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Original Research

Factors affecting participation in web-based Alzheimer's questionnaire surveys: Lessons from the Japanese trial-ready cohort

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ABSTRACT

Background: Web-based approach is considered helpful for the research focused on screening and early detection of individuals with preclinical Alzheimer's disease (AD); obtaining sufficient responses is critical to the success of such online study.
Objectives: This study examined factors influencing response rates to an online survey about disease-modifying drugs for AD among participants in the Japanese Trial-Ready Cohort (J-TRC) webstudy.
Design: This was a retrospective observational study.
Settings: Online survey in Japan using Google Forms.
Participants: We enrolled the eligible J-TRC webstudy participants who had registered before September 2023. We sent them an invitation e-mail including a questionnaire web address on November-December 2023, in order to conduct an online survey regarding their perceptions of disease-modifying therapy drug that was approved in July 2023, Japan.
Measurements: We analyzed the impact of mailed day of the week (DOW), participant gender, age, employment status, and educational background with/without response to the invitation, quantified by the odds ratio of response.
Results: Among approximately 10,400 J-TRC web study participants who sent invitation emails, the overall response rate was approximately 20 %, without significant influence depending on the DOW when the survey invitation was sent. Individuals who were older (50s–70s), retired, or had higher education levels were significantly more likely to respond, regardless of the DOW. Differences in response rates by sex/gender were observed, but were largely influenced by the employment status.
Conclusions: In order to improve response rates and enhance data quality, these findings provide valuable insights for optimizing the design of future online studies/surveys in the field of AD and dementia, particularly for targeting cognitively unimpaired middle-aged and older populations.

1. Introduction

Web-based clinical studies / surveys [1–4] have gained significant traction in recent years, particularly in light of the COVID-19 pandemic [5] which has accelerated the adoption of remote research methods. Online surveys are specifically a valuable tool for screening and early detection of individuals with diseases in their presymptomatic stages or those at risk of the disease [6] because in-person clinical studies or surveys are often not easy.

This approach is also expected to be beneficial for Alzheimer's disease (AD). AD is a prime example of a condition where early intervention before a significant cognitive decline occurs, is considered crucial [7,8]. Although disease-modifying therapy (DMT) for mild AD was approved in 2023 in the United States and Japan [9,10] to slow the clinical deterioration of patients with mild cognitive impairment or early dementia stage of AD [11], the preclinical stage of AD [12], characterized by initial pathological changes in the brain without overt symptoms, has become another key focus of clinical trials aiming to slow or prevent disease progression [13,14]. However, recruiting asymptomatic participants for these trials includes unique challenges for several reasons: first, asymptomatic individuals may lack awareness or perceive their own risk for AD, making them less likely to agree to participate in clinical tri-

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als. Second, detecting and diagnosing preclinical AD in asymptomatic individuals requires high-cost or invasive testings such as amyloid PET scans or cerebrospinal fluid test despite their relatively low positive rates among asymptomatic individuals, further complicating the recruitment process. Thus, the online method may be suitable for recruitment to surveys, clinical studies, or trials for the earliest stage of AD [15].

In a web survey, obtaining sufficient responses is critically important for its success. It is reported that web-based recruitment achieved fewer responses than postcards or mail letters did, but web surveys can achieve a comparable level of response to mailed hard-copy surveys when preceded by an advance notification [16]. This highlights the importance of strategic planning of survey administration to enhance response rates (RRs), including arrangement of which day of the week (DOW) and which time of the day for sending mass emails, which are reported as important to obtain as many responses as possible [17]. However, research on the impact of timing on survey RRs has yielded mixed results: one study reported that sending survey notifications and reminders on Tuesday mornings led to higher RRs [18]. In contrast, another study identified Wednesday morning as the most effective time for sending Internet surveys [17]. Another study reported that the effects of arrangement in DOW and time of the day of survey invitation are small and short-lived, with varied effects by employment status and age [19]. These findings suggest that while certain DOW and time may be more effective for some specific types of surveys, evidence about the detailed impact of the timing of invitation on RRs has not been established. Additionally, the increasing use of mobile devices has significantly changed how people interact with emails and surveys. Mobile device users may check their emails more frequently but may not necessarily respond immediately, requiring additional considerations for timing and survey design [20].

