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# **BMJ Open**

# 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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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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# 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.

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**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,

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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.

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#### 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

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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  $\geq 65$  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.

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#### **METHODS**

Japan has approximately 378,000 km<sup>2</sup> 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

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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.

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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).

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#### 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). Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

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

	Bystander group				
Characteristic	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	Tin	ne course, minute	es, median (Q1–Q	3)
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**).

Prehospitalisation factor	Crude OR	95% CI	<i>p</i> -value	Adjusted OR	95% CI	<i>p</i> -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.	-0	-	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	0.91	0.90–0.92	<0.001	0.95	0.93–0.96	<0.001
(1-minute increments)						
Witness-initial defibrillation	0.89	0.89-0.90	<0.001	0.97	0.95-0.98	<0.001
time (1-minute increments)	0.69	0.89-0.90	<0.001	0.97	0.95-0.96	<0.001
Call to contact time	0.87		<0.001	0.02	0 02 0 04	<0.001
(1-minute increments)	υ.87	0.86-0.89	<b>∽</b> 0.001	0.93	0.92-0.94	SU.UU I

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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.

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

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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 ( $\sim$ 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 ( $\geq$  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

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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  $\geq 65$  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. Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

#### 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 ( $\geq 5$  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

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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 by stander 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. er revie

#### **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.

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Utstein-style registry.

# **COMPETING INTERESTS**

The authors have no competing interests.

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# **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). Js.

Therefore, no additional data are available.

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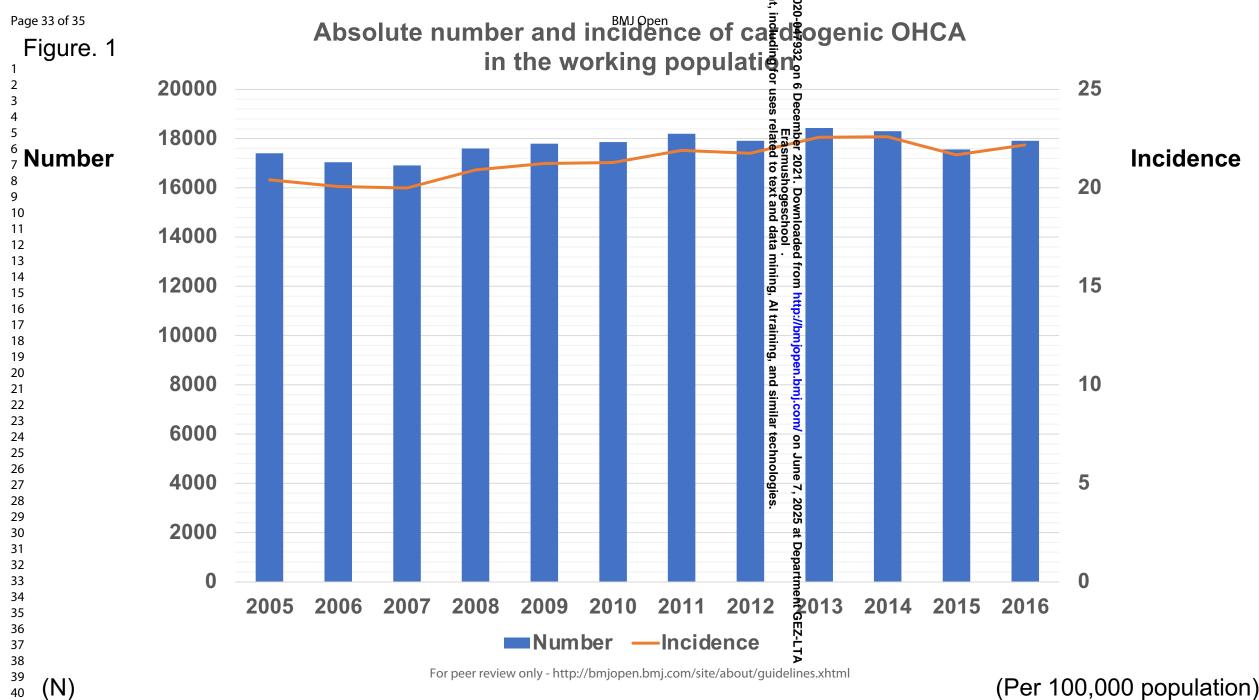
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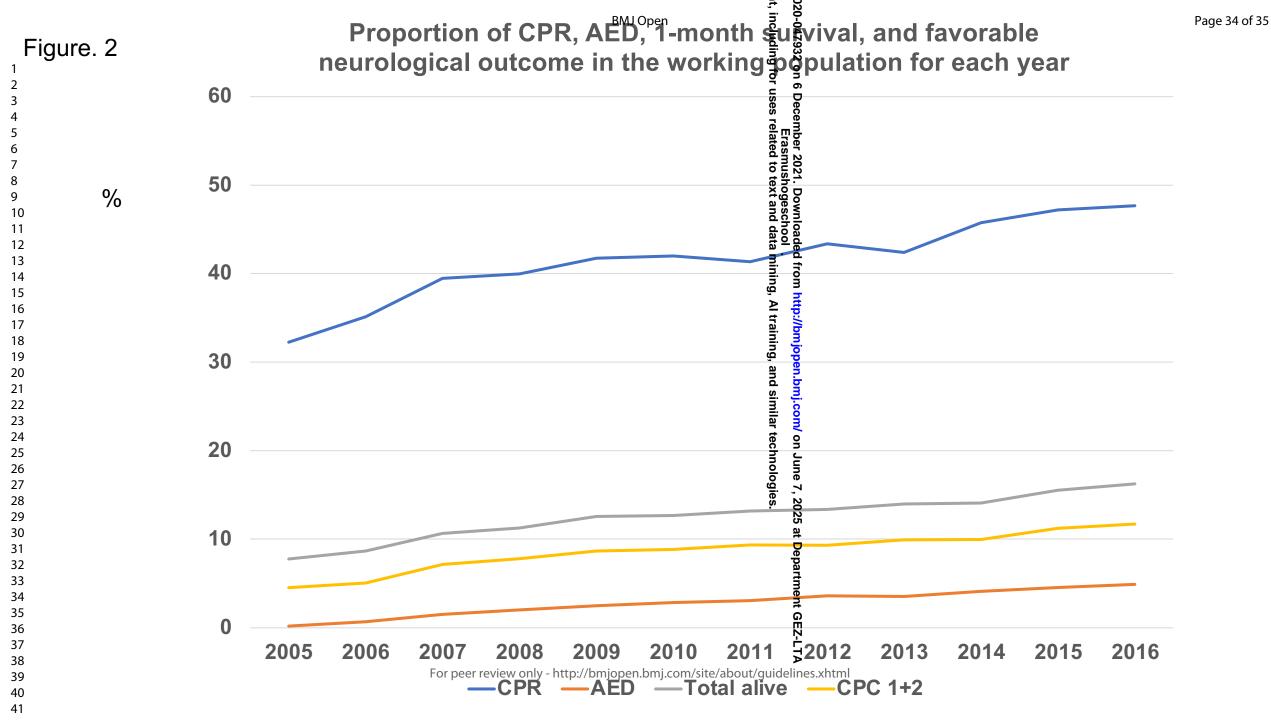
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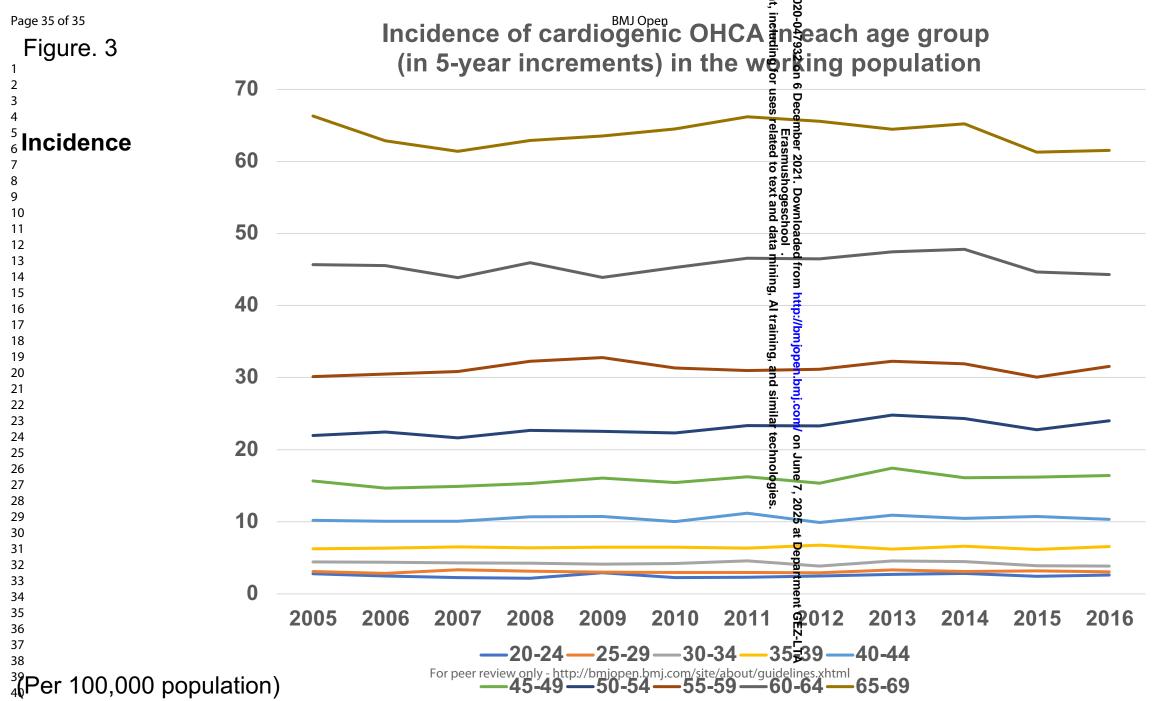
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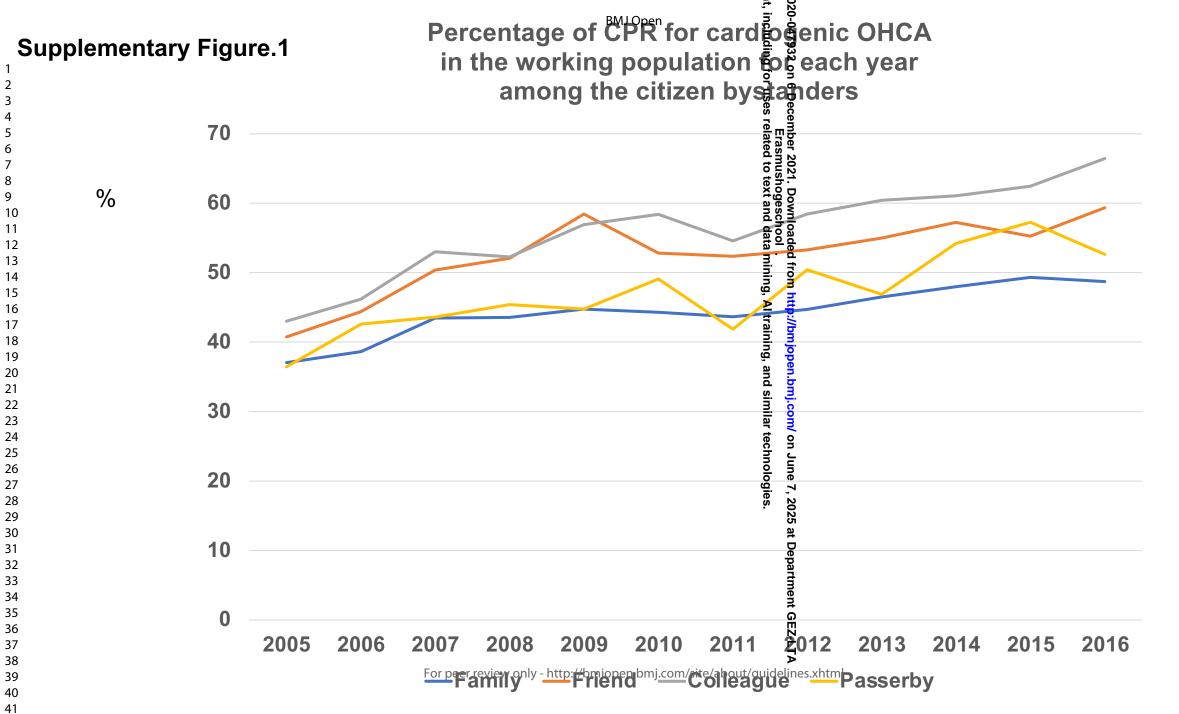
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<sup>(</sup>Per 100,000 population)







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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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Secondary Subject Heading:	Occupational and environmental medicine, Epidemiology, Public health
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12 13 14 15	4	Corresponding author:
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57 58 59 60	18	Word count: 3641words

ABSTRACT

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20	<b>Objectives:</b> The prevention and improvement of the prognosis of out-of-hospital cardiac
21	arrests (OHCAs) are important issues especially with respect to their social and economic
22	significance in working populations. The age distribution of the working population in Japan
23	is expected to change continually due to its aging society and extension of retirement;
24	however, few reports have examined the long-term condition of OHCA in the working
25	population, defined by age. The aim of this study was to determine the incidence of OHCAs
26	and the survival rates after 1 month, among the Japanese working population, defined by age,
27	considering the changing age distribution.
28	Design and setting: We analysed the All-Japan Utstein registry, a prospective, nationwide,
29	population-based, observational registry (2005–2016).
30	Participants: From the registry, 212,961 OHCA patients from the Japanese working
31	population (defined aged 20-69 years), with only cardiogenic aetiology participated in this
32	study. These patients were further divided into four groups according to the type of citizen
33	bystander (family, friends, work-colleagues, and passers-by).
34	Primary and secondary outcome measures: The main outcomes were 1-month survival
35	with favourable neurological outcomes.

