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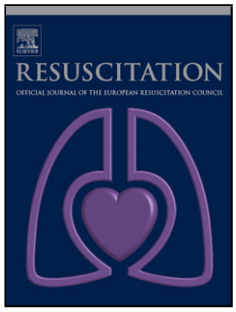

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Out-of-Hospital Cardiac Arrest in Patients With Psychiatric Disorders - Characteristics and Outcomes

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ABSTRACT

Aims – To investigate whether the recent improvements in pre-hospital cardiac arrest-management and survival following out-of-hospital cardiac arrest (OHCA) also apply to OHCA patients with psychiatric disorders.

Methods - We identified all adult Danish patients with OHCA of presumed cardiac cause, 2001-2015. Psychiatric disorders were defined by hospital diagnoses up to 10 years before OHCA and analyzed as one group as well as divided into five subgroups (schizophrenia-spectrum disorders, bipolar disorder, depression, substance-induced mental disorders, other psychiatric disorders). Association between psychiatric disorders and pre-hospital OHCA-characteristics and 30-day survival were assessed by multiple logistic regression.

Results - Of 27,523 OHCA-patients, 4772 (17.3%) had a psychiatric diagnosis. Patients with psychiatric disorders had lower odds of 30-day survival (0.37 [95% confidence interval 0.32-0.43]) compared with other OHCA-patients. Likewise, they had lower odds of witnessed status (0.75 [CI 0.70-0.80]), bystander cardiopulmonary resuscitation (CPR) (0.77 [CI 0.72-0.83]), shockable heart rhythm (0.37 [95% CI, 0.33-0.40]), and return of spontaneous circulation (ROSC) at hospital arrival (0.66 [CI 0.59-0.72]). Similar results were seen in all five psychiatric subgroups. The difference in 30-day survival between patients with and without psychiatric disorders increased in recent years: from 8.4% (CI 7.0-10.0%) in 2006 to 13.9% (CI 12.4-15.4%) in 2015 and from 7.0% (4.3-10.8%) in 2006 to 7.0% (CI 4.5-9.7%) in 2015, respectively.

Conclusion – Patients with psychiatric disorders have lower survival following OHCA compared to non-psychiatric patients and the gap between the two groups has widened over time.

INTRODUCTION

During the last decade great efforts have been made to improve bystander resuscitation attempts in out-of-hospital cardiac arrest (OHCA).[1–4] This has led to increased bystander cardiopulmonary resuscitation (CPR) and bystander defibrillation rates resulting in overall enhanced survival after OHCA.[1,5,6]

Mental and addictive disorders affect about 16% of the world's population and account for about 13% of years of life lost due to premature mortality or disability, as much as cardiovascular diseases.[7] Patients with psychiatric disorders have 10-20 years shorter life-expectancy compared to the general population [8,9] and cardiovascular diseases are the main cause of their premature death.[9–11] Several mechanisms contribute to the excess cardiovascular mortality: metabolic disorders, unhealthy lifestyle, socioeconomic decline, stigmatization and use of psychotropic drugs.[9,11,12]

Notably, patients with psychiatric disorders have been found to have three times higher risk of sudden cardiac arrest.[13] Despite the strong association between mental disorders and cardiac arrest,[14–16] little is known about outcomes of these patients following OHCA and whether they have benefitted from the recent efforts to enhance bystander intervention and survival. Therefore, we investigated possible differences and temporal changes in prehospital OHCA-characteristics and 30-day survival following OHCA between patients with and without psychiatric disorders.

METHODS

Data sources

Data concerning OHCA were obtained from the nationwide Danish Cardiac Arrest Register where all OHCAs with attempts of resuscitation by a bystander or the emergency medical services

(EMS) personnel are recorded. Patients with late signs of death are not included in the register. The register has been described in detail previously.[1]

In Denmark, every resident has a permanent and unique civil registration number that permits individual-level linkage between the national administrative registries. The Danish Civil Registration System provides information about patients' age and gender. All hospital admissions have been recorded since 1978 in the Danish National Patient Register. One primary diagnosis and, when relevant, one or more secondary diagnoses are assigned to every admission and classified according to the International Classification of Diseases (ICD), until 1994 the ICD-8 and from 1994 the ICD-10. The Danish Psychiatric Central Research Register includes all psychiatric hospitalizations, encoded according to ICD-classification, as well as data on patients in psychiatric ambulatory settings and community psychiatric centers. We obtained vital status and causes of death from the Danish Register of Causes of Death. All claimed prescriptions in Denmark have been recorded in the National Prescription Register since 1995. The drugs are classified according to the international Anatomical Therapeutic Chemical (ATC) classification system. Household income was found through Statistics Denmark.

Study population

The study population included all patients with OHCA from June 2001 through 2015. Patients younger than 18 and older than 100 years of age at OHCA, EMS-witnessed arrests and arrests of a presumed non-cardiac cause were excluded. We classified patients as having psychiatric disorder if they had a hospital discharge diagnosis or an ambulatory contact diagnosis from either the Danish Psychiatric Central Research Register or the Danish National Patient Register for at least one of the following diseases up to 10 years before OHCA: 1) schizophrenia or other psychotic disorders, 2) bipolar disorder, 3) depression, 4) substance-induced mental disorders or 5) other psychiatric

disorders (dementia and mental organic disorder were excluded)(see eTable 1 for ICD-codes). If more than one diagnosis was present, the patient was assigned to the most severe subgroup in accordance with the diagnostic hierarchical order in ICD-10.

From the National Prescription Register, we further identified patients who redeemed psychotropic medications i.e. antipsychotics, antidepressants and/or lithium within 90 days prior to OHCA without having a hospital psychiatric diagnosis (eTable 2). Those patients were classified into two subgroups: 1) exposed to antipsychotics and/or lithium and 2) exposed only to antidepressants. Such patients represent a group of individuals treated for their psychiatric disorder only in the primary sector - not reported in the hospital-based registries – and, hence, to study a more homogenous psychiatric population, they were excluded from the main analyses (Figure 1).

