Daylight Saving Time transitions and cardiovascular disease in Andalusia: time series modelling and analysis using visibility graphs

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Abstract

The present study aimed to determine whether transitions both to and from daylight saving time (DST) led to an increase in the incidence of hospital admissions for major acute cardiovascular events (MACE). To support the analysis, Natural Visibility Graphs (NVG) were used with data from Andalusian public hospitals between 2009 and 2019. We calculated the incidence rates of hospital admissions for MACE, and specifically acute myocardial infarction and ischemic stroke during the two weeks leading up to, and two weeks after, the DST transition. NVG were applied to identify dynamic patterns. The study included 157,221 patients diagnosed with MACE, 71,992 with AMI (42,975 ST-segment Elevation Myocardial Infarction (STEMI) and 26,752 non-ST-Elevation myocardial infarction (NSTEMI) and 51,420 with ischemic stroke. Observed/expected ratios shown an increased risk of AMI (1.06; 95%CI (1.00-1.11); p=0.044), NSTEMI (1.12; 95% CI (1.02-1.22); p=0.013) and acute coronary syndrome (1.05; 95%CI (1.00-1.10); p=0.04) around the autumn DST. The NVG showed slight variations in the daily pattern of pre-DST and post-DST hospitalization admissions for all pathologies, but indicated that the increase in the incidence of hospital admissions after the DST is not sufficient to change the normal pattern significantly.

Keywords: Major acute cardiovascular events; Acute coronary syndromes; Cerebrovascular disease; Daylight saving time; Time series analysis.

Introduction

Daylight Saving Time (DST) is when the clocks go forward one hour in spring and then, in autumn, go back again.[1,2] These time changes have been in place in Spain and other European countries since March 2002,[3] and are also used in other non-European countries. The main reason for using DST is to make better use of the hours of daylight, by adapting the increased hours of daylight to those when most working activity takes place.[4,5] On the other hand, it is also known that daylight plays an important role in many circadian rhythms, including the sleep/wake cycle. An alteration in the external stimuli we perceive, such as a change in the number of daylight hours we are exposed to, leads to an alteration in our circadian rhythms. So much so, that they are even altered by time of the additional daylight, whether at the beginning or end of the day;[6] for this reason, any change in daylight hours, such as DST, can lead to chronodisruption.[2]

DST has long been associated with an increased incidence of diseases such as acute myocardial infarction (AMI); [7-9] one meta-analysis showed a slight increase in the risk of AMI following DST transitions, most notably in spring.[10] Other studies have assessed the possible effect that DST may have on other pathologies, such as cerebrovascular diseases (CeVD), reporting an increase in the number of deaths in the first days after the start of spring DST,[11] as well as an increase in hospitalizations for ischemic stroke during the first two days after DST.[12] In this context, a group of international experts recommended the discontinuation of DST, both in Europe and in the United States.[13-15]

In the last decade, the composite endpoint of major adverse cardiovascular (CV) events (MACE) is increasingly used in randomized clinical trials and observational studies. Although there is variability in the definition and components, many authors agree to use as MACE components: AMI, acute coronary syndrome/ischemic heart disease, stroke, heart failure and CV death.[16]

Very recently, the United States Senate voted in favour of the proposed federal law (the Sunshine Protection Act) to adopt DST on a permanent basis in the United States, thus abolishing the twice-yearly time change.[17] In March 2019, the European Commission also voted in favour of ending seasonal clock changes by 2021 in the European Union,[18] although subsequently, EU countries have been unable to agree on whether to apply standard time or DST. In fact, politicians have effectively passed the onus on to scientists to produce conclusive evidence that the dangers to health caused by DST outweigh the benefits.

Analyzing the time series corresponding to hospitalization due to CV diseases before and after DST enable us to evaluate dynamic patterns. Among others, Natural Visibility Graphs (NVG), introduced in Lacasa, et al.,[19] are one of the most recent and easily applied approaches to carry out such analysis. This method transforms the original time series into a complex network (undirected graph), which represents a nonlinear model of the underlying dynamic pattern. This transformation is unique and unambiguous, and allows us to obtain the main points in the original time series.[20] This approach has been successfully applied in fields as diverse as the study of hurricanes[21] and earthquakes,[22] economics[23] or contaminant dynamics.[24,25] It has also been used in healthcare to analyze psychiatric disorders through the brain activity using functional Magnetic Resonance Imaging (fMRI) data,[26] assess brain dysfunctions through electroencephalographic (EEG) time series,[27] detect epilepsy from EEG signals,[28,29] for early detection of sudden cardiac arrests,[30] for the analysis of Multi-omics time series used in precision medicine or for monitoring health events[31] and for establishing the relation between Intracranial Pressure (ICP) and Heart Rate (HR)[32], among others.

One region of special interest for the impact assessment of DST on CV diseases due to its geographical location in the southern part of Spain is Andalusia, which covers 87,268 km² and is one of the areas in Europe with the most hours of sunshine per year. Spain changes to DST like other European countries, and is in the Greenwich Mean Time+2 (GMT+2) time zone during summer, although this corresponds to GMT+1 when DST is in place. Therefore, taking into account that, to our knowledge, no similar studies have been conducted in this region, the main aim of the present work was to find out, through analysis using NVG, whether transitions both to and from DST led to an increase in the incidence of hospital admissions for MACE and specifically for AMI and ischemic stroke.

Methods

This was an observational study analyzing databases including patients aged between 20 and 75 admitted to Andalusian public hospitals between 1 January 2009 and 31 December 2019. Data were obtained from the Andalusian Minimum Basic Data Set (MBDS).

Patients were included according to the International Classification of Diseases (ICD): we used IDC from 2009-2015 and ICD10 from 2016 onwards. As primary endpoint, MACE was considered. MACE component definitions were AMI [ICD9 410 and ICD10 I21-I22], acute coronary syndrome (ACS)/ischemic heart disease (IHD) [ICD9 410-411 and ICD10 I20.0, I21-I22] and stroke [ICD9 433-434, 436 and ICD10 I63, I65-I66] as primary diagnoses; and heart failure [ICD9 428 and ICD10 I50] and all-cause death and CV death [ICD9 411-414, 415-417, 420-429, 432-433, 435-437, 785.51 and ICD10 I20, I23-I25, I30-I52, I62, I63.0-I63.2, I64-I65, I67-I68, R57.0] as secondary diagnoses.[16]

Specifically, the codes for ischemic stroke (IS) were ICD9 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91 and ICD10 I63, while for ST-elevation acute myocardial infarction (STEMI) we used ICD9 410.0-410.6 and 410.8, ICD10 I21.0-

I21.3, I22.0-I22.1 and I22.8-I22.9; and for non-ST-elevation acute myocardial infarction (NSTEMI), ICD9 410.7, ICD-10 I21.4-I21.8 and I22.2-I22.7 were used.

Other variables analyzed were gender, in-hospital mortality and percutaneous intervention performed.

Statistical analysis

Frequencies, means, and standard deviations were obtained. Comparisons between the two transitions (spring and autumn) for continuous variables were assessed by t-test. Categorical data were compared using the χ^2 test. To determine the incidence of disease at DST transitions, we calculated the incidence rates observed in hospital admissions for MACE, AMI (considering STEMI and NSTEMI) and ischemic stroke during the two weeks prior to the DST transition (starting on a Sunday) and the two weeks after the legal time change (ending on a Saturday). From this, we worked out the ratio between the observed number during two weeks after DST and the expected number during the two weeks before DST. The observed/experienced (O/E) ratio was calculated overall and for each day of the week. Assuming the Poisson distribution, the 95% confidence interval (95%CI) was determined with the *pnorm* function of R statistical software (R Foundation for Statistical Computing, Vienna, Austria). The predictive values of the variables were expressed as odds ratios and corresponding p-values. All p-values were bilateral and $p<0.05$ was considered statistically significant.

Finally, to use the time series analysis to extend the findings obtained, we applied an innovative approach using graph theory, called natural visibility graphs (NVG), to identify dynamic patterns of the variables involved. Each NVG node corresponds to a value in the time series connected laterally with other "visible" nodes. Two nodes at times t_a and t_b with corresponding time series values y_a and y_b, respectively, are considered to be connected if any intermediate node at t_c between them ($t_a < t_c < t_b$) with time series value y_c fulfils the visibility criterion (1):

$$y_c < y_a + (y_b - y_a)\frac{t_c - t_a}{t_b - t_a} \qquad (1)$$

The NVG obtained after applying the visibility criterion to every pair of nodes is characterized by a NxN symmetric sparse binary adjacency matrix (2) (with N the number of nodes), where $a_{ij} = 1$ means that nodes i and j are connected by an edge (i.e., they have visibility) and $a_{ij} = 0$ means no connection. This is a hollow matrix (its diagonal elements are zero), because a node has no visibility with itself and the elements adjacent to the diagonal are 1, because a node always has visibility with its surrounding nodes

$$\begin{pmatrix} 0 & 1 & \dots & a_{1N} \\ 1 & 0 & 1 & \dots \\ \dots & 1 & \dots & 1 \\ a_{N1} & \dots & 1 & 0 \end{pmatrix} \qquad (2)$$

Among the properties or centrality measures of the adjacency matrix, the degree of each node k_i can be obtained by looking at the number of nodes connected to it by an edge ($k_i = \sum_j a_{ij}$), showing its relative importance in the time series. Another important property of the NVG, which can characterize the behaviour of the original time series (e.g., chaotic, random, multifractal, etc.),[19,33] is the degree probability distribution $P(k)$, which is equal to the number of nodes with a certain degree divided by the total number of nodes.

Multivariate analysis, i.e., correlation analysis between time series, can be carried out using Multiplex Visibility Graph (MVG), [34] which is based on a multi-layered network. One correlation measure obtained from an MVG is the Average Edge Overlap (ω), [35] which quantifies, on average, the number of overlapping edges across the NVGs in the MVG (3).

$$\omega = \frac{\sum_i \sum_{j>i} \sum_\alpha a_{ij}^{[\alpha]}}{M \cdot \sum_i \sum_{j>i} \left(1 - \delta_{0,\sum_\alpha a_{ij}^{[\alpha]}}\right)} \qquad (3)$$

where $\delta_{0,\sum_\alpha a_{ij}^{[\alpha]}}$ is the Kronecker delta, whose value is 1 if $\sum_\alpha a_{ij}^{[\alpha]}$ is null and 0 otherwise. The maximum value of ω is 1 (the time series involved have identical temporal patterns), and its minimum value is $1/M$ (every edge in the MVG only exists in one layer); therefore, the higher the value of ω, the higher the correlation between the time series. In this work, two time series were compared using ω: the pre-DST time series, which corresponds to the mean of hospitalizations for each day of the two weeks leading up to DST over all the years analyzed, and the post-DST time series, corresponding to the two weeks after DST.

Results

A total of 157,221 participants had some component of MACE, of which 71,992 were AMI registers, 58,327 for stroke and 90,424 for ACS or IHD. Regarding secondary diagnoses of heart failure and all-cause death and CV death, 20,476 and 6,103 were considered, respectively. Specifically, 42,975 patients had STEMI, 26,752 had NSTEMI and 51,420 were registered with IS.

The mean age of the MACE patients was 61.7 (±9.9) years, while for AMI the mean age was 60.1 (±10.0) and 63.0 (±9.8) for ischemic stroke. Table 1 shows the main characteristics of hospital admissions for each of the pathologies between 2009 and 2019 during the weeks before and after the spring and autumn transitions. The presence of hypertension and diabetes mellitus in each pathology is also shown. Specifically, hospital admissions in people with hypertension and diagnosed with heart failure and cardiovascular pathology were higher in the two weeks after the autumn DST when compared with the two weeks before.

Out of the total number of patients admitted for AMI, 59.7% were admitted for STEMI. The analysis of O/E ratios showed a higher percentage increase for DST in autumn in the incidence of cases for NSTEMI (+0.4%). The patients admitted for AMI were predominantly male (77.9%), (specifically, in STEMI (80.3%) and in non-STEMI (74.2%)); similarly, there were more admissions for ischemic stroke in men (66.4%). In general, higher in-hospital mortality is shown for ischemic stroke (6.5%) than for AMI (4.2%). Compared to STEMI, mortality for NSTEMI cases was low (4.6% vs. 2.6%). Although no differences were observed in the spring transition, in the autumn transition there were more hospital admissions for AMI (p=0.045) and NSTEMI (p=0.003) for men during the two weeks after DST than the two weeks leading up to it.

