using McNemar's  $\chi^2$  test. Univariate and multivariable Poisson regression analyses were used to compare the incidence of AF episodes adjusted for patient age and geographical location (US state) to derive incident rate ratios (IRRs) with 95% confidence intervals (CIs). The state with the lowest COVID-19 prevalence was considered the reference group to estimate the IRR for primary events. The association between incidence of AF and COVID-19 prevalence per state was evaluated using logistic regression and reported odd ratios (ORs) with 95% CI. A two-sided  $P$  value of  $< 0.05$  was considered statistically significant. All statistical analyses were performed using Stata 16 (StataCorp LLC, TX, USA).

## Results

### Study population

During the COVID-19 Period, 12 472 patients with a CIED *in situ*, representing 20 centres from 13 states, underwent remote monitoring via PaceMate<sup>TM</sup>. Excluded from the analysis were 2126 patients who were either without an atrial lead *in situ* or were programmed without atrial sensing and pacing, resulting in a primary cohort population of 10 346 patients, including 5177 (50.0%) PPMs, 707 (6.8%) CRT-Ps, 1956 (18.9%) ICDs, and 2506 (24.2%) CRT-Ds (Figure 1 and



2). The mean patient age was  $73 \pm 12$  years. Further details regarding the number of patients monitored per state and device types are provided in [Figure 3](#) and [Supplementary material online, Tables S3 and S4](#).

Of the 10 346 primary cohort patients, 3069 patients had also undergone remote monitoring during the Control Period and were included in the secondary cohort analysis determining the association between COVID-19 and AF occurrence. These patients represented 14 centres in 8 states, and included 1587 (51.7%) PPMs, 189 (6.2%) CRT-Ps, 583 (19.0%) ICDs, and 710 (23.1%) CRT-Ds ([Figure 3](#)). The mean patient age was  $74 \pm 12$  years.

### COVID-19 burden per state

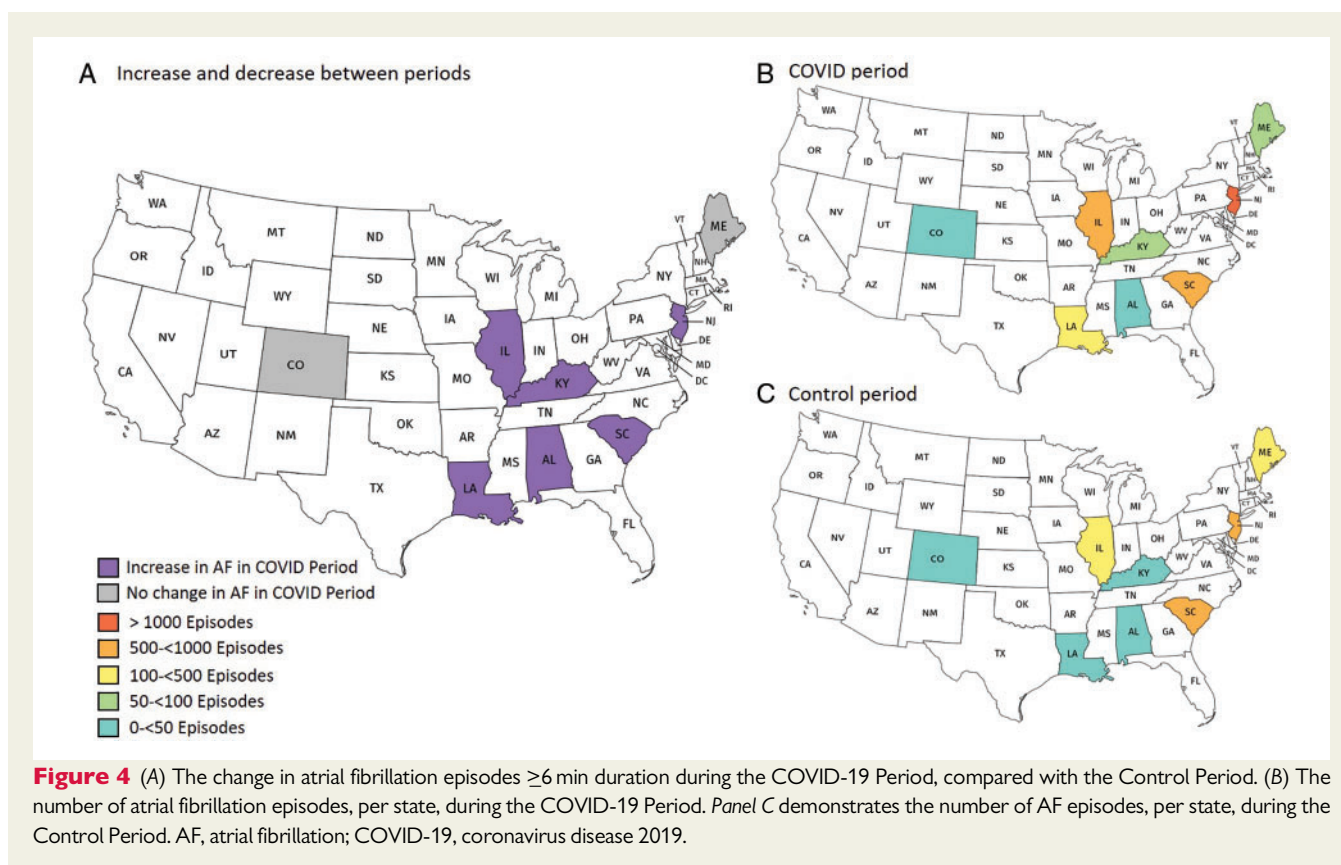
The number of confirmed COVID-19 cases per monitored state as at 29 April 2020 are detailed in [Figure 3](#) and [Supplementary material online, Table S1](#). All states included in the analysis had initial social isolation measures introduced in March 2020 (varying from state-to-state but consisting of either closure of bars and restaurants, or closure of schools). Formal stay-at-home orders were issued in all states between 21 March and 7 April 2020. Further details are provided in [Supplementary material online, Table S2](#).