The impact of the factors as mentioned above on survey RRs has not been thoroughly investigated in the context of AD, and it remains unclear whether findings from other diseases are similarly applicable to AD. Therefore, we investigated the RRs and their relationship with demographic attributes in an AD-related web survey. For this purpose, we used the data from a survey conducted on participants of the Japanese Trial-Ready Cohort (J-TRC) web study [21,22], which we have been conducting since 2019 as one of the online screening registries aiming to recruit preclinical AD individuals ready for clinical trials in Japan [23].

2. Methods

2.1. Ethics

The J-TRC webstudy was approved by the University of Tokyo Graduate School of Medicine Institutional Ethics Committee (ID:2019132NI-(3)), and online informed consent was obtained from individual participants upon registration. The online survey had been also approved by the local ethics committee.

2.2. Study design

This is a retrospective, dropout analysis of web-based survey on the perception about DMT drugs among participants of the J-TRC web study. With the approval of lecanemab in 2023, a DMT drug for early AD [11], we have just conducted an online survey in late 2023 to the J-TRC webstudy participants in terms of perception of healthcare system challenges for the safe, effective, and sustainable delivery of approved DMT drugs. Content results of this survey are available in our report [24].

The details of the J-TRC web study have been described in our previous reports [21]. The J-TRC study for preclinical and prodromal AD was launched in Japan in 2019 under a research license agreement with the Alzheimer's Therapeutic Research Institute. It has two main study components: the J-TRC webstudy and the J-TRC onsite study. The J-TRC webstudy (https://www.j-trc.org/), which is designed based on the Alzheimer's Prevention Trials Webstudy (https://www.aptwebstudy.org/) for Japanese cognitively normal elderly volunteer participants aged 50–85 years, is monitored by web-based remote assessment of the cognitive function instrument (CFI) [25] and CogState [26] every 3 months. The J-TRC website is accessible only domestically within Japan. Within approximately 4 years since its launch, the J-TRC web study has recruited more than 10,000 eligible online participants from all over Japan in the aim to build "trial-ready cohort" for facilitating clinical trials for AD.

Individuals who are considered to have an increased risk of elevated brain amyloid or cognitive decline are referred to the J-TRC onsite study for detailed in-person assessments, *APOE* genotyping, blood biomarker testing (e.g., plasma Aβ and p-tau), and determination of brain amyloid status by amyloid PET. This study, designed based on the TRC-PAD in-person study in the United States, aims to build a large ($n > 300$) cohort of Japanese individuals with preclinical AD.

2.3. Online questionnaire to J-TRC webstudy participants

The procedure of our online survey is largely in accordance with our previous online survey conducted in June 2023 in terms of J-TRC website usability [27]. On September 25, 2023, we extracted the data of J-TRC webstudy participants who had completed registration to the J-TRC website, given consent to participate in the study, and completed one or more CFI tests. Among them, 10,414 web study participants with valid e-mail addresses were included as eligible users to send an invitation e-mail containing the web address of the online questionnaire. Before sending invitations, these participants were randomly allocated a single DOW among five DOWs to send invitation e-mails: from Tuesday (November 28, 2023) to Saturday (December 2). Mainly due to the limitation of the e-mail sending system, we could not send the invitation email on Sunday (Dec 3) or Monday (Nov 27). The allocation of the DOW is randomly determined so that the distribution of the total number of CFI completed by individual J-TRC webstudy participants is equal across the different DOW subgroups: we then confirmed that there was no significant difference in the distribution of other background characteristics (i.e., age, sex/gender, education years, employment status, history of AD/dementia) across the different DOW subgroups. By this random allocation process, we expect that we can minimize bias derived from varied background characteristics, thereby allowing us to make the difference in the degree of response more directly interpretable.

E-mail sending was done in the morning (6:00 am–7:00 am), only once per participant on their allocated DOW. The timing of this survey just corresponds to the interval period between the full approval of lecanemab in Japan in September 2023 and the publication of the Optimal Clinical Use Guideline (OUG) [10] of lecanemab in Japan on December 19, 2023. This means that at the time of this survey, the questionnaire was the content of high public interest. No incentives (e.g., monetary gift or lottery) were provided to the questionnaire respondents. The invitation was sent only once per individual J-TCR web participant, and we have not sent thank-you mass e-mails with a reminder.