For MACE, the O/E analysis showed no significant differences in the two DST periods, although there was a higher percentage in autumn (1.03; 95% CI 1.06-0.99); p=0.170) (Figure 1). The calculated O/E ratio reported an increased risk of AMI (1.06; 95%CI (1.00-1.11); p=0.044), NSTEMI (1.12; 95% CI (1.02-1.22); p=0.013) and acute coronary syndrome (ACS) (1.05; 95% CI (1.00-1.10); p= 0.042) during the autumn DST (Table 2; Figures S1) Regarding the O/E ratios for the days of the week, in the case of NSTEMI, a higher number of hospital admissions was observed on the Wednesdays after the autumn transitions (1.25; 95% CI (1.00-1.55); p=0.05). Specific differences were found by gender analysis (Table S1): in AMI, men tended to have more hospital admissions on the Mondays (p=0.06) and Fridays (p=0.05) after the autumn transitions; in fact, men had higher number of percutaneous interventions (1.37; 95% CI (1.06-1.74); p=0.02) on those Fridays; in women, the Fridays after the autumn transitions showed significantly lower hospital admission (0.68; 95% CI (0.47-0.95); p=0.01), but percutaneous interventions led to more hospital admissions on the Wednesdays after the autumn transitions (p=0.06). In NSTEMI, men tended to have more hospital admissions on the Mondays (p=0.08) and Wednesdays (p=0.08) after autumn transitions and significantly on the Saturdays (1.48; 95% CI (1.08-1.97); p=0.02); in contrast, women tended to have fewer hospital admissions on the Fridays after the autumn transitions (p=0.08). Men had more hospital admissions related to heart failure on the Sundays after the autumn DST (1.54 95% CI (1.05-2.18); p=0.02). With respect to stroke, women had more admissions on the Sundays after the spring transitions (1.36; 95%CI (1.01-1.79); p=0.04), while men tended to have fewer admissions on that day (p=0.07).

Table 3 shows the Average Edge Overlaps (ω) calculated to analyze the correlation between the two weeks pre-DST and post-DST time series for each pathology and percutaneous interventions at the autumn and spring transitions. This analysis showed very small variations in the daily pattern of pre-DST and post-DST hospitalization admissions for all pathologies (high values of ω), therefore indicating a highly similar trend in both cases. Only heart failure at the autumn DST transition had a pattern variation with ω <0.8 (although still with a high value). Also, a slightly higher pattern variation could be observed (further information in supplementary material) in percutaneous interventions, NSTEMI and CV disease at the spring DST transition.

Discussion

The main finding of the present study is a significant increase around the autumn DST transition in the hospital admissions of patients whose diagnosis was AMI and ACS. This statistically significant increase was most clearly observed in those with a diagnosis of NSTEMI at hospital admission. A trend, although not significant, of higher numbers of hospital admissions for MACE or heart failure in the autumn transition is also reported.

The increase in hospital admissions associated with AMI following DST has been described in several articles. Some studies highlight an increase in hospital admissions for AMI in the spring transition.[4,8,36,37] However, to our knowledge, only two studies showed an increased risk of AMI admissions associated with the autumn DST transition. Making it clear that any disruption of the circadian rhythm increases the risk of an acute CV event or MACE.[13]

Another feature of the present study is the specific analysis of the AMI subtypes (STEMI and NSTEMI). Specifically, a higher incidence of NSTEMI events has been found after the autumn DST transition. One study analyzing this difference by subtype[4] found a higher incidence in NSTEMI after the spring DST transition. Authors indicate that a single behavioral variable, sleep deprivation, can cause transient increases in blood pressure and vasoconstriction of coronary arteries, leading to a mismatch between supply and demand and, in turn, to NSTEMI.[38]

An enhanced circadian clock misalignment and sleep deprivation have been considered factors associated with AMI risk.[39,40] Regarding circadian clock misalignment, geographic location[23] has been considered an important factor; the cohort analyzed in this work is located in Andalusia, Southern Spain, which has a warm Mediterranean climate with many hours of sunshine per year; moreover, there is a significant discrepancy between solar time and official time, especially in the westernmost areas.[41]

Another factor is latitude; countries may have more or less hours of sunlight during the day depending on this parameter.[42] To our knowledge, no studies have been carried out in locations on the same latitude as Andalusia and, for this reason, our findings may differ from those from other locations. However, one study carried out in southern Germany [43] found a higher incidence of re-infarction in patients with previous AMI after the autumn DST transitions, highlighting the interaction between sex and geographical location. Similarly, an observational study in southern Croatia [44] reported a significant increase in the incidence of non-fatal AMI after four working days following the autumn DST.

As also referred by Čulić, even if one hour of sleep is 'gained', the findings of the present study suggest that, during autumn DST, other social or psychological factors, although less incident, have more impact in the long term, when compared to spring DST.[44] For example, variables such as gender, age, ethnicity, chronotype or the presence of chronic diseases may predispose subjects to develop AMI.[36,44] In this respect, the sleeping and eating habits of the Andalusian population are different from those of other Europeans, with late mealtimes which delay the sleep pattern. This means that our findings could be explained by specific behavioral characteristics of Andalusians. The thermal perception of the population is also referred to in the scientific literature, which highlights that correct clothing behavior can contribute to preventing excess winter mortality.[45] Regarding to the presence of chronic disease, since hypertension and diabetes mellitus have been reported to affect plaque instability and inflammation in MACE, a sub-analysis has been performed (Table 1). Specifically, it was observed that those with hypertension had more heart failure and CV disease events in the transient two weeks after the autumn DST.

Behavioral characteristics may also predispose people to have an evening chronotype. It is known that people with an evening chronotype have poor eating habits, delaying food intake and tending to make unhealthy food choices.[46] In a recent study carried out in southern Spain as part of the CORDIOPREV project, it was established that patients with an evening chronotype had a higher cardiometabolic risk than those with a morning chronotype. The study also showed that these patients tended to go to bed later, which was in turn linked to a higher caloric intake and lower dietary quality and, as a consequence, obesity, all of which are risk factors for AMI.[47] Furthermore, taking into account the characteristics of the Andalusian population and the fact that there are fewer hours of sunlight after the working day has ended, this could have an impact on the physical activity of the population, and could lead to people leading a more sedentary lifestyle and moving closer to the evening-type chronotype.

Regarding stroke and the development of percutaneous interventions, in general terms, no increased incidence was found after any of the DST transitions although, as other studies report,[1,12, 48] there were differences on some days of the week when sub-analyzing by sex.

One major new feature in the present study was to include an analysis of the trends in hospital admissions for each of the pathologies, using the Average Edge Overlap measurement from the MVG confirmed by the pre-DST and the post-DST mean time series. High ω values (some of them very close to 1) were found, indicating that there are no differences in the trends of hospital admissions between the two weeks before and the two weeks after the DST, either in spring or autumn.

These data results are consistent with those from other studies, in which the pattern for admissions for AMI and the STEMI and NSTEMI subtypes shows a trend towards Mondays being the days when they occur the most and weekends when they occur the least.[46] In fact, there were more hospital admissions on Mondays after the autumn transition in patients admitted for any pathology included in the present study and who had hypertension as a secondary diagnosis (1.11 95% CI (1.01-1.21); p=0.02). For ischemic stroke, no major differences were found between the time series analyzed. However, to our knowledge, no similar studies have been carried out into the temporal pattern of hospital admissions for stroke in Spain. In fact, the findings of the present study show that the geographical location and cultural characteristics of the Andalusian population, highlighting sleep and eating patterns, may influence the better or worse adaptation to the chronodisruption generated by DST. In this sense, future longitudinal studies should consider not only non-behavioral variables such as gender, age, ethnicity or presence of chronic diseases, but also behavioral characteristics such as sleep (siesta) and eating patterns (also type of diet), variables that directly influence the person's chronotype.[47] In fact, behaviours traditionally associated with geographic location (culture and environmental conditions) such as siesta, meal timing or type of diet have been shown to have an effect on cardiometabolic health.[49-50]

Our study has some limitations. Firstly, the data provided have only been taken from hospitals belonging to the Andalusian public health service (attended by the majority of the population), where all hospital admissions are recorded. However, it has not been possible to include the data from private hospitals. Also, the data did not provide information on the time of onset of the pathologies, so it was not possible to carry out a time-dependent analysis of hospital admissions.

Conclusions

Our findings show an increased risk of hospitalization for AMI and ACS after the autumn DST, as well as for the NSTEMI subtype, where this risk is more pronounced. This risk is particularly notable in men. With regard to hospital admissions for ischemic stroke, no differences were found after both DST transitions. Hospital admissions in people with hypertension and diagnosed with heart failure and CV pathology were higher in the two weeks after the autumn DST. The Average Edge Overlap value revealed that the trend in AMI and its subtypes, as well as in ischemic stroke, did not change in any of the DST transitions, despite the increased risk in AMI and NSTEMI after the autumn DST. This indicates that the increase in the incidence of hospital admissions after the DST is not sufficient to change this pattern. On the other hand, this type of analysis has proved useful for these types of cases and, moreover, constitutes a powerful tool that can be used to analyze other time series. Finally, our findings show that the idiosyncrasies of the population in southern Spain may determine the incidence of hospital admissions after DST, particularly in the autumn transition.

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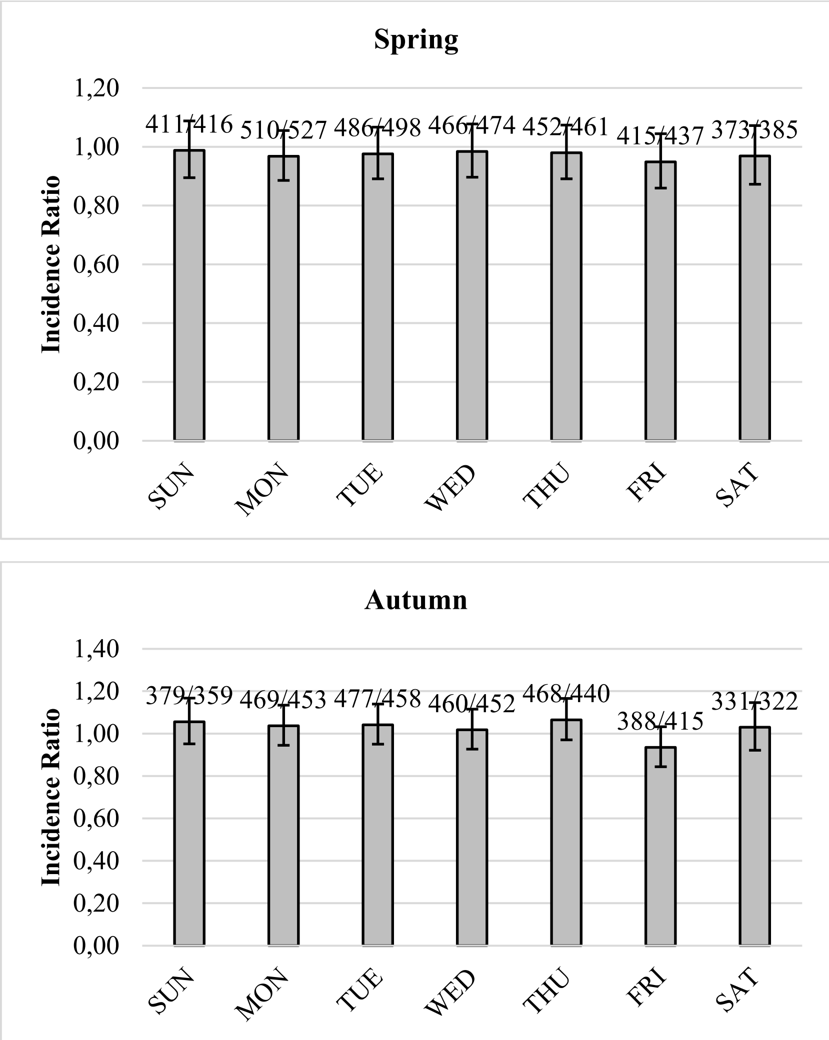


Figure 1. Graphic distribution of O/E in the number of hospital admissions due to MACE

Table 1. General characteristics of the study population in patients admitted during the two weeks leading up to and after the DST for both transitions (spring and autumn). Sub-analysis considering the presence of hypertension and diabetes mellitus.

