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Rainbow of KIBOU project: Effectiveness of invitation materials for improving cancer screening rate using social marketing and behavioral economics approaches

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ABSTRACT

Studies to date have shown that individual invitation (call) and re-invitation (recall) are effective in improving cancer screening rate. Also, by dividing subjects into segments and sending unique messages to each segment, the cancer screening rate is further improved. However, this approach is not realistic in the local governments due to limited resources, so we used social marketing and nudge techniques to develop cancer screening recommendation materials that do not need to send separately. This study therefore aimed to verify the effect of these materials in the real world. We compared the cancer screening rates in municipalities within Japan that used the invitation materials we developed (colorectal, breast, lung, cervical and stomach cancer), with those from the previous year. In addition, the usefulness of the materials in the real world was examined multilaterally using RE-AIM framework (Reach, Effectiveness, Adaption, Implementation, Maintenance). From 2015 to 2018, 4.3 million residents (Reach) from 787 municipalities (Adaption) were sent invitation materials for cancer screening. Of 167 municipalities that were compared, 141 (83%) showed an increase in screening rate when our materials were used. Overall, the screening rate improved by 2.6% or 1.44 fold (p < 0.001) (Effectiveness). However, the screening rate varied greatly depending on how screening is provided. Of the four years studied, 75 municipalities used the same materials for two or more years (Implementation). The material developed in this study improved the cancer screening rate in the real world, and it may be possible to further improve the screening rate if the number of opportunities for screening and its capacity is increased at the timing of sending materials. The materials can be found on the website (http://rokproject.jp/kenshin/) and free electronic files are available to municipalities wishing to use them.

1. Introduction

According to the 2016 National Survey of Living Conditions, the cancer screening rate for people aged 40 or older in Japan ranges from 28% to 48% for the five cancers recommended by the government (colorectal, breast, lung, cervical, and stomach cancer). This rate is below the current goal of 50% in the Third Basic Plan to Promote Cancer Control Programs (MHLW, 2018). The results are lower than those in other countries (OECD, 2018), and it is desirable to achieve higher rates.

The evidence reviewed by the Community Preventive Service Task Force (2021) indicates that client reminders are effective in improving cancer screening rates. In Japan, local governments are responsible for providing cancer screening as health insurers under the Health Promotion Law. In order to improve the rate of cancer screening, the national government recommends individual reminders, by sending (call) and re-sending (recall) print materials individually. However, at present, only 38%–54% of local governments across the country are re-sending reminder to those who have not currently undergone cancer screening although calls are done for more than 80% of the local governments (Cancer Information Service, 2021).

In addition, the effects of call-recall vary greatly depending on the message. There is evidence that tailored messages can help improve

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cancer screening rates (Lauver et al., 2003; Saywell et al., 2004; Sohl et al., 2007; Albada et al., 2009; Ishikawa et al., 2012; Hirai et al., 2016; Lipkus et al., 2019; Huf et al., 2020; Misawa et al., 2020). Ishikawa et al. conducted a randomized controlled trial (RCT) to compare breast cancer screening rate with tailored recommendations versus universal recommendations to the Japanese population. In the tailored message group, the subjects were divided into three segments according to the level of their cancer concern and intention to prepare for cancer screening such as low cancer worry/low screening intention, high cancer worry/low screening intention, and social marketing techniques were used to develop effective messages for each group (Ajzen, 1985; Hay et al., 2005; Harada et al., 2013). The results showed that in all three segments, the group to which the tailored recommendation was sent had a significantly higher screening rate than the group to which the universal recommendation was sent.

However, when sending invitation letters for cancer screening, it is difficult for local municipalities to send different materials to different population segments. In order to send segment-by-segment invitations, it is necessary to conduct a questionnaire survey in advance to allocate each individual to each segment, print materials for each segment, and send tailored messages to each segment. When we first started providing support to local governments, we proposed to send leaflets with three types of messages, which were prepared separately for each segment. However, there were almost no requests from local governments for the use of these leaflets, and the overwhelming opinion was that it was impossible for local government staff to use these leaflets due to lack of resources, including time and cost. In addition, because a pre-survey response is required for segmentation, only a limited number of persons can be invited to cancer screening if the pre-survey response rate is low. For behavioral change interventions, if they are difficult to implement in the real world, they cannot serve as a widespread awarenessraising tool (Brownson et al., 2018; Neta et al., 2018). Not only the efficacy in the experimental field, but also the effectiveness in the actual field is important.

