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## Evaluating the definition of Severely Injured Patients: A Japanese Nationwide 5-Year Retrospective Study

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1 Article

2 **Evaluating the definition of Severely Injured Patients: A**  
3 **Japanese Nationwide 5-Year Retrospective Study**

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**Abstract:**

**Objectives:** The definition of severely injured patients lacks universal consensus based on quantitative measures. The most widely used definition of severe injury is based on the Injury Severity Score (ISS), which is calculated using the Abbreviated Injury Scale (AIS) in Japan. This study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  by age groups.

**Design:** Retrospective cohort study.

**Setting:** Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280 hospitals.

**Participants:** We utilized data of 117,201 injured patients from a national database. We included injured patients who were transferred from the scene of injury by ambulance and/or physician.

**Primary and secondary outcome measures:** Prevalence, in-hospital mortality, and odds ratio (OR) for mortality with respect to age and injury level (ISS group).

**Results:** In all age categories, the in-hospital mortality of patient groups with an  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients aged > 75 years was the highest (20% greater than that of the other age groups). Moreover, in-hospital mortality for age group 5–14 years was the lowest (4.0–10.9%). In all the age groups, the OR for mortality for patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 12.8, 11.0, and 8.4, respectively.

**Conclusions:** Our results revealed the lack of an acceptable definition, with a high in-hospital mortality and high OR for mortality for all age groups.

**Keywords:** severely injured patient; trauma scoring system; anatomical severity definition; mortality risk; Japan Trauma Data Bank

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**Strengths and limitations of this study**

- This study is the first nationwide study in Japan to evaluate in-hospital mortality and odds ratio for mortality in patients with severe injury according to age.
- We used a nationwide multi-institutional trauma database with a large sample size.
- The Japanese nationwide dataset with more missing data may have led to selection bias.
- The Japan Trauma Databank had used AIS 90 until 2018, which is not newest measure.

48

## 1. INTRODUCTION

The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1–5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs,[4,5] the definition lacks a universal consensus with quantitative measures.[2,3]

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq 16$  was defined as ‘severely injured’ because patients with an ISS  $\geq 16$  had an expected mortality rate of  $> 20\%$ . [1] However, the mortality of patients with an ISS  $\geq 16$  and ISS  $\geq 26$  decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  as the commonly used anatomical injury definitions by age group.[2]

## 2. MATERIALS AND METHODS

### 2.1. Study setting and population

This retrospective observational nationwide study was conducted based on data obtained from the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn, and records prehospitalization- and hospital-related information. The JTDB includes data on demographic characteristics, comorbidities, injury types, mechanism of injury, means of transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record the online registration of individual patient data. There were 280 participating hospitals in all 47 prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open

84 access and updating of existing medical information, and the Japan Correlation for Acute Medicine  
85 evaluates the submitted data.

86 In this study, we used the JTDB dataset that included information from January 1, 2014 to  
87 December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for  
88 this study was injured patients who were transferred from the scene of injury by ambulance and/or  
89 physician. Patients with cardiac arrest on hospital arrival or with missing key data such as  
90 mechanism, age, ISS, and/or survival outcome were excluded from this study. Figure 1 presents a  
91 flow diagram of the patient selection process in this study.

92

93

## 94 **2.2. Data collection**

95 We collected information from the JTDB, including the following variables: demographic  
96 characteristics (age [years], sex, injury mechanism, transportation type, transfer process), and  
97 clinical parameters (AIS of the injured region, ISS). In the JTDB, a patient with an AIS of the  
98 injured region  $\geq 3$  was defined as a case of a severely injured region.

99

## 100 **2.4. Ethics statement**

101 This study was approved by the hospital ethics committee of Yokohama City University Medical  
102 Center (approval no. B170900003). The approval authority for data access was provided by the  
103 Japanese Association for the Surgery of Trauma (Trauma Registry Committee). The requirement for  
104 informed consent from the patients was waived owing to the observational nature of the study.

105

## 106 **2.5. Statistical analysis**

107 The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with respect  
108 to age group (0–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74,  $\geq 75$  years) and injury  
109 severity (ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ ; the ISSs of these groups were used as the definitions of  
110 anatomical injury in a previous review article.[2]

111 Continuous variables are presented as medians with interquartile range (IQR, Q1–Q3), and  
112 categorical variables are presented as the number and percentage of patients. The Mann–Whitney U  
113 test and Wilcoxon’s rank-sum test were used to analyze continuous variables, whereas the chi-  
114 square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for  
115 mortality was calculated using a logistic regression model. All statistical analyses were performed

116 using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical  
117 significance was defined as a two-tailed P-value of <0.05.

118

## 119 **2.6. Patient and public involvement**

120 Patients and the public were not involved in the design, or conduct, or reporting, or  
121 dissemination plans of this research. We will not directly disseminate our findings to involved  
122 participants but plan to disseminate them through publication of this study.

123

## 124 **3. RESULTS**

125 During the 5-year study period, we analyzed the data of 117,201 injured patients transferred from  
126 the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The median age  
127 and ISS score were 64 years (IQR, 41–78) and 10 (IQR, 9–19), respectively. The overall in-hospital  
128 mortality rate was 9.0%.

129 Table 1 shows the characteristics by age group and injury severity group during the 5-year study  
130 period. The number of patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  was 48,028 (41% of all the  
131 patients), 32,225 (28%), and 15,343 (13%), respectively.

132 Table 2 shows in-hospital mortality and OR for mortality with respect to age group and injury  
133 severity. In all age categories, the in-hospital mortality of patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  
134  $\geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality for  
135 patients aged > 55 years was higher than that for younger age groups, and that of patients aged > 75  
136 years was higher (by more than 20%) than that of all patient groups for each level of injury severity.  
137 In-hospital mortality for the 5–14 years age group was 4.0–10.9% and lower than that for the other  
138 age groups.

139 In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4–11.6),  
140 and 8.4 (8.0–8.8), respectively, for the three levels of injury severity, and the OR in patients with  
141 ISS  $\geq 16$  or ISS  $\geq 18$  was higher than that in patients group ISS  $\geq 26$ .

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143



144 **Table 1. Characteristics by the nine age groups and three levels of injury severity groups.**

Variables	Overall n = 117,199	Age 0–4 n = 1095	Age 5–14 n = 4079	Age 15–24 n = 10,743	Age 25–34 n = 7919	Age 35–44 n = 9952	Age 45–54 n = 12,188	Age 55–64 n = 13,931	Age 65–74 n = 20,044	Age ≥ 75 n = 36,705
Age, years	64 (41–78)	2 (1–3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42)	49 (47–52)	60 (57–62)	69 (67–72)	83 (79–87)
Male	16,317 (44)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77)	9211 (76)	10017 (72)	12662 (63)	16317 (44)
Mechanism of injury										
Blunt	113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	11,475 (94)	13,383 (96)	19,433 (97)	36,705 (99)
Injury region										
Head injury with AIS ≥ 3	36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25)	3363 (28)	4451 (32)	7384 (37)	12,136 (33)
Facial injury with AIS ≥ 3	940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3)	124 (1.0)	123 (0.9)	133 (0.7)	136 (0.4)
Neck injury with AIS ≥ 3	478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6)	70 (0.6)	77 (0.6)	110 (0.6)	92 (0.3)
Chest injury with AIS ≥ 3	256,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28)	3485 (29)	3726 (27)	4594 (23)	5448 (15)
Abdominal and pelvic injury with AIS ≥ 3	5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7)	709 (6)	684 (5)	831 (4)	893 (2)
Spinal injury with AIS ≥ 3	13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	1120 (11)	1530 (13)	2106 (15)	3053 (15)	3548 (10)
Upper extremity injury with AIS ≥ 3	6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7)	849 (7)	798 (6)	1026 (5)	1428 (4)
Lower extremity injury with AIS ≥ 3	31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21)	2404 (20)	2691 (19)	4358 (22)	15,457 (42)
Injury Severity Score	10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20)	13 (9–21)	14 (9–21)	14 (9–21)	9 (9–17)
Actual in-hospital mortality	3361 (9.0)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7)	533 (7.4)	762 (5.5)	1438 (7.2)	3361 (9.0)
Injury Severity Score ≥ 16	48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41)	5297 (43)	6541 (47)	9711 (48)	13,940 (37)
Injury Severity Score ≥ 18	32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	2985 (30)	3793 (31)	4372 (31)	6256 (31)	8626 (23)
Injury Severity Score ≥ 26	15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	1823 (15)	2038 (15)	2910 (15)	3938 (11)

145 Data are presented as number (percentage) or median (interquartile range Q1–Q3); AIS, Abbreviated Injury Scale

146 **Table 2. In-hospital mortality and odds ratio for mortality of patient groups with ISS  $\geq$  16, ISS  $\geq$  18, and ISS  $\geq$  26.**

