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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047932
Article Type:	Original research
Date Submitted by the Author:	12-Dec-2020
Complete List of Authors:	Yamagishi, Yasunobu; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Oginosawa, Yasushi; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Fujino, Yoshihisa; University of Occupational and Environmental Health Japan, Department of Environmental Epidemiology, Institute of Industrial Ecological Sciences Yagyu, Keishiro; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Miyamoto, Taro; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Tsukahara, Keita ; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Ohe, Hisaharu ; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Kohno, Ritsuko; University of Occupational and Environmental Health Japan, Department of Heart Rhythm Management Abe, Haruhiko; University of Occupational and Environmental Health Japan, Department of Heart Rhythm Management
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Cardiology < INTERNAL MEDICINE, OCCUPATIONAL & INDUSTRIAL MEDICINE

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A population-based study of out-of-hospital cardiac arrest in the Japanese working population: 12-year trends, colleague bystanders, and neurological outcome

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Word count: 3276 words

ABSTRACT

Objectives: To elucidate the long-term characteristics and relationship between a colleague bystander and prognosis following an out-of-hospital cardiac arrest (OHCA) in the Japanese working population.

Design and setting: Prospective, nationwide, population-based OHCA registry (2005–2016).

Participants: Working population of Japan, aged 20–69 years.

Primary and secondary outcome measures: Characteristics of cardiogenic OHCA. Citizen bystanders were classified as family, friends, colleagues, and passers-by. The relationship between prehospitalisation factors and 1-month survival with favourable neurological outcome was examined.

Results: The absolute number and incidence of OHCA were mostly unchanged, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016; while the 1-month survival with favourable neurological outcome increased from 4.5% in 2005 to 11.7% in 2016. The incidence of OHCA, in any age group, was almost constant during the 12-year period, and increased exponentially with increasing age. Colleagues had the highest cardiopulmonary resuscitation/automated external defibrillator proportion and the best prognosis, despite having a significantly longer time from witnessing an OHCA to initial defibrillation compared with passers-by (13 *vs.* 12 minutes, p<0.001); that was independently associated with 1-month survival with favourable neurological outcome (adjusted odds ratio: 0.97 [1-minute increments], 95% confidence interval: 0.95–0.98; $p<0.001$).

Conclusions: In the 12-year period, the incidence of OHCA in any age group remained almost constant, whereas the prognosis improved each year. Reducing the time from witnessing an OHCA to initial defibrillation may further improve the prognosis of OHCA with a colleague bystander.

Keywords: Cardiopulmonary resuscitation, defibrillation, Japan, out-of-hospital cardiac arrest, prognosis, prospective registry, working population.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- In this population-based study, we analysed data collected from 2005 to 2016 in the All-Japan Utstein registry of the Fire and Disaster Management Agency; a prospective, nationwide, population-based registry.
- A large sample size and longer follow-up allowed detailed assessment of the relationship between a colleague bystander and prognosis following an out-of-hospital cardiac arrest (OHCA) in the Japanese working population.
- We assessed independent factors associated with 1-month survival with favourable neurological outcome after OHCA in the Japanese working population.
- The All-Japan Utstein registry did not contain information on actual employment status, individual medical therapy, activities of daily living before the OHCA, or in-hospital treatment interventions.

INTRODUCTION

Despite advancements in preventive and therapeutic options, sudden cardiac death (SCD) remains a leading cause of mortality. The annual incidence of SCD is estimated to range from 50 to 100 per 100,000 among North Americans and Europeans, and from 14.9 to 36 per 100,000 in the Japanese population.[1] Moreover, the relative public health burden of premature death is greater for SCDs than for all individual cancers and most other leading causes of death.[2] Several studies have reported a relationship between out-of-hospital cardiac arrest (OHCA) and location, such as the workplace,[3-6] although detailed information about SCDs in the working population is lacking, because SCDs do not always occur in the workplace.

We previously defined the working population as individuals aged 20–69 years, and we analysed relatively short-term cardiogenic OHCA condition in the Japanese working population, as an approximation of SCD, by using data from the Utstein registry—a prospective, nationwide, population-based OHCA registry—between 2005 and 2008 in Japan.[7] The earlier study revealed that the incidence of SCD in the working population was highest during winter, on Sundays and Mondays, and during early morning hours, whereas the prognosis of SCD was not reported. A previous study found that the key predictor of survival after OHCA is a bystander witness.[8] A family member witnessed most cases of OHCA in Japan, and OHCA had a worse prognosis with a family member bystander than with other bystanders.[9] However, the association between a colleague bystander and the OHCA outcome in the working population has not been fully elucidated.

On January 8, 2020, the Japanese parliament enacted a partial amendment to the law regarding the stabilisation of employment of elderly persons that recommended an extension of the retirement age from 65 to 70 years, with the law coming into effect in companies from April 1, 2021. Another study reported that patients aged ≥ 65 years comprised approximately 76% of patients with OHCA in Japan.[10] Therefore, because individuals in the 65–69 age group are likely to constitute a new working population in the future, investigating the characteristics of SCD in this age group may provide important information with regard to Japanese socioeconomics.

This study aimed to investigate the long-term characteristics of OHCA in the Japanese working population and to determine the prognosis based on age and type of bystander, with a focus on colleagues.

METHODS

Japan has approximately 378,000 km^2 of total land area, and its population in 2019 was estimated to be 126.2 million, of which 67.33 million were employed, including both part-time and full-time workers.[11] In 2019, 726 fire stations with emergency dispatch centres provided emergency services 24 hours a day.[12] OHCA patients who received a resuscitation attempt by emergency medical service (EMS) personnel were transported to a hospital and then registered in the Utstein registry.

In this population-based study, we analysed data collected between 2005 and 2016 in the All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA)—a prospective, nationwide, population-based registry—of OHCA victims based on the standardised Utstein style.[13] As described in previous reports that used the Utstein data,[9 10 14] EMS personnel filled the information sheet and updated the OHCA patient information in the Utstein registry based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation. EMS personnel followed-up these OHCA patients for 1 month to ascertain the survival rate and neurological outcome. The data of 1,423,338 patients were collected between January 1, 2005 and December 31, 2016.

Our patient population was divided into two groups: a cardiogenic and a non-cardiogenic OHCA group. As reported in a previous study,[15] the cardiogenic group was defined as having confirmed absence of signs of circulation, with the following exclusion criteria: cerebrovascular disease, respiratory disease, malignant tumours, external factors, drug overdose, drowning, traffic accident, hypothermia, anaphylactic shock, and other non-cardiac factors. The cardiogenic or non-cardiogenic classification was determined clinically by physicians at the hospitals in collaboration with EMS providers, and was confirmed by the FDMA. In this study, the cardiogenic OHCA group included individuals of the working population alone (aged 20–69 years). After excluding those who did not receive OHCA resuscitation (n=4,907) or those who lacked a witness (n=109,761), the working population was further divided into four bystander groups (family, friends, colleagues, and passers-by). We focused on the absolute number and incidence of OHCA, the proportion that received CPR/AED, the 1-month survival rate following OHCA each year, and the characteristics of bystanders. The incidence of OHCA was calculated as follows: Absolute number of OHCAs in the 20–69 age group divided by the number of individuals in the entire 20–69 age group.

The population size was based on the estimated data obtained from the Statistics Bureau of Japan.[16 17] Neurological outcomes were evaluated by physicians based on the Cerebral Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2, moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or vegetative state; and Category 5, death or brain death.[10 13] Favourable neurological outcome at 1 month after admission was defined as Categories 1 or 2. Some abnormal values were noted in the data on the interval between the emergency call and patient contact (call to contact time), witness to call, time from witnessing an OHCA to bystander-initiated CPR, and time from witnessing an OHCA to initial defibrillation; therefore, we only analysed data recorded between 0 and 60 minutes. According to the FDMA, until 2012, patients with missing data on bystander use of AEDs constituted the group 'without bystander use of AEDs'; however, since 2013, they handled missing data as it is. To homogenise these data, we included all cases with missing AED data (n=8,180) in the group without bystander use of AEDs. The requirement for informed consent was waived owing to the use of anonymised data. This study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (approval number; UOEHCRB19-072).[18]

Statistical analysis

We used the Mann–Whitney *U* test to compare the averages of continuous variables between the study groups. Univariate and multivariate logistic regression models were used to estimate the relationship between prehospitalisation factors, such as age, sex, bystander CPR/AED, first documented rhythm, type of bystander, onset time (call time), time course, and 1-month survival with favourable neurological outcome after OHCA. All statistical analyses were conducted using Stata (version 16.1; StataCorp LLC, College Station, TX, USA).

Patient and public involvement

Patients and public were not involved in the design of this study.

RESULTS

Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and 2016, we excluded cases with missing essential data (n=62) or abnormal values for categorisation (n=8). Cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the total OHCA population (n=1,423,268), respectively. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20–69 years (working population) were enrolled in this study.

Overall trend of OHCA

The total general population reported by the Statistics Bureau of Japan declined from 127,768,000 in 2005 to 126,933,000 in 2016. A transient increase was observed in 2010 alone (n=128,057,000). Both the absolute number and the total incidence of OHCA had increased, from 102,737 (80 per 100,000 population) in 2005 to 123,552 (97 per 100,000 population) in 2016. Moreover, the absolute number and incidence of cardiogenic OHCA in all age groups increased from 56,412 (44 per 100,000 population) in 2005 to 75,109 (59 per 100,000 population) in 2016.

OHCA trend in the working population

In the OHCA population (n=1,423,268), the working population comprised 428,958 (30.1%) OHCA cases, whereas in the cardiogenic OHCA group (n=814,794), the working population comprised 212,961 (26.1%) OHCA cases.

Figure 1 shows that both the absolute number of cases and the incidence of cardiogenic OHCA in the working population mostly remained unchanged, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016. The proportion of CPR and AED performed for cardiogenic OHCA in the working population increased every year, from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively, and the 1-month survival and favourable neurological outcome of cardiogenic OHCA in the working population also increased from 7.8% and 4.5% in 2005 to 16.3% and 11.7% in 2016, respectively (**Figure 2**).

Sixty-five to 69 age group

The Statistics Bureau of Japan reported that the population aged 20–64 years declined from 77,829,000 in 2005 to 70,522,000 in 2016, whereas the population in the 65–69 age group increased, from 7,460,000 in 2005 to 10,275,000 in 2016. **Figure 3** shows the incidence of cardiogenic OHCA in each age group (in 5-year increments) in the working population.

There was no significant improvement in the incidence of cardiogenic OHCA over the last 12 years in any age group, and the incidence increased exponentially with increasing age.

Citizen bystander in OHCAs in the working population

Table 1.1 presents the characteristics (age, sex, CPR/AED proportion, and 1-month survival/neurological outcome) of the cardiogenic OHCA cases in the working population for each type of citizen bystander. The colleague bystander group had the highest percentage of both CPR and AED (56.6% and 10.2%, respectively). Furthermore, the colleague bystander group had the highest 1-month survival and best neurological outcome (28.1% and 20.8%, respectively). When time course data were available (n=13,698), the time course was identified for each citizen bystander group (**Table 1.2**). The colleague bystander group had a significantly longer median interval between witnessing an OHCA and initial defibrillation than the passers-by bystander group (13 vs. 12 minutes, $p < 0.001$).

Table 1.1. Characteristics of patients with cardiogenic OHCA in the working population according to bystander group

Characteristic	Bystander group			
	Family	Friends	Colleagues	Passers-by
Total, n	46,909	6,115	8,457	5,155
Age, years, median (Q1–Q3)	61 (52–66)	59 (48–65)	56 (48–62)	60 (52–65)
Sex, men, %	73.6	83.0	92.2	86.6
CPR, %	44.3	52.7	56.6	47.6
AED (bystander defibrillation), %	0.7	7.1	10.2	9.3
1-month survival rate, %	15.9	22.0	28.1	26.5
1-month neurological outcome (CPC 1+2, %)	10.1	15.8	20.8	18.5

Abbreviations: AED, automated external defibrillator; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

Table 1.2. Characteristics of patients with cardiogenic OHCA in the working population according to bystander group (time course data available)

Characteristic	Time course, minutes, median (Q1–Q3)			
Witness call	2 (1–4)	2 (1–4)	2 (1–4)	2 (1-4)
Call to contact	8 (7–10)	8 (6–11)	8 (6–10)	7 (6–9)
Witness-initiated CPR by bystander	3 (1–5)	2 (1–5)	2 (1–5)	2 (1–4)
Witness-initial defibrillation	13 (11–17)	13 (10–17)	13 (10–16)	12 (9–15)

Abbreviations: CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

In the multivariate logistic regression analysis, age, sex, bystander chest compression, shock by public-access AEDs, first documented rhythm, type of bystander, time from witnessing an OHCA to bystander-initiated CPR, time from witnessing an OHCA to initial defibrillation, and call to contact time were independently associated with 1-month survival with favourable neurological outcome in this study population (**Table 2**).

Table 2. Effect of prehospitalisation factors on 1-month survival with favourable neurological outcome after OHCA

Prehospitalisation factor	Crude OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Age (1-year increments)	0.97	0.97–0.98	<0.001	0.98	0.98–0.99	<0.001
Sex						
male	Ref.	–	–	Ref.	–	–
female	0.67	0.63–0.71	<0.001	1.35	1.21–1.52	<0.001
Bystander chest compression						
no	Ref.	–	–	Ref.	–	–
yes	2.26	2.16–2.37	<0.001	1.87	1.27–2.74	0.001
Shock by public-access AEDs						
no	Ref.	–	–	Ref.	–	–
yes	4.57	4.17–5.01	<0.001	1.73	1.48–2.02	<0.001
First documented rhythm						
VT/VF	Ref.	–	–	Ref.	–	–
PEA	0.16	0.15–0.17	<0.001	0.51	0.40–0.64	<0.001
asystole	0.03	0.03–0.04	<0.001	0.21	0.15–0.29	<0.001
Type of bystander						
family	Ref.	–	–	Ref.	–	–
friends	1.67	1.55–1.80	<0.001	1.26	1.11–1.44	<0.001
colleagues	2.33	2.19–2.47	<0.001	1.29	1.15–1.44	<0.001
passers-by	2.01	1.86–2.17	<0.001	1.25	1.08–1.45	0.003
Onset time						
0:00–7:59	0.75	0.71–0.79	<0.001	0.93	0.84–1.03	0.184
8:00–16:59	Ref.	–	–	Ref.	–	–
17:00–23:59	0.82	0.78–0.87	<0.001	0.93	0.85–1.03	0.157
Witness-initiated CPR by bystander time (1-minute increments)	0.91	0.90–0.92	<0.001	0.95	0.93–0.96	<0.001
Witness-initial defibrillation time (1-minute increments)	0.89	0.89-0.90	<0.001	0.97	0.95-0.98	<0.001
Call to contact time (1-minute increments)	0.87	0.86-0.89	<0.001	0.93	0.92-0.94	<0.001

Abbreviations: AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; Ref., reference; VT/VF, ventricular tachycardia/ventricular fibrillation.

DISCUSSION

Using data obtained from the Utstein registry, collected for 12 years between 2005 and 2016, we investigated OHCA in the Japanese working population with respect to age. We found that: (1) approximately 30% of all OHCA cases occurred in the working population, and the working population comprised 26% of all cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of cardiogenic OHCA in the working population remained mostly unchanged over the 12-year period; (3) in any age group in the working population, there was no significant improvement in the incidence of cardiogenic OHCA over the 12-year period, with the incidence of OHCA increasing exponentially with increasing age; (4) the proportion of CPR and the use of AEDs increased each year, and the prognosis after 1 month improved in the working population; and (5) among citizen bystanders, the colleague bystander group had the highest bystander CPR/AED proportion, highest 1-month survival rate, and best neurological outcome. However, colleague bystanders had a significantly longer time from witnessing an OHCA to initial defibrillation than the passers-by bystander group, and the time from witnessing an OHCA to initial defibrillation was independently associated with 1-month survival with favourable neurological outcome.

Causality of OHCA and its countermeasures in the working population

Acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At least one significant coronary artery lesion was found in 70% of all OHCA patients in the absence of an obvious extracardiac cause.[19] The Kumamoto Acute Coronary Events study of an acute myocardial infarction (AMI) registry revealed that the incidence of AMI decreased from 2004 to 2011 in both men and women.[20] The rate of ST segment elevation myocardial infarction decrease was attributed to the increased use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g. statins).[21-23] However, the Miyagi AMI registry reported that the incidence of AMI in both men and women who were < 59 years has continued to increase over the past 30 years, between 1985 and 2014. This was attributed to the high incidence of dyslipidaemia secondary to the westernisation of young peoples' diets and lifestyles, as well as high smoking rates (~50% and > 30% in young men and women, respectively).[24] Therefore, an improvement in the diet and the cessation of smoking could be important for reducing the incidence of cardiogenic OHCA in this population.