An online questionnaire was administered using Google Forms provided in Japanese language (https://www.google.com), without requiring any personally identifiable information (e.g., name, account ID, e-mail address, or date of birth). It can be accessed via PCs, tablets, or smartphones, although we recommended access to the survey via PCs. We used an anonymous method for collecting responses: we did not require respondents to log in with their Google accounts to answer the Google Form questionnaire or did not require them to fill in their J-TRC webstudy accounts. This is because we wanted to gain as many responses as possible, even at the expense of respondents' traceability. Instead, we were unable to exclude potential duplicate responses from the same individual. However, to reduce double responses, we included a caution statement "Please respond to the questionnaire only once." within the invitation e-mail. Data was acquired 4 weeks after the invitation email was sent.

2.4. Statistical analysis

All statistical analyses were conducted using R software (R Foundation for Statistical Computing, Vienna, Austria). In the following analyses, we presume that we can ignore the possibility of a double response and assume that all survey responses were from the J-TRC web study participants who we sent the survey invitation e-mail. We conducted the following analyses: (1) RRs and its 95 %CI under specified conditions (e.g., those of female and male in a certain DOW) in which the 95 %CI of response rate was calculated based on binomial distribution, and (2) odds ratio (OR) of response, to identify which kind of participant characteristics may be more or less likely to lead to the survey response. We could not conduct multivariable analysis because in this anonymous study, we have not linked ID between the J-TRC participants and the actual survey respondents.

For analysis (2), we obtained OR by comparing the characteristics of the J-TRC participants and the survey respondents. For example, considering that of the 10,000 J-TRC web study participants that were sent a survey invitation mail, 5,000 were women, while 5,000 were men. However, 900 and 850 survey respondents stated that their sex was female and male, respectively. Assuming the exposure factor is the female sex (vs. male sex) and the outcome factor is the response to the survey, a 2-by-2 contingency table was made, as shown in Table S1. The OR of the survey response was calculated using the following equation:

$$OR = \frac{\left(\frac{A:\ N\ of\ female\ among\ respondents}{B:\ N\ of\ female\ among\ non\ -\ respondents}\right)}{\left(\frac{C:\ N\ of\ male\ among\ respondents}{D:\ N\ of\ male\ among\ non\ -\ respondents}\right)}$$

Although we do not know the B and D values directly, values of A, A+B, C, and C+D are known; therefore, the OR can be calculated. The OR in Table S1 was calculated to be 1.072 (95 % CI: 0.965 ~ 1.190), and since its 95 % CI includes 1, we can conclude that sex was not associated with an increased or decreased response to the online survey. Thus, we calculated the ORs of the binarized features of the survey respondents using the R package {*epitools*}. We also conducted Mantel-Haenszel tests by imputing stratified contingency tables to analyze the association of other covariates.

3. Results

3.1. Survey respondent characteristics

Among approximately 10,400 J-TRC webstudy participants who sent invitation emails, 2,050 responses (19.7 % RR) were received within four weeks of the response acceptance period. The background of the participants and respondents is shown in Table 1.

3.2. Comparison of response rates by day of the week

The overall RR slightly varied by the DOW, with Tuesday having the highest RR (20.8 %) and Friday the lowest (18.5 %) (Fig. 1A), although their 95 %CI showed substantial overlap. The OR of individual DOW compared to any other DOW also showed similar results, without a significant decrease or increase in OR (95 %CI spanning 1) (Fig. 1B).

3.3. Sex/Gender and response rates

Differences in RRs by sex/gender were observed (Fig. 1C), with significantly lower RRs for females on Wednesday and Friday. Mantel-Haenszel tests of response by sex/gender while adjusting for DOW showed a significantly lower likelihood of females to respond than males regardless of the DOW (OR 0.870, 95 %CI: 0.789 ~ 0.958).

3.4. Age and response rates

RRs by age seemed to show a certain trend: individuals in the older (i.e., 50's, 60', and 70's) age group had a higher likelihood to respond to a survey when compared to any other age group (Fig. 2B). This trend by age looks retained even when examined by DOW (Fig. 1E). Mantel-Haenszel tests of response by age group, adjusting for DOW, showed significant changes in OR across age groups regardless of the DOW ($p < 0.001$). However, when adjusting for age groups, Mantel-Haenszel tests of response by DOW did not show significant changes in OR by DOW ($p = 0.473$).