	All	Spring DST Transition		Autumn DST Transition	
		2W Pre	2W Post	2W Pre	2W Post
MACE	n=157,221	n=6393	n=6222	n=5793	n=5942
HT	88436 (56.2%)	3621 (56,6%)	3511 (56,4%)	3235 (55,8%)	3383 (56,9%)
DM	56426 (35.9%)	2321 (36,3%)	2232 (35,9%)	1996 (34,5%)	2119 (35,7%)
AMI	n=71,992	n=2,945	n=2,915	n=2,593	n=2,740
HT	36039 (50.1%)	1469 (49.9%)	1486 (51%)	1295 (49.9%)	1389 (50.7%)
DM	23225 (32.3%)	943 (32%)	924 (31.7%)	818 (31.5%)	912 (33.3%)
STEMI	n=42975	n=1,740	n = 1,773	n = 1,585	n = 1,627
HT	19039 (44.3%)	751 (43.2%)	806 (45.5%)	713 (45%)	718 (44.1%)
DM	11738 (27.3%)	459 (26.4%)	460 (25.9%)	432 (27.3%)	456 (28%)
NSTEMI	n=26,752	n=1,111	n=1,061	n = 924	n = 1,034
HT	15845 (59.2%)	671 (60.4%)	636 (59.9%)	539 (58.3%)	627 (60.6%)
DM	10625 (39.7%)	448 (40.3%)	430 (40.5%)	355 (38.4%)	425 (41.1%)
Stroke	n=58327	n=2342	n=2258	n=2235	n=2214
HT	35958 (61.6%)	1448 (61.8%)	1392 (61.6%)	1366 (61.1%)	1379 (62.3%)
DM	21877 (37.5%)	901 (38.5%)	844 (37.4%)	803 (35.9%)	811 (36.6%)
Ischemic Stroke	n=5,1420	n=2,051	n=2,022	n=1,943	n=1,920
HT	31750 (61.7%)	1273 (62.1%)	1257 (62.2%)	1185 (61%)	1186 (61.8%)
DM	19230 (37.4%)	779 (38%)	768 (38%)	693 (35.7%)	686 (35.7%)
ACS	n=90424	n=3644	n=3635	n=3240	n=3406
HT	47027 (52%)	1906 (52.3%)	1909 (52.5%)	1687 (52.1%)	1785 (52.4%)
DM	30480 (33.7%)	1230 (33.8%)	1220 (33.6%)	1067 (32.9%)	1155 (33.9%)
HF	n=20476	n=913	n=842	n=689	n=741
HT	12977 (63.4%)	579 (63.4%)	520 (61.8%)	416 (60.4%)*	487 (65.7%)*
DM	10362 (50.6%)	445 (48.7%)	422 (50.1%)	330 (47.9%)	376 (50.7%)
CVD	n=6103	n=244	n=243	n=215	n=205
HT	3497 (57.3%)	139 (57%)	142 (58.4%)	113 (52.6%)**	131 (63.9%)**
DM	2630 (43.1%)	107 (43.9%)	102 (42%)	84 (39.1%)	88 (42.9%)

2W Pre = Two weeks Pre-DST; 2W Post = Two weeks Post-DST; Levels of significance: *p<0.05; **p≤0.01; Abbreviations: DST: Daylight Saving Time, MACE: major adverse cardiovascular events, AMI: Acute myocardial infarction, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST elevation myocardial infarction, ACS: Acute Coronary Syndrome, HF: Heart Failure, CVD: Cardiovascular Death

Table 2. Ratio of observed/expected (O/E) number of hospital admission due to AMI, STEMI, NSTEMI and IS during spring and autumn transitions.

	Spring DST		Autumn DST	
	O/E (95% CI)	p	O/E (95% CI)	p
MACE	0.97 (0.94-1.01)	0.127	1.03 (0.99-1.06)	0.170
AMI	0.99 (0.94-1.04)	0.689	1.06 (1.00-1.11)	**0.044**
STEMI	1.02 (0.95-1.09)	0.585	1,03 (0,96-1,10)	0.465
NSTEMI	0.95 (0,88-1,04)	0.279	1.12 (1,02-1,22)	**0.013**
Percutaneous interventions	1.04 (0.95-1.13)	0.346	0.98 (0.90-1.07)	0.758
Stroke	0.96 (0.91-1.02)	0.213	0.99 (0.93-1.05)	0.745
Ischemic Stroke	0.99 (0.93-1.05)	0.642	0.99 (0.93-1.05)	0.704
ACS	1.00 (0.95-1.04)	0.910	1.05 (1.00-1.10)	**0.042**
HF	0.92 (0.84-1.01)	0.089	1.08 (0.97-1.19)	0.172
CVD	1.00 (0.83-1.19)	0.940	0.95 (0.78-1.16)	0.604

MACE components are AMI, Stroke, ACS, HF and CVD. Abbreviations: DST: Daylight Saving Time, MACE: major adverse cardiovascular events, AMI: Acute myocardial infarction, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST elevation myocardial infarction, ACS: Acute Coronary Syndrome, HF: Heart Failure, CVD: Cardiovascular Death.

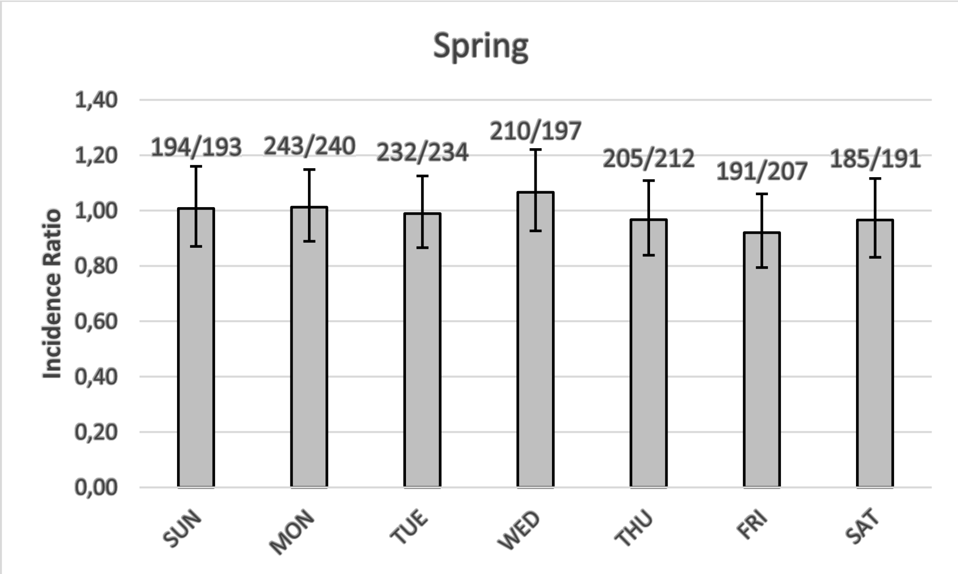
Table 3. Average Edge Overlap (ω) for all pathologies and percutaneous interventions at spring and autumn DST transitions.

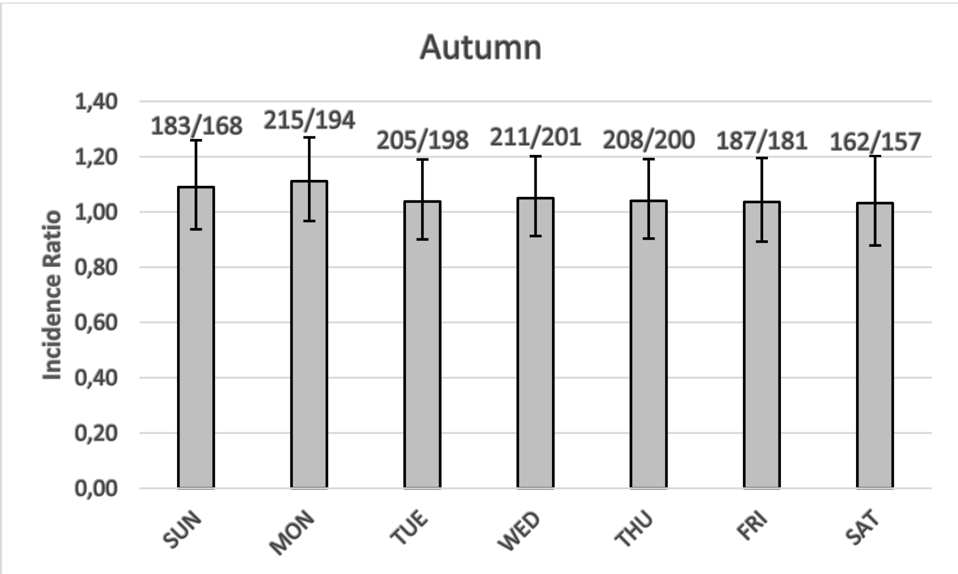
	Spring DST	Autumn DST
	ω	ω
MACE	1	0.8750
AMI	0.8500	0.9286
STEMI	1	0.8889
NSTEMI	0.7917	0.8333
Stroke	0.8000	0.8889
Ischemic Stroke	0.8500	0.8889
ACS	0.8500	0.8000
HF	0.8889	0.7727
CVD	0.7727	0.9000
Percutaneous Interventions	0.7857	0.8000

Abbreviations: DST: Daylight Saving Time, MACE: major adverse cardiovascular events, AMI: Acute myocardial infarction, STEMI: ST-elevation myocardial infarction, NSTEMI: Non-ST elevation myocardial infarction, ACS: Acute Coronary Syndrome, HF: Heart Failure, CVD: Cardiovascular Death

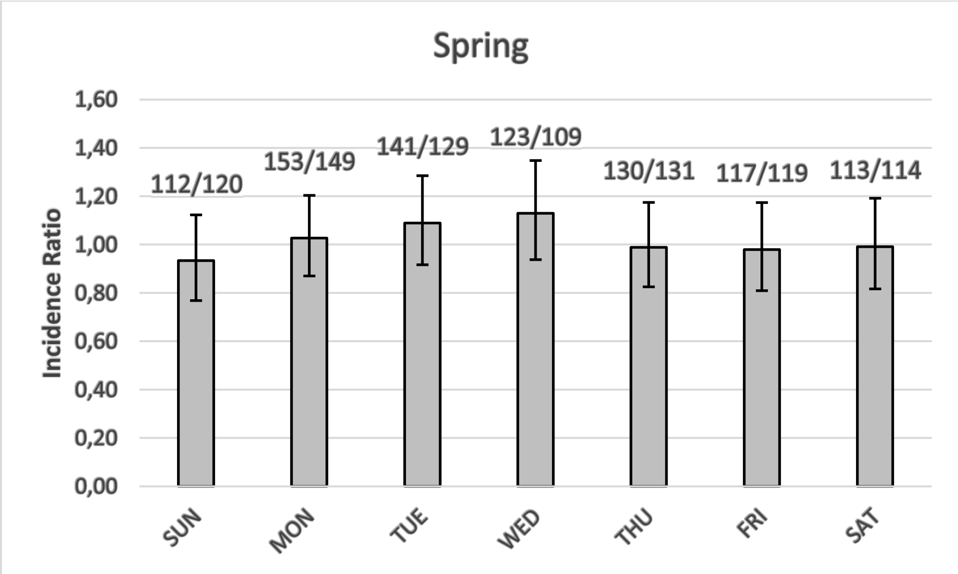
Figure S1. Graphic weekly distribution of O/E in the number of hospital admissions due to AMI, STEMI, NSTEMI, percutaneous interventions, stroke, ischemic stroke, ACS, HF, CVD, diabetes mellitus and hypertension.

