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Assessing the Consumer Acceptability of Vaccine Rice

Yoko Saito[1*], Hideo Aizaki[1] and Hisamitsu Saito[2]

A feature of much recent medical research has been to offer a range of treatment choices for a given condition. It is important therefore to understand patient preferences among the non-medical as well as medical features of these options. An instructive example is a variety of rice currently under development with recombinant DNA technology as an alternative to the vaccine injection conventionally used against cedar pollen allergy as immunotherapy treatment. We use a survey-based discrete choice experiment to examine and decompose the attitudes to this medical food, along with their likely net effects on final demand. Restricting the survey to allergy sufferers allows focus on the rice's maximum perceived welfare benefits, in contrast to the ambiguous conclusions of previous studies. Patient characteristics, such as allergy severity, GM technology familiarity, and opportunity costs of hospital visits necessary for the injection treatment strongly influence the vaccine rice's appeal. A successful marketing program for the new rice will require appealing to these direct benefits.

Key words: discrete-choice experiment, GM technology, medical benefit, non-medical benefits, vaccine rice

1. Introduction

A principal purpose of medical research is to expand the horizon of potentially curative activity. With this greater horizon comes greater uncertainty over the possibilities that will be favored by patients. An understanding of patient preferences can help anticipate such choices, and in so doing, offer a stronger foundation for medical and health policy (Brown *et al*., 2010; Wordsworth *et al*., 2001). Non-medical features of vaccination systems have become increasingly important in patient health and quality-of-life decisions (Jit and Hutubessy, 2016). Coupé *et al*. (2012), for example, attend to non-health as well as health benefits and costs, noting that the vaccine for human *papillomavirus* has the non-health benefit of saving screening visits to the hospital.

Takaiwa (2004) recently developed a new medical-rice vaccine (hereafter, vaccine rice) for use in the treatment of cedar pollen allergy. Although still in its development stage at the Institute of Agrobiological Sciences in Japan[1)], it shows promising evidence of providing allergen resistance equivalent to the current alternative of a vaccine injection. According to Okubo (2015), 80 percent of injected patients report either alleviation in symptoms or a complete cure. Vaccine rice is believed to work by way of intestinal immunity. Injections provide subcutaneous immunity and require regular hospital visits while vaccine rice offers the additional non-medical benefit of saving hospital visits.

Vaccine rice is a gene-recombinant technology and has been controversial in many quarters. Most of the genetically modified (GM) crop varieties were largely developed for the purpose of reducing farm production costs, for instance, by way of herbicides or insect resistance. Cost advantages appeal directly only to the producers; consumers, especially in the EU and Japan, generally see no advantage in them other than in reducing purchase prices. Their concern, instead, is with the possible risks, particularly to health and environment (Costa-Font *et al*., 2008). Consumer perceptions of the risks of novel food technologies have been studied extensively (Frewer *et al*., 1998, 2003; Grunert *et al*.,

[1] Research Faculty of Agriculture, Hokkaido University
[2] Faculty of Economics and Business, Hokkaido University
Corresponding author*: saitoy@agecon.agr.hokudai.ac.jp

1) Following the Cartagena Protocol on Biosafety, vaccine rice is currently planted in an experimental field to investigate its environmental impacts. Pursuant to the Pharmaceutical Affairs Law, it also has to pass clinical trials as a medicine before it can be sold commercially.

2003; Hudson *et al*., 2015; Savadori *et al*., 2004; Siegrist, 2008). Some (e.g., Gaskell *et al*., 2004; Loureiro, 2005) concluded that the slow diffusion of GM foods can be explained not so much by their risk itself as the apparent absence of any countervailing positive benefits.

Recent developments in GM crop and food technology, however, promise direct consumer value (Corrigan *et al*., 2009; Deodhar *et al*., 2008; De Steur *et al*., 2010; Lusk, 2003; and Sabalza *et al*., 2014). It is the exclusively medical applications of GM technology that have found the greatest consumer acceptance (Kirk and Mcintosh, 2005; Gaskell 2000; and Saito *et al*., 2017). Einsiedel and Medlock (2005) in particular find that edible vaccines drawn from GM crop material represent GM's presently most widely accepted use.

Evaluating a product with nutrition, medical, convenience, and price implications simultaneously requires assessing its relative costs and benefits. Given that risk is one aspect of cost, it is essential to consider the preferences for risks as well as for benefits. One important aspect of our approach is to examine whether the respondent is willing to consume vaccine rice that has the same therapeutic effect as injection. As vaccine rice is still in the development stage, preferences are identified in our study through the stated-preference approach, in which respondents indicate choices among a series of conditional treatments. This approach has been widely employed to estimate consumer valuations of health and/or medical features of non-GM agricultural products (e.g., Iwamoto, 2012; Kallas *et al*., 2014; Krystallis and Chrysochou, 2012; and Yuwen and Hsiaoping 2020). By contrast, consumer evaluations of GM agricultural products with specifically medical features have not been adequately addressed. This study fills the gap by evaluating consumer acceptance of vaccine rice. In addition, our limitation of the survey population to direct potential beneficiaries, namely infected respondents, should position stated preferences near the upper bound of those for GM products.

However, we must connect these preferences to the consumer attitudes on interrelated issues, such as environmental protection, food consumption, and the perceived value of one's time. Insofar as vaccine rice is a medicine, it offers allergy patients an additional treatment option, potentially affecting the medical industry. As an agricultural product, it offers food consumers an additional nutrition option, potentially affecting farmers. Products like vaccine rice, therefore, have possible impacts on both the medical and agricultural industries, encouraging a collaborative work between them.

The remainder of this paper is organized as follows. Section 2 discusses the benefits and risks of vaccine rice in Japan. Section 3 outlines our survey design, empirical model specification, and estimation methods. Section 4 presents the results, highlighting the factors affecting willingness-to-pay (WTP) for vaccine rice. Section 5 concludes with a summary of results and policy implications.