Table 1
Background characteristics of J-TRC webstudy participants and survey respondents

		All J-TRC users invited to survey n = 10,414	Survey respondents n = 2,050
Mailed DOW	Tuesday	2,084 (20.0 %)	434 (21.2 %)
	Wednesday	2,084 (20.0 %)	410 (20.0 %)
	Thursday	2,083 (20.0 %)	403 (19.7 %)
	Friday	2,082 (20.0 %)	385 (18.8 %)
	Saturday	2,081 (20.0 %)	418 (20.4 %)
Age	-49	297 (2.9 %)	14 (0.7 %)
	50-59	3,989 (38.3 %)	599 (29.2 %)
	60-69	3,641 (35.0 %)	806 (39.3 %)
	70-79	1,972 (18.9 %)	506 (24.7 %)
	80-	515 (4.9 %)	125 (6.1 %)
Sex: female		5,790 (55.6 %)	1,082 (52.8 %)
Retired		3,348 (32.1 %)	838 (40.9 %)
Education years ≤12		2,406 (23.1 %)	365 (17.8 %)

Abbreviations: DOW, day of the week; J-TRC, Japanese Trial-Ready Cohort.

3.5. Employment status and response rates

Response by retired individuals in each DOW compared to any other DOW showed consistently significantly higher than those with not-retired individuals (Fig. 2A), and Mantel-Haenszel tests of response by employment status while adjusting for DOW showed significantly high OR (1.513, 95 %CI: 1.367 ~ 1.675). Furthermore, since sex/gender may be associated with the relationship between employment status and the degree of response, we separately visualized OR of sex/gender in each DOW compared to any other DOWs, depending on the employment status (Fig. 2B). Among non-retired individuals (left-sided), females seem to have a similar or higher likelihood of response than males. In comparison, among retired individuals (right-sided) females appear to have a similar or lower likelihood of response.

These potential confounding of sex/gender was further examined by Matel-Haenszel tests, where response by employment status while adjusting for sex/gender yet showed significantly high OR (1.508, 95 %CI: 1.363 ~ 1.669). In contrast, Mantel-Haenszel tests of response by sex/gender while adjusting for employment status showed a non-significant change of response (OR 0.933, 95 %CI: 0.844 ~ 1.030), suggesting that the degree of response by sex/gender was rather influenced by that of employment status.

Similarly, potential confounding of age group in the relationship between the employment status and the degree of response was examined by Mantel-Haenszel test, where response by employment status while adjusting for age group also showed significantly high OR (1.180, 95 %CI: 1.048 ~ 1.328). In addition, Mantel-Haenszel tests of response by age group while adjusting for employment status showed a significant change in response ($p < 0.001$), suggesting that the degree of response by age group is not always dependent on the employment status.

3.6. Educational level and response rates

Response by shorter education years (i.e., 12 years or less versus longer than 12 years) in each DOW compared to any other DOW showed consistently significantly lower than those with longer education years (Fig. 2C). Confounding of employment status was examined by Mantel-

