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# Retrospective comparison of the frequency of Do Not Intubate orders among patients diagnosed with sepsis in the emergency room between 2017 and 2022

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The data and code were available upon reasonable request (Nobuichiro Tamura, email address: [nt13991@kchnet.or.jp](mailto:nt13991@kchnet.or.jp))

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## ABSTRACT:

**Background:** This study retrospectively evaluated the frequency of "Do Not Intubate" (DNI) orders in patients with sepsis diagnosed in the emergency room in 2017 and 2022. The objective was to understand the longitudinal adoption of the Advanced Care Planning (ACP) concept over a 5-year span.

**Methods:** We included patients primarily diagnosed with sepsis by emergency physicians at Kurashiki Central Hospital in 2017 and 2022. The primary outcome was the frequency of DNI orders, whereas the secondary outcomes were morbidity and length of hospital stay. We compared the outcomes between 2017 and 2022. Additionally, patient characteristics, such as age, sex, presence of co-resident family members, malignancy status, source of infection, and degree of official care certification were collected.

**Results:** We included 82 and 77 patients with sepsis in 2017 and 2022, respectively. Regarding the primary outcome, 39% (95% confidence interval [CI]: 27-49%) (31/82) of patients with sepsis in 2017 had DNI orders, compared to 44% (95% CI: 33-56%) (34/77) in 2022. There were no significant differences in the primary and secondary outcomes between the two years. The only significant difference noted was in the degree of official care certification among patient characteristics.

**Conclusion:** The frequency of DNI orders remained relatively stable between 2017 and 2022. This suggests that the ACP concept has not yet been widely integrated into the decision-making process for treatment strategies for patients with sepsis.

**Keywords:** Do not intubate order; Emergency room; Sepsis

## INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to an infection [1]. Patients with sepsis account for approximately 20% of admissions to intensive care units (ICUs) [2]. The mortality rate of severe sepsis is approximately 30%, escalating to 50-60% in cases of septic shock [3,4].

Not only does sepsis profoundly affect short-term prognosis, especially mortality rates, but it also has significant implications for long-term outcomes. Discussions regarding the long-term prognosis of sepsis are vital, as the repercussions of the condition span much further than immediate survival. Patients who recover from sepsis experience persistent physical, psychological, and cognitive challenges, commonly referred to as post-sepsis syndrome [5].

Japan is currently facing an accelerated rate of population aging, resulting in a growing older adult population. This demographic transition poses a considerable strain on the healthcare and social care systems [6]. In response to these challenges, in 2018, the Ministry of Health, Labour, and Welfare revised the "Guidelines on the Decision-making Process for Medical Care at the End of Life(Suppl.1)" The updated guidelines underscore the importance of continuous dialogue regarding the direction of medical care and individuals' desired quality of life. This is crucial because personal preferences may evolve based on changes in one's physical and mental well-being [7]. Despite the importance of this subject, there is a dearth of quantitative studies examining the incorporation of advanced care planning (ACP) into the decision-making process for Japanese patients with sepsis. This study aimed to determine whether there has been a shift in the frequency of Do Not Intubate (DNI) orders for patients with sepsis following the revision of the ACP guidelines by the Ministry of Health, Labour, and Welfare. Our study set the frequency of DNI orders, not Do Not Attempt Resuscitation (DNAR) orders, as the primary outcome, as it is a procedure-specific directive and completely objective because there are previous reports regarding DNAR orders [8,9]. In this study, the process of DNI decision making was not restrictively defined; however, these decisions were made mainly among patients, family members, and ER physicians based on sharing information about patient willingness and sickness severity. If patients or their families select DNI orders, they receive treatment including antibiotics and fluid therapy. Regarding vasopressors, 5 patients (16%) in the 2017 DNI group were willing to use them, and 14 patients (41%) in the 2022 DNI group. (Table 1)

## MATERIALS AND METHODS

### Patients

In this study, we included all patients diagnosed with sepsis as their primary condition by emergency physicians at Kurashiki Central Hospital in 2017 and 2022. However, sepsis should be ideally diagnosed based on the SOFA or qSOFA scores; sepsis was subjectively diagnosed based on patients' clinical conditions, including fever, tachycardia,

## KEY MESSAGES:

- Japan is currently facing an accelerated rate of population aging, resulting in a growing older adult population.
- 39% (95% confidence interval [CI]: 27-49%) (31/82) of patients with sepsis in 2017 had DNI orders, compared to 44% (95% CI: 33-56%) (34/77) in 2022.
- The frequency of DNI orders remained relatively stable between 2017 and 2022.

tachypnea, altered mental status, and hypotension due to infection. Individuals below the age of 20 were excluded. Kurashiki Central Hospital is a tertiary care institution situated in Kurashiki, which is the second-largest community within Okayama Prefecture in mid-western Japan. The city's population has remained steady over recent years, reaching 476,595 residents in 2022, and represents a medium-sized Japanese city [10].