	Overall n = 117,199			Age 0–4 n = 1095			Age 5–14 n = 4079			Age 15–24 n = 10,743			Age 25–34 n = 7919		
	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)
ISS $\geq$ 16	48,028	13.3	12.8 (11.9–13.8)	376	5.9	44.6 (6.0–332.4)	1166	4.0	59.8 (14.5–246.7)	3878	8.6	34.1 (21.4–54.2)	3043	9.8	48.2 (26.4–88.1)
ISS $\geq$ 18	32,225	17.4	11.0 (10.4–11.6)	187	11.2	57.3 (13.3–246.7)	747	5.8	40.6 (16.0–103.0)	2954	11.0	33.1 (22.6–48.5)	2305	12.2	25.7 (17.6–37.6)
ISS $\geq$ 26	15,343	23.5	8.4 (8.0–8.8)	62	17.7	18.4 (7.7–43.6)	367	10.9	56.6 (26.3–122.0)	1595	16.1	17.9 (14.1–22.8)	1129	19.9	19.6 (15.2–25.4)

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Age 35–44 n = 9952			Age 45–54 n = 12,188			Age 55–64 n = 13,931			Age 65–74 n = 20,044			Age ≥ 75 n = 36,705		
No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)
4076	8.7	29.2 (18.4–46.5)	5297	9.3	17.1 (12.4–23.6)	6541	10.8	16.2 (12.3–21.3)	9711	13.6	13.2 (11.0–16.0)	13940	20.2	10.5 (9.5–11.5)
2985	11.2	23.7 (16.8–33.4)	3793	11.7	12.0 (9.6–15.1)	4372	14.4	11.9 (9.8–14.4)	6256	18.6	11.2 (9.8–12.9)	8626	27.4	10.5 (9.7–11.3)
1481	18.2	18.3 (14.5–23.2)	1823	17.7	10.3 (8.6–12.4)	2038	20.9	9.1 (7.8–10.6)	2910	24.6	7.4 (6.6–8.3)	3938	34.0	8.0 (7.3–8.6)

157

158 ISS, Injury Severity Score; OR, odds ratio; CI, confidence interval.

#### 159 4. DISCUSSION

160 To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital  
161 mortality and OR for mortality in patients with severe injury according to age. Our study showed  
162 that in all three groups with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$ , which are the commonly used  
163 anatomical injury definitions, in-hospital mortality for patients aged  $< 55$  years was between 4.0%  
164 and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition  
165 for severely injured patients in a Japanese cohort via the detailed classification of the definition  
166 cutoff values and age groups, there was no acceptable definition, with not only a high in-mortality  
167 but also a high OR for mortality for all age groups.

168 Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  $\geq 16$   
169 points, the mortality of patients with an  $ISS \geq 16$  was more than 20%; however, the mortality of  
170 these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining  
171 severely injured patients with a high mortality rate.[1–3,8] This study also showed that patients with  
172  $ISS \geq 26$  had the highest in-hospital mortality in all age categories. However, the OR for mortality in  
173 patients with  $ISS \geq 26$  was lower than that in patients with  $ISS \geq 16$  and  $ISS \geq 18$ . There are possible  
174 explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for  
175 mortality in a Japanese cohort.

176 First, there are differences in the study era and/or cohorts at the time of development.[1] A previous  
177 10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the in-  
178 hospital mortality of patients with  $ISS \geq 16$  decreased from 28.5% to 15.7% due to improvements in  
179 trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort, unlike the aging  
180 population in the rest of the world, the characteristics and survival outcome of severely injured  
181 patients varied widely according to age, and the mortality risk of elderly patients with severe injury  
182 was higher than that of the other age groups.[12] A previous Japanese nationwide study showed that  
183 the incidence rate of severe traumatic brain injury among severely injured patients aged  $> 65$  years  
184 was high (40.7%).[13] Moreover, the in-hospital mortality of these patients was higher than that of  
185 the other age-groups.[13] These results suggest that the elderly patient groups had a higher mortality  
186 because of the high proportion and mortality of severe traumatic head injury. This study also  
187 showed that the prevalence and in-hospital mortality of severely injured patients aged 55–64, 65–  
188 75, and  $\geq 75$  years increased stepwise. However, in pediatric patients, a previous study suggested  
189 that the ISS cutoff of  $\geq 16$  in adult patients was equivalent to that of  $\geq 26$  in pediatric patients.[14] A  
190 Japanese nationwide study using the JTDB dataset also showed that the in-hospital mortality of  
191 pediatric patients with  $ISS \geq 16$  was 8.9% in 2018. However, this study showed that the in-hospital  
192 mortality even for pediatric patients aged 5–14 years with  $ISS \geq 26$  was low (10.9%). Therefore, it is  
193 important to develop an acceptable definition of severe injury by considering the age-related  
194 characteristics and mortality risks in a Japanese cohort.

195 Second, there was a limitation in evaluating only anatomical severity as a definition of severe  
196 injury. A more recent approach suggests that the addition of other physiological variables to the

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3 197 anatomical severity score has the advantage of identifying severely injured patients with a high  
4 198 mortality risk.[2,15,16]. Although the mortality of patients with ISS  $\geq$ 16 was 18.7%, that of patients  
5 199 with ISS  $\geq$ 16 in addition to one other physiological parameter increased from 35% to 38%.[2]  
6 200 Moreover, patients with an increasing number of the physiological variable, such as the Glasgow  
7 201 coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy), may have an  
8 202 increased risk of mortality.[15–17] However, we could not evaluate the variables according to  
9 203 physiological parameters and findings of blood tests. Therefore, it seems important to evaluate these  
10 204 parameters together with the anatomical severity used in this study to develop a well-validated  
11 205 definition of severely injured patients.

12 206 Our study had some limitations. First, there was selection bias because not all Japanese hospitals  
13 207 that treat severely injured patients were registered in the JTDB. Moreover, the JTDB dataset has  
14 208 missing data, especially for pediatric patients.[18] A high-quality Japanese nationwide dataset with  
15 209 less missing data should be constructed to improve the accuracy of predicting the survival of injured  
16 210 patients. Second, because the number of patients aged 0–4 and 5–14 years was small (0.9% and  
17 211 3.5% of all the patients, respectively), it is possible that the ORs of these patient groups with small  
18 212 sample sizes were overestimated. In addition, the number of participating hospitals differed across  
19 213 the study period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the AIS 2005  
20 214 updated 2008 coding scale. Similar studies need to be conducted using the newest measure to verify  
21 215 our results.

## 216 217 **5. CONCLUSIONS**

218 This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mortality, and OR  
219 for mortality in patients with severe injury according to age categories. In all the three levels of  
220 anatomical injury, the in-hospital mortality for patients aged  $<$  55 years was low. Evaluating the  
221 validity of the definition for severely injured patients in a Japanese cohort based on the detailed  
222 classification of the definition cutoff values and age categories revealed the lack of an acceptable  
223 definition, with not only a high in-hospital mortality, but also a high OR for mortality in all age  
224 categories.

225  
226 **Author Contributions:** Conceptualization, CT and TM; methodology, CT; software, CT and TA;  
227 validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, MG, and TA;  
228 resources, CT and TA; data curation, CT and TA; writing—original draft preparation, CT; writing—  
229 review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT; project  
230 administration and funding acquisition, CT All authors have read and agreed to the published version of  
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3 233 **Institutional Review Board Statement:** This study was approved by the institutional ethics committees  
4 234 of Yokohama City University Medical Centre (approval no. B170900003).

5  
6 235 **Informed Consent Statement:** The requirement for informed consent from the patients was waived due  
7 236 to the observational nature of the study design.

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9  
10 237 **Data Availability Statement:** The approving authority for data access was the Japanese Association for  
11 238 the Surgery of Trauma (Trauma Registry Committee).

12  
13 239 **Acknowledgments:** None.

14  
15 240 **Conflicts of Interest:** The authors declare no conflict of interest.

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26 294 Figure Legend

27 295 **Figure 1.** Flow diagram of the patient selection process.