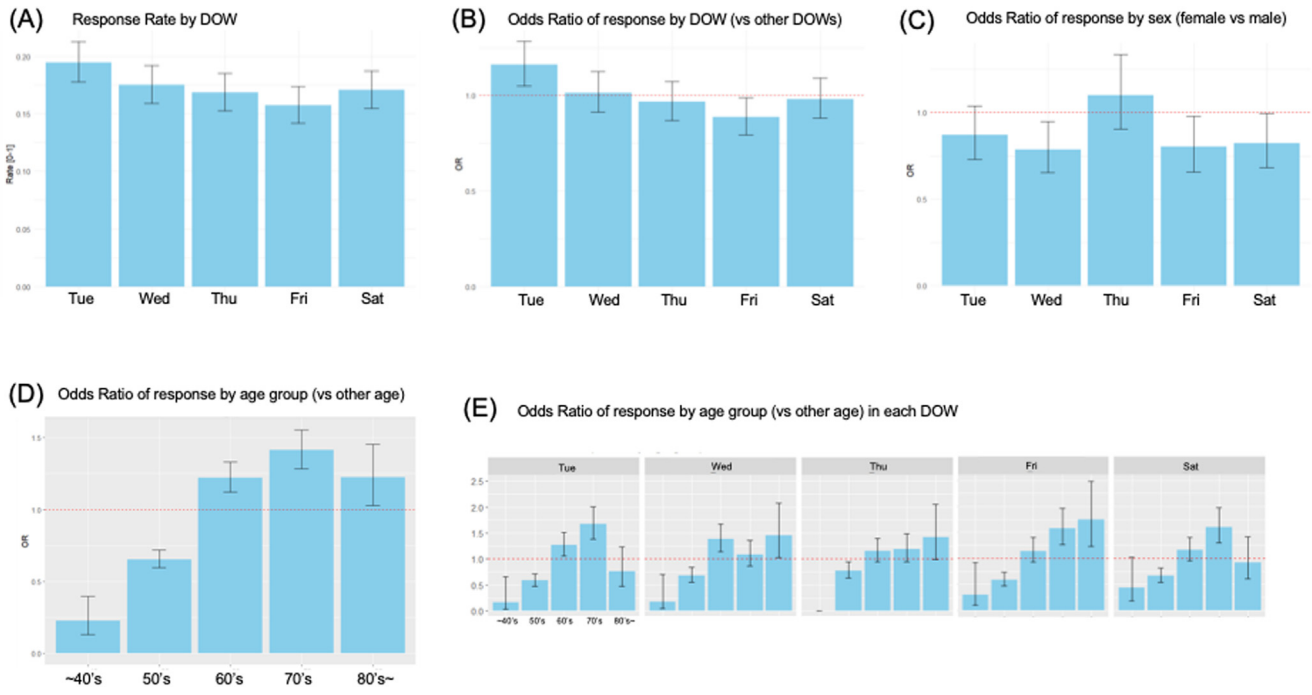

Fig. 1. Response rates and odds ratio by day of the week, sex, and age
Fig. 1A illustrates the response rates by day of the week (DOW), showing that Tuesday had the highest response rate. However, the differences between DOWs were not statistically significant, as indicated by overlapping error bars. Fig. 1B presents the odds ratios (ORs) of response rates for each DOW, comparing responses on a given day to all other days combined. The 95 % confidence intervals (CIs), indicating no significant increase or decrease in response likelihood based on the DOW. Fig. 1C displays odds ratio (OR) for female compared to male respondents for each day DOW of sending invitation e-mail. On Tuesday and Friday, female are less likely to respond than male (upper 95 % OR < 1). Fig. 1D demonstrates OR of response rates of individual age group compared to all other age groups. The results show that older age individuals are more likely to respond than those with younger individuals, suggesting an age-related trend in survey participation. Fig. 1E further explores the age-dependent trend in response rates across DOWs. The general pattern of higher response rates among older individuals was retained across different DOWs, highlighting the consistency of age-related differences in response behavior. Abbreviations: DOW, day of the week.

Haenszel test, where response by education years while adjusting for employment status still showed significantly low OR (0.566, 95 %CI: 0.497 ~ 0.643).

4. Discussion

In this study, we analyzed the impact of DOW, gender, age, employment status, and educational background on online survey RRs among participants of the J-TRC web study. As a result, the overall RR was approximately 20 % without significant differences across the examined DOW. Female respondents were less likely to participate compared to males, older individuals responded more frequently than younger ones, and retired individuals had higher RRs than those not retired. Additionally, participants with shorter education years were less likely to respond. Among these characteristics, employment status (retired vs. non-retired), age (older vs. younger), and education (longer vs. shorter) appear to be independent factors influencing response rates. These findings may guide the design of future online surveys targeting middle-aged and elderly populations, particularly in dementia-related research, to enhance RRs and ensure survey success.

Although substantially overlapped in the 95 % CI, the highest RR was observed on Tuesday, while the lowest was on Friday (Fig. 1A). Our survey invitation was sent in the morning, and prior studies have shown that response rates may vary based on the time of day. Some studies have found higher response rates on Tuesday or Wednesday mornings [17,18]. These findings suggest that sending surveys earlier in the week may be more effective in eliciting responses. However, other prior research has indicated that the influence of DOW and the timing of survey invitation on RR appears to be relatively minimal and transient [19]. Our results are also consistent with this earlier observation, since the 95 % CI of RR considerably overlapped with each other between different DOW.

The decreasing trend of the RR from Tuesday to Friday suggests that participants may be less likely to respond later in the weekdays, possibly due to increasing work-related or personal commitments. The RR on Saturday rebounded to a level comparable to Tuesday, likely because respondents had more time to complete the survey on weekends. These findings suggest that researchers conducting online surveys may benefit from prioritizing invitations on Tuesday, Wednesday, or Saturday while avoiding Friday mornings, at least in studies using a schedule to email in the morning. Also, this trend highlights the importance of considering employment status when designing survey distribution strategies. As our findings indicate, non-retired individuals exhibited lower response rates, likely due to work obligations. Therefore, sending survey invitations on Saturdays may help increase participation among this group by providing them with more flexibility to respond outside of working hours.