### Atrial fibrillation episodes during COVID-19: primary cohort ( $n = 10\,346$ )

During the COVID-19 Period, the primary cohort transmitted 44 021 AF episodes, 16 570 (37.6%) of which were  $\geq 6$  min in duration, translating to 16 AF episodes per 1000 patient days. At least one AF episode  $\geq 6$  min was transmitted by 1254 (12.1%) patients. [Supplementary material online, Table S5](#) provides detail regarding episodes per state. There were 7954 (18.1%) episodes  $\geq 1$  h in duration, transmitted by 953 (9.2%) individual patients, and 3497 (7.9%) episodes  $\geq 6$  h in duration, transmitted by 618 (6.0%) individual patients. This equated to eight episodes  $\geq 1$  h, and three episodes  $\geq 6$  h, per 1000 patient days. Details regarding episodes per state and episodes per 1000-patient days per state, for all three episodes duration cut-offs, are provided in [Supplementary material online, Figure S2](#).

### Association of COVID-19 with atrial fibrillation occurrence: secondary cohort ( $n = 3069$ )

Atrial fibrillation episodes, transmitted by the 3069 secondary cohort patients who were remote monitored during both the COVID-19 Period and the Control Period, were compared. During the



COVID-19 Period, 251 (8.2%) patients experienced 2722 AF episodes  $\geq 6$  min, while during the Control Period, 276 (9.0%) patients were responsible for 2209 AF episodes  $\geq 6$  min. Details regarding episodes  $\geq 6$  min, per state, are provided in [Figure 4](#) and [Supplementary material online, Table S6](#). The number of individual patients in the secondary cohort who experienced an AF episode  $\geq 6$  min duration during the COVID-19 and Control Periods did not significantly differ [odds ratio (OR) 1.21, 95% CI 0.94–1.56,  $P=0.13$ ]. Multivariable Poisson regression analysis demonstrated a significant increase in AF episodes of  $\geq 6$  min duration during the COVID-19 Period compared with the Control Period (IRR 1.33, 95% CI 1.25–1.40,  $P<0.001$ ; [Supplementary material online, Table S7](#)). This difference further increased when comparing episodes of  $\geq 1$  h duration (IRR 1.65, 95% CI 1.53–1.79,  $P<0.001$ ; [Supplementary material online, Table S8](#) and [Figure S3](#)) and  $\geq 6$  h duration (IRR 1.54, 95% CI 1.38–1.73,  $P<0.001$ ; [Supplementary material online, Table S9](#) and [Figure S3](#)). Details regarding episodes for all three episodes duration cut-offs, during both time periods, are provided in [Figure 2](#). Of the 3069 secondary cohort patients, 70 (2.3%) had a change to mode-switch rate programming that occurred during the study period.

### Progression of atrial fibrillation episodes over time: tertiary cohort ( $n = 3359$ )

Atrial fibrillation episodes, transmitted by the 3359 tertiary cohort patients who were remote monitored during both the Control Period and the Pre-COVID Control Period, were compared. Multivariable regression analysis demonstrated an increase in AF

episodes of  $\geq 6$  min duration during the Pre-COVID Control Period compared with the Control Period (IRR 1.24, 95% CI 1.17–1.30,  $P<0.001$ ), and an increase in AF episodes of  $\geq 1$  h duration (IRR 1.19, 95% CI 1.10–1.28,  $P<0.001$ ). There was no significant difference in AF episodes of  $\geq 6$  h duration (IRR 1.12, 95% CI 1.00–1.25,  $P<0.061$ ) between the two time periods.