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29 296 JTDB, Japanese Trauma Data Bank.  
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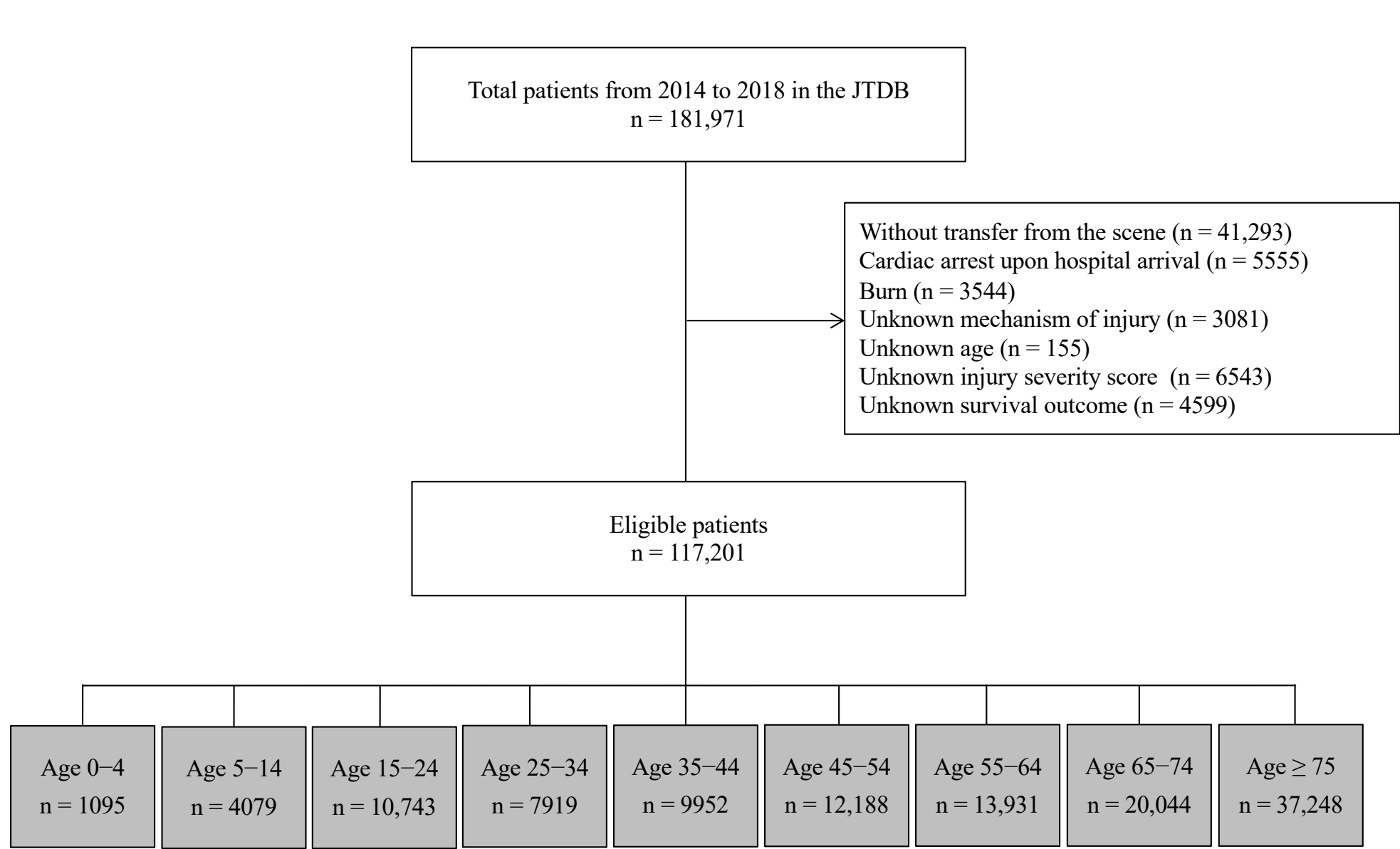


Figure 1. Flow diagram of the patient selection process.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2 2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2,3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3,4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3,4 N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
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	4,5
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	4,5 4,5 3,4 N/A N/A
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5 3,4,5 5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	3,4,5 3 3
Outcome data	15*	Report numbers of outcome events or summary measures over time	5

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5
2			(b) Report category boundaries when continuous variables were categorized	5
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5
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9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
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11	<b>Discussion</b>			
12				
13	Key results	18	Summarise key results with reference to study objectives	9
14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
15				
16	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9,10
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19	Generalisability	21	Discuss the generalisability (external validity) of the study results	9,10
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21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10
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26 \*Give information separately for exposed and unexposed groups.

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

## Evaluating the definition of Severely Injured Patients: A Japanese Nationwide 5-Year Retrospective Study

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1 Article

2 **Evaluating the definition of Severely Injured Patients: A**  
3 **Japanese Nationwide 5-Year Retrospective Study**

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**Abstract:**

**Objectives:** The definition of severely injured patients lacks universal consensus based on quantitative measures. The most widely used definition of severe injury is based on the Injury Severity Score (ISS), which is calculated using the Abbreviated Injury Scale (AIS) in Japan. This study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  by age groups.

**Design:** Retrospective cohort study.

**Setting:** Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280 hospitals.

**Participants:** We utilized data of 117,199 injured patients from a national database. We included injured patients who were transferred from the scene of injury by ambulance and/or physician.

**Primary and secondary outcome measures:** Prevalence, in-hospital mortality, and odds ratio (OR) for mortality with respect to age and injury level (ISS group).

**Results:** In all age categories, the in-hospital mortality of patient groups with an  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients aged > 75 years was the highest (20% greater than that of the other age groups). Moreover, in-hospital mortality for age group 5–14 years was the lowest (4.0–10.9%). In all the age groups, the OR for mortality for patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 12.8, 11.0, and 8.4, respectively.

**Conclusions:** Our results revealed the lack of an acceptable definition, with a high in-hospital mortality and high OR for mortality for all age groups.

**Keywords:** severely injured patient; trauma scoring system; anatomical severity definition; mortality risk; Japan Trauma Data Bank

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**Strengths and limitations of this study**

- This study is the first nationwide study in Japan to evaluate in-hospital mortality and odds ratio for mortality in patients with severe injury according to age.
- We used a nationwide multi-institutional trauma database with a large sample size.
- The Japanese nationwide dataset with more missing data may have led to selection bias.
- The Japan Trauma Databank had used AIS 90 until 2018, which is not newest measure.

## 1. INTRODUCTION

The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1–5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs,[4,5] the definition lacks a universal consensus with quantitative measures.[2,3]

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq 16$  was defined as ‘severely injured’ because patients with an ISS  $\geq 16$  had an expected mortality rate of  $> 20\%$ . [1] However, the mortality of patients with an ISS  $\geq 16$  and ISS  $\geq 26$  decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. We hypothesized that there would be differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical severity. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with an ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  as the commonly used anatomical injury definitions by age group [2].

## 2. MATERIALS AND METHODS

### 2.1. Study setting and population

This retrospective observational nationwide study was conducted based on data obtained from the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn, and records prehospitalization- and hospital-related information. The JTDB includes data on demographic characteristics, comorbidities, injury types, mechanism of injury, means of transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record the online registration of individual patient data. There were 280 participating hospitals in all 47 prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open



85 access and updating of existing medical information, and the Japan Correlation for Acute Medicine  
86 evaluates the submitted data.

87 In this study, we used the JTDB dataset that included information from January 1, 2014 to  
88 December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for  
89 this study was injured patients who were transferred from the scene of injury by ambulance and/or  
90 physician. Patients with cardiac arrest on hospital arrival or with missing key data such as  
91 mechanism, age, ISS, and/or survival outcome were excluded from this study. Figure 1 presents a  
92 flow diagram of the patient selection process in this study.

## 94 **2.2. Data collection**

95 We collected information from the JTDB, including the following variables: demographic  
96 characteristics (age [years], sex, injury mechanism, transportation type, transfer process), and  
97 clinical parameters (AIS of the injured region, ISS). In the JTDB, a patient with an AIS of the  
98 injured region  $\geq 3$  was defined as a case of a severely injured region.

## 100 **2.4. Ethics statement**

101 This study was approved by the hospital ethics committee of Yokohama City University Medical  
102 Center (approval no. B170900003). The approval authority for data access was provided by the  
103 Japanese Association for the Surgery of Trauma (Trauma Registry Committee). The requirement for  
104 informed consent from the patients was waived owing to the observational nature of the study.

## 106 **2.5. Statistical analysis**

107 The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with respect  
108 to age group (0–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74,  $\geq 75$  years) and injury  
109 severity (ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ ; the ISSs of these groups were used as the definitions of  
110 anatomical injury in a previous review article.[2]

111 Continuous variables are presented as medians with interquartile range (IQR, Q1–Q3), and  
112 categorical variables are presented as the number and percentage of patients. The Mann–Whitney U  
113 test and Wilcoxon’s rank-sum test were used to analyze continuous variables, whereas the chi-  
114 square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for  
115 mortality was calculated using a logistic regression model. All statistical analyses were performed  
116 using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical  
117 significance was defined as a two-tailed P-value of  $< 0.05$ .

118

## 119 2.6. Patient and public involvement

120 Patients and the public were not involved in the design, or conduct, or reporting, or  
121 dissemination plans of this research. We will not directly disseminate our findings to involved  
122 participants but plan to disseminate them through publication of this study.

123

## 124 3. RESULTS

125 During the 5-year study period, we analyzed the data of 117,199 injured patients transferred from  
126 the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The median age  
127 and ISS score were 64 years (IQR, 41–78) and 10 (IQR, 9–19), respectively. The overall in-hospital  
128 mortality rate was 6.1%.

