

How does the frame of communication affect cancer patients' decisions?—from a behavioral economics point of view

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Background: It has been said that physicians should provide their patients with accurate evidence in terms of information on treatment options. However, in some cases, although the physician provides accurate and sufficient information, the patient still chooses the medically not-recommended treatment. The purpose of this research is to clarify how patients' decisions differ when a physician changes the frame of an explanation when he/she provides information about cancer treatment.

Methods: An online questionnaire survey was conducted in March 2017. Through the aid of a survey company, we emailed questionnaires to 1,360 cancer patients who received treatment within the last 2 years. We randomly assigned participants to 6 hypotheticals scenario of a terminal cancer patient, and presented hypothetical evidence in different ways. Subsequently, we asked survey participants whether they would choose to receive additional anti-cancer treatment.

Results: Although there was no statistically significant difference between scenarios, the "social burden" groups showed a lower rate of patients who preferred to continue a medically ineffective anti-cancer treatment than the control group, at a 10% significance level. The scenario significantly affected the patients' sense of abandonment [$F_{(5, 1,354)}$ =5.680, P<0.001], sense of distress [$F_{(5, 1,354)}$ =3.920, P=0.002], and necessity of improvement [$F_{(5, 1,354)}$ =2.783, P=0.017].

Conclusions: Nudges were not shown to be effective in situations where discontinuation of anticancer treatment was being considered. On the other hand, some nudges were found to be invasive and should be used with caution.

Keywords: Decision-making; nudge; medical communication; behavioral economics; online survey

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Introduction

Background

Recently, patients' autonomy has been made a priority (1), and physicians try to provide medical information as accurately and objectively as possible (2). However, in some cases, although the physician provides accurate and sufficient information, the patient still chooses the medically not-recommended treatment (3,4). In such cases, many physicians believe their explanation was insufficient

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and try to explain treatment options more accurately. This signifies miscommunication between the physician and the patient. There may be many factors that contribute to this miscommunication, one of which could be the cognitive bias of the patient (5). Of course, an accurate explanation is essential; however, the effort needed to provide accurate information is based on the belief that human beings are rational. According to a behavioral economics point of view, patients' irrational choices are often derived from their cognitive bias (6-9). It may be useful to take the patient's cognitive bias into consideration in medical communication.

In the present study, we focused on "nudge" as a way of combining medical decision-making and the theory of behavioral economics. Nudge is a concept in behavioral economics, political theory, and economics that proposes positive reinforcement and indirect suggestions to try to achieve non-forced compliance to influence the motives, incentives, and decision-making of groups and individuals (10,11). Actually, in some previous studies, the application of behavioral economics in medical settings has been reported (12-14). For example, the study that conducted a randomized controlled trial in an end-of-life care decisionmaking situation reported that 77% of those given a form with a check mark for comfort-oriented care chose comfortoriented care, while only 43% of those given a form with a check mark for life-extending care chose it, indicating the effectiveness of setting a default option (15). Another study reported that sending messages emphasizing cost could

Highlight box

Key findings

- Explaining the "social burden" may reduce the proportion of patients who make medically unrecommended choices, but no statistically significant results were obtained.
- In terms of patients' evaluation, the explanation of "social burden" might be avoided.

What is known and what is new?

- Several studies on medical situations have shown the effectiveness of nudges.
- A thought experiment on a situation in which a patient is considering discontinuing anticancer treatment did not show any effect of nudges.

What is the implication, and what should change now?

- Nudges were not shown to be effective in situations where discontinuation of anticancer treatment was being considered.
- On the other hand, some nudges were found to be invasive and should be used with caution.

reduce the rate of missed hospital appointments (16). Thus, it has been noted that changing the way the message is presented may change the patient's behavior.

Objective

We then planned to explore how to best use nudge in medical communication. The purpose of this research is to clarify how a physician's explanation about cancer treatment using nudge affects (I) patient choice and (II) patient evaluation of the explanation. Though the most powerful nudge would be to set a default, this survey was an experimental method using the Internet, we decided to compare different ways of focusing on the same situation by changing the expressions in the texts presented. We present this article in accordance with the SURGE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-464/rc).

