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Significant regional variation in use of implantable cardioverter-defibrillators in Denmark

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Abstract

Aims: Implantable cardioverter-defibrillator (ICD) treatment prevents sudden cardiac death in high-risk patients. This study examined geographical variation in ICD implantation rates in Denmark and potential causes of variation.

Methods and Results: We obtained numbers of ICD implantations in the 5 Danish regions and 98 municipalities during 2007-2013 from the Danish Pacemaker and ICD Registry. Standardized implantation rates (SIRs) were computed as ICD implantations per 1,000,000 person-years, and age- and gender-standardized to the Danish population. We examined associations of the municipal SIR with mean age and Charlson Comorbidity Index score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre. Based on 7,192 ICD implantations, the nationwide SIR was 186 (95% confidence interval [CI]: 182-190), ranging from 170 (95% CI: 158-183) in the North Denmark Region to 206 (95% CI: 195-218) in the Region of Zealand. Municipalities with higher patient comorbidity scores, higher percentages of implantations with primary prophylactic indication, and shorter distances to ICD implanting centres, had higher SIRs (differences between SIRs of municipalities in highest and lowest quartiles = 22 [95% CI: 10-34], 45 [95% CI: 33-58], and 35 [95% CI: 24-47], respectively). Regional differences in SIRs decreased over time and had become insignificant during 2011-2013.

Conclusion: ICD implantation rates in Denmark varied significantly between regions but variation decreased during 2007-2013. Geographical variation was associated with differences in patient comorbidity score, variation in use of primary prophylactic ICD treatment, and distance to ICD implanting centre.

Keywords: Implantable cardioverter-defibrillator; implantation rate; variation; epidemiology; cross-sectional study

Introduction

Implantable cardioverter-defibrillator (ICD) treatment reduces risk of sudden cardiac death, and international guidelines recommend ICD implantation for high-risk patients.[1] Although evidence-based, adherence to guidelines may vary in clinical practice, and ICD implantation rates vary considerably internationally.[1,2,3] This is partly explained by differences between national economies and health care systems.[3,4] However, significant variation in ICD implantation rates has also been reported within nations,[5,6,7,8] indicating that other factors contribute. Differences in implantation rates may reflect both over- and underuse and it is difficult to assess the optimal implantation rate. While >10% of patients receiving primary prophylactic ICDs did not meet guideline criteria in one study,[5] this potential overuse alone did not explain the geographical variation observed.

Other reports have suggested underuse among eligible patients in areas with low implantation rates as a reason for geographical variation in implantation rates, rather than overuse in areas with high implantation rates.[9] Of notice, areas with increases in ICD utilization have been reported to have larger improvements in heart failure survival.[10] Pokorney *et al.* reported that fewer than 1 in 10 eligible patients received a primary prophylactic ICD within one year after myocardial infarction in the United States during 2007-2010.[11] In a study of 2,093 cases of sudden cardiac arrest in the community during 2003-2012, only 13% of patients eligible for primary prophylactic ICD implantation prior to the event had actually received an ICD.[12] These findings suggest that identification of factors impeding ICD implantation in eligible patients is a paramount issue in the prevention of sudden cardiac death. Regional variation in ICD implantation rates may reflect inequity in access to ICD implantation for eligible patients. However, few studies have identified potential determinants of regional variation in ICD implantation rates.[9]

The aims of the present study were to 1) examine whether regional ICD implantation rates vary significantly in Denmark, 2) identify patient- and device-related factors associated with geographical variation in ICD implantation rates, and 3) examine temporal trends in geographical variation in ICD implantation rates.

Methods

Study design and setting

We conducted this nationwide cross-sectional study in Denmark using the cumulative population of 6.3 million inhabitants during 2007-2013. Health care in Denmark is tax-funded and free-of-charge, guaranteeing all inhabitants unfettered access to general practitioners and hospitals.[13] Each Danish inhabitant has a unique civil registration number allowing for accurate and unambiguous linkage of national registries.[13] Denmark is divided into 98 municipalities within 5 regions: the Capital Region, the Region of Zealand, the North Denmark Region, the Central Denmark Region, and the Region of Southern Denmark. The average number of inhabitants per region is 1.2 million, ranging from 0.59 million in the North Denmark Region to 1.8 million in the Capital Region. The average number of inhabitants per municipality is 59,000, ranging from 1,800 to 613,000. The Danish Civil Registration System contains current and previous addresses of residency for all Danish inhabitants and is updated daily.[13]

In the regions of North Denmark, Central Denmark, and Southern Denmark all ICD implantations are performed in Aalborg University Hospital, Aarhus University Hospital, and Odense University Hospital, respectively. In the Capital Region and the Region of Zealand, all ICD implantations were performed in Gentofte Hospital and Rigshospitalet during the study period. More than 99% of all ICD implantations in Denmark were performed in these five regional ICD centres, and Denmark has a relatively low number of ICD implanting centres compared with other European nations (approximately 0.87 centres per million inhabitants).[3] The geographical localization of the five regional ICD implanting centres is illustrated in Figure 1 and their municipal referral areas are listed in Table S1.

Data sources

The Danish Pacemaker and ICD Registry (DPIR) contains information about all ICD implantations performed in Denmark. The registry includes information about the ICD recipient (date of birth, gender, underlying cardiac diagnosis) and the implantation (date, indication, ICD centre, device type [ICD or cardiac resynchronization therapy (CRT-D)]).

The Danish National Patient Registry (DNPR) maintains records of all hospitalizations in Denmark.[14] Upon hospital discharge, the treating physician records a primary diagnosis describing the main reason for diagnostic work-up and treatment, and up to several secondary diagnoses describing comorbid conditions.[14] Diagnoses are coded according to the World Health Organization's *International Classification of Diseases, Eighth Revision* (ICD-8) before 1993 and *Tenth Revision* (ICD-10) thereafter. Both primary and secondary hospital inpatient and outpatient discharge diagnoses were included in our analyses.