Charlson score[17] (scores range from 0 to 33, with higher scores indicating more coexisting comorbidities) and comorbidity at baseline were determined from hospital diagnoses up to 10 years before OHCA, except for diabetes, which was defined as claimed prescriptions for glucose-lowering medicine within 180 days before OHCA.[17]

Outcomes

The primary outcome was 30-day survival. The secondary outcomes were pre-hospital OHCA-characteristics (location of OHCA, witnessed status, bystander CPR, bystander CPR among witnessed OHCAs, bystander defibrillation and first registered heart rhythm) and return of spontaneous circulation (ROSC) upon hospital arrival.

Statistical methods

To investigate changes over time in bystander CPR, ROSC and 30-day survival, we present percentage of patients per year with their corresponding exact binomial 95% confidence intervals.

We employed multiple logistic regression models adjusted for age, sex and year of arrest in a three-step analysis to compare patients with and without psychiatric disorders:

1. We assessed differences in odds of 30-day survival;

2. We investigated the associations of having psychiatric disorders with pre-hospital OHCA-characteristics and ROSC.

3. To assess the effects of differences in baseline characteristics between patients with and without psychiatric disorders, we repeated survival-analysis (step 1) in subsets of patients defined by the presence of predefined pre-hospital OHCA-characteristics, ROSC and according to Charlson score at baseline. A complete list of subsets that we examined is available in Supplementary method.

In the main analysis, patients with a previous psychiatric diagnosis were pooled in a single group and compared with patients without psychiatric disorders (neither prior psychiatric diagnoses nor redeemed prescriptions for psychotropic drugs). In subanalyses, the five mutually exclusive subgroups of psychiatric disorders (schizophrenia, bipolar disorder, depression, substance-induced mental disorders, other psychiatric disorders) were investigated separately.

We performed additional analyses repeating the steps 1 and 2:

- Stratifying by gender;
- Comparing patients not having a former psychiatric diagnosis but in treatment with psychotropic drugs within 90 days before OHCA with patients without psychiatric disorders.

To assess the role of psychotropic drugs, we performed survival-analysis stratified by the number of drugs redeemed by our total psychiatric population - i.e. both patients identified by hospital contacts and redemption of psychotropic medications - within 90 days prior to OHCA,

divided as follows: 1) patients not taking psychotropic drugs, 2) taking only one drug and 3) taking two or more drugs.

Lastly, we conducted sensitivity analyses 1) including OHCAs of both presumed cardiac and non-cardiac cause of arrest and 2) among OHCA-patients for whom complete information on all variables was available (complete case analysis).

Missing data was handled using multiple imputations. Analyses were performed based on 200 imputed data sets using the smcfcs package in R.[18] SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 3.5.2 (R Development Core Team) were used for data management and statistical analyses.

Ethics

The study has been approved by the Danish Data Protection Agency (Ref.no. 2007-58-0015, local ref.no. GEH-2014-017, I-Suite.nr. 02735). For register studies based on anonymous data in Denmark ethical approval is not required.

RESULTS

The main population consisted of 27,523 OHCA-patients, 4772 (17.3%) of whom had a known psychiatric diagnosis (Figure 1).

Main analyses

Compared to other OHCA-patients, patients with psychiatric disorders were younger, less likely to be male and have overall a large burden of comorbidity: particularly, almost two-fold more chronic obstructive pulmonary disease (COPD) and cerebrovascular disease, five-fold more dementia and seven-fold more liver disease and epilepsy. (Table 1, for missing values eTable 3).

In the adjusted analysis, patients with psychiatric disorders had significantly lower odds of 30-day survival (odds ratio [OR] 0.37 [95% confidence interval, (CI), 0.32-0.43]) compared with patients without psychiatric disorders, Figure 2. Patients with psychiatric disorders were less likely to have witnessed OHCA, bystander CPR (even among witnessed OHCAs), initial shockable rhythm, bystander defibrillation, and ROSC upon hospital arrival, compared with patients without psychiatric disorders, Figure 3. There were no differences in location of OHCA between the two groups.

Patients with psychiatric disorders were associated with lower probability of 30-day survival irrespectively of location of arrest (notably, lower in public locations than in private homes), witnessed status and whether they received bystander CPR, as compared to patients without psychiatric disorders, Figure 4. Patients with psychiatric disorders had lower odds of 30-day survival compared to patients without psychiatric disorders even in the subgroups of bystander witnessed OHCAs who received CPR, and OHCAs with initial shockable rhythm who attained ROSC upon hospital arrival, Figure 4. Moreover, the lower survival was still present when we stratified the analysis according to the burden of comorbidity (Charlson score) (eFigure 1).

The stratification by gender did not change the results considerably; however, among women, patients with psychiatric disorders had more often OHCA in public location and the same chances of receiving bystander CPR, compared to patients without psychiatric disorders (eFigure 2).

Temporal trends

OHCA-patients both with and without psychiatric disorders experienced a large and parallel increment in the number of individuals who received bystander CPR and achieved ROSC (Figure 5A and 5B, eTable 4 and 5). Nevertheless, the increase in 30-day survival was comparable only until 2006, thereafter the two curves diverged: for non-psychiatric patients the survival-rate raised from 8.4% (CI 7.0-10.0%) in 2006 to 13.9% (CI 12.4-15.4%) in 2015, while it stagnated for patients with psychiatric disorders: 7.0% (4.3-10.8%) in 2006 to 7.0% (4.5-9.7%) in 2015 (Figure 5C, eTable 6).