Methods

Subjects and procedures

A cross-sectional survey was conducted with cancer patients who met the following inclusion criteria: (I) diagnosed with cancer within 2 years; (II) under anti-cancer treatment or during follow-up; (III) age 20 to 74 years; (IV) be at ease with Internet usage. Responses were considered as consent to participate.

In as much this study aimed to explore patients' preferences in terms of choice of treatment within a wider range or region, a web-based survey was selected as an appropriate research method. The web-based survey company was selected based on published monitoring data, such as tracking demographic information and the frequency of information updates. The research targets, that is, cancer patients who meet the inclusion criteria, were recruited from monitors for screening purposes. The purpose of the research and ethical considerations was explained, and through the survey website, the patients were requested to participate in the research. Responses to the questionnaire were voluntary, and confidentiality was maintained throughout the investigations and analyses. No identification numbers were corrected. The questionnaire was administered via website. After participating in the survey, the participants received payment from the Internet research company.

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was

approved from review by the Institutional Review Board (IRB) based on the IRB policy of Kawauchi South Campus, Tohoku University (approval No. 2016-003). Consent was considered to have been obtained upon submission of the response.

Measurements

Demographic data

The investigated patients' characteristics included sex and age. The patients' disease conditions included the site of cancer, clinical stage, duration since diagnosis, anti-cancer treatment (surgery, chemotherapy, hormonal therapy, and radiation therapy) relapse, metastasis, and current treatment status.

Preference for treatment based on the hypothetical scenario

We used an experimental setting with a hypothetical scenario. An original scenario was developed for our survey as there were no previous studies that used such a scenario. To create the scenario, first, four researchers discussed the draft scenario from psychological and economical points of view. The scenario presented that the anti-cancer treatment no longer had any effect on the patient's cancer, and that there is only one anti-cancer treatment (treatment A) without effective evidence. This means the medically recommended choice was to end anti-cancer treatment. We created six different scenarios. The first scenario maintained a neutral explanation and was identified as the control scenario. The other five scenarios were made to explore the effect of a nudge. In each scenario, the physician explained treatment A and its possible side effects. Subsequently, the physician incorporated one nudge to recommend ending anti-cancer treatment. We assessed five different nudges as follows: direct recommendation, presentation of norm, presentation of benefit for the patient, presentation of benefit for the family members, and presentation of social burden. We named each scenario as follows: (I) control, (II) direct suggestion, (III) norm, (IV) benefit for the patient, (V) benefit for the family members, and (VI) social burden. Direct suggestion was the scenario similar to default setting. Norm, benefit for the patient and benefit for the family members were scenarios using the nudge to emphasize benefit. And social burden was the scenario using the nudge to emphasize loss. After creating the draft scenario, we asked three oncologists to review the original scenario to ensure its clinical validity and to make any changes that they

deemed necessary. The final scenarios are shown in Table 1.

We randomly assigned the participants to six different scenarios, and then asked them: "If you were told the above by your primary physician, what would you do?" Response options were as follows: (I) I prefer to receive treatment A, (II) I do not prefer to receive treatment A.

Patients' evaluation of the explanation

To assess the patients' evaluation after reading the hypothetical scenario, we asked the following four questions: "Did you feel like you were abandoned by the physician?" (Sense of abandonment); "Did you feel like you can rely on the physician?" (Sense of reliability); "Did you feel distressed?" (Sense of distress); and "Do you think the explanation has to be improved?" (Necessity of improvement). The response options were (I) not at all, (II) not quite, (III) yes and no, (IV) a little, and (V) very much.

Statistical analysis

To explore the potential influence of the various scenarios on the treatment preference, a chi-squared test was performed. We compared the rate of the participants who answered that they prefer to receive treatment A between the control scenario and the other five scenarios with nudges. Subsequently, we performed one-way analysis of variance to compare the evaluation scores between the six scenarios.

For all statistical evaluations, P values of 0.05 or lower were considered significant, and 0.10 or lower were considered as marginally significant, given the exploratory nature of the study. All analyses were performed using SPSS Statistics 21.0 (IBM Corp., Armonk, NY, USA).

Results

Participants' characteristics

Web-based questionnaires were sent to patients who fulfilled the inclusion criteria. A total of 1,360 patients were recruited, and all were included for data analysis. Patient characteristics are summarized in *Table 2*.