2. Medical/Non-Medical Benefit and Human/Environmental Risk

According to an epidemiological survey conducted by Baba and Nakae (2008), approximately 30 percent of the Japanese population suffers from allergic reactions to cedar pollen and other allergens. Currently, two types of treatments are available for cedar pollen allergy: (i) symptomatic treatment and (ii) immunotherapy treatment including injection and vaccine rice. Symptomatic treatment is aimed at temporarily alleviating these reactions. For example, patients take over-the-counter drugs when they suffer from allergic reactions during the pollen-spreading season. If the reactions are severe, they may make time to visit a hospital to receive prescription drugs. In contrast, immunotherapy treatment is aimed at completely curing the allergic reactions. Thus, patients can start receiving the treatment even in the non-pollen spreading season. However, the treatment, particularly injection, requires constant and frequent hospital visits for three to four years, likely reducing their incentive to receive the treatment (Ogihara *et al*., 2010). Vaccine rice offers the same medical benefits as injections, while providing the additional non-medical benefit of saving hospital visits.

Patients presumably choose their treatments based on the expected net benefits, calculated subjectively from information about the therapeutic mechanism, possible side-effects, treatment fees, treatment length, and the inconvenience, and the costs of clinic visits. Further, it is the preference for the relative risks of the medical and non-medical benefits that are relevant to these choices. The purpose of this study is to examine patients' evaluation of the medical and non-medical benefits of the two immunotherapy treatments. Several factors affect evaluations. For instance, schedule flexibility may be important. If patients have a baby to take care of, they may prefer to postpone taking injections for some years until their schedule becomes flexible while receiving symptomatic treatment. Alternatively, if vaccine rice is available, they may want to receive immunotherapy treatment immediately.

However, for some, when the medicine is gene-recombinant, those risks include environmental risks, such as the prospects of GM crops cross pollinating

Suppose the nearest hospital is 20 minutes away. The medical fee is fixed no matter which treatment you choose (rice or injection). However, the treatment fee does vary. For injection treatment, you must visit the hospital once a week or once a month, while for vaccine rice, you will eat one bowl of vaccine rice per day and visit the hospital once a month. You have to continue this treatment for 2 to 3 years, including during cedar pollen's non-spreading season. With regard to the rice production site, you have two options: (a) open-field (conventional production technology); (b) closed-factory (indoor negative-pressure ventilation).

Based on this information, choose your most preferred treatment. If you do not prefer any of the options listed, choose [c]. Please note that the "I do not choose" option implies that you prefer continuing your current treatment (opt-out).

	[a]	[b]	[c]
Treatment method	Vaccine rice	Injection	I do not choose (current treatment)
Fee per month (Yen)	1,000	500	
Rice production site	Closed factory		

Figure 1. Survey script and sample choice set

with local varieties or weed mutations if the crop is herbicide-tolerant. Possible solutions to the environmental influences are beginning to emerge. One is the recent development of the 'plant factory', in which negative-pressure ventilation minimizes the chances of pollen dispersal, reducing the chances of interactions with surrounding ecosystems. Patients concerned with this issue will presumably compare the likely effectiveness of the environmental protection technology with the corresponding medical benefits. Given that vaccine rice is ingested, its healthfulness might also be a concern, despite the fact that risks of this sort are normally put aside for GM chemotherapies used in cancer treatments. Although there is little data on the side effects of vaccine rice, its higher net benefits, which are less known, will likely be discounted in view of the general suspicions surrounding transgenic technology.

3. Data and Methods

1) Survey design

As vaccine rice is not yet marketed, we carried out discrete-choice experiments to examine patient acceptability (Louviere *et al*., 2000). In the online survey conducted for us by the Japanese survey firm Macromill (March 2015), respondents were limited to Japanese residents allergic to cedar pollen. We obtained 1,060 respondents – about half female and half male; nine were excluded because they were already under immunotherapy. Our sample data, thus, consists only of those who have never been treated. An equal number of responses were obtained from those in their 20s, 30s, 40s, 50s, and 60s.

In the discrete-choice questions, respondents were asked to indicate their preference among the three treatment attribute options in Figure 1, including the option of "I do not choose." They were informed that the "I do not choose" option implies they would continue their current treatment or opt-out option.[2] Attributes examined were: (1) the treatment method; (2) the fee; and (3) if the chosen treatment is vaccine rice, its production site (see Table 1 for each attribute level). Since injection and vaccine rice always appear in a choice set (that is, treatment method is itself considered an attribute, namely #1 in Table 1), only the per-month fee (#2) and the siting of rice production (an open field vs. a plant factory, #3) vary across sets. Price categories were determined on the basis of a preliminary survey. We excluded sublingual immunotherapy because it has only recently been developed and is not yet under major consideration. Hospital visit frequency and treatment duration are also non-medical service attributes, although not considered explicitly

2) We asked in the survey whether respondents take the following measures during cedar pollen season: (i) over- the-counter medicines, (ii) prescription medicines, and (iii) a diet considered effective against cedar pollen allergy. Cross-tabulating this information with the results of the discrete-choice experiment, we find that the probability of choosing the opt-out option in every choice set is 10 percentage points (30 percent vs. 20 percent) higher among respondents taking none of the above three actions than is the probability of taking *at least one* of the three. This suggests respondents who have only a weak intention to alleviate cedar pollen allergy symptoms (i.e., those taking *none* of the three actions) were indicating their preferences unbiasedly in our discrete-choice experiments. That in turn points to the validity of our present approach.

Table 1. Product attributes in the choice experiment

Product attribute	Level
Treatment method #1	(a) Rice (b) Injection (c) I do not choose ('opt-out')
Treatment fee (yen per month) #2	(a) 500 (b) 1,000 (c) 1,500 (d) 2,000 (e) 2,500 (f) 3,000
Rice production site #3	(a) Open field (b) Closed factory

Table 2. Variable definitions and summary statistics

Variable	Definition	Mean	Std. dev.	Min	Max
Choice experiment variable					
ASC_{TR}	1 if choose immunotherapy (injection or rice), 0 otherwise				
FEE	Fee, in 1,000 yen/month				
RICE	1 if choose vaccine rice, 0 otherwise				
FACTORY	1 if choose vaccine rice produced in plant factory, 0 if in open-field				
Respondent characteristic					
AGE	Respondent's age	44.66	13.763	20	69
SKD_flex	Schedule flexibility: 0 (enough spare time) to 1 (not enough spare time)	0.503	0.277	0	1
SEVERE	Allergic reaction severity to cedar pollen: 0 (not severe) to 1 (severe)	0.825	0.174	0	1
FAM_imm	Familiarity with immunotherapy: 0 (unfamiliar) to 1 (familiar)	0.313	0.268	0	1
FAM_gm	Familiarity with GM foods or technology: 0 (unfamiliar) to 1 (familiar)	0.184	0.202	0	1
ENV	Environmental concerns with GM technology: 0 (less) to 1 (more)	0.616	0.249	0	1

Note: The bottom five variables are denominated in decimals between 0 and 1. See Appendix B.

here because they are simultaneously determined with the treatment method, information about which was provided in the survey script. Thirty-six possible choice sets were generated by way of orthogonal design, divided into six groups, each of which contains six sub-sets.[3] Each respondent was randomly assigned to one of the six groups.

