Original Investigation

Association of National Initiatives to Improve Cardiac Arrest Management With Rates of Bystander Intervention and Patient Survival After Out-of-Hospital Cardiac Arrest

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IMPORTANCE Out-of-hospital cardiac arrest is a major health problem associated with poor outcomes. Early recognition and intervention are critical for patient survival. Bystander cardiopulmonary resuscitation (CPR) is one factor among many associated with improved survival.

OBJECTIVE To examine temporal changes in bystander resuscitation attempts and survival during a 10-year period in which several national initiatives were taken to increase rates of bystander resuscitation and improve advanced care.

DESIGN, SETTING, AND PARTICIPANTS Patients with out-of-hospital cardiac arrest for which resuscitation was attempted were identified between 2001 and 2010 in the nationwide Danish Cardiac Arrest Registry. Of 29 111 patients with cardiac arrest, we excluded those with presumed noncardiac cause of arrest (n = 7390) and those with cardiac arrests witnessed by emergency medical services personnel (n = 2253), leaving a study population of 19 468 patients.

MAIN OUTCOMES AND MEASURES Temporal trends in bystander CPR, bystander defibrillation, 30-day survival, and 1-year survival.

RESULTS The median age of patients was 72 years; 67.4% were men. Bystander CPR increased significantly during the study period, from 21.1% (95% CI, 18.8%-23.4%) in 2001 to 44.9% (95% CI, 42.6%-47.1%) in 2010 ($P < .001$), whereas use of defibrillation by bystanders remained low (1.1% [95% CI, 0.6%-1.9%] in 2001 to 2.2% [95% CI, 1.5%-2.9%] in 2010; $P = .003$). More patients achieved survival on hospital arrival (7.9% [95% CI, 6.4%-9.5%] in 2001 to 21.8% [95% CI, 19.8%-23.8%] in 2010; $P < .001$). Also, 30-day survival improved (3.5% [95% CI, 2.5%-4.5%] in 2001 to 10.8% [95% CI, 9.4%-12.2%] in 2010; $P < .001$), as did 1-year survival (2.9% [95% CI, 2.0%-3.9%] in 2001 to 10.2% [95% CI, 8.9%-11.6%] in 2010; $P < .001$). Despite a decrease in the incidence of out-of-hospital cardiac arrests during the study period (40.4 to 34.4 per 100 000 persons in 2001 and 2010, respectively; $P = .002$), the number of survivors per 100 000 persons increased significantly ($P < .001$). For the entire study period, bystander CPR was positively associated with 30-day survival, regardless of witnessed status (30-day survival for nonwitnessed cardiac arrest, 4.3% [95% CI, 3.4%-5.2%] with bystander CPR and 1.0% [95% CI, 0.8%-1.3%] without; odds ratio, 4.38 [95% CI, 3.17-6.06]). For witnessed arrest the corresponding values were 19.4% (95% CI, 18.1%-20.7%) vs 6.1% (95% CI, 5.4%-6.7%); odds ratio, 3.74 (95% CI, 3.26-4.28).

CONCLUSIONS AND RELEVANCE In Denmark between 2001 and 2010, an increase in survival following out-of-hospital cardiac arrest was significantly associated with a concomitant increase in bystander CPR. Because of the co-occurrence of other related initiatives, a causal relationship remains uncertain.

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Out-of-hospital cardiac arrest affects approximately 300 000 individuals in North America annually, with an incidence of treated out-of-hospital cardiac arrest of approximately 56 per 100 000 person-years.[1,2] In Denmark, the corresponding incidence has previously been calculated to be 62 per 100 000 person-years, with approximately 3500 treated annually.[3] Despite efforts to improve prognosis, survival remains low, with aggregated survival-to-discharge rates less than 8%.[1,4,5] In many cases, time from recognition of cardiac arrest to the arrival of emergency medical services (EMS) is long,[5] leaving bystanders in a critical position to potentially influence patient prognosis through intervention before EMS arrival.[5-7] However, only a minority of cardiac arrests receive bystander cardiopulmonary resuscitation (CPR).[1,5,8]