Preference for treatment based on the bypothetical scenario

Table 3 presents the rate of the patients who answered that they prefer to receive treatment. A total of 259 (19.0%) patients preferred to continue the anti-cancer treatment, that is, to go against the medically recommended choice.

The scenarios	Wordings
(I) Comparison	I recommend no additional anti-cancer treatment options for you. However, if you insist on additional treatment, there is one option. However, there is no evidence that the treatment will be effective for you. Furthermore, it is likely that there will be side effects
(II) Direct suggestion	There is one treatment that you can undergo using your health insurance. However, there is no evidence that it will be effective for you. Furthermore, it is likely that there will be side effects. <i>Unfortunately, considering the situation, I think that the best choice for you is to discontinue treatment</i>
(III) Presentation of norm	There is one treatment that you can undergo using your health insurance. However, there is no evidence that it will be effective for you. Furthermore, it is likely that there will be side effects. <i>In a similar situation, most patients choose to discontinue treatment</i>
(IV) Presentation of benefit for the patient	There is one treatment that you can undergo using your health insurance. However, there is no evidence that it will be effective for you. Furthermore, it is likely that there will be side effects. <i>If you choose to discontinue treatment, you will be free from side effects and be able to stay at home or go out</i>
(V) Presentation of benefit for the family members	There is one treatment that you can undergo using your health insurance. However, there is no evidence that it will be effective for you. Furthermore, it is likely that there will be side effects. <i>If you choose to discontinue treatment, you will be free from side effects and be able to stay at home or go out. In addition, your family members will be able to spend good time</i>
(VI) Presentation of social burden	There is one treatment that you can undergo using your health insurance. However, there is no evidence that it will be effective for you. Furthermore, it is likely that there will be side effects. <i>If you choose to undergo the treatment, it will cost 10 million Yen to social insurance premiums</i>

Table 1 Hypothetical scenarios used in the survey

Common part: you have received anti-cancer treatment for several years. However, there are no more effective treatment options that can cure you or extend your life. Currently, your physical symptoms are well controlled and you can stay at home. Your physician said, "*The result of the exam showed that your cancer has progressed. Even if you continue the current treatment, it is no longer expected to have a positive effect, and there are no more effective treatments available for you.*" In addition to the sentences shown in the "common part", the participants were presented with one of the scenarios I–VI.

Although there was no statistically significant difference between the scenarios, "social burden" groups (χ^2 =2.966, P=0.085) showed lower rates of patients who preferred to continue the medically ineffective anti-cancer treatment than the control group, at a 10% significance level.

Patients' evaluation of the explanation

Table 4 presents the patients' evaluation of the explanation. The scenario significantly affected the patients' sense of abandonment [$F_{(5, 1,354)}$ =5.680, P<0.001], sense of distress [$F_{(5, 1,354)}$ =3.920, P=0.002], and necessity of improvement [$F_{(5, 1,354)}$ =2.783, P=0.017]. The results of the multiple comparison, the scenario control, "direct suggestion", and "social burden" have had a negative impact on the patients' evaluation. From the result of the multiple comparison using the Tukey test, the "benefit for the patient" and "benefit for the family members" groups showed a lower sense of abandonment than the control and "social burden"

groups. The "benefit for the family members" group also showed a lower sense of abandonment than the "direct suggestion" group. Likewise, the "benefit for the patient" and "benefit for the family members" groups showed a lower sense of distress than the control group. The "benefit for the family members" group also showed a lower sense of distress than the "direct suggestion" group. Additionally, the "benefit for the family members" group showed a lower necessity of improvement than the "social burden" group.

Discussion

This study is one of the few to investigate the effect of nudge on cancer patients' choice within a medical setting. There have been many studies on patients' decisionmaking and medical communication. Most researches were conducted based on the belief that "if physicians provide accurate explanations and show sufficient evidence, patients can choose the medically appropriate treatment." However,