### Association of COVID-19 state prevalence with atrial fibrillation occurrence

Of the 13 states with centres undergoing remote monitoring during COVID-19, seven were classified as high-COVID-prevalent ( $\geq 10\,000$  COVID-19 cases: CO, IL, LA, NJ, OH, TX, and VA), and six were classified as low-COVID-19-prevalent ( $<10\,000$  COVID-19 cases: AL, KS, KY, ME, OK, and SC). High-COVID-19-prevalent states saw a significantly higher proportion of patients with AF during the COVID-19 Period, compared with low-COVID-19-prevalent states (OR 1.34, 95% CI 1.21–1.48,  $P<0.001$ ).

### Discussion

The impact of global events on the AF burden has been relatively poorly studied. Using a remotely monitored multi-centre cohort of CIED patients we evaluated the association of the COVID-19 pandemic and related social disruptions with AF occurrence. The major finding of this study is a significant increase in AF episodes during the

COVID-19 pandemic compared with the identical period a year earlier. This escalation in AF was present across episodes of  $\geq 6$  min,  $\geq 1$  h, and  $\geq 6$  h duration, with a 33%, 65%, and 54% increase, respectively. In addition, there was a strong relationship between COVID-19 prevalence and the occurrence of AF, with 34% more patients being affected by AF in high-COVID-19-prevalent states, compared with lower prevalent states. Though pandemic circumstances were associated with increased frequency of AF episodes in affected patients, we did not see a significantly higher proportion of patients experiencing AF.

AF is a progressive disease, and over time patients may experience longer-duration episodes.<sup>8</sup> Our study demonstrated only a 24% increase in episodes of  $\geq 6$  min and a 19% increase in episodes of  $\geq 1$  h between the control period in early 2019, and a second control period in late 2019, just prior to the pandemic onset in the USA. Furthermore, there was no difference in AF episodes of  $\geq 6$  h duration between early and late 2019. When contrasted with the far larger differences seen between early 2019 and the COVID-19 Period, these data support that the increase in AF episodes seen during the COVID pandemic is not solely attributable to the natural history of AF over time.

A recent Danish study identified a 47% reduction in the nationwide diagnosis of *de novo* AF during pandemic-related lockdown, compared with the same time period in 2019.<sup>9</sup> Our study did not specifically differentiate *de novo* AF episodes from AF recurrence. Our cohort has underlying cardiac disease necessitating a CIED implant, a population in which AF is common,<sup>5</sup> and unlike the prior study, CIED patients will have all AF episodes detected and recorded, regardless of symptoms. The observations in Denmark may be attributable to a reduction in patients accessing healthcare, rather than being reflective of a true decrease in AF incidence. For many patients AF is an asymptomatic and thus incidental diagnosis; if patients avoid routine contact with healthcare systems during lockdown, incidental AF may go undiagnosed.

Given the multitude of ways in which the COVID-19 pandemic has altered lives of people across the globe, and the associated stress, we hypothesized that the pandemic would be associated with a rise in AF episodes. The lifestyle impacts of the pandemic are far-reaching, as a large proportion of the population is forced to adapt their usual daily routine due to circumstances including social distancing, stay-at-home orders, work-from-home arrangements, loss of employment, and individual economic struggles. The observed increase in AF incidence is likely multifactorial, and may relate to the complex interactions between chronic stress, diet, physical activity, weight gain, alcohol use, and economic circumstances, all of which have been impacted during the pandemic. Possible contributory effects of COVID-19 infection cannot be excluded.

Various online surveys have examined the impact of COVID-19 restrictions on dietary behaviours. Both Sidor and Rzymiski<sup>10</sup> and Scarmozzino and Visioli<sup>11</sup> reported an increase in food consumption during the pandemic, in 43% and 46% of respondents, respectively. Ammar *et al.*<sup>12</sup> found an increase in poorer eating behaviours in a cohort of over 1000 patients in Africa, Asia, and Europe, with 20% reporting binge-eating and 23% reporting unhealthy food choices 'most of the time' during the pandemic. Another study of individuals attending an obesity clinic found 61% of participants reported stress-eating during the lockdown.<sup>13</sup> A reduction in the quality of food

consumed during the pandemic may be attributable to reduced fresh produce availability, restrictions in store opening hours, reluctance to venture out to buy fresh food, purchase of non-perishables due to fear of future food availability,<sup>14</sup> and individual economic circumstances limiting choice.<sup>15</sup> An increase in food consumption may be due to pandemic-related stress, which has been linked to poorer food-related choices.

