Implantable electrical devices for prevention of sudden cardiac death: data on implant rates from a ‘real world’ regional registry

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Aims
International and national consensus guidelines define appropriate indications for implantable cardioverter–defibrillators (ICDs), but the variability in implant rates in ‘real world’ clinical practice is still unknown.

Methods and results
In Emilia-Romagna, an Italian region with around 4.3 million inhabitants, a web-based registry was instituted to collect data for all ICDs implanted. Between January 2006 and December 2008, data from all consecutive patients resident in this region who underwent first implant of an ICD or a biventricular ICD were collected and standardized, considering each regional area (i.e. each of the nine provinces). The overall number of implanted ICDs had an increase in years 2007 and 2008, with a relative increase in comparison to 2006, by 14 and 48% respectively, reaching an average value of 16.2 per 100 000 inhabitants in 2008. Most of the increase was due to a rise in ICDs for primary prevention. The ratio between the implant rates of the provinces with the highest and the lowest implant rates, respectively, was around 2 in 2008.

Conclusion
Implant rates for ICDs, considering both primary and secondary prevention of sudden death, show up to two-fold variations even in a geographical region where the general level of health care is advanced and well appreciated by the population. The lack of a common strategy for sudden death prevention, approved by both physicians and institutional regional authorities, together with some degree of variability in translating guidelines into clinical practice, were identified as the main factors explaining the heterogeneity in ICD implant rates.

Keywords
Guideline • Implantable cardioverter–defibrillator • Registry • Sudden death

Introduction
One of the most relevant problems of current cardiology practice is the appropriate deployment, in patients appropriately selected according to consensus guidelines, of a series of treatments whose proven efficacy is accompanied by relatively high upfront costs.1 Such treatments include implantable cardioverter–defibrillator (ICDs), devices for cardiac resynchronization therapy (CRT), drug-eluting stents, and devices for left ventricular assistance. In the particular setting of sudden cardiac death (SCD) prevention, the high upfront cost of ICDs and CRT devices has been considered one of the limiting factors to full implementation of consensus guidelines. Randomized controlled studies showed that in selected high-risk patients on optimized medical treatment,
an ICD or a CRT device can reduce SCD and improve overall survival, both in the setting of primary and secondary prevention,\textsuperscript{2–4} and this bulk of evidence was the basis for current indications for device therapy.\textsuperscript{5–7} In the ‘real world’, an analysis of the actual barriers to implementation of guidelines on electrical devices for SCD prevention has to consider not only financial, but also administrative, organizational, and cultural factors.\textsuperscript{8–10} These factors may explain the relatively wide heterogeneity in device implant rates within Europe and the great differences existing between European countries and the USA.\textsuperscript{9,11,12} It is, however, expected that these factors would exert a relatively homogeneous effect in the context of a relatively limited regional area, thus leading to relatively homogeneous implant rates. The issue of monitoring the implementation of consensus guidelines is currently topical and constitutes one of the more challenging fields of health care interventions.\textsuperscript{1,13–15}

The aim of our study was to assess the results of the implementation of current guidelines on secondary and primary prevention of SCD, through analysis of implant rates of ICDs in the specific context of our Italian region, Emilia Romagna, where a prospective registry on device implants has been instituted. Emilia Romagna is an administrative region of Northern Italy with a population of around 4.3 million inhabitants.\textsuperscript{16} In Italy, the aim of the National Health Service is to guarantee the uniform provision of care to citizens, but responsibility for healthcare is shared between the central government and the 20 Italian regions. Considerable and growing differences in regional health service organization and provision exist,\textsuperscript{17} but these differences should be minimal within the same regional area where the process of health care delivery is expected to be fairly homogeneous. Our analysis was focused on ICD implant rates, and on their evolution over time in a 3-year period, in all the provinces that are part of our regional area, taking into consideration ICD implants performed either for primary or secondary prevention of SCD.