In addition to the discreet-choice questions, we asked respondents about their familiarity with immunotherapy (*FAM_imm*) and GM technology (*FAM_gm*), as well as their concerns about the environmental risks of GM (*ENV*). We also inquired into the subjective severity of their allergic reactions (*SEVERE*) and their schedule flexibility (*SKD_flex*). These variables are constructed by aggregating the answers to Likert-scale questions. See Appendix B for further details. Schedule flexibility is intended to measure the opportunity cost of their immunization visits to the hospital. The opportunity cost of hospital visits is considered to be a principal factor affecting the demand for medical services (Acton, 1975; Goto and Ibuka, 2020; Grossman 1972; and Ii and Ohkusa 1999ab, 2001). Several measures have been used in the literature. For example, Acton (1975) uses the distance to the hospital. Similarly, Kondo *et al.* (2009) employ the geographical density of hospitals. However, since our respondents have not received immunotherapy treatment in a hospital setting, we cannot ask them about the actual distance they have to travel to receive the treatment. Instead, we consider a more direct measure. The first measure is obtained by asking respondents to record their daily activities. This measure is precise but not suitable for a one-time online survey. The second measure is obtained based on past daily activities. We can inquire as to the actual amount of their spare time or ask respondents to indicate the level of their spare time on a Likert scale. Note that because of the heavy burden on respondents, the former measure does not necessarily provide a precise result in an online survey without interviewers. As a result, we employ a measure that asks for schedule flexibility on a Likert scale. However, caution must be exercised when interpreting

3) We use R Core Team (2014) and its add-on package (Aizaki, 2012, 2014; Aizaki *et al.*, 2014) to construct choice sets. See Appendix A for the complete list of choice sets.

the results. In case it is imprecisely measured, we also estimate the model without *SKD_flex* to see how its introduction affects our results.

With these responses, we tested four hypotheses: (a) the more severely the patient suffers from allergic reaction or the greater the familiarity with immunotherapy, the more the patient prefers that treatment; (b) the less familiar with GM technology, the less desired the vaccine rice; (c) the greater the opportunity cost of a hospital visit, the greater the preference for vaccine rice; and finally (d) the more the environmental awareness of the respondent, the greater the preference for a GM crop to be cultivated in a plant factory.

Definitions and summary statistics of the variables are provided in Table 2. Average familiarity with immunotherapy treatment (*FAM_imm*) is 0.31 with a standard deviation of 0.27, implying that the respondents' knowledge of immunotherapy as a definitive treatment for cedar pollen allergy varies considerably. Average familiarity with GM products (*FAM_gm*) is 0.18, indicating consumer knowledge of GM crops remains limited. The average level of concern for environmental risks (*ENV*) of GM crops is 0.62. Given the moderate level of this concern, GM crop production in a plant factory might effectively mitigate environmental worries. Average allergy severity (*SEVERE*) is 0.83, suggesting that most respondents consider their cedar pollen reactions to be very severe and that their quality of life significantly worsens during cedar pollen season. Finally, the average schedule flexibility (*SKD_flex*), a proxy for the opportunity cost of hospital visits, is 0.50 with a standard deviation of 0.28, suggesting that our data incorporate a variety of lifestyles, ranging from flexible to inflexible schedules. The timesaving advantages of vaccine rice should appeal to those with high hospital-visit opportunity costs.

2) Estimation model

We model patient preferences as discrete-choice problems. Suppose the utility that cedar-pollen-allergic patient *i* expects to gain from treatment *j* can be expressed as

$$U_{ij}=V_{ij}+\varepsilon_{ij} \tag{1}$$

where the V_{ij} are the systematic components of the utility of alternatively choosing vaccine rice ($j=1$), injection ($j=2$), or the current treatment (opt-out) option ($j=3$), which excludes any form of immunotherapy. Let V_{ij} take the following compound form:

Immunotherapy (Vaccine rice)

$$V_{i1}=\beta_{1i}ASC_{TR}+\beta_2 FEE_1 + (\beta_{3i}+\beta_{4i}FACTORY_1)RICE_1 \tag{2}$$

Immunotherapy (Injection)

$$V_{i2}=\beta_{1i}ASC_{TR}+\beta_2 FEE_2 \tag{3}$$

Opt-Out Options (Current treatment or possible options)

$$V_{i3}=0 \tag{4}$$

in which ASC_{TR} is equal to 1 if either vaccine rice or injection immunotherapy is selected, or else 0. FEE_j denotes the treatment fee in 1,000 yen per month. $RICE_j$ is 1 if vaccine rice is chosen for immunotherapy, or else 0. $FACTORY_j = 1$ if the vaccine rice selected is to be produced in a plant factory and 0 if it is to be produced in open-field conditions.

Parameters β_{1i}, β_2, β_{3i}, and β_{4i} in equations (2) and (3) measure the welfare impacts of receiving immunotherapy, paying the treatment fee, choosing vaccine rice, or choosing vaccine rice produced in a plant factory, respectively. Note that β_{1i}, β_{3i}, and β_{4i} are indexed *i*, so that the utility gained from immunotherapy or its vaccine rice form varies according to the respondent's personal characteristics. The characteristics are entered as follows:

$$\beta_{1i}=\beta_{10}+\beta_{11}MALE_i+\beta_{12}AGE_i, + \beta_{13}SEVERE_i+\beta_{14}FAM\_imm_i, \tag{5}$$

$$\beta_{3i}=\beta_{30}+\beta_{31}MALE_i+\beta_{32}AGE_i, \text{ and } + \beta_{33}FAM\_gm_i+\beta_{34}SKD\_flex_i, \text{ and} \tag{6}$$

$$\beta_{4i}=\beta_{40}+\beta_{41}ENV_i. \tag{7}$$

We expect that the more severe the allergic reaction, the greater the preference for immunotherapy. Moreover, as patients become more familiar with immunotherapy in general (*FAM_imm*), their preference for it should rise. Hence, both β_{13} and β_{14} in equation (5) should be positive. The choice between vaccine rice and injection in (6) depends on patient familiarity with GM technology and on the time-saving benefits of vaccine rice. Familiarity with GM technology should increase the likelihood of choosing vaccine rice. The greater the opportunity cost of a hospital visit, the more likely the choice of consuming it at home as a rice. Thus, both β_{33} and β_{34} are expected to be positive. Finally, the more environmental the patient's attitude, the stronger should be the preference for a vaccine rice produced in a plant factory, suggesting β_{41} in equation (7) should be positive as well.

