Implantable Cardioverter Defibrillators Have Reduced the Incidence of Resuscitation for Out of Hospital Cardiac Arrest Caused by Lethal Arrhythmias

Running title: Hullemen et al; ICDs decline VF incidence

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Journal Subject Codes: [22] Ablation/ICD/surgery; [25] CPR and emergency cardiac care
Abstract:

Background - Over the last decades, a gradual decrease in ventricular fibrillation (VF) as initial recorded rhythm during resuscitation for out of hospital cardiac arrest (OHCA) has been noted. We aimed to establish the contribution of Implantable Cardioverter Defibrillator (ICD) therapy to this decline.

Methods and Results - Using a prospective database of all OHCA resuscitation in the province North-Holland in The Netherlands (ARREST), we collected data on all patients in whom resuscitation for OHCA was attempted in 2005-2008. VF OHCA incidence (per 100,000 inhabitants/year) was compared with VF OHCA incidence data from 1995-1997, collected in a similar way. We also collected ICD interrogations of all ICD patients from North-Holland and identified all appropriate ICD shocks in 2005-2008; we calculated the number of prevented VF OHCA episodes considering that only part of the appropriate shocks would result in avoided resuscitation. VF OHCA incidence decreased from 21.1/100,000 in 1995-1997 to 17.4/100,000 in 2005-2008 (p<0.001). Non-VF OHCA increased from 12.2/100,000 to 19.4/100,000 (p<0.001). VF as presenting rhythm declined from 63% to 47%. In 2005-2008, 1972 ICD patients received 977 shocks. Of these shocks, 339 were caused by a life-threatening arrhythmia. We estimate that these 339 shocks have prevented 81 (min 39, max 152) cases of VF OHCA, corresponding with 33% (min 16%, max 63%) of the observed decline in VF OHCA incidence.

Conclusions - The incidence of VF-OHCA decreased over the last 10 years in North-Holland. ICD therapy explained a decrease of 1.2/100,000 inhabitants/year, corresponding with 33% of the observed decline in VF OHCA.

Key words: cardiopulmonary resuscitation; heart arrest; implantable cardioverter-defibrillator; incidence; ventricular fibrillation
**Introduction**

Multiple studies from Europe and the United States noted a gradual decrease in the incidence of ventricular fibrillation (VF) during resuscitation for out-of-hospital cardiac arrest (OHCA) over the last decades. These studies showed that the proportion of OHCA with VF as initial rhythm during a resuscitation attempt (VF OHCA) declined on average from 54% to 38% over a 15-year period.\(^1-^5\) There is no clear one-dimensional explanation for this widely observed decline in VF incidence. The introduction of the Implantable Cardioverter Defibrillator (ICD) has been linked to the decline in VF OHCA incidence.\(^1\)

The purpose of this investigation was to confirm whether the incidence of VF OHCA in the Netherlands has declined over the years, and to calculate to what extent this decline could be explained by ICD usage. We used a prospective database of all resuscitation efforts in the province North-Holland in The Netherlands. This ARREST (AmsteRdam REscucitation STudies) registry covers the period 1995-1997 and from 2005 onwards.

Importantly, while the first ICD implantation in The Netherlands was performed in 1984, ICD implantation remained rare until 1997.\(^6\) Only after large randomized controlled trials, first published in 1997, demonstrated the efficacy of ICD usage, ICD implantations became common.\(^7-^9\) This allowed us to study changes in VF-OHCA incidence between both periods, and to what extent these changes were associated with ICD usage.

**Methods**

We compared the incidence of VF OHCA in 2005-2008 with the VF OHCA incidence in 1995-1997 (*VF OHCA incidence*). Additionally, we calculated the number of prevented VF OHCA by ICD shocks in 2005-2008 (*ICD therapy*), and compared this with the observed decrease in VF OHCA incidence, assuming that ICD implantation was hardly performed before 1997 and that no
VF OHCA was avoided by ICD shocks in the period 1995-1997. The Medical Ethics Review Board of the Academic Medical Center, Amsterdam approved the study and gave a waiver for the requirement of (written) informed consent.