A low frequency of bystander CPR (<20%) and low 30-day survival (<6%) were identified nearly 10 years ago in Denmark,[3] which led to several national initiatives to strengthen bystander resuscitation attempts and advanced care. These strategies included (1) implementation of mandatory resuscitation training in elementary schools (since January 2005), as well as when acquiring a driver's license (since October 2006), combined with an increase in voluntary first aid training[9]; (2) the free distribution of approximately 150 000 CPR self-instruction training kits between 2005 and 2010[10]; (3) the nationwide improvement of telephone guidance from emergency dispatch centers to bystanders witnessing a cardiac arrest, including the addition of health care professionals at dispatch centers, starting from 2009; (4) a large increase in the number of automated external defibrillators located outside hospitals (approximately 15 000 were in place by 2011)[11]; (5) efforts to improve advanced care with updates of clinical guidelines,[7,12] including introduction of therapeutic hypothermia starting from 2004, and increasing focus on early revascularization; and (6) overall strengthening of the EMS system with training of the ambulance personnel, including implementation of paramedics, mobile emergency care units staffed with specialized anesthesiologists dispatched as rendezvous with basic life support ambulances, or both. Despite these nationwide efforts, it is unknown whether there have been changes in resuscitation attempts by bystanders and improvements in survival. To answer this question we examined temporal trends in prehospital factors directly related to cardiac arrest as well as trends in survival during the past 10 years.

Methods

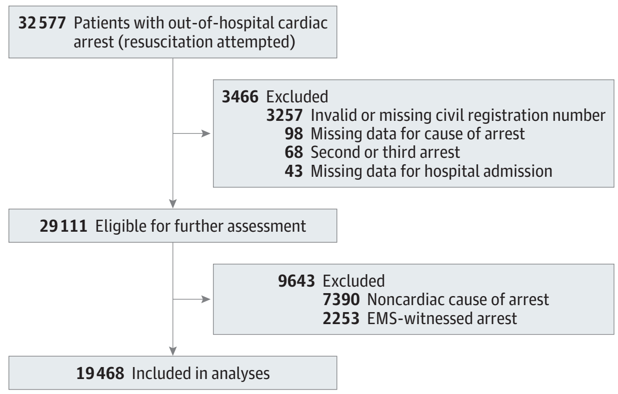
Setting and Population

This nationwide study was conducted from June 1, 2001, to December 31, 2010, in Denmark, which has approximately 5.6 million inhabitants.[13] The study was approved by the Danish Data Protection Agency (2007-58-0015, internal reference GEH-2010-001). In Denmark, ethical approval is not required for retrospective register-based studies.

Definitions and Recording of Out-of-Hospital Cardiac Arrest

An out-of-hospital cardiac arrest was included when a clinical condition of cardiac arrest resulted in resuscitation efforts either by bystanders (with activation of the EMS system) or by EMS personnel. The capture of cardiac arrest cases was nearly complete because the EMS system is activated for all emergencies concerning cardiac arrest, and the definition excludes cases with obvious late signs of death (eg, rigor mortis) for which resuscitative efforts are not initiated. Importantly, EMS personnel are required to complete a short case report form for the Danish Cardiac Arrest Register for every out-of-hospital cardiac arrest. For this study we included date; time; location of cardiac arrest (private home vs outside private home); whether the actual collapse was a nonwitnessed, bystander-witnessed, or EMS-witnessed arrest; whether the bystander performed CPR, defibrillated the patient, or both; first recorded heart rhythm (shockable rhythm [ventricular fibrillation or tachycardia] or nonshockable rhythm [asystole or pulseless electrical activity]); time interval, an estimate from recognition of cardiac arrest (based on the time of receipt of EMS call, as well as on a subsequent interview of the caller conducted by EMS at the scene) to rhythm analysis by EMS; and survival on arrival at the hospital. A bystander was defined as an individual who witnessed the collapse or who found the person unresponsive and activated the EMS system.

Figure 1. Patient Selection, 2001-2010



EMS indicates emergency medical services.

Diagnosis codes were used to define presumed cause of cardiac arrest. Death certificates and discharge diagnoses with cardiac disease, unknown disease, or unexpected collapse were defined as cardiac cause of arrest. Death certificates and discharge diagnoses with other medical disorders (without diagnosis mentioned above) were defined as noncardiac causes. Trauma, drug overdose, attempted suicide, and violent attack were considered noncardiac causes, regardless of other diagnoses. We used the Danish National Population Registry to obtain age, sex, and survival status. Admission dates, discharge dates, and discharge diagnoses were gathered from the Danish National Patient Registry. Causes of deaths were obtained from the National Causes of Deaths Registry. Discharge diagnoses and causes of death were coded according to the *International Statistical Classification of Diseases, Tenth Revision*. Patients with noncardiac causes of arrest and EMS-witnessed arrests were excluded from further analysis (**Figure 1**).