The primary outcome of interest was the frequency of DNI orders in 2017 and 2022. DNI decisions were made collaboratively, involving patients, their families, physicians, and nursing staff. No fixed protocol was followed to arrive at a DNI order. For this study, we included patients with sepsis whose treatment preferences were known prior to hospital transportation and for whom decisions were made post-transport.

Our decision to examine data from the years 2017 and 2022 stemmed from a significant development: in 2018, the Ministry of Health, Labour, and Welfare released a revised version of the "Guidelines for Decision-making Processes in End-of-Life Medical Care." The updated guidelines emphasize continuous engagement in discussions related to healthcare and end-of-life decisions. They emphasized the importance of considering an individual's preferences, documenting these dialogues and choices in writing, and ensuring that they are shared between the patients, their families, and medical and caregiving teams. These modifications were rooted in the evolving demographics of the aging Japanese population, with rising mortality rates and increasing recognition of research and initiatives that integrate the ACP concept [7]. Given the potential influence of this announcement on the prevalence of ACPs in Japanese society, the aim of our study was to assess whether there was a difference in the frequency of DNI orders before and after the official declaration. Since 2017 corresponds to the year immediately preceding 2018, when the guidelines were announced, we selected 2017 as the cohort year before the guidelines were released. And it is believed that it takes several years for these guidelines to permeate society, and since 2022 was the latest year with sufficient information regarding the present study, it was designated as the cohort year following the release of the guidelines.

The ethics committee of the Kurashiki Central Hospital approved this study (Approval No. 4129). In line with

the regulations on the protection of personal information, opt-out consent was obtained for this study.

### Comparison items

In this study, our primary outcome was the frequency of DNI orders. The secondary outcomes included morbidity and the duration of the hospital stay. We compared these outcomes between the years 2017 and 2022. Additionally, we collected data on patient characteristics such as age, sex, presence of a co-resident family member, malignancy status, infection source, and level of long-term care certification. The long-term care certification is an integral component of the public health insurance system, established to assess and determine the level of care necessary for older adults or those with disabilities who require assistance with daily activities. Table 4 presents the definition of the level of long-term care certification. All data were collected retrospectively from electronic medical records.

### Statistical analyses

For analyses, we utilized the statistical software EZR version 1.61 [11]. Univariate analysis was conducted to compare the independent variables. For continuous variables, we reported the means and standard deviations (SDs). Pearson's chi-squared test was chosen for categorical variables, while the two-sided Wilcoxon rank-sum test was employed for continuous variables. A multivariate logistic regression analysis was conducted. In this analysis, we set DNI orders as dependent variables and age, co-resident family, malignancy, sex, and group (2017-2022) as independent variables. We select independent variables based on previous research that reported that age, sex, marital status, and cultural and societal characteristics affect DNAR orders [12,13]. A P-value of <0.05 was deemed statistically significant.

**Table 1.** Patient characteristics.

Comparison	2017 group (N=82)			2022 group (N=77)			P value <sup>a</sup>
	DNI (N=31)	non DNI (N=51)	Total	DNI (N=34)	non DNI (N=43)	Total	
Age	81.7±7.45	72.4±10.5	77.3±10.5	78.6±8.8	75.6±11.9	75.7±11.9	0.39
Sex (Male)	17	30	47	23	23	46	0.87
Co-residing family (Yes)	22	40	62	23	29	52	0.29
Malignancy	8	7	15	4	5	9	0.27
Official care certification							0.01
None	9	32	41	14	30	44	
Requiring support	1	3	4	1	2	3	
Requiring care level I	7	2	9	0	0	0	
Requiring care level II	2	4	6	4	4	8	
Requiring care level III	8	4	12	5	1	6	
Requiring care level IV	1	4	5	7	6	13	
Requiring care level V	3	2	5	3	0	3	
Source of infection							0.30
Pneumoniae	7	8	15	6	3	9	
Intra-abdominal	4	10	14	5	4	9	
Urinary tract infection	7	18	25	7	10	17	
Soft tissue infection	1	2	3	3	2	5	
Meningitis	1	0	1	1	0	1	
Ricketia	0	0	0	0	2	2	
Infectious Endocarditis	2	0	2	1	2	3	
Unidentified	9	13	22	10	21	31	
Admission ward							0.17
ICU	11	42	53	14	31	45	
HCU	14	2	16	5	5	10	
General	6	7	13	15	6	21	
Willing to use vasopressor	5	51	56	14	43	57	0.53
Mortality	12	4	16	14	5	19	0.55