Significant differences in RRs by sex/gender were observed, with males showing higher RRs on Wednesday, Friday, and overall (as indicated by the Mantel-Haenszel test) (Fig. 1C). Meanwhile, employment status was also associated with the degree of response (e.g., higher OR in retired individuals) as reported in earlier studies [19], and Mantel-Haenszel test further revealed that the effect of sex and gender on response rates was largely influenced by employment status. Specifically, among retired individuals, males were more likely to respond than females, whereas among non-retired individuals, females were more likely to respond than males (Fig. 2B).

Analysis by age group revealed that participants in their 70s had the highest RRs on Tuesdays, significantly higher than other age groups (Fig. 1D, E). The observation that older adults are more likely to en-

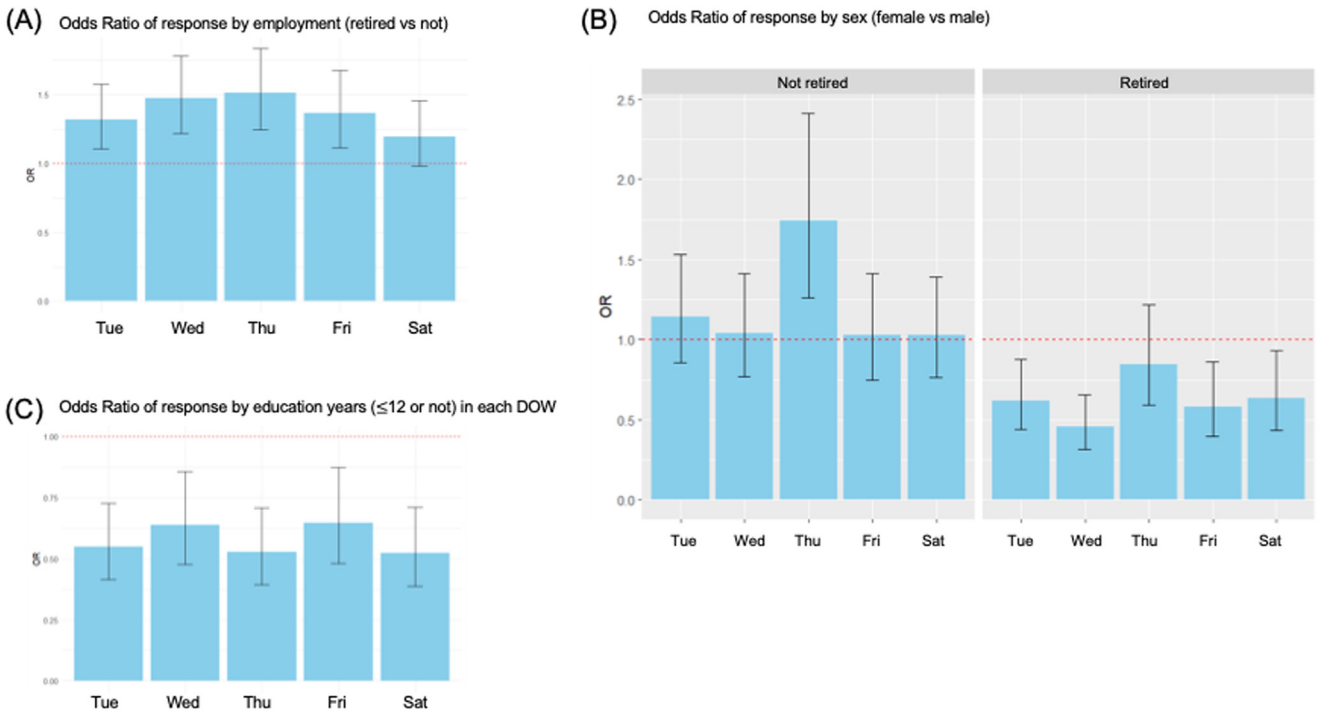

Fig. 2. Odds ratio of response by employment status and education years

Fig. 2A illustrates the response rates by employment status, showing that retired individuals are consistently more likely to respond across all DOWs compared to non-retired individuals.

Fig. 2B examines the association between sex/gender and response rates, stratified by employment status. The results reveal that among retired individuals, females were less likely to respond compared to males, whereas among non-retired individuals, females were more likely to respond than males.