Table 1. Changes in Characteristics for Patients During the Study Period

	Year											No. (%)	
Characteristic	2001[a]	2002	2003	2004	2005	2006	2007	2008	2009	2010	P Value[b]	2001-2010	Missing Data
OHCA, No. (%)	1262 (6.5)	2282 (11.7)	2278 (11.7)	2100 (10.8)	2095 (10.8)	1890 (9.7)	1819 (9.3)	1849 (9.5)	1987 (10.2)	1906 (9.8)		19 468 (100)	
Age, median (IQR), y	71 (62-80)	71 (61-80)	71 (61-80)	72 (61-81)	72 (62-80)	72 (61-80)	72 (61-81)	71 (60-80)	72 (62-81)	73 (63-81)	<.001	72 (61-80)	0[c]
Men	71 (61-78)	70 (59-78)	70 (59-79)	70 (60-79)	70 (61-79)	71 (60-78)	70 (60-79)	69 (59-79)	70 (61-79)	70 (61-79)	.60	70 (60-79)	0[c]
Women	73 (63-82)	75 (65-82)	73 (64-83)	75 (65-83)	75 (64-84)	75 (65-83)	77 (66-84)	75 (64-83)	76 (65-85)	77 (66-85)	<.001	75 (65-83)	0[c]
Men, No. (%)	884 (70.1)	1509 (66.1)	1531 (67.2)	1386 (66.0)	1432 (68.4)	1297 (68.6)	1207 (66.4)	1252 (67.7)	1355 (68.2)	1258 (66.0)	.73	13 111 (67.4)	0[c]
Cardiac arrest in private home, No. (%)	601 (69.6)	1243 (72.2)	1309 (72.4)	1279 (73.7)	1331 (74.1)	1080 (77.2)	1146 (75.8)	1260 (74.6)	1447 (75.7)	1387 (75.0)	<.001	12 083 (74.2)	3182 (16.3)
Bystander-witnessed arrest, No. (%)	599 (51.6)	992 (48.8)	1113 (53.2)	971 (50.2)	996 (50.4)	898 (52.7)	844 (51.2)	972 (53.3)	1069 (54.2)	1020 (53.9)	.001	9474 (52.0)	1231 (6.3)
Bystander CPR, No. (%)	247 (21.1)	408 (20.0)	496 (23.6)	492 (25.4)	539 (27.2)	514 (30.2)	563 (34.1)	714 (39.3)	799 (40.5)	849 (44.9)	<.001	5621 (30.8)	1193 (6.1)
AED use by bystander, No. (%)	13 (1.1)	23 (1.1)	21 (1.0)	18 (0.9)	33 (1.7)	22 (1.3)	29 (1.8)	22 (1.3)	24 (1.4)	36 (2.2)	.003	241 (1.4)	1829 (9.4)
Time interval, median (IQR), min[d]	11 (6-19)	11 (6-18)	10 (5-17)	10 (6-17)	11 (6-20)	11 (6-19)	11 (6-19)	11 (7-18)	12 (7-19)	13 (8-20)	<.001	11 (6-18)	3394 (17.4)
Shockable heart rhythm, No. (%)	351 (32.2)	498 (25.6)	484 (23.5)	457 (22.6)	542 (26.5)	559 (30.8)	488 (29.4)	513 (29.9)	570 (30.4)	519 (28.7)	<.001	4981 (27.6)	1429 (7.3)
Survival, No. (%)													
On arrival at hospital	91 (7.9)	140 (7.0)	202 (9.8)	193 (10.2)	203 (10.4)	211 (12.5)	217 (13.8)	310 (18.8)	362 (20.7)	354 (21.8)	<.001	2283 (13.2)	2145 (11.0)
30-d	44 (3.5)	86 (3.8)	102 (4.5)	102 (4.9)	104 (5.0)	143 (7.6)	136 (7.5)	189 (10.2)	203 (10.2)	206 (10.8)	<.001	1315 (6.8)	0[c]
1-y	37 (2.9)	75 (3.3)	90 (4.0)	87 (4.1)	100 (4.8)	133 (7.0)	122 (6.7)	173 (9.4)	184 (9.3)	195 (10.2)	<.001	1196 (6.1)	0[c]

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; IQR, interquartile range; OHCA, out-of-hospital cardiac arrest.

[a] 2001 consists of 7 months from June to December.

[b] $P < .05$ considered statistically significant.

[c] Patients with invalid or missing civil registration number, used to link information on patient's age, sex, and survival status, were excluded from the analysis.

[d] Estimated time interval from recognition of OHCA to rhythm analysis by emergency medical service.