Compared to Western countries, ischaemic heart disease is less common in Japan,[25] whereas the prevalence of Brugada syndrome is relatively high.[26 27] Brugada syndrome was described by Pedro and Josep Brugada in 1992 as a disease that causes ventricular fibrillation despite the absence of obvious structural cardiac disease, electrolyte abnormalities, or QT prolongation.[28] The Brugada-type electrocardiogram (ECG; right bundle branch block and ST segment elevation in V1 through V3) may be closely associated with a sudden unexplained death syndrome, such as Lai Tai ('death during sleep') in northeast Thailand, Bangungut ('moaning and dying during sleep') in the Philippines, and Pokkuri ('sudden unexpected death at night') in Japan.[29] A troublesome characteristic of Brugada syndrome is its nocturnal tendency, which may delay therapeutic intervention and thus lead to worse prognosis. In the univariate analysis of this study, night-time onset of OHCA was associated with a worse prognosis than daytime onset, although this tendency was not detected in multivariate analysis (**Table 2**). A 12-lead ECG at screening, history of syncope, and family history of SCD could help identify patients who are in need of preventive pharmacological and non-pharmacological therapy (e.g. implantable cardioverter defibrillator).[30]

Previous meta-analyses of prospective cohort studies have revealed associations between work stressors and cardiovascular disease. The summary relative risk for long working hours (≥ 55 hours per week) compared with the standard 35–40 hours per week was 1.13 (95% confidence interval [CI]: 1.02–1.26).[31] The total working hours tended to decline in Japan [32] however, the reduction in the number of working hours was minor, and it is unknown whether it contributed significantly to the incidence of OHCA in the working population.

Analysis of OHCA in the 65–69 age group

In 2018, the Japanese Cabinet Office reported that the proportion of workers in the 65–69 age group was low; in the 5-year age groups, the proportions of male and female workers were 91.0% (55–59), 79.1% (60–64), and 54.8% (65–69) and 70.5% (55–59), 53.6% (60–64), and 34.4% (65–69), respectively.[33] Considering the extension of retirement age that will come into effect from 2021, the employment rates are expected to increase for people in the 65–69 age group. Thus, we investigated the characteristics of cardiogenic OHCA in the 65–69 age group.

In fact, the proportion of workers aged ≥ 65 years in the total labour force population has been increasing every year, from 7.6% in 2005 to 12.8% in 2018.[34] We identified that there was no significant improvement in the incidence of cardiogenic OHCA in any age group over the last 12 years, and the incidence increased exponentially with increasing age (**Figure 3**). A study of OHCA in Osaka Prefecture, Japan, that was conducted for 2 years revealed that the incidence of OHCA increased exponentially with increasing age.[35] This study revealed that the incidence of cardiogenic OHCA in any age group was almost constant over the 12-year period. It should be noted that the incidence of OHCA in the 65–69 age group (extended retirement age group) was high, and age was independently associated with 1-month survival with favourable neurological outcome (adjusted odds ratio [OR]: 0.98 [1-year increments], 95% CI: 0.98–0.99; $p < 0.001$). Therefore, it is important for companies with older employees to take this factor into account.

Effect of colleagues and other types of bystanders

The worst 1-month survival and neurological outcome was observed in the family bystander group. This unfavourable result could be attributed to the lowest CPR/AED proportion (44.3% and 0.7%) among all of the study groups. Another study reported a similar association for the bystander-patient relationship: family members had a worse 1-month survival and neurological outcome than friends and colleagues. They reported that large delays (≥ 5 minutes) in the witness call interval and a large witness bystander CPR interval were most frequent in the family bystander group.[36]

A previous systematic review revealed that the OHCA survival rate was better at the workplace,[3] and the findings of our study are similar, whereby colleague bystander was associated with a better 1-month survival and favourable neurological outcome. A possible reason for such a favourable prognosis is that the CPR/AED proportion was highest in the colleague bystander group. Furthermore, we found room for further improvement of the prognosis of OHCA in the colleague bystander group. The colleague bystander group had a significantly longer median interval between witnessing an OHCA and initial defibrillation than the passers-by bystander group (13 *vs.* 12 minutes, respectively; $p < 0.001$), and the time from witnessing an OHCA to initial defibrillation was independently associated with 1-month survival with favourable neurological outcome in the working population (adjusted OR: 0.97 [1-minute increments], 95% CI: 0.95–0.98; $p < 0.001$). A possible reason why colleagues took longer to perform the first defibrillation compared with passers-by is that most of the initial defibrillations were performed by EMS providers, and the median call to contact interval was significantly longer in the colleague bystander group than in the passers-by bystander group (8 *vs.* 7 minutes, respectively; $p < 0.001$). It is assumed that travel distance and time within the building contribute to the delay. Another study that used the model of a large-scale skyscraper calculated the length of time taken by the emergency services to reach a patient within the building (i.e. travel time). The minimum travel time was approximately 19 seconds, the intermediate value was 2 minutes, and the worst value was 4 minutes.[37]

Recently, the importance of CPR has become widely known, and the findings of this study supported this fact, given that the CPR proportion in the working population has increased over the years (**Figure 2**). However, our present study revealed that there were > 30% of cases wherein CPR was not performed despite the cardiogenic OHCA being witnessed by colleagues in 2016 (shown in **Supplementary Figure 1**). More opportunities for CPR awareness activities in companies may be useful to prevent cardiac death and poor neurological outcome in OHCA patients in the working population. A previous study reported that approximately two-thirds of OHCA survivors return to work,[38] which is crucially important in terms of public health and socioeconomic significance.

Limitations

This study has several limitations. First, this was a retrospective population-based study of data obtained from a prospective registry, with some instances where data were missing or abnormal values were present. Second, the actual employment status of the OHCA patients in the 20–69 age group (working population) was unknown. Third, the Utstein registry did not contain information on individual medical therapy, activities of daily living before the OHCA, or the details of in-hospital treatment interventions. Finally, there may be unmeasured confounding factors that may have influenced the 1-month survival with favourable neurological outcome.

CONCLUSIONS

Over the 12-year period (2005–2016), both the absolute number and incidence of cardiogenic OHCA in the working population remained mostly unchanged, whereas the prognosis of OHCA at 1-month improved. Among citizen bystanders, the colleague bystander group had the highest CPR/AED proportion, highest 1-month survival rate, and best neurological outcome, despite a significantly longer time from witnessing an OHCA to initial defibrillation than the passers-by bystander group. Reducing the time from witnessing an OHCA to initial defibrillation may further improve the prognosis of patients with an OHCA witnessed by a colleague.

ACKNOWLEDGEMENTS

We wish to thank all of the emergency medical service personnel and the Fire and Disaster Management Agency of Japan for their cooperation in collecting data and managing the Utstein-style registry.

COMPETING INTERESTS

The authors have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHORS' CONTRIBUTIONS

YY was involved in data analysis and writing of the manuscript. YO was involved in data verification, the design of the study, supervision, and revising the manuscript. YF was involved in data verification, supervision, and statistical analysis. KY, TM, and KT were involved in data verification. HO and RK were involved in data verification and supervision. HA was involved in data verification, supervision, and revising the manuscript.

DATA SHARING

The data used in this study are not publicly available. The data are only accessible through the Fire and Disaster Management Agency (2-1-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan; Tel.: +03-5253-7529; Fax: +03-5253-7532; E-mail: fdma-goiken@ml.soumu.go.jp). Therefore, no additional data are available.

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Figure. 1

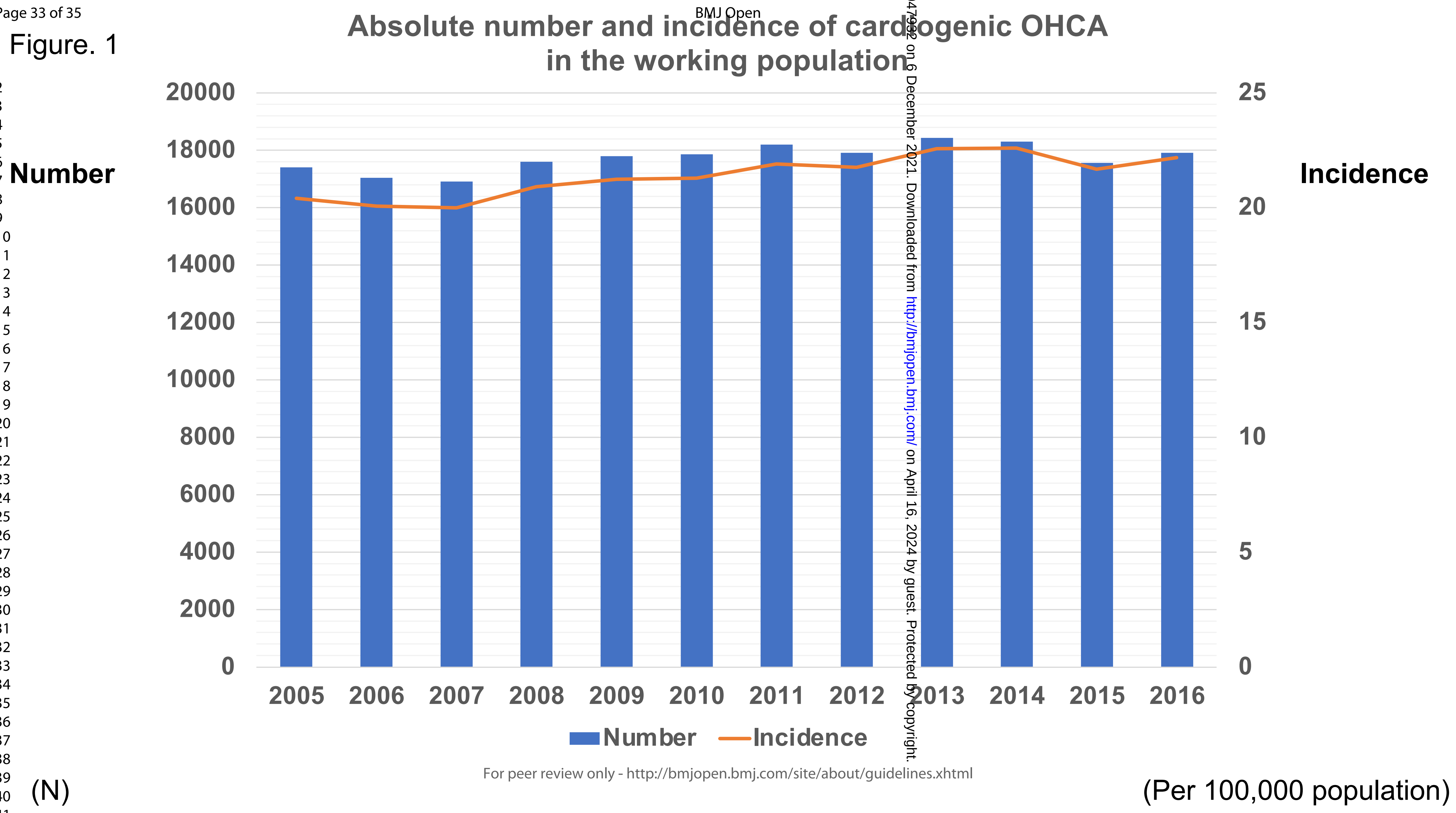

Absolute number and incidence of cardiogenic OHCA
in the working population
Number
Incidence
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
25
20
15
10
5
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Number
Incidence
(N)
(Per 100,000 population)

Figure. 2

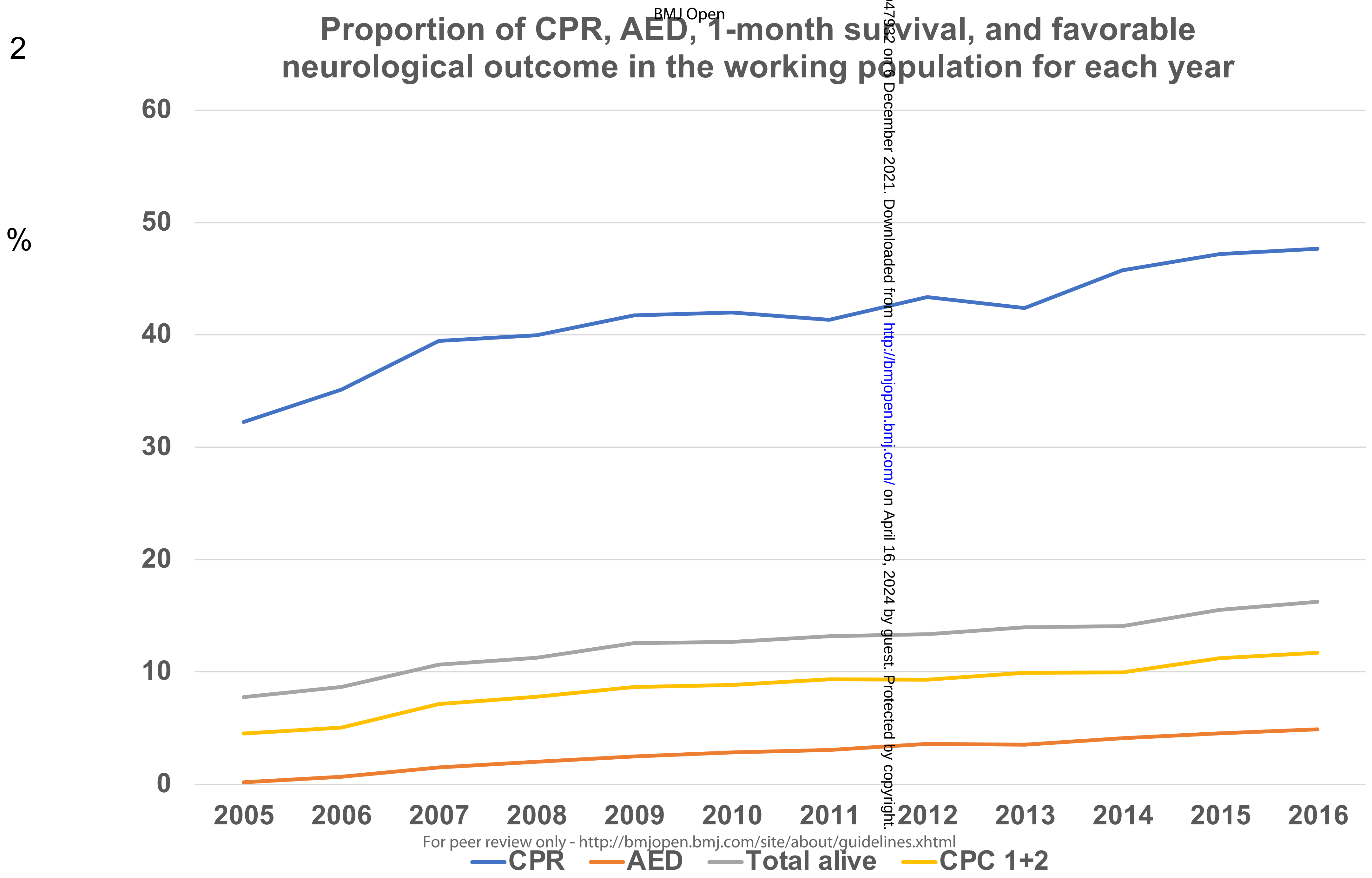
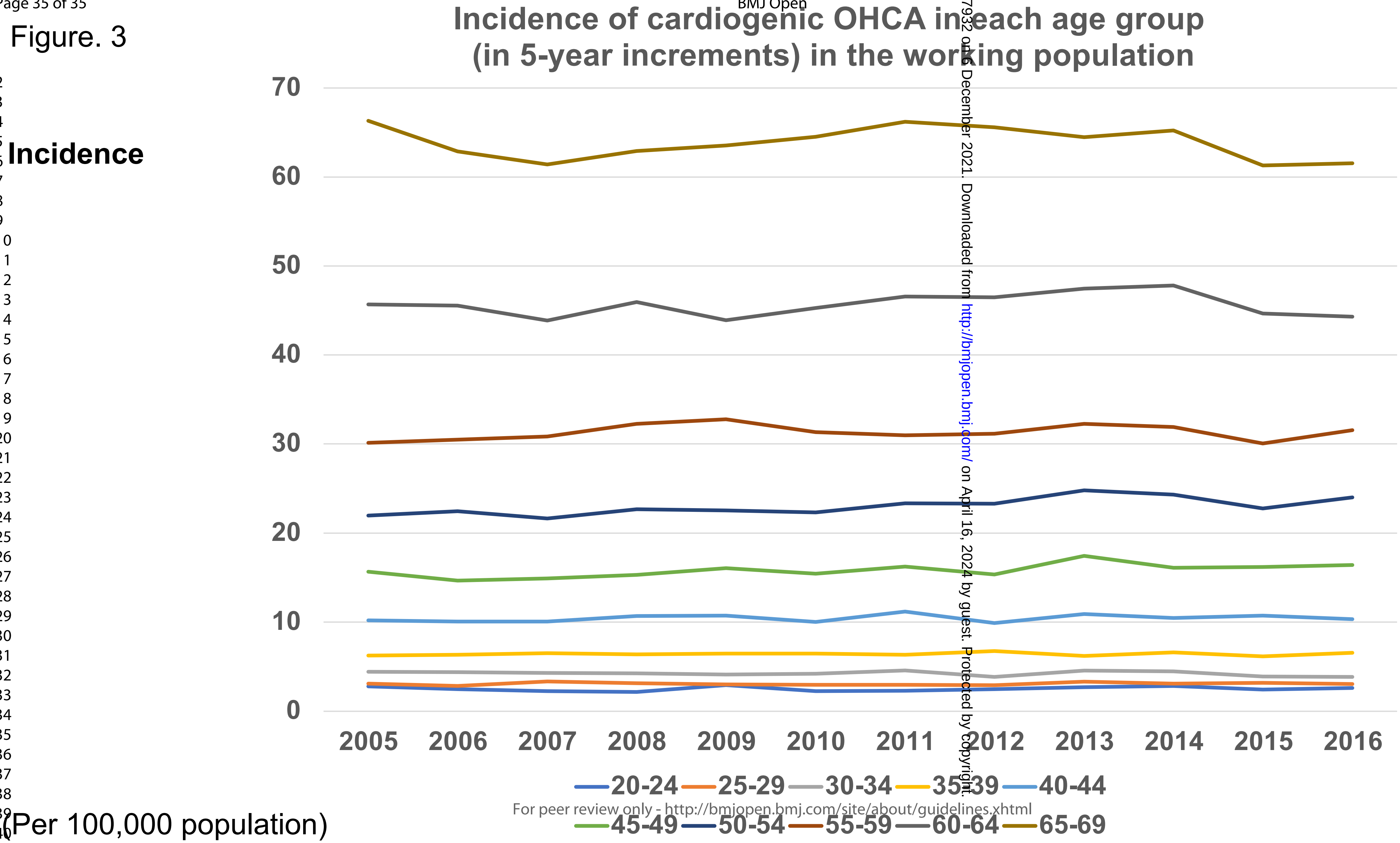
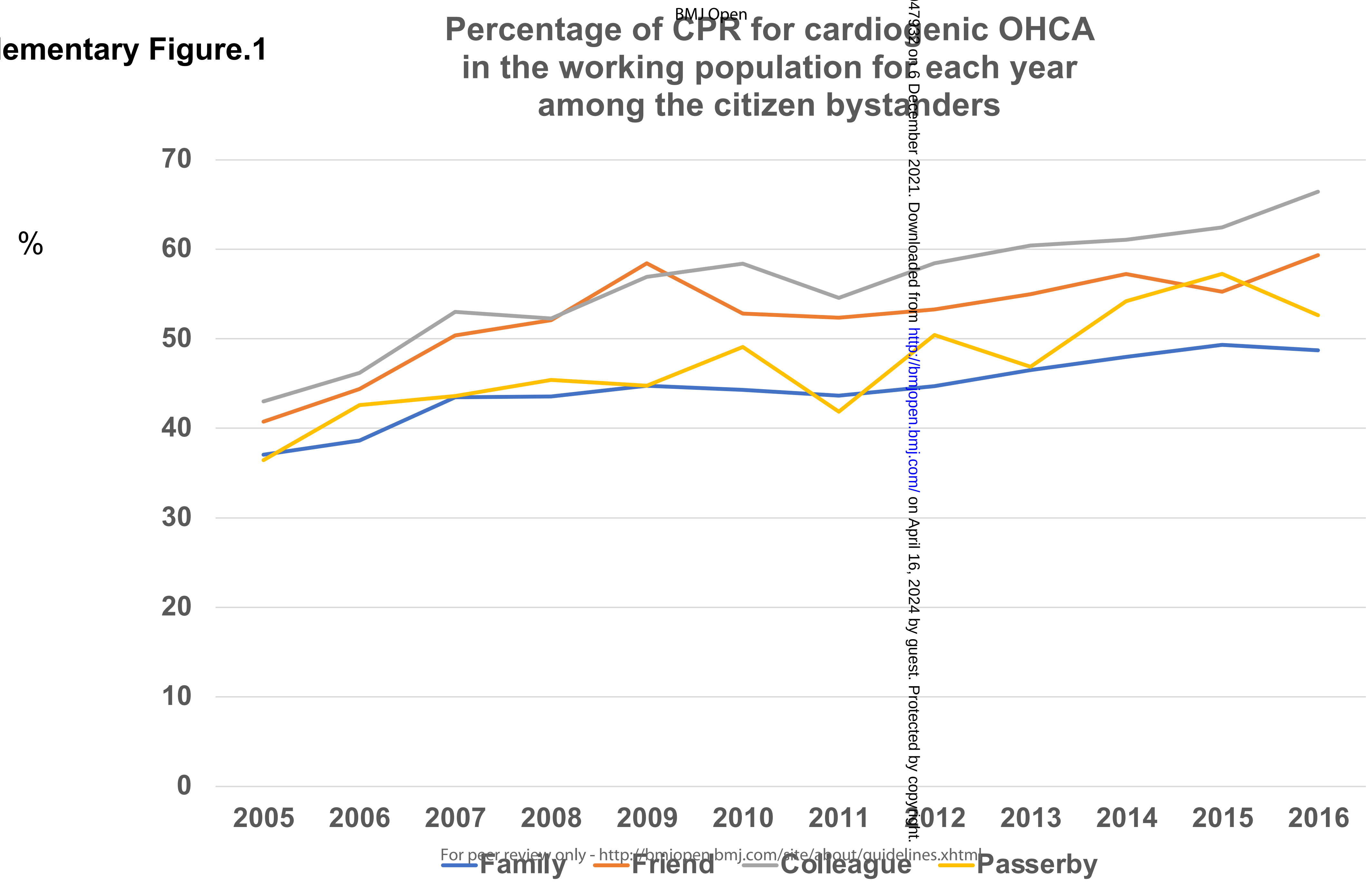