If ε_{ij} follows a type I extreme-value distribution, equations (1)-(7) can be estimated using a conditional logit model. Its underlying assumption − the independence of irrelevant alternatives (IIA) − is that the relative probability of choosing any two alternatives is independent of the availability of any third one (Hensher, Rose, and Greene, 2015). For example, IIA

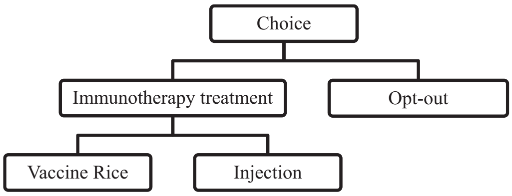

Figure 2. Tree structure of nested logit model

implies the choice between injection and the opt-out options is independent of the availability of a vaccine rice alternative. However, when the rice is unavailable, severe pollen-allergy sufferers may prefer immunotherapy and be more likely to choose injection over the opt-out options. This logic is represented in the Figure 2 decision tree. The upper portion of the tree represents the choice between immunotherapy and opt-out, while the lower consists of two options: vaccine rice or injection. If this tree is valid, then IIA does not hold and conditional logit estimates are no longer consistent because the choice of an immunotherapy option is no longer independent of the third or opt-out option. In Section 4 we therefore present both the conditional and nested logit results corresponding to the Figure 2 decision tree.[4)] All estimates are obtained from NLOGIT Version 5.

4. Estimation Results

1) Utility function estimates

Table 3 presents the utility-function parameter estimates of allergy treatment choice. See columns (1) and (2) for the parameter estimates of the conditional logit model and columns (3) and (4) for the nested logit estimates. Both the conditional and nested logit models give qualitatively and quantitatively similar results. Furthermore, the inclusive-value parameters, constrained to 1.0 in the conditional logit and associated with choosing immunotherapy, are not significantly different from unity even at the 10 percent level, suggesting the data are consistent with the IIA assumption imposed by the conditional logit. We therefore base our principal findings on the conditional logit model.

Fee coefficient β_2 is negative and significant, implying the higher the treatment fee, the greater the utility loss. Parameters β_{10} to β_{14} exhibit the effect of personal characteristics on preferences for immunotherapy relative to the opt-out options. Both β_{13} and β_{14} are positive and significant as expected: the more severe the allergic reaction (*SEVERE*) and the greater the understanding of immunotherapy (*FAM_imm*), the greater the preference for treatment.

Parameters β_{30} to β_{33} in column (1) reflect the influence of personal characteristics on vaccine-rice preferences relative to injection. The β_{30} is positive and significant. Because every variable does not take a negative value by construction, this result implies that all respondents highly evaluate the non-medical benefits of vaccine rice. β_{33}'s positive sign suggests that those familiar with GM technology (*FAM_gm*) would receive higher utility with vaccine-rice treatment. The statistical non-significance of β_{41} suggests little evidence that the production of GM crops in closed factories would mitigate any environmental concerns (*ENV*) over GM technology.

We add the respondent's schedule flexibility (*SKD_flex*) in columns (2) and (4). Its sign is positive and significant, indicating that patients with less schedule flexibility are more likely to choose vaccine rice. In contrast, β_{30} becomes insignificant, suggesting that vaccine rice is mostly appreciated by consumers with schedule inflexibility. However, we need to interpret the results cautiously for patients with mild symptoms because they may have little incentive to receive immunotherapy treatment regardless of their schedule flexibility. Note that our empirical methodology can partly address this issue. Instead of choosing between injection and vaccine rice, patients who are not interested in immunotherapy treatment can choose the opt-out option. Moreover, as Table 2 or Table B1 indicates, most respondents considered their cedar pollen reactions to be very severe. Lastly, to check the robustness of our results to the inclusion of patients with mild symptoms, we re-estimate equations (1)-(7) by excluding respondents who indicated that the discomfort from the allergic reaction to cedar pollen is not severe in Table B1.[5)] The results are similar to those in Table 3; namely, *SKD_flex* has a positive and significant sign. These findings suggest that it is less likely that the choices by patients with mild symptoms significantly affect our estimation results.

2) WTP estimates for vaccine rice

To facilitate the economic interpretation of these findings, let us now examine the comparative WTP between vaccine rice and injection. The WTP, obtained

4) Hynes *et al.* (2021), for instance, apply several models to their discrete-choice experiment responses. See also de Bekker-Grob *et al.* (2020) and Johnson *et al.* (2019).

5) We estimated the model five times. In the first model, we excluded respondents who indicated that the level of their discomfort is less than or equal to four in Table B1. In the following models, we increased the cut-off level of severity one by one. The last model only included respondents with the maximum level of discomfort.