ICD patients

Using the DPIR, we identified all first-time ICD recipients in Denmark during 2007-2013. We excluded immigrants because data on previous comorbidities could have been missing for hospitalizations prior to ICD implantation. Residents of Greenland, an autonomous constituent country within the Kingdom of Denmark, were excluded because of the distinctive culture and remote geographical position of the island. Residents of the Faroe Islands, another autonomous country within the Kingdom of Denmark, are not registered in the Danish Civil Registration System and were not included in the study.

Based on all discharge diagnoses registered in DNPR before or on the day of ICD implantation, we computed the comorbidity score according to the Charlson Comorbidity Index for each patient.[15] The Charlson Comorbidity Index has been validated for use with DNPR hospital discharge data[15] and has proved an adequate tool for measuring the prognostic impact of comorbidity in ICD patients.[16] Each patient's municipal address on the day of ICD implantation was obtained from the Danish Civil Registration System.[13] The distance from regional ICD implanting centre to each of the municipalities in the respective referral area was ascertained using the web mapping service Google Maps, © 2015 Google Inc. (Table S1).

Statistical analysis

We ascertained the number of first-time ICD implantations performed in each region and municipality of Denmark, overall and for the first and latter part of the study period, 2007-2010 and 2011-2013, respectively. Implantation rates were computed as number of implantations per 1,000,000 person-years, and standardized to the age- and gender-distribution of all Danish inhabitants during 2007-2013. Implantation rates were computed overall, and for men and women, respectively. The approximate bootstrap method was used to compute 95% confidence intervals (CIs) of the standardized implantation rates (SIRs). We computed implantation rate ratios (IRRs), comparing the lowest and highest regional SIRs, and comparing regional SIRs with the nationwide SIR, overall and for the periods 2007-2010 and 2011-2013, respectively.

We categorized ICD implantations according to gender, age (<60 years, 60-69 years, or ≥70 years), and Charlson Comorbidity Index score (≤1, 2, 3, or ≥4 points) of ICD recipients, as well as device type (ICD or CRT-D) and indication (primary or secondary prophylaxis), overall and according to region and municipality. The mean age and comorbidity score of ICD recipients were computed overall and for each region and municipality.

To examine its association with potential determinants of geographical variation, the SIR was plotted against 1) the municipal mean age of ICD recipients, 2) the municipal mean comorbidity score of ICD recipients, 3) the municipal percentage of implantations performed as primary prophylaxis, and 4) the distance from patient residency to ICD implanting centre. As a measure of the strength of association, the Pearson correlation coefficient, r, was computed. Furthermore, SIRs were compared for municipalities in the lowest versus highest quartile according to 1) the municipal mean age of ICD recipients, 2) the municipal mean comorbidity score of ICD recipients, 3) the municipal percentage of implantations performed as primary prophylaxis, and 4) the distance from patient residency to ICD implanting centre. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). The study was approved by the Danish Data Protection Agency (record no. 1-16-02-267-12) and by the steering committee of the DPIR. According to Danish legislation, approval from an ethics committee was not needed for this registry-based study.

Results

Implantations overall

After exclusion of 46 patients (23 with unknown address, 14 with no registered identification of the implantation site, and 9 residents of Greenland), we included 7,192 first-time ICD recipients. Men constituted 80% of the study population (Table 1). The mean age of ICD recipients was 63 (median = 66 [IQR: 57-72]) years and the mean Charlson Comorbidity Index score was 2.3 (median = 2.0 [IQR: 1.0-3.0]) points (Table 1). The indication for implantation was primary prophylactic in 50% of cases and 26% of devices were CRT-Ds (Table 1). The SIR was 186 (95% CI: 182-190) per million person-years, 300 (95% CI: 292-308) for men (Table S3) and 74 (95% CI: 70-78) for women (Table S4).

Regional variation

SIRs were higher in the Capital Region and the Region of Zealand than in the Regions of North Denmark, Central Denmark, and Southern Denmark (Figure 1A and Table 2), particularly for men (Table S3). The ratio comparing the lowest regional SIR with the highest was 1.21, 1.27 for men and 1.14 for women. Ratios comparing regional SIRs with the nationwide SIR ranged from 0.91

to 1.11 (Table 2), from 0.88 to 1.12 for men (Table S3) and from 0.96 to 1.10 for women (Table S4). Men constituted less than 80% of ICD recipients in the regions of North Denmark and Southern Denmark, and more than 80% of ICD recipients in the regions of Central Denmark, Zealand and the Capital (Table 1). ICD recipients in the Region of Zealand, which had the highest SIR, were older with higher comorbidity scores than ICD recipients in Denmark overall, while ICD recipients in the regions of North Denmark and Southern Denmark had lower mean comorbidity scores than ICD recipients in Denmark overall (Table 1). The proportion of implantations with primary prophylactic indication ranged from 39% in the North Denmark Region to 60% in the Region of Zealand (Table 1). The proportion of CRT-Ds ranged from approximately 23% in the Region of Southern Denmark and the Capital Region to 32% in the Central Denmark Region (Table 1).

Factors associated with implantation

Figure 1 illustrates municipal SIRs in Denmark. Overall, municipal SIRs did not correlate, or correlated poorly, with mean age and comorbidity score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre (Figure 2). However, the strength of correlations varied between regions (Table 3). In particular, municipal SIRs in the region of North Denmark correlated inversely with distance from patient residency to ICD implanting centre, while this correlation was weaker in other regions of Denmark (Table 3). In the Region of Central Denmark, we found that municipal SIRs correlated moderately with the mean comorbidity score of ICD recipients (Table 3).