Therefore, we developed a single integrated leaflet for breast cancer that does not need to be sent separately by segment but does simultaneously include a tailored message to each segment. In addition to messages developed for each segment based on the findings of Ishikawa et al. this material contains messages that may be more effective using behavioral science methods such as the Health Belief Model (Rosenstock, 1974) and behavioral economics methods, such as nudges (Thaler and Sunstein, 2008; Institute for Government, 2010; Kawachi, 2014; Halpern, 2015). Health Belief Model has been proven to be useful to increase screening rates by meta-analysis and systematic review for breast cancer (Sohl and Moyer, 2007; Saei Ghare Naz et al., 2018b), for colorectal cancer (Lau et al., 2020), and cervical cancer (Saei Ghare Naz et al.,). Nudge are used to modify the social and physical environment to enhance capacity for subconscious behaviors that align with the intrinsic values of an individual, without actively restricting options. Examples of nudges used to improve the cancer screening rate include making cancer screening a default option and using the tendency of people to avoid losing money. This is a relatively new concept, but a number of studies on screening behavior have been conducted, some of which have reported significant findings (Gupta et al., 2016; Schwartz et al., 2017; Aasbø et al., 2019; Fukuma et al., 2019; Stoffel et al., 2019; Huf et al., 2020; Gong et al., 2020; Misawa et al., 2020; Fukuyoshi et al., 2021). Using the same method, we developed screening invitation materials that do not need to be divided into segments, for the screening of other cancers such as colorectum, lung, cervix and stomach. We have introduced these materials to more than 1700 municipalities throughout Japan via 47 prefectural governments, providing the design of the materials to those who wish to use them, and inviting residents throughout the country to undergo cancer screening.

In the real world, evaluation should be multifaceted, reflecting varied use and difficulty in assessments. As endpoints of usefulness, it is important to examine not only effectiveness, but also how they were widely used and how many persons were impacted. The purpose of this study was therefore to evaluate the usefulness of the materials developed, in the real world, which were designed using behavioral science and behavioral economics methods to be more widely used and more effective.

2. Methods

2.1. Development of cancer screening invitation materials

Target cancer screenings included a fecal occult blood test for colorectal cancer, mammography for breast cancer, chest x-ray for lung cancer, cytology for cervical cancer, and barium x-ray and endoscopy for stomach cancer as recommended by the national guideline in Japan (MHLW, 2016) (Table 1).

Individual and focus group interviews were repeated with individuals who had not yet undergone any cancer screening to confirm the insights for the three segments defined by cancer worry and screening intention for cancer types such as colorectal, breast, cervical and stomach cancer. As for lung cancer, different segmentation and insights were found. Based on each insight, we developed messages that should be conveyed for behavioral change using social marketing methods, and included them in a single document (Table 2) (McKenzie and Smeltzer, 2000; Gordon et al., 2006; Weinreich, 2010; The NSMC, 2011; Thorgeirsson and Kawachi, 2013; Roberto and Kawachi, 2014; Lee and Kotler, 2016). The messages were also developed based on the Health Belief Model (Rosenstock, 1974; Saei Ghare Naz et al., 2018a, b; Lau et al., 2020). Among the constructs of the Health Belief Model, as a message to raise perceived susceptibility, we conveyed high morbidity and high mortality rates of each type of cancer, and also conveyed the possibility of having cancer even if there are no symptoms. As perceived severity and perceived benefit, we conveyed the message that the probability of a cure for advanced cancer is low, but the probability of a cure is high if it is detected early through cancer screening. In addition, as a perceived benefit, we conveyed the message that although the price of cancer screening is high, it can be very cheap (or free) with a subsidy. As for cervical cancer and breast cancer screening, a female doctor can be reserved at the time of appointment. In particular, with regard to costs, the benefits were emphasized by clearly stating the price including the price of subsidies received (Table 3). As for the cues to action, specific instructions were shown (easy-to-understand, specific steps to take to undergo cancer screening). Using behavioral economics methods such as nudge, we developed messages that incorporate nudge constructs such as incentives and attractive, timeliness, norms/social, and messenger (Table 3) (Institute for Government, 2010; Ploug et al., 2012; Voyer, 2015; The BIT, 2014; Purnell et al., 2015; Stoffel et al., 2019; Misawa et al., 2020; Huf et al., 2020; Fukuyoshi et al., 2021).

Using these methods, we developed a leaflet and a pressure-printed postcard for call and/or recall invitation to cancer screening for each of the five cancer types: colorectal, breast, lung, cervical, and stomach cancer. In response to national guidelines, two types of materials for stomach cancer were developed, one recommended yearly endoscopic and X-ray screenings and the other recommended every two years. As a result, a total of 21 kinds of materials were developed using the same method, including invitation materials for all five cancers (five-cancer leaflet), three envelopes for sending leaflets, and a leaflet invitation for a combination of three (colorectal, lung, and stomach cancer) screenings (set flyer) (https://rokproject.jp/kenshin/).