Table 3. Allergy treatment choice, utility function estimates

Variable	Conditional logit		Nested logit	
	(1)	(2)	(3)	(4)
ASC_{TR}				
Constant (β_{10})	−0.620***	−0.606***	−0.674***	−0.647***
	(0.187)	(0.187)	(0.214)	(0.209)
MALE (β_{11})	0.036	0.037	0.077	0.070
	(0.069)	(0.069)	(0.081)	(0.080)
AGE (β_{12})	−0.006**	−0.006***	−0.008***	−0.007***
	(0.003)	(0.003)	(0.003)	(0.003)
SEVERE (β_{13})	1.150***	1.136***	1.316***	1.269***
	(0.155)	(0.155)	(0.211)	(0.205)
FAM_imm (β_{14})	1.148***	1.144***	1.329***	1.291***
	(0.109)	(0.109)	(0.176)	(0.170)
FEE				
Constant (β_2)	−0.621***	−0.622***	−0.653***	−0.648***
	(0.025)	(0.025)	(0.032)	(0.032)
RICE				
Constant (β_{30})	0.479***	0.234	0.491***	0.237
	(0.130)	(0.146)	(0.132)	(0.149)
MALE (β_{31})	0.428***	0.411***	0.434***	0.415***
	(0.071)	(0.071)	(0.072)	(0.072)
AGE (β_{32})	−0.004	−0.002	−0.004	−0.002
	(0.003)	(0.003)	(0.003)	(0.003)
FAM_gm (β_{33})	0.431***	0.416***	0.421***	0.409***
	(0.142)	(0.142)	(0.149)	(0.148)
SKD_flex (β_{34})		0.378***		0.387***
		(0.101)		(0.106)
FACTORY				
Constant (β_{40})	−0.121	−0.128	−0.144	−0.146
	(0.114)	(0.114)	(0.122)	(0.120)
ENV (β_{41})	0.142	0.154	0.181	0.184
	(0.162)	(0.162)	(0.173)	(0.172)
Inclusive value				
Treatment			0.868	0.890
			(0.079)	(0.080)
Opt-out (current treatment)			1.000	1.000
Log likelihood	−6,243.974	−6,236.995	−6,242.705	−6,236.117
Observations	6,306	6,306	6,306	6,306

Note: Standard errors are in parentheses. *, **, and *** indicate statistical significance at the 10, 5, and 1 percent levels, respectively. The inclusive value parameter for a nest "Opt-out" is constrained to 1 in the nested logit estimation.

as the ratio of the respective parameter in Table 3 to the negative of price parameter β_2, measures the maximum amount patients will pay relative to the opt-out options. In particular, Table 4 shows how WTP for the stated treatment type, relative respectively to the opt-out options (β_{10}—β_{14}), injection (β_{30}—β_{34}), or open field (β_{40}—β_{41}), is affected when a given patient characteristic changes by one standard deviation. The 95% confidence intervals are also shown.

Consider first the WTP for immunotherapy relative to the opt-out options. At its sample mean (Table 2), a unit change in reaction severity to cedar pollen (*SEVERE*) lifts relative WTP for immunotherapy by 1,506 ($=1.826\times0.825\times1{,}000$) yen. At sample mean *FAM_imm*, a unit improvement in one's understanding of immunotherapy lifts relative WTP by 576 ($=1.840\times0.313\times1{,}000$) yen. Thus, allergic reaction severity and adequacy of understanding immunotherapy are the keys to drawing patients into immunotherapy. Next, look at the WTP for vaccine rice relative to injection. Gender (β_{31}) has non-negligible impact on vaccine rice's WTP advantage: men are willing to pay 660 ($=0.660\times1\times1{,}000$) yen more for vaccine rice, relative to injection, than women are. This is consistent

Table 4. Willingness-to-pay estimates

Variable	WTP	95% Confidence Interval	1 std. dev. change in variable
ASC(*Immunotherapy*)$_{TR}$			
Constant (β_{10})	−0.974	(−1.448, −0.418)	
MALE (β_{11})	0.059	(−0.148, 0.302)	
AGE (β_{12})	−0.010	(−0.017, −0.002)	−0.138
SEVERE (β_{13})	1.826	(1.239, 2.514)	0.317
FAM_imm (β_{14})	1.840	(1.387, 2.370)	0.493
RICE			
Constant (β_{30})	0.376	(−0.078, 0.907)	
MALE (β_{31})	0.660	(0.403, 0.961)	
AGE (β_{32})	−0.004	(−0.011, 0.005)	−0.055
FAM_gm (β_{33})	0.668	(0.205, 1.211)	0.135
SKD_flex (β_{34})	0.608	(0.267, 1.008)	0.168
FACTORY			
Constant (β_{40})	−0.206	(−0.524, 0.166)	
ENV (β_{41})	0.248	(−0.243, 0.823)	0.062

Note: Unit is 1,000 Yen per month. A 95 percent confidence interval is obtained following Krinsky and Robb (1986). 1 std.dev.change in variable is calculated as WTP times 1std.dev. of each variable in Table 2.

with Kirk and McIntosh (2005), who find women generally favoring injections more than men do. A unit increase in the patient's familiarity with GM technology (*FAM_gm*) improves rice's WTP advantage by 123 (=0.668×0.184×1,000) yen. Finally, a unit rise in the patient's schedule inflexibility (*SKD_flex*) improves vaccine rice's WTP advantage over injection by 306 (=0.608×0.503×1,000) yen.

As Table 2 shows, our respondents vary greatly – in both positive and negative directions – in personal characteristics, the greatest variation being in schedule flexibility (*SKD_flex*) and immunotherapy familiarity (*FAM_imm*). WTP sensitivity to personal characteristics and situations should, therefore, also be rather high. This is confirmed in the fourth column of Table 4, which shows the WTP variation corresponding to a one-standard-deviation change in the respective characteristic. Evaluated at the mean for instance, allergy severity has greater effect than familiarity does (1,506 yen vs. 576 yen) on the WTP for immunotherapy. But since familiarity varies more than severity, it has the greater overall WTP effect. In Table 4 also, WTP for vaccine rice relative to injection is 135 yen in a patient a standard deviation above mean GM familiarity, and 168 yen greater in a patient one standard deviation above mean schedule flexibility, than at their respective means. Overall, preferences for vaccine rice over injection depend greatly on the patient's personal situation.

5. Discussion and Conclusions

We have investigated an allergy patient's possible responses to a vaccine rice produced with GM technology. Although recombinant DNA has been nearly universally accepted for strictly medical interventions such as for cancer treatment, its perceived health and environmental risks have, especially in developed countries, impeded its adoption in food products. Unlike recombinant technology's medical uses, which appeal to the consumer-patient directly, its agricultural and food applications have heretofore appealed directly only to producers—and to food buyers only indirectly through price reductions. Successfully alleviating these consumer concerns, therefore, appears to hold the greatest promise of wider applications of recombinant methods. More immediately, a GM-based medical rice vaccine now appears to be effective in curing the widely prevalent cedar pollen allergy, economizing on costly hospital visits, especially for patients with schedule inflexibility.