Proportion of CPR, AED, 1-month survival, and favorable neurological outcome in the working population for each year
%
60
50
40
30
20
10
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
CPR
AED
Total alive
CPC 1+2

Figure. 3


Incidence of cardiogenic OHCA in each age group
(in 5-year increments) in the working population
Incidence
(Per 100,000 population)
70
60
50
40
30
20
10
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69

Supplementary Figure.1



BMJ Open

The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047932.R1
Article Type:	Original research
Date Submitted by the Author:	26-Aug-2021
Complete List of Authors:	Yamagishi, Yasunobu; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Oginosawa, Yasushi; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Fujino, Yoshihisa; University of Occupational and Environmental Health Japan, Department of Environmental Epidemiology, Institute of Industrial Ecological Sciences Yagyu, Keishiro; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Miyamoto, Taro; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Tsukahara, Keita ; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Ohe, Hisaharu ; University of Occupational and Environmental Health Japan, The Second Department of Internal Medicine Kohno, Ritsuko; University of Occupational and Environmental Health Japan, Department of Heart Rhythm Management Abe, Haruhiko; University of Occupational and Environmental Health Japan, Department of Heart Rhythm Management
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Occupational and environmental medicine, Epidemiology, Public health
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Cardiology < INTERNAL MEDICINE, OCCUPATIONAL & INDUSTRIAL MEDICINE

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The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study

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Word count: 3641words

ABSTRACT

Objectives: The prevention and improvement of the prognosis of out-of-hospital cardiac arrests (OHCAs) are important issues especially with respect to their social and economic significance in working populations. The age distribution of the working population in Japan is expected to change continually due to its aging society and extension of retirement; however, few reports have examined the long-term condition of OHCA in the working population, defined by age. The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution.

Design and setting: We analysed the All-Japan Utstein registry, a prospective, nationwide, population-based, observational registry (2005–2016).

Participants: From the registry, 212,961 OHCA patients from the Japanese working population (defined aged 20–69 years), with only cardiogenic aetiology participated in this study. These patients were further divided into four groups according to the type of citizen bystander (family, friends, work-colleagues, and passers-by).

Primary and secondary outcome measures: The main outcomes were 1-month survival with favourable neurological outcomes.

Results: The incidence of OHCAs, in any age group, was almost constant during the 12-year period. The work-colleagues had the best prognosis despite having significantly longer times to initial defibrillations compared with the passers-by (13 vs. 12 min, respectively, *P* <0.001) that was associated independently with 1-month survival with favourable neurological outcomes (adjusted odds ratio: 0.94 [1-min increments], *P* <0.001).

Conclusions: In the 12-year period, the incidence of OHCAs in any age group remained almost constant, whereas the prognosis improved each year. Reducing the time to initial defibrillation may further improve the prognosis of OHCAs with a work-colleague bystander.

Keywords: Cardiopulmonary resuscitation, defibrillation, Japan, out-of-hospital cardiac arrest, prognosis, prospective registry, working population.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- In this population-based study, we analysed data collected between 2005 to 2016 in the All-Japan Utstein registry of the Fire and Disaster Management Agency; a prospective, nationwide, population-based registry.
- A large sample size and longer follow-up allowed for the detailed assessment of the relationship between a work-colleague bystander and the prognosis following an out-of-hospital cardiac arrest (OHCA) in the Japanese working population.
- We assessed independent factors associated with 1-month survival with favourable neurological outcomes after OHCAs in the Japanese working population.
- The All-Japan Utstein registry did not contain information on the actual employment status, individual medical therapy, activities of daily living before the OHCAs, or in-hospital treatment interventions.

INTRODUCTION

The prevention and improvement of the prognosis of out-of-hospital cardiac arrests (OHCAs) are important issues especially with respect to their social and economic significance in working populations.

Japan and other developed countries have aging populations.[1] Out of concern for future labour shortages due to the aging population, the Japanese parliament enacted a partial amendment to the law with respect to the stabilisation of the employment of elderly persons that recommended an extension of the retirement age from 65 to 70 years. This reform bill came into effect for companies from April 1, 2021. In addition, a study reported that patients aged ≥ 65 years comprised approximately 76% of patients with OHCAs in Japan.[2] Although the age distribution of the working population is expected change continuously, few reports have examined the long-term condition of OHCAs in the working population, according to age.

We defined the working population as individuals aged 20–69 years previously, and we analysed relatively short-term cardiogenic OHCAs in the Japanese working population using data from the Utstein registry, in Japan — a prospective, nationwide, population-based OHCA registry — between 2005 and 2008.[3] Although this earlier study revealed that the incidence of OHCAs in the working population was the highest during winter, on Sundays and Mondays, and during the early hours of the morning, it did not report on the prognosis of the OHCAs.

The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution.

METHODS

The population of Japan in 2019 was estimated to be 126.2 million, of which 67.33 million were employed, including both part-time and full-time workers.[4] In 2019, 726 fire stations with emergency dispatch centres provided emergency services 24 hours a day.[5] OHCA patients who underwent resuscitation attempts by emergency medical service (EMS) personnel were transported to hospitals and then registered in the Utstein registry.

In this population-based study, we analysed data collected between 2005 and 2016 from the All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA); a prospective, nationwide, population-based registry of OHCA victims based on the standardised Utstein style.[6] As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation. The person who performed the basic cardiopulmonary resuscitation, or defibrillation using a public-access AEDs was defined as a bystander. The EMS personnel followed-up these OHCA patients for 1 month to ascertain the survival rates and neurological outcomes. The data of 1,423,338 patients were collected between January 1, 2005 and December 31, 2016.

We excluded the non-cardiogenic OHCA group, and only the cardiogenic OHCA group participated in our present study. As reported in a previous study,[9] the cardiogenic group was defined as those having confirmed absence of signs of circulation, with the following exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and other non-cardiac factors. The cardiogenic or non-cardiogenic classification was determined clinically by physicians at the hospitals in collaboration with the EMS providers and was confirmed by the FDMA. In this study, the cardiogenic OHCA group of the working population (aged 20–69 years) were analysed. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). We focused on the absolute number and incidences of OHCAs, the proportion that received CPR/AEDs, the 1-month survival rate following the OHCAs each year, and the characteristics of the bystanders. The incidence of the OHCAs was calculated as follows: the absolute number of OHCAs in the 20–69 age group divided by the number of individuals in the entire 20–69 age group.

The population size was based on the estimated data obtained from the Statistics Bureau of Japan.[10,11] The neurological outcomes were evaluated by physicians based on the Cerebral Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2, moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes at 1 month after admission were defined as Categories 1 or 2. Since some abnormal values were noted in the data in the intervals between the emergency calls and the patient contact times (call to contact time), witness to call times, times from witnessing OHCAs to bystander-initiated CPRs, and times from witnessing OHCAs to the times of the initial defibrillations, we only analysed the data recorded between 0 and 60 min (**Supplementary Table 1**). According to the FDMA (Fire and Disaster Management Agency), until 2012, patients with null values for bystander use of AEDs were converted automatically into the group 'without bystander use of AEDs'; however, since 2013, they did not automatically convert the null value into the group ‘without bystander use of AEDs’ and these data were handled as missing data. To homogenise these data, we included all the cases with missing AED data (n = 8,180) in the group without bystander use of AEDs. The requirement for informed consent was waived due to the use of anonymised data. This study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (approval number; UOEHCRB19-072).[12]

Statistical analysis

We used the Mann-Whitney U test to compare the differences between the two independent groups, when the dependent variable was either ordinal or continuous but not normally distributed. The incidence rate ratios (IRRs) for the incidence of cardiogenic OHCAs were estimated using a Poisson regression analysis, with the age groups separated by five years and a dummy variable for the year included in the model. A log-transformed version of each age group (in 5-year increments) for each year, was obtained from the official statistics, was used as the offset. Univariate and multivariable logistic regression models were used to estimate the relationships between the prehospitalisation factors, such as age, sex, bystander chest compressions, shock by public-access AEDs, first documented rhythms, types of bystander, onset times of day, onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to the initial defibrillations, call to contact times, and 1-month survival with favourable neurological outcomes after OHCAs. For the multivariable regression models, Cook's distance and variance inflation factors (VIFs) were determined to ascertain the presence of influential observations and multicollinearity, respectively. All the statistical analyses were conducted using Stata (version 16.1; StataCorp LLC, College Station, TX, USA).

Patient and public involvement

The patients and the public were not involved in the design of this study.

RESULTS

Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and 2016, we excluded cases with missing age data (n = 62) or patients who were over 120 years old (n = 8). The cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the total OHCA population (n = 1,423,268), respectively. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20–69 years (working population) were enrolled in this study. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked ~~a~~ witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). **Figure 1** shows a flow diagram of patients with OHCAs.

Overall trend of OHCAs

The total general population reported by the Statistics Bureau of Japan declined from 127,768,000 in 2005 to 126,933,000 in 2016, while a transient increase was observed in 2010 alone (n = 128,057,000). Both the absolute number and the total incidence of OHCAs increased, from 102,737 (80 per 100,000 population) in 2005 to 123,552 (97 per 100,000 population) in 2016. Moreover, the absolute number and incidence of cardiogenic OHCAs in all age groups increased from 56,412 (44 per 100,000 population) in 2005 to 75,109 (59 per 100,000 population) in 2016.

OHCA trend in the working population

Of the OHCA population (n = 1,423,268), the working population comprised 428,958 (30.1%) of the OHCA cases, whereas in the cardiogenic OHCA group (n = 814,794), the working population comprised 212,961 (26.1%) OHCA cases.

Figure 2 shows that both the absolute number of cases and the incidence of cardiogenic OHCA in the working population mostly remained unchanged, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016. The proportion of CPRs and AEDs performed for the cardiogenic OHCAs in the working population increased every year, from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively, and the 1-month survival and favourable neurological outcomes of the cardiogenic OHCAs in the working population also increased from 7.8% and 4.5% in 2005 to 16.3% and 11.7% in 2016, respectively (**Figure 3**).

Sixty-five to 69 age group

The Statistics Bureau of Japan reported that the population aged 20–64 years declined from 77,829,000 in 2005 to 70,522,000 in 2016, whereas the population in the 65–69 age group increased, from 7,460,000 in 2005 to 10,275,000 in 2016. **Table 1** shows the incidence of cardiogenic OHCAs in each age group (in 5-year increments) in the working population. A Poisson regression analysis revealed that there were no significant improvements in the incidence of cardiogenic OHCAs over the last 12 years in any age group, and the IRRs for the incidence of cardiogenic OHCAs in age groups separated by five years, was 1.08.

Table 1. Incidence of cardiogenic OHCAs in each age group (in 5-year increments) in the working population

	Incidence by year (per 100,000 population)											
Age (years)	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
20-24	2.8	2.5	2.3	2.2	2.9	2.3	2.3	2.5	2.7	2.8	2.4	2.6
25-29	3.1	2.8	3.3	3.1	3.0	3.0	3.0	2.9	3.3	3.1	3.2	3.1

30-34	4.5	4.4	4.3	4.2	4.1	4.2	4.6	3.9	4.6	4.5	3.9	3.9
35-39	6.3	6.4	6.5	6.4	6.5	6.5	6.3	6.8	6.2	6.6	6.2	6.6
40-44	10.2	10.1	10.1	10.7	10.8	10.0	11.2	9.9	10.9	10.5	10.7	10.3
45-49	15.7	14.7	14.9	15.3	16.1	15.4	16.2	15.4	17.5	16.1	16.2	16.4
50-54	22.0	22.4	21.6	22.7	22.6	22.4	23.3	23.3	24.8	24.3	22.8	24.0
55-59	30.2	30.5	30.9	32.3	32.8	31.4	31.0	31.2	32.3	31.9	30.1	31.6
60-64	45.7	45.5	43.9	45.9	43.9	45.3	46.6	46.5	47.4	47.8	44.7	44.3
65-69	66.3	62.9	61.4	62.9	63.5	64.5	66.2	65.6	64.5	65.2	61.3	61.5

Abbreviations: OHCA, out-of-hospital cardiac arrest.

Citizen bystander in OHCAs in the working population

Table 2.1 presents the characteristics (age, sex, CPR/AED proportions, and 1-month survival/neurological outcomes) of the cardiogenic OHCA cases in the working population for each type of citizen bystander. The work-colleague bystander group had the highest percentage for both CPRs and AEDs (56.6% and 10.2%, respectively). Furthermore, the work-colleague bystander group had the highest 1-month survival and best neurological outcomes (28.1% and 20.8%, respectively). When the time course data were available (n = 13,698), the time course was identified for each citizen bystander group (**Table 2.2**). The work-colleague bystander group had significantly longer median intervals between witnessing OHCAs and the initial defibrillations than the passers-by bystander group (13 vs. 12 min, respectively, $P < 0.001$).