129 Table 1 shows the characteristics by age group and injury severity group during the 5-year study  
130 period. The number of patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 48,028 (41% of all the  
131 patients), 32,225 (28%), and 15,343 (13%), respectively.

132 Table 2 shows in-hospital mortality and OR for mortality with respect to age group and injury  
133 severity. In all age categories, the in-hospital mortality of patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS$   
134  $\geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality for  
135 patients aged > 55 years was higher than that for younger age groups, and that of patients aged > 75  
136 years was higher (by more than 20%) than that of all patient groups for each level of injury severity.  
137 In-hospital mortality for the 5–14 years age group was 4.0–10.9% and lower than that for the other  
138 age groups.

139 In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4–11.6),  
140 and 8.4 (8.0–8.8), respectively, for the three levels of injury severity, and the OR in patients with  
141  $ISS \geq 16$  or  $ISS \geq 18$  was higher than that in patients group  $ISS \geq 26$ .

142

143

144 **Table 1. Characteristics by the nine age groups and three levels of injury severity groups.**

Variables	Overall n = 117,199	Age 0–4 n = 1095	Age 5–14 n = 4079	Age 15–24 n = 10,743	Age 25–34 n = 7919	Age 35–44 n = 9952	Age 45–54 n = 12,188	Age 55–64 n = 13,931	Age 65–74 n = 20,044	Age ≥ 75 n = 36,248
Age, years	64 (41–78)	2 (1–3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42)	49 (47–52)	60 (57–62)	69 (67–72)	83 (79–87)
Male	16,317 (44)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77)	9211 (76)	10017 (72)	12662 (63)	16317 (44)
Mechanism of injury										
Blunt	113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	11,475 (94)	13,383 (96)	19,433 (97)	36,705 (99)
Injury region										
Head injury with AIS ≥ 3	36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25)	3363 (28)	4451 (32)	7384 (37)	12,136 (33)
Facial injury with AIS ≥ 3	940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3)	124 (1.0)	123 (0.9)	133 (0.7)	136 (0.4)
Neck injury with AIS ≥ 3	478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6)	70 (0.6)	77 (0.6)	110 (0.6)	92 (0.3)
Chest injury with AIS ≥ 3	25,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28)	3485 (29)	3726 (27)	4594 (23)	5448 (15)
Abdominal and pelvic injury with AIS ≥ 3	5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7)	709 (6)	684 (5)	831 (4)	893 (2)
Spinal injury with AIS ≥ 3	13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	1120 (11)	1530 (13)	2106 (15)	3053 (15)	3548 (10)
Upper extremity injury with AIS ≥ 3	6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7)	849 (7)	798 (6)	1026 (5)	1428 (4)
Lower extremity injury with AIS ≥ 3	31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21)	2404 (20)	2691 (19)	4358 (22)	15,457 (42)
Injury Severity Score	10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20)	13 (9–21)	14 (9–21)	14 (9–21)	9 (9–17)
Actual in-hospital mortality	7201 (6.1)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7)	533 (4.4)	762 (5.5)	1438 (7.2)	3361 (9.0)
Injury Severity Score ≥ 16	48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41)	5297 (43)	6541 (47)	9711 (48)	13,940 (37)
Injury Severity Score ≥ 18	32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	2985 (30)	3793 (31)	4372 (31)	6256 (31)	8626 (23)
Injury Severity Score ≥ 26	15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	1823 (15)	2038 (15)	2910 (15)	3938 (11)

145 Data are presented as number (percentage) or median (interquartile range Q1–Q3); AIS, Abbreviated Injury Scale

146 **Table 2. In-hospital mortality and odds ratio for mortality of patient groups with ISS  $\geq$  16, ISS  $\geq$  18, and ISS  $\geq$  26.**

	Overall			Age 0–4			Age 5–14			Age 15–24			Age 25–34		
	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)
ISS $\geq$ 16	48,028	13.3 (6383)	12.8 (11.9–13.8)	376	5.9 (22)	44.6 (6.0–332.4)	1166	4.0 (46)	59.8 (14.5–246.7)	3878	8.6 (335)	34.1 (21.4–54.2)	3043	9.8 (299)	48.2 (26.4–88.1)
ISS $\geq$ 18	32,225	17.4 (5602)	11.0 (10.4–11.6)	187	11.2 (21)	57.3 (13.3–246.7)	747	5.8 (43)	40.6 (16.0–103.0)	2954	11.0 (325)	33.1 (22.6–48.5)	2305	12.2 (280)	25.7 (17.6–37.6)
ISS $\geq$ 26	15,343	23.5 (3605)	8.4 (8.0–8.8)	62	17.7 (11)	18.4 (7.7–43.6)	367	10.9 (40)	56.6 (26.3–122.0)	1595	16.1 (257)	17.9 (14.1–22.8)	1129	19.9 (225)	19.6 (15.2–25.4)

156

Age 35–44			Age 45–54			Age 55–64			Age 65–74			Age ≥ 75		
No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)
4076	8.7 (353)	29.2 (18.4–46.5)	5297	9.3 (492)	17.1 (12.4–23.6)	6541	10.8 (707)	16.2 (12.3–21.3)	9711	13.6 (1317)	13.2 (11.0–16.0)	13940	20.2 (2812)	10.5 (9.5–11.5)
2985	11.2 (335)	23.7 (16.8–33.4)	3793	11.7 (442)	12.0 (9.6–15.1)	4372	14.4 (629)	11.9 (9.8–14.4)	6256	18.6 (1163)	11.2 (9.8–12.9)	8626	27.4 (2364)	10.5 (9.7–11.3)
1481	18.2 (270)	18.3 (14.5–23.2)	1823	17.7 (322)	10.3 (8.6–12.4)	2038	20.9 (426)	9.1 (7.8–10.6)	2910	24.6 (716)	7.4 (6.6–8.3)	3938	34.0 (1338)	8.0 (7.3–8.6)

157

158 ISS, Injury Severity Score; OR, odds ratio; CI, confidence interval.

#### 159 4. DISCUSSION

160 To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital  
161 mortality and OR for mortality in patients with severe injury according to age. Our study showed  
162 that in all three groups with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$ , which are the commonly used  
163 anatomical injury definitions, in-hospital mortality for patients aged  $< 55$  years was between 4.0%  
164 and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition  
165 for severely injured patients in a Japanese cohort via the detailed classification of the definition  
166 cutoff values and age groups, there was no acceptable definition, with not only a high in-hospital  
167 mortality but also a high OR for mortality for all age groups.

168 Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  $\geq 16$   
169 points, the mortality of patients with an  $ISS \geq 16$  was more than 20%; however, the mortality of  
170 these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining  
171 severely injured patients with a high mortality rate.[1–3,8] This study also showed that patients with  
172  $ISS \geq 26$  had the highest in-hospital mortality in all age categories. However, the OR for mortality in  
173 patients with  $ISS \geq 26$  was lower than that in patients with  $ISS \geq 16$  and  $ISS \geq 18$ . There are possible  
174 explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for  
175 mortality in a Japanese cohort.

176 First, there are differences in the study era and/or cohorts at the time of development.[1] A previous  
177 10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the in-  
178 hospital mortality of patients with  $ISS \geq 16$  decreased from 28.5% to 15.7% due to improvements in  
179 trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort, unlike the aging  
180 population in the rest of the world, the characteristics and survival outcome of severely injured  
181 patients varied widely according to age, and the mortality risk of elderly patients with severe injury  
182 was higher than that of the other age groups.[12] A previous Japanese nationwide study showed that  
183 the incidence rate of severe traumatic brain injury among severely injured patients aged  $> 65$  years  
184 was high (40.7%).[13] Moreover, the in-hospital mortality of these patients was higher than that of  
185 the other age-groups.[13] These results suggest that the elderly patient group had a higher mortality  
186 because of the high proportion and mortality of severe traumatic head injury. This study also  
187 showed that the prevalence and in-hospital mortality of severely injured patients aged 55–64, 65–  
188 75, and  $\geq 75$  years increased stepwise. On the other hand, previous studies suggested that the ISS  
189 cutoff of  $\geq 16$  in adult patients was equivalent to a cut-off  $\geq 26$  in pediatric patients aged  $< 16$   
190 years.[14,15] This study showed different results from those of a previous study [15], wherein the  
191 in-hospital mortality of pediatric patients aged 0–4 years with an  $ISS \geq 26$  was high (17.7%) and that  
192 of pediatric patients aged 5–14 years with an  $ISS \geq 26$  was low (10.9%), as shown in Table 2.  
193 Moreover, a previous study showed that there was a difference in the optimal cut off value of ISS in  
194 predicting severely injury mortality risk by region and/or mechanism of injury among pediatric  
195 patients. Therefore, it is important to develop an acceptable definition of severe injury by  
196 considering the age-related characteristics and mortality risks in a Japanese cohort. Moreover, this  
197 study showed that the mortality rate and mortality risk of injured patients in Japan differed by age  
198 groups and did not have a linear correlation with age in years. For a better predictive accuracy in  
199 mortality, it may be effective to add age categories as a predictive variable for mortality and to