Here too though, worries and other downsides of vaccine rice will have to be allayed, and we have used discrete-choice experiments to examine the relative importance of these various diffusion factors. Our findings stand out in sharp relief. Patients, particularly technologically acquainted ones, generally appreciate the non-medical benefit of vaccine rice. The results also suggest that patients with the least schedule flexibility are the most likely to choose vaccine rice over hospital injections. The WTP effect of patient immunotherapy acquaintance, and of allergic reaction severity, are the highest two we encountered. A focus on especially severe allergy cases and immunotherapy education would, therefore, be crucial for vaccine rice's success. However, we do not find strong evidence that producing the GM crop in a plant-factory rather than an open-field setting would be very persuasive to people with environmental concerns.

Broadening the public's knowledge of GM technology will not be easy. About twenty years have passed since the first GM food – the FLAVR SAVR tomato – was introduced; yet a real understanding of genetic modification continues to be confined to small circles (Hallman *et al*., 2013). A balance of medical and nonmedical costs and benefits in GM research design will thus be important to future crop transgenics. For example, grains have long shelf lives, requiring little of the handling that most vaccines do and hence easily shipped when a health outbreak occurs. Efforts are already underway to engineer foods with resistance to infectious diseases like cholera. Nevertheless, our study suggests that attention be paid early in the research program to the envisioned technology's market acceptability, in terms not only of its cost to consumers but its medical opportunities for patients, and that a conscious marketing program be designed around these features.

JEL codes: Q13, D12, I10

References

Acton, J.P. (1975) Nonmonetary Factors in the Demand for Medical Services: Some Empirical Evidence, *Journal of Political Economy* 83: 595–614.

Aizaki, H. (2012) Basic Functions for Supporting An Implementation of Choice Experiments in R, *Journal of Statistical Software*, 50(C2): 1–24.

Aizaki, H. (2014) support.CEs: Basic Functions for Supporting an Implementation of Choice Experiments, version 0.1.2, http://CRAN.R-project.org/package=support.CEs.

Aizaki, H., T. Nakatani, and K. Sato (2014) Stated Preference Methods Using R, Boca Raton, FL: CRC Press.

Baba, K. and K. Nakae (2008) Epidemiological Survey of Nasal Allergy in 2008: Comparison with 1998 Result, *Progress in Medicine* 28: 2001–2012.

Brown, D.S., F. R. Johnson, C. Poulos, and M. Messonnier (2010) Mothers' Preferences and Willingness to Pay for Vaccinating Daughters against Human Papillomavirus, *Vaccine* 28: 1702–1708.

Corrigan, J.R., D.P.T. Depositario, R. Nayga Jr., X. Wu and T.P. Laude (2009) Comparing Open-Ended Choice Experiments and Experimental Auctions: An Application to Golden Rice, *American Journal of Agricultural Economics* 93: 837–853.

Costa-Font, M., J.M. Gil and B. Traill (2008) Consumer Acceptance, Valuation of and Attitudes Towards Genetically Modified Food: Review and Implications for Food Policy, *Food Policy* 33: 99–111.

Coupé, V. M. H., J. A. Bogaards, C. L. M. Meijer, and J. Berkhof (2012) Impact of Vaccine Protection against Multiple HPV Types on the Cost-Effectiveness of Cervical Screening, *Vaccine* 30: 1813–1822.

de Bekker-Grob, E.W., B. Donkers, J. Veldwijk, M. Jonker, S. Buis, J. Huisman, and P. Bindels, (2020) What Factors Influence Non-Participation Most in Colorectal Cancer Screening? A Discrete Choice Experiment, The Patient-Patient-Centered Outcomes Research, https://doi.org/10.1007/s40271-020-00477-w.

Deodhar, S.Y., S. Ganesh, and W.S. Chern (2008) Emerging Markets for GM Foods: An Indian Perspective on Consumer Understanding and the Willingness to Pay, *International Journal of Biotechnology* 10: 570–587.

De Steur, H., X. Gellynck, S. Storozhenko, G. Liqun, W. Lambert, D. Van Der Straeten, and J. Viaene (2010) Willingness-to-Accept and Purchase Genetically Modified Rice with High Folate Content in Shanxi Province, China, *Appetite* 54: 118–125.

Einsiedel, E.F., and J. Medlock (2005) A Public Consultation on Plant Molecular Farming, *AgBioForum* 8: 26–32.

Frewer L.J., C. Howard, and J.I. Aaron (1998) Consumer Acceptance of Transgenic Crops, *Pesticide Science* 52: 388–393.

Frewer, L., J. Scholderer, and N. Lambert (2003) Consumer Acceptance of Functional Foods: Issues for the Future, *British Food Journal* 105: 714–731.

Gaskell, G., N. Allum, W. Wagner, N. Kronberger, H. Torgersen, J. Hampel, and J. Bardes (2004) GM Foods and the Misperception of Risk Perception, *Risk Analysis* 24: 185–194.

Gaskell, G. (2000) Agricultural Biotechnology and Public Attitudes in the European Union, *AgBioForum* 3: 87–96.

Goto, R. and Y. Ibuka (2020) Health Economics, Tokyo: Yuhikaku.

Grossman, H. (1972) On the Concept of Health Capital and the Demand for Health, *Journal of*

Political Economy 80: 223–255.

Grunert, K. G., L. Bredahl, and J. Scholderer (2003) Four Questions on European Consumers' Attitudes toward the Use of Genetic Modification in Food Production, *Innovative Food Science & Emerging Technologies* 4: 435–445.

Hallman, W.K., C.L. Cuite, and X.K. Morin (2013) Public Perceptions of Labeling Genetically Modified Foods, Working Paper 2013-01. New Brunswick, New Jersey: Rutgers, The State University of New Jersey, New Jersey Agricultural Experiment Station.

Hensher, D. A., J. M. Rose, and W. H. Greene (2015) Applied Choice Analysis, Cambridge, U.K.: Cambridge University Press.

Hudson, J., A. Capalanova, and M. Novak (2015) Public Attitudes to GM Foods: The Balancing of Risks and Gains, *Appetite* 92: 303–313.

Hynes, S., W. Chen, K. Vondolia, C. Armstrong, and E. O'Connor (2021) Valuing the Ecosystem Service Benefits from Kelp Forest Restoration: A Choice Experiment from Norway, *Ecological Economics* 179, 106833.

Ii, M. and Y. Ohkusa (1999a) Interchangeability between Medical Services and Over-the-Counter Medication in the Case of Common Cold: Analysis Based on an Original Survey, *Iryo to Shakai* 9: 69–82.