<sup>a</sup> P value was calculated between 2017 total group and 2022 total group

## RESULTS

Table 1 presents the patient's characteristics. We included 82 patients diagnosed with sepsis in 2017 and 77 patients diagnosed in 2022. We present them in each group (DNI, non-DNI and total) in 2017 and 2022. The average age of the 2017 and 2022 cohorts was 77.3 years (SD = 10.5 years) and 75.7 years (SD = 11.9 years), respectively. The male-to-female ratio was 47 (57.3%) to 35 (42.7%) in 2017 and 46 (59.7%) to 31 (40.3%) in 2022. In 2017, 15 (18.3%) patients had either a history of malignancy or were newly diagnosed with malignancies in the emergency room (ER), compared to 9 (11.7%) in 2022. Furthermore, 41 (50.0%) patients received some degree of official care certification in 2017, which decreased to 33 (42.9%) in 2022. A total of 62 (75.6%) patients had a co-resident family member in 2017, compared to 52 (67.5%) in 2022. Based on a report by Chang et al. [14], we categorized the sources of infection. Pneumonia, intra-abdominal infections, and urinary tract infections were the most prevalent in both groups. Regarding ward admissions in 2017, 53 (64.6%) patients were admitted to ICUs, 16 (19.5%) to High Care Units (HCUs), and 13 (15.9%) to general wards. These fig-

ures changed in 2022 to 45 (58.4%) in ICUs, 10 (13.0%) in HCUs, and 21 (27.3%) in general wards. Regarding vasopressors, 5 patients (16%) in the 2017 DNI group were willing to use them, and 14 patients (41%) in the 2022 DNI group. Only long-term care certification showed a significant difference between the two groups when comparing patient characteristics. In the 2017 group, DNI patients' mortality rate was 38.7% (12/31) and non-DNI was 7.8% (4/51). In the 2022 group, DNI mortality was 41.1% (14/34) and non-DNI mortality was 11.6% (5/43). Mortality rates were not significantly different between the two groups.

Table 2 displays the primary and secondary outcomes. The primary outcome, the frequency of DNI orders, was 39% (31/82) in 2017 and 44% (34/77) in 2022. Regarding secondary outcomes, 2017 showed a mortality rate of 19.5% (16/82) and an average length of stay of 20.7 days (SD = 18.5 days). For 2022, these figures were 24.7% (19/77) and 16.6 days (SD = 19.9 days), respectively. No significant difference was observed between the two groups for the primary and secondary outcomes.

Table 3 shows the result of multivariate logistic regression for DNI orders. Only age and the presence of ma-

**Table 2.** Primary and secondary outcomes.

Comparison	2017 group (N=82)	2022 group (N=77)	P value (95% CI)
Frequency of DNI <sup>a</sup>	31(39%)	34(44%)	0.43 (0.66-2.57)
Mortality	16(20%)	19(25%)	0.45 (0.32-1.68)
Length of stay (day)	20.7±18.5	16.6±19.9	0.19 (-1.98-10.07)

DNI<sup>a</sup>: Do Not Intubate

**Table 3.** Multivariate logistic regression for Do Not Intubation Orders.

	Odds Ratio(95% CI)	P value
Age (per 1 year)	1.12 (1.07-1.17)	0.00
Co-residing family	1.40 (0.62-3.11)	0.41
Malignancy	2.96 (1.06-8.21)	0.04
Sex	1.55 (0.73-3.29)	0.25
Group (2017-2022)	0.62 (0.30-1.27)	0.19

**Table 4.** The definition of level of long-term care certification.

Requiring support	I. Able to manage meals and toileting independently II. Some assistance or supervision may be required for certain activities of daily living
Requiring care level I	I. Partial assistance is required in daily activities II. Mild cognitive impairment is present
Requiring care level II	I. Assistance is required in all aspects of daily life, including meals and toileting II. Moderate to severe cognitive impairment is present
Requiring care level III	I. There are difficulties in movements such as self-transfer, requiring almost complete assistance in all activities II. Problematic behaviors are observed
Requiring care level IV	I. It is difficult to carry out daily activities without assistance II. Problematic behaviors become pronounced
Requiring care level V	I. Bedridden and unable to independently manage meals and toileting, requiring caregiving for basic functioning II. Difficulty in communication

lignancy have a significant association with DNI orders. Group (2017-2022) was not a significant independent factor. This result was consistent with the univariate analysis in Table 2.

