



Cost-effectiveness of a New Opportunistic Screening Strategy for Walk-in Fingertip HbA_{1c} Testing at Community Pharmacies in Japan

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Aiko Shono,^{1,2} Masahide Kondo,² Shuling Hoshi,² Reiko Okubo,³ and Naoya Yahagi^{4,5,6}

OBJECTIVE

A new opportunistic community-based strategy was launched in Japan in April 2014 to detect lifestyle-related diseases, including diabetes, by creating Specimen Measurement Offices (SMOs). SMOs offer walk-in fingertip HbA_{1c} testing. This article aimed to assess the value-for-money of HbA_{1c} testing services at SMOs by conducting a cost-effectiveness analysis.

RESEARCH DESIGN AND METHODS

We compared two scenarios: 1) status quo, defined as HbA_{1c} testing that is available only through conventional screening; and 2) HbA_{1c} testing available at SMOs as a complement to the status quo scenario. The model consisted of a screening module with a decision tree and a disease progression module with a Markov model. We calculated incremental cost-effectiveness ratios (i.e., cost per quality-adjusted life-years [QALYs]) over the lifetime analytic horizon as the primary end point of the cost-effectiveness analysis. In this model, we assumed the participant cohort to be people 40–74 years of age who sought walk-in fingertip HbA_{1c} testing at SMOs on the premises of community pharmacies. Costs and outcomes were discounted at a rate of 3%. The cost-effectiveness was analyzed from a societal perspective.

RESULTS

The incremental cost per individual for those 40–74 years of age was estimated to be –527 U.S. dollars (USD) (–52,722 Japanese yen [JPY]) for HbA_{1c} testing at SMOs compared with the status quo. Incremental effectiveness was estimated to be 0.0203 QALYs for HbA_{1c} testing at SMOs compared with the status quo. Therefore, this cost-effectiveness analysis showed that, compared with the status quo, HbA_{1c} testing at SMOs was more effective and had lower cost for the population studied.

CONCLUSIONS

We consider our results to be robust because most simulations were under the threshold of USD 50,000 (JPY 5,000,000) per QALYs gained, by sensitivity analysis. These results will be useful to managers of pharmacies or other health institutions and/or policy makers in local government.

¹Department of Public Health and Epidemiology, Faculty of Pharmaceutical Sciences, Meiji Pharmaceutical University, Tokyo, Japan

²Department of Health Care Policy and Health Economics, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

³Department of Nephrology, University of Tsukuba, Tsukuba, Japan

⁴Nutrigenomics Research Group, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

⁵Revolution of Access to Diabetes Diagnosis (RADD) Project, Tsukuba, Japan

⁶The Cooperation Council for Specimen Measurement Offices, Tokyo, Japan

Corresponding author: Aiko Shono, shono@my-pharm.ac.jp.

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Type 2 diabetes is often asymptomatic and can remain undiagnosed and untreated for many years, until complications appear (1,2). Detection of prediabetes or early-stage diabetes would provide an opportunity to intervene and delay the development of type 2 diabetes; however, there are disputes about the direct evidence of screening itself (3–6).

There are several different approaches to screening for type 2 diabetes, namely, universal, targeted, community-based, and opportunistic screening. These approaches have been used alone and in combination (6). Nationwide universal screening (Specific Health Checkup [SHC]) includes type 2 diabetes screening in Japan (7) and the National Health Service Health Check program in the U.K., a nationwide targeted screening, which includes a diabetes check as well (8). Opportunistic screening is also common in many countries (6). This involves testing for type 2 diabetes that is conducted at the time of scheduled clinical visits for the management of other diseases (8). Also, opportunistic screening at community pharmacies has been in place in some countries, such as the U.S., Switzerland, the U.K., and Australia (8,9).