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2  
3 200 calculate the coefficient for coded value according to mortality risk by each age group, as shown in  
4 201 the Trauma and injury Severity Score methodology [16].  
5 202 Second, there was a limitation in evaluating only anatomical severity as a definition of severe  
6 203 injury. A more recent approach suggests that the addition of other physiological variables to the  
7 204 anatomical severity score has the advantage of identifying severely injured patients with a high  
8 205 mortality risk.[2,17,18] Although the mortality of patients with  $ISS \geq 16$  was 18.7%, that of patients  
9 206 with  $ISS \geq 16$  in addition to one other physiological parameter increased from 35% to 38%.[2]  
10 207 Moreover, patients with an increasing number of the physiological variable, such as the Glasgow  
11 208 coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy), may have an  
12 209 increased risk of mortality.[17–19] However, we could not evaluate the variables according to  
13 210 physiological parameters and findings of blood tests. Therefore, it seems important to evaluate these  
14 211 parameters together with the anatomical severity used in this study to develop a well-validated  
15 212 definition of severely injured patients.

16 213 Our study had some limitations. First, there was selection bias because not all Japanese hospitals  
17 214 that treat severely injured patients are registered in the JTDB. The 280 tertiary centers equivalent to  
18 215 Level I trauma centers in the United States participated, including 92% of the Japanese government-  
19 216 approved tertiary emergency medical centers in March 2019. Therefore, the JTDB is not a  
20 217 population-based sample of injured patients and the data are registered voluntarily. Moreover, the  
21 218 JTDB dataset has missing data, especially for pediatric patients.[20] The number of pediatric  
22 219 patients were lower than that of adult patients. Therefore, missing data may have a more significant  
23 220 influence on the analysis of the pediatric patients' data than that of the adult patients' data. A high-  
24 221 quality Japanese nationwide dataset with less missing data should be constructed to improve the  
25 222 accuracy of predicting the survival of injured patients in the data analysis for all age categories.  
26 223 Second, because the number of patients aged 0–4 and 5–14 years was small (0.9% and 3.5% of all  
27 224 the patients, respectively), it is possible that the ORs of these patient groups with small sample sizes  
28 225 were overestimated. In addition, the number of participating hospitals differed across the study  
29 226 period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the AIS 2005 updated 2008  
30 227 coding scale. Similar studies need to be conducted using the newest measure to verify our results.  
31 228

## 32 229 **5. CONCLUSIONS**

33 230 This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mortality, and OR  
34 231 for mortality in patients with severe injury according to age categories. This study showed that there  
35 232 were differences in in-hospital mortality rate and risk among Japanese injured patients by age and  
36 233 anatomical severity; therefore, the use of correlation between mortality and injury severity score  
37 234 such as the ISS may be hardly justified in the definition of severely injured patients in all age  
38 235 categories. In the future, it will be important to evaluate the other parameters such as age,  
39 236 physiological variables, and laboratory variables together with the anatomical severity by using the  
40 237 population-based database to develop a well-validated definition of severely injured patients.  
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3 240 **Author Contributions:** Conceptualization, CT and TM; methodology, CT; software, CT and TA;  
4 241 validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, MG, and TA;  
5 242 resources, CT and TA; data curation, CT and TA; writing—original draft preparation, CT; writing—  
6 243 review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT; project  
7 244 administration and funding acquisition, CT All authors have read and agreed to the published version of  
8 245 the manuscript.

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11  
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14 248 Yokohama City University Medical Centre (approval no. B170900003).

15  
16  
17 249 **Informed Consent Statement:** The requirement for informed consent from the patients was waived due  
18 250 to the observational nature of the study design.

19  
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21 251 **Data Availability Statement:** The approving authority for data access was the Japanese Association for  
22 252 the Surgery of Trauma (Trauma Registry Committee).

23  
24  
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26  
27 254 **Conflicts of Interest:** The authors declare no conflict of interest.

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29 255



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314 Figure Legend

315 **Figure 1.** Flow diagram of the patient selection process.

316 JTDB, Japanese Trauma Data Bank.

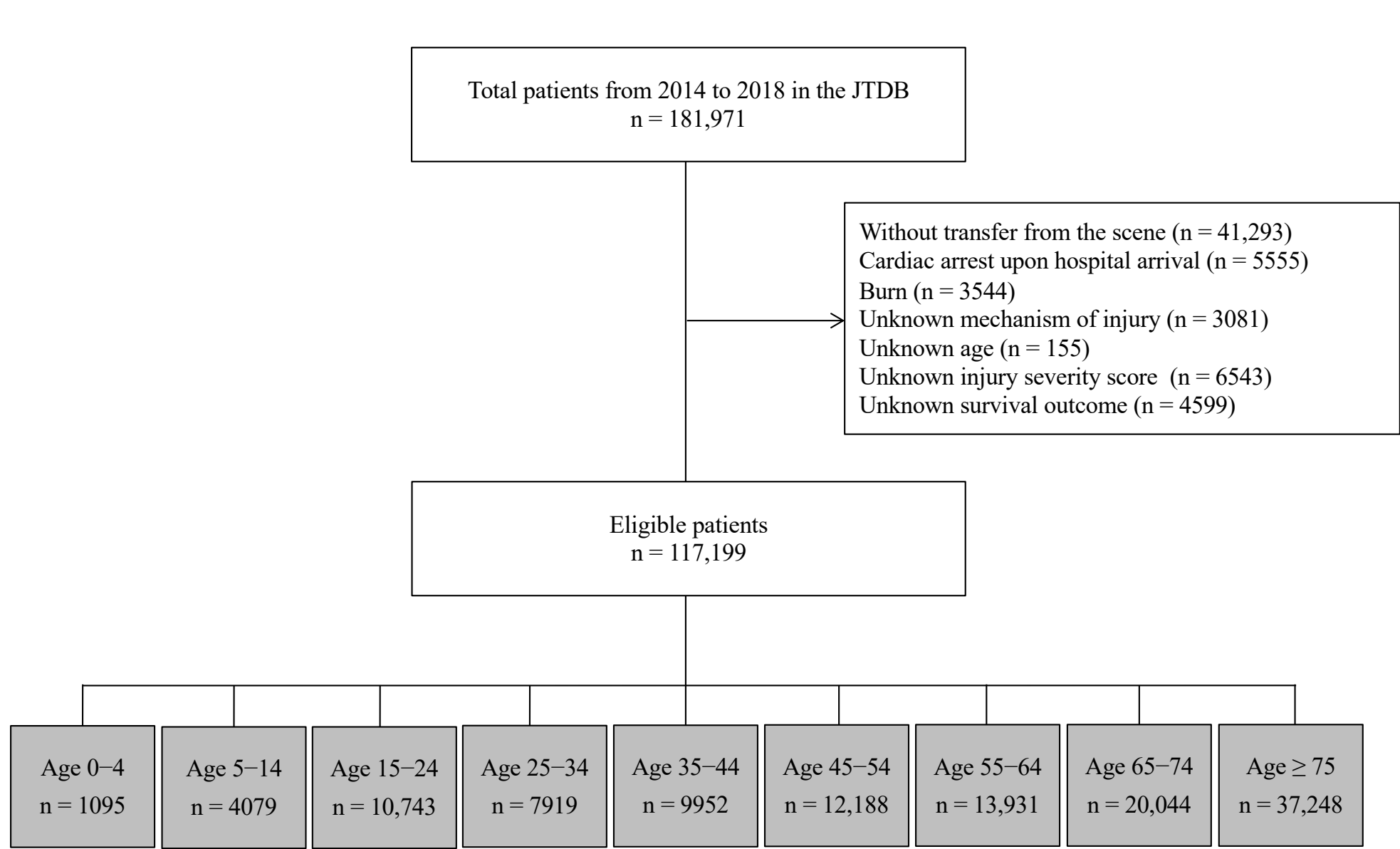


Figure 1. Flow diagram of the patient selection process.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2 2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2,3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3,4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3,4 N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
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	4,5
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	4,5 4,5 3,4 N/A N/A
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5 3,4,5 5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	3,4,5 3 3
Outcome data	15*	Report numbers of outcome events or summary measures over time	5

1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5
2			(b) Report category boundaries when continuous variables were categorized	5,6
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,7,8
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6	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5,7,8
7				
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11	<b>Discussion</b>			
12	Key results	18	Summarise key results with reference to study objectives	9
13	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
14				
15	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9,10
16				
17	Generalisability	21	Discuss the generalisability (external validity) of the study results	9,10
18				
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21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10
23				
24				

25  
26 \*Give information separately for exposed and unexposed groups.