2.2. Study design to evaluate effectiveness of the invitation materials

A total of 787 municipalities used our materials in fiscal years 2015, 2016, 2017, and 2018. They decided for themselves what type of materials they would use (cancer type, leaflet or card type, one or several, etc.), how to use the materials (to call or recall) and to whom they would be sent (whole population, specific age group, specific sex, those without

Table 1

Recommended screening by the Ministry of Health, Labour and Welfare of Japan.

Cancer site	Crude Incidence rate ^{*1}	Crude Mortality rate ^{*1}	Screening method	Subjects	Interval
Colorectal Cancer	120.9	41.6	Interview and fecal occult blood test	40 years or older* ²	Every year
Breast Cancer	72.8	23.4	Interview and breast X-ray examination (mammography) *3	40 years or older ^{*2}	Every two years
Lung Cancer	98.3	60.9	Question (interview), chest X-ray examination and sputum cytology	40 years or older* ²	Every year
Cervical Cancer	16.9	4.6	Interview, inspection, cervical cytology and pelvic examination	20 years or older ^{*2}	Every two years
Stomach	102.2	34.7	In addition to the interview, either stomach X-ray examination or endoscopy	50 years and over* ² * ⁴	Every two years* ⁵

*1 Rates are expressed as 100,000 person-year.

*2 There is no upper limit for age.

*3 Inspection and palpation are not recommended.

*4 For the time being, stomach X-ray examination can be performed for people aged 40 years or older.

*5 For the time being, stomach X-ray examination can be conducted annually.

Table 2

Insights about not undergoing cancer screening and effective messaging to encourage screening participation.

Cancer Segment Insight Messages to be sent Colorectum Indifferent Loss-Framed Message: I will never get Breast (Low cancer cancer "1 in 10 people get breast Cervix worry/low cancer "Mortality rate is 40% if Stomach screening intention) not detected early Interested (High I'm afraid of Gain-framed message: cancer worry/ finding cancer. "Detecting cancer early can lead to a higher low screening intention) chance of cure' Intended How do I get Clear information about where/when/how they (High screening cancer intention) screening? can receive screening Smoker I'm tired of Communicating the Lung listening to effectiveness of Screening "tobacco = lung without mentioning cancer' "tobacco" I know smoking is bad, but I don't want to be blamed. Non-smoker "Lung cancer = "Non-smokers can get tobacco' lung cancer.' It has nothing to do with nonsmokers

past screening history, etc.) based on their interest and available resources. In order to evaluate effectiveness of the materials, the annual screening rate of these municipalities were compared with the rate up to the previous year of the same municipalities as a historical control for each cancer type for which the materials were sent. The screening rate of the persons who actually received the materials was compared with the screening rate of the controls. Since screening was done as a municipalities' health practice rather than research, additional data was not available for the study and possible confounding could not be adequately adjusted. However, in order to reduce confounding as much as possible, data from a control group was collected from the same sex and age group for one of the past three years in the same municipalities. Therefore, these historical controls consist of almost the same subjects (one year younger or at most three year younger themselves) as those to whom the materials were sent. Even for the municipalities which did not have control data for the same sex and age group in the past three years, we collected data for similar age groups during these 3 years as controls for exploratory analysis (incomplete control).

Table 3

Examples of insights and messages based on behavioral economics and nudge
concepts based on MINDSPACE ^a and EAST ^b framework.

Nudge concept	Insight	Messages
Incentives ^a / Attractive ^b	"If you miss this timing, you can't get a discount." Emphasizing that "Actually, expensive screening is cheaper with subsidies."	You can get a subsidy "this year"! Instead of stating only "You can take the screening for 'Free' or '500 yen", stating "The examination fee is 10,000 yen, and the municipality provides a subsidy of 9500 yen, so that you can only pay 500 yen ^C ."
Timely ^b	Use the turning point of 40 years old to promote behavior change. Deadline is close.	"Get Breast Cancer Screening When You Are Over 40!" "Please make an appointment as soon as possible."
Norms ^a / Social ^b	Imply everyone's getting it.	"It gets very crowded every year when the deadline approaches."
Messenger ^a	The information provider is an official entity.	"This leaflet was created by the National Cancer Center."

^a Institute for Government (2010).

^b The Behavioural Insights Team (2014).

^c Prices are hypothetical examples.

2.3. Data collection and survey measures

Regarding the invitation materials, data on cancer type, materials used, purpose of the materials (call or recall), attributes of the recipients and control group (year, age, past screening participation history, etc.), and the frequency and timing of cancer screening provided, were collected.

Regarding screening rate, we collected data on the number of persons to whom materials were sent and the number of persons undergoing cancer screening for each recipient and control group.