We found significant differences between the SIRs when municipalities were sorted into lowest and highest quartiles according to mean age of ICD recipients, mean comorbidity score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre, respectively (Table 4).

Temporal changes

The nationwide SIR increased by approximately 20% from 2007-2010 to 2011-2013 (Table 2), by 22% for men (Table S3) and by 13% for women (Table S4). The proportion of male recipients, mean age and CCI score showed slightly increasing trends over time (Table 1). The proportion of implantations performed as primary prophylaxis increased from 47% during 2007-2010 to approximately 54% during 2011-2013 (Table 1), while the proportion of devices that were CRT-Ds increased from approximately 24% to 28%. The SIR increased significantly in almost all regions (Table 2, Figures 1B and 1C). The largest relative increases occurred in the Central Denmark Region (29%), the Southern Denmark Region (29%), and the North Denmark Region (18%), while relative increases were smaller in the Capital Region (13%) and the Region of Zealand (10%). Accordingly, the span in ratios comparing regional SIRs with the nationwide SIR decreased over time (Table 2), and while SIRs in the Capital Region and the Region of Zealand were significantly higher than SIRs in other regions during 2007-2010, SIRs did not differ significantly between regions during 2011-2013 (Table 2). The ratio comparing the lowest regional SIR with the highest decreased by 9% (from 1.28 during 2007-2010 to 1.16 during 2011-2013), by 4% for men (from 1.29 to 1.24) and by 17% for women (from 1.55 to 1.28).

The observed differences in SIRs between upper and lower quartiles of municipalities also decreased over time (Table 4). While statistically significant when sorted by mean comorbidity score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre during 2007-2010, only SIRs of upper and lower quartile municipalities sorted by distance from patient residency to ICD implanting centre differed significantly during 2011-2013 (Table 4).

Discussion

Main findings

This nationwide study, in a country with a tax-paid health care system offering universal coverage to all inhabitants, showed significant geographical variation in ICD implantation rates in Denmark during 2007-2013. Implantation rates were four times higher among men than among women, but gender differences were not larger in regions with lower implantation rates. We observed moderate to strong linear correlations of municipal implantation rates with mean comorbidity score of ICD recipients and distance from patient residency to ICD implanting centre in some regions. The regional differences in ICD implantation rates were significant during 2007-2010, but decreased over time and were not significant anymore during 2011-2013.

Lower comorbidity score of ICD recipients, lower percentage of implantations with primary prophylactic indication, and longer distance from patient residency to ICD implanting centre were significantly associated with lower municipal implantation rates during 2007-2010, while only distance from patient residency to ICD implanting centre remained significantly associated with implantation rate during 2011-2013.

Comparison with other countries

Regional variation in ICD implantation rates has been reported in other European countries and in the United States during the same study period as ours.[5-7,9] Ratios comparing regional rates of primary prophylactic ICD implantation with the national average in the United States during 2006-2007 ranged from 0.39 to 1.77.[5] In comparison, ratios in our study ranged from 0.91 to 1.16 during 2007-2010 when regional differences were most significant. In a systematic review of 58 European cardiac implantable electronic implant studies, Valzania *et al.* demonstrated that the ratio between the regions with the highest and lowest ICD implantation rates within the same country ranged from 1.7 to 44.0.[9] Our ratio of 1.21 demonstrated that regional variation is less pronounced in Denmark than reported in any other country. The most likely reason is that Denmark is a small country with socioeconomic homogeneity and equal access to the public health care system independent of individual socioeconomic status. Regional differences in gross domestic products and health care expenditures per capita, suggested to account for significant differences in ICD implantation rates in other parts of Europe,[9] are less pronounced in Denmark.[14] Still, significant differences in implantation rates were observed between Western and Eastern Denmark, supporting previous reports suggesting that factors other than gross domestic products and health care expenditures per capita are determinants of ICD use.[3,9]

Variation in indication for ICD implantation

In agreement with our findings, a French study previously reported that patients in regions with higher rates of ICD implantation were more likely to undergo implantation for primary prevention.[7] The underlying explanation for the geographical differences in proportions of primary prophylactic ICD implantation probably is multifactorial. Differences in both patient referral and propensity to accept ICD treatment may influence implantation rates and barriers to referral include both physician- and patient-related factors. For instance, women have been reported to have lower likeliness of referral for and receiving primary prophylactic ICD implantation,[11,17] and to decline implantation more often than men.[18] The difference in SIRs for men and women in our study seem to support a lower likeliness of ICD implantation in women than in men in general, but the gender differences in ICD implantation rates were not more pronounced in regions with lower overall ICD implantation rates. Thus, lower implantation rates among women are unlikely to explain the regional variation observed. However, regional differences in ICD implantation rates decreased more for women than for men during the study period, and increased awareness of indications for ICD implantation in women in certain regions possibly contributed to the overall decrease in regional variation.

Another possible explanation for the differences observed, is varying awareness of the indications for primary prophylactic ICD implantation among health care professionals. Since 2006, Danish guidelines have recommended ICD implantation as primary prophylaxis for patients with ischaemic heart disease and left ventricular ejection fraction ≤35% in New York Heart Association class II-III despite optimal medical treatment. During the study period, primary prophylactic ICD implantation was not recommended for patients with heart failure of non-ischaemic origin. The results of the present study may indicate that these guidelines were implemented faster in the Eastern part of Denmark than in the Western part, resulting in higher implantation rates in the Eastern part. This interpretation supports that education and more widespread knowledge about ICD indications reduce geographical differences in implantation rates. The decrease in regional differences of ICD implantation rates over time may reflect increasing implementation of guidelines for primary prophylactic implantation in Denmark and decreasing inequity in access to ICD treatment for eligible patients.