**VF OHCA incidence**

The ARREST research group maintains a prospective database of all resuscitation efforts in North-Holland, a province of The Netherlands, which includes Greater Amsterdam. This province has a population of approximately 2.4 million people and covers 2671 km², including both urban and rural communities. The organization of the emergency medical services (EMS) and data collection in the study region has been described previously. Only OHCA cases from presumed cardiac causes which were not witnessed by paramedics were included in this analysis. OHCA was defined as cardiac if the EMS rescuers or the physicians at the hospital could not identify an unequivocal non-cardiac condition for OHCA.

Data was collected according to the Utstein recommendations. Between July 4, 2005 and May 1, 2008, we prospectively collected data on all patients in whom EMS personnel attempted resuscitation during an OHCA. After each resuscitation attempt, ambulance personnel routinely sent the continuous ECG recording from their manual defibrillators to the study center by modem. These data were stored and analyzed with dedicated software (Code Stat Reviewer 7.0, Physio Control, Redmond, WA). Paramedics reported whether an automatic external defibrillator (AED) had been used prior to ambulance arrival. Study personnel visited the site of the AED shortly after the cardiac arrest and collected the ECG recording from the AED. The initial rhythm retrieved from the AED or manual defibrillator was categorized as VF (including pulseless ventricular tachycardia (VT)) or non-VF (asystole, bradycardia, supraventricular tachycardia (SVT), or normal rhythm).
The reference data set for VF OHCA incidence were the results from the ARREST study conducted in 1995-1997. This prospective cohort study was performed in Amsterdam and surroundings (Greater Amsterdam, approximately 1.3 million inhabitants, 1030 km²) between June 1, 1995 and August 1, 1997, employing the same method of data collection as in 2005-2008.

**ICD therapy**

All ICD implanting hospitals in North-Holland and adjacent regions participated in this study. Patients who received an ICD or visited the ICD clinic in one of the participating hospitals between July 4, 2005 and May 1, 2008 and lived in North-Holland were included in the analysis. Age, gender, ICD implantation dates and stored electrogram (EGM) data were obtained from the included patients. Only shocks from which the provoking rhythm was documented and EGMs were available were included in the analysis. ICD shocks that did not prevent OHCA were not included in the analysis.

The rhythm before and after the ICD shock was classified as VF, polymorphic ventricular tachycardia (PVT), monomorphic ventricular tachycardia (MVT), non-sustained ventricular tachycardia (NSVT), SVT, bradycardia, asystole, normal or unknown rhythm. In 20 ICD shocks (2.0% of all ICD shocks) we were no able to differentiate MVT from PVT because only a near field (tip-ring) ventricular electrogram was available. These VTs were classified as MVT, in order not to overestimate the potential prevention of VF OHCA.

Cycle length of the provoking rhythm and programmed cycle length of the lower limit of VF zone was documented. An experienced electrophysiologist evaluated all EGMs.

**Calculation of the number of prevented VF OHCA by ICD shocks**

We calculated the number of VF OHCA cases that were prevented by ICD shocks by
multiplying the number of life-threatening arrhythmias that were successfully terminated by ICD shocks by the probability that the life-threatening arrhythmia would have led to an EMS-call and a subsequent OHCA attempt. We defined a life-threatening arrhythmia as VF or PVT, regardless of cycle length, or MVT faster than the lower limit of the programmed VF zone.

We considered the probability that resuscitation for OHCA was attempted at all must be taken into account, because not all OHCA patients without ICDs undergo resuscitation. First, some of these patients succumb before an EMS-call is made. To estimate the probability of an EMS call following a collapse of a patient at risk of a lethal arrhythmia, we used results from Bardy et al.13 From this study, we estimated that 62% of all OHCA instances led to an EMS-call. Second, if the collapse had led to an EMS call, the patient could have died before EMS arrival, and EMS personnel would not have attempted OHCA. To estimate this probability, we determined the number of EMS dispatches for suspected OHCA in which no resuscitation was attempted from ARREST data collected in 2005-2008.