Ii, M. and Y. Ohkusa (1999b) Is There any Substitution between Medical Services and Over-the-Counter Medications? *Japanese Journal of Health Economics and Policy* 6: 5–17.

Ii, M. and Y. Ohkusa (2001) An Empirical Research for Demand of Influenza Vaccination, *Japanese Journal of Public Health* 48: 16–27.

Iwamoto, H. (2012) The Effect of Low-Calorie Content Information on Consumers' Choice of Rice, *Journal of Rural Problems* 186: 116–119.

Jit, M. and R. Hutubessy (2016) Methodological Challenges to Economic Evaluations of Vaccines: Is a Common Approach Still Possible? *Applied Health Economics and Health Policy* 14: 245–252.

Johnson, J., K. Howard, A. Wilson, M. Ward, G. Gilbert, and C. Degeling (2019) Public Preferences for One Health Approaches to Emerging Infectious Diseases: A Discrete Choice Experiment, *Social Science & Medicine* 228: 164–171.

Kallas, Z., C.E. Realini, and J.M. Gil (2014) Health Information Impact on the Relative Importance of Beef Attributes Including Its Enrichment with Polyunsaturated Fatty Acids (Omega-3 and Conjugated Linoleic Acid), *Meat Science* 97: 497–503.

Kirk, D.D. and K. McIntosh (2005) Social Acceptance of Plant-Made Vaccines: Indications from a Public Survey, *AgBioForum* 8: 228–234.

Kondo, M., S. Hoshi, and I. Okubo (2009) Does Subsidy Work? Price Elasticity of Demand for Influenza Vaccination among the Elderly in Japan, *Health Policy* 91: 269–276.

Krinsky, I. and L. Robb (1986) On Approximating the Statistical Properties of Elasticities, *Review of Economics and Statistics* 68: 715–719.

Krystallis, A. and P. Chrysochou (2012) Do Health Claims and Prior Awareness Influence Consumers' Preferences for Unhealthy Foods? The Case of Functional Children's Snacks, *Agribusiness* 28: 86–102.

Loureiro, M. L. and M. Bugbee (2005) Enhanced GM Foods: Are Consumers Ready to Pay for the Potential Benefits of Biotechnology? *The Journal of Consumer Affairs* 39(1):52–70.

Louviere, J.J., D.A. Hensher, and J.D. Swait (2000) Stated Choice Methods. Cambridge, U.K.: Cambridge University Press.

Lusk, J.L. (2003) Effects of Cheap Talk on Consumer Willingness-to Pay for Golden Rice, *American Journal of Agricultural Economics* 85: 840–856.

Ogihara, H., A. Yuta, Y. Miyamoto, T. Takeo, and K. Takeuchi (2010). Quality of Life in Allergic Rhinitis Immunotherapy for Japanese Cedar Pollen, *Japanese Journal of Rhinology* 49: 26–32.

Okubo, K. (2015). Guide for Allergy Treatment, Health Labor Sciences Research Grant Report.

R Core Team (2014) R: A Language and Environment for Statistical Computing, Version 3.1.2, Vienna, Austria: R Foundation for Statistical Computing, http://www.R-project.org/

Sabalza, M., P. Christou, and T. Capell (2014) Recombinant Plant-Derived Pharmaceutical Proteins: Current Technical and Economic Bottlenecks, *Biotechnology Letter* 36: 2367–2379.

Saito, Y., Y. Sasakawa, Y. Tabei, S. Ito (2017) Health-Risk Concerns vs. Medical Benefits of the GM Technology, *AgBioForum* 20: 46–53.

Savadori, L., S. Savio, E. Nicotra, R. Rumiati, M. Finucane, and P. Slovic (2004) Expert and Public Perception of Risk from Biotechnology, *Risk Analysis* 24: 1289–1299.

Siegrist, M. (2008) Factors Influencing Public Acceptance of Innovative Food technologies and Products, *Trends in Food Science & Technology* 19: 603–608.

Takaiwa, F. (2004) Development of GM Rice for

Cedar Pollen Allergy Control, *Food Science Journal* 312: 32–38.
Wordsworth, S., M. Ryan, and N. Waugh (2001) Costs and Benefits of Cervical Screening IV: Valuation by Women of the Cervical Screening Programme, *Cytopathology* 12: 367–376.
Yuwen, F. and C. Hsiaoping (2020) Consumers' Preferences towards Nutrition-Modified Milk in Urban Areas of China with Rating-Based Conjoint Analysis, *Japanese Journal of Agricultural Economics* 22: 112–117.

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Appendix A: List of choice sets

Group	Question	Method	Fee	Site	Group	Question	Method	Fee	Site
1	1	Rice	1,000	Factory	4	1	Rice	500	Field
1	1	Injection	500	–	4	1	Injection	1,500	–
1	2	Rice	1,500	Field	4	2	Rice	3,000	Factory
1	2	Injection	2,500	–	4	2	Injection	2,000	–
1	3	Rice	500	Factory	4	3	Rice	1,000	Factory
1	3	Injection	2,000	–	4	3	Injection	1,000	–
1	4	Rice	2,000	Field	4	4	Rice	1,500	Field
1	4	Injection	1,000	–	4	4	Injection	3,000	–
1	5	Rice	2,500	Field	4	5	Rice	2,000	Factory
1	5	Injection	3,000	–	4	5	Injection	500	–
1	6	Rice	3,000	Factory	4	6	Rice	2,500	Field
1	6	Injection	1,500	–	4	6	Injection	2,500	–
2	1	Rice	2,500	Factory	5	1	Rice	500	Factory
2	1	Injection	1,000	–	5	1	Injection	2,500	–
2	2	Rice	1,000	Field	5	2	Rice	2,500	Factory
2	2	Injection	2,000	–	5	2	Injection	500	–
2	3	Rice	3,000	Factory	5	3	Rice	1,000	Field
2	3	Injection	2,500	–	5	3	Injection	1,500	–
2	4	Rice	1,500	Field	5	4	Rice	1,500	Factory
2	4	Injection	500	–	5	4	Injection	1,000	–
2	5	Rice	500	Factory	5	5	Rice	3,000	Field
2	5	Injection	3,000	–	5	5	Injection	3,000	–
2	6	Rice	2,000	Field	5	6	Rice	2,000	Field
2	6	Injection	1,500	–	5	6	Injection	2,000	–
3	1	Rice	2,000	Factory	6	1	Rice	2,500	Factory
3	1	Injection	2,500	–	6	1	Injection	1,500	–
3	2	Rice	2,500	Field	6	2	Rice	2,000	Factory
3	2	Injection	2,000	–	6	2	Injection	3,000	–
3	3	Rice	1,000	Factory	6	3	Rice	3,000	Field
3	3	Injection	3,000	–	6	3	Injection	500	–
3	4	Rice	1,500	Factory	6	4	Rice	500	Field
3	4	Injection	1,500	–	6	4	Injection	1,000	–
3	5	Rice	500	Field	6	5	Rice	1,000	Field
3	5	Injection	500	–	6	5	Injection	2,500	–
3	6	Rice	3,000	Field	6	6	Rice	1,500	Factory
3	6	Injection	1,000	–	6	6	Injection	2,000	–