2.4. Endpoints

As a primary endpoint, we compared the cancer screening rate after sending the invitation materials and the cancer screening rate of the same age group up to the previous year. That is, if the invitation material is used as the first call, the annual screening rate is used, whereas if it is used as a recall, the screening rate after recall is used as the endpoint. For comparison, the difference and ratio of screening rates are then calculated and a 2-sided χ^2 test conducted with an alpha of 5%. As a subgroup analysis, screening rates were also compared for each year and each cancer type. In addition, subgroup analyses were also conducted by calls and recalls and the number of invitations. In the control group, calls or recalls were (1) conducted also using our materials, (2) conducted using materials developed by the municipality, or (3) not conducted.

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Only the case of (2) and (3) were used as controls for comparison since the effect cannot be evaluated in the case of (1).

As a secondary endpoint, the usefulness of the invitation materials in the real world was examined in a multifaceted manner using the RE-AIM framework of Dissemination & Implementation research (King et al., 2010; Brownson et al., 2018).

Reach: Number of persons who received the invitation material developed in this research

Effectiveness: Cancer screening rate (same as the primary endpoint) Adoption: Number of municipalities using invitation materials developed in this research

Implementation: Percentage of municipalities that used materials as originally intended

Maintenance: Number of municipalities that continuously used material for 2 years or more

The original intention in the evaluation of the implementation is defined by the thickness of the paper, the size, and the presence/absence of changes other than the permitted parts.

2.5. Ethical consideration

This study was approved by the Research Ethics Committee of the National Cancer Center. This study only used existing aggregated data obtained in the health services, and personal information was not used. Therefore, it corresponds to research that does not require informed consent according to the Japanese research ethics guideline "Ethical Guidelines for Medical and Health Research Involving Human Subjects".

3. Results

The number of local municipalities evaluated for each year is shown in Table 4. Overall, our cancer screening invitation materials were sent to 4.3 million residents in a total of 787 municipalities between 2015 and 2018. The number of materials used was highest for breast cancer and cervical cancer, and slightly lower for stomach cancer and lung cancer. Although the number of municipalities for which comparative data were available varied, there was no year-to-year trend in the number of municipalities using the materials and the number of materials sent. It was also seen that not only invitation materials for each of the five types of cancer, but also materials for the five-cancer leaflet and the set flyer are often used. In many cases, the five-cancer leaflet or set flyer was used as calls and materials for each cancer type was used as recalls, which was our recommended usage. However, many local municipalities only used the five-cancer leaflet as a call, without combining material for each cancer type as a recall.

The results of the screening rate are shown in Table 5. Of the 167 municipalities where a comparison could be done with the same age group in the previous 1–3 years (complete control in Table 4), 141 (83%) showed an increase in screening rate and there was a statistically significant increase in all types of cancer. Overall, the screening rate improved by 2.6% or 1.44-fold (p < 0.001). The average improvement in the screening rate was 1.7–3.7% compared to the previous 1–3 years, regardless of cancer type, with the greatest reduction among individual municipalities being –15.3% and the greatest increase 27.1% (Fig. 1). In terms of the ratio, the average increase was 1.32–1.55, with the lowest being 0 and the highest 9.8. On subgroup analyses, for calls, screening rates were 14.6% for our material group and 9.8% for control group with an increase of 4.8% or 1.48-fold (p < 0.001) and for recalls, screening

Table 4

Number of municipalities that use the invitation materials for cancer screening.

	Number of municipalities	Number of people with materials sent	Number of municipalities with data sent	Number of municip	oalities with control data
				Complete control	Complete and incomplete controls
Colored	ctal cancer				
2015	20	53,058	14	12	13
2016	20	72,328	9	3	5
2017	32	437,900	20	9	11
2018	30	167,244	23	6	10
total	102	730,530	66	30	39
Breast	cancer	,			
2015	40	168,628	22	7	19
2016	55	235,660	14	5	9
2017	65	155,433	28	11	15
2018	56	217,199	33	11	17
total	216	776,920	97	34	60
Lung ca	ancer				
2015	11	34,990	10	10	10
2016	14	33,030	4	2	4
2017	14	46,634	8	4	5
2018	14	60,847	15	8	9
total	53	175,501	37	24	28
Cervica	al cancer				
2015	32	123,375	20	7	17
2016	39	233,920	17	9	12
2017	53	257,306	34	20	26
2018	58	260,013	42	17	22
total	182	874,614	113	53	77
Stomac	h cancer				
2015	19	88,297	14	12	12
2016	16	75,089	7	5	7
2017	8	19,582	7	3	3
2018	18	88,833	16	6	8
total	61	271,801	44	26	30
Other 1	naterials				
2015	24	227,968	-	-	-
2016	50	345,379	_	-	-
2017	53	378,953	_	-	-
2018	46	528,093	-	-	-
total	173	1,480,393	-	-	-