Factors associated with ICD implantation

In accordance with the previous finding that patients receiving primary prophylactic ICDs have higher Charlson Comorbidity Index scores than patients receiving secondary prophylactic ICDs,[19] we found higher comorbidity scores of ICD recipients in regions with more frequent use of primary prophylactic ICD treatment. Comorbidity may be associated with a significant risk of non-arrhythmic death and the disadvantages of ICD treatment may attenuate the benefits in some patients with severe comorbidity. The risk-benefit analysis of ICD implantation in patients with comorbidity often is complicated, and the association between the SIR and the mean CCI score of ICD recipients observed in our study may result from regional differences in the individual judgment of primary prophylactic ICD indication with different levels of comorbidity.

Even though Denmark is a small country with relatively short distances, we observed that the SIR decreased with increasing distance from patient home to ICD implanting centre. Several factors may explain this association. Patients living far from an ICD implanting centre may be less likely to be referred for ICD implantation or more likely to decline implantation. As ICD implantation is without any direct financial costs for the recipient and all expenses are reimbursed to the implanting centre, reluctance to receive or offer ICD implantation for financial reasons is unlikely to occur in Denmark. Implantation is usually performed ≥90 days after myocardial infarction and regional differences in cardiac rehabilitation programs and patient participation may therefore play an important role. Patients living far from the local hospital offering cardiac rehabilitation more often refuse to participate in cardiac rehabilitation programs or drop out from such programs.[20] Consequently, primary prophylactic ICD treatment may be offered less frequently to eligible patients living far from the local hospital. This may partly explain the association between distance to ICD implanting centre and the SIR, as most patients living far from the local hospital also live far from the regional ICD implanting centre. Of notice, longer distance from patient residency to ICD implanting centre remained significantly associated with lower implantation rate during 2011-2013, thereby uncovering a possible potential for further improvement of the prevention of sudden cardiac death.

Strengths and Limitations

The strengths of this study lie in its nationwide design within the setting of a tax-paid health care system offering universal coverage to all inhabitants and its use of national registries with prospectively recorded data of high quality. Due to longitudinal data and a large sample size, we were able to observe temporal changes in ICD implantation rates and identify several factors associated with implantation, thereby uncovering potential causes for inequity in access to ICD treatment.

Our study is limited by its observational study design precluding causal inference, and we could not show a consistent reason for variation in ICD implantation rates, or that correcting it increased implantation rates. Another limitation is that some municipal SIRs were based on small numbers of implantations, leading to imprecise estimates requiring cautious interpretation. We controlled for confounding by age and gender through standardization of implantation rates, but residual confounding cannot be excluded. Although a previous study conducted in England reported no associations between ICD implantation rates and multiple socioeconomic factors,[8] including income, employment, and education, socioeconomic differences that were not corrected for in the statistical analyses may have affected our results. Some of the variation observed in our study may be attributable to epidemiological differences, for instance regional differences in the incidence of myocardial infarction. However, a visual comparison of municipal SIRs in our study with municipal incidences of myocardial infarction in Denmark during the study period (not shown) did not suggest a remarkable association, nor did previous studies demonstrate that ICD implantation rates were associated with incidence of myocardial infarction[9] or standardized mortality rates for acute myocardial infarction.[8,9]

Conclusions

This nationwide study showed significant regional variation in ICD implantation rates in Denmark during 2007-2013, but regional differences decreased over time and became statistically insignificant during 2011-2013. Although significant gender differences in ICD implantation rates were found, gender differences in ICD implantation rates did not explain the regional variation observed. Lower mean comorbidity score of ICD recipients, lower percentage of implantations with primary prophylactic indication, and longer distance from patient residency to ICD implanting centre were associated with lower implantation rates during 2007-2010, while only distance to ICD implanting centre remained significantly associated with the SIR throughout our study period. Our findings indicate that regional inequity in access to ICD treatment in Denmark has decreased over time, but that distance to ICD implanting centre may still be an obstacle to ICD treatment in eligible patients. Future studies are needed to further elucidate and address the underlying causes for variation in ICD implantation rates.

Supplementary Data

Registry codes used in the current study and distances from municipalities to implantation centres are provided in the supplementary online material.

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Conflict of Interests

J.C.N. has received grants from the Novo Nordisk Foundation, Denmark [grant number NNF16OC0018658]. J.B.J. has received speakers' fees from Medtronic and is on the advisory board for Merit Medical.

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Figure Legend

Figure 1. Municipal age- and gender-standardized implantation rates of first-time implantable cardioverter-defibrillators in Denmark during A) 2007-2013, B) 2007-2010, and C) 2011-2013. Regional borders and implantation centres are black. C = Central Denmark Region; CA = Capital Region; N = North Denmark Region; S = Region of Southern Denmark; Z = Region of Zealand.

Figure 2. Linear correlations between municipal standardized implantation rates of cardioverter-defibrillators during 2007-2013 in Denmark and A) mean age of ICD recipients, B) mean Charlson Comorbidity Index score of ICD recipients, C) percentage of implantations with primary prophylactic indication, and D) distance from patient residency to ICD implanting centre.