**Methods**

In July 2005, the Regional Health Care and Social Agency of Emilia-Romagna, an Italian region, launched a prospective web-based registry called Registro Regionale di Aritmologia Interventistica (RERAI), aimed at collecting clinical and implant data for all cardiac devices implanted in the Emilia-Romagna region. All 21 public and 3 private cardiology centres implanting ICDs and CRT devices in this region participated in the data collection. In the present study (conceived in accordance with the principles of the most recent revision of the Declaration of Helsinki), we analysed data from all consecutive patients resident in the Emilia-Romagna region who underwent first implant of an ICD or a biventricular ICD (CRT device) for secondary and primary prevention of SCD between January 2006 and December 2008. Device replacements and upgrades of a previous implant were excluded. Because the RERAI registry was designed to observe current clinical practice, the ethics committees of each participating hospital required only ordinary written informed consent for implant (in line with national regulations) and anonymous publication of scientific data, which was obtained from all patients.

In these centres, national and international consensus guidelines were followed with regard to indications to implant an ICD, either in the field of secondary prevention, or in the field of primary prevention of sudden death, for all the possible cardiac substrates (ischaemic heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, Brugada syndrome, primary electrical disease, etc.). Implant of a device was classified as primary prevention if performed in a patient identified as a subject at increased risk of SCD, according to current guidelines, in the absence of previously documented sustained ventricular tachyarrhythmias or cardiac arrest.\textsuperscript{5–7} Implants performed for providing CRT through a biventricular defibrillator, in the absence of previously documented sustained ventricular tachyarrhythmias or previous cardiac arrest, were included in primary prevention of SCD.

On the basis of actual implants performed in the resident population (independently of the hospital where implants had been performed), the implantation rates for 100 000 inhabitants were calculated annually for each of the nine provinces of residence, for all indications and separately for primary and secondary prevention. Crude rates of ICD implantations for each province were adjusted for differences in age and sex, using the regional population during the year 2007 as the standard population.\textsuperscript{16} The standardization was performed in order to compare implant rates in provinces with different distributions in age and sex. Histograms and box-plots were used to graphically represent results. Spearman’s rank correlation indices were calculated to evaluate the correlation between ICD implantation rates in every year of the 3-year period we analysed and the number of implanting centres for province. Statistical analyses were conducted using SAS Software version 9.1.3 (SAS Institute Inc, Cary, NC, USA) and STATA Software version 10.1 (StataCorp, College Station, TX, USA).

**Results**

In our region, Emilia Romagna, the overall number of implanted ICDs increased in years 2007 and 2008, with a relative increase in comparison to 2006, by 14 and 45%, respectively, reaching an average value of 16.2 per 100 000 inhabitants in 2008 (Table 1). Most of the increase was due to a rise in devices implanted for primary prevention (relative increase of 28 and 69% for years 2008 and 2007, respectively, in comparison to 2006), while the number of devices implanted for secondary prevention of SCD showed smaller changes.

As shown in Table 1, most of the implanted patients were male, and the median age was 67–69 years, younger for patients with a primary prevention indication. With regard to clinical characteristics, around half of the patients had ischaemic heart disease, and the presence of moderate–severe functional impairment, expressed by an advanced NYHA class, was more common in primary prevention, similarly to the presence of a widened QRS complex (Table 2).

The distribution of implanted devices according to type (single-chamber, dual-chamber, and biventricular) is shown in Table 3.

Implant rates per 100 000 inhabitants are shown for the entire region and for each province in Figures 1 and 2, with regard to the overall number of device implants (for either secondary or primary prevention) (Figure 1) and the number of implants performed only for primary prevention (Figure 2), respectively.

No significant correlation was found between the number of implanting centres per province (ranging from 1 to 6) and standardized implant rates per each province (data of the 3 years were included in the same analysis) ($r = 0.247$ at Pearson’s test, $P = 0.213$ and $r = 0.174$ at Spearman’s test, $P = 0.344$). The four
provinces including a university/teaching hospital, compared with the five without, tended to have higher implant rates (averaged values 2006–2008) when considering the setting for primary prevention (median 11.4 vs. 8.3 per 100 000 inhabitants, $P_{\text{,}0.05}$ at non parametric equality-of-medians test), but not in the setting of secondary prevention (median 3.5 vs. 4.5 per 100 000 inhabitants, not significant).

Analysis of variations in standardized implant rates in 2007 vs. 2006 and 2008 vs. 2006 showed a trend towards a negative correlation with implant rates in year 2006 ($\rho_{\text{,}0.55}$, $P_{\text{,}0.125}$ in 2007 vs. 2006 and $\rho_{\text{,}0.70}$, $P_{\text{,}0.036}$ in 2008 vs. 2006, respectively). This analysis suggests that the largest increase over time occurred in the provinces that had a lowest implant rate in 2006.