Table 2 Background of participants

Variables	Values		
Demographic information			
Sex (male), n (%)	707 (52.0)		
Age (years), mean \pm standard deviation	57.2±10.4		
Marital status, n (%)			
Married	1,023 (75.2)		
Single or divorced/widowed	337 (24.8)		
Education, n (%)			
High school/college	718 (52.8)		
University/graduate school	570 (41.9)		
Employment status, n (%)			
Employed	583 (42.9)		
Unemployed	590 (43.4)		
Disease information			
Cancer site, n (%)			
Breast	340 (25.0)		
Urinary organs	196 (14.4)		
Colon and rectum	193 (14.2)		
Esophagus and stomach	138 (10.1)		
Head and neck	103 (7.6)		
Uterus and ovary	94 (6.9)		
Leukemia and lymphoma	67 (4.9)		
Lung	52 (3.8)		
Liver and pancreas	42 (3.1)		
Others	135 (9.9)		
Clinical stage, n (%)			
0	195 (14.3)		
1	403 (29.6)		
2	248 (18.2)		
3	170 (12.5)		
4	108 (7.9)		
Unknown	236 (17.4)		
Time since diagnosis (years), mean \pm SD	5±5.6		
Relapse (+), n (%)	228 (16.8)		
Metastasis (+), n (%)	194 (14.3)		
Chemotherapy (+), n (%)	529 (38.9)		
Surgery (+), n (%)	1,131 (83.2)		
Radio therapy (+), n (%)	384 (28.2)		
Hormonal therapy (+), n (%)	368 (27.1)		

Table 2 (continued)

 Table 2 (continued)

Variables	Values		
Current status, n (%)			
Inpatient treatment	12 (0.9)		
Outpatient treatment	356 (26.2)		
Follow-up	850 (62.5)		
No more treatment	128 (9.4)		
Others	14 (1.0)		

in behavioral economic studies, it is presumed that people may not necessarily make rational choices (6-9). This study aimed to bring such behavioral economics insights into a medical setting.

The most important finding was that there was no statistically significant difference between scenarios at a 5% significance level. There are some possible reasons for the lack of effect of the nudge used in the scenario experiment. First, this survey was an experimental survey using a hypothetical scenario, and the physician's explanation using nudges was neither realistic nor clear for the subjects. Second, the content of the message may have been complex, and it may have been difficult for the subject to fully understand the message from the text alone. Most of the previous studies examining the effects of nudges have focused on behaviors with relatively simple gains and losses (16,17), but the choice of anticancer treatment at the end of life, for which there is little medical evidence, may have resulted in very complex and uncertain gains and losses. In addition, none of the information used in our scenario (e.g., the "stay at home" as a benefit of not receiving treatment) can be expressed numerically. These characteristics of the situation may have prevented the nudges from being effective. We need to further investigate whether there is room for improvement in the use of nudges and the experimental setting, or whether nudges themselves are ineffective in selecting anticancer therapy at the end of life.

In addition, the effect of nudges using sentences is smaller than other nudges such as default settings, and the current sample size may not have been sufficient to obtain sufficient power. In fact, the effect sizes of the scenarios used in this study ranged from 0.02 to 0.15. As a result of post-hoc calculation, the power for the scenarios other than "social burden" were evaluated as small. Therefore, we provide supplementary discussion on the scenarios that showed significant differences at the 10% level.

Scenario	Ν	%	χ^2	Р			
(I) Control (n=227)	49	21.6	-	-			
(II) Direct suggestion (n=226)	41	18.1	0.866	0.352			
(III) Presentation of norm (n=239)	48	20.1	0.271	0.603			
(IV) Presentation of benefit for the patient (n=219)	36	16.4	2.683	0.101			
(V) Presentation of benefit for the family members (n=227)	51	22.5	0.002	0.960			
(VI) Presentation of social burden (n=222)	34	15.3	2.966	0.085*			

Table 3 Participants who did not prefer the medically recommended choice

*, P<0.10.

The "social burden" group exhibited lower rate of patients who preferred to continue undergoing the medically ineffective anti-cancer treatment than the control group, at a 10% significance level. This result can be interpreted by two behavioral economics concepts: selfish or altruistic motivation (18), and social norms (19).

In behavioral economics, there are two types of motivations: selfish and altruism (18). Selfish individuals maximize their utility by considering their own benefits and costs. For these people, if we intend to recommend one choice, in the present case of ending anti-cancer treatment, it may be useful to emphasize how much benefit the patient can gain from the choice. When it comes to the end stage in cancer patients, the concept of good death in Japan includes some benefits for the patients such as being free from pain and physical distress, being able to stay at one's favorite place, having some pleasure in daily life, and spending enough time with one's family (20). Concurrently, "not being a burden to others" is one of the 10 core domains of the Japanese cancer patients' good death (20). The "social burden" scenario referred to the economic burden on society of receiving treatment A, and this means that withholding the anti-cancer treatment can reduce the "burden to others". This message can be an individual benefit for the persons who are hostile toward "being a burden to others" itself, and works as a selfish motivation to withhold treatment A. As seen above, we can explain the effect of the "social burden" scenario.