Table 2.1. Characteristics of patients with cardiogenic OHCAs in the working population according to the bystander group

Characteristic	Bystander group			
	Family	Friends	Work-colleagues	Passers-by
Total, n	46,909	6,115	8,457	5,155
Age, years, median (Q1–Q3)	61 (52–66)	59 (48–65)	56 (48–62)	60 (52–65)
Sex, men, %	73.6	83.0	92.2	86.6
CPR, %	44.3	52.7	56.6	47.6
AED (bystander defibrillation), %	0.7	7.1	10.2	9.3
1-month survival rate, %	15.9	22.0	28.1	26.5
1-month neurological outcome (CPC 1+2, %)	10.1	15.8	20.8	18.5

Abbreviations: AED, automated external defibrillator; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

Table 2.2. Characteristics of patients with cardiogenic OHCAs in the working population according to the bystander group (time course data available)

Characteristic	Family	Friends	Work-colleagues	Passers-by
	Time course, min, median (Q1–Q3)			
Witness call	2 (1–4)	2 (1–4)	2 (1–4)	2 (1-4)
Call to contact	8 (7–10)	8 (6–11)	8 (6–10)	7 (6–9)
Witness-initiated CPR by bystander	3 (1–5)	2 (1–5)	2 (1–5)	2 (1–4)
Witness-initial defibrillation	13 (11–17)	13 (10–17)	13 (10–16)	12 (9–15)

Abbreviations: CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

Using a multivariable logistic regression, 13,698 patients were analysed. There were 11,808 (86.2%) males, 13,509 (98.6%) patients received bystander chest compression, 1,062 (7.8%) were shocked by public-access AEDs (automated external defibrillator), 13,698 first documented rhythms were analysed. The VT/VF rhythm was 11,882 (86.7%), PEA 741 (5.4%), asystole 834 (6.1%), and others 241 (1.7%). There were 8,564 (62.5%) family bystanders, 1,551 (11.3%) friends bystanders, 2,465 (18.0%) work-colleagues bystanders, and 1,118 (8.2%) passers-by bystanders. With respect to the onset time of day, 13,698 were analysed, of which the time period 0:00-7:59 comprised 3,835 (28.0%), 8:00-16:59 5,696 (41.6%), and 17:00-23:59 4,167 (30.4%). Age, sex, bystander chest compressions, shock by

219 public-access AEDs, first documented rhythms, types of bystander, onset years, times from
220 witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to initial
221 defibrillations, and the call to contact times were associated independently with 1-month
222 survival with favourable neurological outcomes in this study population (**Table 3**).
223 According to the Cook's distance calculation, none were above 0.5. The mean VIF was 1.27
224 and none of the variables exceeded a VIF of 3.

225

Table 3. Effect of prehospitalisation factors on the 1-month survival with favourable neurological outcomes after OHCAs

Prehospitalisation factor	Crude OR	95% CI	*P*-value	Adjusted OR	95% CI	*P*-value
Age (10-year increments)	0.98	0.98–0.99	<0.001	0.98	0.98–0.99	<0.001
Sex						
male	Ref.	–	–	Ref.	–	–
female	1.16	1.04-1.29	0.006	1.33	1.19–1.50	<0.001
Bystander chest compression						
no	Ref.	–	–	Ref.	–	–
yes	1.77	1.23–2.56	0.002	1.54	1.05–2.22	0.027
Shock by public-access AEDs						
no	Ref.	–	–	Ref.	–	–

yes	1.72	1.51–1.95	<0.001	1.53	1.31–1.77	<0.001
First documented rhythm						
VT/VF	Ref.	–	–	Ref.	–	–
PEA	0.35	0.28–0.43	<0.001	0.49	0.39–0.61	<0.001
asystole	0.13	0.09–0.17	<0.001	0.21	0.15–0.29	<0.001
Others	2.16	1.67-2.79	<0.001	1.73	1.31-2.29	<0.001
Type of bystander						
family	Ref.	–	–	Ref.	–	–
friends	1.42	1.26–1.59	<0.001	1.28	1.13–1.46	<0.001
work-colleagues	1.55	1.41–1.71	<0.001	1.28	1.15–1.44	<0.001
passers-by	1.69	1.48–1.93	<0.001	1.25	1.08–1.45	0.003
Onset time of day						
0:00–7:59	0.76	0.69–0.84	<0.001	0.92	0.83–1.03	0.141
8:00–16:59	Ref.	–	–	Ref.	–	–
17:00–23:59	0.90	0.82–0.98	0.018	0.93	0.84–1.02	0.116
Onset year (1-year increments)	1.08	1.07-1.09	<0.001	1.09	1.08-1.11	<0.001
Witness-initiated CPR by bystander time (1-min increments)	0.91	0.90–0.92	<0.001	0.96	0.95–0.98	<0.001

Witness-initial defibrillation time (1-min increments)	0.89	0.89-0.90	<0.001	0.94	0.93-0.95	<0.001
Call to contact time (1-min increments)	0.87	0.86-0.89	<0.001	0.93	0.91-0.95	<0.001

Abbreviations: AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; Ref., reference; VT/VF, ventricular tachycardia/ventricular fibrillation.

DISCUSSION

Using the data obtained from the Utstein registry, that were collected for 12 years between 2005 and 2016, we investigated OHCAs in the Japanese working population with respect to age. We found that: (1) approximately 30% of all the OHCA cases occurred in the working population, and that the working population comprised 26% of all the cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of cardiogenic OHCAs in the working population remained mainly unchanged over the 12-year period; (3) in any age group in the working population, there was no significant improvement in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased each year, and the prognosis after 1 month improved in the working population; and (5) among the citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes. However, the work-colleague bystanders had a significantly longer time from witnessing OHCAs to the initial defibrillations than the passers-by bystander group, and the time from witnessing OHCAs to initial defibrillations was associated independently with 1-month survival with favourable neurological outcomes.

Causality of OHCAs and their countermeasures in the working population

The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At least one significant coronary artery lesion was found in 70% of all OHCA patients in the absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial infarction decrease was attributed to the increased use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g. statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the incidence of AMIs in both men and women who were < 59 years continued to increase. This was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of young peoples' diets and lifestyles, as well as the high smoking rates (~50% and > 30% in

256 young men and women, respectively).[18] Therefore, an improvement in the diet and the cessation of smoking may be important in the reduction of the incidence of cardiogenic OHCAs in this population.

259 Compared to Western countries, ischaemic heart disease is less common in Japan,[19] whereas the prevalence of the Brugada syndrome is relatively high.[20,21] The Brugada syndrome was described by Pedro and Josep Brugada in 1992, as a disease that causes ventricular fibrillation despite the absence of obvious structural cardiac diseases, electrolyte abnormalities, or QT prolongations.[22] The Brugada-type electrocardiogram (ECG; right bundle branch block and ST segment elevation in V1 through V3) may be associated closely with a sudden unexplained death syndrome, such as Lai Tai ('death during sleep') in northeast Thailand, Bangungut ('moaning and dying during sleep') in the Philippines, and Pokkuri ('sudden unexpected death at night') in Japan.[23] A troublesome characteristic of the Brugada syndrome is its nocturnal tendency, which may delay therapeutic interventions and thus lead to worse prognosis. In the univariate analysis of this study, a night-time onset (0:00–7:59 and 17:00–23:59) of OHCAs was associated with a worse prognosis than a daytime onset (8:00–16:59), although this tendency was not shown in the multivariable analysis (**Table 3**). Using a 12-lead ECG at screening, a history of syncope, and a family history of sudden cardiac death may help identify patients who are in need of preventive

274 pharmacological and non-pharmacological therapy (e.g. use of an implantable cardioverter defibrillator).[24]

276 Previous meta-analyses of prospective cohort studies have revealed associations between work stressors and cardiovascular diseases. The summary relative risk for long working hours (≥ 55 hours per week) compared with the standard 35–40 hours per week was 1.13 (95% confidence interval [CI]: 1.02–1.26).[25] The total working hours tended to decline in Japan [26] however, the reduction in the number of working hours was minor, and it is unknown whether it contributed significantly to the incidence of OHCAs in the working population.

282 **Analysis of OHCAs in the 65–69 age group**

283 In 2018, the Japanese Cabinet Office reported that the proportion of workers in the 65–69 age group was low; in the 5-year age groups, the proportions of male and female workers were 91.0% (55–59), 79.1% (60–64), and 54.8% (65–69) and 70.5% (55–59), 53.6% (60–64), and 34.4% (65–69).[27] Considering the extension of the retirement age that came into effect from 2021, the employment rates are expected to increase for people in the 65–69 age group. Thus, we investigated the characteristics of cardiogenic OHCAs in the 65–69 age group.

289 In fact, the proportion of workers aged ≥ 65 years in the total labour force population has been increasing every year, by 7.6% in 2005 to 12.8% in 2018.[28] We identified that there were no significant improvements in the incidence of cardiogenic OHCAs in any age group

292 over the last 12 years, and the incidence increased with increasing age (**Table 1**). A study of
293 OHCAs in the Osaka Prefecture, Japan, that was conducted for two years revealed that the
294 incidence of OHCAs increased exponentially with increasing age.[29] Our present study
295 revealed that the incidence of cardiogenic OHCAs in any age group was almost constant over
296 the 12-year period. It should be noted that the incidence of OHCAs in the 65–69 age group
297 (extended retirement age group) was high, and that age was associated independently with
298 1-month survival with favourable neurological outcomes (adjusted odds ratio [OR]: 0.98
299 [10-year increments], 95% CI: 0.98–0.99; $P < 0.001$). Therefore, it is important for
300 companies with older employees to take this into account. Nevertheless, this is not a problem
301 that is limited to Japan; the aging of the population is progressing worldwide, especially in
302 developed countries.[1] In the future, there is a possibility that the retirement age will be
303 extended in many countries around the world.

304 **Effect of work-colleagues and other types of bystanders**

305 A previous study found that a key predictor of survival after OHCAs is the bystander
306 witness.[30] Another previous study reported that most of the cases of OHCAs in Japan that
307 were witnessed by family members and family bystanders had a worse prognosis than those
308 witnessed by other bystanders.[7] Moreover, in our present study, the worst 1-month survival
309 and neurological outcomes was observed in the family bystander group. This unfavourable
310 result may be attributed to the lowest CPR/AED proportions (44.3% and 0.7%, respectively).

Another study that reported a similar association for the bystander-patient relationship indicated that the large delays (≥ 5 min) in the witness call interval and large witness bystander CPR interval were most frequent in the family bystander group.[31]

A previous systematic review revealed that the OHCA survival rate was better in the workplace,[32] and the findings of our study were similar: work-colleague bystanders were associated with a better 1-month survival and favourable neurological outcomes. A possible reason for such a favourable prognosis was that the CPR/AED proportion was highest in the work-colleague bystander group. Furthermore, we found further improvements in the prognosis of OHCAs in the work-colleague bystander group. The work-colleague bystander group had significantly longer median intervals between the witnessing OHCAs and initial defibrillations than the passers-by bystander group (13 vs. 12 min, respectively; $P < 0.001$). It is known that a 1-min delay can reduce the survival rate by 7–10%,[33] and the results from Table 3 also indicate that a 1-min difference does have a clinically meaningful benefit for 1-month survival with favourable neurological outcomes (adjusted OR: 0.94 [1-min increments], 95% CI: 0.93–0.95; $P < 0.001$). A possible reason why work-colleagues took longer to perform the first defibrillation compared with passers-by may have been due to most of the initial defibrillations being performed by EMS providers, and that the median call to contact intervals were significantly longer in the work-colleague bystander group than in the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$). The travel distance and time to travel within buildings may also have contributed to the delays. Another study that used the model of a large-scale skyscraper, calculated the length of time taken by the emergency services to reach a patient within the building (i.e. travel time) and found that the minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]

Recently, the importance of CPR has become known widely, and the findings of this study supported this, given that the CPR proportion in the working population has increased over the years (**Figure 3**). However, our present study revealed that in 2016 in > 30% of the cases CPR was not performed despite the witnessing of the cardiogenic OHCAs by work-colleagues (shown in **Supplementary Figure 1**). More opportunities for CPR awareness activities in companies may be useful in preventing cardiac death and poor neurological outcomes in OHCA patients in the working population. A previous study reported that approximately two-thirds of OHCA survivors return to work,[35] which is important in terms of public health and socioeconomic significance.

Limitations

This study had several limitations. First, this was a retrospective population-based study of data obtained from a prospective registry, with some instances where data were missing or abnormal values were present. Second, the actual employment status of the OHCA patients in the 20–69 age group (working population) was unknown. Third, the Utstein registry did not contain any information on individual medical therapy, and activities of daily living before the OHCAs, or the details of the in-hospital treatment interventions. Finally, there may have been unmeasured confounding factors that may have influenced the 1-month survival with favourable neurological outcomes.

CONCLUSIONS

Over the 12-year period (2005–2016), both the absolute number and incidence of cardiogenic OHCAs in the working population remained mainly unchanged, whereas the prognosis of OHCAs at 1-month improved. Among the citizen bystanders, the work-colleague bystander group showed the highest CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes, despite significantly longer times from witnessing OHCAs to initial defibrillations than the passers-by bystander group. Reducing the time from witnessing OHCAs to initial defibrillations may further improve the prognosis of patients with OHCAs that have been witnessed by work-colleagues.

ACKNOWLEDGMENTS

We wish to thank all of the emergency medical service personnel and the Fire and Disaster Management Agency of Japan for their cooperation in collecting data and managing the Utstein-style registry.

COMPETING INTERESTS

The authors have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHORS' CONTRIBUTIONS

YY was involved in data analysis and writing of the manuscript. YO was involved in data verification, the design of the study, supervision, and revising the manuscript. YF was involved in data verification, supervision, and statistical analysis. KY, TM, and KT were involved in data verification. HO and RK were involved in data verification and supervision. HA was involved in data verification, supervision, and revising the manuscript.

DATA SHARING

The data used in this study are not publicly available. The data are only accessible through the Fire and Disaster Management Agency (2-1-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan; Tel.: +03-5253-7529; Fax: +03-5253-7532; E-mail: fdma-goiken@ml.soumu.go.jp). Therefore, no additional data are available.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (approval number; UOEHCRB19-072).

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LEGENDS

Figure 1. A flow diagram of patients with OHCAs

Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and 2016, we excluded cases with missing data of age (n=62) or patients who were over 120 years old (n=8). Cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the total OHCA population (n=1,423,268), respectively. We excluded non-cardiogenic OHCA group. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20–69 years (working population) were enrolled in this study. After excluding those who did not receive OHCA resuscitation (n = 4,907) or those who lacked a witness (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.

Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working population. Both the absolute number and incidence of cardiogenic OHCAs in the working population were mostly unchanged over the period of 12 years, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016. Abbreviation: OHCA, out-of-hospital cardiac arrest.

Figure 3. Proportion of CPR, AED, 1-month survival, and favourable neurological outcome in the working population for each year. The percentage of CPR and AED increased each year from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively. One-month survival rate of cardiogenic OHCAs in the working population increased from 7.8% in 2005 to 16.3% in 2016, and the 1-month survival with favourable neurological outcome also increased from 4.5% in 2005 to 11.7% in 2016. Abbreviations: CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; CPC, cerebral performance category.