The main outcome parameters were resuscitative efforts from bystanders and patient survival.

Statistics

For temporal trends, we compared binary variables and continuous variables (calendar year) using Wilcoxon rank-sum tests. Spearman rank correlation coefficients were used when comparing continuous variables. Poisson regression analyses were used to analyze temporal trends based on changes in numbers of survivors per 100 000 persons. Furthermore, joinpoint regression models were used to test if any joinpoints were statistically significant with a change in slope for temporal trends in bystander CPR and survival. $P < .05$ (2-sided) was considered statistically significant.

Odds ratios (ORs) with 95% CIs were calculated by logistic regression analyses to examine the association between prehospital factors and 30-day survival for the entire study period. Estimates are presented as unadjusted and adjusted for age and sex. There was no indication of colinearity, and all relevant interactions were taken into account. When calculating fractions, medians, and ORs, observations with missing value for the covariate involved in calculation were excluded.

To test whether missing data could introduce bias into the study we applied the MICE (multivariate imputation by chained equations) method. Overall, 10 imputed data sets were constructed using information from all covariates in **Table 1**. We then compared estimates from the observed data set with estimates from the imputed data sets.

Data management and analyses were performed using SAS version 9.2 (SAS Institute Inc), R version 2.15.2 (R Development Core Team), and Joinpoint Regression Program version 4.0.1 (National Cancer Institute, National Institutes of Health).

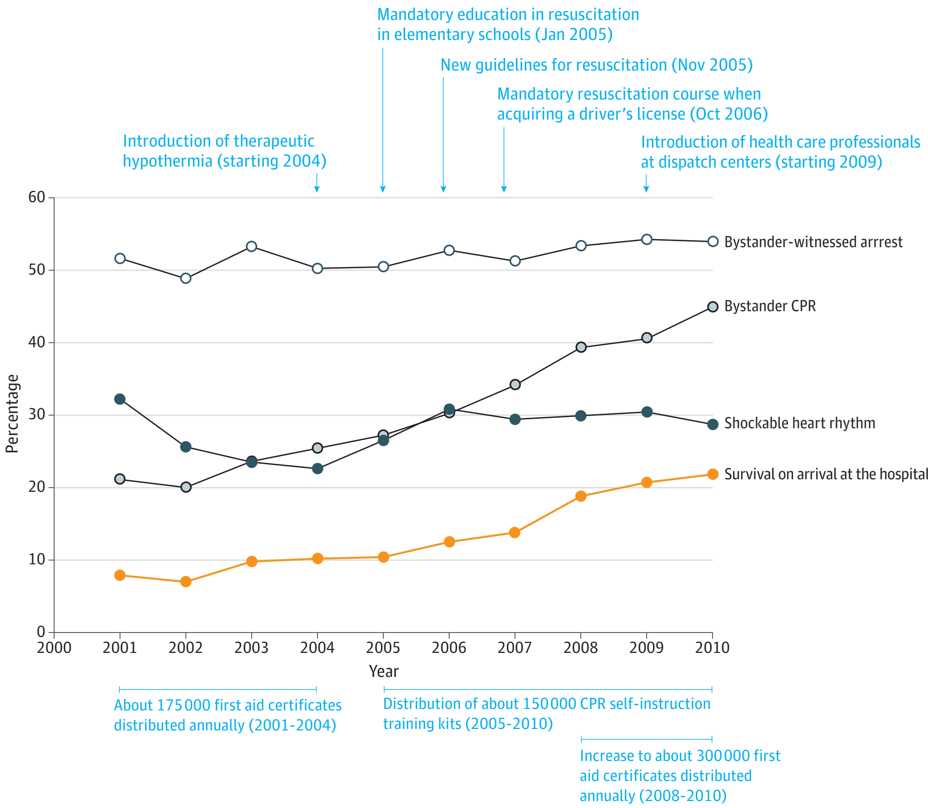
Results

A total of 19 468 patients with out-of-hospital cardiac arrests were included in the final study population (Figure 1). Patient-related and cardiac arrest–related characteristics are reported in Table 1.