In Japan, undiagnosed cases of type 2 diabetes have been estimated to account for ~35% of the total 9.4 million cases among adults in 2015 (10). Currently, the SHC represents one of three available opportunities for type 2 diabetes screening, in addition to conventional opportunistic screening in clinics and walk-in fingertip HbA_{1c} testing at a Specimen Measurement Office (SMO). The Japanese government launched the SHC and Specific Counseling Guidance in 2008 as a nationwide mass screening program to detect metabolic syndrome among adults 40–74 years of age. Insurers are required to allow insured persons 40–74 years of age to participate in the SHC program. During an SHC visit, HbA_{1c} or fasting blood glucose level should be screened to detect type 2 diabetes (11). However, although it is a nationwide program, the SHC coverage was only ~48.6% in 2014 (12).

A new opportunistic community-based strategy was launched in Japan to detect lifestyle-related diseases including diabetes, by creating the SMOs, which offer HbA_{1c} testing, in April 2014. This legislation was prompted by the success of a

trial diabetes screening project, “Revolution of Access to Diabetes Diagnosis” (RADD), which was implemented at 10 pharmacies in Adachi Ward, Tokyo, as a joint program of the nonprofit Adachi Diabetes Mellitus Society and the Adachi Ward Pharmacist Association (13). On 28 February 2018, there were 1,586 SMOs in Japan, mostly established on the premises of community pharmacies or drug stores (14). In Adachi Ward, the RADD evolved in 2015 into an official subsidized program for HbA_{1c} testing at SMOs, to increase participation in diabetes screening. In this locally subsidized program, only 5 U.S. dollars (USD) (equivalent to 500 Japanese yen [JPY]) per test is charged to residents of Adachi Ward, compared with the regular fee of USD 10 (JPY 1,000) at the 10 RADD pharmacies (15).

HbA_{1c} testing at the SMOs is mainly targeted to people who miss or fail to present at SHC visits. The screening complements conventional health services using an innovative approach. If opportunistic screening at SMOs becomes widespread in Japan, it could offer an important resource for people who are not tested by the SHC program. It is suggested that it could also provide a new mode of care in community settings for diverse health care professionals seeking better management of people with diabetes. This article aimed to assess the value-for-money of HbA_{1c} testing services at SMOs from a societal perspective by conducting a cost-effectiveness analysis.

RESEARCH DESIGN AND METHODS

We conducted a cost-effectiveness analysis to evaluate the introduction of HbA_{1c} testing services at SMOs in Japan by adopting a societal perspective. We compared two scenarios: 1) status quo, defined as HbA_{1c} testing that is available only during SHC visits and conventional opportunistic screening in clinics; and 2) HbA_{1c} testing that is available at SMOs as a complement to the status quo scenario.

In the model, the data on SMOs were taken from the RADD Project (16). Data were used from 1,296 people who were 40–74 years of age from a total of 2,024 people who provided HbA_{1c} data to SMOs between October 2010 and May 2014. The total study population ($n = 2,024$) had a mean age of 52.1 years (age range, 17–92 years), and 48% were male. We also carried out a literature search to find relevant available evidence on type 2

diabetes and its complications in Japan; The PubMed database; Igaku Chuo Zasshi (Japan Medical Abstracts Society), a Japanese medical literature database; annual government statistical reports; Ministry of Health, Labour and Welfare (MHLW) grant system; local government reports and tariffs were accessed using various combinations of relevant terms, such as “type 2 diabetes.” We then used those sources to estimate the annual transition probabilities of complications as well as costs.