AMI

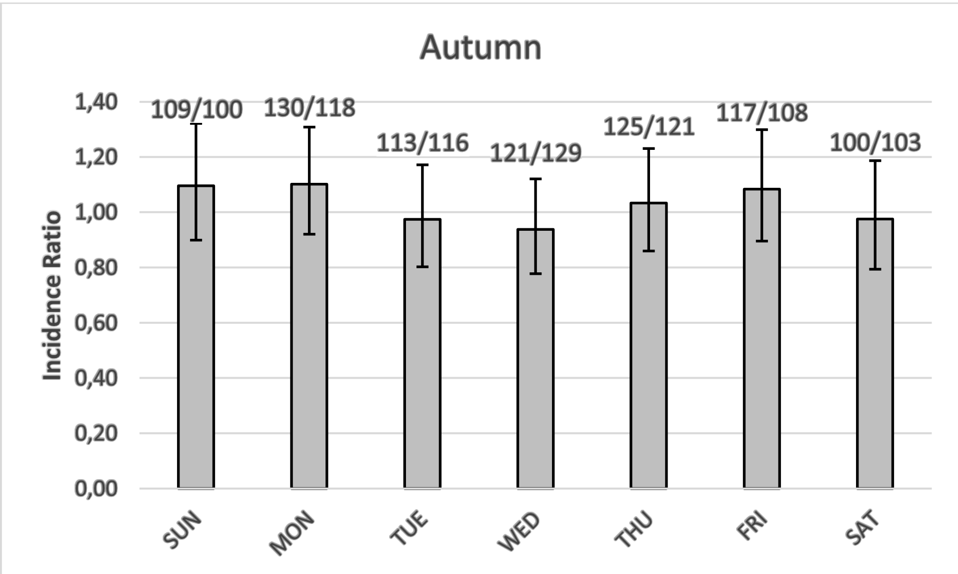




STEMI

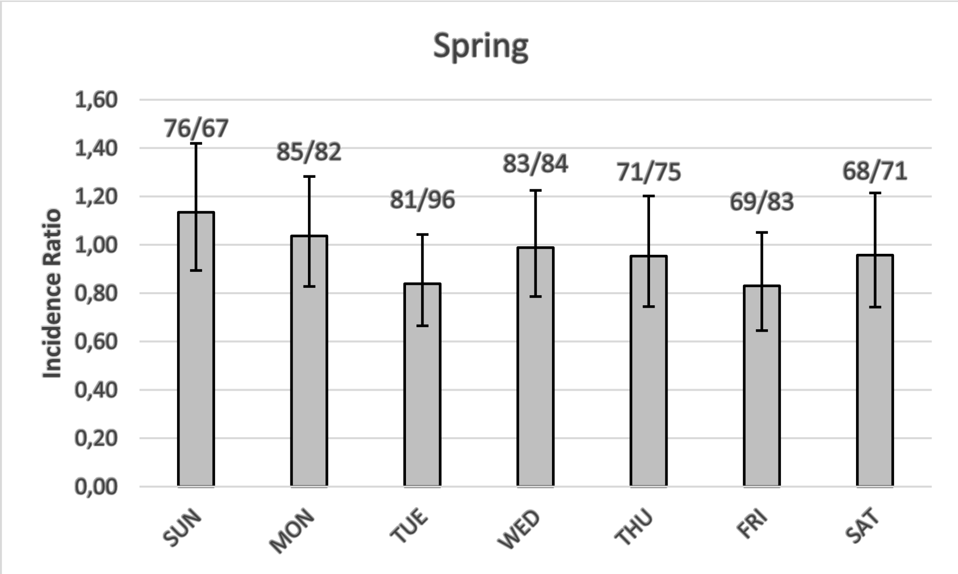


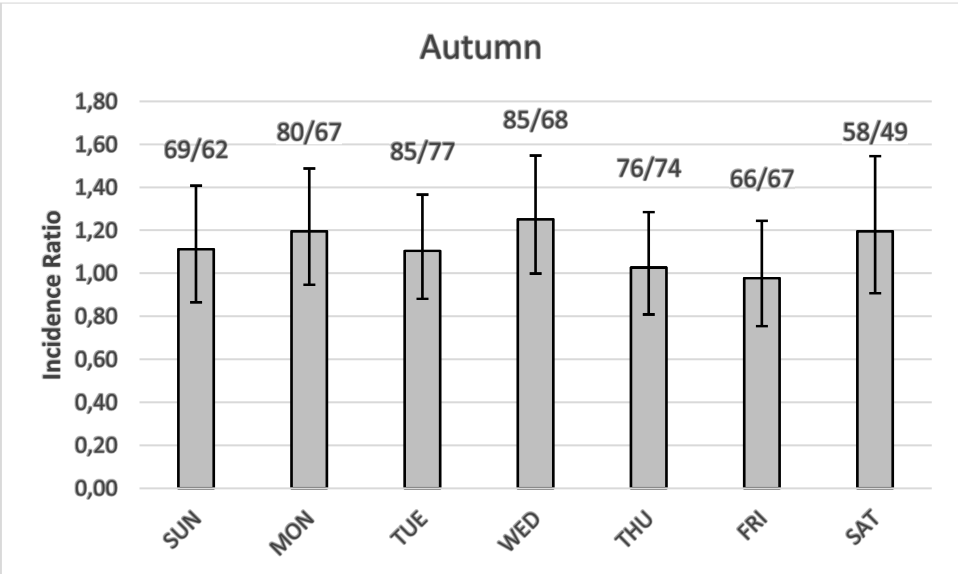
Spring
Incidence Ratio
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
112/120
153/149
141/129
123/109
130/131
117/119
113/114
SUN
MON
TUE
WED
THU
FRI
SAT



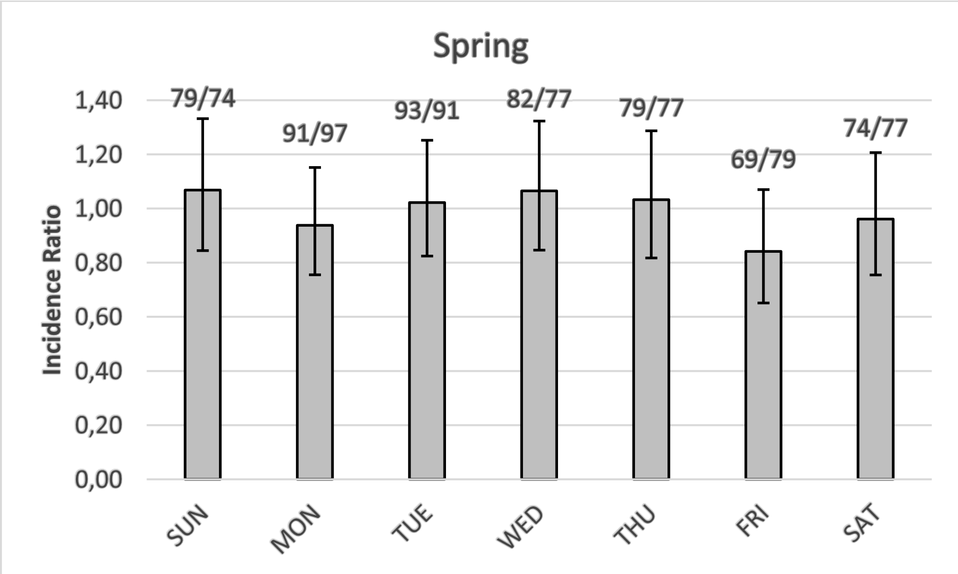
Autumn
Incidence Ratio
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
109/100
130/118
113/116
121/129
125/121
117/108
100/103
SUN
MON
TUE
WED
THU
FRI
SAT

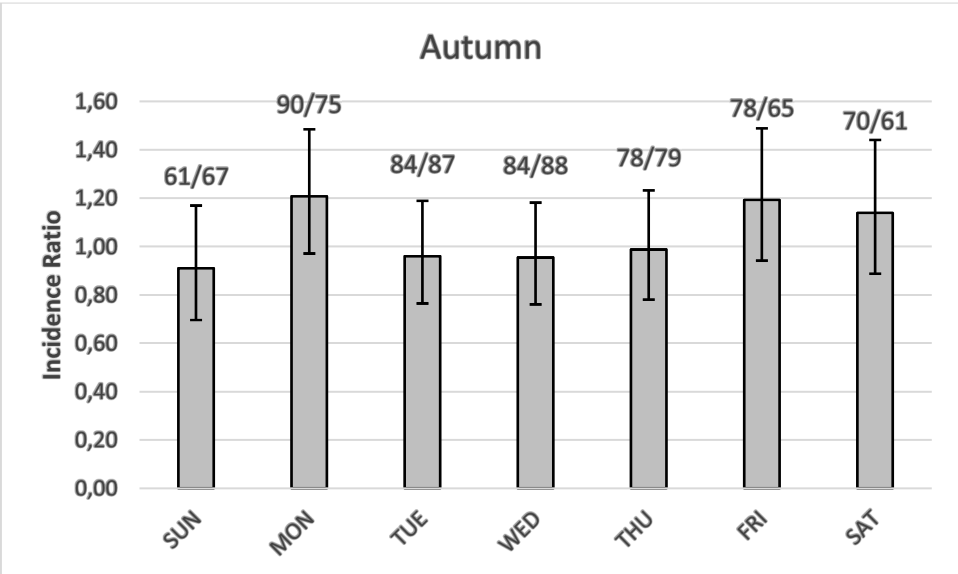
NSTEMI


Spring
Incidence Ratio
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
76/67
85/82
81/96
83/84
71/75
69/83
68/71
SUN
MON
TUE
WED
THU
FRI
SAT

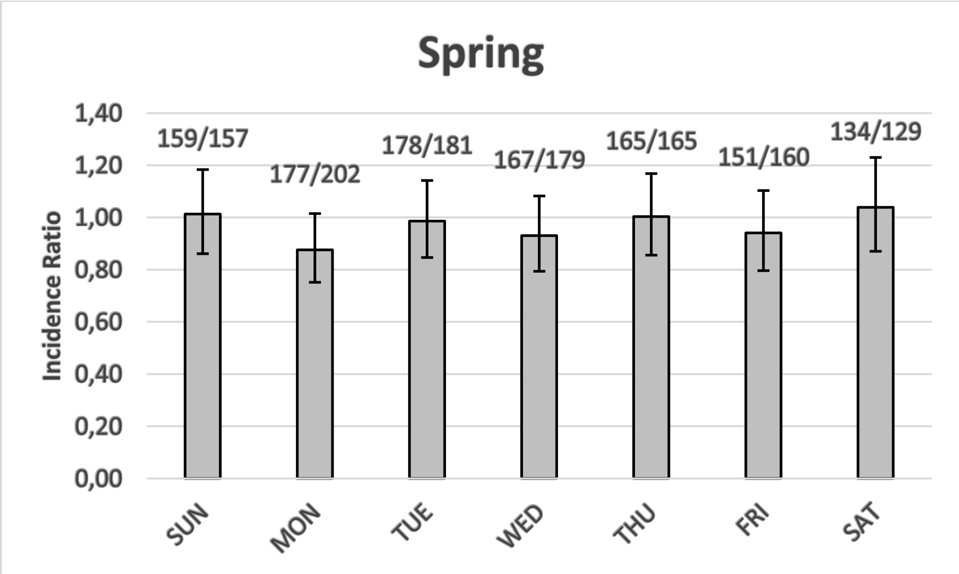

Autumn
Incidence Ratio
1,80
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
69/62
80/67
85/77
85/68
76/74
66/67
58/49
SUN
MON
TUE
WED
THU
FRI
SAT