Witnessed Status and Bystander Resuscitation Attempt

Altogether, 52.0% (95% CI, 51.2%-52.7%) of the patients had a bystander-witnessed arrest, with a small increase over

Figure 2. Bystander-Witnessed Arrest, Bystander Cardiopulmonary Resuscitation (CPR), Shockable Heart Rhythm as First Recorded Rhythm, and Survival on Arrival at the Hospital, Denmark, 2001-2010



Throughout the study period, there was a large increase in the number of automated external defibrillators located outside hospitals (approximately 15 000 in 2011) and implementation of paramedics and mobile emergency care units staffed with anesthesiologists. $P < .001$ for all changes over time, except for bystander-witnessed arrest ($P = .001$). $P < .05$ (2-sided) considered statistically significant.

time ($P = .001$) (**Figure 2**). Throughout the study period, there was a large increase in the proportion of patients receiving bystander CPR (21.1% [95% CI, 18.8%-23.4%] in 2001 to 44.9% [95% CI, 42.6%-47.1%] in 2010; $P < .001$). The increase was significant, irrespective of witnessed status and location of arrest (eTable 1 in Supplement). Only a small proportion were defibrillated with an automatic defibrillator by a bystander (1.1% [95% CI, 0.6%-1.9%] in 2001 to 2.2% [95% CI, 1.5%-2.9%] in 2010; $P = .003$).

First Recorded Heart Rhythm and Time Interval

The proportion of patients with a shockable rhythm was 27.6% (95% CI, 27.0%-28.3%) for the entire study period, with some variation over time (Figure 2). The median time interval from recognition of cardiac arrest to rhythm analysis by EMS was 11 minutes (interquartile range, 6-18), with a small but significant ($P < .001$) increase from 2001 (11 minutes) to 2010 (13 minutes).

Survival on Arrival at the Hospital, 30-Day Survival, and 1-Year Survival

There was a significant increase in the proportion of patients achieving survival on arrival at the hospital, from 7.9% (95% CI, 6.4%-9.5%) in 2001 to 21.8% (95% CI, 19.8%-23.8%) in 2010 ($P < .001$) (Figure 2). Also, 30-day survival increased from 3.5% (95% CI, 2.5%-4.5%) in 2001 to 10.8% (95% CI, 9.4%-12.2%) in 2010 ($P < .001$) (**Figure 3**). Thirty-day survival increased from 10.5% (95% CI, 7.3%-13.8%) in 2001 to 32.0% (95% CI, 28.0%-36.0%) in 2010 ($P < .001$) among patients with a shockable rhythm and from 0.5% (95% CI, 0.01%-1.1%) in 2001 to 2.4% (95% CI, 1.6%-3.2%) in 2010 ($P < .001$) among those with a nonshockable rhythm. The improvements in survival were still significant, and only slightly reduced, when 1-year survival was assessed (Figure 3).

Changes in Absolute Incidence of Out-of-Hospital Cardiac Arrests and Numbers of Survivors

For patients included in the final study population the average incidence was 37.5 (95% CI, 35.9-39.1) out-of-hospital cardiac arrests per 100 000 persons per year. During the study period, there was some annual variation in the number of cardiac arrests and overall a decrease was observed, from 40.4 (95% CI, 38.2-42.6) per 100 000 persons in 2001 to 34.4 (95% CI, 32.8-35.9) per 100 000 persons in 2010 ($P = .002$). Despite this decrease, there was a significant increase in number of patients achieving survival on arrival at the hospital, from 2.9 (95% CI, 2.3-3.5) per 100 000 persons in 2001 to 6.4 (95% CI, 5.7-7.1) per 100 000 persons in 2010 ($P < .001$). The number of 30-day survivors also increased, from 1.4 (95% CI, 1.0-1.8) per 100 000 persons in 2001 to 3.7 (95% CI, 3.2-4.2) per 100 000 persons in 2010

(*P* < .001), as did the number of 1-year survivors (1.2 [95% CI, 0.8-1.6] per 100 000 persons in 2001 to 3.5 [95% CI, 3.0-4.0] per 100 000 persons in 2010; *P* < .001).

Changes in Slope for Bystander CPR and Survival Following National Initiatives

Joinpoints were identified as statistically significant with a change in slope for temporal trends in bystander CPR and in survival on arrival at the hospital. In both cases, the slope increased in the second half of the study period along with the national initiatives (eFigures 1 and 2 in Supplement). A joinpoint was not identified as statistically significant for 30-day survival (*P* = .09) (eFigure 3 in Supplement).

Changes In 30-Day Survival in Relation to Resuscitative Efforts From Bystanders

Patients both with and without bystander CPR had a significant increase in 30-day survival over time (eFigure 4 in Supplement). Throughout the study period the increase among 30-day survivors was achieved mainly among patients who had received bystander CPR (eFigure 5 in Supplement).