Table1

Table 1. Characteristics of ICD recipients and implantations in Denmark during 2007-2013.			
Characteristics, n (%) or mean (95% CI)	**2007-2013**	**2007-2010**	**2011-2013**
All regions			
Implantations	7,192 (100.0)	3,680 (100.0)	3,512 (100.0)
Male	5,752 (79.9)	2,919 (79.3)	2,833 (80.7)
Age	63.1 (62.8-63.4)	62.8 (62.4-63.2)	63.3 (62.9-63.8)
CCI score	2.3 (2.2-2.3)	2.2 (2.2-2.3)	2.3 (2.2-2.4)
CRT-D	1,866 (25.9)	887 (24.1)	979 (27.9)
Primary prophylaxis	3,622 (50.4)	1,739 (47.3)	1,883 (53.6)
North Denmark Region			
Implantations	729 (100.0)	377 (100.0)	352 (100.0)
Male	564 (77.4)	285 (75.6)	279 (79.3)
Age	62.4 (61.4-63.5)	62.5 (61.1-63.9)	62.3 (60.8-63.9)
CCI score	2.0 (1.9-2.1)	2.1 (2.0-2.3)	1.8 (1.6-2.0)
CRT-D	192 (26.3)	104 (27.6)	88 (25.0)
Primary prophylaxis	283 (39.0)	139 (37.0)	144 (41.3)
Central Denmark Region			
Implantations	1,512 (100.0)	740 (100.0)	772 (100.0)
Male	1,214 (80.3)	604 (81.6)	610 (79.0)
Age	63.1 (62.5-63.8)	62.6 (61.7-63.6)	63.6 (62.6-64.5)
CCI score	2.4 (2.3-2.5)	2.3 (2.2-2.4)	2.4 (2.3-2.5)
CRT-D	490 (32.4)	236 (31.9)	254 (32.9)
Primary prophylaxis	764 (50.4)	347 (46.8)	417 (53.8)
Region of Southern Denmark			
Implantations	1,528 (100.0)	754 (100.0)	774 (100.0)
Male	1,207 (79.0)	593 (78.6)	614 (79.3)
Age	62.3 (61.6-62.9)	62.0 (61.1-62.9)	62.6 (61.7-63.5)
CCI score	2.0 (2.0-2.1)	2.0 (1.9-2.2)	2.0 (1.9-2.2)
CRT-D	346 (22.6)	120 (15.9)	226 (29.2)
Primary prophylaxis	622 (40.7)	283 (37.5)	339 (43.8)
Capital Region			
Implantations	2,128 (100.0)	1,121 (100)	1,007 (100.0)
Male	1,722 (80.9)	904 (80.6)	818 (81.2)
Age	63.2 (62.6-63.7)	63.1 (62.3-63.9)	63.2 (62.4-64.0)
CCI score	2.4 (2.3-2.4)	2.3 (2.2-2.4)	2.5 (2.3-2.6)
CRT-D	489 (23.0)	255 (22.7)	234 (23.2)
Primary prophylaxis	1,180 (55.5)	601 (53.6)	579 (57.5)
Region of Zealand			
Implantations	1,295 (100.0)	688 (100.0)	607 (100.0)
Male	1,045 (80.7)	533 (77.5)	512 (84.3)
Age	64.2 (63.5-64.8)	63.6 (62.7-64.6)	64.8 (63.9-65.7)
CCI score	2.5 (2.4-2.6)	2.4 (2.3-2.6)	2.6 (2.4-2.7)
CRT-D	349 (26.9)	172 (25.0)	177 (29.2)
Primary prophylaxis	773 (59.7)	369 (53.6)	404 (66.6)

CI = confidence interval; CCI = Charlson Comorbidity Index; CRT-D = cardiac resynchronization therapy defibrillator.

Table2

Table 2. Implantation rates of cardioverter-defibrillators in Denmark during 2007-2013.

Region	**2007-2013**			**2007-2010**			**2011-2013**			**2007-2010 versus 2011-2013**	
	IR† (95% CI)	SIR† (95% CI)	IRR	IR† (95% CI)	SIR† (95% CI)	IRR	IR† (95% CI)	SIR† (95% CI)	IRR	SIR difference (95% CI)	*p*‡
All	186 (182-190)	186 (182-190)	ref	168 (162-173)	171 (166-177)	ref	210 (203-217)	205 (198-211)	ref	34 (25-42)	<0.0001
North	180 (167-193)	170 (158-183)	0.91	162 (146-179)	158 (142-173)	0.92	202 (181-223)	187 (168-207)	0.91	30 (4-55)	0.02
Central	173 (164-181)	178 (169-186)	0.96	149 (139-160)	157 (146-168)	0.92	203 (190-218)	203 (189-218)	0.99	46 (28-64)	<0.0001
Southern	182 (174-192)	175 (166-184)	0.94	158 (147-169)	155 (144-166)	0.91	215 (200-230)	200 (186-214)	0.98	46 (28-64)	<0.0001
Capital	181 (173-189)	198 (189-206)	1.06	169 (160-179)	187 (176-198)	1.09	196 (184-208)	211 (198-224)	1.03	23 (6-40)	0.007
Zealand	226 (214-239)	206 (195-218)	1.11	210 (194-226)	198 (184-213)	1.16	248 (228-268)	217 (200-235)	1.06	19 (-4-42)	0.11

† Implantations per million person-years.

‡ P-value for the difference between SIRs of 2007-2010 and 2011-2013.

CI = confidence interval; IR = implantation rate; IRR = standardized implantation rate ratio; ref = reference; SIR = age- and gender-standardized implantation rate.

Table3

Table 3. Linear correlations between the standardized implantation rate and mean age of ICD recipients, mean Charlson Comorbidity Index score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre in Denmark during 2007-2013.

Region	**Pearson correlation coefficient, *r*†**			
	Mean age	Mean CCI score	Primary prophylactic indication	Distance
Overall	-0.008	0.35	0.38	-0.29
North Denmark	-0.46	-0.03	0.28	-0.73
Central Denmark	0.11	0.63	0.41	-0.46
Southern Denmark	-0.08	0.18	0.37	-0.29
Capital	0.13	0.12	-0.32	-0.22
Zealand	0.10	-0.22	0.41	-0.20

† A value of 1 indicates total positive linear correlation, a value of -1 indicates total inverse linear correlation, while a value of 0 indicates no linear correlation.

CCI = Charlson Comorbidity Index; ICD = implantable cardioverter-defibrillator.