Opportunistic HbA_{1c} Screening at SMOs

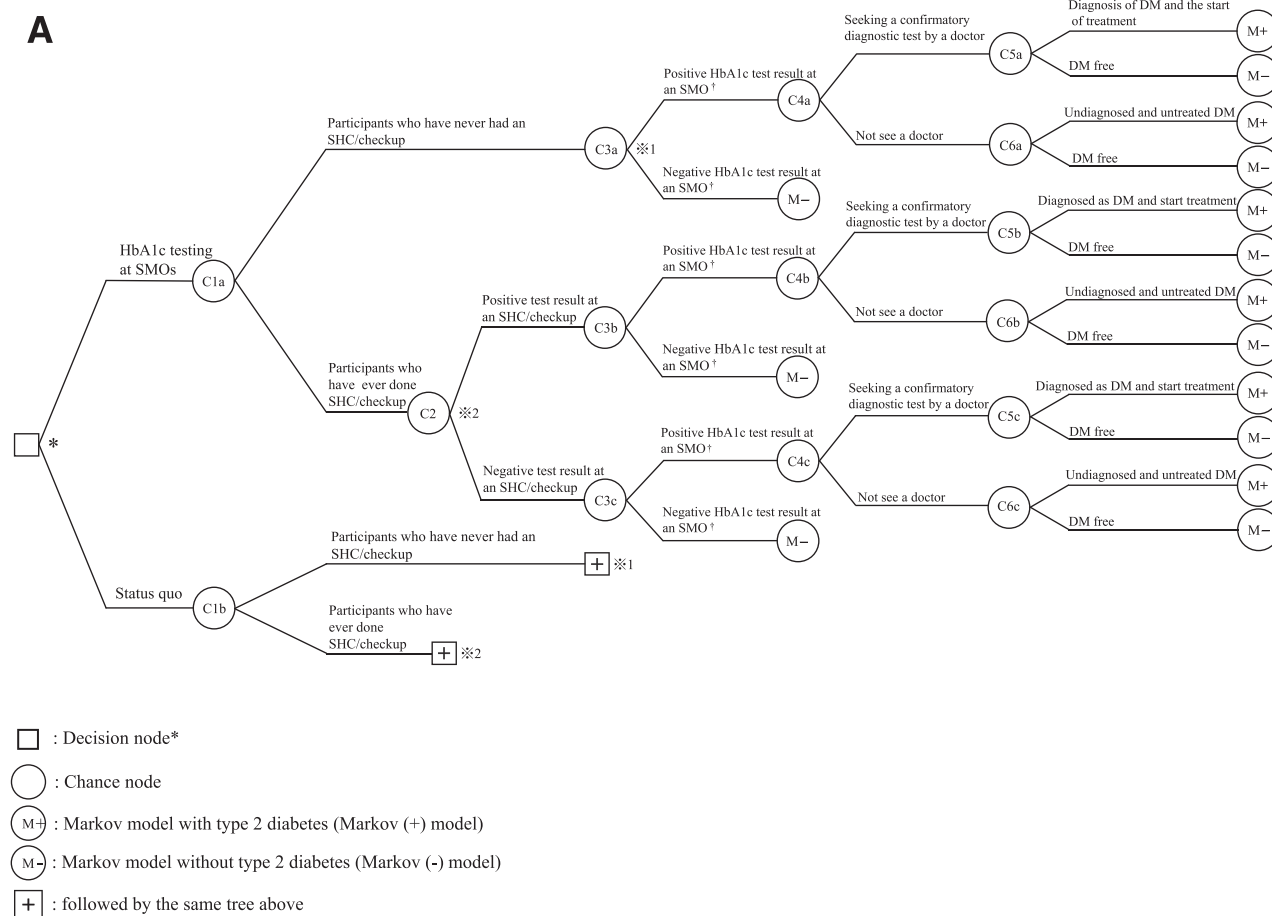
The process modeled for HbA_{1c} testing in pharmacy settings at SMOs is as follows. A customer at a pharmacy asks the pharmacist to have their HbA_{1c} tested. The pharmacist confirms that the customer is not being treated for diabetes mellitus, to exclude patients who have received a diagnosis of type 2 diabetes. After receiving an explanation about the HbA_{1c} test from the pharmacist, the customer undergoes testing. The pharmacist gives the customer their results together with information about how to interpret the results. The customer is advised to visit their family doctor if their HbA_{1c} level is not <6.0% (42 mmol/mol) (16).