Appendix B: Variable construction

The reaction severity and schedule flexibility variables are constructed by asking respondents to indicate, respectively, the level of discomfort from cedar pollen on a scale of 0 to 9 (Table B1) and their schedule flexibilities from 0 to 4 (Table B2). The discomfort variable is then constructed by dividing responses by 9 and the hospital visit opportunity cost variable by 4, so that each takes decimal values between 0 and 1. The immunotherapy and GM familiarity, and environmental concern variables are constructed by first providing information on immunotherapy treatment (Table B3) and GM technology (Table B4), and potential environmental risks of GM crop cultivation (Table B5) and then asking respondents to indicate each item on a Likert scale from 0 to 4. To construct the composite Likert variable *FAM_imm*, we sum the ranks of all Table B3 items and divide by 24 to render it as decimal values between 0 and 1. *FAM_gm* and *ENV* are similarly constructed by summing the ranks in Tables B4 and B5, dividing by 40 and 20, respectively.

Table B1. Discomfort from allergic reactions

What is the extent of your discomfort from the allergic reaction to cedar pollen?	No.	%
0 (Least)	1	0.1
1	1	0.1
2	4	0.4
3	13	1.2
4	40	3.8
5	46	4.4
6	166	15.8
7	247	23.5
8	160	15.2
9 (Severe)	373	35.5

Table B2. Schedule flexibility

How flexible is your schedule?	No.	%
0 (Enough spare time)	98	9.3
1	258	24.6
2	313	29.8
3	297	28.3
4 (Not enough spare time)	85	8.1

Table B3. Familiarity with immunotherapy treatment

How familiar are you with the following information about immunotherapy treatment?	Do not know at all				Know very well
	0	1	2	3	4
Diluted allergen is ingested to alleviate allergic reaction	224 (21.3)	290 (27.6)	248 (23.6)	201 (19.1)	88 (8.4)
Occasionally causes anaphylactic shock	415 (39.5)	248 (23.6)	184 (17.5)	137 (13.0)	67 (6.4)
Two to five years required for definitive cure	446 (42.4)	210 (20.0)	180 (17.1)	146 (13.9)	69 (6.6)
Not all patients definitively cured	393 (37.4)	247 (23.5)	195 (18.6)	153 (14.6)	63 (6.0)
Only definitive treatment for cedar pollen allergy	514 (48.9)	209 (19.9)	180 (17.1)	108 (10.3)	40 (3.8)
Only injection or sublingual application available	440 (41.9)	252 (24.0)	191 (18.2)	125 (11.9)	43 (4.1)

Note: Numbers in parentheses represent share of respondents (%).

Table B4. Familiarity with GM foods

How familiar are you with the following information about GM food?	Do not know at all				Know very well
	0	1	2	3	4
GM plants with herbicide tolerance are commercially produced in foreign countries	536 (51.0)	250 (23.8)	148 (14.1)	88 (8.4)	29 (2.8)
GM crops are used in many processed products, such as cooking oil in Japan	475 (45.2)	289 (27.5)	190 (18.1)	79 (7.5)	18 (1.7)
60% of cooking oil processed in Japan is made from GM crops	647 (61.6)	216 (20.6)	127 (12.1)	49 (4.7)	12 (1.1)
Japan imports a lot of GM crops for several purposes, such as animal feeds	523 (49.8)	269 (25.6)	163 (15.5)	75 (7.1)	21 (2.0)
90% of soybeans produced in the U.S. and Brazil are GM crops	642 (61.1)	190 (18.1)	133 (12.7)	66 (6.3)	20 (1.9)
The use of GM crops may not be displayed on the labels of cooking oil in Japan	723 (68.8)	145 (13.8)	116 (11.0)	39 (3.7)	28 (2.7)
The use of GM soybeans must be displayed on the labels of food products in Japan	472 (44.9)	214 (20.4)	199 (18.9)	114 (10.9)	52 (5.0)
Cross-breeding has occurred between wild and GM species in Japan	760 (72.3)	136 (12.9)	104 (9.9)	38 (3.6)	13 (1.2)
Research on GM crops is regulated by law	602 (57.3)	224 (21.3)	140 (13.3)	70 (6.7)	15 (1.4)
Except for flowers, GM plants are not commercially produced in Japan	770 (73.3)	136 (12.9)	99 (9.4)	34 (3.2)	12 (1.1)

Note: Numbers in parentheses represent share of respondents (%).

Table B5. Environmental concerns over GM technology

How much are you concerned about the following potential environmental risks of GM crop cultivation?	Not at all				Very much
	0	1	2	3	4
Interactions between GM species and surrounding ecosystems might cause serious environmental problems	81 (7.7)	120 (11.4)	326 (31.0)	373 (35.5)	151 (14.4)
GM crop production spreads due to cross-breeding between non-GM and GM crops	84 (8.0)	112 (10.7)	325 (30.9)	374 (35.6)	156 (14.8)
GM crops might produce and spread toxic chemicals into the environment	71 (6.8)	78 (7.4)	287 (27.3)	384 (36.5)	231 (22.0)
GM crop cultivation might facilitate herbicide-tolerant weed mutations	74 (7.0)	92 (8.8)	357 (34.0)	368 (35.0)	160 (15.2)
Overuse of insect-resistant GM crops makes insects resistant to those crops	78 (7.4)	66 (6.3)	322 (30.6)	393 (37.4)	192 (18.3)

Note: Numbers in parentheses represent share of respondents (%).