Percutaneous interventions

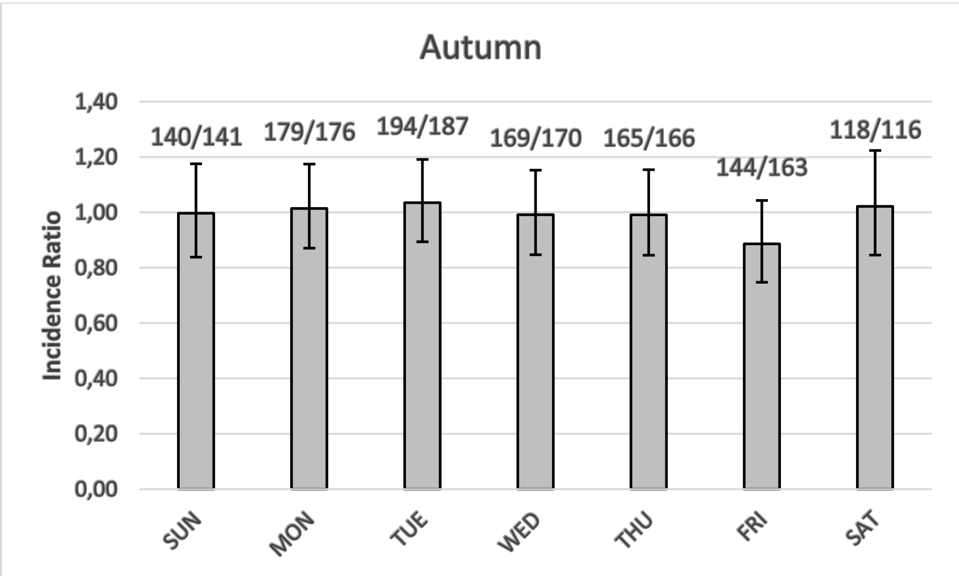




Stroke

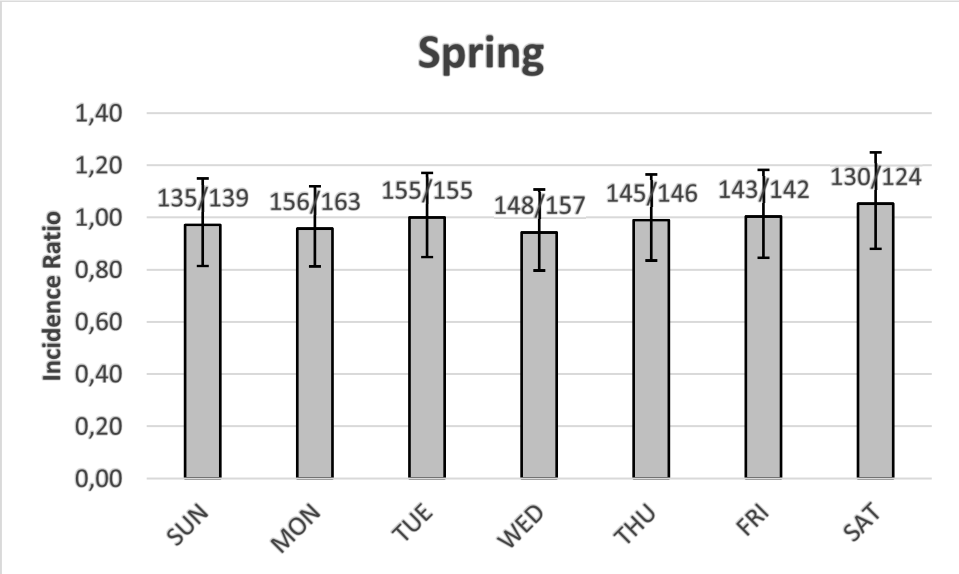


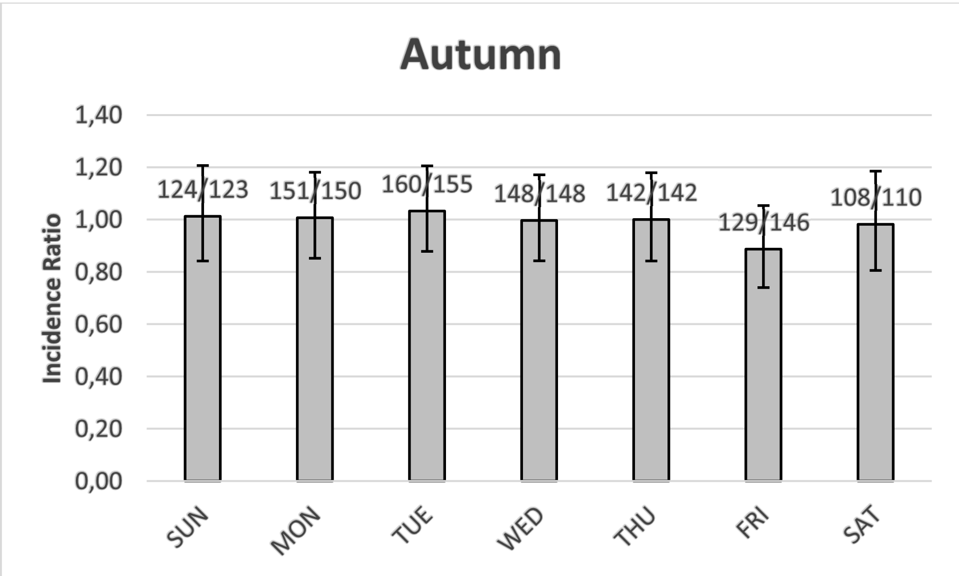
Spring
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
Incidence Ratio
159/157
177/202
178/181
167/179
165/165
151/160
134/129
SUN
MON
TUE
WED
THU
FRI
SAT



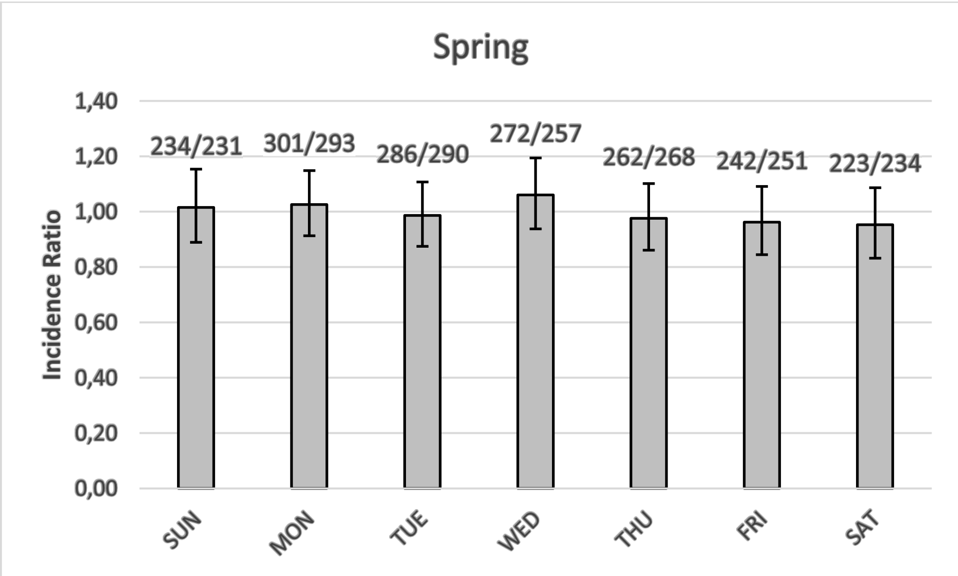
Autumn
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
Incidence Ratio
140/141
179/176
194/187
169/170
165/166
144/163
118/116
SUN
MON
TUE
WED
THU
FRI
SAT

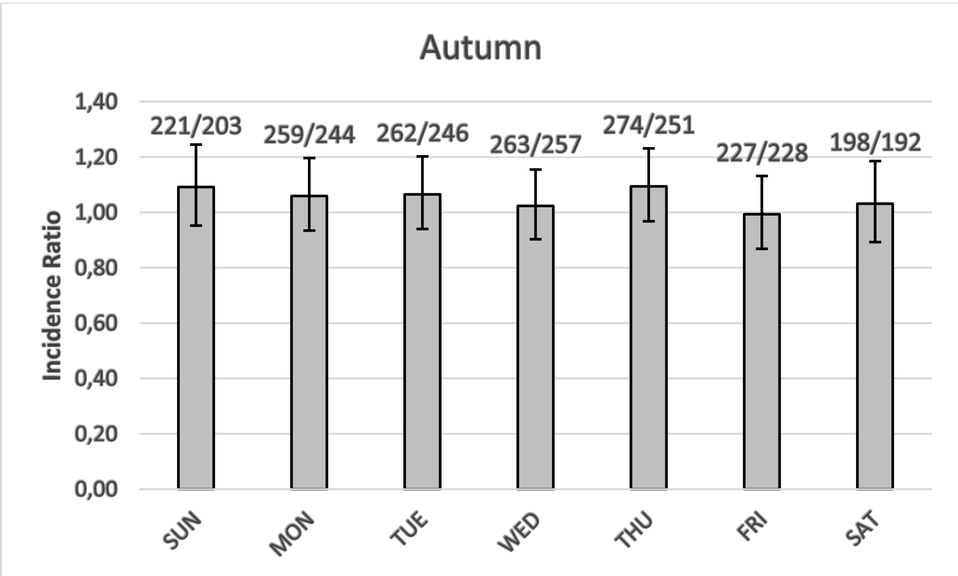
Ischemic stroke



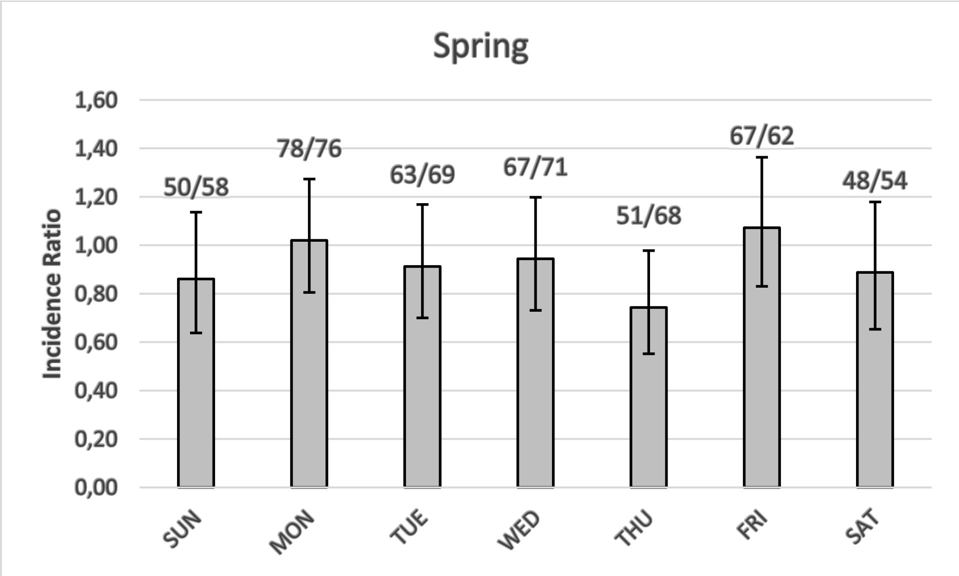


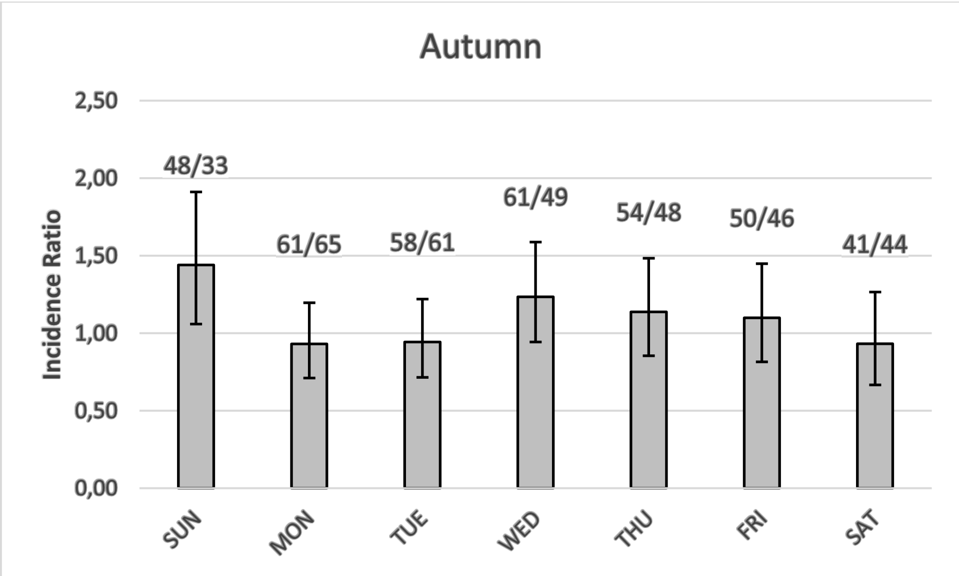
ACS


Spring
Incidence Ratio
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
234/231
301/293
286/290
272/257
262/268
242/251
223/234
SUN
MON
TUE
WED
THU
FRI
SAT

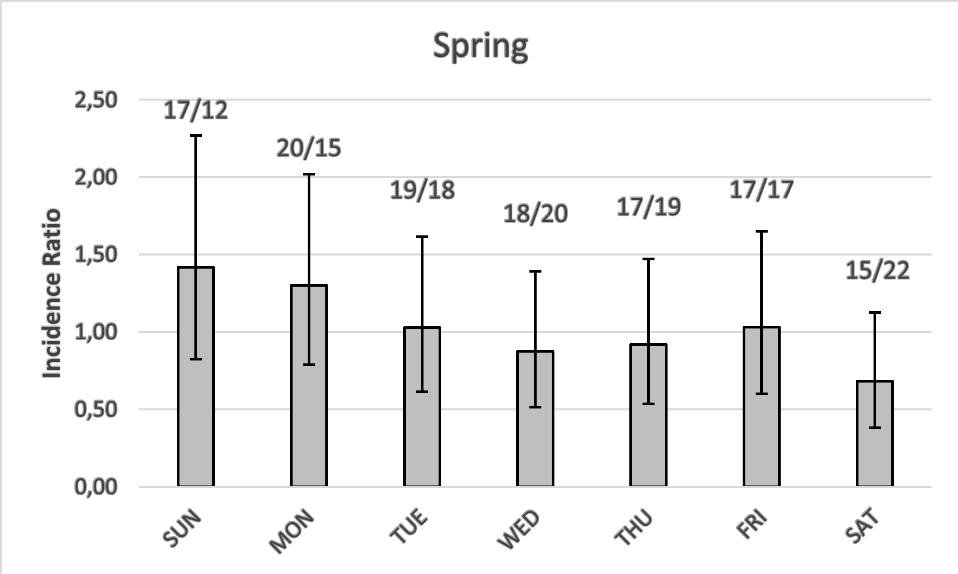

Autumn
Incidence Ratio
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
221/203
259/244
262/246
263/257
274/251
227/228
198/192
SUN
MON
TUE
WED
THU
FRI
SAT