**Correction for multiple successful ICD shocks**

Some ICD patients experienced multiple successful ICD shocks during the study period. Addition of all these ICD shocks to calculate the number of OHCA episodes that were prevented by ICD therapy would lead to overestimation of this number, because most patients without ICDs, would not have survived the OHCA episode to have an opportunity to suffer a subsequent resuscitation for OHCA. To correct for this, we calculated a corrected total number of successful ICD shock instances per patient (NICDt). NICDt is a measure of the number of life-threatening arrhythmias that would have occurred without ICD usage, considering that only the first successful ICD shock per patient contributed fully to the calculated NICDt; the contribution of every next shock was corrected for the probability that the patient would survive the previous
OHCA episode. This could be expressed as:

\[ NICDt = \sum_{i=1}^{N} Z \]

NICDt = total number of successful ICD shock instances

N = total number of appropriate shocks on life-threatening arrhythmias per patient

Z = average survival rate from VF OHCA of patients without ICD in ARREST in 2005-2008

All calculated NICDts per patient were added to estimate the total number of life-threatening arrhythmias potentially leading to resuscitation for VF OHCA.

**Statistical analyses**

OHCA incidence and baseline demographic and resuscitation characteristics were calculated for Greater Amsterdam in 1995-1997, for Greater Amsterdam in 2005-2008 and for North-Holland in 2005-2008. No substantial differences existed between Greater Amsterdam and North-Holland without Greater Amsterdam in 2005-2008 (data shown in online Data Supplement). Therefore, in this analysis, we used the results of North-Holland including Greater Amsterdam for the 2005-2008 time period. Comparisons of baseline demographic and resuscitation characteristics between VF OHCA in 1995-1997 and in 2005-2008 were analyzed by Student t test, Chi-square test or Kolmogorov-Smirnoff test where appropriate. Continuous data were shown as mean±standard deviation. All time intervals were expressed as median (25th to 75th percentile).

All incidence rates were reported per 100,000 person-years. Incidences were modelled as intensities (\( \lambda \)) of a Poisson process. Changes with confidence intervals between 1995-1997 and 2005-2008 were tested assuming independent \( \lambda \) values. For 2005-2008, we added the calculated number of prevented VF OHCA by ICD shocks to the observed incidence of VF OHCA, and compared this with the observed VF OHCA incidence in 1995-1997.

We performed a sensitivity analysis for our calculated number of prevented VF OHCA to
account for patients with missing ICD read-out data and ICD shocks without an available EGM, as well as our assumption that all MVT faster than the lower limit of the VF zone would have led to a VF OHCA. All statistical tests were 2-tailed, and a p-value of <0.05 was considered to be statistically significant. Statistics were performed in SPSS 16.0 for Mac (Chicago, Illinois) and Excel 11.5 for Mac (Chicago, Illinois).

**Results**

**OHCA Incidence and resuscitation characteristics**

In Greater Amsterdam in 1995-1997, 581 persons experienced a VF OHCA in a period of 26 months, amounting to a yearly incidence of 21.1/100,000 (Table 1). In North-Holland in 2005-2008, 1173 persons experienced a VF OHCA in 34 months, amounting to a reduced yearly incidence of 17.4/100,000. The VF OHCA incidence decreased statistically significant by 3.6/100,000 (95% CI 1.6-5.6) over time (p<0.001). The yearly non-VF OHCA incidence increased from 12.2/100,000 in 1995-1997 to 19.4/100,000 in 2005-2008. The non-VF OHCA incidence increased statistically significant by 7.2/100,000 (95% CI 5.5-8.9) over time (p<0.001). Thus, the proportion of patients with OHCA with VF as presenting rhythm declined from 63 to 47% (p<0.001). In 2005-2008, 3696 dispatches for OHCA occurred. Resuscitation was not attempted in 33% of these dispatches, because the patient was considered dead upon arrival.

**Table 2** shows the baseline demographic and resuscitation characteristics of all OHCA cases of both periods. Median time of EMS call to initial rhythm assessment increased from 9.0 to 10.5 minutes. In 2005-2008 an AED was attached in 21% of all OHCA cases. The median time of EMS call to shock decreased from 11.0 to 10.7 minutes (Table 2).
Survival of all OHCA patients increased from 9% to 14% (p<0.001, not shown). Survival of patients with VF OHCA increased from 17 to 31% (p< 0.001, not shown).

**Prevented VF OHCA by ICD shocks**

In 2005 and 2008, 1972 patients living in North-Holland had or received an ICD. Of the 1972 patients, 475 (24%) received the ICD prior to the study period and 1497 (76%) patients received the ICD between July 4, 2005 and May 1, 2008. During the study period, the yearly ICD implantation rate increased from 11/100,000 in 2005 to 26/100,000 in 2008. The mean age of the ICD patients at entry in the cohort (either at July 4, 2005 or at implantation during the study period) was 62.2±12.6 years. Of the 1972 ICD patients, 1539 (78%) were male (not shown).