Subgroups of psychiatric disorders

Baseline comorbidities and cardiac arrest-related characteristics for each subgroup of psychiatric disorders are presented in eTable 7.

All five subgroups of psychiatric disorders had lower odds of shockable heart rhythm, ROSC and 30-day survival (Figure 2, eFigure 3), compared with patients without psychiatric disorders. Patients with substance-induced mental disorders and schizophrenia had lower odds of witnessed arrest and bystander CPR compared with patients without psychiatric disorders, but the former were associated with arrest in public locations, the latter in private locations (eFigure 3). No differences in terms of bystander CPR were seen for patients with depression and bipolar disorder, compared with patients without psychiatric disorders (eFigure 3).

As in main analysis, we detected a progressive increase in bystander CPR and ROSC in all psychiatric subgroups during the study period (eFigure 4), while the trends for 30-day survival were inconclusive because of a few events.

Patients who redeemed psychotropic drugs

In total, 3707 patients redeemed psychotropic drugs within 90 days prior to OHCA and did not have a psychiatric diagnosis in hospital settings: 2897 claimed only prescriptions for antidepressants, and 810 for antipsychotics and/or lithium (baseline characteristics in eTable 8). Both these two groups had lower probability of 30-day survival, shockable heart rhythm and ROSC compared with patients without psychiatric disorders (eFigure 5).

Analysis stratified by number of psychotropic drugs

Totally, 6742 (79.5%) of the total psychiatric population (8479 patients) were in treatment with at least one psychotropic medication (eTable 9). Patients with psychiatric disorders had lower probability of 30-day survival compared with non-psychiatric patients regardless of the number of redeemed medications; however, the probability of survival was particularly low for patients redeeming two or more drugs (eFigure 6).

Sensitivity analyses

The results of sensitivity analyses including OHCAs of both presumed cardiac and non-cardiac causes (37,433 OHCAs - eFigure 7) and complete case analyses (20,959 cases - eFigure 8) did not differ from the main analyses.

DISCUSSION

This nationwide study shows that patients with psychiatric disorders have less than half the probability of 30-day survival following OHCA–when compared to patients without psychiatric disorders. Moreover, having a psychiatric disorder is generally associated with unfavorable OHCA-

characteristics. The gap in 30-day survival between patients with and without psychiatric disorders increased over time; and during the last ten years of the study period there was no increase in 30-day survival for patients with psychiatric disorders, while a 1.5-fold increase in 30-day survival was seen for patients without psychiatric disorders.

Our study underlines the relevance of epidemiological research in the field of cardiac arrest to identify OHCA-characteristics in specific populations considering the sudden nature of the event, the unfeasibility of randomized clinical trials and the still low survival.

30-day survival

The lower survival following OHCA associated with mental disorders have diverse possible explanations.

Firstly, the overall correlation with unfavorable pre-hospital OHCA-factors, especially non-shockable heart rhythm, which is one of the main determinants of post-OHCA survival.[1] However, a poorer survival was still evident in the subsets of patients with more favourable OHCA-characteristics such as shockable rhythm and ROSC upon hospital arrival. Notably, the poorer outcomes among those with ROSC suggest a higher in-hospital post-arrest mortality for patients with psychiatric disorders, which may be caused by greater rates of complications and lower tolerance to intensive treatment due to a general frail physical condition and a larger burden of comorbidity.[19]

Secondly, psychotropic drugs affect negatively the outcomes following an acute cardiac event.[20] Accordingly, our results suggest that the combined use of these drugs reduces the post-arrest survival. Besides their prolonging action on QT-interval, psychotropic drugs have adverse metabolic effects, interact with other medications, drugs and alcohol, and may induce hypotension and have negative inotropic effects.[9,11,21,22]

Our analyses suggest that the difference in mortality following OHCA between the two groups became more pronounced in the second part of the study period. This progressive disparity in survival has been widely documented and appears primarily due to a lack of reduction in cardiovascular mortality amongst patients with psychiatric disorders.[19,23] Since 2006, both the American and the European guidelines have recommended a more aggressive approach in the post-resuscitation treatment of survivors of cardiac arrest.[24] Concurrently, several papers have demonstrated inequalities in healthcare provision for patients with mental illness compared to the general population, even in case of life-threatening diseases.[12,25] Hence, it may be hypothesised that the progressive lower survival following OHCA could be, at least partly, caused by a less aggressive in-hospital post-arrest management.

Finally, the initiation of bystander CPR might be delayed in patients with psychiatric disorders since OHCA can be misdiagnosed with other manifestations of their disease such as psychogenic unresponsiveness, catatonia, epilepsy or substance intoxication [26] with terrible consequences for survival.[27]

OHCA-characteristics

The extensive efforts to improve bystander intervention in Denmark [1] have resulted in a temporal increase in the number of subjects who received CPR and attained ROSC upon hospital arrival irrespectively of the psychiatric status. However, in the adjusted analyses, we found having a psychiatric disorder to be associated with lower odds of ROSC: a larger prevalence of unfavorable pre-hospital OHCA-factors could explain such relation.[1]

Interestingly, we observed a strong association between psychiatric disorders and non-shockable rhythm, which may be due to the effects of psychotropic drugs and to a large prevalence

of comorbidities [9] related to non-shockable rhythm such as COPD and liver disease.[22,28] In light of this association with non-shockable heart rhythm, patients with psychiatric disorders can only slightly benefit from the recent widespread diffusion of automated external defibrillators.[1,22]

Moreover, patients with psychiatric disorders had more often unwitnessed arrest and received less often bystander CPR compared to non-psychiatric patients, which could be explained by their solitary lifestyle and by the characteristics of their neighborhood.[29,30] It may be also speculated that the lower rate of bystander intervention could be related to the stigma that still marks mental disorders.[31,32] The fact that their probability of survival compared to non-psychiatric OHCA-patients was lower in public locations than in private homes and that they received less bystander CPR even in the subsets of witnessed OHCAs strengthens this assumption.