Figure. 1

A flow diagram of patients with OHCAs

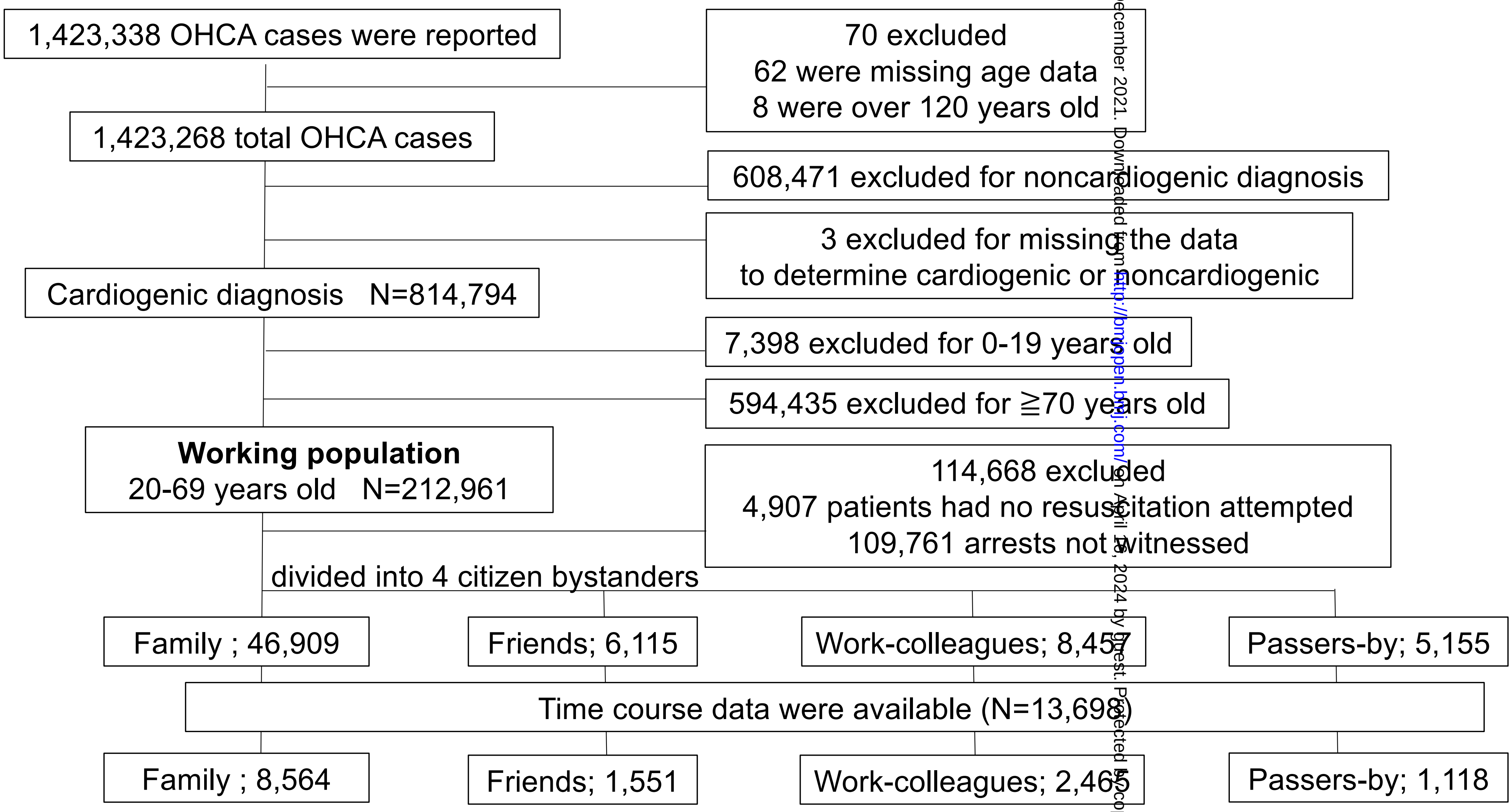


Figure. 2

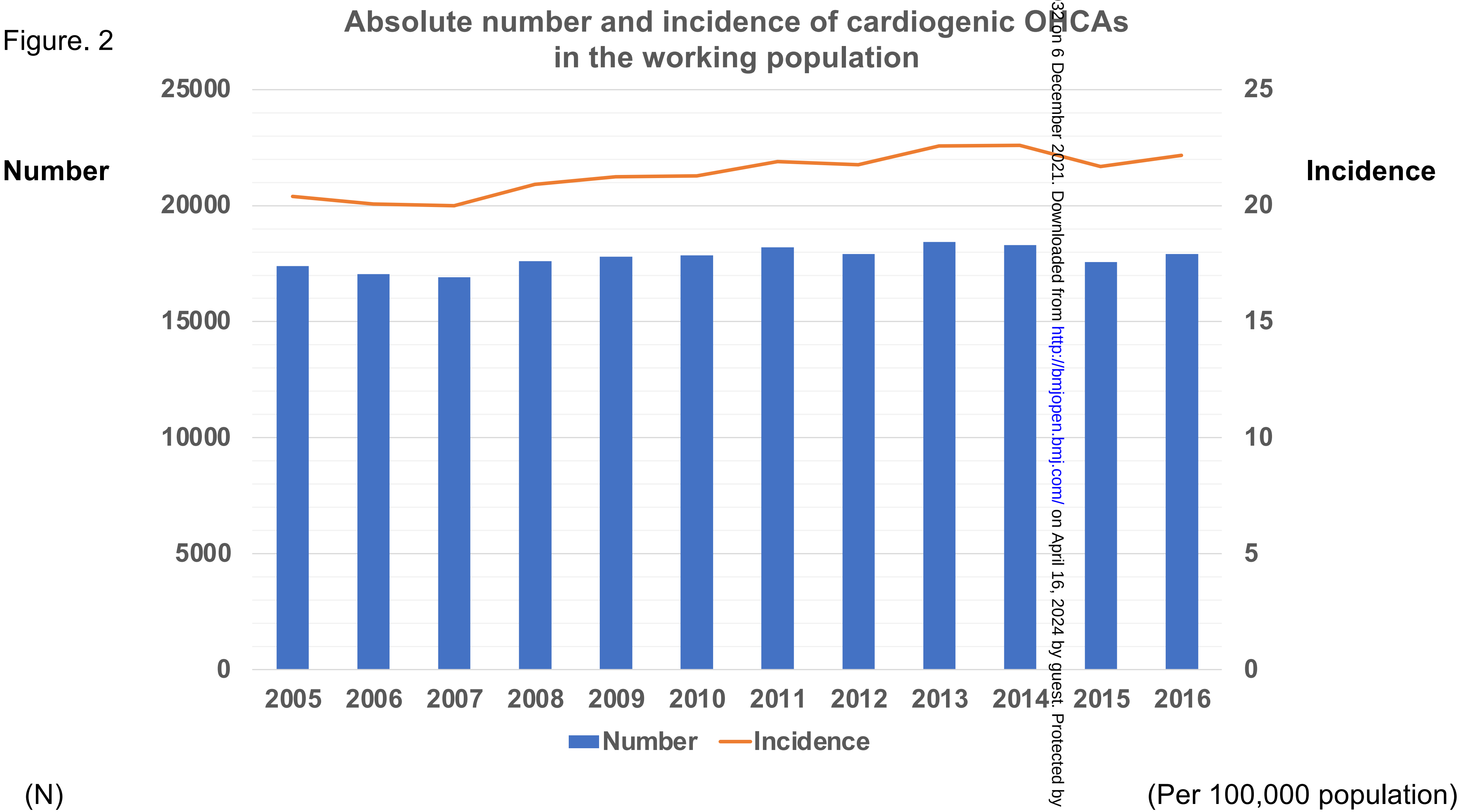
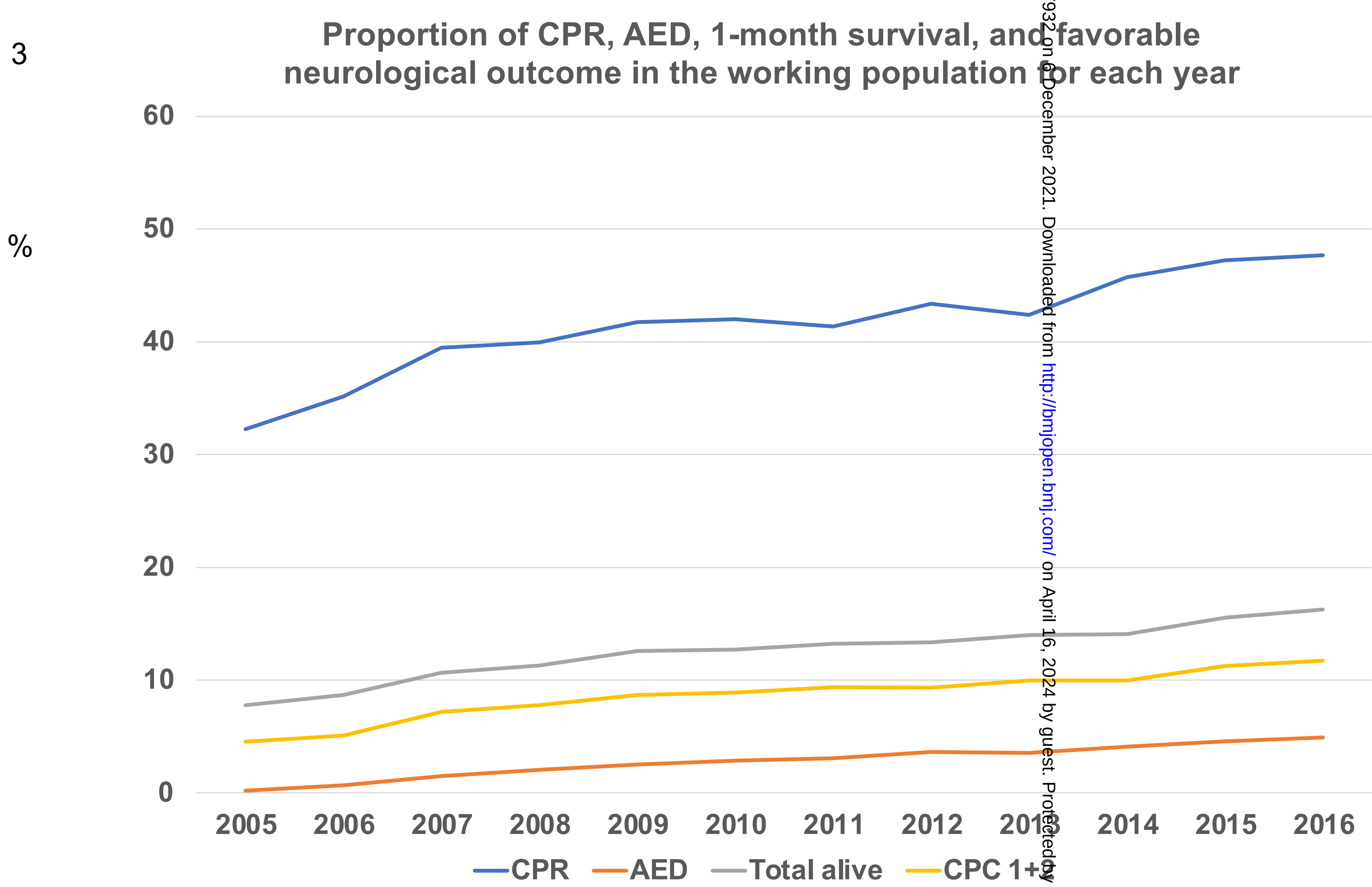
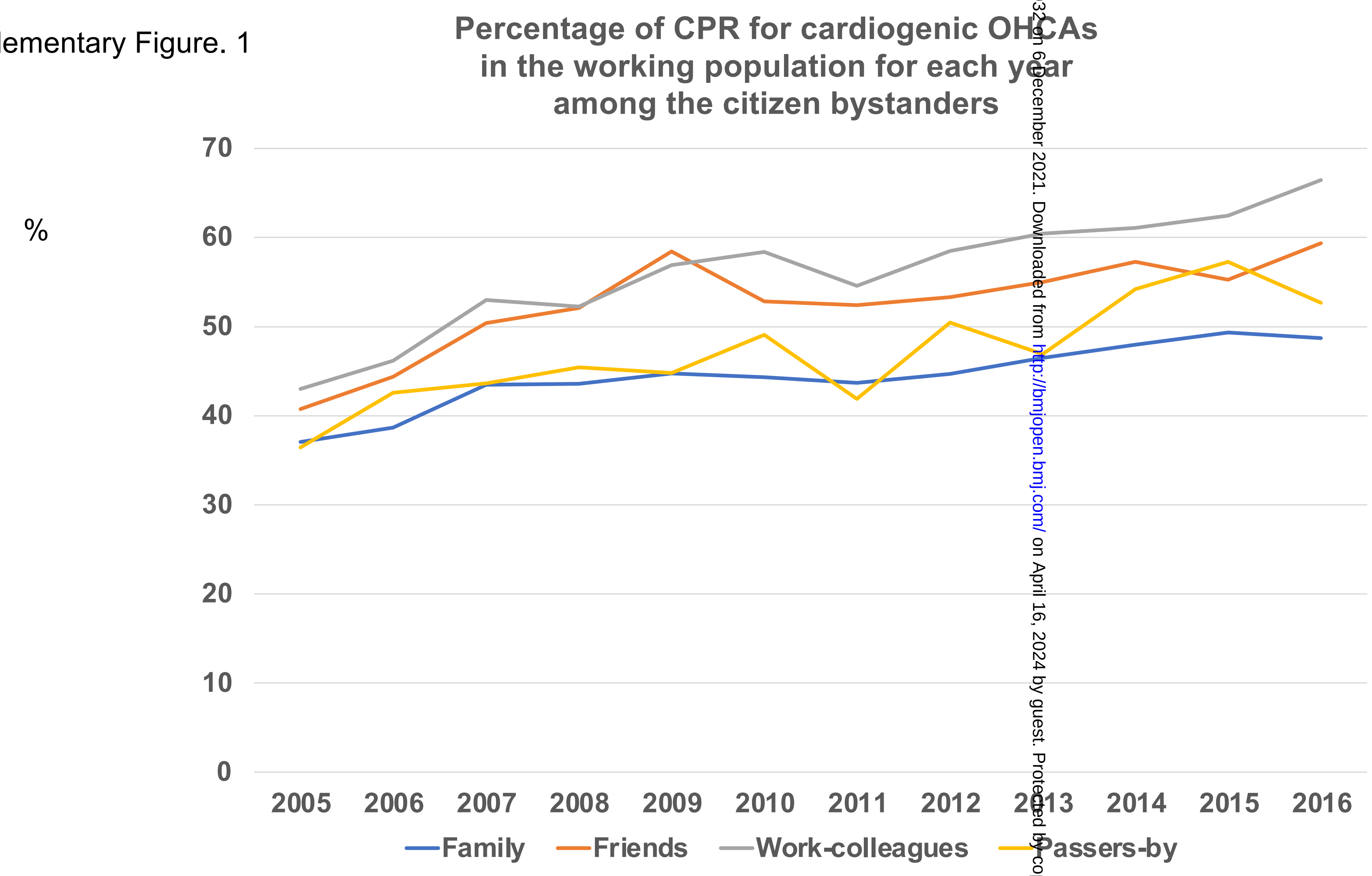

Absolute number and incidence of cardiogenic OHCAs in the working population
Number
Incidence
25000
20000
15000
10000
5000
0
25
20
15
10
5
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Number
Incidence
(N)
(Per 100,000 population)

Figure. 3


Proportion of CPR, AED, 1-month survival, and favorable neurological outcome in the working population for each year
%
60
50
40
30
20
10
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
CPR
AED
Total alive
CPC 1+2

Supplementary Figure. 1



Supplementary Table 1. Information about the abnormal value of time course

	Time course, minutes		
	< 0	0 - 60	60 <
Witness call, n (%)	13.784 (20.7)	52.281 (78.6)	472 (0.7)
Call to contact, n (%)	20 (0.0)	66,440 (99.9)	83 (0.1)
Witness-initiated CPR by bystander, n (%)	40 (0.1)	30,264 (99.4)	152 (0.5)
Witness-initial defibrillation, n (%)	112 (0.4)	31,190 (98.8)	253 (0.8)

Abbreviations: CPR, cardiopulmonary resuscitation.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract →Page 1, Lines 1-2: **The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found →Page 2-3, Lines 19-43: **ABSTRACT**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported →Page 5, Lines 62-70: Japan and other developed countries have aging populations.[1] Out of concern for future labour shortages due to the aging population, the Japanese parliament enacted a partial amendment to the law with respect to the stabilisation of the employment of elderly persons that recommended an extension of the retirement age from 65 to 70 years. This reform bill came into effect for companies from April 1, 2021.
Objectives	3	State specific objectives, including any prespecified hypotheses →Page 5, Lines 68-70: Although the age distribution of the working population is expected change continuously, few reports have examined the long-term condition of OHCAs in the working population, according to age. (hypotheses) →Page 6, Lines 78-80: The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution. (objectives)
Methods		
Study design	4	Present key elements of study design early in the paper →Page 6, Lines 88: In this population-based study, we analysed data collected between 2005 and 2016 from the All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA); a prospective, nationwide, population-based registry of OHCA victims based on the standardised Utstein style.[6]
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection →Page 6-7, Lines 91-97: As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of

		selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants →Page 7-8, Lines 109-113: In this study, the cardiogenic OHCA group of the working population (aged 20–69 years) were analysed. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by).
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case →not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable →Page 7, Lines 103-107: As reported in a previous study,[9] the cardiogenic group was defined as those having confirmed absence of signs of circulation, with the following exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and other non-cardiac factors. →Page 8, Line 119-123: The neurological outcomes were evaluated by physicians based on the Cerebral Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2, moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes at 1 month after admission were defined as Categories 1 or 2.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group →Page 6-7, Lines 91-97: As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation.
Bias	9	Describe any efforts to address potential sources of bias →Page 9-10, Lines 144-149: Univariate and multivariable logistic regression models were used to estimate the relationships between the prehospitalisation factors, such as age, sex, bystander chest compressions, shock by public-access AEDs, first documented rhythms, types of bystander, onset times of day, onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to the initial defibrillations, call to contact times, and 1-month survival with favourable neurological outcomes after OHCAs.

Study size	10	Explain how the study size was arrived at →Page 7, Lines 100-101: The data of 1,423,338 patients were collected between January 1, 2005 and December 31, 2016.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why →Page 9, Lines 138-140: We used the Mann-Whitney U test to compare the differences between the two independent groups, when the dependent variable was either ordinal or continuous but not normally distributed
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding →Page 9-10, Lines 137-153: **Statistical analysis ~**
		(*b*) Describe any methods used to examine subgroups and interactions →Page 9-10, Lines 137-153: **Statistical analysis ~**
		(*c*) Explain how missing data were addressed →Figure 1 →Page 8-9, Lines 128-133: According to the FDMA (Fire and Disaster Management Agency), until 2012, patients with null values for bystander use of AEDs were converted automatically into the group 'without bystander use of AEDs'; however, since 2013, they did not automatically convert the null value into the group 'without bystander use of AEDs' and these data were handled as missing data. To homogenise these data, we included all the cases with missing AED data (n = 8,180) in the group without bystander use of AEDs.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy →not applicable
		(*e*) Describe any sensitivity analyses →As sensitivity analyses, univariate and multivariable logistic regression are performed with and without time data. We confirmed that these methods of data analysis did not change the main results.