Target Population

In this model, we assumed the participant cohort to be individuals 40–74 years of age who sought walk-in fingertip HbA_{1c} testing. In addition, we assumed a hypothetical scenario of only one HbA_{1c} test at an SMO for the age groups 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74 years. At the initial stage of the model, every person is assumed to have no diagnosis of or have not been treated for type 2 diabetes. The model consisted of a screening module with a decision tree (Fig. 1A) and a disease progression module with a Markov model (Fig. 1B).

Model Assumption

Two scenarios were modeled as follows: 1) status quo; and 2) complementary HbA_{1c} testing at SMOs. The model was a combination of a decision tree and a Markov model. The decision tree included two main nodes, as follows: 1) the decision node, which represented the decision made by pharmacy managers about whether to establish an SMO that provided HbA_{1c} testing on the pharmacy premises; and 2) chance nodes, which



SMO: Specimen measurement office

SHC: Specific health checkup

DM: type 2 diabetes

*Target population: aged 40–74 years those who sought walk-in fingertip HbA_{1c} testing at SMOs. Individuals who do not undergo HbA_{1c} testing at SMOs were omitted in this model

† “positive test result” is as over the cut-off point; 6% (42 mmol/mol), and “negative test result” is as less than cut-off point

Figure 1—A: Model: decision tree. **B:** Model: Markov model with type 2 diabetes state. **C:** Model: Markov model with no type 2 diabetes.

represented the possible events that could occur (17). In Japan, 6% (42 mmol/mol) has been adopted by the National Health and Nutrition Survey as the cutoff value for defining the risk for the development of type 2 diabetes. Therefore, in the current study, a participant with an HbA_{1c} test result above this cutoff value was defined as a person at risk for diabetes. Additional details are shown in the Supplementary Appendix, and other probabilities assigned to the chance nodes are shown in Supplementary Table 1.

The following two kinds of Markov models followed the decision tree: a Markov positive model (Markov [+]) model, which suggests the prognosis for a person with type 2 diabetes (Fig. 1B); and a

Markov negative model (Markov [–]) model, which suggests the future for a person without type 2 diabetes (Fig. 1C).

The Markov (+) model comprised a series of five health states that a patient can have at a given point in time (17): 1) type 2 diabetes without complications 2); end-stage renal disease (ESRD) 3); cardiovascular disease (CVD) 4); amputation 5); blindness; and 6) death. For type 2 diabetes, each person was assumed to have a single complication rather than multiple complications. Each transition probability defines the rate at which each complication is reached with or without treatment as well as the probability of death from no diabetes or diabetes without complications as well as

diabetes with a complication. We assumed that the age-specific probability of death for those without diabetes and those with diabetes without complications or with blindness only were the same (18).

The Markov (–) model comprised the following two states 1): no type 2 diabetes at a given point in time; and 2) death. Annual transition probabilities (death with no type 2 diabetes) were determined using vital statistics (19). The effects of early intervention for type 2 diabetes were included in the Markov (+) model. One Markov cycle was set at 1 year. Individuals who did not undergo HbA_{1c} testing at SMOs were omitted from this model because they would have