Prehospital Factors Associated With 30-Day Survival

The association between prehospital factors and 30-day survival for the entire study period is shown in **Table 2**. Importantly, bystander CPR was positively associated with 30-day survival, irrespective of witnessed status.

New Onset of Anoxic Brain Damage in 1-Year Survivors

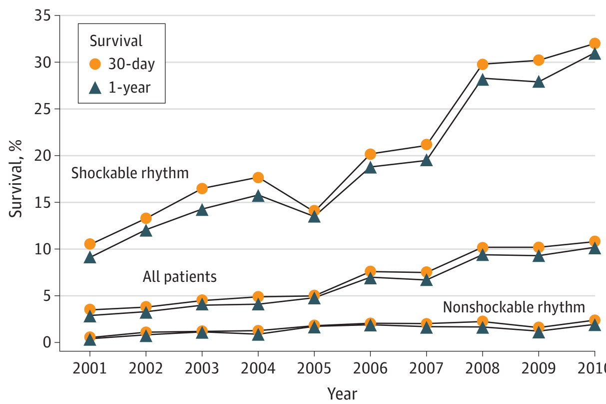
In total, 10.3% (95% CI, 8.6%-12.0%) of the 1-year survivors were diagnosed with anoxic brain damage during the period from hospital discharge to 30 days after discharge following cardiac arrest. There was some variation during the study period, and overall a small decline in anoxic brain damage was observed (eTable 2 in Supplement).

Other Analyses

The increases in rates of bystander CPR and survival over time were also persistent when patients with presumed noncardiac cause were included in the analyses (n = 26 076). Rates of bystander CPR increased from 19.4% (95% CI, 17.5%-21.3%) in 2001 to 43.3% (95% CI, 41.4%-45.2%) in 2010; survival on arrival at the hospital increased from 6.5% (95% CI, 5.3%-7.7%) in 2001 to 19.1% (95% CI, 17.5%-20.7%) in 2010; and 30-day survival increased from 2.8% (95% CI, 2.0%-3.6%) in 2001 to 8.6% (95% CI, 7.6%-9.7%) in 2010 (*P* < .001 for all).

Regarding missing data and temporal trends, the associations between 1-year increase in calendar year and (1) receiving bystander CPR and (2) achieving survival on arrival at the hospital were OR, 1.149 (95% CI, 1.136-1.162) and OR, 1.167 (95% CI, 1.148-1.186), respectively, in the observed data set and OR, 1.154 (95% CI, 1.141-1.168) and OR, 1.173 (95% CI, 1.154-1.192), respectively, in the imputed data sets using multiply imputed pooled analysis.

Figure 3. Survival Following Out-of-Hospital Cardiac Arrest, 2001-2010



Proportion of patients achieving 30-day and 1-year survival, overall as well as for patients with a shockable rhythm and patients with a nonshockable rhythm, respectively, according to calendar year. *P* < .05 (2-sided) was considered statistically significant. *P* < .001 for all comparisons.

Discussion

Our nationwide study had 4 major findings: rates of bystander CPR increased substantially; survival rates at 30 days and 1 year more than tripled; the number of survivors per 100 000 persons more than doubled; and rates of defibrillation by bystanders remained low.

Changes in Bystander CPR and Survival

The large temporal increase in bystander CPR in conjunction with the large increase in numbers of patients achieving survival on arrival at the hospital is a strong indicator of improvements made in prehospital settings. This notion is also indicated by the change in slopes, with a steeper increase in bystander CPR and survival on arrival at the hospital in the second half of the study period, along with national initiatives (eFigures 1 and 2 in Supplement). Additionally, 30-day survival and 1-year survival increased, which likely reflects improvements in prehospital as well as in-hospital settings, including the strengthening of the EMS system and the advanced care. Hence, the reason for improved survival is probably multifactorial and most likely related to improvements in each of the links in the chain of survival[6,7,12] as well as other factors that influence survival.[14] This notion is supported by the observation that 30-day survival increased among patients both with and without bystander CPR. Thus, bystander CPR was only 1 important factor among many associated with good outcome. However, survival rates remained low for patients without bystander CPR, and the large increase in 30-day survivors over time was observed primarily in patients who had received bystander CPR. Our study design does not allow any conclusion to be drawn related to which specific factors have contributed most to the increase in survival. But the closely parallel time course for the increase in bystander CPR and survival, together with the large positive association between bystander CPR and survival, may suggest a positive effect of increasing

Table 2. Association Between Prehospital Factors and 30-Day Survival for the Entire Study Period