Subgroups of psychiatric disorders

In our study, patients with schizophrenia seemed to have the lowest chances of survival following OHCA among the diverse subgroups. Accordingly, schizophrenia is associated more often than other psychiatric disorders with medical causes of death, including cardiovascular death.[8]

Unwitnessed cardiac arrest and reduced probability of bystander intervention were seen in patients with schizophrenia and substance-abuse; possibly because of a stronger social isolation and public stigmatization towards these types of mental illness.[33] Compared to patients without psychiatric disorders, patients with substance-induced mental disorders were related to private location, while patients with bipolar disorder and schizophrenia had more often arrest in public locations, which might be due to the high number of homeless among them.[34]

Limitations

The main limitation of the present study is inherited in its observational nature; therefore, any conclusion on causality should be drawn with caution.

The Danish registries do not hold important clinical information, such as blood pressure, detailed drug abuse, or alcohol consumption. Therefore, we cannot completely rule out residual confounding due to these factors.

The Danish Cardiac Arrest Registry present a limited amount of missing data regarding OHCA-characteristics: to address this issue, we employed multiple imputations. Moreover, results of complete case analyses did not differ from main analyses.

We determined hospital contacts up to 10 years before OHCA to identify patients with psychiatric disorders, which could misclassify patients with diagnoses with a more temporary pattern, such as depression or anxiety. Nevertheless, mental disorders are often relapsing: a recurrence rate over 85% within a decade from the first episode is documented for depression and of 40-55% for anxiety disorders.[35] Moreover, in our cohort about 80% of patients classified as depressed redeemed prescriptions for antidepressants shortly before OHCA, implying that the diagnosis was still actual at the time of OHCA.

Potential differences among health care systems reduce the generalizability of our results. Nevertheless, several studies from other countries have documented a higher prevalence of cardiovascular morbidity and mortality in patients with psychiatric disorders compared to the general population.[9,12]

Lastly, we lacked information about the indication for psychotropic drugs. Depression accounts for about 80% of prescribed antidepressants in general population, followed by anxiety disorders.[36,37] However, non-psychiatric conditions such as neuropathic pain are also treated with antidepressants. Therefore, we conducted a sensitivity analysis excluding tricyclic antidepressants - the antidepressants most used in pain treatment - which did not change the results.

Conclusions

Patients with psychiatric disorders have unfavorable pre-hospital OHCA-factors and lower 30-day survival following OHCA compared to non-psychiatric OHCA-patients. Despite improvements over time in bystander CPR, their chances of survival did not increase in the last eight years of the study period. A greater awareness towards patients with psychiatric disorders is warranted to improve their survival following OHCA via a better prevention and more efficient peri-arrest treatment. Future studies should aim to investigate possible inequalities in post-resuscitation management between patients with and without psychiatric disorders.

Conflicts of Interest

Dr. Kragholm has received research grant from The Laerdal Foundation, and lecture fees from Novartis Healthcare. Dr. Hansen reports receiving support from The Danish Heart Foundation, The Danish Foundation TrygFonden, and The Laerdal Foundation. Dr. Lippert is supported by unrestricted grants from the Danish foundation TrygFonden and unrestricted research grants and center support from the Laerdal Foundation. Dr. Folke has received unrestricted funding from The Laerdal Foundation. Dr. Torp-Pedersen has received grant support and honoraria from Bayer, grant support from Biotronik and he has been a consultant for Merck, Sanofi and Daiichi. Dr. Kessing is expert witness for Sunovion. Dr. Gislason has received unrestricted clinical research scholarship from the Novo Nordisk Foundation.

These institutions had not influenced the study design, data collection and analyses, preparation and approval of the manuscript. All the results and conclusions in this paper are solely representative of the authors.

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FIGURES LEGENDS

Figure 1: Selection of the study population. OHCA: out-of-hospital cardiac arrest, EMS: emergency medical services.