HF

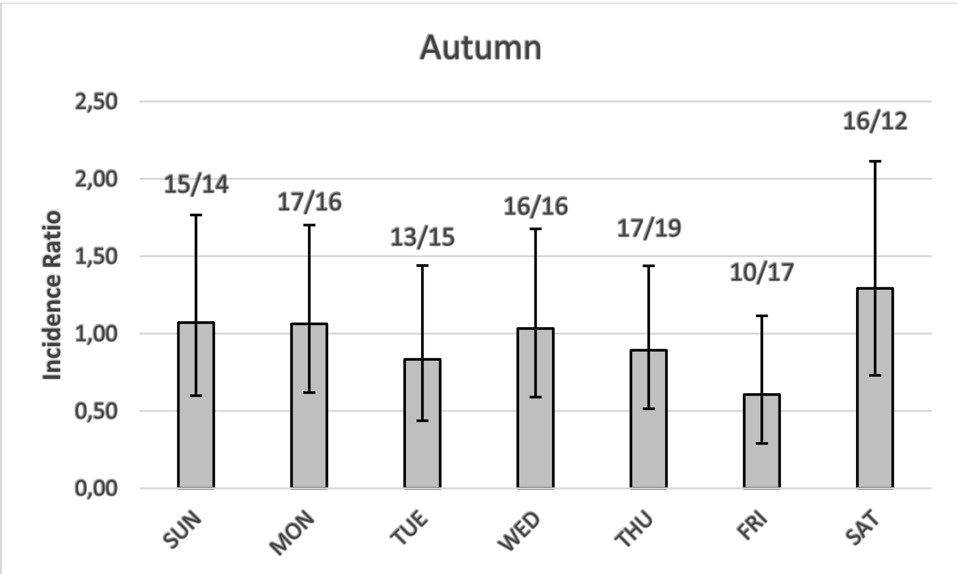

Spring
Incidence Ratio
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
50/58
78/76
63/69
67/71
51/68
67/62
48/54
SUN
MON
TUE
WED
THU
FRI
SAT


Autumn
Incidence Ratio
2,50
2,00
1,50
1,00
0,50
0,00
48/33
61/65
58/61
61/49
54/48
50/46
41/44
SUN
MON
TUE
WED
THU
FRI
SAT

CVD

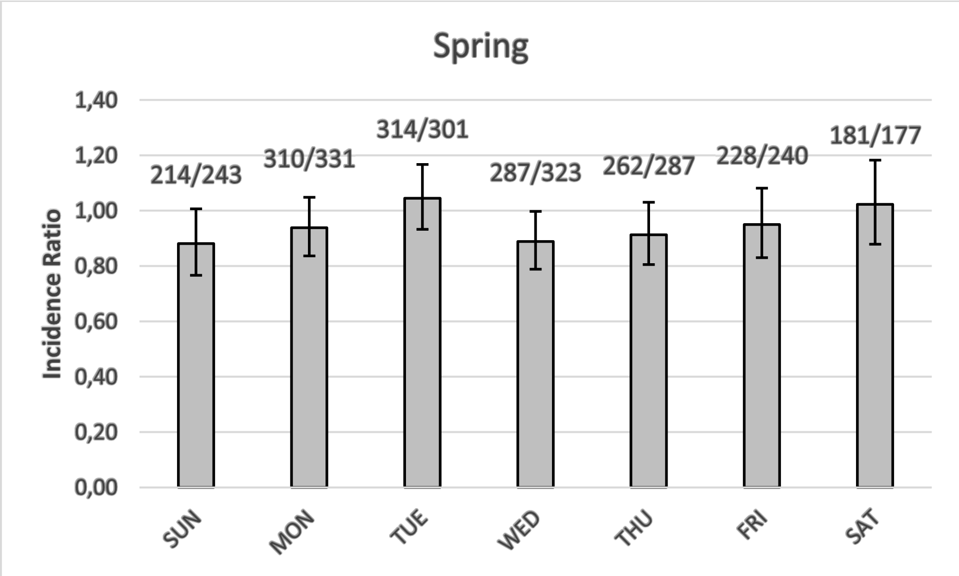


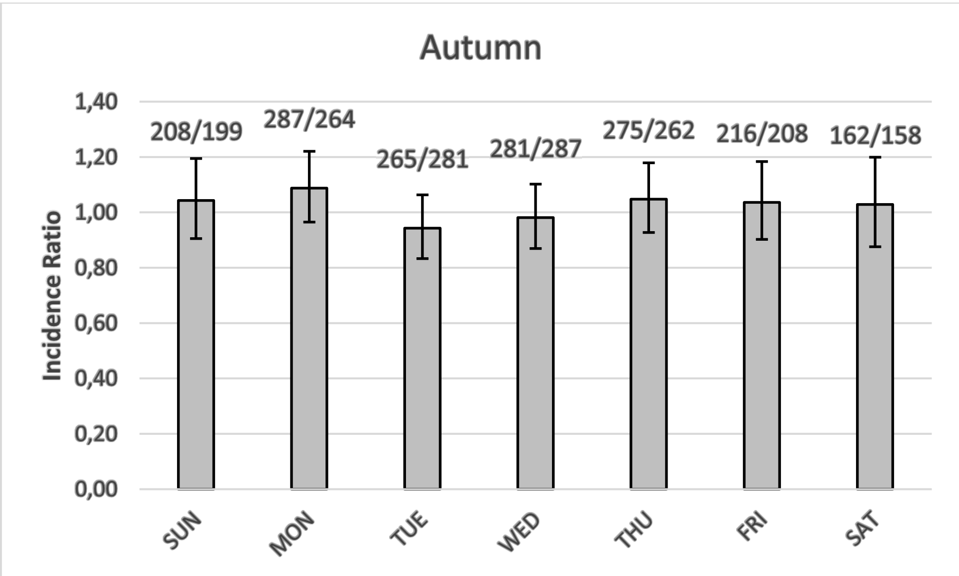
Spring
Incidence Ratio
2,50
2,00
1,50
1,00
0,50
0,00
17/12
20/15
19/18
18/20
17/19
17/17
15/22
SUN
MON
TUE
WED
THU
FRI
SAT



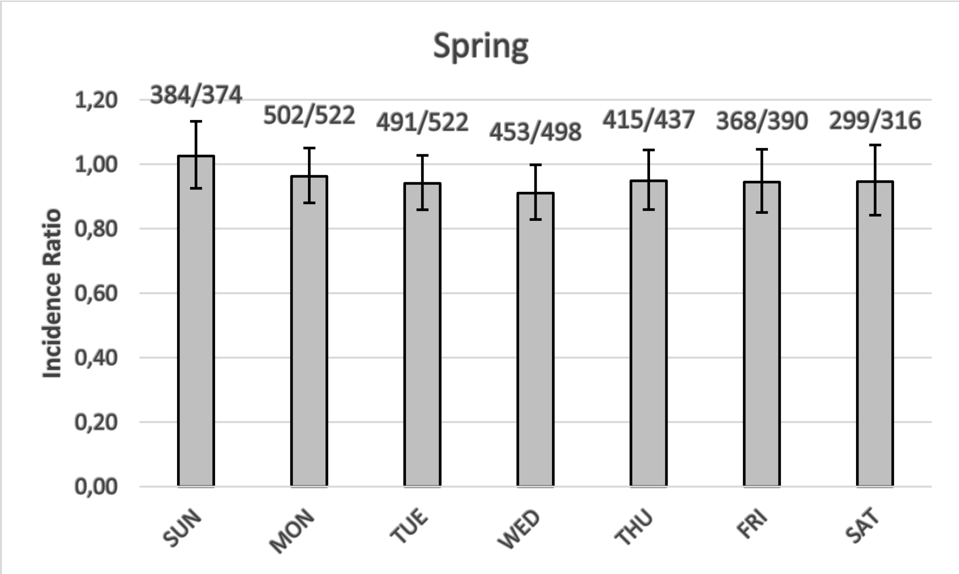
Autumn
Incidence Ratio
2,50
2,00
1,50
1,00
0,50
0,00
15/14
17/16
13/15
16/16
17/19
10/17
16/12
SUN
MON
TUE
WED
THU
FRI
SAT

Diabetes mellitus





Hypertension



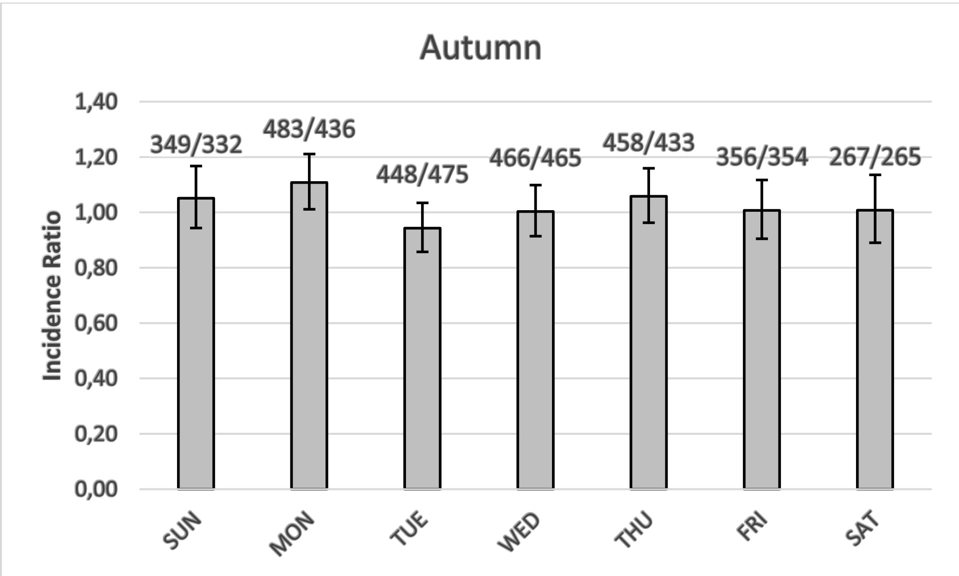
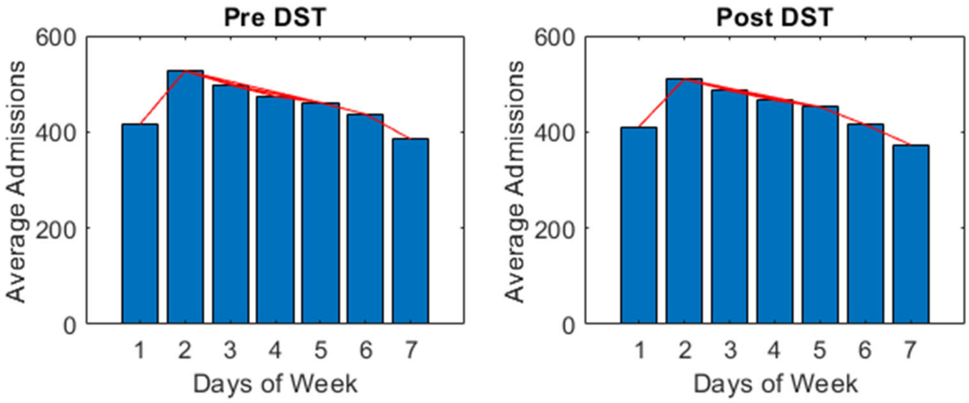
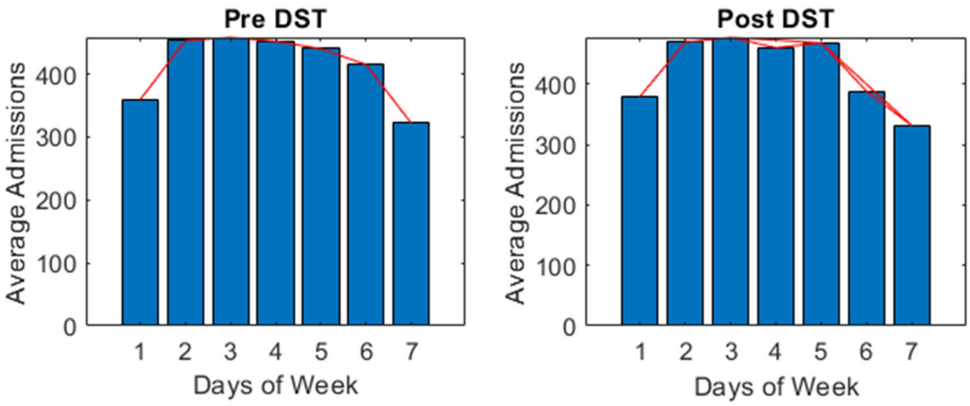