**Figure 1** shows the calculation of the estimated number of prevented resuscitation for VF OHCA by ICD shocks. Thirty-two patients were resuscitated despite carrying an ICD, therefore these patients the ICD did not prevent an OHCA. These patients were excluded from the calculation of prevented VF OHCA. Furthermore, no ICD read-outs were available for 121 patients. As we could not establish whether OHCA was prevented by ICD shocks in these patients, we also excluded them from our calculation. The analysis cohort thus consisted of 1819 analyzable ICD patients. The duration of the ICD read-out period for these patients varied between 1 and 1032 days, with a mean of 567±367 days (not shown). In total, 977 shocks were given to 303 patients. Of these shocks, 371 shocks were excluded from further analysis, because they were inappropriate, mainly due to SVT (272 shocks). We excluded another 132 ICD shocks, because they were given for MVT with a cycle length outside the VF zone (which was on average set at 290±22ms), and would not have led to a life-threatening arrhythmia either. We further ignored 135 ICD shocks, because EGMs were not available. As a result, we identified 339 ICD shocks given to 166 patients for a proven life-threatening arrhythmia. Of these 166
patients 41 received 2 shocks, 21 received 3 shocks, 6 received 4 shocks, and 8 patients received 5, 6, 7, 8, 9, 10, 12, and 23 shocks, respectively. Because we found in ARREST that only 31% of patients without an ICD would have survived an episode of a life-threatening arrhythmia, and using the calculation for multiple successful ICD shocks (NICDt), we estimate that in this population 194 instances of life-threatening arrhythmia in 166 patients were successfully aborted by ICD shocks. Under the assumption that a life-threatening arrhythmia would have led to an EMS-call in 62% and subsequently a resuscitation effort for VF OHCA in 67% of the cases, we estimate that appropriate ICD shocks have prevented 81 cases of presumed VF OHCA. This amounts to an incidence of 1.2/100,000 in North-Holland in 2005-2008 (Figure 2). As the VF OHCA incidence declined by 3.6/100,000 between 1995-1997 and 2005-2008, ICD usage thus accounted for 33% of the decline in VF OHCA.

Sensitivity Analysis

To account for the possible contribution of missing ICD data and the influence of our assumption that only MVT faster than the lower limit of the VF zone would have led to a VF OHCA, we performed a sensitivity analysis (Table 3). Assuming that 121 patients with missing read-out data 135 ICD shocks without an available EGM and 132 patients with MVT rate below the VF zone would have contributed to the analysis with a clinical course and shock distribution as in Figure 1, a maximum of 152 cases of prevented VF OHCA episodes could be calculated. This would account for 63% of the decline in VF OHCA incidence. To calculate the minimal number of prevented VF OHCA, we excluded, in addition to the patients and ICD shocks that we excluded in Figure 1, also the 189 shocks for MVT within the VF zone, assuming that such fast MVT would not have resulted in VF OHCA in the absence of an ICD. Using this calculation, only 39 cases of VF OHCA would have been prevented by ICD shocks. This corresponds to 16%
Discussion

This study shows that VF OHCA incidence decreased by 3.6 per 100,000 person-years during the 10-year period between 1995-1997 and 2005-2008 in the province North-Holland in The Netherlands. We estimated that in 2005-2008 ICD shocks prevented 81 cases of resuscitation for VF OHCA, i.e. 1.2 VF OHCA/100,000 person-years. Hence, approximately 33% of the decline in VF OHCA incidence could be explained with ICD shocks. The decline in VF OHCA is accompanied by a statistically significant increase in non-VF OHCA. As a consequence, there is a small increase in total OHCA incidence between 1995-1997 and 2005-2008. Both the lower numerator and higher denominator contribute to the observed decreased proportion of VF OHCA. The decline in VF OHCA incidence has consistently been observed in multiple other reports, albeit at different levels, but not the increase in overall OHCA incidence.1-4,14,15