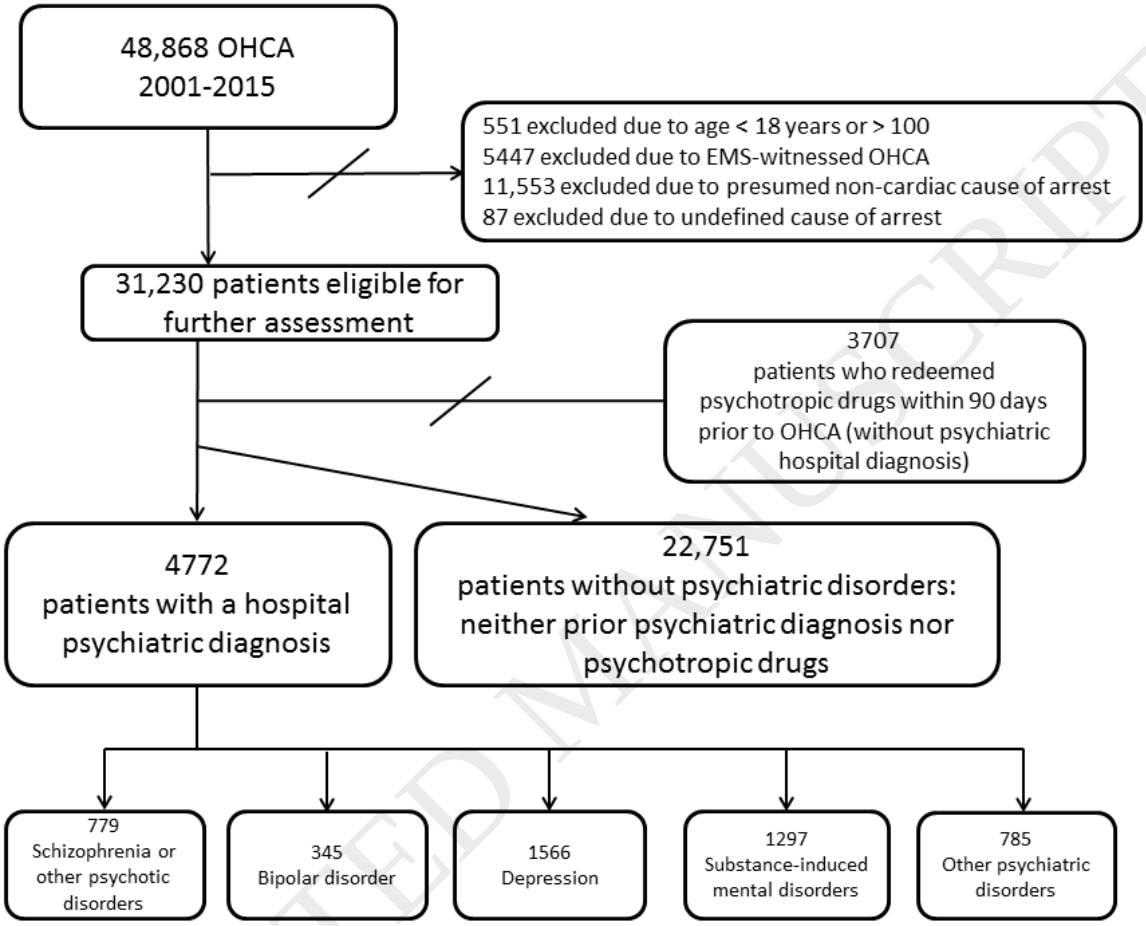

Figure 2: Association between psychiatric-status and 30-day survival following OHCA.

Odds Ratio of 30-day survival in patients with any psychiatric disorders and in subgroups of patients with psychiatric disorders, as compared with patients without psychiatric disorders. Multiple logistic regression models were adjusted for age, sex and year of arrest. OHCA: out-of-hospital cardiac arrest

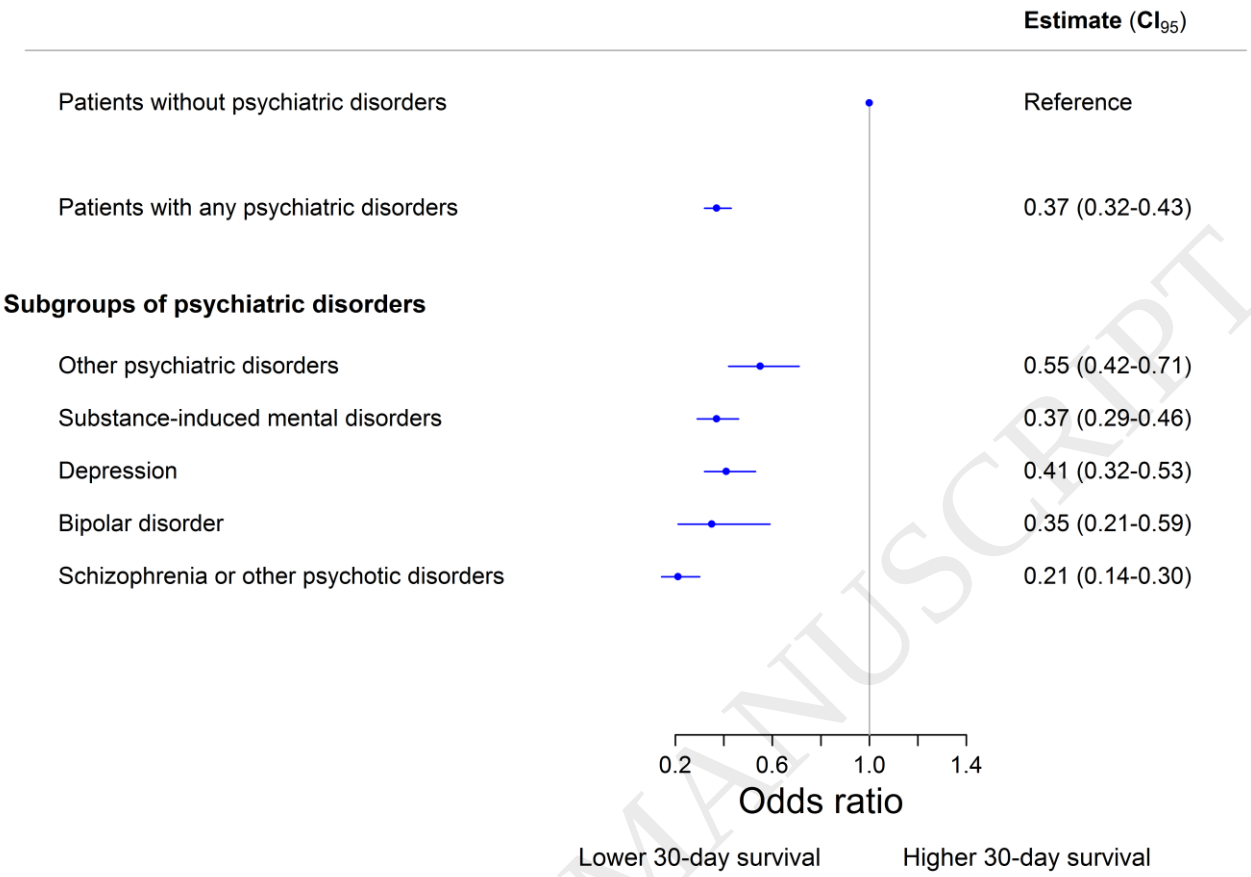

Figure 3: Association between psychiatric-status and pre-hospital OHCA characteristics.