Fig. 2C explores the association between education level and response rates. The results indicate that individuals with shorter education years (≤12 years) were consistently less likely to respond, regardless of the DOW.

Abbrevations: DOW, day of the week.

gage with online surveys has been supported by recent studies, including our findings. Research suggests that older adults, particularly those who have retired or have limited mobility, may be more inclined to participate in surveys due to increased time availability and familiarity with certain communication technologies. Additionally, studies indicate that clear communication and user-friendly survey platforms further encourage their engagement, as seen in the StayWELL study, which reported high adherence rates among older participants during the COVID-19 pandemic [28]. However, Mantel-Haenszel test, where response by employment status while adjusting for age group also showed significantly high OR (1.180, 95 %CI: 1.048 ~ 1.328). In addition, Mantel-Haenszel tests of response by age group while adjusting for employment status showed a significant change in response ($p < 0.001$), suggesting that the degree of response by age group is not always dependent on the employment status. The effect of older age might include respondents' self-perception about their risk of acquiring AD or dementia along with aging. Comparing RRs by the length of educational years showed that participants with a college education had significantly higher RRs compared to those with only a high school education (Fig. 2C). Higher educational levels may be associated with better understanding and greater willingness to participate in surveys. In particular, our survey consisted of 55 questions requiring 30-40 minutes to complete, being somewhat burdensome for respondents to complete the survey, which by itself may have led to survey fatigue. A similar positive association between educational level and the RR has been reported in previous research [29]. This finding suggests that using clearer, more accessible language in survey invitations and questionnaire instructions could help enhance participation among individuals with lower education years. Simplifying survey structures and providing concise, easy-to-understand explanations of survey objectives and procedures may be effective strategies to improve response rates in this demographic.

Our study includes some limitations, such as using an anonymous survey design, which prevented the blocking of potential dual responses from the same respondents as well as the linkage of respondents' identities with specific attributes. Consequently, it was not possible to perform multivariate analyses to assess the relative risk of response presence or absence in relation to certain background characteristics. This limitation makes it difficult to determine the independent effects of factors such as age, gender, employment status, and education level on response rates, as potential confounders could not be adjusted for. Future studies that incorporate participant-specific identifiers while ensuring confidentiality could enable more refined statistical adjustments and provide a more detailed understanding of response behavior. In addition, since the J-TRC web study participants are those who are interested in dementia research or treatment, the obtained knowledge from our study about the characteristics leading to eligible responses cannot always be directly applicable to surveys targeting general middle-aged or elderly populations with diverse backgrounds, for whom we need further research [30]. Our study population likely exhibited a higher level of awareness and motivation toward participation compared to the general population, potentially leading to an overestimation of response rates. Comparatively utilizing data from similar web-based registries in different cultural contexts, such as the APT Web study [31], may be helpful in investigating cross-cultural variations in survey response rates and participation engagement patterns, including whether the trends observed in this study are unique to Japan or reflect broader patterns applicable to other countries. However, no earlier studies have conducted an online survey of clinical registry participants in the context of AD treatment.

Finally, this study emphasizes that employment status, age, and education significantly influence online survey RRs in dementia-related research. To improve RRs, future surveys should optimize invitation timing and carefully consider the target population's demographic charac-

teristics. Additionally, further research should explore how these factors interact across more diverse populations to enhance the generalizability of the findings.

In conclusion, this study evaluated the impact of DOW, gender, age, employment status, and educational background on RR in online surveys among J-TRC web study participants. Employment status, age, and educational level emerged as independent factors significantly influencing RR. These findings offer valuable insights for improving survey design and distribution, potentially leading to higher RRs and enhanced data quality, particularly in research involving middle-aged and elderly populations.

Data sharing statement

The J-TRC data supporting the findings of this study may be shared upon reasonable request.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Kenichiro Sato reports financial support was provided by Japan Society for the Promotion of Science. Takeshi Iwatsubo reports financial support was provided by Japan Agency for Medical Research and Development. Yoshiki Niimi reports financial support was provided by Japan Agency for Medical Research and Development. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Saki Nakashima: Writing – original draft, Visualization, Methodology, Conceptualization. **Kenichiro Sato:** Writing – review & editing, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yoshiki Niimi:** Writing – review & editing, Project administration, Conceptualization. **Tatsushi Toda:** Writing – review & editing, Supervision. **Takeshi Iwatsubo:** Writing – review & editing, Supervision.

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Supplementary materials

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