36	Results: The incidence of OHCAs, in any age group, was almost constant during the 12-year
37	period. The work-colleagues had the best prognosis despite having significantly longer times
38	to initial defibrillations compared with the passers-by (13 vs. 12 min, respectively, $P < 0.001$ )
39	that was associated independently with 1-month survival with favourable neurological
40	outcomes (adjusted odds ratio: 0.94 [1-min increments], P < 0.001).
41	Conclusions: In the 12-year period, the incidence of OHCAs in any age group remained
42	almost constant, whereas the prognosis improved each year. Reducing the time to initial
43	defibrillation may further improve the prognosis of OHCAs with a work-colleague bystander.
44	Keywords: Cardiopulmonary resuscitation, defibrillation, Japan, out-of-hospital cardiac arrest, prognosis,
45	prospective registry, working population.

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4	46	STRENGTHS AND LIMITATIONS OF THIS STUDY
5	70	STRENGTING AND LIMITATIONS OF THIS STOD I
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7 8	47	
9	47	• In this population-based study, we analysed data collected between 2005 to 2016 in
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11	48	the All-Japan Utstein registry of the Fire and Disaster Management Agency; a
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13 14	40	
15	49	prospective, nationwide, population-based registry.
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18	50	• A large sample size and longer follow-up allowed for the detailed assessment of the
19 20		
20	51	relationship between a work-colleague bystander and the prognosis following an
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24	52	out-of-hospital cardiac arrest (OHCA) in the Japanese working population.
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28	53	• We assessed independent factors associated with 1-month survival with favourable
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30	54	neurological outcomes after OHCAs in the Japanese working population.
31	01	neuronogieur outcomes uner orreris in the supunese working population.
32 33		
34	55	• The All-Japan Utstein registry did not contain information on the actual employment
35	00	The fill supul observices of and not contain information on the actual employment
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37 38	56	status, individual medical therapy, activities of daily living before the OHCAs, or
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40	57	in-hospital treatment interventions.
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## 

58 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  $\geq 65$  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

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and Mondays, and during the early hours of the morning, it did not report on the prognosis ofthe 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

80 changing age distribution.

# 82 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

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93	information based on the information recorded by the treating physician, including sex, age,
94	prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time
95	course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an
96	automated external defibrillator (AED), administration of intravenous fluids, tracheal
97	intubation, and prehospitalisation return of spontaneous circulation. The person who
98	performed the basic cardiopulmonary resuscitation, or defibrillation using a public-access
99	AEDs-was defined as a bystander. The EMS personnel followed-up these OHCA patients for
100	1 month to ascertain the survival rates and neurological outcomes. The data of 1,423,338
101	patients were collected between January 1, 2005 and December 31, 2016.
102	We excluded the non-cardiogenic OHCA group, and only the cardiogenic OHCA group
103	participated in our present study. As reported in a previous study,[9] the cardiogenic group
104	was defined as those having confirmed absence of signs of circulation, with the following
105	exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external
106	factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and
107	other non-cardiac factors. The cardiogenic or non-cardiogenic classification was determined
108	clinically by physicians at the hospitals in collaboration with the EMS providers and was
109	confirmed by the FDMA. In this study, the cardiogenic OHCA group of the working
110	population (aged 20-69 years) were analysed. After excluding those who did not receive
111	OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = $109,761$ ), the working

3 4 5	112	population was further divided into four bystander groups (family, friends, work-colleagues,
6 7 8	113	and passers-by). We focused on the absolute number and incidences of OHCAs, the
9 10 11	114	proportion that received CPR/AEDs, the 1-month survival rate following the OHCAs each
12 13 14	115	year, and the characteristics of the bystanders. The incidence of the OHCAs was calculated as
15 16 17 18	116	follows: the absolute number of OHCAs in the 20–69 age group divided by the number of
19 20 21 22	117	individuals in the entire 20–69 age group.
23 24 25	118	The population size was based on the estimated data obtained from the Statistics Bureau of
26 27 28	119	Japan.[10,11] The neurological outcomes were evaluated by physicians based on the Cerebral
29 30 31	120	Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2,
32 33 34	121	moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or
35 36 37	122	vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes
38 39 40	123	at 1 month after admission were defined as Categories 1 or 2. Since some abnormal values
41 42 43	124	were noted in the data in the intervals between the emergency calls and the patient contact
44 45 46	125	times (call to contact time), witness to call times, times from witnessing OHCAs to
47 48 49	126	bystander-initiated CPRs, and times from witnessing OHCAs to the times of the initial
50 51 52	127	defibrillations, we only analysed the data recorded between 0 and 60 min (Supplementary
53 54 55	128	Table 1). According to the FDMA (Fire and Disaster Management Agency), until 2012,
56 57 58	129	patients with null values for bystander use of AEDs were converted automatically into the
59 60	130	group 'without bystander use of AEDs'; however, since 2013, they did not automatically

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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

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2 3		
5 4 5 6	149	contact times, and 1-month survival with favourable neurological outcomes after OHCAs.
7 8 9	150	For the multivariable regression models, Cook's distance and variance inflation factors (VIFs)
9 10 11 12	151	were determined to ascertain the presence of influential observations and multicollinearity,
13 14	152	respectively. All the statistical analyses were conducted using Stata (version 16.1; StataCorp
15 16 17 18 19	153	LLC, College Station, TX, USA).
20 21 22	154	Patient and public involvement
23 24 25 26 27	155	The patients and the public were not involved in the design of this study.
28 29 30 31	156	
32 33 34 35	157	RESULTS
36 37 38	158	Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and
39 40 41	159	2016, we excluded cases with missing age data ( $n = 62$ ) or patients who were over 120 years
42 43 44	160	old (n = 8). The cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the
45 46 47	161	total OHCA population ( $n = 1,423,268$ ), respectively. In the cardiogenic OHCA group,
48 49 50	162	212,961 OHCA patients aged 20-69 years (working population) were enrolled in this study.
51 52 53	163	After excluding those who did not receive OHCA resuscitations ( $n = 4,907$ ) or those who
54 55 56 57 58 59	164	lacked a-witnesses (n = $109,761$ ), the working population was further divided into four

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4 5	165	bystander groups (family, friends, work-colleagues, and passers-by). Figure 1 shows a flow
6 7 8 9	166	diagram of patients with OHCAs.
10 11 12 13	167	Overall trend of OHCAs
14 15 16 17	168	The total general population reported by the Statistics Bureau of Japan declined from
18 19 20	169	127,768,000 in 2005 to 126,933,000 in 2016, while a transient increase was observed in 2010
21 22 23	170	alone (n = $128,057,000$ ). Both the absolute number and the total incidence of OHCAs
24 25 26	171	increased, from 102,737 (80 per 100,000 population) in 2005 to 123,552 (97 per 100,000
27 28 29	172	population) in 2016. Moreover, the absolute number and incidence of cardiogenic OHCAs in
30 31 32	173	all age groups increased from 56,412 (44 per 100,000 population) in 2005 to 75,109 (59 per
33 34 35 36	174	100,000 population) in 2016.
37 38 39	175	OHCA trend in the working population
40 41 42 43	176	Of the OHCA population ( $n = 1,423,268$ ), the working population comprised 428,958
44 45 46	177	(30.1%) of the OHCA cases, whereas in the cardiogenic OHCA group ( $n = 814,794$ ), the
47 48 49 50	178	working population comprised 212,961 (26.1%) OHCA cases.
51 52 53	179	Figure 2 shows that both the absolute number of cases and the incidence of cardiogenic
54 55 56	180	OHCA in the working population mostly remained unchanged, from 17,403 (20 per 100,000
57 58 59	181	population) in 2005 to 17,917 (22 per 100,000 population) in 2016. The proportion of CPRs
60	182	and AEDs performed for the cardiogenic OHCAs in the working population increased every

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183 year, from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively, and the 184 1-month survival and favourable neurological outcomes of the cardiogenic OHCAs in the 185 working population also increased from 7.8% and 4.5% in 2005 to 16.3% and 11.7% in 2016, 186 respectively (Figure 3). 187 Sixty-five to 69 age group 188 The Statistics Bureau of Japan reported that the population aged 20–64 years declined from 189 77,829,000 in 2005 to 70,522,000 in 2016, whereas the population in the 65–69 age group 190 increased, from 7,460,000 in 2005 to 10,275,000 in 2016. Table 1 shows the incidence of 191 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 192 incidence of cardiogenic OHCAs over the last 12 years in any age group, and the IRRs for 193 194 the incidence of cardiogenic OHCAs in age groups separated by five years, was 1.08. 195 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) 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 Age (years) 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

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3 4 5		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
6 7 8 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
9 10 11 12		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
13 14 15		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
16 17 18		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
19 20 21		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
22 23 24		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
25 26 27		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
28 29 30		Abbreviations: OHCA, out-of-hospital cardiac arrest.												
31 32 33 34	196													
35 36 37	197	Citizen bystander in OHCAs in the working population												
38 39 40 41	198	Table 2.1 presents the characteristics (age, sex, CPR/AED proportions, and 1-month)												
42 43 44	199	survival/neurological outcomes) of the cardiogenic OHCA cases in the working population												
45 46 47	200	for each type of citizen bystander. The work-colleague bystander group had the highest												
48 49 50	201	percentag	e for both	n CPRs	and A	EDs (5	6.6% a	nd 10.2	2%, res	pective	ly). Fu	rthermo	ore, the	
51 52 53	202	work-coll	league by	stander	group	had the	e highe	st 1-mo	onth su	rvival a	and bes	t neuro	logical	
54 55 56	203	outcomes				-								
57 58 59	204	13,698), t							-	_				e
60	205	work-coll	league by	stander	group	had sig		ntly lon	ger me	dian in	tervals	betwee	en	

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+ 5 5	206	witnessing OHCAs and the initia	il defibrillations th	ian the passer	rs-by bystander gi	roup (13 vs.
7 8 9	207	12 min, respectively, $P < 0.001$ ).				
9 10						
11	208					
12 13						
14						
15		Table 2.1. Characteristics of patients wi	th cardiogenic OHCA	s in the working	population according	g to the
16 17						
18		bystander group				
19 20						
20 21				Bysta	nder group	
22		Characteristic		Dysta		
23 24						
25			Family	Friends	Work-colleagues	Passers-by
26						
27 28		Total, n	46,909	6,115	8,457	5,155
29						
30		Age, years, median (Q1–Q3)	61 (52–66)	59 (48–65)	56 (48–62)	60 (52–65)
31 32						
33		Sex, men, %	73.6	83.0	92.2	86.6
34 35						
35 36		CPR, %	44.3	52.7	56.6	47.6
37		CFR, 70	44.5	52.7	50.0	47.0
38 39						
40		AED (bystander defibrillation), %	0.7	7.1	10.2	9.3
41						
42 43		1-month survival rate, %	15.9	22.0	28.1	26.5
44						
45		1-month neurological outcome				
46 47			10.1	15.8	20.8	18.5
48		(CPC 1+2, %)				
49						
50 51		Abbroviations: AED, automated externa				

Abbreviations: AED, automated external defibriliator; 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	e data	available)
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Characteristic	Family	Friends	Work-colleagues	Passers-by
		Time course, m	in, 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.				
			1 1 71	11.000

35 36	210	Using a multivariable logistic regression, 13,698 patients were analysed. There were 11,808
37 38 39 40	211	(86.2%) males, 13,509 (98.6%) patients received bystander chest compression, 1,062 (7.8%)
41 42	212	were shocked by public-access AEDs (automated external defibrillator), 13,698 first
43 44 45 46	213	documented rhythms were analysed. The VT/VF rhythm was 11,882 (86.7%), PEA 741
40 47 48	214	(5.4%), asystole 834 (6.1%), and others 241 (1.7%). There were 8,564 (62.5%) family
49 50 51 52	215	bystanders, 1,551 (11.3%) friends bystanders, 2,465 (18.0%) work-colleagues bystanders,
53 54	216	and 1,118 (8.2%) passers-by bystanders. With respect to the onset time of day, 13,698 were
55 56 57 58	217	analysed, of which the time period 0:00-7:59 comprised 3,835 (28.0%), 8:00-16:59 5,696
58 59 60	218	(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 co	ontact times	s were asso	ciated in	dependently	with 1-m	onth
222	survival with favourable neurol	ogical outco	omes in thi	s study p	opulation (	Table 3).	
223	According to the Cook's distanc	e calculatio	on, none w	ere above	e 0.5. The m	nean VIF w	vas 1.27
224	and none of the variables exceed	led a VIF o	of 3.				
225							
	Table 3. Effect of prehospitalisation factors	on the 1-montl	h survival with	favourable r	neurological outo	comes after Ol	HCAs
	Prehospitalisation factor	Crude OR	95% CI	<i>P</i> -value	Adjusted OR	95% CI	<i>P</i> -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.	-	-