27  
28 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and  
29 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely  
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31 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is  
32 available at <http://www.strobe-statement.org>.  
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# BMJ Open

## Evaluating the definition of Severely Injured Patients: A Japanese Nationwide 5-Year Retrospective Study

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1 Article

2 **Evaluating the definition of Severely Injured Patients: A**  
3 **Japanese Nationwide 5-Year Retrospective Study**

4 **Chiaki Toida <sup>1,2\*</sup>, Takashi Muguruma <sup>2</sup>, Masayasu Gakumazawa <sup>2</sup>, Mafumi Shinohara <sup>2</sup>,**  
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## 17 Abstract:

18 **Objectives:** The definition of severely injured patients lacks universal consensus based on  
19 quantitative measures. The most widely used definition of severe injury is based on the Injury  
20 Severity Score (ISS), which is calculated using the Abbreviated Injury Scale in Japan. This study  
21 aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in  
22 patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  by age groups.

23 **Design:** Retrospective cohort study.

24 **Setting:** Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280  
25 hospitals.

26 **Participants:** We utilized data of 117,199 injured patients from a national database. We included  
27 injured patients who were transferred from the scene of injury by ambulance and/or physician.

28 **Primary and secondary outcome measures:** Prevalence, in-hospital mortality, and OR for  
29 mortality with respect to age and injury level (ISS group).

30 **Results:** In all age categories, the in-hospital mortality of patient groups with an  $ISS \geq 16$ ,  $ISS \geq 18$ ,  
31 and  $ISS \geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients  
32 aged  $> 75$  years was the highest (20% greater than that of the other age groups). Moreover, in-  
33 hospital mortality for age group 5–14 years was the lowest (4.0–10.9%). In all the age groups, the  
34 OR for mortality for patients with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$  was 12.8, 11.0, and 8.4,  
35 respectively.

36 **Conclusions:** Our results revealed the lack of an acceptable definition, with a high in-hospital  
37 mortality and high OR for mortality for all age groups.

39 Keywords: severely injured patient; trauma scoring system; anatomical injury severity; mortality  
40 risk; Japan Trauma Data Bank

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## 42 Strengths and limitations of this study

- 43 ➤ We used data from a large nationwide Japanese trauma registry to evaluate in-hospital  
44 mortality and odds ratio (OR) for mortality in patients with severe injury according to age.
- 45 ➤ This is the first study to reveal that no definition of severe injury was acceptable, with not only  
46 high in-hospital mortality but also a high OR for mortality for all age groups.
- 47 ➤ The Japanese nationwide dataset with more missing data may have led to selection bias.

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## 1. INTRODUCTION

The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1–5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs,[4,5] the definition lacks a universal consensus with quantitative measures.[2,3]

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq 16$  was defined as “severely injured” because patients with an ISS  $\geq 16$  had an expected mortality rate of  $> 20\%$ .[1] However, the mortality of patients with an ISS  $\geq 16$  and ISS  $\geq 26$  decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than that in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. We hypothesized that there would be differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical injury severity. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with an ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  as the commonly used anatomical injury definitions by age group [2].

## 2. MATERIALS AND METHODS

### 2.1. Study setting and population

This retrospective observational nationwide study was conducted based on data obtained from the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn,

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4 78 and records prehospitalization- and hospital-related information. The JTDB includes data on  
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6 79 demographic characteristics, comorbidities, injury types, mechanism of injury, means of  
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8 80 transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as  
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10 81 indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record  
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12 82 the online registration of individual patient data. There were 280 participating hospitals in all 47  
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14 83 prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency  
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16 84 medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open  
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18 85 access and updating of existing medical information, and the Japan Correlation for Acute Medicine  
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20 86 evaluates the submitted data.

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22 87 In this study, we used the JTDB dataset that included information from January 1, 2014 to  
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24 88 December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for  
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26 89 this study was injured patients who were transferred from the scene of injury by ambulance and/or  
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28 90 physician. Patients with cardiac arrest on hospital arrival or with missing key data, such as  
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30 91 mechanism, age, ISS, and/or survival outcome, were excluded from this study. Figure 1 presents a  
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32 92 flow diagram of the patient selection process in this study.

## 33 34 93 35 94 **2.2. Data collection**

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37 95 We collected information from the JTDB, including the following variables: demographic  
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39 96 characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and  
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41 97 clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the  
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43 98 injured region  $\geq 3$  was defined as a case of a severely injured region.

## 44 45 99 46 47 48 100 **2.3. Ethics statement**

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51 101 This study was approved by the hospital ethics committee of Yokohama City University  
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53 102 Medical Center (approval no. B170900003). The approval authority for data access was provided by  
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55 103 the Japanese Association for the Surgery of Trauma (Trauma Registry Committee). The  
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57 104 requirement for informed consent from the patients was waived owing to the observational nature of  
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59 105 the study.  
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## 107 2.4. Statistical analysis

108 The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with  
109 respect to age group (0–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, and  $\geq 75$  years) and  
110 injury severity (ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ ); the ISSs of these groups were used as the  
111 definitions of anatomical injury in a previous review article.[2]

112 Continuous variables are presented as medians with interquartile range (IQR, Q1–Q3), and  
113 categorical variables are presented as the number and percentage of patients. The Mann–Whitney U  
114 test and Wilcoxon’s rank-sum test were used to analyze continuous variables, whereas the chi-  
115 square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for  
116 mortality was calculated using a logistic regression model. All statistical analyses were performed  
117 using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical  
118 significance was defined as a two-tailed P-value of  $< 0.05$ .

## 120 2.5. Patient and public involvement

121 Patients and the public were not involved in the design, conduct, reporting, or dissemination of  
122 this research. We will not directly disseminate our findings to involved participants. However, we  
123 plan to disseminate them through the publication of an article.

## 125 3. RESULTS

126 During the 5-year study period, we analyzed the data of 117,199 injured patients transferred  
127 from the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The median  
128 age and ISS score were 64 years (IQR, 41–78) and 10 (IQR, 9–19), respectively. The overall in-  
129 hospital mortality rate was 6.1%.

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4 130 Table 1 shows the characteristics by age group and injury severity group during the 5-year  
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6 131 study period. The number of patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  was 48,028 (41% of all  
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8 132 the patients), 32,225 (28%), and 15,343 (13%), respectively.

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11 133 Figure 2 shows in-hospital mortality and OR for mortality with respect to age group and injury  
12  
13 134 severity. In all age categories, the in-hospital mortality of patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  
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15 135  $\geq 26$  was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality for  
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17 136 patients aged  $> 55$  years was higher than that for younger age groups, and that of patients aged  $> 75$   
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19 137 years was higher (by more than 20%) than that of all patient groups for each level of injury severity.  
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21 138 In-hospital mortality for the 5–14 years age group was 4.0–10.9% and lower than that for the other  
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23 139 age groups.

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26 140 In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4–  
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28 141 11.6), and 8.4 (8.0–8.8), respectively, for the three levels of injury severity, and the OR in patients  
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30 142 with ISS  $\geq 16$  or ISS  $\geq 18$  was higher than that in patients group ISS  $\geq 26$ .

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145 **Table 1. Characteristics by the nine age groups and three levels of injury severity groups.**

Variables	Overall n = 117,199	Age 0–4 n = 1095	Age 5–14 n = 4079	Age 15–24 n = 10,743	Age 25–34 n = 7919	Age 35–44 n = 9952	Age 45–54 n = 12,188	Age 55–64 n = 13,931	Age 65–74 n = 20,044	Age ≥ 75 n = 36,248
Age, years	64 (41–78)	2 (1–3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42)	49 (47–52)	60 (57–62)	69 (67–72)	83 (79–87)
Male	73,680 (63)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77)	9211 (76)	10017 (72)	12662 (63)	16317 (44)
Mechanism of injury										
Blunt	113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	11,475 (94)	13,383 (96)	19,433 (97)	36,705 (99)
Injury region										
Head injury with AIS ≥ 3	36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25)	3363 (28)	4451 (32)	7384 (37)	12,136 (33)
Facial injury with AIS ≥ 3	940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3)	124 (1.0)	123 (0.9)	133 (0.7)	136 (0.4)
Neck injury with AIS ≥ 3	478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6)	70 (0.6)	77 (0.6)	110 (0.6)	92 (0.3)
Chest injury with AIS ≥ 3	25,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28)	3485 (29)	3726 (27)	4594 (23)	5448 (15)
Abdominal and pelvic injury with AIS ≥ 3	5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7)	709 (6)	684 (5)	831 (4)	893 (2)
Spinal injury with AIS ≥ 3	13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	1120 (11)	1530 (13)	2106 (15)	3053 (15)	3548 (10)
Upper extremity injury with AIS ≥ 3	6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7)	849 (7)	798 (6)	1026 (5)	1428 (4)
Lower extremity injury with AIS ≥ 3	31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21)	2404 (20)	2691 (19)	4358 (22)	15,457 (42)
Injury Severity Score	10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20)	13 (9–21)	14 (9–21)	14 (9–21)	9 (9–17)
Actual in-hospital mortality	7201 (6.1)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7)	533 (4.4)	762 (5.5)	1438 (7.2)	3361 (9.0)
Injury Severity Score ≥ 16	48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41)	5297 (43)	6541 (47)	9711 (48)	13,940 (37)
Injury Severity Score ≥ 18	32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	2985 (30)	3793 (31)	4372 (31)	6256 (31)	8626 (23)
Injury Severity Score ≥ 26	15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	1823 (15)	2038 (15)	2910 (15)	3938 (11)