			OR (95% CI)			
					Imputed Data Sets[a]	
Factor	No.	Crude 30-d Survival, % (95% CI)	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
Sex						
Women	6357	4.4 (3.9-4.9)	0.54 (0.47-0.62)	0.66 (0.57-0.76)[c]	0.54 (0.47-0.62)	0.66 (0.57-0.76)[c]
Men	13 111	7.9 (7.4-8.4)				
Age, per 10 additional years	19 468	NA	0.70 (0.67-0.72)	0.70 (0.68-0.72)[d]	0.70 (0.67-0.72)	0.70 (0.68-0.72)[d]
Cardiac arrest in private home						
No	4203	15.2 (14.1-16.3)	4.04 (3.57-4.56)	3.33 (2.94-3.78)	3.98 (3.51-4.51)	3.31 (2.91-3.76)
Yes	12 083	4.3 (3.9-4.6)				
Bystander-witnessed arrest						
Yes	9474	11.3 (10.7-12.0)	7.28 (6.13-8.66)	7.38 (6.20-8.79)	7.12 (5.99-8.47)	7.24 (6.08-8.63)
No	8763	1.7 (1.5-2.0)				
Bystander CPR overall						
Yes	5621	14.3 (13.4-15.2)	4.88 (4.32-5.52)	3.92 (3.45-4.44)	4.77 (4.22-5.40)	3.79 (3.34-4.31)
No	12 654	3.3 (3.0-3.6)				
Bystander CPR in nonwitnessed arrest						
Yes	1874	4.3 (3.4-5.2)	4.38 (3.17-6.06)	3.48 (2.50-4.84)	4.38 (3.17-6.06)	3.47 (2.50-4.84)
No	6858	1.0 (0.8-1.3)				
Bystander CPR in witnessed arrest						
Yes	3709	19.4 (18.1-20.7)	3.74 (3.26-4.28)	2.98 (2.59-3.42)	3.73 (3.26-4.27)	2.98 (2.59-3.42)
No	5730	6.1 (5.4-6.7)				
AED use by bystander						
Yes	241	27.8 (22.1-33.5)	5.93 (4.44-7.91)	4.42 (3.28-5.95)	6.13 (4.53-8.29)	4.51 (3.31-6.14)
No	17 398	6.1 (5.8-6.5)				
Shockable heart rhythm						
Yes	4981	21.0 (19.9-22.2)	15.9 (13.7-18.5)	14.0 (12.0-16.3)	16.0 (13.8-18.6)	14.0 (12.0-16.3)
No	13 058	1.7 (1.4-1.9)				
Estimated time interval, 1 additional min from recognition of OHCA to rhythm analysis by EMS	16 074	NA	0.97 (0.96-0.97)	0.97 (0.96-0.97)	0.97 (0.96-0.99)	0.97 (0.96-0.99)
Estimated time interval >10 min from recognition of OHCA to rhythm analysis by EMS						
Yes	8565	3.8 (3.4-4.2)	0.35 (0.31-0.40)	0.35 (0.30-0.40)	0.40 (0.35-0.47)	0.40 (0.35-0.47)
No	7509	10.0 (9.3-10.7)				

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; NA, not applicable; OHCA, out-of-hospital cardiac arrest; OR, odds ratio.

[a] In the analysis using imputed data sets missing value for information on prehospital factor was imputed. Therefore, these analyses correspond to entire study population (n = 19 468), except for subanalysis on nonwitnessed (n = 8763) and witnessed (n = 9474) arrest.

[b] Adjusted for sex and age.

[c] Adjusted only for age.

[d] Adjusted only for sex.

rates of bystander CPR and, subsequently, survival, although this cannot be confidently concluded with the data presented. Nevertheless, these findings are supported by other studies in this field.[15-21]

Additionally, we found that bystander CPR was positively associated with 30-day survival among patients with both witnessed and nonwitnessed arrests. This important finding suggests that the beneficial effects of bystander CPR are not entirely driven by early recognition of cardiac arrest with early alarm call and faster arrival of EMS personnel. Further, it underlines the importance of bystander CPR, irrespective of witnessed status.

Last, the improvement in survival was observed despite a small increase in time from recognition of cardiac arrest to rhythm analysis by EMS personnel. Multiple reasons could account for the small prolongation in time interval, and overall we do not have a clear explanation for this trend.