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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	1.08	1.07-1.09	<0.001	1.09	1.08-1.11	<0.001
(1-year increments)	1.00	1.01-1.00	-0.001	1.00	1.00-1.11	-0.001
Witness-initiated CPR by bystander time	0.91	0.90–0.92	<0.001	0.96	0.95–0.98	<0.001
(1-min increments)	0.01	5.50 5.0 <u>2</u>	0.001	5.00	0.00	0.001

0.89-0.90

< 0.001

0.94

0.93-0.95

< 0.001

0.89

2		
3 4 5		Witness-initial defibrillation time
6 7 8		(1-min increments)
9 10 11		Call to contact time
12 13 14		(1-min increments)
15 16 17		Abbreviations: AED, automated
18 19 20		out-of-hospital cardiac arrest; Of
21 22 23		tachycardia/ventricular fibrillatior
24 25		
26	226	
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28 29		
30	227	DISCUSSION
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32 33		
34	228	Using the data obtained
35	220	Using the data obtained
36		
37 38	229	2005 and 2016, we inve
39		
40	230	age. We found that: (1)
41 42		<b>C</b> ()
42	231	population, and that the
44	201	population, and that the
45		
46 47	232	cardiogenic OHCA grou
48		
49	233	OHCAs in the working
50 51		
52	234	in any age group in the
53	204	in any age group in the
54 55		
55 56	235	incidence of cardiogenie
57		
58	236	increasing with increasi
59 60		

ents) time 0.87 0.86-0.89 < 0.001 0.93 0.91-0.95 <0.001 ents) AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; OHCA, cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; Ref., reference; VT/VF, ventricular ntricular fibrillation. eer (c **ON** lata obtained from the Utstein registry, that were collected for 12 years between 016, we investigated OHCAs in the Japanese working population with respect to und that: (1) approximately 30% of all the OHCA cases occurred in the working and that the working population comprised 26% of all the cases in the c OHCA group; (2) both the absolute number and the incidence of cardiogenic the working population remained mainly unchanged over the 12-year period; (3) group in the working population, there was no significant improvement in the of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs with increasing age; (4) the proportion of CPRs and the use of AEDs increased

<ul> <li>CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes.</li> <li>However, the work-colleague bystanders had a significantly longer time from witnessing</li> <li>OHCAs to the initial defibrillations than the passers-by bystander group, and the time from</li> <li>witnessing OHCAs to initial defibrillations was associated independently with 1-month</li> <li>survival with favourable neurological outcomes.</li> <li><b>Causality of OHCAs and their countermeasures in the working population</b></li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> </ul>			
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<ul> <li>However, the work-colleague bystanders had a significantly longer time from witnessing</li> <li>OHCAs to the initial defibrillations than the passers-by bystander group, and the time from</li> <li>witnessing OHCAs to initial defibrillations was associated independently with 1-month</li> <li>survival with favourable neurological outcomes.</li> <li><b>Causality of OHCAs and their countermeasures in the working population</b></li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>		238	among the citizen bystanders, the work-colleague bystander group had the highest bystander
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<ul> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	3 9 )	248	of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of
<ul> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	 2 3	249	AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial
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<ul> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	7 3 9	251	inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.
<ul> <li>254 was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	)   <u>2</u>	252	statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the
	3 4 5	253	incidence of AMIs in both men and women who were < 59 years continued to increase. This
255 young peoples' diets and lifestyles, as well as the high smoking rates ( $\sim$ 50% and > 30% in	5 7 3	254	was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of
	) )	255	young peoples' diets and lifestyles, as well as the high smoking rates ( $\sim$ 50% and > 30% in

3 4 5 6	256	young men and women, respectively).[18] Therefore, an improvement in the diet and the
7 8	257	cessation of smoking may be important in the reduction of the incidence of cardiogenic
9 10 11 12	258	OHCAs in this population.
13 14 15	259	Compared to Western countries, ischaemic heart disease is less common in Japan,[19]
16 17 18	260	whereas the prevalence of the Brugada syndrome is relatively high.[20,21] The Brugada
19 20 21	261	syndrome was described by Pedro and Josep Brugada in 1992, as a disease that causes
22 23 24	262	ventricular fibrillation despite the absence of obvious structural cardiac diseases, electrolyte
25 26 27	263	abnormalities, or QT prolongations.[22] The Brugada-type electrocardiogram (ECG; right
28 29 30	264	bundle branch block and ST segment elevation in V1 through V3) may be associated closely
31 32 33	265	with a sudden unexplained death syndrome, such as Lai Tai ('death during sleep') in
34 35 36	266	northeast Thailand, Bangungut ('moaning and dying during sleep') in the Philippines, and
37 38 39	267	Pokkuri ('sudden unexpected death at night') in Japan.[23] A troublesome characteristic of
40 41 42	268	the Brugada syndrome is its nocturnal tendency, which may delay therapeutic interventions
43 44 45	269	and thus lead to worse prognosis. In the univariate analysis of this study, a night-time onset
46 47 48	270	(0:00–7:59 and 17:00–23:59) of OHCAs was associated with a worse prognosis than a
49 50 51	271	daytime onset (8:00–16:59), although this tendency was not shown in the multivariable
52 53 54	272	analysis (Table 3). Using a 12-lead ECG at screening, a history of syncope, and a family
55 56 57 58 59 60	273	history of sudden cardiac death may help identify patients who are in need of preventive

3 4 5	274	pharmacological and non-pharmacological therapy (e.g. use of an implantable cardioverter
6 7 8 9	275	defibrillator).[24]
10 11 12 13	276	Previous meta-analyses of prospective cohort studies have revealed associations between
14 15 16	277	work stressors and cardiovascular diseases. The summary relative risk for long working hours
17 18	278	( $\geq$ 55 hours per week) compared with the standard 35–40 hours per week was 1.13 (95%)
19 20 21	279	confidence interval [CI]: 1.02–1.26).[25] The total working hours tended to decline in Japan
22 23 24	280	[26] however, the reduction in the number of working hours was minor, and it is unknown
25 26 27 28	281	whether it contributed significantly to the incidence of OHCAs in the working population.
29 30 31 32	282	Analysis of OHCAs in the 65–69 age group
33 34 35	283	In 2018, the Japanese Cabinet Office reported that the proportion of workers in the 65–69 age
36 37 38	284	group was low; in the 5-year age groups, the proportions of male and female workers were
39 40 41	285	91.0% (55–59), 79.1% (60–64), and 54.8% (65–69) and 70.5% (55–59), 53.6% (60–64), and
42 43 44	286	34.4% (65–69).[27] Considering the extension of the retirement age that came into effect
45 46 47	287	from 2021, the employment rates are expected to increase for people in the 65–69 age group.
48 49 50 51	288	Thus, we investigated the characteristics of cardiogenic OHCAs in the 65-69 age group.
52 53 54	289	In fact, the proportion of workers aged $\geq 65$ years in the total labour force population has
55 56 57	290	been increasing every year, by 7.6% in 2005 to 12.8% in 2018.[28] We identified that there
58 59 60	291	were no significant improvements in the incidence of cardiogenic OHCAs in any age group

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4 5	292	over the last 12 years, and the incidence increased with increasing age (Table 1). A study of
5 7 3	293	OHCAs in the Osaka Prefecture, Japan, that was conducted for two years revealed that the
9 10 11	294	incidence of OHCAs increased exponentially with increasing age.[29] Our present study
12 13 14	295	revealed that the incidence of cardiogenic OHCAs in any age group was almost constant over
15 16 17	296	the 12-year period. It should be noted that the incidence of OHCAs in the 65–69 age group
18 19 20	297	(extended retirement age group) was high, and that age was associated independently with
21 22 23	298	1-month survival with favourable neurological outcomes (adjusted odds ratio [OR]: 0.98
24 25 26	299	[10-year increments], 95% CI: 0.98–0.99; $P < 0.001$ ). Therefore, it is important for
27 28 29	300	companies with older employees to take this into account. Nevertheless, this is not a problem
30 31 32	301	that is limited to Japan; the aging of the population is progressing worldwide, especially in
33 34	302	developed countries.[1] In the future, there is a possibility that the retirement age will be
35 36 37	303	extended in many countries around the world.
38 39 40		0.
41 42 43	304	Effect of work-colleagues and other types of bystanders
44 45 46	305	A previous study found that a key predictor of survival after OHCAs is the bystander
47 48 49	306	witness.[30] Another previous study reported that most of the cases of OHCAs in Japan that
50 51 52	307	were witnessed by family members and family bystanders had a worse prognosis than those
51 52 53 54 55 56 57 58	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
59 50	310	result may be attributed to the lowest CPR/AED proportions (44.3% and 0.7%, respectively).
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	311	Another study that reported a similar association for the bystander-patient relationship
	312	indicated that the large delays ( $\geq$ 5 min) in the witness call interval and large witness
)   <u>2</u>	313	bystander CPR interval were most frequent in the family bystander group.[31]
3 1 5	314	A previous systematic review revealed that the OHCA survival rate was better in the
5 7 3	315	workplace,[32] and the findings of our study were similar: work-colleague bystanders were
) ) 	316	associated with a better 1-month survival and favourable neurological outcomes. A possible
2 3 1	317	reason for such a favourable prognosis was that the CPR/AED proportion was highest in the
5	318	work-colleague bystander group. Furthermore, we found further improvements in the
3 ) )	319	prognosis of OHCAs in the work-colleague bystander group. The work-colleague bystander
 <u>2</u> 3	320	group had significantly longer median intervals between the witnessing OHCAs and initial
+ 5 5	321	defibrillations than the passers-by bystander group (13 vs. 12 min, respectively; $P < 0.001$ ). It
7 3 9 1	322	is known that a 1-min delay can reduce the survival rate by $7-10\%$ ,[33] and the results from
,   <u>2</u>	323	Table 3 also indicate that a 1-min difference does have a clinically meaningful benefit for
3 1 5	324	1-month survival with favourable neurological outcomes (adjusted OR: 0.94 [1-min
5 7 3	325	increments], 95% CI: 0.93–0.95; $P < 0.001$ ). A possible reason why work-colleagues took
)   	326	longer to perform the first defibrillation compared with passers-by may have been due to
2 3 1	327	most of the initial defibrillations being performed by EMS providers, and that the median call
5	328	to contact intervals were significantly longer in the work-colleague bystander group than in
3 9 )	329	the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$ ). The travel distance and

3 4 5	330	time to travel within buildings may also have contributed to the delays. Another study that
6 7 8 9	331	used the model of a large-scale skyscraper, calculated the length of time taken by the
10 11 12 13 14 15	332	emergency services to reach a patient within the building (i.e. travel time) and found that the
	333	minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst
16 17 18	334	value 4 min.[34]
19 20 21	335	Recently, the importance of CPR has become known widely, and the findings of this study
22 23 24	336	supported this, given that the CPR proportion in the working population has increased over
25 26 27	337	the years (Figure 3). However, our present study revealed that in 2016 in > 30% of the cases
28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43	338	CPR was not performed despite the witnessing of the cardiogenic OHCAs by
	339	work-colleagues (shown in Supplementary Figure 1). More opportunities for CPR
	340	awareness activities in companies may be useful in preventing cardiac death and poor
	341	neurological outcomes in OHCA patients in the working population. A previous study
	342	reported that approximately two-thirds of OHCA survivors return to work,[35] which is
44 45 46	343	important in terms of public health and socioeconomic significance.
47 48 49 50	344	Limitations
51 52 53	345	This study had several limitations. First, this was a retrospective population-based study of
54 55 56	346	data obtained from a prospective registry, with some instances where data were missing or
57 58 59 60	347	abnormal values were present. Second, the actual employment status of the OHCA patients in

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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.

2 3		
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6 7		
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9 10 11 12 13	365	Management Agency of Japan for their cooperation in collecting data and managing the
14	366	Utstein-style registry.
15 16 17 18 19	367	
20 21	368	COMPETING INTERESTS
22 23		
23 24 25	369	The authors have no competing interests.
26		
27 28	370	
29 30 31 32	371	FUNDING
33 34 35	372	This research received no specific grant from any funding agency in the public, commercial,
36 37 38	373	or not-for-profit sectors.
39 40 41 42	374	
43 44 45	375	AUTHORS' CONTRIBUTIONS
46 47 48 49	376	YY was involved in data analysis and writing of the manuscript. YO was involved in data
49 50 51 52 53 54	377	verification, the design of the study, supervision, and revising the manuscript. YF was
	378	involved in data verification, supervision, and statistical analysis. KY, TM, and KT were
55 56 57	379	involved in data verification. HO and RK were involved in data verification and supervision.
58 59 60	380	HA was involved in data verification, supervision, and revising the manuscript.