Table4

Table 4. Differences between standardized implantation rates of municipalities in the lowest versus highest quartile according to mean age and Charlson Comorbidity Index score of ICD recipients, percentage of implantations with primary prophylactic indication, and distance from patient residency to ICD implanting centre.

	2007-2013				2007-2010				2011-2013			
	SIR^L	SIR^U	Difference (95% CI)	p	SIR^L	SIR^U	Difference (95% CI)	p	SIR^L	SIR^U	Difference (95% CI)	p
Mean age	181	194	13 (1-25)	0.04	157	173	16 (-1-34)	0.06	201	192	-9 (-28-10)	0.34
Mean CCI score	179	201	22 (10-34)	0.0003	142	178	36 (20-52)	0.0000	200	206	6 (-12-25)	0.51
Primary prophylaxis percentage	158	203	45 (33-58)	0.0000	141	189	48 (32-63)	0.0000	197	207	11 (-10-32)	0.32
Distance to ICD centre	206	171	-35 (-47--24)	0.0000	197	157	-40 (-54--25)	0.0000	219	188	-31 (-49--13)	0.0008

CCI = Charlson Comorbidity Index; CI = confidence interval; ICD = implantable cardioverter defibrillator; SIR^L = standardized implantation rate of municipalities in the lowest quartile; SIR^U = standardized implantation rate of municipalities in the highest quartile.