Widespread CPR Training

The large temporal increase in rates of bystander CPR observed in our study is most likely attributable to the overall increasing level of attention to resuscitation by bystanders in Denmark, including an increase in both mandatory and voluntary first aid training, with an estimate of more than 15% of the Danish population having taken CPR courses between 2008 and 2010.[9] A relationship between CPR training and an increase in resuscitation attempts by bystanders has also been suggested by other studies.[15,17,18,22-24] Changing the habits of a whole population is difficult, and although our study design does not allow us to determine how much each initiative has actually contributed to the changes observed, it is reassuring that the sum of initiatives seems to have had an early influence on bystander CPR rates, including in private homes, and underlines that the changes are somewhat robust, also in relation to the setting of cardiac arrest.

Public-Access Defibrillation

Rates of defibrillation by bystanders using automated external defibrillators remained low throughout the study period, but when used, defibrillation by bystanders was positively associated with survival, and public defibrillators have already been proven effective if they are placed in strategic locations where large numbers of people are located.[25-30] Overall, the low use of defibrillators by bystanders was expected, because the largest increase in placement of out-of-hospital defibrillators (and implementation of emergency dispatch guidance to the nearest available defibrillator) occurred during the last year of the study period. As a result, we did not expect the full effect of these initiatives to be visible in our study. Furthermore, nearly three-fourths of the cardiac arrests occurred in private homes, which presumably provide limited access to public defibrillators.

Changes in Incidence

There was a small decrease in the incidence of cardiac arrests over time. To adjust for the possibility that the improved survival could be driven by changes in reporting, we performed separate analyses focusing only on changes in absolute numbers of survivors (numerator) as dependent on population size (denominator), which did not change the main findings. Therefore, we did not find any indication that the observed improvement in survival was driven by changes in reporting.

Limitations

The main limitation is that our study is observational in nature. In this context, the national initiatives taken overlapped in time, and although the data suggest a positive effect of bystander CPR education, the findings are largely ecological, and although supportive, they offer no direct causal link between initiatives and outcomes. Second, we were able to analyze only a limited number of covariates without data on several important factors: the quality of CPR given, whether CPR was dispatcher-assisted, and advanced treatment provided, including therapeutic hypothermia, revascularization, etc. Thus, it was not possible to take these factors into account. In addition, we did not have qualitative data on more advanced outcome measurements, including standardized neurologic outcome scores such as the Cerebral Performance Category score.[31] Overall, this must be considered an important limitation. However, we used discharge diagnosis codes to report new onset of anoxic brain damage in 1-year survivors. Rates of anoxic brain damage were relatively low, which could reflect that 1-year survivors represent a favorable group with fairly good neurologic outcome and that only patients with major cognitive impairment were coded with anoxic brain damage. Nevertheless, other studies have shown good length and quality of life in survivors discharged from the hospital,[32,33] and 72% of the patients in a large US study had a good or moderate cerebral performance (Cerebral Performance Category score) at hospital discharge.[8]

Third, a number of patients had missing data (Table 1); however, comparing estimates from the observed data set with estimates from the imputed data sets did not change our main findings. Hence, we did not find any indication that missing data influenced our main conclusions. Last, data collection was consecutive, and the more detailed and accurate decisions concerning the study design were conducted retrospectively. Yet the Danish Cardiac Arrest Register was in place before the national initiatives described in this study were introduced.

Conclusions

In Denmark between 2001 and 2010, there was an increase in survival following out-of-hospital cardiac arrest that was significantly associated with a concomitant increase in bystander CPR. Because of the co-occurrence of other initiatives to improve outcome after cardiac arrest, a causal relationship between bystander CPR and survival remains uncertain.

ARTICLE INFORMATION

Author Contributions: Dr Wissenberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Wissenberg, Lippert, Folke, Christensen, Olesen, Gislason, Torp-Pedersen.
Acquisition of data: Wissenberg, Lippert, Folke, Jans, P. A. Hansen, Lang-Jensen, Nielsen, Torp-Pedersen.
Analysis and interpretation of data: Wissenberg, Lippert, Weeke, C. M. Hansen, Christensen, Jans, Olesen, Lindhardsen, Fosbol, Nielsen, Gislason, Kober.
Drafting of the manuscript: Wissenberg, Folke, C. M. Hansen.
Critical revision of the manuscript for important intellectual content: All Authors.
Statistical analysis: Wissenberg, C. M. Hansen, Olesen, Lindhardsen, Fosbol, Gislason.
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Administrative, technical, or material support: Folke, Christensen, Jans, P. A. Hansen, Lindhardsen, Nielsen, Gislason, Torp-Pedersen.
Study supervision: Lippert, Folke, Christensen, Jans, Lang-Jensen, Gislason, Kober.

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