Table 5

Comparison of cancer screening rates between group using the ROK* materials and control.

	n	Invitees to screening ROK/	Participants ROK/	Participati	p-value		
	Municipalities (screening rate increase/ decrease**)	control	control	Rate (%)	Difference (ROK- control) (%)	Ratio (ROK/ control)	
Colored	ctum, FY***						
2015	12(11/1)	101104/101727	6171/4760	6.1/4.7	1.4	1.30	< 0.001
2016	3(2/1)	2450/2698	316/250	12.9/	3.6	1.39	< 0.001
				9.3			
2017	9(8/1)	17723/18425	1526/983	8.6/5.3	3.3	1.61	< 0.001
2018	6(4/2)	19611/19760	896/538	4.6/2.7	1.8	1.68	< 0.001
total	30(25/5)	140888/142610	8909/6531	6.3/4.6	1.7	1.38	< 0.001
Breast,	FY***						
2015	7(5/2)	53443/51482	3769/2177	7.1/4.2	2.8	1.67	< 0.001
2016	5(4/1)	25690/39262	2387/2366	9.3/6.0	3.3	1.54	< 0.001
2017	11(11/0)	18856/19730	2859/2132	15.2/	4.4	1.40	< 0.001
				10.8			
2018	11(7/4)	26634/26286	3037/2429	11.4/	2.2	1.23	< 0.001
		104600 (106560	10050 (0104	9.2	0.0	1.45	0.001
total	34(2///)	124623/136760	12052/9104	9.7/6.7	3.0	1.45	<0.001
Lung, F	10(10/0)	22226 /24220	6911 /4074	107/	4.4	1.01	<0.001
2015	10(10/0)	33820/34820	0311/49/4	16.//	4.4	1.51	<0.001
2016	2(1/1)	17526/17803	790/694	45/39	0.6	1 16	< 0.01
2010	2(1/1) 4(4/0)	81049/81707	3331/2300	4.3/3.9	1.3	1.10	< 0.01
2017	8(6/2)	54321/54716	5942/4624	10.9/	2.5	1.45	< 0.001
2010	3(0/2)	01021/01/10	0512/1021	8.5	2.0	1.29	<0.001
total	24(21/3)	186722/189136	16374/12601	8.8/6.7	2.1	1.32	< 0.001
Cervix,	FY***						
2015	7(6/1)	66590/64690	5321/3052	8.0/4.7	3.3	1.69	< 0.001
2016	9(8/1)	43047/45927	3166/2286	7.4/5.0	2.4	1.48	< 0.001
2017	20(17/3)	63191/66968	7572/5202	12.0/	4.2	1.54	< 0.001
				7.8			
2018	17(13/4)	49721/52455	6242/4622	12.6/	3.7	1.43	< 0.001
				8.8			
total	53(44/9)	272270/282495	28543/19784	10.5/	3.5	1.50	< 0.001
				7.0			
Stomac	h, FY***						
2015	12(12/0)	38282/39547	2379/1358	6.2/3.4	2.8	1.81	< 0.001
2016	5(3/2)	4822/4686	433/410	9.0/8.7	0.2	1.03	0.693
2017	3(2/1)	6011/6325	708/597	11.8/	2.3	1.25	< 0.001
				9.4			
2018	6(5/1)	18211/18824	718/497	3.9/2.6	1.3	1.49	< 0.001
total	26(22/4)	67326/69382	4238/2862	6.3/4.1	2.2	1.53	< 0.001

*ROK: Rainbow of KIBOU project.

**Number of municipalities which screening rate increased / decreased by the ROK materials.

***FY: Fiscal year.

rates were 7.3% for our material group and 5.2% for control group with an increase of 2.1% or 1.41-fold (p < 0.001). When the number of individual invitations was the same in our material group and the control group (call vs. call or call + recall vs. call + recall, etc.), the average improvement in screening rate was 2.2% or 1.35 fold. When the number of invitations was high in the intervention group (such as call vs. none or call + recall vs. call), the average improvement in screening rate was 3.1% or 1.54 fold.

The difference in screening rate is shown in Fig. 1 for municipalities where age was not necessarily the same in the control group as in our material group (complete and incomplete controls in Table 4). The average improvement in the screening rate was 3.9% or 1.83 fold, which was a little larger than that of the comparable control group, but the municipalities with further improvement in the screening rate werewas also observed. There are 12 municipalities where the screening rate increased by 15% or more and four municipalities where the rate decreased by 10% or more in our material group. The difference in characteristics of screening and its subjects are shown in Table 6. The results suggested the screening rate increased when more invitations were sent, the subjects were older, increased screenings were provided after the invitations were sent, the invitations were sent to those with past screening history, and screening fee was lower.