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed →Figure 1
		(b) Give reasons for non-participation at each stage →Figure 1
		(c) Consider use of a flow diagram →Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders →Page 6, Lines 85-87: OHCA patients who underwent resuscitation attempts by emergency medical service (EMS) personnel were transported to hospitals and then registered in the Utstein registry.
		(b) Indicate number of participants with missing data for each variable of interest →Figure 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) →Page 7, Lines 99-100: The EMS personnel followed-up these OHCA patients for 1 month to ascertain the survival rates and neurological outcomes.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time →Table 2.1 and 2.2.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure →not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures →not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included →Table 3.
		(*b*) Report category boundaries when continuous variables were categorized →Table 3.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period →not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses →Page 9-10, Lines 137-153: **Statistical analysis ~**
Discussion		
Key results	18	Summarise key results with reference to study objectives →Page 18-19, Lines 230-243: We found that: (1) approximately 30% of all the OHCA cases occurred in the working population, and that the working population comprised 26% of all the cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of cardiogenic OHCAs in the working population remained mainly unchanged over the 12-year

		period; (3) in any age group in the working population, there was no significant improvement in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased each year, and the prognosis after 1 month improved in the working population; and (5) among the citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes. However, the work-colleague bystanders had a significantly longer time from witnessing OHCAs to the initial defibrillations than the passers-by bystander group, and the time from witnessing OHCAs to initial defibrillations was associated independently with 1-month survival with favourable neurological outcomes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias →Page 24-25, Lines 344-352: **Limitations** ~
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence →Page 23-24, Lines 325-334: A possible reason why work-colleagues took longer to perform the first defibrillation compared with passers-by may have been due to most of the initial defibrillations being performed by EMS providers, and that the median call to contact intervals were significantly longer in the work-colleague bystander group than in the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$). The travel distance and time to travel within buildings may also have contributed to the delays. Another study that used the model of a large-scale skyscraper, calculated the length of time taken by the emergency services to reach a patient within the building (i.e. travel time) and found that the minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]
Generalisability	21	Discuss the generalisability (external validity) of the study results →Page 22, Lines 300-303: Nevertheless, this is not a problem that is limited to Japan; the aging of the population is progressing worldwide, especially in developed countries.[1] In the future, there is a possibility that the retirement age will be extended in many countries around the world.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based →Page 26, Line 371-373: **FUNDING~**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047932.R2
Article Type:	Original research
Date Submitted by the Author:	24-Oct-2021
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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Occupational and environmental medicine, Epidemiology, Public health
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Cardiology < INTERNAL MEDICINE, OCCUPATIONAL & INDUSTRIAL MEDICINE

The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study

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Word count: 3639 words

ABSTRACT

Objectives: The prevention and improvement of the prognosis of out-of-hospital cardiac arrests (OHCAs) are important issues especially with respect to their social and economic significance in working populations. The age distribution of the working population in Japan is expected to change continually due to its aging society and extension of retirement; however, few reports have examined the long-term condition of OHCA in the working population, defined by age. The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution.

Design and setting: We analysed the All-Japan Utstein registry, a prospective, nationwide, population-based, observational registry (2005–2016).

Participants: From the registry, 212,961 OHCA patients from the Japanese working population (defined aged 20–69 years), with only cardiogenic aetiology participated in this study. These patients were further divided into four groups according to the type of citizen bystander (family, friends, work-colleagues, and passers-by).

Primary and secondary outcome measures: The main outcomes were 1-month survival with favourable neurological outcomes.

Results: The incidence of OHCAs, in any age group, was almost constant during the 12-year period. The work-colleagues had the best prognosis despite having significantly longer times to initial defibrillations compared with the passers-by (13 vs. 12 min, respectively, P <0.001) that was associated independently with 1-month survival with favourable neurological outcomes (adjusted odds ratio: 0.94 [1-min increments], P <0.001).

Conclusions: In the 12-year period, the incidence of OHCAs in any age group remained almost constant, whereas the prognosis improved each year. Reducing the time to initial defibrillation may further improve the prognosis of OHCAs with a work-colleague bystander.

Keywords: Cardiopulmonary resuscitation, defibrillation, Japan, out-of-hospital cardiac arrest, prognosis, prospective registry, working population.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- In this population-based study, we analysed data collected between 2005 to 2016 in the All-Japan Utstein registry of the Fire and Disaster Management Agency; a prospective, nationwide, population-based registry.
- A large sample size and longer follow-up allowed for the detailed assessment of the relationship between a work-colleague bystander and the prognosis following an out-of-hospital cardiac arrest (OHCA) in the Japanese working population.
- We assessed independent factors associated with 1-month survival with favourable neurological outcomes after OHCAs in the Japanese working population.
- The All-Japan Utstein registry did not contain information on the actual employment status, individual medical therapy, activities of daily living before the OHCAs, or in-hospital treatment interventions.

INTRODUCTION

The prevention and improvement of the prognosis of out-of-hospital cardiac arrests (OHCAs) are important issues especially with respect to their social and economic significance in working populations.

Japan and other developed countries have aging populations.[1] Out of concern for future labour shortages due to the aging population, the Japanese parliament enacted a partial amendment to the law with respect to the stabilisation of the employment of elderly persons that recommended an extension of the retirement age from 65 to 70 years. This reform bill came into effect for companies from April 1, 2021. In addition, a study reported that patients aged ≥ 65 years comprised approximately 76% of patients with OHCAs in Japan.[2] Although the age distribution of the working population is expected change continuously, few reports have examined the long-term condition of OHCAs in the working population, according to age.

We defined the working population as individuals aged 20–69 years previously, and we analysed relatively short-term cardiogenic OHCAs in the Japanese working population using data from the Utstein registry, in Japan — a prospective, nationwide, population-based OHCA registry — between 2005 and 2008.[3] Although this earlier study revealed that the incidence of OHCAs in the working population was the highest during winter, on Sundays and Mondays, and during the early hours of the morning, it did not report on the prognosis of the OHCAs.

The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution.

METHODS

The population of Japan in 2019 was estimated to be 126.2 million, of which 67.33 million were employed, including both part-time and full-time workers.[4] In 2019, 726 fire stations with emergency dispatch centres provided emergency services 24 hours a day.[5] OHCA patients who underwent resuscitation attempts by emergency medical service (EMS) personnel were transported to hospitals and then registered in the Utstein registry.

In this population-based study, we analysed data collected between 2005 and 2016 from the All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA); a prospective, nationwide, population-based registry of OHCA victims based on the standardised Utstein style.[6] As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation. The person who performed the basic cardiopulmonary resuscitation, or defibrillation using a public-access AEDs ~~was~~ was defined as a bystander. The EMS personnel followed-up these OHCA patients for 1 month to ascertain the survival rates and neurological outcomes. The data of 1,423,338 patients were collected between January 1, 2005 and December 31, 2016.

We excluded the non-cardiogenic OHCA group, and only the cardiogenic OHCA group participated in our present study. As reported in a previous study,[9] the cardiogenic group was defined as those having confirmed absence of signs of circulation, with the following exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and other non-cardiac factors. The cardiogenic or non-cardiogenic classification was determined clinically by physicians at the hospitals in collaboration with the EMS providers and was confirmed by the FDMA. In this study, the cardiogenic OHCA group of the working population (aged 20–69 years) were analysed. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). We focused on the absolute number and incidences of OHCAs, the proportion that received CPR/AEDs, the 1-month survival rate following the OHCAs each year, and the characteristics of the bystanders. The incidence of the OHCAs was calculated as follows: the absolute number of OHCAs in the 20–69 age group divided by the number of individuals in the entire 20–69 age group.

The population size was based on the estimated data obtained from the Statistics Bureau of Japan.[10,11] The neurological outcomes were evaluated by physicians based on the Cerebral Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2, moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes at 1 month after admission were defined as Categories 1 or 2. Since some abnormal values were noted in the data in the intervals between the emergency calls and the patient contact times (call to contact time), witness to call times, times from witnessing OHCAs to bystander-initiated CPRs, and times from witnessing OHCAs to the times of the initial defibrillations, we only analysed the data recorded between 0 and 60 min (**Supplementary Table 1**). According to the FDMA (Fire and Disaster Management Agency), until 2012, patients with null values for bystander use of AEDs were converted automatically into the group 'without bystander use of AEDs'; however, since 2013, they did not automatically

131 convert the null value into the group 'without bystander use of AEDs' and these data were handled as missing data. To homogenise these data, we included all the cases with missing AED data (n = 8,180) in the group without bystander use of AEDs. The requirement for informed consent was waived due to the use of anonymised data. This study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (approval number; UOEHCRB19-072).[12]

137 **Statistical analysis**

138 We used the t-test to compare the differences between the two independent groups, when the dependent variable was continuous. The incidence rate ratios (IRRs) for the incidence of cardiogenic OHCAs were estimated using a Poisson regression analysis, with the age groups separated by five years and a dummy variable for the year included in the model. A log-transformed version of the numbers in each age group (in 5-year increments) for each year, was obtained from the official statistics, was used as the offset. Univariate and multivariable logistic regression models were used to estimate the relationships between the prehospitalisation factors, such as age, sex, bystander chest compressions, shock by public-access AEDs, first documented rhythms, types of bystander, onset times of day, onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to the initial defibrillations, call to contact times, and 1-month survival with

favourable neurological outcomes after OHCAs. For the multivariable regression models, Cook's distance and variance inflation factors (VIFs) were determined to ascertain the presence of influential observations and multicollinearity, respectively. All the statistical analyses were conducted using Stata (version 16.1; StataCorp LLC, College Station, TX, USA).

Patient and public involvement

The patients and the public were not involved in the design of this study.

RESULTS

Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and 2016, we excluded cases with missing age data (n = 62) or patients who were over 120 years old (n = 8). The cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the total OHCA population (n = 1,423,268), respectively. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20–69 years (working population) were enrolled in this study. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked ~~a~~ witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). **Figure 1** shows a flow diagram of patients with OHCAs.

Overall trend of OHCAs

The total general population reported by the Statistics Bureau of Japan declined from 127,768,000 in 2005 to 126,933,000 in 2016, while a transient increase was observed in 2010 alone (n = 128,057,000). Both the absolute number and the total incidence of OHCAs increased, from 102,737 (80 per 100,000 population) in 2005 to 123,552 (97 per 100,000 population) in 2016. Moreover, the absolute number and incidence of cardiogenic OHCAs in all age groups increased from 56,412 (44 per 100,000 population) in 2005 to 75,109 (59 per 100,000 population) in 2016.

OHCA trend in the working population

Of the OHCA population (n = 1,423,268), the working population comprised 428,958 (30.1%) of the OHCA cases, whereas in the cardiogenic OHCA group (n = 814,794), the working population comprised 212,961 (26.1%) OHCA cases.

Figure 2 shows that both the absolute number of cases and the incidence of cardiogenic OHCA in the working population mostly remained unchanged, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016. The proportion of CPRs and AEDs performed for the cardiogenic OHCAs in the working population increased every year, from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively, and the 1-month survival and favourable neurological outcomes of the cardiogenic OHCAs in the working population also increased from 7.8% and 4.5% in 2005 to 16.3% and 11.7% in 2016, respectively (**Figure 3**).

Sixty-five to 69 age group

The Statistics Bureau of Japan reported that the population aged 20–64 years declined from 77,829,000 in 2005 to 70,522,000 in 2016, whereas the population in the 65–69 age group increased, from 7,460,000 in 2005 to 10,275,000 in 2016. **Table 1** shows the incidence of cardiogenic OHCAs in each age group (in 5-year increments) in the working population. A Poisson regression analysis revealed that there were no significant improvements in the incidence of cardiogenic OHCAs over the last 12 years in any age group, and the IRRs for the incidence of cardiogenic OHCAs in age groups separated by five years, was 1.08.

Table 1. Incidence of cardiogenic OHCAs in each age group (in 5-year increments) in the working population

	Incidence by year (per 100,000 population)											
Age (years)	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
20-24	2.8	2.5	2.3	2.2	2.9	2.3	2.3	2.5	2.7	2.8	2.4	2.6
25-29	3.1	2.8	3.3	3.1	3.0	3.0	3.0	2.9	3.3	3.1	3.2	3.1

30-34	4.5	4.4	4.3	4.2	4.1	4.2	4.6	3.9	4.6	4.5	3.9	3.9
35-39	6.3	6.4	6.5	6.4	6.5	6.5	6.3	6.8	6.2	6.6	6.2	6.6
40-44	10.2	10.1	10.1	10.7	10.8	10.0	11.2	9.9	10.9	10.5	10.7	10.3
45-49	15.7	14.7	14.9	15.3	16.1	15.4	16.2	15.4	17.5	16.1	16.2	16.4
50-54	22.0	22.4	21.6	22.7	22.6	22.4	23.3	23.3	24.8	24.3	22.8	24.0
55-59	30.2	30.5	30.9	32.3	32.8	31.4	31.0	31.2	32.3	31.9	30.1	31.6
60-64	45.7	45.5	43.9	45.9	43.9	45.3	46.6	46.5	47.4	47.8	44.7	44.3
65-69	66.3	62.9	61.4	62.9	63.5	64.5	66.2	65.6	64.5	65.2	61.3	61.5

Abbreviations: OHCA, out-of-hospital cardiac arrest.

Citizen bystander in OHCAs in the working population

Table 2.1 presents the characteristics (age, sex, CPR/AED proportions, and 1-month survival/neurological outcomes) of the cardiogenic OHCA cases in the working population for each type of citizen bystander. The work-colleague bystander group had the highest percentage for both CPRs and AEDs (56.6% and 10.2%, respectively). Furthermore, the work-colleague bystander group had the highest 1-month survival and best neurological outcomes (28.1% and 20.8%, respectively). When the time course data were available (n = 13,698), the time course was identified for each citizen bystander group (**Table 2.2**). The work-colleague bystander group had significantly longer median intervals between

206 witnessing OHCAs and the initial defibrillations than the passers-by bystander group (13 vs.

207 12 min, respectively, $P < 0.001$).

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Table 2.1. Characteristics of patients with cardiogenic OHCAs in the working population according to the bystander group

Characteristic	Bystander group			
	Family	Friends	Work-colleagues	Passers-by
Total, n	46,909	6,115	8,457	5,155
Age, years, median (Q1–Q3)	61 (52–66)	59 (48–65)	56 (48–62)	60 (52–65)
Sex, men, %	73.6	83.0	92.2	86.6
CPR, %	44.3	52.7	56.6	47.6
AED (bystander defibrillation), %	0.7	7.1	10.2	9.3
1-month survival rate, %	15.9	22.0	28.1	26.5
1-month neurological outcome (CPC 1+2, %)	10.1	15.8	20.8	18.5

Abbreviations: AED, automated external defibrillator; CPC, Cerebral Performance Category; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

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Table 2.2. Characteristics of patients with cardiogenic OHCAs in the working population according to the bystander group (time course data available)

Characteristic	Family	Friends	Work-colleagues	Passers-by
	Time course, min, median (Q1–Q3)			
Witness call	2 (1–4)	2 (1–4)	2 (1–4)	2 (1-4)
Call to contact	8 (7–10)	8 (6–11)	8 (6–10)	7 (6–9)
Witness-initiated CPR by bystander	3 (1–5)	2 (1–5)	2 (1–5)	2 (1–4)
Witness-initial defibrillation	13 (11–17)	13 (10–17)	13 (10–16)	12 (9–15)

Abbreviations: CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; Q1–Q3, first to third quartile.

Using a multivariable logistic regression, 13,698 patients were analysed. There were 11,808 (86.2%) males, 13,509 (98.6%) patients received bystander chest compression, 1,062 (7.8%) were shocked by public-access AEDs (automated external defibrillator), 13,698 first documented rhythms were analysed. The number of patients with VT/VF rhythm was 11,882 (86.7%), PEA 741 (5.4%), asystole 834 (6.1%), and others 241 (1.7%). There were 8,564 (62.5%) family bystanders, 1,551 (11.3%) friends bystanders, 2,465 (18.0%) work-colleagues bystanders, and 1,118 (8.2%) passers-by bystanders. With respect to the onset time of day, 13,698 were analysed, of which the time period 0:00-7:59 comprised 3,835 (28.0%), 8:00-16:59 5,696 (41.6%), and 17:00-23:59 4,167 (30.4%). Age, sex, bystander chest compressions, shock by public-access AEDs, first documented rhythms, types of bystander, onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to initial defibrillations, and the call to contact times were associated independently with 1-month survival with favourable neurological outcomes in this study population (**Table 3**). According to the Cook's distance calculation, none were above 0.5. The mean VIF was 1.27 and none of the variables exceeded a VIF of 3.