In the only other study determining coexisting trends of ICD therapy and declining VF OHCA incidence, 3.5 per 100,000 potentially life-threatening arrhythmias were terminated by ICD shocks in Rochester, Minnesota, with increasing ICD implantation rates up to 2002.1 According to their calculation, ICD shocks had an impact of 10-33% of on the reduced incidence of VF OHCA. However, the authors did not account for the correction of multiple successful shocks, nor for the less than 100% likelihood a life-threatening arrhythmia leads to a resuscitation attempt.15 Furthermore, some potentially life-threatening arrhythmias that triggered an appropriate shock may only have resulted in a short syncope with spontaneous recovery if no ICD had been present. This may be the case in up to half of all appropriate shocks.16 At all, an appropriate ICD shock might not be a reliable surrogate for sudden cardiac death leading to a
resuscitation effort. For all these reasons, we believe correction factors must be applied to appropriate ICD-shocks to achieve the most reliable estimate of prevented resuscitation for VF OHCA.

**Other explanations for the decline in VF OHCA**

The declined incidence of VF as first recorded rhythm may be explained by an intrinsically reduced incidence of VF as the cause of OHCA, either from ICD use or other changing biological mechanisms in the population at risk for VF. However, also an increased delay to the documentation of this first recorded rhythm or an increased speed of deterioration from VF to another rhythm, specifically asystole, might explain a declined incidence of VF. Between 1995-1997 and 2005-2008, the total incidence and proportion of collapse in public locations and of witnessed collapse decreased - two factors that may be related - resulting in a delay to call the dispatch center and in more deterioration of VF in asystole.\(^\text{17}\) This is in line with recent observations of a lower proportion of VF OHCA at home, possibly due to differences in patient characteristics.\(^\text{18}\) However, overall bystander CPR in 2005-2008 had increased, which might have prevented some cases of VF from deteriorating to asystole.\(^\text{17}\) We also noted an increased median time from call to first rhythm analysis for all patients, which may have caused more VF to deteriorate to asystole. However, the median time to first shock decreased. This can be attributed to the group of patients who received an early shock from an AED.

Beta-blocker use has also been associated with the reduced incidence of VF. In an animal model, duration of VF was significantly reduced with beta-blocker use.\(^\text{19}\) In a retrospective cohort study, it was shown that OHCA victims taking beta-blockers were 5 times more likely to show non-VF than VF as first documented rhythm.\(^\text{20}\) If beta-blocker use would hasten VF deterioration without changing the initial incidence of VF, one would then expect to observe a
still high VF OHCA incidence if time to initial rhythm recording is short, such as when an AED is used. Indeed, when on site or dispatched AED use was compared with attachment of manual defibrillators by EMS personnel, a considerable higher percentage of shockable rhythms was noted (59% or 76% vs. 24% or 47%, respectively).\textsuperscript{21,22} In situations in which the response time is extremely short, such as in airports or casinos equipped with AEDs, VF is also the presenting rhythm in a high proportion of the cases.\textsuperscript{23,24} These observations suggest that VF incidence might not have declined per se, but that it possibly rather reflects faster deteriorating VF.

\textbf{Increase in non-VF OHCA}

The overall increase in OHCA, larger than the decline in VF OHCA indicates that more patients suffered an OHCA. The cause of this increase is not clear. We report on 100% of all known OHCA in both time periods with an unchanged system of case collection, which makes it less likely that we missed such a large number of non-VF OHCA cases in the period 1995-1997.

Trends for cardiovascular and acute MI hospital admissions and mortality have shown a decline between the two study periods. Mortality from competing illnesses like malignancies have shown a (less pronounced) decline in the same time period and therefore cannot have caused an increased number of non-VF OHCA.

\textbf{Limitations}

The population of the study region of the period 2005-2008 was 43% larger than, but included the whole study region of 1995-1997 (Greater Amsterdam). Data shown in \textbf{Supplemental Table 1} indicate that there was no statistically significant difference in VF and non-VF OHCA incidence in the area that contributed to both study periods compared to the area added in 2005-2008. Some covariates related to resuscitation were statistically significant different (\textbf{Supplemental Table 2}), probably related to the more rural characteristics of the added region.
The prevented VF OHCA incidence in the Greater Amsterdam region only (1.21/100,000) was identical to the prevented incidence in the whole study region in 2005-2008 (1.20/100,000). The joint analysis therefore is not biased by the extension of the region in 2005-2008.