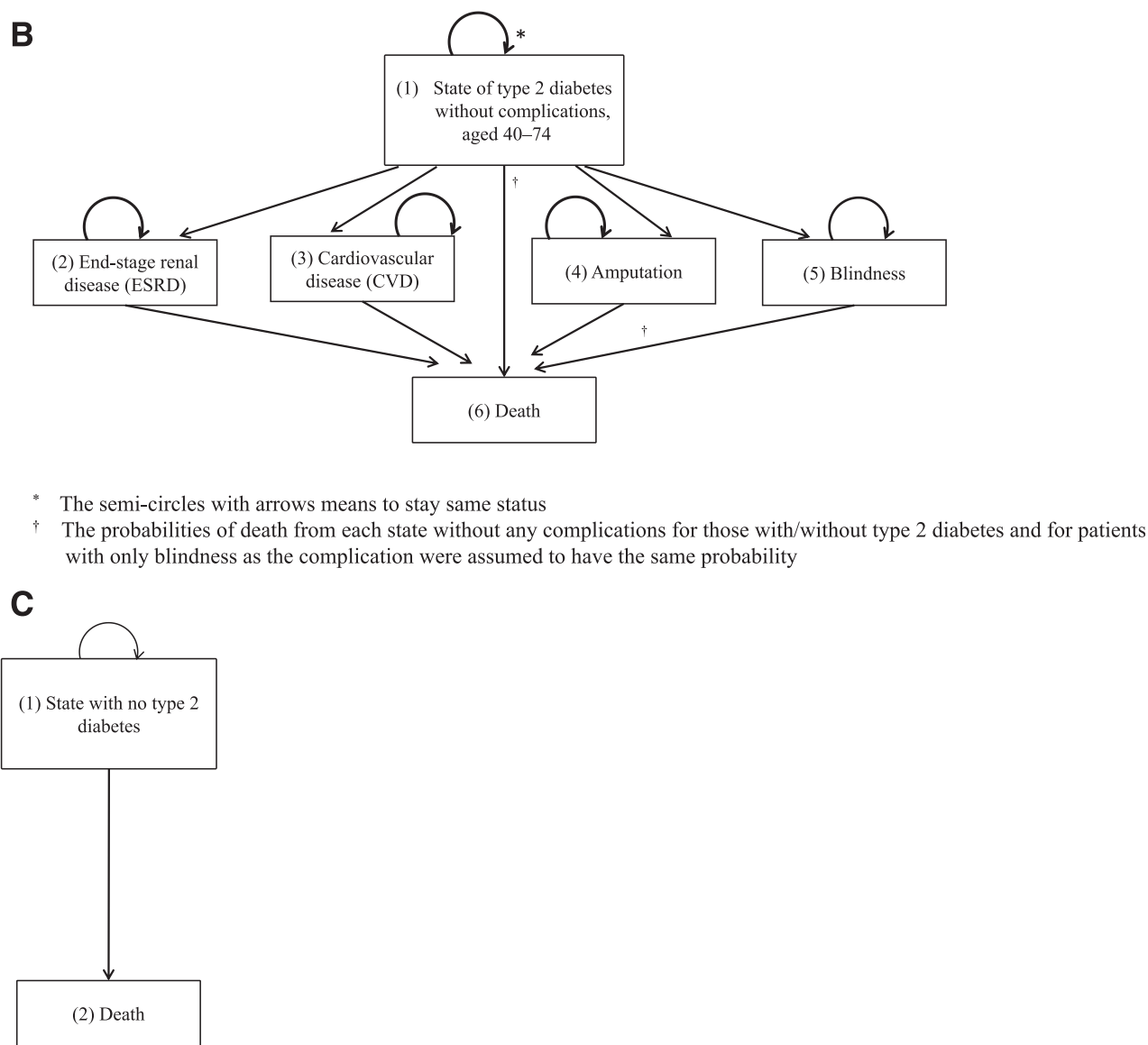


Figure 1—Continued.

produced no effects in terms of cost and effectiveness in either scenario.

Utilities

Utility weights used to calculate quality-adjusted life-years (QALYs) were 1.0 for individuals without type 2 diabetes, 0.910 for individuals with early-stage type 2 diabetes without complications (20), 0.884 for individuals with advanced type 2 diabetes without complications (20), 0.746 for individuals with CVD (21), 0.620 for individuals with ESRD (22), 0.559 for individuals with amputation (22), 0.536 for individuals with blindness (22), and 0 for the individual who died. The deterioration of utility is assumed to occur at years 6 and 10 for untreated case patients and treated case

patients, respectively (23,24). The utility weight for each undetected case of type 2 diabetes was assumed to be the same as the value for each detected case of type 2 diabetes without complications (25).