Table 3. Effect of prehospitalisation factors on the 1-month survival with favourable neurological outcomes after OHCAs

Prehospitalisation factor	Crude OR	95% CI	*P*-value	Adjusted OR	95% CI	*P*-value
Age (10-year increments)	0.98	0.98–0.99	<0.001	0.98	0.98–0.99	<0.001
Sex						
male	Ref.	–	–	Ref.	–	–
female	1.16	1.04-1.29	0.006	1.33	1.19–1.50	<0.001
Bystander chest compression						
no	Ref.	–	–	Ref.	–	–
yes	1.77	1.23–2.56	0.002	1.54	1.05–2.22	0.027
Shock by public-access AEDs						
no	Ref.	–	–	Ref.	–	–

yes	1.72	1.51–1.95	<0.001	1.53	1.31–1.77	<0.001
First documented rhythm						
VT/VF	Ref.	–	–	Ref.	–	–
PEA	0.35	0.28–0.43	<0.001	0.49	0.39–0.61	<0.001
asystole	0.13	0.09–0.17	<0.001	0.21	0.15–0.29	<0.001
Others	2.16	1.67-2.79	<0.001	1.73	1.31-2.29	<0.001
Type of bystander						
family	Ref.	–	–	Ref.	–	–
friends	1.42	1.26–1.59	<0.001	1.28	1.13–1.46	<0.001
work-colleagues	1.55	1.41–1.71	<0.001	1.28	1.15–1.44	<0.001
passers-by	1.69	1.48–1.93	<0.001	1.25	1.08–1.45	0.003
Onset time of day						
0:00–7:59	0.76	0.69–0.84	<0.001	0.92	0.83–1.03	0.141
8:00–16:59	Ref.	–	–	Ref.	–	–
17:00–23:59	0.90	0.82–0.98	0.018	0.93	0.84–1.02	0.116
Onset year (1-year increments)	1.08	1.07-1.09	<0.001	1.09	1.08-1.11	<0.001
Witness-initiated CPR by bystander time (1-min increments)	0.91	0.90–0.92	<0.001	0.96	0.95–0.98	<0.001

Witness-initial defibrillation time (1-min increments)	0.89	0.89-0.90	<0.001	0.94	0.93-0.95	<0.001
Call to contact time (1-min increments)	0.87	0.86-0.89	<0.001	0.93	0.91-0.95	<0.001

Abbreviations: AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; Ref., reference; VT/VF, ventricular tachycardia/ventricular fibrillation.

DISCUSSION

Using the data obtained from the Utstein registry, that were collected for 12 years between 2005 and 2016, we investigated OHCAs in the Japanese working population with respect to age. We found that: (1) approximately 30% of all the OHCA cases occurred in the working population, and that the working population comprised 26% of all the cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of cardiogenic OHCAs in the working population remained mainly unchanged over the 12-year period; (3) in any age group in the working population, there was no significant improvement in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased each year, and the prognosis after 1 month improved in the working population; and (5) among the citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes. However, the work-colleague bystanders had a significantly longer time from witnessing OHCAs to the initial defibrillations than the passers-by bystander group, and the time from witnessing OHCAs to initial defibrillations was associated independently with 1-month survival with favourable neurological outcomes.

Causality of OHCAs and their countermeasures in the working population

The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At least one significant coronary artery lesion was found in 70% of all OHCA patients in the absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial infarction decrease was attributed to the increased use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g. statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the incidence of AMIs in both men and women who were < 59 years continued to increase. This was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of young peoples' diets and lifestyles, as well as the high smoking rates (~50% and > 30% in young men and women, respectively).[18] Therefore, an improvement in the diet and the cessation of smoking may be important in the reduction of the incidence of cardiogenic OHCAs in this population.

Compared to Western countries, ischaemic heart disease is less common in Japan,[19] whereas the prevalence of the Brugada syndrome is relatively high.[20,21] The Brugada syndrome was described by Pedro and Josep Brugada in 1992, as a disease that causes ventricular fibrillation despite the absence of obvious structural cardiac diseases, electrolyte abnormalities, or QT prolongations.[22] The Brugada-type electrocardiogram (ECG; right bundle branch block and ST segment elevation in V1 through V3) may be associated closely with a sudden unexplained death syndrome, such as Lai Tai ('death during sleep') in northeast Thailand, Bangungut ('moaning and dying during sleep') in the Philippines, and Pokkuri ('sudden unexpected death at night') in Japan.[23] A troublesome characteristic of the Brugada syndrome is its nocturnal tendency, which may delay therapeutic interventions and thus lead to worse prognosis. In the univariate analysis of this study, a night-time onset (0:00–7:59 and 17:00–23:59) of OHCAs was associated with a worse prognosis than a daytime onset (8:00–16:59), although this tendency was not shown in the multivariable analysis (**Table 3**). Using a 12-lead ECG at screening, a history of syncope, and a family history of sudden cardiac death may help identify patients who are in need of preventive

274 pharmacological and non-pharmacological therapy (e.g. use of an implantable cardioverter
275 defibrillator).[24]

276 Previous meta-analyses of prospective cohort studies have revealed associations between
277 work stressors and cardiovascular diseases. The summary relative risk for long working hours
278 (≥ 55 hours per week) compared with the standard 35–40 hours per week was 1.13 (95%
279 confidence interval [CI]: 1.02–1.26).[25] The total working hours tended to decline in Japan
280 [26] however, the reduction in the number of working hours was minor, and it is unknown
281 whether it contributed significantly to the incidence of OHCAs in the working population.

282 **Analysis of OHCAs in the 65–69 age group**

283 In 2018, the Japanese Cabinet Office reported that the proportion of workers in the 65–69 age
284 group was low; in the 5-year age groups, the proportions of male and female workers were
285 91.0% (55–59), 79.1% (60–64), and 54.8% (65–69) and 70.5% (55–59), 53.6% (60–64), and
286 34.4% (65–69).[27] Considering the extension of the retirement age that came into effect
287 from 2021, the employment rates are expected to increase for people in the 65–69 age group.
288 Thus, we investigated the characteristics of cardiogenic OHCAs in the 65–69 age group.

289 In fact, the proportion of workers aged ≥ 65 years in the total labour force population has
290 been increasing every year, by 7.6% in 2005 to 12.8% in 2018.[28] We identified that there
291 were no significant improvements in the incidence of cardiogenic OHCAs in any age group

over the last 12 years, and the incidence increased with increasing age (**Table 1**). A study of OHCAs in the Osaka Prefecture, Japan, that was conducted for two years revealed that the incidence of OHCAs increased exponentially with increasing age.[29] Our present study revealed that the incidence of cardiogenic OHCAs in any age group was almost constant over the 12-year period. It should be noted that the incidence of OHCAs in the 65–69 age group (extended retirement age group) was high, and that age was associated independently with 1-month survival with favourable neurological outcomes (adjusted odds ratio [OR]: 0.98 [10-year increments], 95% CI: 0.98–0.99; $P < 0.001$). Therefore, it is important for companies with older employees to take this into account. Nevertheless, this is not a problem that is limited to Japan; the aging of the population is progressing worldwide, especially in developed countries.[1] In the future, there is a possibility that the retirement age will be extended in many countries around the world.

Effect of work-colleagues and other types of bystanders

A previous study found that a key predictor of survival after OHCAs is the bystander witness.[30] Another previous study reported that most of the cases of OHCAs in Japan that were witnessed by family members and family bystanders had a worse prognosis than those witnessed by other bystanders.[7] Moreover, in our present study, the worst 1-month survival and neurological outcomes was observed in the family bystander group. This unfavourable result may be attributed to the lowest CPR/AED proportions (44.3% and 0.7%, respectively).

Another study that reported a similar association for the bystander-patient relationship indicated that the large delays (≥ 5 min) in the witness call interval and large witness bystander CPR interval were most frequent in the family bystander group.[31]

A previous systematic review revealed that the OHCA survival rate was better in the workplace,[32] and the findings of our study were similar: work-colleague bystanders were associated with a better 1-month survival and favourable neurological outcomes. A possible reason for such a favourable prognosis was that the CPR/AED proportion was highest in the work-colleague bystander group. Furthermore, we found further improvements in the prognosis of OHCAs in the work-colleague bystander group. The work-colleague bystander group had significantly longer median intervals between the witnessing OHCAs and initial defibrillations than the passers-by bystander group (13 vs. 12 min, respectively; $P < 0.001$). It is known that a 1-min delay can reduce the survival rate by 7–10%,[33] and the results from Table 3 also indicate that a 1-min difference does have a clinically meaningful benefit for 1-month survival with favourable neurological outcomes (adjusted OR: 0.94 [1-min increments], 95% CI: 0.93–0.95; $P < 0.001$). A possible reason why work-colleagues took longer to perform the first defibrillation compared with passers-by may have been due to most of the initial defibrillations being performed by EMS providers, and that the median call to contact intervals were significantly longer in the work-colleague bystander group than in the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$). The travel distance and time to travel within buildings may also have contributed to the delays. Another study that used the model of a large-scale skyscraper, calculated the length of time taken by the emergency services to reach a patient within the building (i.e. travel time) and found that the minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]

Recently, the importance of CPR has become known widely, and the findings of this study supported this, given that the CPR proportion in the working population has increased over the years (**Figure 3**). However, our present study revealed that in 2016 in > 30% of the cases CPR was not performed despite the witnessing of the cardiogenic OHCAs by work-colleagues (shown in **Supplementary Figure 1**). More opportunities for CPR awareness activities in companies may be useful in preventing cardiac death and poor neurological outcomes in OHCA patients in the working population. A previous study reported that approximately two-thirds of OHCA survivors return to work,[35] which is important in terms of public health and socioeconomic significance.

Limitations

This study had several limitations. First, this was a retrospective population-based study of data obtained from a prospective registry, with some instances where data were missing or abnormal values were present. Second, the actual employment status of the OHCA patients in the 20–69 age group (working population) was unknown. Third, the Utstein registry did not contain any information on individual medical therapy, and activities of daily living before the OHCAs, or the details of the in-hospital treatment interventions. Finally, there may have been unmeasured confounding factors that may have influenced the 1-month survival with favourable neurological outcomes.

CONCLUSIONS

Over the 12-year period (2005–2016), both the absolute number and incidence of cardiogenic OHCAs in the working population remained mainly unchanged, whereas the prognosis of OHCAs at 1-month improved. Among the citizen bystanders, the work-colleague bystander group showed the highest CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes, despite significantly longer times from witnessing OHCAs to initial defibrillations than the passers-by bystander group. Reducing the time from witnessing OHCAs to initial defibrillations may further improve the prognosis of patients with OHCAs that have been witnessed by work-colleagues.

ACKNOWLEDGMENTS

We wish to thank all of the emergency medical service personnel and the Fire and Disaster Management Agency of Japan for their cooperation in collecting data and managing the Utstein-style registry.

COMPETING INTERESTS

The authors have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHORS' CONTRIBUTIONS

YY was involved in data analysis and writing of the manuscript. YO was involved in data verification, the design of the study, supervision, and revising the manuscript. YF was involved in data verification, supervision, and statistical analysis. KY, TM, and KT were involved in data verification. HO and RK were involved in data verification and supervision. HA was involved in data verification, supervision, and revising the manuscript.

DATA SHARING

The data used in this study are not publicly available. The data are only accessible through the Fire and Disaster Management Agency (2-1-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan; Tel.: +03-5253-7529; Fax: +03-5253-7532; E-mail: fdma-goiken@ml.soumu.go.jp). Therefore, no additional data are available.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (approval number; UOEHCRB19-072).

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LEGENDS

Figure 1. A flow diagram of patients with OHCAs

Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and 2016, we excluded cases with missing data of age (n=62) or patients who were over 120 years old (n=8). Cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the total OHCA population (n=1,423,268), respectively. We excluded non-cardiogenic OHCA group. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20–69 years (working population) were enrolled in this study. After excluding those who did not receive OHCA resuscitation (n = 4,907) or those who lacked a witness (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.

Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working population. Both the absolute number and incidence of cardiogenic OHCAs in the working population were mostly unchanged over the period of 12 years, from 17,403 (20 per 100,000 population) in 2005 to 17,917 (22 per 100,000 population) in 2016. Abbreviation: OHCA, out-of-hospital cardiac arrest.

Figure 3. Proportion of CPR, AED, 1-month survival, and favourable neurological outcome in the working population for each year. The percentage of CPR and AED increased each year from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively. One-month survival rate of cardiogenic OHCAs in the working population increased from 7.8% in 2005 to 16.3% in 2016, and the 1-month survival with favourable neurological outcome also increased from 4.5% in 2005 to 11.7% in 2016. Abbreviations: CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; CPC, cerebral performance category.