We did not consider anti-tachycardia pacing therapy to have prevented an OHCA in our analysis, unless the anti-tachycardia pacing was unsuccessful and a (appropriate) shock followed. We also assumed that no VF OHCA was prevented by ICD shocks in 1995-1997. In that period only a very limited number of patients had an ICD implanted, and therefore ICD therapy in this period was almost negligible. Furthermore, ICD-patient data from the time period 1995-1997 could not be retrieved.

In our model, we made a number of assumptions to estimate the contribution of multiple successful shock episodes in the study period in the same patient, the probability of an EMS-call after collapse and the probability of a resuscitation effort after EMS arrival. The sensitivity analysis indicates the limits of the potential impact of ICD use; our estimate of attributed reduction ranges from 16% to 63%. We did not account for the possibility that prevented VF could have deteriorated to asystole before the rhythm could be detected; i.e. we assumed in our calculations that all life-threatening arrhythmias would be attended soon enough to identify VF as initial rhythm. It is possible that, despite our correction factors, we still overestimated the probability that a sudden cardiac death would have led to a resuscitation attempt.

Conclusions

The incidence of VF OHCA decreased in the province of North-Holland in The Netherlands over the last decade. ICD therapy explained 1.2/100,000 inhabitants/year of the decrease, corresponding with approximately 33% of this decline, with a range between 16 and 63%. There must be other factors that at least contribute equally to the declined incidence of VF.
Acknowledgements: We are indebted to all ICD technicians and cardiologists in the participating hospitals; Academisch Medisch Centrum Amsterdam, Vrije Universiteit Medisch Centrum Amsterdam, Onze Lieve Vrouwe Gasthuis Amsterdam (G.S. de Ruiter, MD, PhD), Leids Universitair Medisch Centrum, Medisch Centrum Alkmaar (J.H. Ruiter, MD, PhD), Kennemer Gasthuis Haarlem (R. Tukkie, MD, PhD), St. Lucas Andreas Amsterdam (W.G. de Voogt, MD, PhD), Spaarne Ziekenhuis Hoofddorp (J.P. Ezechiels, MD, PhD), Universitair Medisch Centrum Utrecht (M.M. Meine, MD, PhD) and St. Antonius Ziekenhuis Nieuwegein (L.V.A. Boersma, MD, PhD), for their contribution to the data collection. We thank Claire Nolte who helped retrieving the data of the ICD patients.

Funding Sources: The ARREST database is maintained by an unconditional grant of Physio Control Inc, Redmond WA, USA, and a grant from the Netherlands Heart Foundation, grant number 2006B179. Joris de Groot is supported by a personal grant from the Netherlands Heart Foundation, 2009T021. Hanno Tan was supported by the Netherlands Organization for Scientific Research (NWO, grant ZonMW Vici 918.86.616) and the Dutch Medicines Evaluation Board (MEB/CBG)

Conflict of Interest Disclosures: None.

References:


15. Raitt MH. Have increasing rates of defibrillator implantation reduced the incidence of out-of-


Table 1. Population and OHCA incidence in Greater Amsterdam and North-Holland.

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<thead>
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<tbody>
<tr>
<td>Area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater Amsterdam</td>
<td>1,273,382</td>
<td>2,373,302</td>
<td></td>
</tr>
<tr>
<td>North-Holland</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Inhabitants research area (n)</td>
<td>1,273,382</td>
<td>2,373,302</td>
<td></td>
</tr>
<tr>
<td>Duration of data collection (months)</td>
<td>26</td>
<td>34</td>
<td>p</td>
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**OHCA incidence***

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<tr>
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<tbody>
<tr>
<td>EMS dispatches</td>
<td>1685 (61.1)</td>
<td>3696 (55.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OHCA</td>
<td>918 (33.3)</td>
<td>2478 (36.9)</td>
<td>0.007</td>
</tr>
<tr>
<td>VF OHCA</td>
<td>581 (21.1)</td>
<td>1173 (17.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>non-VF OHCA</td>
<td>337 (12.2)</td>
<td>1305 (19.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Variables are denoted as cases (incidence per 100,000 person-years). OHCA denotes Out-of-Hospital Cardiac Arrest; EMS denotes Emergency Medical Service; VF denotes Ventricular Fibrillation.