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4 5	381	
6 7 8 9	382	DATA SHARING
9 10 11 12	383	The data used in this study are not publicly available. The data are only accessible through
13 14 15	384	the Fire and Disaster Management Agency (2-1-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan;
16 17 18	385	Tel.: +03-5253-7529; Fax: +03-5253-7532; E-mail: fdma-goiken@ml.soumu.go.jp).
19 20 21	386	Therefore, no additional data are available.
22 23 24 25	387	
26 27 28 29	388	ETHICS STATEMENT
30 31 32 33	389	This study was approved by the Institutional Review Board of the University of Occupational
34 35	390	and Environmental Health, Japan (approval number; UOEHCRB19-072).
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	487 488 489 490 491 492 493 494 495 494 495 496 497 498 497 498 499 500 501 501	<ul> <li>487</li> <li>488</li> <li>489</li> <li>(29)</li> <li>490</li> <li>491</li> <li>492</li> <li>(30)</li> <li>493</li> <li>493</li> <li>494</li> <li>495</li> <li>496</li> <li>497</li> <li>(31)</li> <li>498</li> <li>499</li> <li>500</li> <li>501</li> <li>(32)</li> <li>503</li> </ul>

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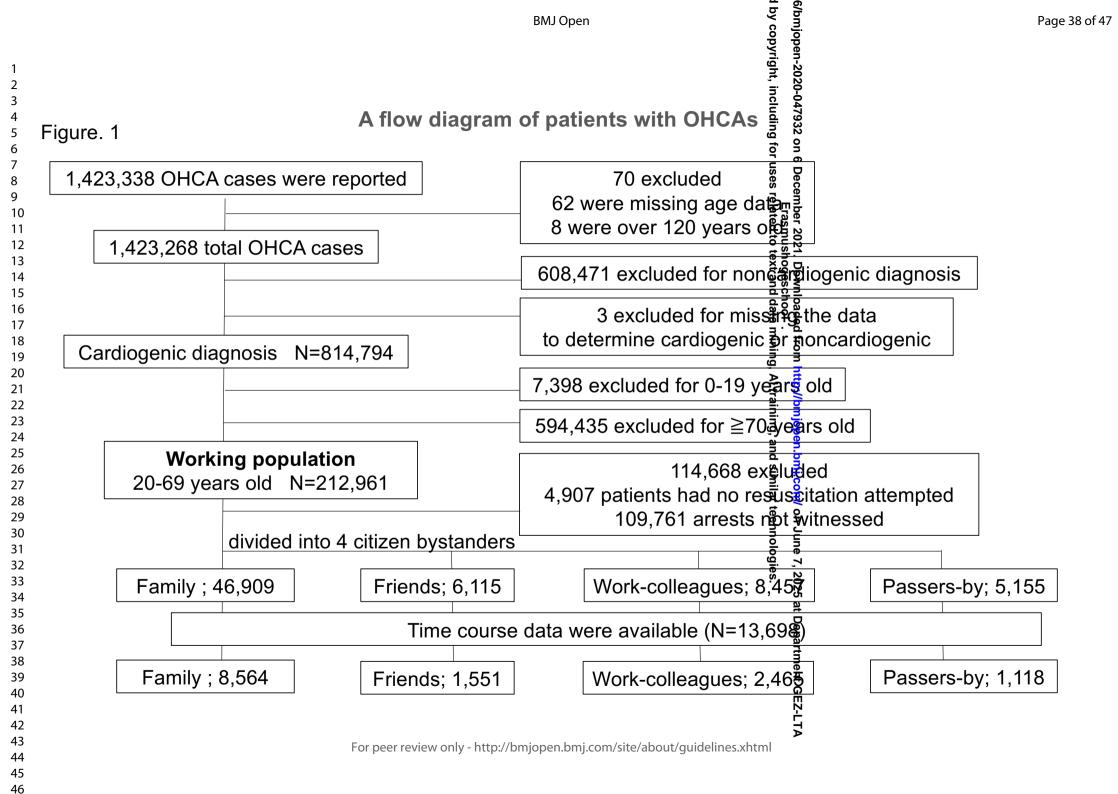
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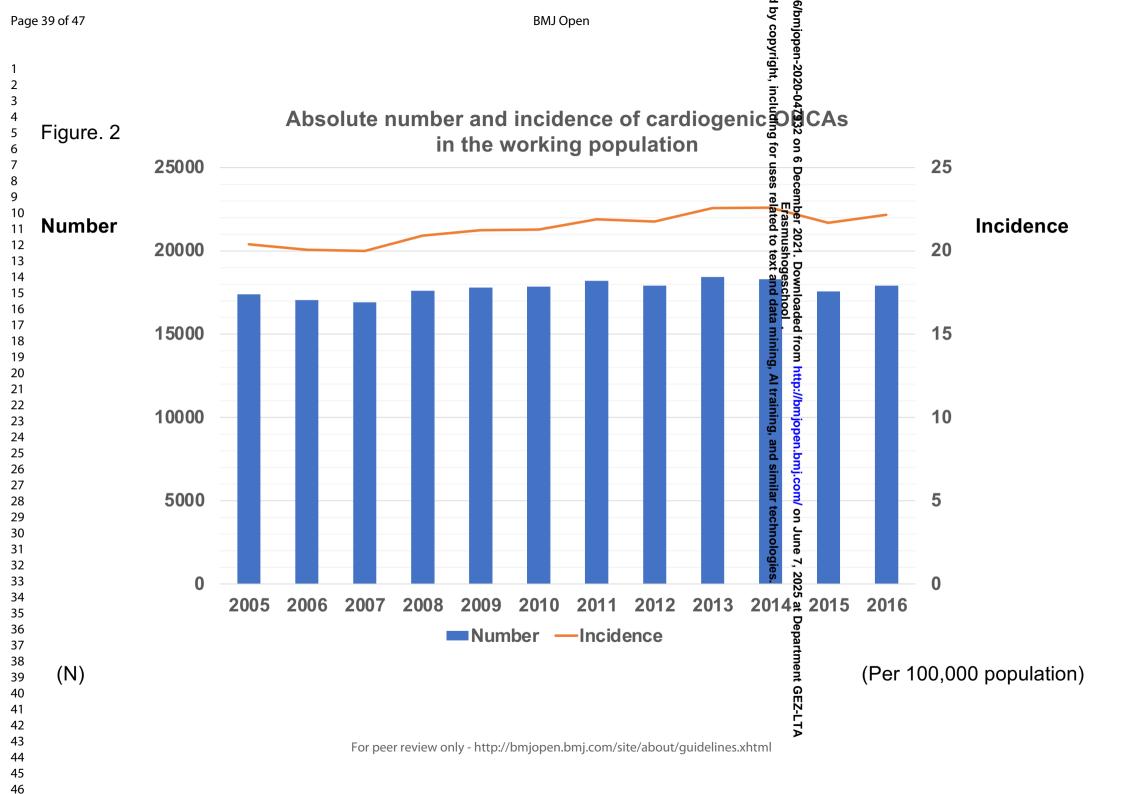
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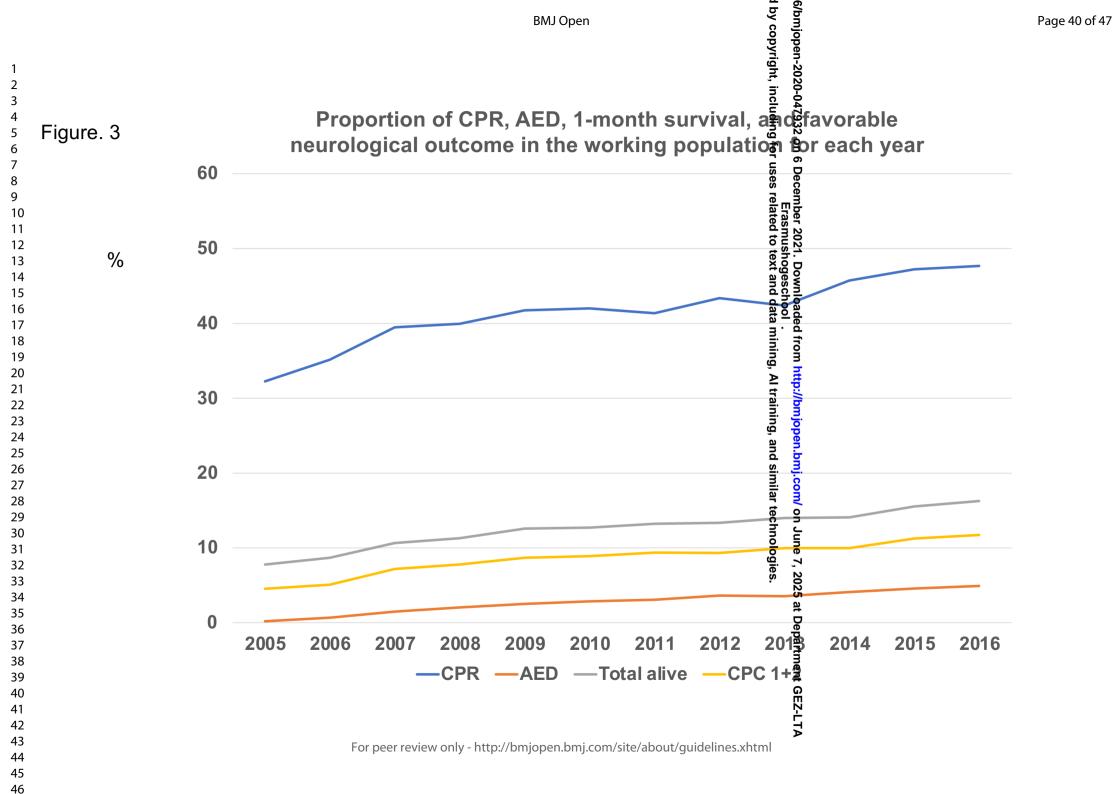
525	Figure 1. A flow diagram of patients with OHCAs
526	Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and
527	2016, we excluded cases with missing data of age $(n=62)$ or patients who were over 120
528	years old (n=8). Cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the
529	total OHCA population (n=1,423,268), respectively. We excluded non-cardiogenic OHCA
530	group. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20-69 years (working
531	population) were enrolled in this study. After excluding those who did not receive OHCA
532	resuscitation ( $n = 4,907$ ) or those who lacked a witness ( $n = 109,761$ ), the working population
533	was further divided into four bystander groups (family, friends, work-colleagues, and
534	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.
534 535	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.
	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest. Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working
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535 536	Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working
535 536 537	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
535 536 537 538	<b>Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working</b> 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
535 536 537 538 539	<b>Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working</b> 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,

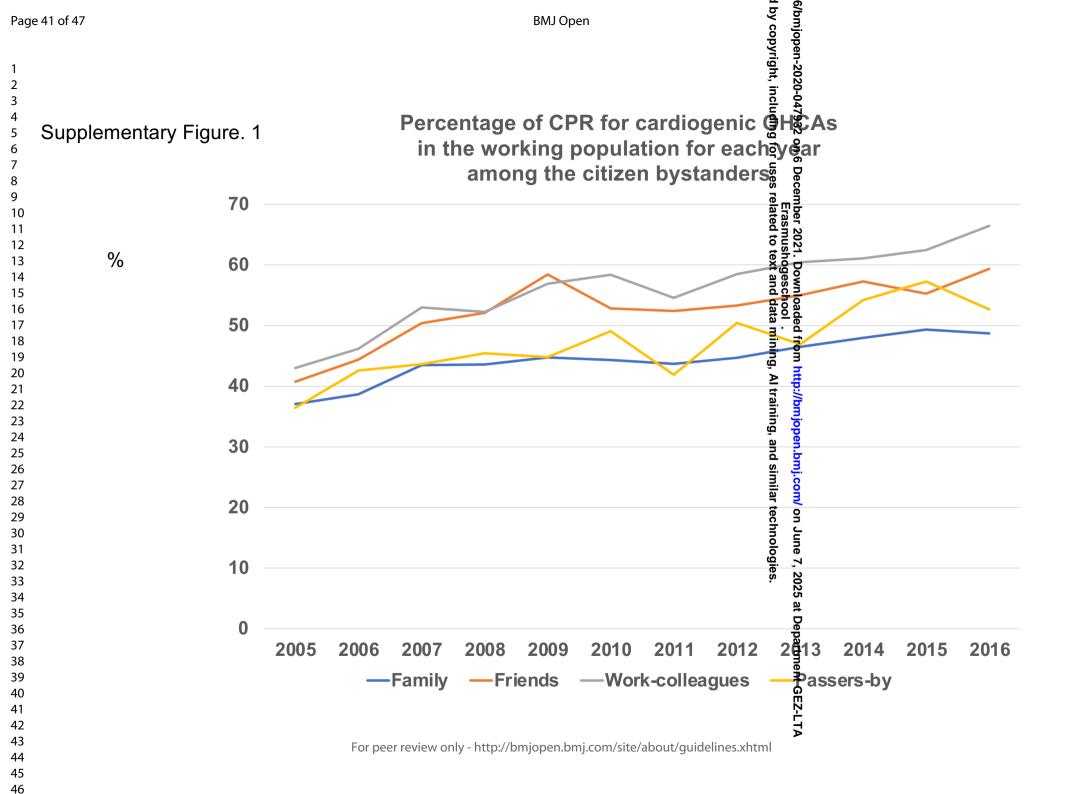
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543	Figure 3. Proportion of CPR, AED, 1-month survival, and favourable neurological
544	outcome in the working population for each year. The percentage of CPR and AED
545	increased each year from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively.
546	One-month survival rate of cardiogenic OHCAs in the working population increased from
547	7.8% in 2005 to 16.3% in 2016, and the 1-month survival with favourable neurological
548	outcome also increased from 4.5% in 2005 to 11.7% in 2016. Abbreviations: CPR,
549	cardiopulmonary resuscitation; AED, automated external defibrillator; CPC, cerebral
550	performance category.
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## Supplementary Table 1. Information about the abnormal value of time course