Changes in patterns of physical activity have emerged during the pandemic. As people are encouraged to stay at home, and in many instances prohibited from attending gyms and sports centres, a trend of increased sedentary behaviour has been observed. In addition to home confinement restrictions making exercise-conducive environments less available, stress likely plays a role, reducing willingness to engage in physical activity.<sup>16</sup> One study noted a total 28% increase in sitting time amongst over 1000 survey respondents,<sup>12</sup> while two other studies have found almost half of participants (47.9% and 48.6%, respectively) had reduced their physical activity during pandemic lockdown.<sup>13</sup> Poorer cardiorespiratory fitness has been associated with an increase in AF,<sup>17</sup> and thus these observed patterns related to sedentary behaviour and exercise may contribute to the increase in AF occurrence that we observed.

Weight gain during the COVID-19 pandemic is a predictable outcome in the context of adverse changes in eating habits and reductions in physical activity, and has been linked to stress.<sup>18</sup> Weight gain during the pandemic was reported in 48.6% of 3500 participants and 19.5% of 1932 participants in two Italian studies,<sup>11</sup> and in 30% of over 1000 survey respondents in a Polish study.<sup>10</sup> Obesity is an important risk factor for AF, with studies demonstrating a reduction in AF with implementation of appropriate weight management strategies<sup>4</sup>; the effects of pandemic weight gain have likely contributed to an increase in AF occurrence.

Alcohol consumption has been identified as a risk for AF.<sup>19</sup> During the COVID-19 pandemic, two analyses have reported an increase in alcohol consumption in 10% and 14.6% of surveyed participants, respectively.<sup>10,11</sup> Alcohol intake may compound or even cause other AF risk factors, such as hypertension, weight gain, and obstructive sleep apnoea, to ultimately significantly contribute to AF occurrence.

As patients adhere to stay-at-home orders, work from home, or are newly unemployed, opportunity for sleep may increase. Alternatively, pandemic-related stress may translate to shorter sleep duration for some patients. A survey undertaken during the lockdown period in China reported reduced sleep quality (of which sleep duration was one measure) in 15.3% of 7236 respondents.<sup>20</sup> Both relatively long and short sleep duration have associations with AF incidence. Khawaja *et al.* reported an elevated risk of AF with longer sleep duration in a cohort of over 18 000 male physicians in the USA. In the same cohort, for patients with obstructive sleep apnoea shorter sleep duration lead to a modest elevation in risk of AF.<sup>21</sup> Substantial nightly variation in sleep apnoea severity has been demonstrated and correlates with the risk of AF.<sup>22</sup>

Pharmacologic compliance may be a factor influencing AF burden. Previous studies have identified medication cost and financial strain as factors influencing adherence to medications for some patients.<sup>23,24</sup> In the setting of unprecedented unemployment figures, and economic uncertainty, purchase of usual prescribed medications may be compromised, leading to emergence of AF in patients who usually maintain sinus rhythm on antiarrhythmic agents.

Whilst there are several plausible explanations for the increase in device-detected AF episodes during the COVID-19 period, we have recently reported that the frequency of ventricular arrhythmias requiring device therapies during the COVID-19 period was significantly reduced.<sup>25</sup> The contrasting relationship of isolation measures with ventricular and atrial arrhythmias, highlight differences in arrhythmia perpetrators that are potentially important elements in the management of arrhythmias.

## Limitations

The data for this study have been obtained from a real-world remote monitoring registry and are observational in nature. In addition, we do not have available data from preceding years for comparison. Details regarding device implant indication, clinical characteristics, individual patient management, and health care utilization are not available. Further, there is no information on behavioural changes that were adapted by individuals included in this analysis or their exposure to COVID-19 infection. It is thus unclear if a direct relationship between COVID-19 infection and AF occurrence exists. Similarly, our analysis does not account for inter-state, inter-city, and inter-county variance in pandemic-related restrictions and lockdown. As a result, confounding variables may exist. Finally, AF is known to be a progressive condition<sup>26</sup> and in itself may have partially influenced the outcome of the study.

## Conclusions

The COVID-19 pandemic has been associated with a marked increase in AF episodes in CIED patients. Atrial fibrillation occurrence was most dramatically increased in states with a greater prevalence of COVID-19 infection, suggesting a potential relationship between the degree of social disruption and AF risk factors.

## Supplementary material

Supplementary material is available at *Europace* online.

## Funding

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**Conflict of interest:** C.H., N.R., and K.C. are employees of Pacemate. D.H.L. reports the University of Adelaide has received on

his behalf lecture and/or consulting fees from Abbott Medical, Bayer, Biotronik, Boehringer Ingelheim, Medtronic, Microport, and Pfizer/BMS. P.S. reports having served on the advisory board of Medtronic, Abbott Medical, Boston Scientific, CathRx, and PaceMate. P.S. reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Medtronic, Abbott Medical, and Boston Scientific. P.S. reports that the University of Adelaide has received on his behalf research funding from Medtronic, Abbott Medical, Boston Scientific, and Microport. All other authors report no conflicts.

## Data availability

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

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