Table 2. Demographic and resuscitation characteristics of all OHCA cases in Greater Amsterdam and North-Holland.

<table>
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<tr>
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<tbody>
<tr>
<td>Age, y *</td>
<td>64.1±14.4</td>
<td>64.8±16.2</td>
<td>0.276</td>
</tr>
<tr>
<td>Male gender †</td>
<td>712 (78%)</td>
<td>1825 (74%)</td>
<td>0.037</td>
</tr>
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</table>

**Demographic characteristics**

**Resuscitation characteristics**

<table>
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<tr>
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<tbody>
<tr>
<td>Witnessed collapse †</td>
<td>779 (85%)</td>
<td>1888 (76%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bystander CPR †</td>
<td>497 (54%)</td>
<td>1486 (60%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Collapse at home †</td>
<td>564 (61%)</td>
<td>1715 (69%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time call to initial rhythm †</td>
<td>9.0 (8.0-12.0)</td>
<td>10.5 (8.1-13.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time call to shock †</td>
<td>11.0 (9.0-14.0)</td>
<td>10.7 (8.2-13.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AED connected</td>
<td>-</td>
<td>527 (21%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Plus minus values are means±SD, group differences tested with Student t-test
† Variables are denoted as cases (percentage), group differences were tested with Chi-square test
‡Time intervals are presented in median in minutes (25th to 75th percentile). Group differences tested with Kolmogorov-Smirnoff test.
CPR denotes Cardio-Pulmonary Resuscitation; AED denotes Automated External Defibrillator
Table 3. Part of decline of VF OHCA explained by ICD shocks: sensitivity analysis

<table>
<thead>
<tr>
<th>Estimation</th>
<th>Calculated prevented VF OHCA (n)</th>
<th>Calculated incidence prevented VF OHCA</th>
<th>Percentage of VF OHCA decline explained by ICD shocks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimates as Figure 1*</td>
<td>81</td>
<td>1.20</td>
<td>33%</td>
</tr>
<tr>
<td>Maximal †</td>
<td>152</td>
<td>2.26</td>
<td>63%</td>
</tr>
<tr>
<td>Minimal ‡</td>
<td>39</td>
<td>0.60</td>
<td>16%</td>
</tr>
</tbody>
</table>

* Assumptions as in Figure 1: excludes patients without follow-up, excludes shocks without EGM, only MVT < VF zone
† Includes patients without follow-up and includes all shocks with missing EGM. We assume that the clinical course of 121 patients without an ICD read-out would have been the same as patients with an ICD read-out. We further assume that the characteristics of the 135 shocks with missing EGM would have been the same as the shocks were EGMs were available (Figure 1).
‡ Assumptions as in Figure 1, but also excludes all MVT, regardless of cycle length.
VF denotes Ventricular Fibrillation. OHCA denotes Out-of-Hospital Cardiac Arrest; ICD denotes Implantable Cardioverter Defibrillator

Figure Legends:

Figure 1. Data flow and calculation of estimated number of prevented VF OHCA by successful ICD shocks. * Some patients experienced successful ICD shocks due to a life-threatening arrhythmia more than once. If the patient had not received an ICD, only a small percentage would have survived the initial episode of a life-threatening arrhythmia. Only the first successful ICD shock per patient contributed fully to the total number of successful shock instances (NICDt). The contribution of every next shock was corrected for a survival probability of 31% for VF OHCA patients experiencing a resuscitation effort. Hence, a second successful ICD shock per patient contributed for 0.31 instances of NICDt, a third successful ICD shock contributed for 0.096 instances to the total number of NICDt, etc. ICD denotes Implantable Cardioverter Defibrillator; OHCA denotes Out-of-Hospital Cardiac Arrest; MVT denotes Monomorphic Ventricular Tachycardia; EGM denotes electrogram; VF denotes Ventricular Fibrillation; PVT
denotes Polymorphic Ventricular Tachycardia; NICDt denotes total number of successful shock instances; EMS denotes Emergency Medical Service.