	-	Time course, minutes	
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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 $\rightarrow$ Page 1, Lines 1-2: The incidence of out-of-hospital cardiac arrests and surviva
		rates after one-month among the Japanese working population: A cohort study
		( <i>b</i> ) 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 $\rightarrow$ 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 $\rightarrow$ 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)
		$\rightarrow$ 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		O,
Study design	4	Present key elements of study design early in the paper
		$\rightarrow$ 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
		$\rightarrow$ 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.

		selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants $\rightarrow$ 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) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case inct ampliable
Variables	7	<ul> <li>→not applicable</li> <li>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</li> <li>→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.</li> <li>→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.</li> </ul>
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 $\rightarrow$ 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
		$\rightarrow$ 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 $\rightarrow$ 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
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was
		addressed
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of
		sampling strategy
		→not applicable
		( <u>e</u> ) Describe any sensitivity analyses
		$\rightarrow$ 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		

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible,
1		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
		$\rightarrow$ Figure 1
		(c) Consider use of a flow diagram
		→Figure 1
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and informat
data		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
		$\rightarrow$ Figure 1
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)
		$\rightarrow$ Page 7, Lines 99-100: The EMS personnel followed-up these OHCA patients for 1 month
Outcomo data	15*	ascertain the survival rates and neurological outcomes.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time
		$\rightarrow$ Table 2.1 and 2.2.
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of
		exposure
		→not applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	→not applicable (a) Cive was divised estimates and if any lister as four day a divised estimates and their
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 an
		why they were included
		$\rightarrow$ Table 3. (b) Borrow and a size when continuous previous contactorized
		(b) Report category boundaries when continuous variables were categorized
		<ul> <li>→Table 3.</li> <li>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaning</li> </ul>
		-
		time period
Oth an an always	17	→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 $\rightarrow$ 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 t
		$\alpha_{1}$ and $\alpha_{2}$ in the cardiogenetic OUCA group: (2) both the absolute number and the incidence of
		cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of

<b>Other information</b> Funding	<u>n</u> 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 $\rightarrow$ Page 26, Line 371-373: FUNDING~
		the world.
		future, there is a possibility that the retirement age will be extended in many countries around
		aging of the population is progressing worldwide, especially in developed countries.[1] In the
Seneransaomity	<u>~1</u>	$\rightarrow$ Page 22, Lines 300-303: Nevertheless, this is not a problem that is limited to Japan; the
Generalisability	21	Discuss the generalisability (external validity) of the study results
		approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]
		a patient within the building (i.e. travel time) and found that the minimum travel time was
		a large-scale skyscraper, calculated the length of time taken by the emergency services to read
		within buildings may also have contributed to the delays. Another study that used the model of
		by stander group (8 vs. 7 min, respectively; $P < 0.001$ ). The travel distance and time to travel
		were significantly longer in the work-colleague bystander group than in the passers-by
		defibrillations being performed by EMS providers, and that the median call to contact interva
		$\rightarrow$ Page 23-24, Lines 323-334. A possible reason why work-coneagues took longer to perform the first defibrillation compared with passers-by may have been due to most of the initial
		$\rightarrow$ Page 23-24, Lines 325-334: A possible reason why work-colleagues took longer to perform
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicit of analyses, results from similar studies, and other relevant evidence
		→Page 24-25, Lines 344-352: Limitations ~
	- /	Discuss both direction and magnitude of any potential bias
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.
		favourable neurological outcomes.
		OHCAs to initial defibrillations was associated independently with 1-month survival with
		initial defibrillations than the passers-by bystander group, and the time from witnessing
		work-colleague bystanders had a significantly longer time from witnessing OHCAs to the
		proportion, highest 1-month survival rate, and best neurological outcomes. However, the
		citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED
		year, and the prognosis after 1 month improved in the working population; and (5) among the
		increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased ea
		in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCA

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\*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.

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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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1 2		
3 4 5	1	The incidence of out-of-hospital cardiac arrests and survival rates after one-month
6 7 8 9	2	among the Japanese working population: A cohort study
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57 58 59 60	18	Word count: 3639 words

ABSTRACT

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20	<b>Objectives:</b> The prevention and improvement of the prognosis of out-of-hospital cardiac
21	arrests (OHCAs) are important issues especially with respect to their social and economic
22	significance in working populations. The age distribution of the working population in Japan
23	is expected to change continually due to its aging society and extension of retirement;
24	however, few reports have examined the long-term condition of OHCA in the working
25	population, defined by age. The aim of this study was to determine the incidence of OHCAs
26	and the survival rates after 1 month, among the Japanese working population, defined by age,
27	considering the changing age distribution.
28	Design and setting: We analysed the All-Japan Utstein registry, a prospective, nationwide,
29	population-based, observational registry (2005–2016).
30	Participants: From the registry, 212,961 OHCA patients from the Japanese working
31	population (defined aged 20-69 years), with only cardiogenic aetiology participated in this
32	study. These patients were further divided into four groups according to the type of citizen
33	bystander (family, friends, work-colleagues, and passers-by).
34	Primary and secondary outcome measures: The main outcomes were 1-month survival
35	with favourable neurological outcomes.

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36	Results: The incidence of OHCAs, in any age group, was almost constant during the 12-year
37	period. The work-colleagues had the best prognosis despite having significantly longer times
38	to initial defibrillations compared with the passers-by (13 vs. 12 min, respectively, $P < 0.001$ )
39	that was associated independently with 1-month survival with favourable neurological
40	outcomes (adjusted odds ratio: 0.94 [1-min increments], P < 0.001).
41	Conclusions: In the 12-year period, the incidence of OHCAs in any age group remained
42	almost constant, whereas the prognosis improved each year. Reducing the time to initial
43	defibrillation may further improve the prognosis of OHCAs with a work-colleague bystander.
44	Keywords: Cardiopulmonary resuscitation, defibrillation, Japan, out-of-hospital cardiac arrest, prognosis,
45	prospective registry, working population.

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2 3		
4	46	STRENGTHS AND LIMITATIONS OF THIS STUDY
5 6		
7 8 9	47	• In this population-based study, we analysed data collected between 2005 to 2016 in
10 11 12	48	the All-Japan Utstein registry of the Fire and Disaster Management Agency; a
13 14 15 16	49	prospective, nationwide, population-based registry.
17 18 19	50	• A large sample size and longer follow-up allowed for the detailed assessment of the
20 21 22	51	relationship between a work-colleague bystander and the prognosis following an
23 24 25	52	out-of-hospital cardiac arrest (OHCA) in the Japanese working population.
26 27 28 29	53	• We assessed independent factors associated with 1-month survival with favourable
30 31 32	54	neurological outcomes after OHCAs in the Japanese working population.
33 34 35	55	• The All-Japan Utstein registry did not contain information on the actual employment
36 37 38	56	status, individual medical therapy, activities of daily living before the OHCAs, or
39 40 41 42	57	in-hospital treatment interventions.
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## 

58 INTRODUCTION

59 The prevention and improvement of the prognosis of out-of-hospital cardiac arrests (OHCAs)
60 are important issues especially with respect to their social and economic significance in
61 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  $\geq 65$  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

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and Mondays, and during the early hours of the morning, it did not report on the prognosis ofthe 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

80 changing age distribution.

## 82 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

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93	information based on the information recorded by the treating physician, including sex, age,
94	prefecture, time of occurrence, initial cardiac rhythm, witness status, type of bystander, time
95	course of resuscitation, bystander-initiated cardiopulmonary resuscitation (CPR), use of an
96	automated external defibrillator (AED), administration of intravenous fluids, tracheal
97	intubation, and prehospitalisation return of spontaneous circulation. The person who
98	performed the basic cardiopulmonary resuscitation, or defibrillation using a public-access
99	AEDs-was defined as a bystander. The EMS personnel followed-up these OHCA patients for
100	1 month to ascertain the survival rates and neurological outcomes. The data of 1,423,338
101	patients were collected between January 1, 2005 and December 31, 2016.
102	We excluded the non-cardiogenic OHCA group, and only the cardiogenic OHCA group
103	participated in our present study. As reported in a previous study,[9] the cardiogenic group
104	was defined as those having confirmed absence of signs of circulation, with the following
105	exclusion criteria: cerebrovascular diseases, respiratory diseases, malignant tumours, external
106	factors, drug overdoses, drownings, traffic accidents, hypothermia, anaphylactic shocks, and
107	other non-cardiac factors. The cardiogenic or non-cardiogenic classification was determined
108	clinically by physicians at the hospitals in collaboration with the EMS providers and was
109	confirmed by the FDMA. In this study, the cardiogenic OHCA group of the working
110	population (aged 20-69 years) were analysed. After excluding those who did not receive
111	OHCA resuscitations (n = 4,907) or those who lacked witnesses (n = $109,761$ ), the working

3 4 5	112	population was further divided into four bystander groups (family, friends, work-colleagues,
6 7 8	113	and passers-by). We focused on the absolute number and incidences of OHCAs, the
9 10 11	114	proportion that received CPR/AEDs, the 1-month survival rate following the OHCAs each
12 13 14	115	year, and the characteristics of the bystanders. The incidence of the OHCAs was calculated as
15 16 17 18	116	follows: the absolute number of OHCAs in the 20–69 age group divided by the number of
19 20 21 22	117	individuals in the entire 20–69 age group.
23 24 25	118	The population size was based on the estimated data obtained from the Statistics Bureau of
26 27 28	119	Japan.[10,11] The neurological outcomes were evaluated by physicians based on the Cerebral
29 30 31	120	Performance Category (CPC) scale: Category 1, good cerebral performance; Category 2,
32 33 34	121	moderate cerebral disability; Category 3, severe cerebral disability; Category 4, coma or
35 36 37	122	vegetative state; and Category 5, death or brain death.[2,6] Favourable neurological outcomes
38 39 40	123	at 1 month after admission were defined as Categories 1 or 2. Since some abnormal values
41 42 43	124	were noted in the data in the intervals between the emergency calls and the patient contact
44 45 46	125	times (call to contact time), witness to call times, times from witnessing OHCAs to
47 48 49	126	bystander-initiated CPRs, and times from witnessing OHCAs to the times of the initial
50 51 52	127	defibrillations, we only analysed the data recorded between 0 and 60 min (Supplementary
53 54 55	128	Table 1). According to the FDMA (Fire and Disaster Management Agency), until 2012,
56 57 58	129	patients with null values for bystander use of AEDs were converted automatically into the
59 60	130	group 'without bystander use of AEDs'; however, since 2013, they did not automatically

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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 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

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3 4 5	149	favourable neurological outcomes after OHCAs. For the multivariable regression models,
6 7 8	150	Cook's distance and variance inflation factors (VIFs) were determined to ascertain the
9 10 11	151	presence of influential observations and multicollinearity, respectively. All the statistical
12 13 14	152	analyses were conducted using Stata (version 16.1; StataCorp LLC, College Station, TX,
15 16 17 18	153	USA).
19 20 21 22	154	Patient and public involvement
23 24 25 26	155	The patients and the public were not involved in the design of this study.
27 28 29 30 31	156	
32 33 34 35 36 37 38	157	RESULTS
	158	Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and
39 40 41	159	2016, we excluded cases with missing age data ( $n = 62$ ) or patients who were over 120 years
42 43 44	160	old (n = 8). The cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the
45 46 47	161	total OHCA population ( $n = 1,423,268$ ), respectively. In the cardiogenic OHCA group,
48 49 50	162	212,961 OHCA patients aged 20-69 years (working population) were enrolled in this study.
51 52 53	163	After excluding those who did not receive OHCA resuscitations ( $n = 4,907$ ) or those who
54 55 56 57 58 59 60	164	lacked a-witnesses (n = 109,761), the working population was further divided into four