146 Data are presented as number (percentage) or median (interquartile range Q1–Q3); AIS, Abbreviated Injury Scale

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#### 148 4. DISCUSSION

149 To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital  
150 mortality and OR for mortality in patients with severe injury according to age. Our study showed  
151 that in all three groups with  $ISS \geq 16$ ,  $ISS \geq 18$ , and  $ISS \geq 26$ , which are the commonly used  
152 anatomical injury definitions, in-hospital mortality for patients aged  $< 55$  years was between 4.0%  
153 and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition  
154 for severely injured patients in a Japanese cohort via the detailed classification of the definition  
155 cutoff values and age groups, there was no acceptable definition, with not only a high in-hospital  
156 mortality, but also a high OR for mortality for all age groups.

157 Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  
158  $\geq 16$  points, the mortality of patients with an  $ISS \geq 16$  was more than 20%; however, the mortality of  
159 these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining  
160 severely injured patients with a high mortality rate.[1–3,8] This study also showed that patients with  
161  $ISS \geq 26$  had the highest in-hospital mortality in all age categories. However, the OR for mortality in  
162 patients with  $ISS \geq 26$  was lower than that in patients with  $ISS \geq 16$  and  $ISS \geq 18$ . There are possible  
163 explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for  
164 mortality in a Japanese cohort.

165 First, there are differences in the study era and/or cohorts at the time of development.[1] A  
166 previous 10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the  
167 in-hospital mortality of patients with  $ISS \geq 16$  decreased from 28.5% to 15.7% owing to  
168 improvements in trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort,  
169 unlike the aging population in the rest of the world, the characteristics and survival outcome of  
170 severely injured patients varied widely according to age, and the mortality risk of elderly patients  
171 with severe injury was higher than that of the other age groups.[12] A previous Japanese nationwide  
172 study showed that the incidence rate of severe traumatic brain injury among severely injured  
173 patients aged  $> 65$  years was high (40.7%).[13] Moreover, the in-hospital mortality of these patients  
174 was higher than that of the other age groups.[13] These results suggest that the elderly patient  
175 groups had a higher mortality because of the high proportion and mortality of severe traumatic head  
176 injury. This study also showed that the prevalence and in-hospital mortality of severely injured

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4 177 patients aged 55–64, 65–75, and  $\geq 75$  years increased stepwise. On the other hand, previous studies  
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6 178 suggested that the ISS cutoff of  $\geq 16$  in adult patients was equivalent to a cutoff of  $\geq 26$  in pediatric  
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8 179 patients aged  $< 16$  years.[14,15] This study showed different results from those of a previous study  
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10 180 [15], wherein the in-hospital mortality of pediatric patients aged 0–4 years with an ISS  $\geq 26$  was  
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12 181 high (17.7%) and that of pediatric patients aged 5–14 years with an ISS  $\geq 26$  was low (10.9%), as  
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14 182 shown in Figure 2. Moreover, a previous study showed that there was a difference in the optimal cut  
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16 183 off value of ISS in predicting severely injury mortality risk by region and/or mechanism of injury  
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18 184 among pediatric patients. Therefore, it is important to develop an acceptable definition of severe  
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20 185 injury by considering the age-related characteristics and mortality risks in a Japanese cohort.  
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22 186 Moreover, this study showed that the mortality rate and risk of injured patients in Japan differed by  
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24 187 age groups and did not have a linear correlation with age in years. For a better predictive accuracy  
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26 188 in mortality, it may be effective to add age categories as a predictive variable for mortality and to  
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28 189 calculate the coefficient for coded value according to mortality risk by each age group, as shown in  
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30 190 the Trauma and Injury Severity Score methodology [16]. Second, there was a limitation in  
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32 191 evaluating only anatomical injury severity as a definition of severe injury. A more recent approach  
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34 192 suggests that the addition of other physiological variables to the anatomical injury severity score has  
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36 193 the advantage of identifying severely injured patients with a high mortality risk.[2,17,18] Although  
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38 194 the mortality of patients with ISS  $\geq 16$  was 18.7%, that of patients with ISS  $\geq 16$  in addition to one  
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40 195 other physiological parameter increased from 35% to 38%.[2] Moreover, patients with an increasing  
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42 196 number of the physiological variable, such as the Glasgow Coma Scale, hypotension, and laboratory  
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44 197 values (e.g., acidosis and/or coagulopathy), may have an increased risk of mortality.[17–19]  
45  
46 198 However, we could not evaluate the variables according to physiological parameters and findings of  
47  
48 199 blood tests. Therefore, it seems important to evaluate these parameters together with the anatomical  
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50 200 injury severity used in this study to develop a well-validated definition of severely injured patients.

51  
52 201 Our study had some limitations. First, there was selection bias because not all Japanese  
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54 202 hospitals that treat severely injured patients are registered in the JTDB. The 280 tertiary centers  
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56 203 equivalent to Level I trauma centers in the United States participated, including 92% of the  
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58 204 Japanese government-approved tertiary emergency medical centers in March 2019. Therefore, the  
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60 205 JTDB is not a population-based sample of injured patients and the data are registered voluntarily.



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4 206 Moreover, the JTDB dataset has missing data, especially for pediatric patients.[20] The number of  
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6 207 pediatric patients were lower than that of adult patients. Therefore, missing data may have a more  
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8 208 significant influence on the analysis of the pediatric patients' data than that of the adult patients'  
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10 209 data. A high-quality Japanese nationwide dataset with less missing data should be constructed to  
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12 210 improve the accuracy of predicting the survival of injured patients in the data analysis for all age  
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14 211 categories. Second, because the number of patients aged 0–4 and 5–14 years was small (0.9% and  
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16 212 3.5% of all the patients, respectively), it is possible that the ORs of these patient groups with small  
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18 213 sample sizes were overestimated. In addition, the number of participating hospitals differed across  
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20 214 the study period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the AIS 2005  
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22 215 updated 2008 coding scale. Similar studies need to be conducted using the newest measure to verify  
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24 216 our results. Last, we did not evaluate which definition would be effective for each age group. A  
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26 217 recent study showed significant discrepancies in the mortality risk of severely injured patients by  
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28 218 each injury region.[21] We intend to calculate the coefficient for the coded value according to  
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30 219 mortality risk by age group and injury region for a better mortality estimate.

## 31 32 33 34 221 **5. CONCLUSIONS**

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36 222 This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mortality, and  
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38 223 OR for mortality in patients with severe injury according to age categories. This study showed that  
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40 224 there were differences in in-hospital mortality rate and risk among Japanese injured patients by age  
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42 225 and anatomical injury severity; therefore, the use of correlation between mortality and injury  
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44 226 severity score, such as the ISS, may be hardly justified in the definition of severely injured patients  
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46 227 in all age categories. In the future, it will be important to evaluate the other parameters, such as age,  
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48 228 physiological variables, and laboratory variables, together with the anatomical injury severity by  
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50 229 using the population-based database to develop a well-validated definition of severely injured  
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52 230 patients.

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56 232 **Author Contributions:** Conceptualization, CT and TM; methodology, CT; software, CT and TA;  
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58 233 validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, MG, and  
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60 234 TA; resources, CT and TA; data curation, CT and TA; writing—original draft preparation, CT;

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4 235 writing—review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT;  
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6 236 project administration and funding acquisition, CT All authors have read and agreed to the  
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8 237 published version of the manuscript.

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12 239 **Ethical Approval Statement:** This study was approved by the institutional ethics committees of  
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14 240 Yokohama City University Medical Centre (approval no. B170900003).

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17 241 **Informed Consent Statement:** The requirement for informed consent from the patients was  
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19 242 waived owing to the observational nature of the study design.

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21 243 **Data Availability Statement:** No additional data available.

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24 244 **Acknowledgments:** None.

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26 245 **Conflicts of Interest:** The authors declare no conflict of interest.