Figure. 1

A flow diagram of patients with OHCAs

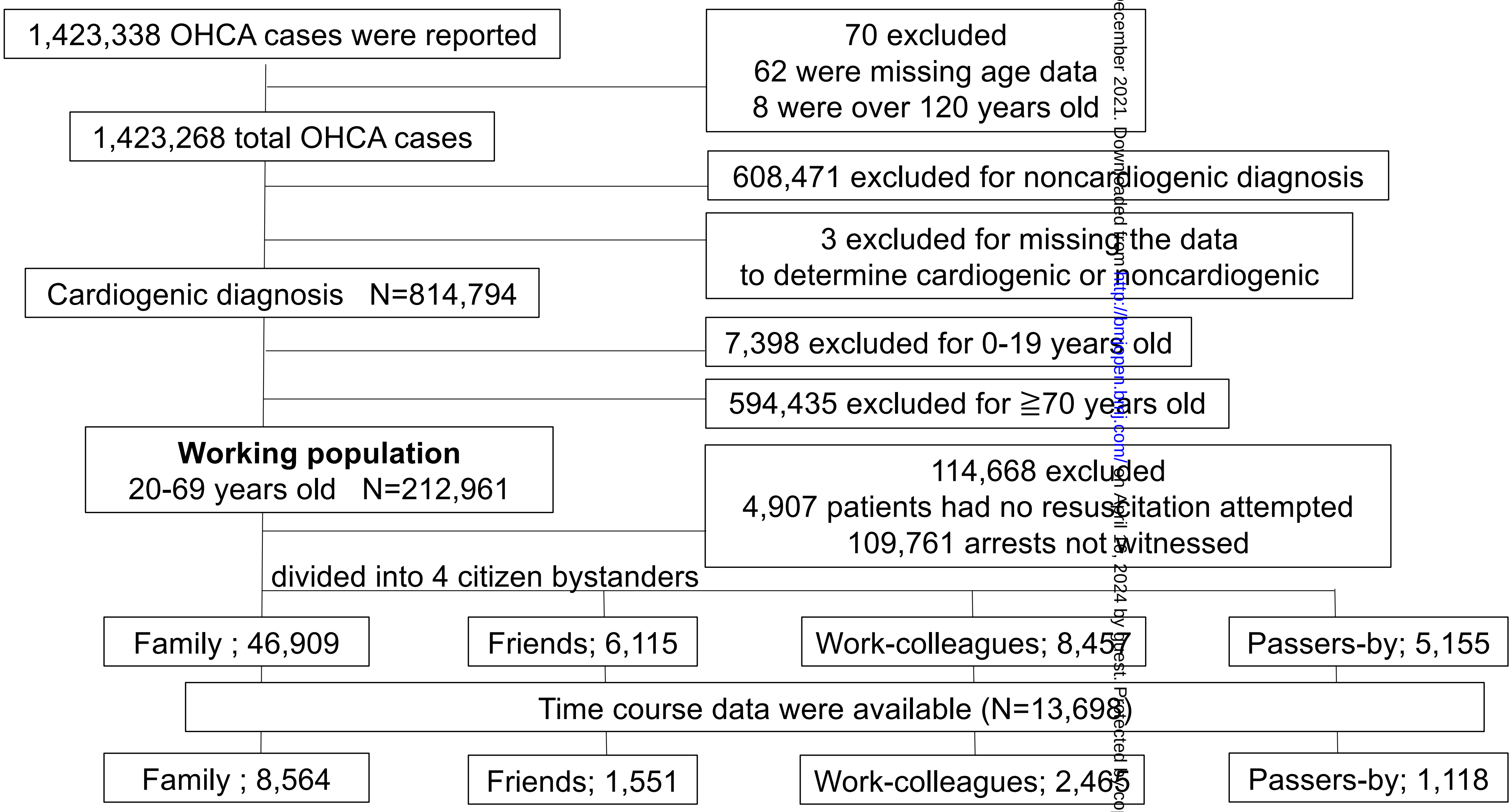


Figure. 2

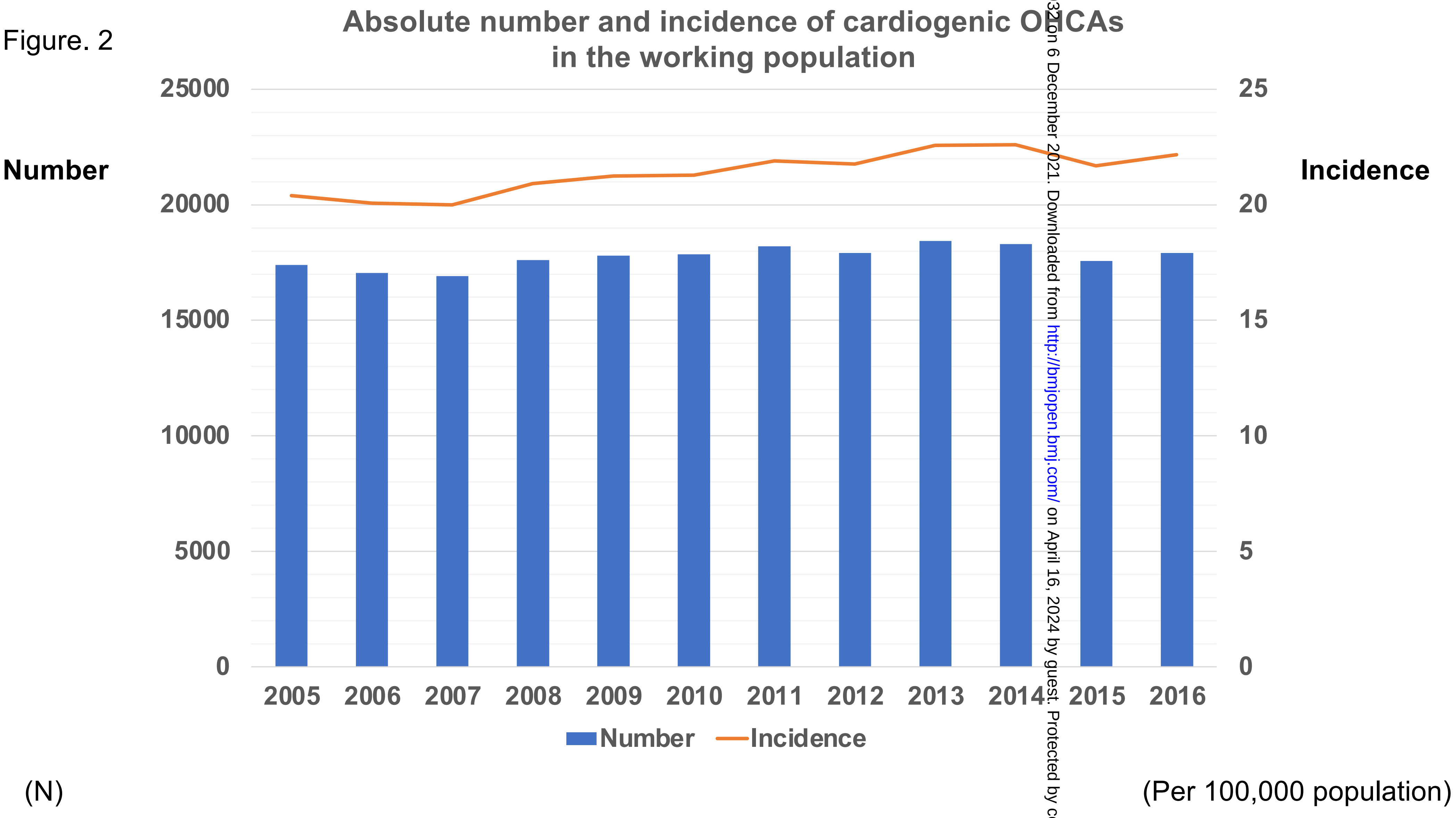
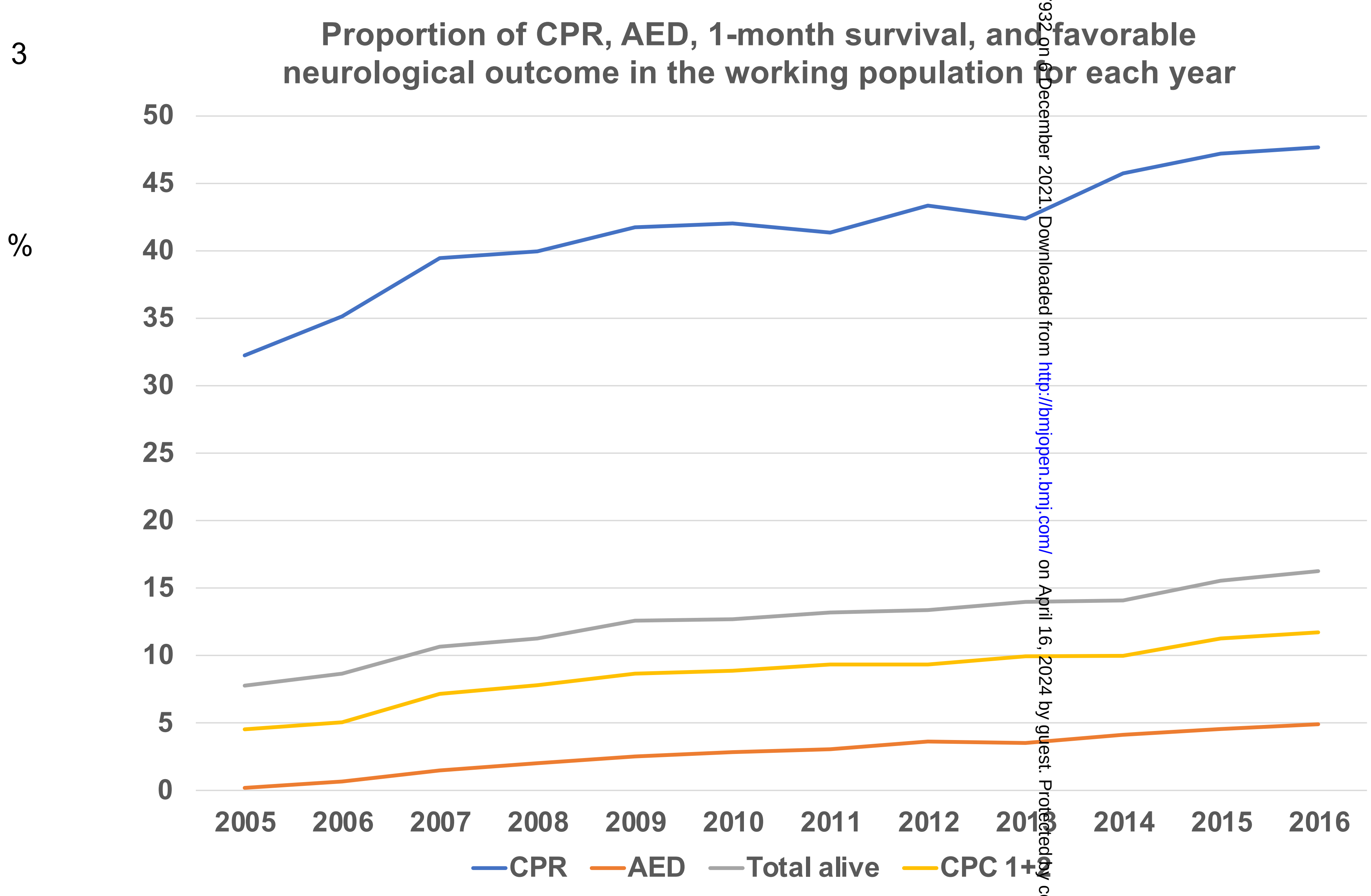
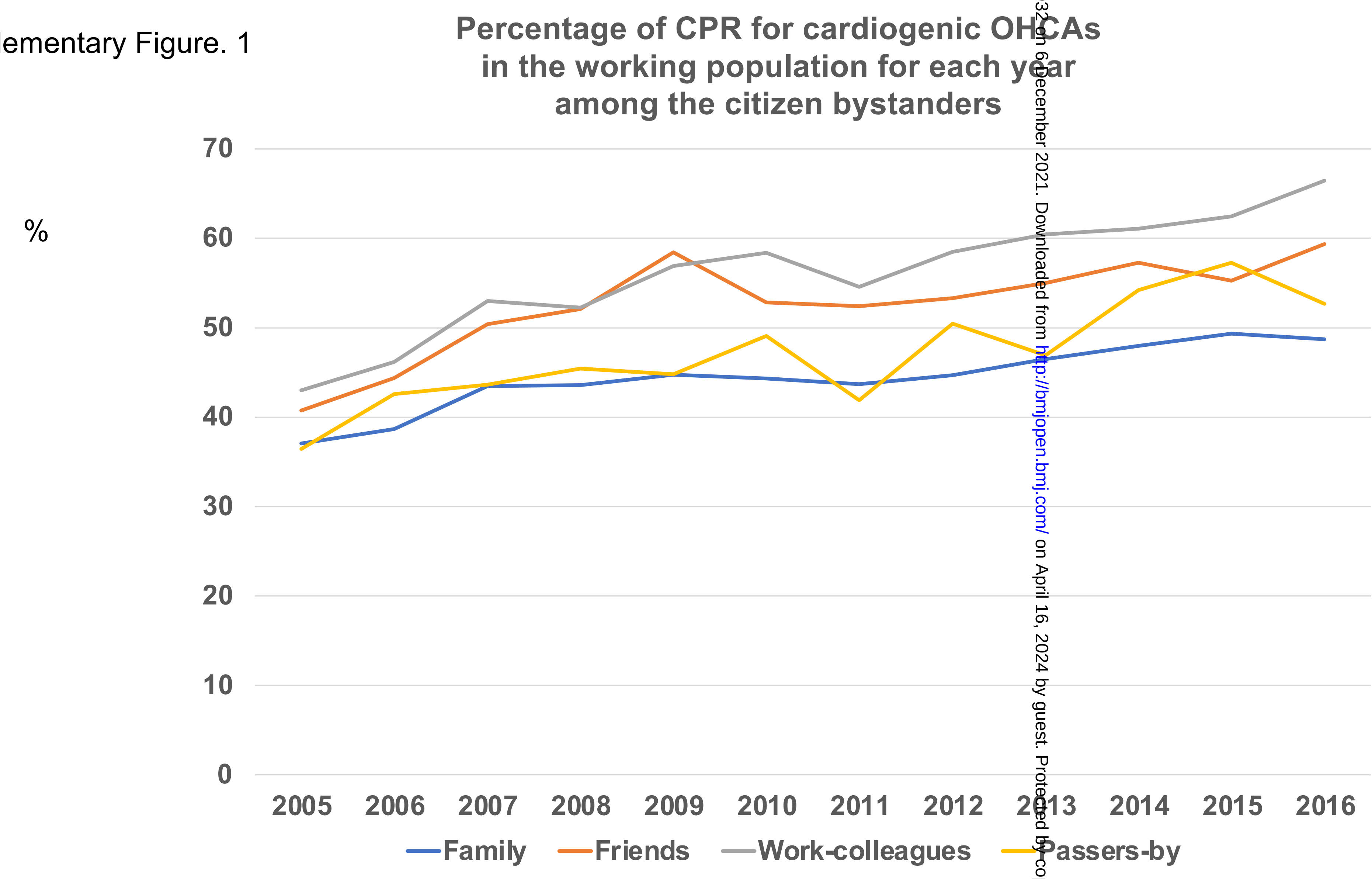

Absolute number and incidence of cardiogenic OHCAs in the working population
Number
Incidence
25000
20000
15000
10000
5000
0
25
20
15
10
5
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Number
Incidence
(N)
(Per 100,000 population)

Figure. 3


Proportion of CPR, AED, 1-month survival, and favorable neurological outcome in the working population for each year
%
50
45
40
35
30
25
20
15
10
5
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
CPR
AED
Total alive
CPC 1+2

Supplementary Figure. 1



Supplementary Table 1. Information about the abnormal value of time course

	Time course, minutes		
	< 0	0 - 60	60 <
Witness call, n (%)	13.784 (20.7)	52.281 (78.6)	472 (0.7)
Call to contact, n (%)	20 (0.0)	66,440 (99.9)	83 (0.1)
Witness-initiated CPR by bystander, n (%)	40 (0.1)	30,264 (99.4)	152 (0.5)
Witness-initial defibrillation, n (%)	112 (0.4)	31,190 (98.8)	253 (0.8)

Abbreviations: CPR, cardiopulmonary resuscitation.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract →Page 1, Lines 1-2: **The incidence of out-of-hospital cardiac arrests and survival rates after one-month among the Japanese working population: A cohort study**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found →Page 2-3, Lines 19-43: **ABSTRACT**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported →Page 5, Lines 62-70: Japan and other developed countries have aging populations.[1] Out of concern for future labour shortages due to the aging population, the Japanese parliament enacted a partial amendment to the law with respect to the stabilisation of the employment of elderly persons that recommended an extension of the retirement age from 65 to 70 years. This reform bill came into effect for companies from April 1, 2021.
Objectives	3	State specific objectives, including any prespecified hypotheses →Page 5, Lines 68-70: Although the age distribution of the working population is expected change continuously, few reports have examined the long-term condition of OHCAs in the working population, according to age. (hypotheses) →Page 6, Lines 78-80: The aim of this study was to determine the incidence of OHCAs and the survival rates after 1 month, among the Japanese working population, defined by age, considering the changing age distribution. (objectives)
Methods		
Study design	4	Present key elements of study design early in the paper →Page 6, Lines 88: In this population-based study, we analysed data collected between 2005 and 2016 from the All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA); a prospective, nationwide, population-based registry of OHCA victims based on the standardised Utstein style.[6]
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection →Page 6-7, Lines 91-97: As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of

		selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants →Page 7-8, Lines 109-113: In this study, the cardiogenic OHCA group of the working population (aged 20–69 years) were analysed. After excluding those who did not receive OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = 109,761), the working population was further divided into four bystander groups (family, friends, work-colleagues, and passers-by).
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case →not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable →Page 7, Lines 103-107: As reported in a previous study,[9] the cardiogenic group was defined as those having confirmed absence of signs of circulation, with the following exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and other non-cardiac factors. →Page 8, Line 119-123: The neurological outcomes were evaluated by physicians based on the Cerebral Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2, moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes at 1 month after admission were defined as Categories 1 or 2.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group →Page 6-7, Lines 91-97: As described in previous reports that used the Utstein data,[2,7,8] EMS personnel filled the information sheet and updated the OHCA patient information based on the information recorded by the treating physician, including sex, age, prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an automated external defibrillator (AED), administration of intravenous fluids, tracheal intubation, and prehospitalisation return of spontaneous circulation.
Bias	9	Describe any efforts to address potential sources of bias →Page 9-10, Lines 144-149: Univariate and multivariable logistic regression models were used to estimate the relationships between the prehospitalisation factors, such as age, sex, bystander chest compressions, shock by public-access AEDs, first documented rhythms, types of bystander, onset times of day, onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from witnessing OHCAs to the initial defibrillations, call to contact times, and 1-month survival with favourable neurological outcomes after OHCAs.

Study size	10	Explain how the study size was arrived at →Page 7, Lines 100-101: The data of 1,423,338 patients were collected between January 1, 2005 and December 31, 2016.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why →Page 9, Lines 138-140: We used the Mann-Whitney U test to compare the differences between the two independent groups, when the dependent variable was either ordinal or continuous but not normally distributed
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding →Page 9-10, Lines 137-153: **Statistical analysis ~**
		(*b*) Describe any methods used to examine subgroups and interactions →Page 9-10, Lines 137-153: **Statistical analysis ~**
		(*c*) Explain how missing data were addressed →Figure 1 →Page 8-9, Lines 128-133: According to the FDMA (Fire and Disaster Management Agency), until 2012, patients with null values for bystander use of AEDs were converted automatically into the group 'without bystander use of AEDs'; however, since 2013, they did not automatically convert the null value into the group 'without bystander use of AEDs' and these data were handled as missing data. To homogenise these data, we included all the cases with missing AED data (n = 8,180) in the group without bystander use of AEDs.
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy →not applicable
		(*e*) Describe any sensitivity analyses →As sensitivity analyses, univariate and multivariable logistic regression are performed with and without time data. We confirmed that these methods of data analysis did not change the main results.

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed →Figure 1
		(b) Give reasons for non-participation at each stage →Figure 1
		(c) Consider use of a flow diagram →Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders →Page 6, Lines 85-87: OHCA patients who underwent resuscitation attempts by emergency medical service (EMS) personnel were transported to hospitals and then registered in the Utstein registry.
		(b) Indicate number of participants with missing data for each variable of interest →Figure 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) →Page 7, Lines 99-100: The EMS personnel followed-up these OHCA patients for 1 month to ascertain the survival rates and neurological outcomes.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time →Table 2.1 and 2.2.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure →not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures →not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included →Table 3.
		(*b*) Report category boundaries when continuous variables were categorized →Table 3.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period →not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses →Page 9-10, Lines 137-153: **Statistical analysis ~**
Discussion		
Key results	18	Summarise key results with reference to study objectives →Page 18-19, Lines 230-243: We found that: (1) approximately 30% of all the OHCA cases occurred in the working population, and that the working population comprised 26% of all the cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of cardiogenic OHCAs in the working population remained mainly unchanged over the 12-year

		period; (3) in any age group in the working population, there was no significant improvement in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased each year, and the prognosis after 1 month improved in the working population; and (5) among the citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes. However, the work-colleague bystanders had a significantly longer time from witnessing OHCAs to the initial defibrillations than the passers-by bystander group, and the time from witnessing OHCAs to initial defibrillations was associated independently with 1-month survival with favourable neurological outcomes.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias →Page 24-25, Lines 344-352: **Limitations** ~
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence →Page 23-24, Lines 325-334: A possible reason why work-colleagues took longer to perform the first defibrillation compared with passers-by may have been due to most of the initial defibrillations being performed by EMS providers, and that the median call to contact intervals were significantly longer in the work-colleague bystander group than in the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$). The travel distance and time to travel within buildings may also have contributed to the delays. Another study that used the model of a large-scale skyscraper, calculated the length of time taken by the emergency services to reach a patient within the building (i.e. travel time) and found that the minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]
Generalisability	21	Discuss the generalisability (external validity) of the study results →Page 22, Lines 300-303: Nevertheless, this is not a problem that is limited to Japan; the aging of the population is progressing worldwide, especially in developed countries.[1] In the future, there is a possibility that the retirement age will be extended in many countries around the world.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based →Page 26, Line 371-373: **FUNDING~**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.