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4 5	165	bystander groups (family, friends, work-colleagues, and passers-by). Figure 1 shows a flow
6 7 8 9	166	diagram of patients with OHCAs.
10 11 12 13	167	Overall trend of OHCAs
14 15 16 17	168	The total general population reported by the Statistics Bureau of Japan declined from
18 19 20	169	127,768,000 in 2005 to 126,933,000 in 2016, while a transient increase was observed in 2010
21 22 23	170	alone (n = $128,057,000$ ). Both the absolute number and the total incidence of OHCAs
24 25 26	171	increased, from 102,737 (80 per 100,000 population) in 2005 to 123,552 (97 per 100,000
27 28 29	172	population) in 2016. Moreover, the absolute number and incidence of cardiogenic OHCAs in
30 31 32	173	all age groups increased from 56,412 (44 per 100,000 population) in 2005 to 75,109 (59 per
33 34 35 36	174	100,000 population) in 2016.
37 38 39	175	OHCA trend in the working population
40 41 42 43	176	Of the OHCA population ( $n = 1,423,268$ ), the working population comprised 428,958
44 45 46	177	(30.1%) of the OHCA cases, whereas in the cardiogenic OHCA group ( $n = 814,794$ ), the
47 48 49 50	178	working population comprised 212,961 (26.1%) OHCA cases.
51 52 53	179	Figure 2 shows that both the absolute number of cases and the incidence of cardiogenic
54 55 56	180	OHCA in the working population mostly remained unchanged, from 17,403 (20 per 100,000
57 58 59	181	population) in 2005 to 17,917 (22 per 100,000 population) in 2016. The proportion of CPRs
60	182	and AEDs performed for the cardiogenic OHCAs in the working population increased every

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183 year, from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively, and the 184 1-month survival and favourable neurological outcomes of the cardiogenic OHCAs in the 185 working population also increased from 7.8% and 4.5% in 2005 to 16.3% and 11.7% in 2016, 186 respectively (Figure 3). 187 Sixty-five to 69 age group 188 The Statistics Bureau of Japan reported that the population aged 20–64 years declined from 189 77,829,000 in 2005 to 70,522,000 in 2016, whereas the population in the 65–69 age group 190 increased, from 7,460,000 in 2005 to 10,275,000 in 2016. Table 1 shows the incidence of 191 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 192 incidence of cardiogenic OHCAs over the last 12 years in any age group, and the IRRs for 193 194 the incidence of cardiogenic OHCAs in age groups separated by five years, was 1.08. 195 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) 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 Age (years) 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

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3 4 5		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
6 7 8 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
9 10 11 12		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
13 14 15		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
16 17 18		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
19 20 21		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
22 23 24		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
25 26 27		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
28 29 30		Abbreviations: OHCA, out-of-hospital cardiac arrest.												
31 32 33 34	196													
35 36 37	197	Citizen bystander in OHCAs in the working population												
38 39 40 41	198	Table 2.1 presents the characteristics (age, sex, CPR/AED proportions, and 1-month)												
42 43 44	199	survival/neurological outcomes) of the cardiogenic OHCA cases in the working population												
45 46 47	200	for each type of citizen bystander. The work-colleague bystander group had the highest												
48 49 50	201	percentag	e for both	n CPRs	and A	EDs (5	6.6% a	nd 10.2	2%, res	pective	ly). Fu	rthermo	ore, the	
51 52 53	202	work-coll	league by	stander	group	had the	e highe	st 1-mo	onth su	rvival a	and bes	t neuro	logical	
54 55 56	203	outcomes				-								
57 58 59	204	13,698), t							-	_				e
60	205	work-coll	league by	stander	group	had sig		ntly lon	ger me	dian in	tervals	betwee	en	

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3 4						(1.2
+ 5 5	206	witnessing OHCAs and the initia	il defibrillations th	ian the passer	rs-by bystander gi	roup (13 vs.
7 8 9	207	12 min, respectively, $P < 0.001$ ).				
9 10						
11	208					
12 13						
14						
15		Table 2.1. Characteristics of patients wi	th cardiogenic OHCA	s in the working	population according	g to the
16 17						
18		bystander group				
19 20						
20 21				Bysta	nder group	
22		Characteristic		Dysta		
23 24						
25			Family	Friends	Work-colleagues	Passers-by
26						
27 28		Total, n	46,909	6,115	8,457	5,155
29						
30		Age, years, median (Q1–Q3)	61 (52–66)	59 (48–65)	56 (48–62)	60 (52–65)
31 32						
33		Sex, men, %	73.6	83.0	92.2	86.6
34 35						
35 36		CPR, %	44.3	52.7	56.6	47.6
37		CFR, 70	44.5	52.7	50.0	47.0
38 39						
40		AED (bystander defibrillation), %	0.7	7.1	10.2	9.3
41						
42 43		1-month survival rate, %	15.9	22.0	28.1	26.5
44						
45		1-month neurological outcome				
46 47			10.1	15.8	20.8	18.5
48		(CPC 1+2, %)				
49						
50 51		Abbroviations: AED, automated externa				

Abbreviations: AED, automated external defibriliator; 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

Characteristic	Family	Friends	Work-colleagues	Passers-by
		Time course, m	in, 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 res	uscitation; OHCA, o	out-of-hospital c	ardiac arrest; Q1–Q3	, first to third
quartile.				

5	210	Using a multivariable logistic regression, 13,698 patients were analysed. There were 11,808
/ 3 9 1	211	(86.2%) males, 13,509 (98.6%) patients received bystander chest compression, 1,062 (7.8%)
1 2	212	were shocked by public-access AEDs (automated external defibrillator), 13,698 first
5 4 5	213	documented rhythms were analysed. The number of patients with VT/VF rhythm was 11,882
5 7 3	214	(86.7%), PEA 741 (5.4%), asystole 834 (6.1%), and others 241 (1.7%). There were 8,564
9 ) 1 )	215	(62.5%) family bystanders, 1,551 (11.3%) friends bystanders, 2,465 (18.0%) work-colleagues
2 3 4 -	216	bystanders, and 1,118 (8.2%) passers-by bystanders. With respect to the onset time of day,
5 7	217	13,698 were analysed, of which the time period 0:00-7:59 comprised 3,835 (28.0%),
3 9 )	218	8:00-16:59 5,696 (41.6%), and 17:00-23:59 4,167 (30.4%). Age, sex, bystander chest

219 compressions, shock by public-access AEDs, first documented rhythms, types of bystander, 220 onset years, times from witnessing OHCAs to bystander-initiated CPRs, times from 221 witnessing OHCAs to initial defibrillations, and the call to contact times were associated 222 independently with 1-month survival with favourable neurological outcomes in this study 223 population (Table 3). According to the Cook's distance calculation, none were above 0.5. 224 The mean VIF was 1.27 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 0.98 0.98-0.99 < 0.001 0.98 < 0.001 Age (10-year increments) 0.98 - 0.99Sex male Ref. Ref. female 1.16 1.04-1.29 0.006 1.33 1.19-1.50 < 0.001 Bystander chest compression Ref. no Ref 0.027 1.77 1.23 - 2.560.002 1.54 1.05 - 2.22yes Shock by public-access AEDs

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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	1.08	1.07-1.09	<0.001	1.09	1.08-1.11	<0.001
(1-year increments)	1.00	1.07-1.03	-0.001	1.00	1.00-1.11	-0.001
Witness-initiated CPR by bystander time	0.91	0.90–0.92	<0.001	0.96	0.95–0.98	<0.001
(1-min increments)	0.01	5.50 5.0 <u>2</u>	0.001	5.00	0.00	0.001

0.89-0.90

< 0.001

0.94

0.93-0.95

< 0.001

0.89

2		
3 4 5		Witness-initial defibrillation time
6 7 8		(1-min increments)
9 10 11		Call to contact time
12 13 14		(1-min increments)
15 16 17		Abbreviations: AED, automated
18 19 20		out-of-hospital cardiac arrest; Of
21 22 23		tachycardia/ventricular fibrillation
24 25		
26	226	
27		
28 29		
30	227	DISCUSSION
31	221	DISCUSSION
32		
33 34		
34 35	228	Using the data obtained
36		
37	229	2005 and 2016, we inve
38		
39 40		
40	230	age. We found that: (1)
42		
43	231	population, and that the
44 45		
45 46	000	
47	232	cardiogenic OHCA grou
48		
49 50	233	OHCAs in the working
50 51		
52	234	in any age group in the
53	204	In any age group in the
54		
55 56	235	incidence of cardiogenie
57		
57		
58	236	increasing with increasi
58 59	236	increasing with increasi
58	236	increasing with increasi

ents) time 0.87 0.86-0.89 < 0.001 0.93 0.91-0.95 <0.001 ents) AED, automated external defibrillator; CI, confidence interval; CPR, cardiopulmonary resuscitation; OHCA, cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; Ref., reference; VT/VF, ventricular ntricular fibrillation. eer (c **ON** lata obtained from the Utstein registry, that were collected for 12 years between 016, we investigated OHCAs in the Japanese working population with respect to und that: (1) approximately 30% of all the OHCA cases occurred in the working and that the working population comprised 26% of all the cases in the c OHCA group; (2) both the absolute number and the incidence of cardiogenic the working population remained mainly unchanged over the 12-year period; (3) group in the working population, there was no significant improvement in the of cardiogenic OHCAs over the 12-year period, with the incidence of OHCAs with increasing age; (4) the proportion of CPRs and the use of AEDs increased

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<ul> <li>CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes.</li> <li>However, the work-colleague bystanders had a significantly longer time from witnessing</li> <li>OHCAs to the initial defibrillations than the passers-by bystander group, and the time from</li> <li>witnessing OHCAs to initial defibrillations was associated independently with 1-month</li> <li>survival with favourable neurological outcomes.</li> <li><b>Causality of OHCAs and their countermeasures in the working population</b></li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> </ul>			
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<ul> <li>However, the work-colleague bystanders had a significantly longer time from witnessing</li> <li>OHCAs to the initial defibrillations than the passers-by bystander group, and the time from</li> <li>witnessing OHCAs to initial defibrillations was associated independently with 1-month</li> <li>survival with favourable neurological outcomes.</li> <li><b>Causality of OHCAs and their countermeasures in the working population</b></li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>		238	among the citizen bystanders, the work-colleague bystander group had the highest bystander
<ul> <li>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.</li> <li>Causality of OHCAs and their countermeasures in the working population</li> <li>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 &lt; 59 years continued to increase. This was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	) I	239	CPR/AED proportion, highest 1-month survival rate, and best neurological outcomes.
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<ul> <li>survival with favourable neurological outcomes.</li> <li>Causality of OHCAs and their countermeasures in the working population</li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	5 5 7	241	OHCAs to the initial defibrillations than the passers-by bystander group, and the time from
<ul> <li>Causality of OHCAs and their countermeasures in the working population</li> <li>The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At</li> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	3 9 )	242	witnessing OHCAs to initial defibrillations was associated independently with 1-month
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	1 2 3	243	survival with favourable neurological outcomes.
<ul> <li>least one significant coronary artery lesion was found in 70% of all OHCA patients in the</li> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	4 5 5 7 3	244	Causality of OHCAs and their countermeasures in the working population
<ul> <li>absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study</li> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	)	245	The acute coronary syndrome is the leading cause of cardiac arrest in Western countries. At
<ul> <li>of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of</li> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	<u>2</u> 3 4	246	least one significant coronary artery lesion was found in 70% of all OHCA patients in the
<ul> <li>AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial</li> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	5 5 7	247	absence of an obvious extracardiac cause.[13] The Kumamoto Acute Coronary Events study
<ul> <li>infarction decrease was attributed to the increased use of angiotensin-converting enzyme</li> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	3 9 )	248	of acute myocardial infarctions (AMIs) revealed that from 2004 to 2011, the incidence of
<ul> <li>inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.</li> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	 2 3	249	AMIs decreased in both men and women.[14] The rate of ST segment elevation myocardial
<ul> <li>statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the</li> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	4 5 5	250	infarction decrease was attributed to the increased use of angiotensin-converting enzyme
<ul> <li>incidence of AMIs in both men and women who were &lt; 59 years continued to increase. This</li> <li>was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	7 3 9	251	inhibitors, angiotensin II receptor blockers, and lipid-lowering medications (e.g.
<ul> <li>254 was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of</li> </ul>	)   <u>2</u>	252	statins).[15-17] However, the Miyagi AMI registry reported that between 1985 and 2014, the
	3 4 5	253	incidence of AMIs in both men and women who were < 59 years continued to increase. This
255 young peoples' diets and lifestyles, as well as the high smoking rates ( $\sim$ 50% and > 30% in	5 7 3	254	was attributed to the high incidence of dyslipidaemia, secondary to the westernisation of
	) )	255	young peoples' diets and lifestyles, as well as the high smoking rates ( $\sim$ 50% and > 30% in