As the secondary endpoint, the usefulness of the invitation materials in the real-world setting was investigated from various aspects using the RE-AIM framework. Reach (the number of persons who received the invitation materials developed in this study), adaptation (the number of municipalities using the materials developed in this study), and effectiveness (the effect of improving the screening) were already reported (Tables 4 and 5). Regarding implementation (the proportion of municipalities that used the materials as originally intended), we asked the municipalities who used the materials to mail the materials actually used and to confirm them. It was found that the papers and sizes were different from those specified for some municipalities, but many municipalities could not provide the actual materials sent and we could not make a quantitative evaluation. As maintenance, out of the four years studied, the number of municipalities that used the same material for 2 years was 41, the number of municipalities that used the same material for 3 years was 8.

4. Discussion

Our study demonstrated an increase in the screening rate when our materials were used, with an overall improvement of 2.6% or 1.44-fold. The materials developed in this study were therefore useful for improving the rate of cancer screening in the real world.

Previous studies have shown that sending tailored messages to patients improves the screening rate. However, in order to send tailored





Fig. 1. Improvement in cancer screening rate by the ROK materials compared to control (A: Comparison with comparative data; B: comparison with all available data).

messages, tailoring or segmentation by questioning each subject must be done in advance, which is not always possible. In that case, one solution may be to use material that does not need to be sent separately, by including a message for each target in one document. Although it is expected that the combined materials will be effective to some extent, it is useful to examine how effective they are, how easy they are to use, and how many municipalities can use them. The aforementioned RCT of Ishikawa et al. examined the efficacy of material developed using a social marketing approach under limited conditions, but it is not known if similar efficacy can be expected when used in the real world. This study examined whether results obtained by this RCT are really effective when used in the real world. While the new anticancer drug is clinically introduced after confirming its efficacy by RCT in a clinical trial, studies that examine how effective they are when used in clinical practice should be conducted. In this kind of research, usefulness is evaluated by comparing real-world data in clinical practice with the historical control, in terms of how much efficacy obtained in clinical trials is reproduced. Although the study design is inferior to RCTs, it is reasonable to evaluate as an observational study using clinical practice data, because RCTs cannot confirm whether the results can be reproduced in a real clinical setting. Based on this method, we compared the cancer screening rates in fiscal year 2015, 2016, 2017, and 2018 when the materials developed in this study were actually used in municipalities, with those of the same subjects in the previous 1-3 fiscal years, as historical controls.

To evaluate the usefulness of the invitation materials, it is important to evaluate how much it contributed to the improvement in the number of screening participants, and this can be evaluated by combining the effect on improving the screening rate and how widely it was used (adaptiveness). It is also important to check process indicators such as how well the method is compliant to the original method (maintenance) in order to fully examine the effect. The research field that actually disseminates effective intervention methods to the real world, such as this research, is called Dissemination & Implementation Research (D&I Research). In this study, the RE-AIM framework was used to evaluate

Table 6

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Year	Type of	Comparison between material group vs. control group								
Cancer		Difference in screening rate	Number of invitation sent	Target age	Number of screening provided after invitation	Past screening history considered	Screening fee			
Extrem	ely higher in the n	naterial group								
2015	Breast	36.4%	Two times more	Same	Same	Not considered	Same			
2018	Lung	27.1%	Same	Same	Three times more	Not considered	Same			
2018	Cervix	26.8%	One time more	Same	Same	Not considered	Same			
2017	Cervix	23.9%	One time more	Same	Same	Not considered	Same			
2018	Colorectum	21.8%	One time more	Dire time more Same S		Having past screening history vs. not considered	Same			
2018	Breast	19.9%	One time more	Same	Same	Having past screening history vs. not considered	Same			
2016	Lung	19.3%	One time more	Same	Same	Not considered	Same			
2016	Colorectum	18.5%	One time more	Same	Same	Not considered	Same			
2017	Breast	16.6%	Same	Same	Same	Not considered	Same			
2015	Cervix	15.7%	On time more	older (30's vs. 20's)	Same	Not considered	Same			
2017	Breast	15.6%	Same	Same	Same	Not considered	Same			
2018	Breast	15.4%	One time more	Younger	Same	Not considered	Free vs. not			
				(age 41 vs. 49)			free			
Extrem	ely higher in the c	ontrol group								
2018	Breast	-10.0%	Same	Same	Ten times more	No history for 2 years vs. No history for 1 year	Same			
2016	Lung	-13.6%	Same	Younger (age 41–63 vs.65–74)	Four times less	Not considered	Same			
2015	Breast	-15.3%	Same	Same	Same Same No history ys. not considered		Same			
2016	Breast	-17.8%	Same	Older	Same	No history	Same			
				(age 40 vs.40 + 45)		vs. not considered				