## DISCUSSION

In 1974, the 'Standards for CPR and Emergency Cardiac Care (ECC)' introduced the term 'Orders not to resuscitate' for the first time [15]. In 1991, the American College of Emergency Physicians Ethics Manual addressed DNAR policies and encouraged emergency physicians to respect advance directives [16]. However, clinical practices sometimes diverge from these guidelines. Rueda et al. [17] reported that 5.28% of patients who died in their hospital did not receive CPR, despite lacking a recorded DNAR order in their medical chart. Furthermore, Rubins [8] highlighted that 16.1% of patients might be wrongly denied intubation without informed refusal, and 16.4% could be intubated against their wishes because of the confusion between DNARs and DNIs. This confusion exists both in the in-hospital system and in the patients' understanding of their medical conditions. Notably, there was a significant discordance (between 30% and 40%) between medical record documentation and patient understanding and consent [9]. Given these challenges, our study set the frequency of DNI orders as the primary outcome, as it is a procedure-specific directive and completely objective.

Our primary outcome, the frequency of DNI orders, was 39% (95% confidence interval [CI]: 27-49%) (31/82) in 2017 and 44% (95% CI: 33-56%) (34/77) in 2022. Notably, there was no significant difference between the two groups despite the introduction of guidelines on the decision-making process for end-of-life medical care in 2018. The frequency of DNI orders is affected by a variety of factors. For example, factors such as sex, age, marital status, cancer diagnosis, and hospital size reportedly influence the frequency of DNAR orders in hospitalized Taiwanese patients [13]. In this study, we also conducted multivariate analysis, within which we examined the frequency of DNI orders in 2017 and 2022 while adjusting for other factors. In univariate analysis, parameters such as age, sex, presence of a co-resident family member, malignancy, and infection source showed no significant differences between 2017 and 2022, and group (2017-2022) was not a significant independent factor in multivariate analysis. These results suggest that the concept of ACPs may not have been widely adopted in sepsis treatment strategy decisions. Multivariate analysis in this study showed only age and the presence of malignancy had a significant association with DNI orders. The fact that these factors were found to influence the frequency of DNI orders partially aligns with the findings reported in previous studies [12,13]. In this study, focusing on sepsis patients in the emergency room, the time from diagnosis to DNI order is short. The result in our multivariate analysis could be attributed to discussions regarding ACP among patients and their families triggered by aging or cancer diagnosis before the onset of sepsis. In the Netherlands, the DNR order frequency increased from 67% in 1990 to 79% in 2001 among all in-hospital patients with stable vital signs,

and physicians provided information on DNAR orders [18]. In contrast, our study focused on patients with unstable sepsis in ERs, where DNI orders resulted from discussions among doctors, patients, and their families. Such variations in the participant profiles can significantly influence the DNAR/DNI order frequency. The rate of DNAR orders varies considerably based on factors such as country, care location, illness type, and period. For instance, between 2008 and 2010, 9.4% of 712 patients with sepsis admitted to ICUs in Taiwan had DNR orders [19]. A United States-based study noted that 13.3% of 376 patients with severe sepsis in a teaching hospital ER received DNR orders between 2009 and 2010 [20]. The 39%-44% DNI order frequency in our study is higher than that in these references, possibly due to differing definitions of DNI and DNAR, as well as Japan's status as one of the world's oldest societies.

In this study, the mortality rate in the 2017 DNI group was 38.7% and 41.2% in the 2022 DNI group. DNR orders are said to have a high risk of mortality. In previous studies, mortality rates for patients with severe sepsis or septic shock who had DNR orders ranged from 50% to 90% [19,20]. While there were differences in patient characteristics between this study and previous studies, the mortality rate in this study tended to be lower compared to the findings of previous research. However, even if elderly patients with sepsis survive, they often experience various disabilities that affect their subsequent quality of life. Therefore, in the treatment of sepsis in an aging society, healthcare providers should not only focus on short-term outcomes such as mortality rates but also consider medium to long-term outcomes such as quality of life scores[21].

Our study had several limitations. First, this was a retrospective study, although we had access to comprehensive information without data gaps. Second, this single-center, small-sample study might not be generalizable, even if our hospital serves as the only tertiary care center in the southwestern area of Okayama Prefecture. Third, we did not calculate the sample sizes, and our results may contain the risk of beta error. However, we are unaware of any previous studies reporting the frequency of DNI orders or temporal changes in patients with sepsis in Japan. This is an exploratory study, and further studies with a larger number of cases are needed. Finally, the diagnosis of sepsis was mainly based on an emergency physician's perspective, making it somewhat subjective. Ideally, sepsis should be diagnosed or suspected based on the presence of infection and either the SOFA or qSOFA scores [22]. However, our study's mortality rates of 19.5% in 2017 and 24.7% in 2022 align with Powell et al.'s findings [20], suggesting that our diagnosis of sepsis was accurate.