Figure S2. Visibility graphs

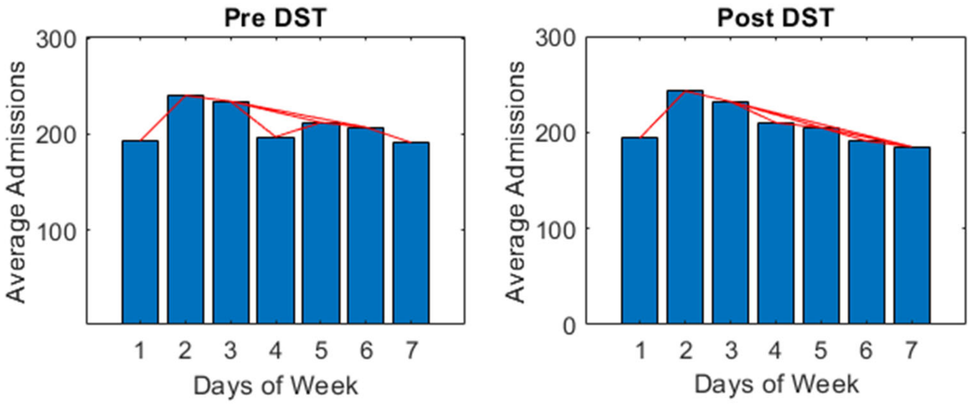
MACE SPRING



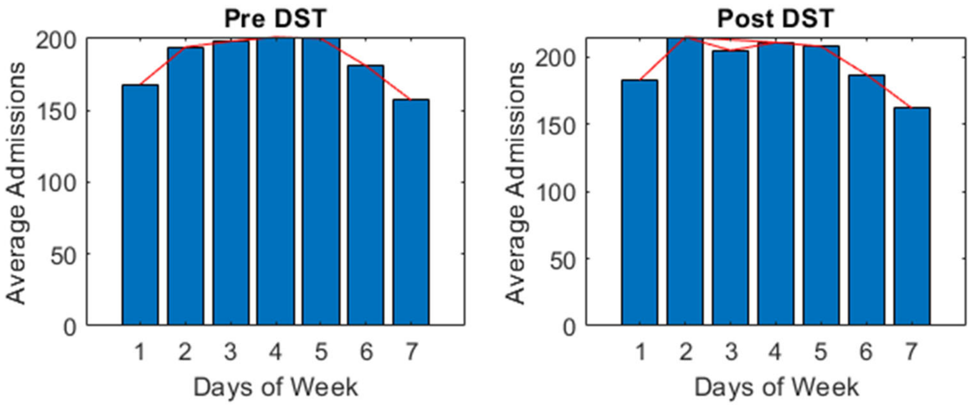
MACE AUTUMN



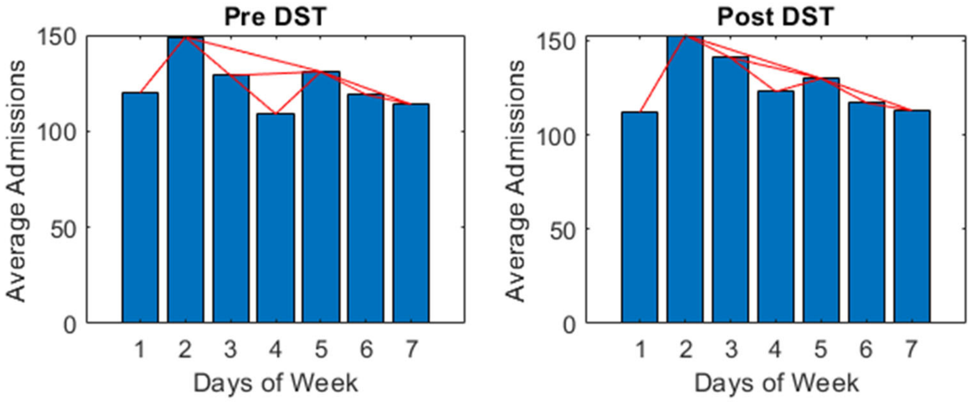
AMI SPRING



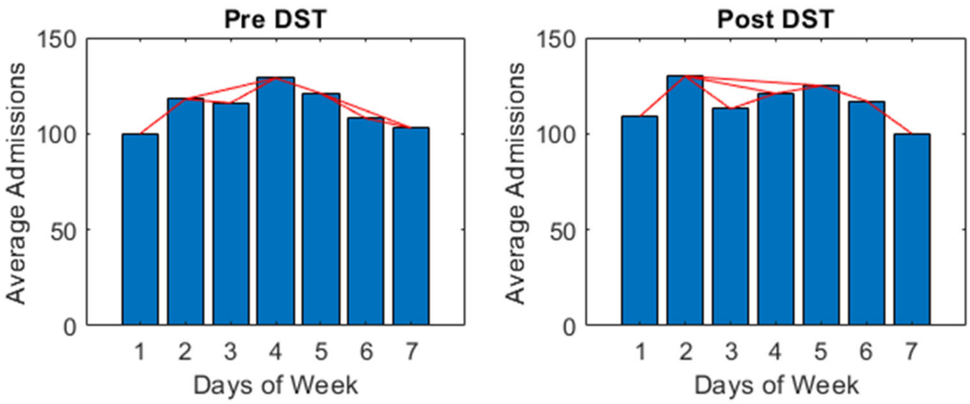
AMI AUTUMN



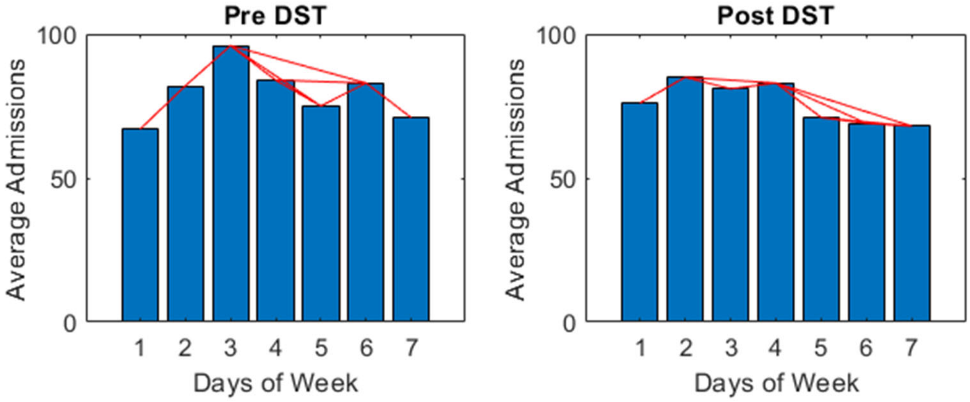
STEMI SPRING



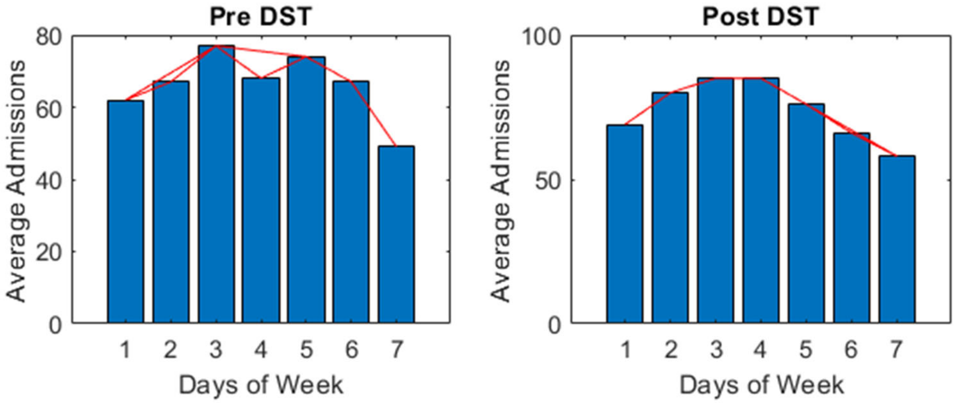
STEMI AUTUMN



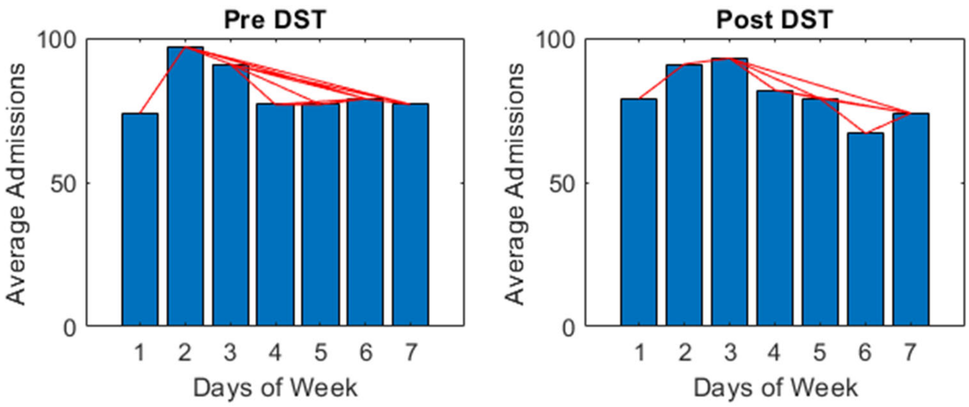
NSTEMI SPRING



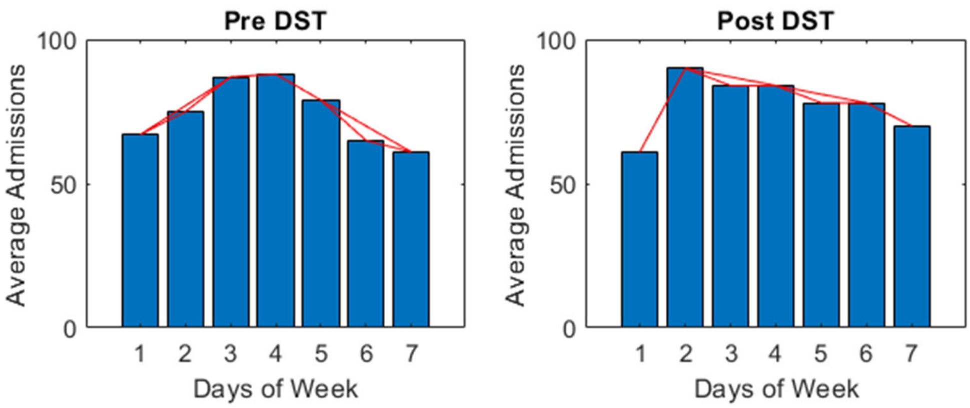
NSTEMI AUTUMN



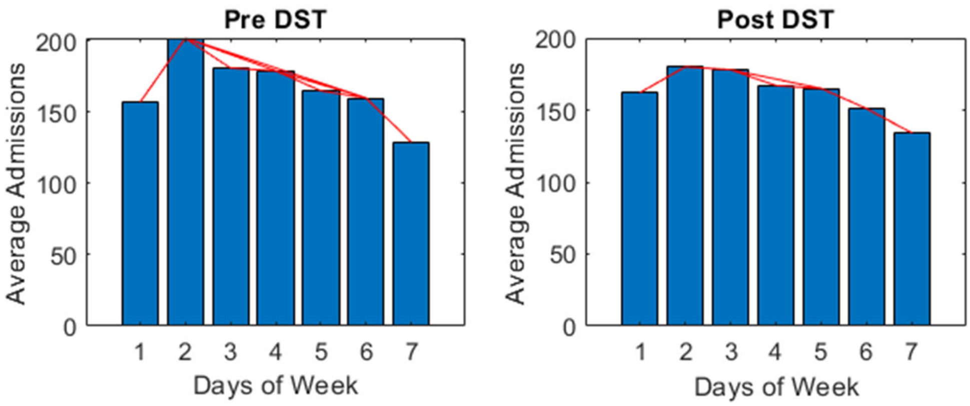
AMI PTCA SPRING



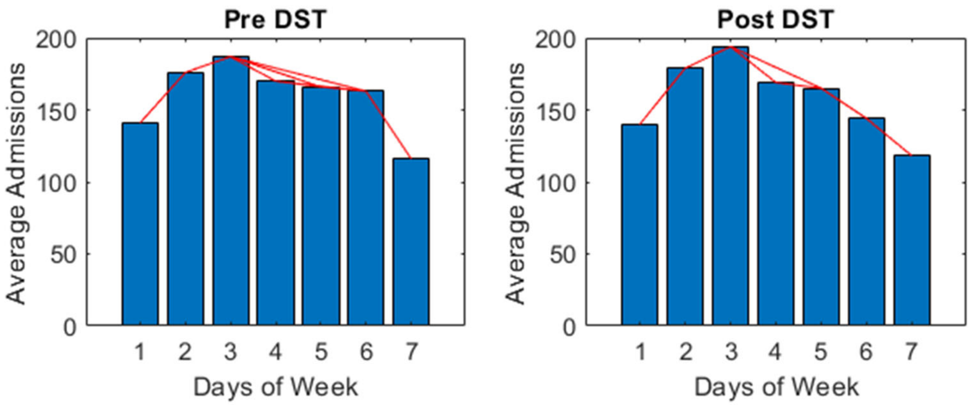
AMI PTCA AUTUMN



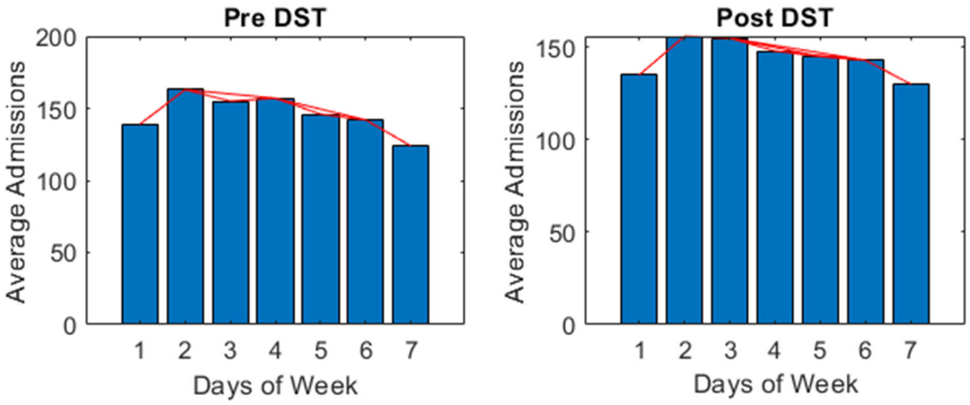
STROKE SPRING



STROKE AUTUMN



IS SPRING



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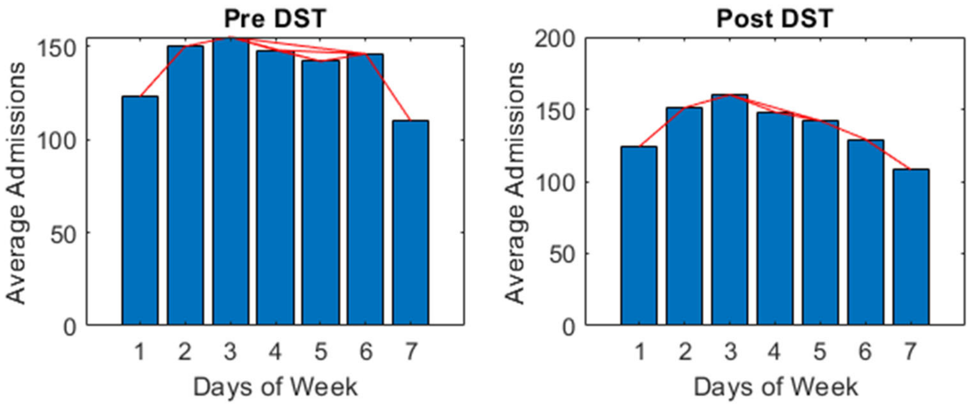

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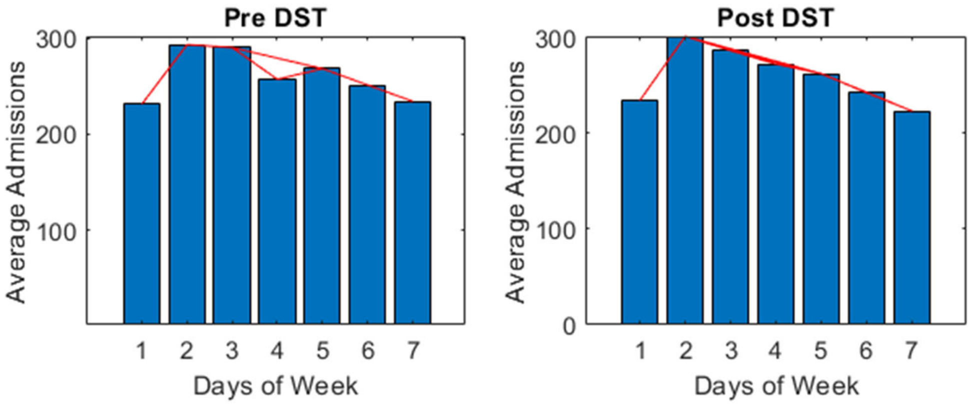

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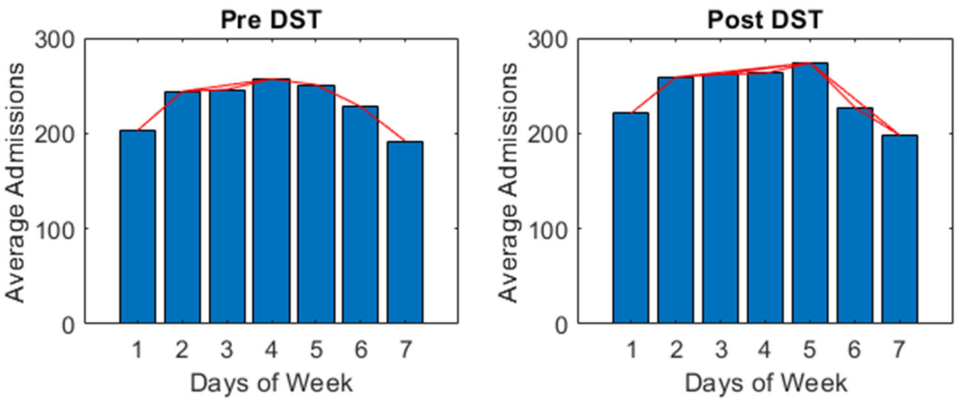

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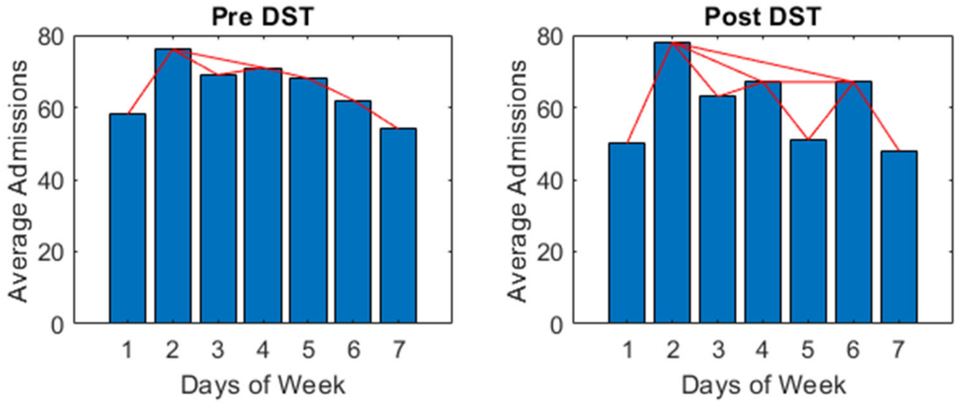

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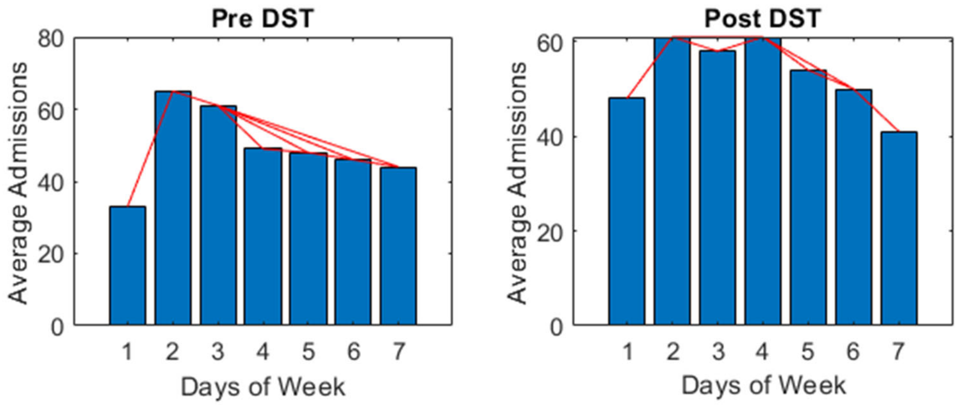
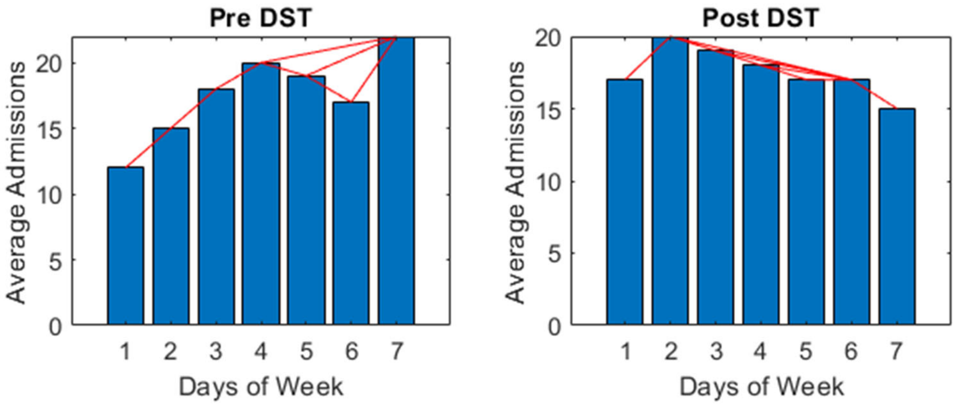


CVD SPRING



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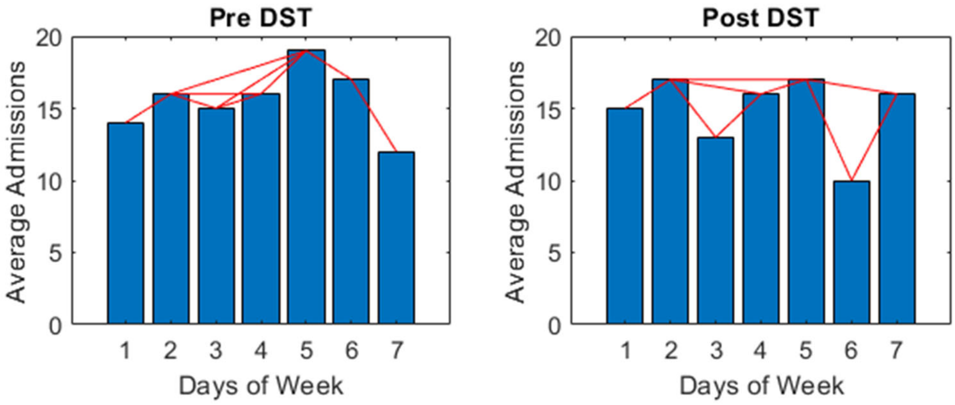