how much we could contribute to the increase in number of persons receiving cancer screenings. The RCT by Ishikawa et al. showed an improvement in the consultation rate by 18.2%, 12.6%, and 8.7% for each of the three segments mentioned above, but the improvement with our materials was 3% on average. Even in a real-world situation, our materials showed a statistically significant improvement in the screening rate, but the effect was much smaller than that shown in the RCT. The reason may be that our materials were not sent by segment, so the targeting effect was not sufficient. On the other hand, in the RCT, in addition to the selection bias where only active persons who responded to the segment survey were research participants, researchers and local governments were more actively involved in improving screening rates because of the research settings. This is probably another reason why the improvement effect was larger. This shows that RCT results are not always true in the real world. Through our effort to maximize awareness of the materials using a website, mailing list and workshops for municipalities, the materials we developed were adopted by 787 municipalities in four years and were used under a very wide range of conditions and were able to reach 4.3 million people. Therefore, it can be estimated that our materials increased the number of people who received cancer screening by about 130,000 with the effect of improving the screening rate by 3%.

As maintenance measure of the RE-AIM framework, we showed that some of the municipalities used the same material for 2, 3, and 4 years. Unfortunately, however, since most municipalities changed the subjects year by year, the trends in screening rates could not be examined. For the few municipalities where the subjects were the same, clear trends were not observed. Although we did not collect data systematically regarding how municipalities decided if they used the materials, the feedback from those that used continuously was that they tended to continue to use the same materials or to choose materials for other cancer types if they experienced screening rates increased using our materials.

According to the definition of Kreuter and Skinner (2000), tailored intervention is defined as evaluating the psychosocial aspects of an individual and sending individual messages based on them. On the other hand, sending a uniform message to a group with certain characteristics such as demographic variables is defined as targeted intervention. In this sense, our cancer screening invitation is a targeted intervention because the same materials are sent to everyone, but we aim for the same effect as a tailored intervention by including a message that evaluates the psychosocial aspects of each subject. Although with this type of tailored intervention it is expected that the effect will be reduced because the materials are not sent separately, if the materials are well-made, it will be very easy to use and effective in practice. Since it can be used for a wider range of subjects due to its easy implementation, it may have a greater effect than those that are highly effective but difficult to be implemented.

Rothman and Salovey (1997) suggested how to frame a message advocating health behavior in response to perceived risk from the perspective of prospect theory of behavioral economics (Kahneman and Tversky, 1979). In order to motivate people to get screening, Rothman and Salovey (1997) suggested that loss-framed messages such as "If you do not get cancer screening, you are increasing your chances of dying from breast cancer" are effective since cancer screening has the risk of discovering a serious disease. However, loss-framed messages were not necessarily effective in promoting cancer screening (Abood et al., 2005; O'Keefe and Jensen, 2009; Gallagher et al., 2011; Lipkus et al., 2019). This may be explained as effect modification by the constructs of the Health Belief Model and the framed message recommending cancer screening. Therefore, we aimed to enhance the effect of behavioral change by changing the framed message according to the degree of cancer worry as the perceived threat construct. This method is based on the hypothesis that the reference point that is the value standard of prospect theory differs depending on the degree of cancer worry. People with low cancer worry who have a positive reference point, that is, who

think they will never get cancer, are thought to recognize taking a cancer screening as a loss that would incur new costs to their current lives. Therefore, a loss-framed message was included in the materials with the aim of changing the reference point that he/she will never get cancer to the reference point that he/she might get cancer. This was intended to make them recognize not taking a cancer screening is a loss. On the other hand, people with high cancer worry who have a negative reference point, that is, who are too worried about getting cancer, are thought to recognize not taking a cancer screening as a gain in that they do not face the possibility of being diagnosed with cancer. Therefore, a gain-framed message was also included in the materials with the aim of changing the reference point that he/she was too worried about getting cancer to the reference point that he/she can find him/herself not having cancer or he/she can be cured by taking a cancer screening. This was intended to make them recognized taking a cancer screening as a gain. As a caveat, a loss-framed message for this segment can enhance negative emotions that increase fear of cancer and should be avoided as much as possible. Our material is for both the high and low cancer-worry segments, so both the loss-framed message and the gain-framed message were included in the same material. One problem is a possible adverse effect of the loss-framed message on the high cancer worry segment. Therefore, we decided not to make the loss-framed message very strong, such as "1 in 10 women will get breast cancer", but to make the overall tone and presentation such as illustrations and colors mild. In addition, previous studies have shown that the effect of framing on the low cancer worry segment is limited (Gallagher et al., 2011; Ishikawa et al., 2012; Lipkus et al., 2019), so to make single invitation material for the three segments, gain framing was considered to be the main approach by targeting the high cancer worry segment. The analysis with the complete and incomplete controls in our study showed that among the people who did not take screening, the municipality that sent our materials to those without any screening history did not show a significant effect on improving the screening rate. On the other hand, when it was sent to a subject who had not taken a screening recently but had a screening history in the past, a large effect on improving the screening rate was observed. It may be that while the subjects without any screening history included many people with low cancer worry and low screening intention, the subjects who had not taken a screening recently but had a screening history in the past included many people with higher cancer worry and higher screening intention. The results imply that it is efficient to send invitation letters to the latter to improve the screening rate in practical settings, where sending separately to each segment is difficult.