## CONCLUSION

We found that the frequency of DNI orders remained largely consistent between 2017 and 2022. Key factors, such as age, sex, presence of a co-resident family member, malignancy, and infection source, which are known to significantly influence the frequency of DNIs, showed no discernible differences between the two groups. This

suggests that the concept of ACPs has yet to be widely adopted in shaping treatment strategies for patients with sepsis.

## CONFIDENTIALITY

None

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None

## AUTHORS' CONTRIBUTIONS

(I) Conceptualization: Nobuichiro Tamura; (II) Data curation: Nobuichiro Tamura; (III) Formal analysis: Atsushi Yamamoto; (IV) Funding acquisition: None; (V) Methodology: Nobuichiro Tamura; (VI) Project administration: Ryosuke Echigoya; (VII) Visualization: Nobuichiro Tamura; (VIII) Writing – original draft: Nobuichiro Tamura; (IX) Writing – review & editing: Atsushi Yamamoto, Ryosuke Echigoya, Tetsunori Ikegami

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## SUPPLEMENTARY MATERIALS

**Suppleness 1.** Guidelines for decision-making processes regarding medical and care approaches in the end stage of life.

### 1. Approach to Medical and Care in the Final Stage of Life

1. Proper information and explanation should be provided by healthcare professionals such as physicians. Based on this, discussions should be held between the individual receiving medical and care services and a multidisciplinary healthcare team, with decision-making primarily based on the individual's wishes. Considering the potential for the individual's wishes to change, support should be provided by the healthcare team to ensure that the individual can express their wishes as needed, with repeated discussions taking place. Additionally, given the possibility that the individual may not be able to communicate their wishes, it is important to engage trusted family members or others in repeated discussions with the individual. Before these discussions, it is also crucial for the individual to designate specific family members or others as proxies to represent their presumed wishes.

2. Regarding medical and care approaches in the final stage of life, decisions such as initiating or withholding medical and care interventions, altering the content of medical and care services, or discontinuing medical and care interventions should be carefully evaluated by the healthcare team based on medical validity and appropriateness.

3. The healthcare team should strive to provide comprehensive medical and care services, including effective relief of pain and other discomforts, as well as psychological and social support for the individual and their family.

4. Active euthanasia with the intention of shortening life is not addressed in these guidelines.

2. Procedure for Determining Policies for Medical and Care Approaches in the Final Stage of Life The determination of policies for medical and care approaches in the final stage of life should follow these steps:

#### (1) When the Individual's Wishes Can Be Confirmed

1. The determination of policies should involve professional medical considerations based on the individual's condition, followed by appropriate information provision and explanation from healthcare professionals such as physicians.

2. Subsequently, decisions regarding policies should be made by the healthcare team, considering agreements reached through thorough discussions between the individual and the healthcare team. Given the potential for changes in the individual's wishes due to the passage of time, changes in their physical or mental condition, or revisions in medical assessments, support should be provided to enable the individual to express their wishes as needed, with family involvement in discussions if necessary.

3. The discussions and decisions made in this process should be documented in writing each time.

(2) When the Individual's Wishes Cannot Be Confirmed In cases where the individual's wishes cannot be confirmed, careful judgment within the healthcare team is necessary, following these steps:

1. If family members or others can estimate the individual's wishes, these presumed wishes should be respected in determining the best course of action for the individual.

2. If family members or others cannot estimate the individual's wishes, discussions should be held extensively with them to determine the best course of action for the individual. This process should be repeated as needed based on changes in circumstances.

3. If there are no family members available or if family members delegate decision-making to the healthcare team, the focus should remain on determining the best course of action for the individual.

4. The discussions and decisions made in this process should be documented in writing each time.

(3) Establishment of a Forum for Discussions Involving Multiple Experts In cases outlined in (1) and (2) above, where decisions regarding policies need additional consideration:

1. When healthcare decisions are challenging due to the individual's physical or mental condition within the healthcare team.

2. When agreement on appropriate medical and care approaches cannot be reached between the individual and the healthcare team, or within the family. It is necessary to establish a separate forum for discussions involving multiple experts, including individuals outside the healthcare team, to deliberate and provide advice on policies and related matters.