On the other hand, altruistic individuals maximize their utility by considering both of their own and others' benefits and costs (18). For these people, the "social burden" scenario also could work to promote withholding treatment A, even though their life might be shortened. This is because reducing social burden is an altruistic decision for society. Concurrently, "social norms" can also explain the effect of the "social burden" scenario. Social norms refer to the standard of behaviors based on common beliefs accepted by groups or societies about how people should behave in a given situation, such as justice, fairness or cooperation (19). In Japan, there is a public, social insurance system that provides universal health insurance coverage. Recently, the aging of the population and the sophistication in medical care have led to a large increase in health-care costs (21). Considering this Japanese situation, to withhold a medically ineffective treatment might be regarded as consistent with social norms, and may have made the participants decide to withhold treatment A.

Contrary to our expectations, significant impact of the "benefit for the patient" was not observed. Considering the aforementioned selfish motivation, the "benefit for the patient" scenario was expected to result in a lower rate for treatment A, since it included the components of the good death, such as being able to stay at one's favorite place, and having some pleasure in daily life (20). However, unlike the "social burden" scenario, no such result was obtained. One possible reason for this is that the scenarios presented as examples of staying at home or going out did not necessarily work as a gain for the subjects. This is because "favorite place" may be home for some patient and be hospital for others. In actual clinical situations, this approach may work because patient characteristics are taken into account and benefits are explained accordingly, but this point requires further study. Supplementally, the "benefit for the family members" scenario did not work in this survey. As the Japanese population tend to emphasize the relationship with family members rather than autonomy (22,23), we expected the "benefit for the family members" to be effective for withholding treatment A. However, this hypothesis was not supported. There are some possible reasons. First, the "benefit for the family members" scenario included

Table 4 Evaluation for the explanation

<u> </u>	Average	Standard deviation	95% confidence interval			Multiple
Scenario			Lower	Upper	Р	comparisons
Sense of abandoned					<0.001	I, VI > IV, V
(I) Control	3.08	1.28	2.91	3.25		11 > V
(II) Direct suggestion	3.00	1.21	2.85	3.16		
(III) Presentation of norm	2.89	1.10	2.75	3.03		
(IV) Presentation of benefit for the patient	2.74	1.15	2.59	2.89		
(V) Presentation of benefit for the family members	2.63	1.05	2.49	2.77		
(VI) Presentation of social burden	3.08	1.22	2.92	3.24		
Sense of reliability					0.162	
(I) Control	3.42	1.06	3.28	3.56		
(II) Direct suggestion	3.34	1.08	3.20	3.48		
(III) Presentation of norm	3.39	1.00	3.26	3.52		
(IV) Presentation of benefit for the patient	3.26	1.09	3.12	3.41		
(V) Presentation of benefit for the family members	3.47	1.04	3.33	3.60		
(VI) Presentation of social burden	3.24	1.07	3.10	3.38		
Sense of distress					0.002	I > IV, V;
(I) Control	3.96	1.15	3.81	4.11		11 > V
(II) Direct suggestion	3.87	1.14	3.72	4.02		
(III) Presentation of norm	3.80	1.21	3.65	3.95		
(IV) Presentation of benefit for the patient	3.64	1.19	3.48	3.80		
(V) Presentation of benefit for the family members	3.55	1.16	3.40	3.70		
(VI) Presentation of social burden	3.85	1.20	3.69	4.01		
Necessity for the improvement					0.017	VI > V
(I) Control	3.19	1.09	3.05	3.34		
(II) Direct suggestion	3.19	1.05	3.05	3.32		
(III) Presentation of norm	3.17	1.08	3.03	3.30		
(IV) Presentation of benefit for the patient	3.01	1.02	2.87	3.15		
(V) Presentation of benefit for the family members	2.96	0.91	2.84	3.08		
(VI) Presentation of social burden	3.26	1.17	3.11	3.42		