Figure 1A_revised

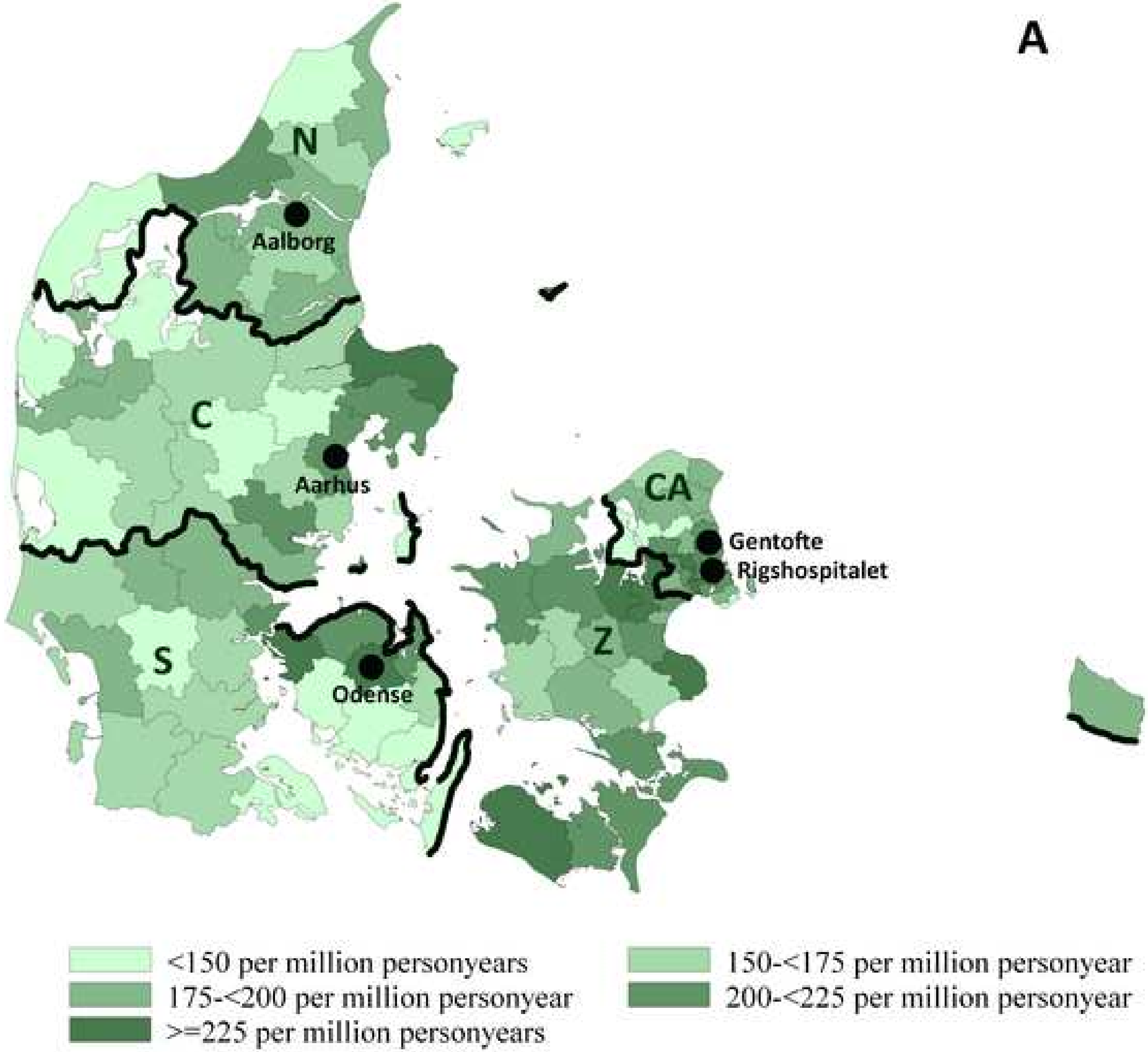


Figure 1B_revised

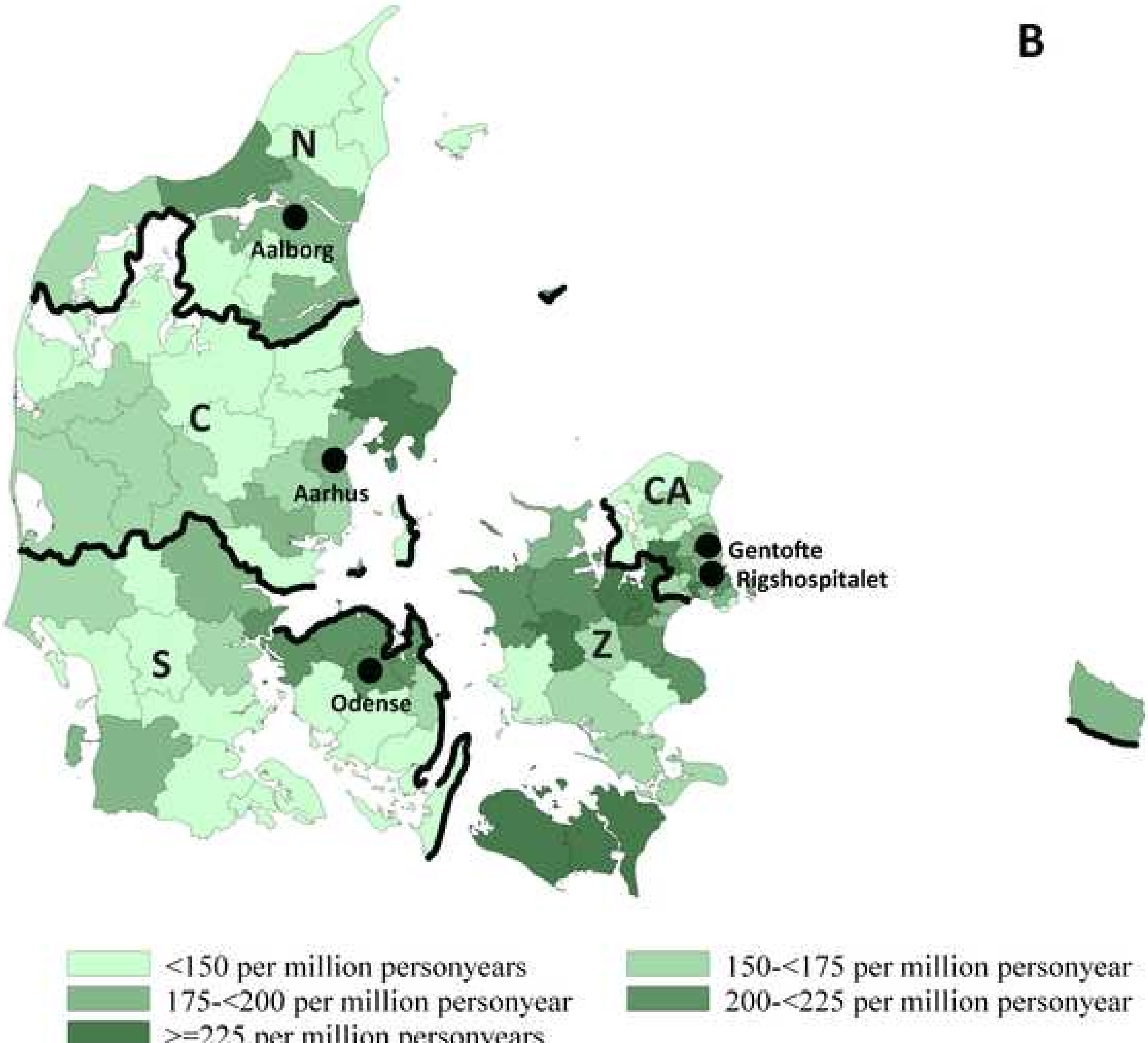


Figure 1C_revised

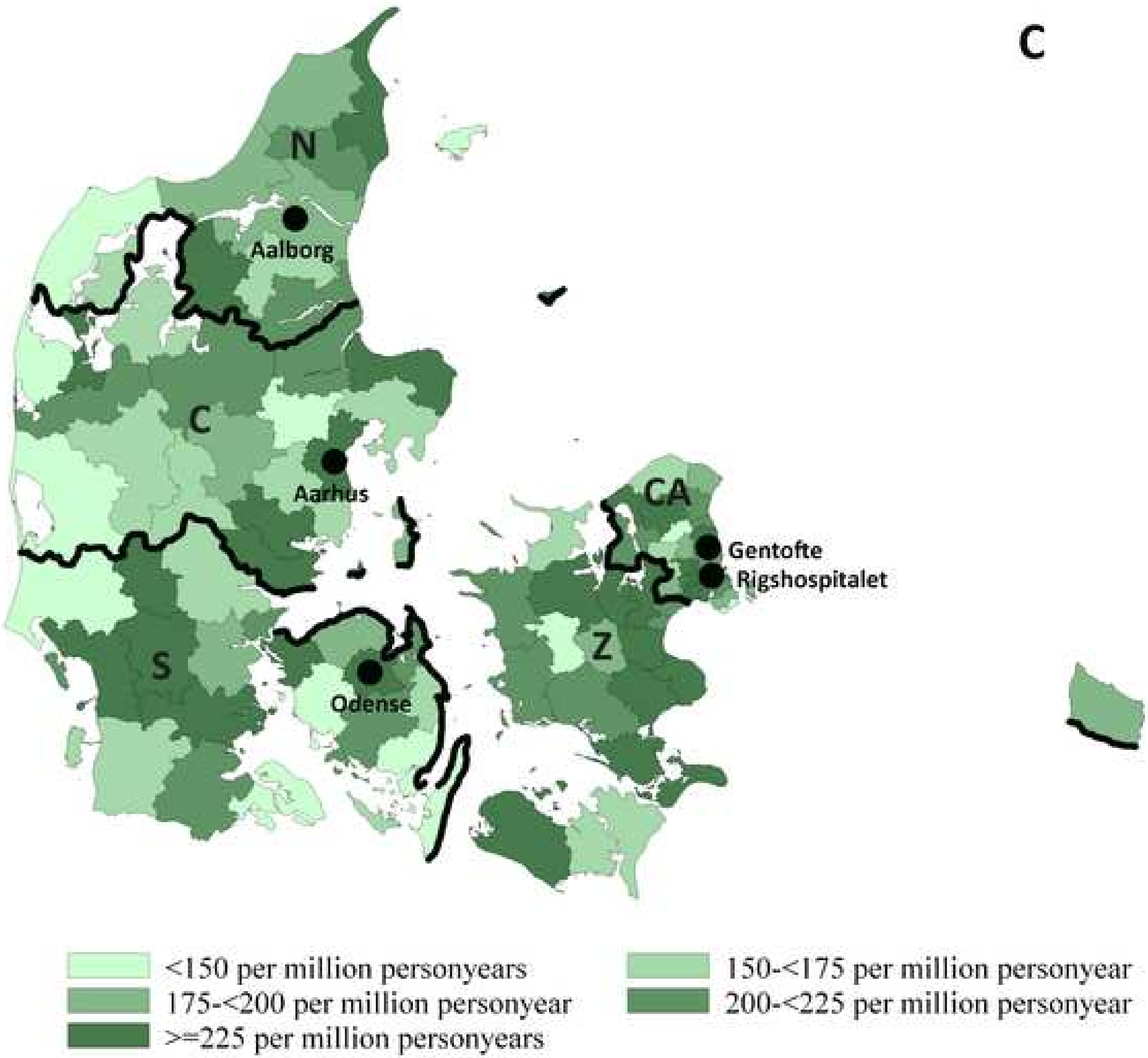
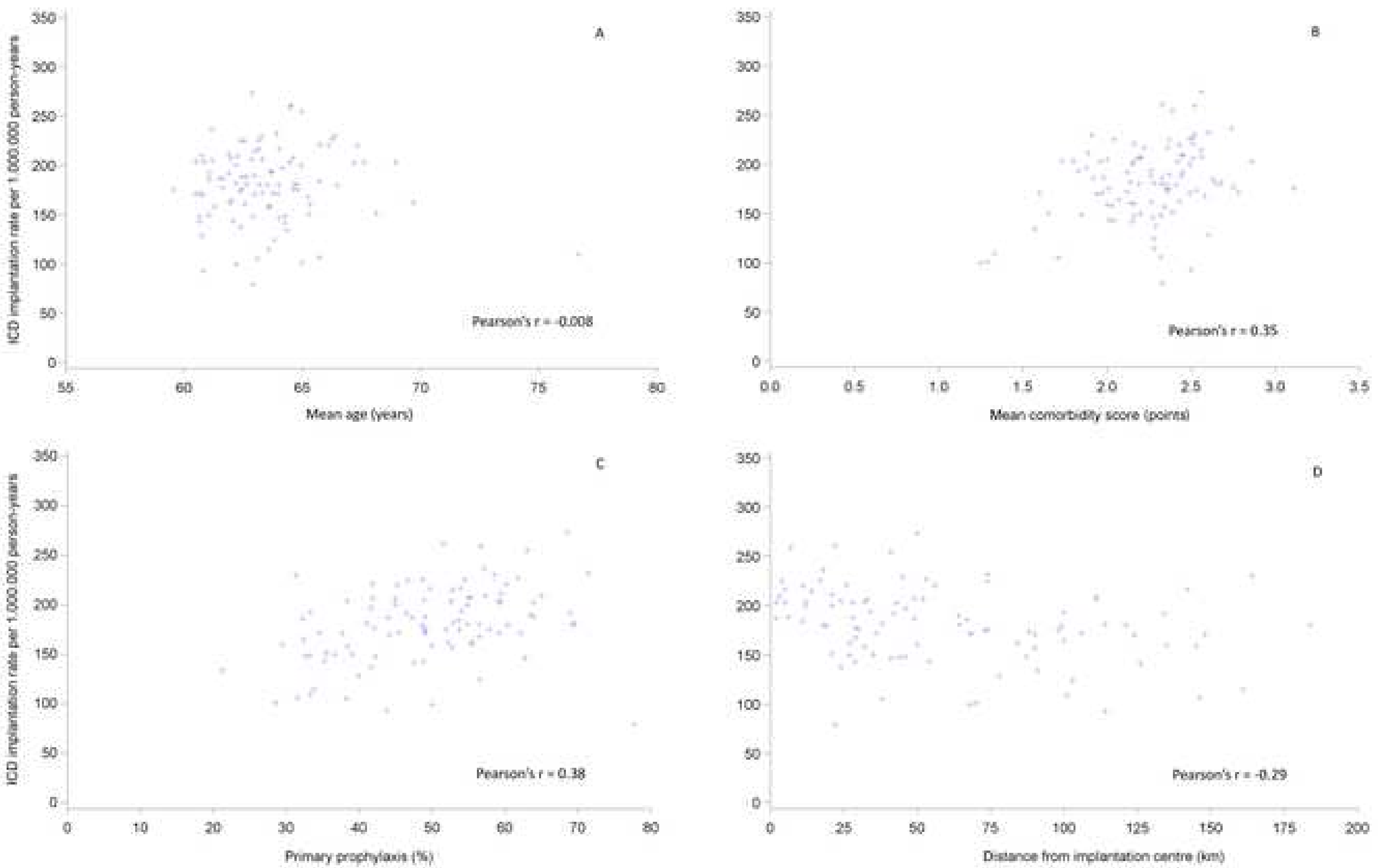


Figure 2


A
B
C
D
ICD implantation rate per 1.000.000 person-years
Mean age (years)
Mean comorbidity score (points)
Primary prophylaxis (%)
Distance from implantation centre (km)
Pearson's r = -0.008
Pearson's r = 0.35
Pearson's r = 0.38
Pearson's r = -0.29