The median and interquartile ranges of standardized implant rates for all the provinces are shown in Figure 3. It appears that there is a trend toward a reduction in dispersion of overall implant rates, although this appears mostly related to a reduction in dispersion of implant rates for secondary prevention, while considerable variability persists for implant rates related to primary prevention.

The ratio between the implant rates of the provinces with the highest and the lowest implant rates, respectively, was 1.8 in 2006, 1.7 in 2007, and 1.8 in 2008 for overall implants (original data on implant rates shown in Figure 1). For implants performed for primary prevention, it was 2.9 in 2006, 2.8 in 2007, and 2.1 in 2008 (original data on implant rates shown in Figure 2).

**Discussion**

The present study is focused on assessment of standardized implant rates for ICDs, in a 3-year period in an Italian region,
Emilia Romagna, where the general level of health care is advanced and no major limitations to access to care are usually detectable. Indications for both secondary prevention (i.e. in patients with previous cardiac arrest or previously documented ventricular tachyarrhythmias) and primary prevention (i.e. in patients considered at high risk of developing ventricular tachyarrhythmias) of SCD were considered and in all the cases, consensus guidelines were the reference for device implant indication.5 – 7 It is noteworthy that the Regional health authorities recently began monitoring the activity of electrophysiology through a prospective web-based registry and until now did not provide any guidance on device implants. Our study shows that implant rates of ICDs may vary within the same regional area, with up to a two-fold ratio in standardized implant rates per inhabitant between areas with the highest and the lowest implant rates. The same ratios appear higher when implant rates for primary prevention are considered. The temporal trend between 2006 and 2008 showed a rise in implant rates, more pronounced for those areas with the lowest implant rates, with an overall trend towards reduction of heterogeneity between different regional areas, more evident for secondary rather than for primary prevention indications. In this perspective, the heterogeneity in implant rates that we found within relatively close geographical areas, with a range of variations that are higher than what was expected, may be the basis for considering promotion of initiatives, at the level of health care providers and hospital institutions for a more homogenous access to ICD therapy, according to available evidence,8 in a comprehensive strategy for SCD prevention. Data derived from various registries have been published, but analyses of implant rates in relatively limited geographical areas may present some biases, since, with few exceptions,18 data are not usually related to resident population,11,12 with a potential bias due to migration of patients to centres in another geographical area. The latter bias may be of secondary relevance when an analysis is performed at a national level, but may be important when the analysis is focused on a restricted area, with potential implications for funding of device therapy.

In a national survey of ICD implants in the UK for years 1998–2002, Cunningham et al.18 reported a more than four-fold ratio between implant rates of the regions within the UK with the highest and the lowest implant rates. These findings were interpreted as the result of different strategies for screening and referral
in secondary care, rather than the result of systematic differences in selection criteria between implanting centres. However, the same group, in a subsequent report by McComb et al., highlighted that it was not possible to find a precise explanation of variations in regional implant rates, even if factors related both to the need for ICD implantation and service provision, in addition to socio-economic deprivation, were considered. An analysis of our data suggests that the variability in implant rates may be lower (variations in the range of two-fold, rather than four-fold) in a different context, where patient referral may have a different value because more centres may be available for performing device implants.

Also in the context of our region, any interpretation of differences in implant rates for ICDs has to consider that, potentially, multiple barriers may limit translation of current knowledge into daily practice. In our region, the lack of a common strategy for SCD prevention, including ICD implant in appropriately selected patients, approved by both physicians and institutional regional authorities, together with some degree of variability in translating guidelines into clinical practice, were identified as the main factors explaining the heterogeneity in ICD implant rates across our geographic area. Moreover, in the absence of a commonly accepted regional policy for SCD, a series of priorities may compete, at local level, for different allocation of financial resources, especially when financial constraints dominate.