Odds ratio for the presence of pre-hospital OHCA-characteristics and ROSC upon hospital arrival in patients with any psychiatric disorders, as compared to patients without psychiatric disorders. Models were adjusted for age, sex and year of arrest. OHCA: out-of-hospital cardiac arrest, CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation.

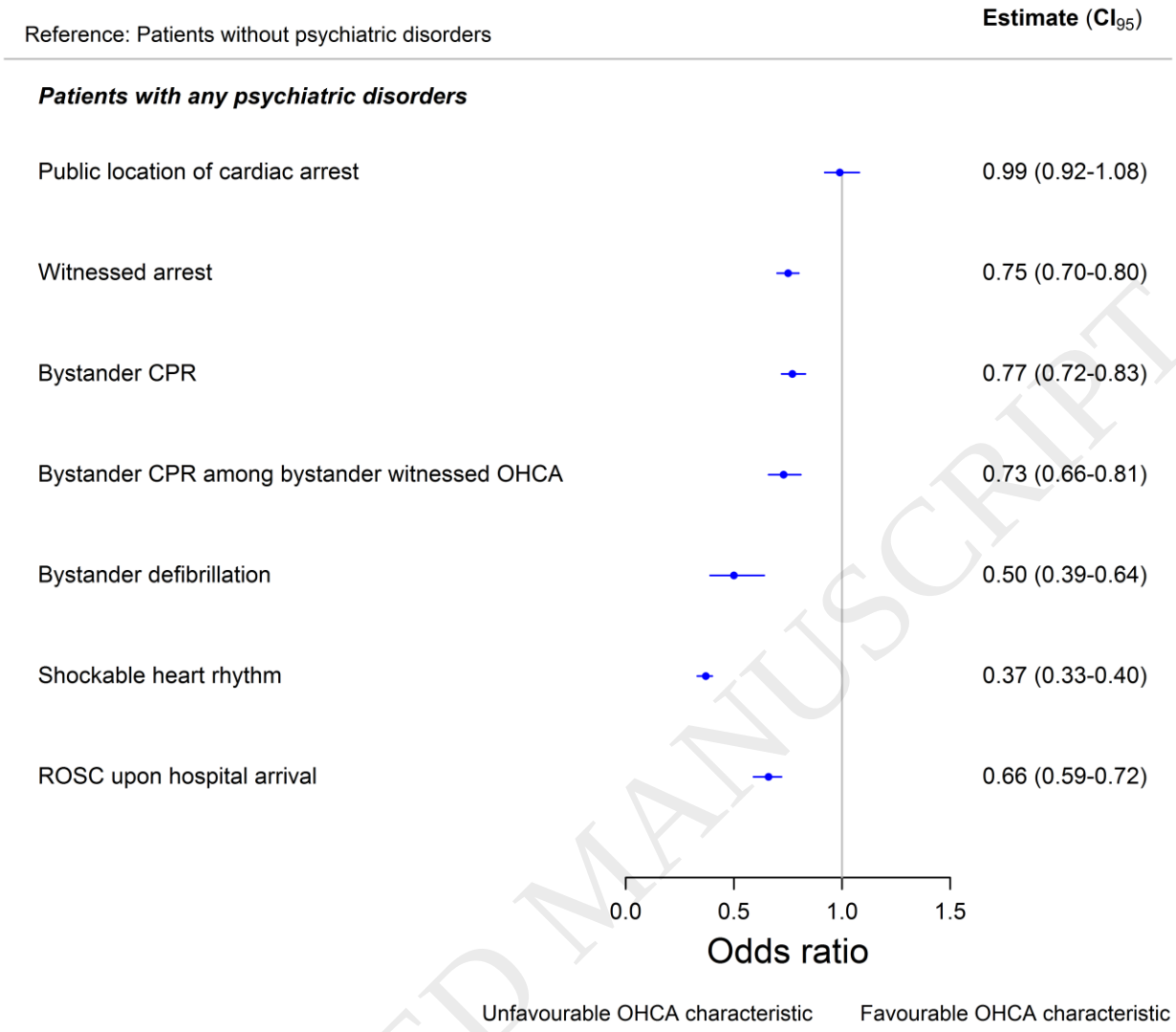

Figure 4: Association between psychiatric-status and 30-day survival following OHCA in patients with the same OHCA-characteristics. Subset analysis of 30-day survival in patients with and without psychiatric disorders in relation to the presence of pre-hospital OHCA-characteristics. Only the patients with the pre-specified characteristics were included in the analysis: the number of OHCAs contributing to the analysis is reported. Multiple logistic regression models were adjusted for age, sex and year of arrest. OHCA: out-of-hospital cardiac arrest, CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation.