**Figure 2.** Incidence of VF and non-VF cardiac arrest in 1995-1997 and 2005-2008 and the estimated avoided episodes of OHCA from ICD use. In 2005-2008 the incidence of VF OHCA has declined, while the incidence of non-VF OHCA increased. ICD shocks in 2005-2008 avoided 1.2/100,000 resuscitations for VF OHCA, which explains 33% of the decline in VF OHCA. VF denotes Ventricular Fibrillation; ICD denotes Implantable Cardioverter Defibrillator.
1972 patients with ICD in 2005-2008

1940 patients with ICD without OHCA

1819 patients without OHCA and with ICD read-out

977 shocks in 303 patients

339 shocks on life-threatening arrhythmia in 166 patients
- 98 VF
- 52 PVT
- 189 MVT <VF zone

32 OHCA's not prevented

121 patients without ICD read-out

371 inappropriate shocks
132 shocks on MVT >VF zone
135 shocks with missing EGM

Contribution of multiple shocks per patient to NICDT

194 instances of aborted sudden cardiac death in 166 patients

Probability NICDT leads to EMS call = 62%

Probability EMS call leads to resuscitation = 67%

81 cases of prevented VF OHCA resuscitation

Incidenc e1.20 VF OHCA/100,000
Implantable Cardioverter Defibrillators Have Reduced the Incidence of Resuscitation for Out of Hospital Cardiac Arrest Caused by Lethal Arrhythmias

_Circulation_. published online August 6, 2012;
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/early/2012/07/17/CIRCULATIONAHA.111.089425

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Supplemental Material
**Supplemental Tables**

Supplemental Table 1. Population and OHCA incidence in Greater Amsterdam and North-Holland without Greater Amsterdam in 2005-2008.

<table>
<thead>
<tr>
<th>Area</th>
<th>Greater Amsterdam (GA)</th>
<th>North-Holland without GA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhabitants research area (n)</td>
<td>1,365,897</td>
<td>1,007,405</td>
</tr>
<tr>
<td>Duration of data collection (months)</td>
<td>34</td>
<td>34</td>
</tr>
</tbody>
</table>

**OHCA incidence***

<table>
<thead>
<tr>
<th></th>
<th>Greater Amsterdam (GA)</th>
<th>North-Holland without GA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMS dispatches</td>
<td>2072 (53.6)</td>
<td>1624 (57.0)</td>
<td>0.15</td>
</tr>
<tr>
<td>OHCA</td>
<td>1406 (36.4)</td>
<td>1072 (37.6)</td>
<td>0.41</td>
</tr>
<tr>
<td>VF OHCA</td>
<td>657 (17.0)</td>
<td>516 (18.1)</td>
<td>0.29</td>
</tr>
<tr>
<td>non-VF OHCA</td>
<td>749 (19.4)</td>
<td>556 (19.5)</td>
<td>0.91</td>
</tr>
</tbody>
</table>

* Variables are denoted as cases (incidence per 100,000 person-years). OHCA denotes Out-of-Hospital Cardiac Arrest; EMS denotes Emergency Medical Service; VF denotes Ventricular Fibrillation.
Supplemental table 2. Demographic and resuscitation characteristics of all OHCA cases in Greater Amsterdam and North-Holland in 2005-2008 excluding greater Amsterdam.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Greater Amsterdam (GA)</th>
<th>North-Holland without GA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 1406</td>
<td>N = 1072</td>
<td></td>
</tr>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y *</td>
<td>64.0±16.9</td>
<td>65.7±15.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Male gender †</td>
<td>1030 (73%)</td>
<td>795 (74%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Resuscitation characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Witnessed collapse †</td>
<td>1075 (76%)</td>
<td>813 (76%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Bystander CPR †</td>
<td>811 (58%)</td>
<td>675 (63%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Collapse at home †</td>
<td>1001 (71%)</td>
<td>714 (67%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Time call to initial rhythm ‡</td>
<td>10.3 (7.9-13.12)</td>
<td>10.5 (8.4-13.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Time call to shock (min) ‡</td>
<td>11.0 (8.4-13.5)</td>
<td>10.2 (8.1-13.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>AED connected</td>
<td>300 (21%)</td>
<td>227 (21%)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* Plus minus values are means±SD, group differences tested with Student t-test

† Variables are denoted as cases (percentage), group differences were tested with Chi-square test
Time intervals are presented in median in minutes (25th to 75th percentile). Group differences tested with Kolmogorov-Smirnoff test.

CPR denotes Cardio-Pulmonary Resuscitation; AED denotes Automated External Defibrillation