Both objective and subjective reasons may influence the decision of not providing patients with an indication for primary prevention of SCD with an ICD. A registry from the USA, focused on a large cohort of in-hospital patients affected by heart failure, showed that the overall proportion of patients actually implanted with an ICD or with planned implantation was only 20% of eligible patients, ranging from 0 to 80%, and that at hospital level, the variability in ICD use in eligible patients was huge, being in the range of a 35-fold variation between the hospital with the highest and the lowest implant rates. The reasons for such incomplete adoption of ICD therapy in the USA are complex, and involve hospital size and characteristics, such as the ability to implant electrical devices, and translate into
important disparities related to age, sex, ethnicity, and lack of insurance.21,22

Scott et al.23 reported on the implant of ICDs and CRT devices in a UK regional centre, taking into account patients referred by hospitals with or without device specialists among the staff members, thus addressing the topical issue of patient referral to implanting centres. The study showed that standardized ICD implant rates had two-fold variations, according to the characteristics of the local hospital, being higher in centres actually able to perform the implant. Even greater variations, up to three-fold differences in implant rates, were found focusing only on ICDs implanted for primary prevention in coronary artery disease.

Overall, implant rates appeared lower in the UK in comparison with our analysis of an Italian region, although the implant rates for the population served by the regional cardiothoracic centre in Southampton were in line with the implant rates of our region. In our analysis, implant rates were independent of the number of implanting centres per regional area, i.e. per province, and this seems to exclude a prevalent role of lack of implanters in influencing actual implants. This finding is in agreement with what reported by McComb et al.19 in an analysis of ICD implants in the UK. Indeed, the chain of referral may work well also in areas with only one implanting centre, if appropriate pathways for access to implant are defined and developed. Our study suggests that the presence of a teaching/university hospital in a specific regional area tends to promote ICD use for primary prevention of SCD, and this may reflect both an increased referral and an enhanced predisposition to apply technological advances.

The results of a recent survey of a group of cardiologists and general physicians in New Zealand revealed how lack of financial resources, lack of local expertise, no diffusion of guidelines, and difficulties in the referral process as well as in access to cardiac investigations were judged as significant barriers to ICD referral in that area.10 Our data suggest that careful analysis of implant rates is interesting also for areas where marked variations are not expected. These approaches may be the basis for providing physicians with a series of feedbacks on their performance and for carrying out audits, in order to validate physicians’ decisions and improve adherence to consensus guidelines. At the same time, the regional and local health trust authorities may also take into account these data in planning health care policy strategies and resource allocation, in order to offer a more homogeneous access to ICD therapy. In this perspective, analyses derived from a registry involving all the centres working in a specific area may also provide inputs for defining benchmarks, as well as for predicting the need for financial resources.

According to consensus of expert8 and studies examining the implementation of evidence-based therapies,24 it appears that the potential barriers to device therapy are more complex than those existing for pharmacological therapy8 and a systematic approach at the level of patients, providers, hospitals, and health care organization systems is required. In this perspective, analyses focused on the potential number of eligible patients in the ‘real world’20 as well as on actual implant rates21-24 are extremely useful for investigating the current status of appropriateness in guideline implementation, for improving all the organizational aspects of access to device therapy, as well as for monitoring the complex process of guideline implementation.

The present report provides an accurate overview of ICD implant rates in a 3-year period. However, it does not provide a detailed analysis of implant rates for specific types of devices (i.e. biventricular ICDs for CRT versus single or dual-chamber ICDs) and does not investigate the rates of eligible patients for device therapy in each regional area. The latter is an important aspect for a comprehensive analysis of appropriateness of actual rates of device implants that require different perspectives25 and that are not covered by current national registries on device implant rates.26,27
Conclusions

Implant rates for ICDs, considering both primary and secondary prevention of SCD, show up to two-fold variations and this is detectable also in a geographical region where the general level of health care is advanced and no major limitations to access to care are usually detectable. The temporal trend in a 3-year period showed a progressive increase in implant rates, with a tendency towards a reduction in the variability of implant rates per local area, although the increased homogeneity was mainly observed for secondary prevention indications. Multiple factors and barriers may affect knowledge translation into daily practice, but the lack of a common strategy for SCD prevention, including ICD implant in appropriately selected patients, approved by both physicians and institutional regional authorities, together with some degree of variability in translating guidelines into clinical practice, were identified as the main factors explaining the heterogeneity in ICD implant rates across our geographic area. This type of analysis may be the basis for providing physicians with a series of feedbacks on their performance and for carrying out audits, in order to validate physicians’ decisions. This type of analysis may also provide inputs for defining benchmarks, as well as for predicting the need for financial resources.

Conflict of interest: none declared.

Appendix

List of RERAI Investigators:

References