Analysis of variance was performed with scenarios as independent variables. When significant differences were found between groups, multiple comparisons were conducted by Tukey. The numbers written in the "multiple comparisons" column mean scenario numbers.

messages from two perspectives, the patients themselves and their family members. This framework is more complex. Second, the explanation of this scenario was longer than that of the other scenarios. Excluding the "benefit for the family members", the messages in which the concept of nudge was applied consisted of just one sentence and 35–65 Japanese characters; this amounts to approximately one line. On the contrary, the "benefit for the family members" scenario included two sentences, 110 characters. One of the principles for using a nudge is to make it easy, and simplifying messages is recommended (24). The complexity and length of the message might have reduced the effect of the "benefit for the family members" scenario. However, we cannot prove this discussion with the present data, and we need to conduct further investigation on this point.

Our second most important finding was that the method of explanation could affect the patients' evaluation. The explanation of benefit for the patient and others showed a lower score in the sense of abandonment, sense of distress, and necessity for improvement. On the other hand, a neutral explanation (control group) and direct suggestion showed higher scores in the senses of abandonment and distress. The explanation of "social burden" also showed higher scores in abandonment and necessity for improvement. Previous studies that explored patients' preferences in terms of medical communication pointed out that communication that supports the patients' hopes and shows compassion was preferable (22,23). It is also noted that many patients do not prefer a declaratory explanation (25). A direct suggestion may be considered as a declarative explanation, and to emphasize the social burden may imply lack of compassion for patients' emotions. Our primary result showed that the explanation of "social burden" might reduce the rate of patients who choose the medically notrecommended choice. However, in terms of the patients' evaluation, the explanation of "social burden" might be avoided. A similar finding has been observed in a previous study that discussed the nudging of families to give consent for organ donation (11). It is pointed out that when we measure the effect of the framing of explanation, we should assess it by multiple aspects including clinical, economic, patient-reported, and surrogate-reported outcomes (12). Our result showed that an "effective" frame was different between clinical and patient-reported outcomes. This result indicates that ethical considerations should be focused on when bringing cognitive bias into medical communication.

Limitations

However, this study has several limitations. First, the survey was web-based, and the cancer patients are self-enumerated. Early in the project, we had planned to conduct a paper questionnaire survey. However, there are few studies that have explored the effect of a nudge on medical decisionmaking, and we did not have enough reason to perform the survey with cancer patients in a hospital setting. Due to lack of previous surveys, we could not focus on a specific nudge as the experimental scenario. Thus, we created six different scenarios, and made it necessary to include many patients in order to test the effect of nudging. We selected an online survey as our preliminary tool. Therefore, the participants had various disease conditions and we can't verify whether the participants met the eligibility criteria. In addition, although the scenario used in the survey was related to the terminal stage of cancer, most of the subjects were patients who were not in the terminal stage of cancer, so there was no sense of reality, and their responses may have been far from realistic. Consequently, caution needed to be applied in the discussion of the result. Second, due to the lack of relevant scenarios in previous studies, hypothetical scenarios were created as original works. We discussed the scenarios with professionals in various specialties. However, we discovered the scenarios might not be able to reflect both the medical reality and the theory of behavioral economics. Concurrently, the scenarios were short, and it might have been difficult for patients to imagine the situation. In actual medical settings, many physicians combine nudges, and some scenarios were considered to be unnatural. Third, we extracted statistically significant differences between scenarios regarding patients' evaluation. However, no statistical significance was extracted in terms of the participants' choices. Consequently, a cautious approach should be applied in the discussion of the effect of nudges. In the next step, we are planning to perform experimental surveys using videos. Our survey showed that some nudges can affect patients' choices, and this result must be taken into consideration when producing the videos.

Conclusions

Nudges were not shown to be effective in situations where discontinuation of anticancer treatment was being considered. On the other hand, some nudges were found to be invasive and should be used with caution.

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Footnote

Reporting Checklist: The authors have completed the SURGE reporting checklist. Available at https://apm. amegroups.com/article/view/10.21037/apm-23-464/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board (IRB) based on the IRB policy of Kawauchi South Campus, Tohoku University (approval No. 2016-003). The Participants' consent was obtained upon submission of the response.

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