In terms of limitations, our study was conducted using the results of health services provided by municipalities that were not researchoriented. Therefore, the validity of this study depends on how the municipalities provided cancer screening and what can be obtained as routine data in the services. In this study, the comparison of primary endpoints was conducted with the same age group and those living in the same area up to the previous year, so that there was no or little confounding due to these factors. However, even if these are the same, it is not possible to remove the effects that were not the effect of the materials, such as differences in the number of times screenings were provided, or past examination history. As for age, some local governments sent the materials only to certain ages such as 40 and 50, some sent them to even ages such as 40, 42 and 44, and others sent them to those aged 40-69. Not all municipalities have age-specific screening rate data, so it was not possible to make age-specific comparisons. It is known from the results of exploratory analysis that the older the age, the higher the screening rate, but it was not clear from this study whether the effect of the materials differs depending on age. It was not also possible to examine whether the effects of our materials differ depending on factors such as health literacy, family history, employment status, constructs of the Health Belief Model or the nudge. (Champion and Skinner, 2008; Allahverdipour et al., 2011; Arnold et al., 2012; Tsunematsu et al., 2013; Glanz et al., 2015; Talley et al., 2016). Further studies are needed to

clarify these effect modifications.

Since our ultimate goal is to increase screening, the major objective of this study is not to correctly examine the effects of the materials themselves, but to clarify how materials, including screening providing methods, can be used to increase the screening rate more efficiently, and to find ways to contribute to increasing the screening rate in the future. In the framework of D&I research, the study investigated the multicomponent effect between call/recall of the invitation materials and the environment in which screening is provided. Although not necessarily quantitative, this study suggests the following; 1) The paper size and paper quality (thickness) of the materials should not be changed. 2) In accordance with the timing of the invitations sent, the number of opportunities for screening and its capacity should be increased, so applicants for screening will not be refused. 3) Sending more invitation is effective, 4) Since it is easier to increase the screening rate by sending invitations to subjects with a previous screening history, it is better to start by targeting these subjects, when the budget is limited.

In addition to social marketing approaches, this study showed behavioral economics approaches such as nudges to be effective in behavioral changes for cancer screening. From the perspective of behavioral economics and nudges, the following methods would be expected to be effective in increasing cancer screening rates (Thaler and Sunstein, 2008). Limit the days people can get cancer screening, rather than making it available at all times. Elicit participant commitment by asking them to write down their scheduled dates when they apply, or by informing their workplace or family about the screening date. Also, utilize the timing of turning points in life for each person, such as age (e. g., 40, 50, 60, etc.), moving, marriage, childbirth, and timing of changing careers. Do not end any event or campaign with conveying the message, but provide the opportunity for them to take cancer screening on the spot. Furthermore, take advantage of the tendency to apply near the deadline. Utilize any chance of another health checkup by setting cancer screening as an opt-out option. As a libertarian paternalist, nudges can be an effective way to convey the benefits and disadvantages of cancer screening while providing an opportunity for individual choices. Further research is expected to evaluate which nudge types of concept are effective.

In the near future, it may be possible to make personalized invitations for cancer screening using information about individuals such as personal health records and life logs stored digitally. For example, as a COVID-19 countermeasure, smartphone location information of each individual is beginning to be used for infection prevention (World Economic Forum, 2020). How to use personal information while protecting individual rights will become a more important issue in the near future.

In conclusion, our materials are expected to increase the cancer screening rate by about 3% on average by just sending them. However, by combining materials with the above method, an even greater improvement in the screening rate can be expected. In order to improve the cancer screening rate, it is important to carry out various measures in combination.

Credit author statement

Yuri Mizota: Conceptualization; Data curation; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Roles/Writing - original draft; Writing - review & editing. Seiichiro Yamamoto: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing review & editing.

Declaration of competing interest

The authors have no conflict of interests.

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