3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25	256	young men and women, respectively).[18] Therefore, an improvement in the diet and the
	257	cessation of smoking may be important in the reduction of the incidence of cardiogenic
	258	OHCAs in this population.
	259	Compared to Western countries, ischaemic heart disease is less common in Japan,[19]
	260	whereas the prevalence of the Brugada syndrome is relatively high.[20,21] The Brugada
	261	syndrome was described by Pedro and Josep Brugada in 1992, as a disease that causes
	262	ventricular fibrillation despite the absence of obvious structural cardiac diseases, electrolyte
25 26 27	263	abnormalities, or QT prolongations.[22] The Brugada-type electrocardiogram (ECG; right
28 29 30	264	bundle branch block and ST segment elevation in V1 through V3) may be associated closely
<ul> <li>31</li> <li>32</li> <li>33</li> <li>34</li> <li>35</li> <li>36</li> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>42</li> </ul>	265	with a sudden unexplained death syndrome, such as Lai Tai ('death during sleep') in
	266	northeast Thailand, Bangungut ('moaning and dying during sleep') in the Philippines, and
	267	Pokkuri ('sudden unexpected death at night') in Japan.[23] A troublesome characteristic of
	268	the Brugada syndrome is its nocturnal tendency, which may delay therapeutic interventions
43 44 45	269	and thus lead to worse prognosis. In the univariate analysis of this study, a night-time onset
46 47 48	270	(0:00–7:59 and 17:00–23:59) of OHCAs was associated with a worse prognosis than a
49 50 51	271	daytime onset (8:00–16:59), although this tendency was not shown in the multivariable
52 53 54	272	analysis (Table 3). Using a 12-lead ECG at screening, a history of syncope, and a family
55 56 57 58 59 60	273	history of sudden cardiac death may help identify patients who are in need of preventive

3 4 5	274	pharmacological and non-pharmacological therapy (e.g. use of an implantable cardioverter
6 7 8 9	275	defibrillator).[24]
10 11 12 13	276	Previous meta-analyses of prospective cohort studies have revealed associations between
14 15 16	277	work stressors and cardiovascular diseases. The summary relative risk for long working hours
17 18	278	( $\geq$ 55 hours per week) compared with the standard 35–40 hours per week was 1.13 (95%)
19 20 21	279	confidence interval [CI]: 1.02–1.26).[25] The total working hours tended to decline in Japan
22 23 24	280	[26] however, the reduction in the number of working hours was minor, and it is unknown
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54	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 $\geq 65$ years in the total labour force population has
55 56 57	290	been increasing every year, by 7.6% in 2005 to 12.8% in 2018.[28] We identified that there
58 59 60	291	were no significant improvements in the incidence of cardiogenic OHCAs in any age group

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4 5	292	over the last 12 years, and the incidence increased with increasing age (Table 1). A study of
5 7 3	293	OHCAs in the Osaka Prefecture, Japan, that was conducted for two years revealed that the
9 10 11	294	incidence of OHCAs increased exponentially with increasing age.[29] Our present study
12 13 14	295	revealed that the incidence of cardiogenic OHCAs in any age group was almost constant over
15 16 17	296	the 12-year period. It should be noted that the incidence of OHCAs in the 65–69 age group
18 19 20	297	(extended retirement age group) was high, and that age was associated independently with
21 22 23	298	1-month survival with favourable neurological outcomes (adjusted odds ratio [OR]: 0.98
24 25 26	299	[10-year increments], 95% CI: 0.98–0.99; $P < 0.001$ ). Therefore, it is important for
27 28 29	300	companies with older employees to take this into account. Nevertheless, this is not a problem
30 31 32	301	that is limited to Japan; the aging of the population is progressing worldwide, especially in
33 34	302	developed countries.[1] In the future, there is a possibility that the retirement age will be
35 36 37	303	extended in many countries around the world.
38 39 40		0.
41 42 43	304	Effect of work-colleagues and other types of bystanders
44 45 46	305	A previous study found that a key predictor of survival after OHCAs is the bystander
47 48 49	306	witness.[30] Another previous study reported that most of the cases of OHCAs in Japan that
50 51 52	307	were witnessed by family members and family bystanders had a worse prognosis than those
51 52 53 54 55 56 57 58	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
59 50	310	result may be attributed to the lowest CPR/AED proportions (44.3% and 0.7%, respectively).
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	311	Another study that reported a similar association for the bystander-patient relationship
	312	indicated that the large delays ( $\geq$ 5 min) in the witness call interval and large witness
)   <u>2</u>	313	bystander CPR interval were most frequent in the family bystander group.[31]
3 1 5	314	A previous systematic review revealed that the OHCA survival rate was better in the
5 7 3	315	workplace,[32] and the findings of our study were similar: work-colleague bystanders were
) ) 	316	associated with a better 1-month survival and favourable neurological outcomes. A possible
2 3 1	317	reason for such a favourable prognosis was that the CPR/AED proportion was highest in the
5	318	work-colleague bystander group. Furthermore, we found further improvements in the
3 ) )	319	prognosis of OHCAs in the work-colleague bystander group. The work-colleague bystander
 <u>2</u> 3	320	group had significantly longer median intervals between the witnessing OHCAs and initial
+ 5 5	321	defibrillations than the passers-by bystander group (13 vs. 12 min, respectively; $P < 0.001$ ). It
7 3 9 1	322	is known that a 1-min delay can reduce the survival rate by $7-10\%$ ,[33] and the results from
,   <u>2</u>	323	Table 3 also indicate that a 1-min difference does have a clinically meaningful benefit for
3 1 5	324	1-month survival with favourable neurological outcomes (adjusted OR: 0.94 [1-min
5 7 3	325	increments], 95% CI: 0.93–0.95; $P < 0.001$ ). A possible reason why work-colleagues took
)   	326	longer to perform the first defibrillation compared with passers-by may have been due to
2 3 1	327	most of the initial defibrillations being performed by EMS providers, and that the median call
5	328	to contact intervals were significantly longer in the work-colleague bystander group than in
3 9 )	329	the passers-by bystander group (8 vs. 7 min, respectively; $P < 0.001$ ). The travel distance and

3 4 5	330	time to travel within buildings may also have contributed to the delays. Another study that
6 7 8 9	331	used the model of a large-scale skyscraper, calculated the length of time taken by the
10 11 12	332	emergency services to reach a patient within the building (i.e. travel time) and found that the
12 13 14 15	333	minimum travel time was approximately 19 s, the intermediate value 2 min, and the worst
16 17 18	334	value 4 min.[34]
19 20 21	335	Recently, the importance of CPR has become known widely, and the findings of this study
22 23 24	336	supported this, given that the CPR proportion in the working population has increased over
25 26 27	337	the years (Figure 3). However, our present study revealed that in 2016 in > 30% of the cases
28 29 30 31 32 33 34	338	CPR was not performed despite the witnessing of the cardiogenic OHCAs by
	339	work-colleagues (shown in Supplementary Figure 1). More opportunities for CPR
34 35 36 37	340	awareness activities in companies may be useful in preventing cardiac death and poor
38 39 40	341	neurological outcomes in OHCA patients in the working population. A previous study
40 41 42 43	342	reported that approximately two-thirds of OHCA survivors return to work,[35] which is
44 45 46	343	important in terms of public health and socioeconomic significance.
47 48 49 50	344	Limitations
51 52 53	345	This study had several limitations. First, this was a retrospective population-based study of
54 55 56	346	data obtained from a prospective registry, with some instances where data were missing or
57 58 59 60	347	abnormal values were present. Second, the actual employment status of the OHCA patients in

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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.

2 3								
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6 7								
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10 11 12 13	365	Management Agency of Japan for their cooperation in collecting data and managing the						
14 15	366	Utstein-style registry.						
16 17 18 19	367							
20 21	368	COMPETING INTERESTS						
22 23								
24	369	The authors have no competing interests.						
25 26								
27 28	370							
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33 34 35	372	This research received no specific grant from any funding agency in the public, commercial,						
36 37 38	373	or not-for-profit sectors.						
39 40 41 42	374							
43 44 45 46	375	AUTHORS' CONTRIBUTIONS						
40 47 48 49	376	YY was involved in data analysis and writing of the manuscript. YO was involved in data						
50 51 52	377	verification, the design of the study, supervision, and revising the manuscript. YF was						
52 53 54 55	378	involved in data verification, supervision, and statistical analysis. KY, TM, and KT were						
56 57	379	involved in data verification. HO and RK were involved in data verification and supervision.						
58 59 60	380	HA was involved in data verification, supervision, and revising the manuscript.						

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6 7 8 9	382	DATA SHARING
9 10 11 12	383	The data used in this study are not publicly available. The data are only accessible through
13 14 15	384	the Fire and Disaster Management Agency (2-1-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan;
16 17 18	385	Tel.: +03-5253-7529; Fax: +03-5253-7532; E-mail: fdma-goiken@ml.soumu.go.jp).
19 20 21	386	Therefore, no additional data are available.
22 23 24 25	387	
26 27 28 29	388	ETHICS STATEMENT
30 31 32 33	389	This study was approved by the Institutional Review Board of the University of Occupational
34 35	390	and Environmental Health, Japan (approval number; UOEHCRB19-072).
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	487 488 489 490 491 492 493 494 495 494 495 496 497 498 497 498 499 500 501 501	<ul> <li>487</li> <li>488</li> <li>489</li> <li>(29)</li> <li>490</li> <li>490</li> <li>491</li> <li>492</li> <li>(30)</li> <li>493</li> <li>493</li> <li>494</li> <li>495</li> <li>496</li> <li>497</li> <li>(31)</li> <li>498</li> <li>499</li> <li>500</li> <li>(32)</li> <li>502</li> <li>503</li> </ul>