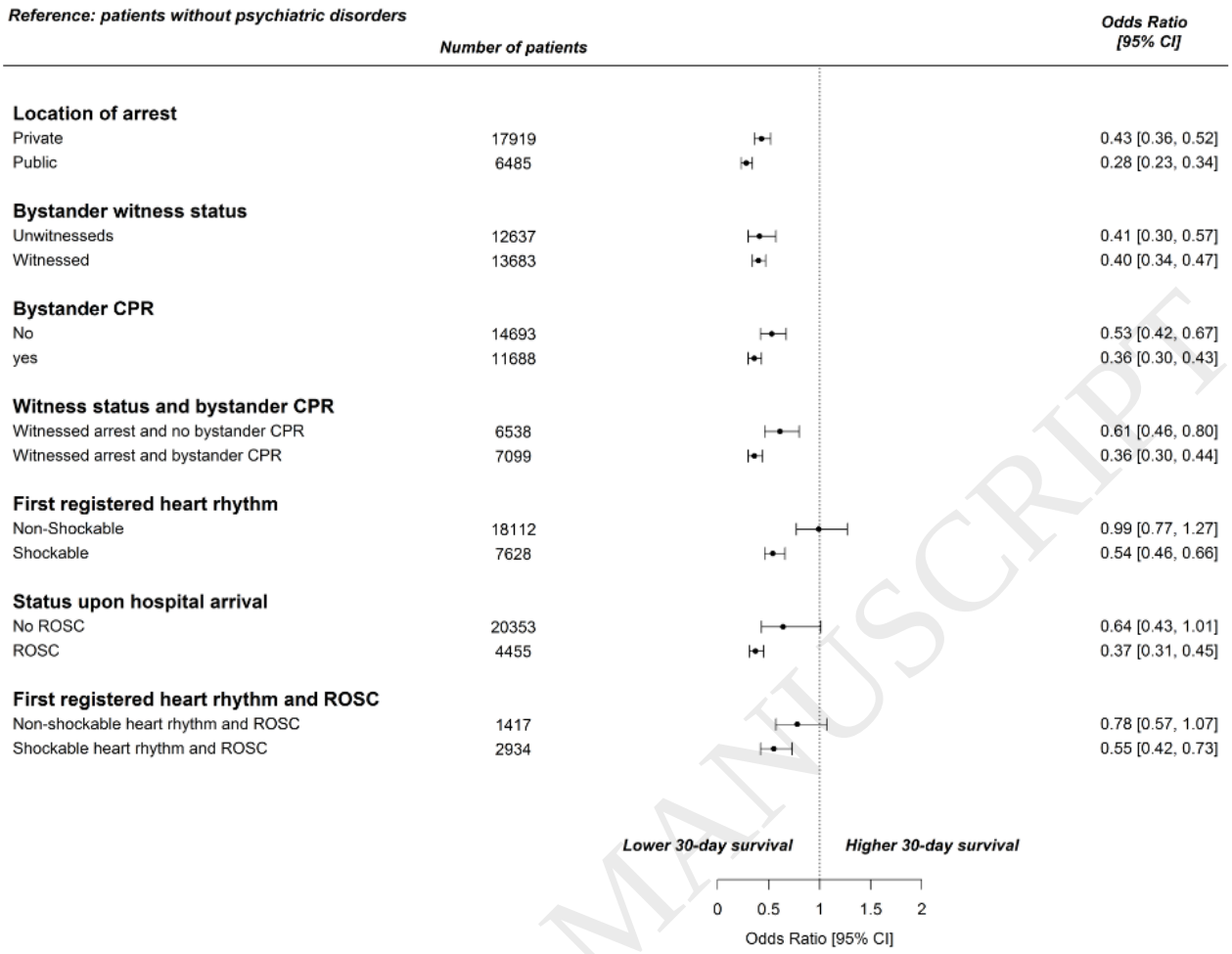

Figure 5: Temporal changes in bystander CPR, ROSC and 30-day survival according to psychiatric-status.

Temporal trends in A) bystander CPR, B) ROSC upon hospital arrival and C) 30-day survival following OHCA in patients with and without psychiatric disorders from 2001 to 2015. Trends were reported as percentage of patients per year with corresponding 95% confidence intervals. CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation.