Table S1. Differences by sex and diagnosis during the two weeks before and after DST for both transitions (spring and autumn).

	All	Spring DST Transition		Autumn DST Transition	
		2W Pre	2W Post	2W Pre	2W Post
MACE	n = 157221	6393	6222	5793	5942
Men †	113507 (72.2%)	4626 (72.4%)	4503 (72.4%)	4114 (71%)	4309 (72.5%)
Women †	43685 (27.8%)	1767 (27.6%)	1717 (27.6%)	1678 (29%)	1633 (27.5%)
AMI	n = 71992	n = 2.945	n = 2.915	n = 2.593	n = 2.740
Men ††	56.050 (77,9%)	2.283 (77,5%)	2.291 (78,6%)	1.972 (76,1%) *	2.157 (78,7%) *
Women ††	15.926 (22,1%)	662 (22,5%)	622 (21,3%)	621 (23,9%)	583 (21,3%)
STEMI	n = 42975	n = 1.740	n = 1.773	n = 1.585	n = 1.627
Men	34.498 (80,3%)	1.391 (79,9%)	1.433 (80,8%)	1.279 (80,7%)	1.311 (80,6%)
Women	8.465 (19,7%)	349 (20,1%)	338 (19,1%)	306 (19,3%)	316 (19,4%)
NSTEMI	n = 26752	n = 1.111	n = 1.061	n = 924	n = 1.034
Men	19.857 (74,2%)	825 (74,3%)	796 (75%)	634 (68,6%) **	782 (75,6%) **
Women	6.892 (25,8%)	286 (25,7%)	265 (25%)	290 (31,4%)	252 (24,4%)
Ischemic Stroke	n = 51420	n = 2.051	n = 2.022	n = 1.943	n = 1.920
Men †††	34.166 (66,4%)	1.391 (67,8%)	1.334 (66%)	1.290 (66,4%)	1.260 (65,6%)
Women †††	17.243 (33,5%)	660 (32,2%)	688 (34%)	652 (33,6%)	660 (34,4%)

2W Pre = Two weeks Pre-DST; 2W Post = Two weeks Post-DST; Levels of significance: *p<0.05; **p≤0.01; † The sex was not determined for 28 subjects. ††The sex was not determined for 16 subjects. ††† The sex was not determined for 11 subjects.