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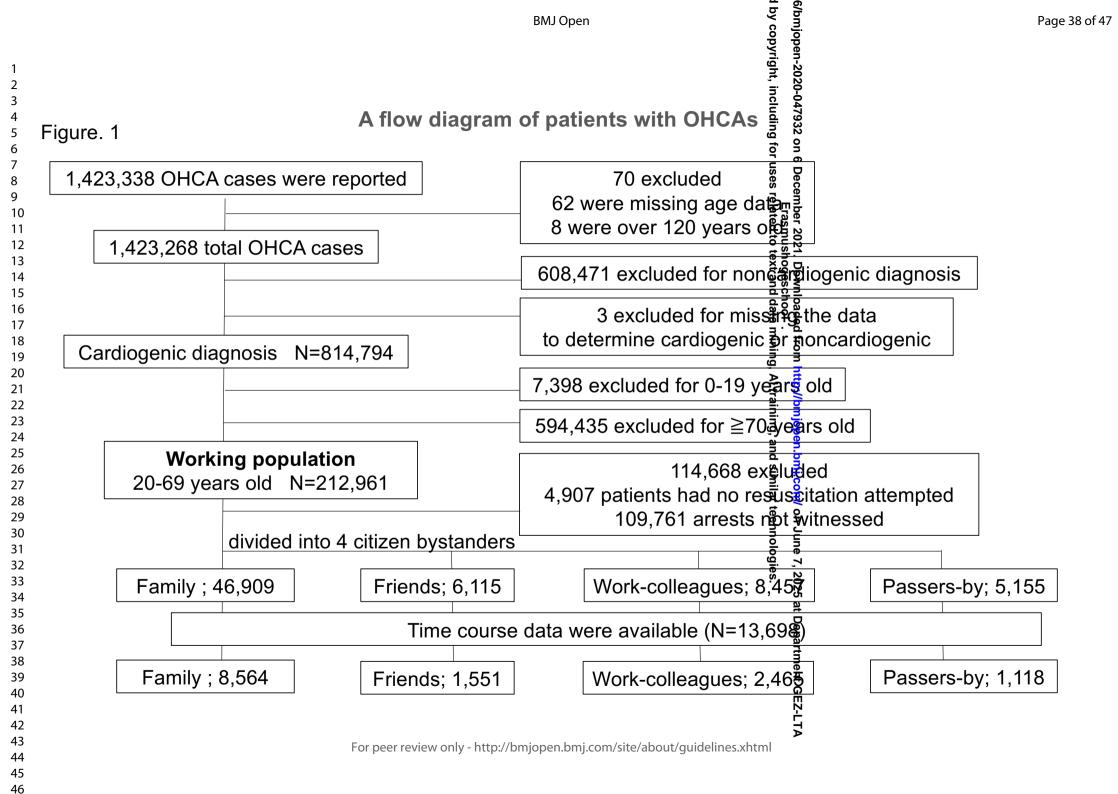
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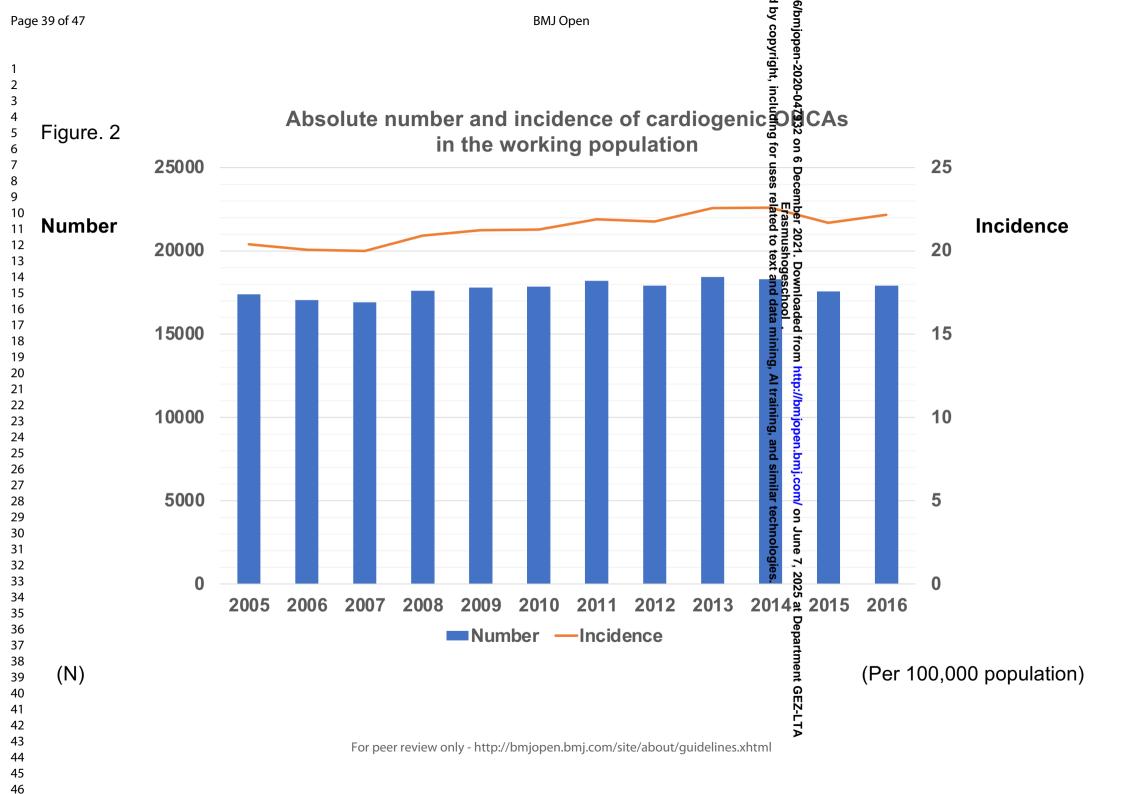
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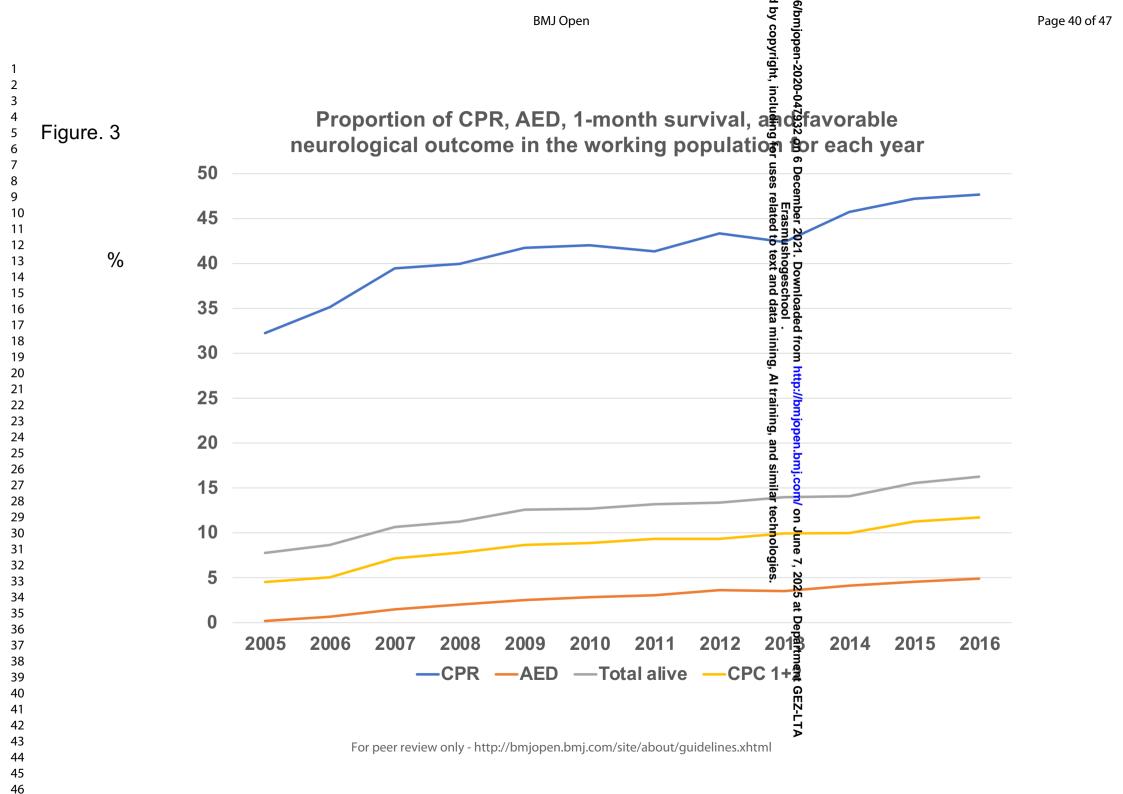
525	Figure 1. A flow diagram of patients with OHCAs
526	Of the 1,423,338 OHCA patients included in the All-Japan Utstein registry between 2005 and
527	2016, we excluded cases with missing data of age $(n=62)$ or patients who were over 120
528	years old (n=8). Cardiogenic and non-cardiogenic groups comprised 57.2% and 42.8% of the
529	total OHCA population (n=1,423,268), respectively. We excluded non-cardiogenic OHCA
530	group. In the cardiogenic OHCA group, 212,961 OHCA patients aged 20-69 years (working
531	population) were enrolled in this study. After excluding those who did not receive OHCA
532	resuscitation (n = 4,907) or those who lacked a witness (n = $109,761$ ), the working population
533	was further divided into four bystander groups (family, friends, work-colleagues, and
534	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.
534 535	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest.
	passers-by). Abbreviation: OHCA, out-of-hospital cardiac arrest. Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working
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535 536	Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working
535 536 537	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
535 536 537 538	<b>Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working</b> 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
535 536 537 538 539	<b>Figure 2. Absolute number and incidence of cardiogenic OHCAs in the working</b> 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,

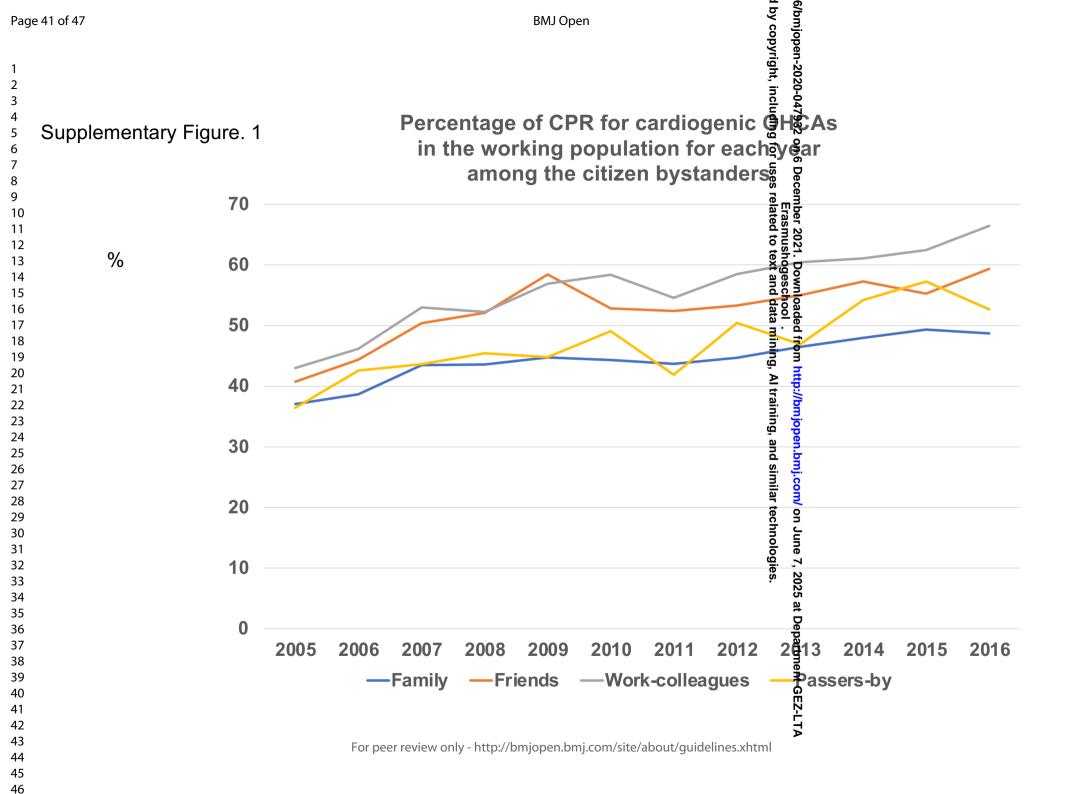
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543	Figure 3. Proportion of CPR, AED, 1-month survival, and favourable neurological
544	outcome in the working population for each year. The percentage of CPR and AED
545	increased each year from 32.3% and 0.2% in 2005 to 47.7% and 4.9% in 2016, respectively.
546	One-month survival rate of cardiogenic OHCAs in the working population increased from
547	7.8% in 2005 to 16.3% in 2016, and the 1-month survival with favourable neurological
548	outcome also increased from 4.5% in 2005 to 11.7% in 2016. Abbreviations: CPR,
549	cardiopulmonary resuscitation; AED, automated external defibrillator; CPC, cerebral
550	performance category.
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#### 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 $\rightarrow$ Page 1, Lines 1-2: The incidence of out-of-hospital cardiac arrests and surviva
		rates after one-month among the Japanese working population: A cohort study
		( <i>b</i> ) 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 $\rightarrow$ 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 $\rightarrow$ 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)
		$\rightarrow$ 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		O,
Study design	4	Present key elements of study design early in the paper
		$\rightarrow$ 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
		$\rightarrow$ 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.

		selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants $\rightarrow$ 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) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case inct ampliable
Variables	7	<ul> <li>→not applicable</li> <li>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</li> <li>→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.</li> <li>→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.</li> </ul>
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 $\rightarrow$ 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
		$\rightarrow$ 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 $\rightarrow$ 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
		<i>Case-control study</i> —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
		( <u>e</u> ) Describe any sensitivity analyses
		$\rightarrow$ 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		

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible,
<b>F</b>		examined for eligibility, confirmed eligible, included in the study, completing follow-up, as
		analysed
		→Figure 1
		(b) Give reasons for non-participation at each stage
		$\rightarrow$ Figure 1
		(c) Consider use of a flow diagram
		$\rightarrow$ Figure 1
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and informat
data		on exposures and potential confounders
		$\rightarrow$ 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
		$\rightarrow$ Figure 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
		$\rightarrow$ Page 7, Lines 99-100: The EMS personnel followed-up these OHCA patients for 1 month
		ascertain the survival rates and neurological outcomes.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time
	-	$\rightarrow$ 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 a
		why they were included
		$\rightarrow$ Table 3.
		(b) Report category boundaries when continuous variables were categorized
		$\rightarrow$ Table 3.
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaning
		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
		$\rightarrow$ Page 18-19, Lines 230-243: We found that: (1) approximately 30% of all the OHCA case
		occurred in the working population, and that the working population comprised 26% of all t
		cases in the cardiogenic OHCA group; (2) both the absolute number and the incidence of

<b>Other information</b> Funding	n 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 $\rightarrow$ Page 26, Line 371-373: FUNDING~
		the world.
		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
		$\rightarrow$ Page 22, Lines 300-303: Nevertheless, this is not a problem that is limited to Japan; the
Generalisaolility	∠ 1	
Generalisability	21	Discuss the generalisability (external validity) of the study results
		approximately 19 s, the intermediate value 2 min, and the worst value 4 min.[34]
		a patient within the building (i.e. travel time) and found that the minimum travel time was
		a large-scale skyscraper, calculated the length of time taken by the emergency services to read
		within buildings may also have contributed to the delays. Another study that used the model of
		by stander group (8 vs. 7 min, respectively; $P < 0.001$ ). The travel distance and time to travel
		defibrillations being performed by EMS providers, and that the median call to contact interval were significantly longer in the work-colleague bystander group than in the passers-by
		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 interval
		$\rightarrow$ Page 23-24, Lines 325-334: A possible reason why work-colleagues took longer to perform the first defibrillation compared with percent by may have been due to most of the initial
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicit of analyses, results from similar studies, and other relevant evidence
		→Page 24-25, Lines 344-352: <b>Limitations</b> ~
	.,	Discuss both direction and magnitude of any potential bias
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.
		favourable neurological outcomes.
		OHCAs to initial defibrillations was associated independently with 1-month survival with
		initial defibrillations than the passers-by bystander group, and the time from witnessing
		work-colleague bystanders had a significantly longer time from witnessing OHCAs to the
		proportion, highest 1-month survival rate, and best neurological outcomes. However, the
		citizen bystanders, the work-colleague bystander group had the highest bystander CPR/AED
		year, and the prognosis after 1 month improved in the working population; and (5) among the
		increasing with increasing age; (4) the proportion of CPRs and the use of AEDs increased ea
		in the incidence of cardiogenic OHCAs over the 12-year period, with the incidence of OHCA

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\*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.

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