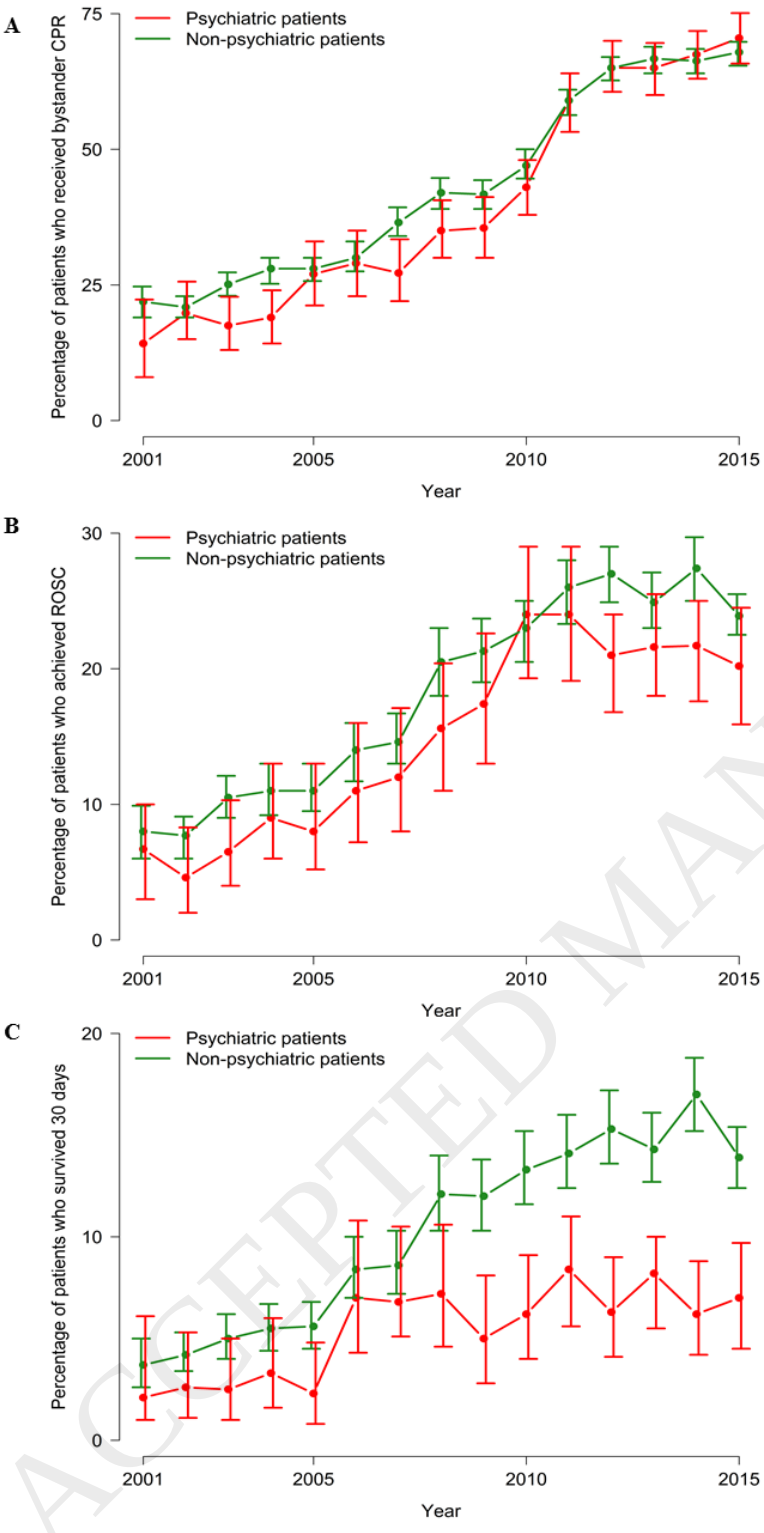

Table 1 - Baseline characteristics and cardiac arrest characteristics of OHCA-patients with and without psychiatric disorders

Characteristics	**Total Population**	**Patients without psychiatric disorders (%)**	**Patients with psychiatric disorders (%)**	**P-values**
Total patients	27,523	22,751 (82.7)	4772 (17.3)	
Median age, y (IQR)	71 (62-81)	72 (63-81)	66 (56-77)	<0.0001
Men, no. (%)	18,985 (69.0)	16,241 (71.4)	2744 (57.5)	<0.0001
Comorbidities and concomitant medications				
Charlson score				
0	10,881 (39.5)	9595 (42.1)	1286 (27.0)	<0.0001
1	5845 (21.2)	4766 (21.0)	1079 (22.6)	
≥ 2	10,797 (39.2)	8390 (36.9)	2407 (50.4)	
Ischemic heart disease [a], no. (%)	7663 (27.8)	6429 (28.3)	1234 (25.9)	0.0972
Congestive heart failure, no. (%)	5429 (19.7)	4416 (19.4)	1013 (21.2)	0.0041
Chronic obstructive pulmonary disease, no. (%)	3859 (14.0)	2805 (12.3)	1054 (22.1)	<0.0001
Diabetes mellitus, no. (%)	4028 (14.6)	3248 (14.3)	780 (16.4)	0.0002

Malignancy, no. (%)	3047 (11.1)	2538 (11.2)	509 (10.7)	0.3275
Peripheral artery disease, no. (%)	2869 (10.4)	2328 (10.2)	541 (11.3)	0.0232
Cerebrovascular disease, no. (%)	3486 (12.7)	2563 (11.3)	923 (19.3)	<0.0001
Liver disease, no. (%)	651 (2.4)	257 (1.1)	394 (8.3)	<0.0001
Chronic kidney disease, no. (%)	1669 (6.1)	1311 (5.8)	358 (7.5)	<0.0001
Epilepsy, no. (%)	646 (2.4)	311 (1.4)	335 (7.0)	<0.0001
Dementia, no. (%)	1059 (3.9)	526 (2.3)	533 (11.2)	<0.0001
Antipsychotics, no. (%)	1542 (5.6)	0 (0.0)	1485 (31.1)	<0.0001
Antidepressants, no. (%)	2413 (8.8)	0 (0.0)	2413 (50.6)	<0.0001
Lithium, no. (%)	125 (0.5)	0 (0.0)	125 (2.6)	<0.0001
Anxiolytics, no. (%)	2501 (9.8)	1417 (6.2)	1208 (25.3)	<0.0001
SES [b]				
Low, no. (%)	8976 (32.6)	6890 (30.3)	2086 (43.7)	<0.001
Medium, no. (%)	9047 (32.9)	7419 (32.6)	1628 (34.1)	
High, no. (%)	9500 (34.5)	8442 (37.1)	1058 (22.2)	
OHCA-factors				

Arrest in private home, no. (%)	17,919 (73.4)	14,782 (73.5)	3137 (73.1)	0.6207
Bystander-witnessed arrest, no. (%)	13,683 (52.0)	11,593 (53.1)	2090 (46.4)	<0.0001
Bystander CPR, no. (%)	11,688 (44.3)	9668 (44.2)	2020 (44.7)	0.5371
Bystander CPR in witnessed OHCAs, no. (%) [c]	7099 (51.9)	6042 (52.1)	1057 (50.6)	0.3798
Bystander defibrillation, no. (%)	679 (2.7)	609 (2.9)	70 (1.7)	<0.0001
Median time interval from recognition of OHCA to EMS arrival, in mins (IQR)	11 (7-17)	11 (7-17)	11 (7-17)	0.8870
Shockable heart rhythm, no. (%)	7628 (29.6)	6884 (32.3)	744 (16.8)	<0.0001
ROSC at hospital arrival, no. (%)	4455 (18.0)	3802 (18.4)	653 (15.8)	<0.0001
30-day survival, no. (%)	2684 (9.8)	2400 (10.6)	284 (6.0)	<0.0001
1-year survival, no. (%)	2472 (9.0)	2228 (9.8)	244 (5.1)	<0.0001

[a] Previous myocardial infarction included

[b] Socioeconomic status (SES): based on an average family income over the past five years prior to OHCA

[c] Percentage of witnessed OHCA

Abbreviations: OHCA, out-of-hospital cardiac arrest; IQR, interquartile range; SD, standard deviation; SES, socioeconomic status; CPR, cardiopulmonary resuscitation; EMS, emergency medical system; ROSC, return of spontaneous circulation.

Note: in the calculation of percentages, we only included observations with data for the covariate involved.