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17 309 Figure Legends

18 310 **Figure 1. Flow diagram of the patient selection process.**

19 311 JTDB, Japanese Trauma Data Bank

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23 313 **Figure 2. Association between odds ratio for in-hospital mortality and age groups by patients with**  
24 314 **Injury Severity Score (ISS)  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ .**

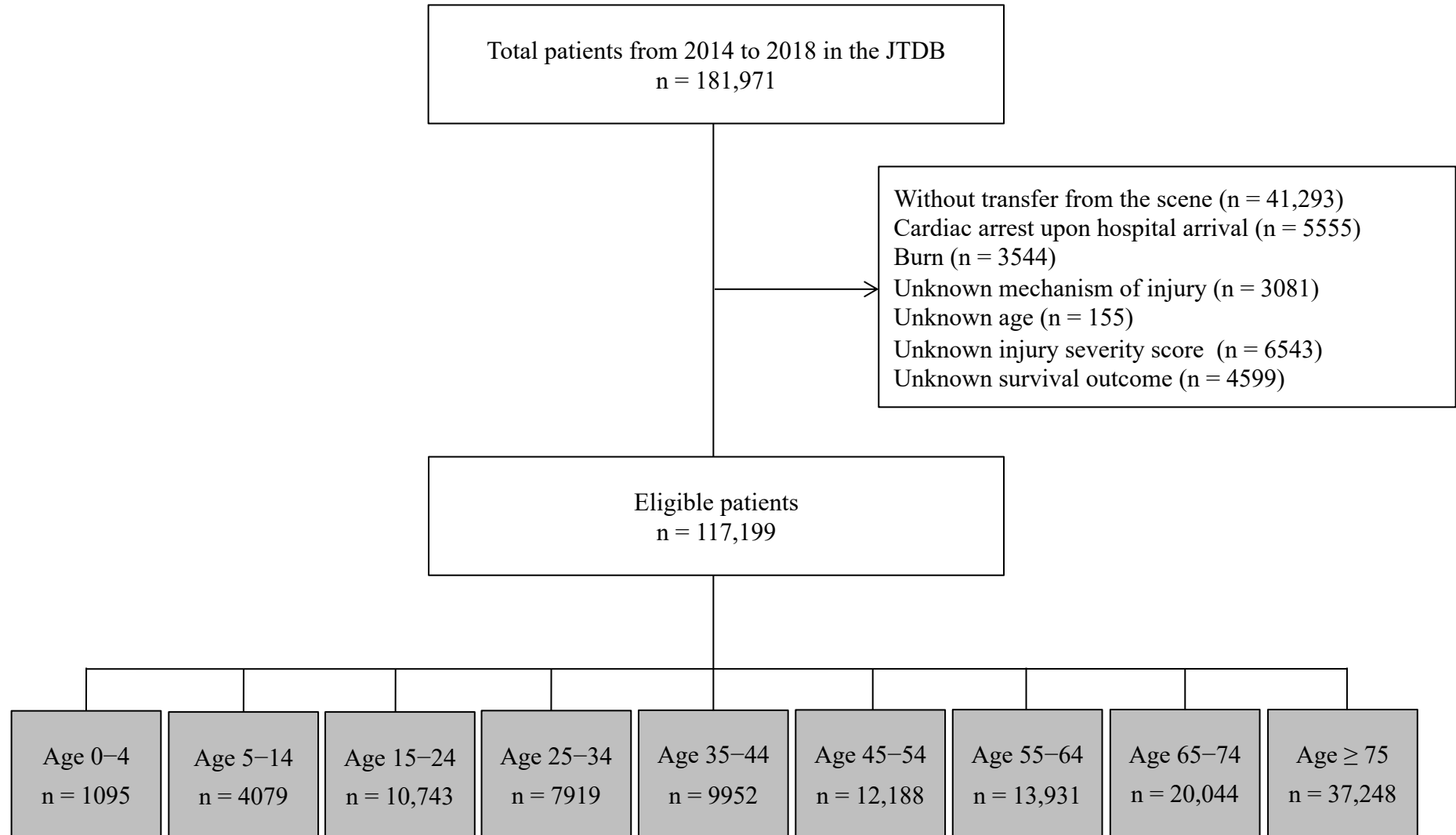
25 315 In a Japanese cohort, using the detailed definition cutoff values and age groups, there

26 316 was no acceptable definition, with not only a high in-hospital mortality, but also a high odds ratio

27 317 for mortality for all age groups.

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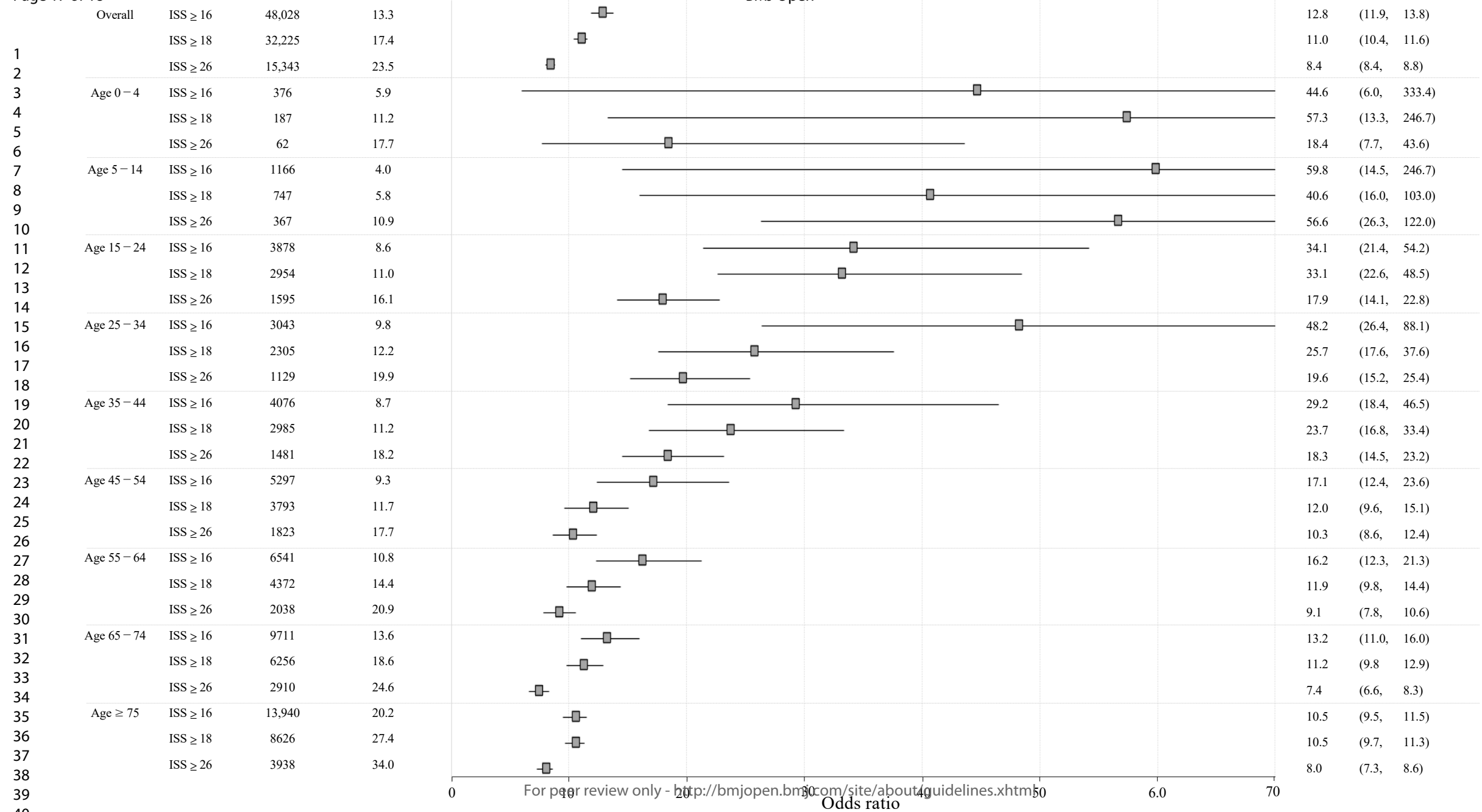


Figure 2. Association between odds ratio for in-hospital mortality and age groups by patients with Injury Severity Score (ISS) ≥16, ISS ≥18, and ISS ≥26.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2 2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2,3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3,4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	3,4 N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
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	4,5
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	4,5 4,5 3,4 N/A N/A
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	5 3,4,5 5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	3,4,5 3 3
Outcome data	15*	Report numbers of outcome events or summary measures over time	5



1	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5
2			(b) Report category boundaries when continuous variables were categorized	5,6
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,6,7
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6	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5,6,7
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11	<b>Discussion</b>			
12	Key results	18	Summarise key results with reference to study objectives	8
13	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9,10
14				
15	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9,10
16				
17	Generalisability	21	Discuss the generalisability (external validity) of the study results	9,10
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21	<b>Other information</b>			
22	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11
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26 \*Give information separately for exposed and unexposed groups.

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