Costs

In this study, costs were considered for HbA_{1c} testing and treatment for type 2 diabetes and complications, including the costs of confirmatory HbA_{1c} testing by a doctor. These cost data were mainly estimated using the published literature and expert opinion. Costs are expressed in USD as well as JPY. Cost was not adjusted for the consumer price index in this article because consumer prices have barely changed. These costs were used for modeling in the decision tree

and Markov model (Table 1). The cost for HbA_{1c} testing at SMOs is shared by pharmacies and individuals. The costs for confirmatory testing and treatment for type 2 diabetes and complications are shared by social insurance and patients. The direct costs for treatment for type 2 diabetes were mainly estimated using medical fee tariffs; costs for sectors other than health and productivity losses were uncounted for in this study.

The cost of each HbA_{1c} test at SMOs, USD 12 (JPY 1,229), was estimated based on data from the RADD Project. The costs consist of fixed/variable capital costs and labor cost. The fixed capital cost, USD 1 (JPY 122), is calculated from the annualized capital cost of the testing equipment and an expected 732 tests, according

Table 1—Model assumption on costing

Annual cost per persons	Base-case value		References
	USD	JPY	
HbA _{1c} check in SMO	12	1,229	(26) and expert opinion
HbA _{1c} check in SHC	9	918	(27)
Detailed examination	78	7,800	(22)
Type 2 diabetes treatment	3,700	370,000	(28)
ESRD treatment	48,230	4,823,000	(29)
CVD treatment			(21)
First year	19,990	1,999,000	
Second year	1,790	179,000	(21)
Amputation treatment (1st year)	22,910	2,291,000	(30)
Blindness treatment	760	76,000	(30)

to the RADD Project, in a year. The variable capital cost includes the price of a test kit: USD 6 (JPY 560) per participant. The pharmacist's labor cost for a 15-min test, USD 5 (JPY 547), is calculated from an average hourly wage of USD 22 (JPY 2,189) for a pharmacist (26). The cost of an HbA_{1c} test at the SHC was estimated to be USD 9 (JPY 918) (27).

The costs of confirmatory testing and treatment for type 2 diabetes and complications were estimated as follows. For people with positive HbA_{1c} test results at SMOs, a cost of USD 78 (JPY 7,800) was set for additional testing (22). The annual costs for outpatient treatment for type 2 diabetes was set at USD 3,700 (JPY 370,000) (28). The annual cost for ESRD treatment was set at USD 48,230 (JPY 4,823,000) (29). The cost in the first year for CVD treatment was set at USD 19,990 (JPY 1,999,000), and USD 1,790 (JPY 179,000) in the second year (21). The cost of amputation in the first year was set at USD 22,910 (JPY 2,291,000) (30). The annual cost of blindness was set at USD 760 (JPY 76,000) (30). Most data were estimated from the medical care fee schedule in Japan.

We took a life-long time horizon, and the Markov cycle was repeated as the age stratum reached 100 years old.

Discounting

Costs and outcomes were discounted at a rate of 3% (17).

Sensitivity Analysis

In this study, we performed one-way sensitivity analyses for our model assumptions. In the analyses, lower and upper limits were applied as plausible values from references in case there was an absence of information on values, such as 95% CI (Supplementary Table 1).

We also conducted a probabilistic sensitivity analysis using a set of 1,000 Monte Carlo simulations. The distributions for variables of probabilities, utilities, and the discount rate were assumed to have triangular distribution, and those for variables of costs were assumed to have a γ -distribution. The lower and upper limit ranges in the triangular distribution were applied in the same way as in the one-way sensitivity analysis.

Comparison

In this study, we compared two scenarios to be chosen by pharmacy managers: 1) status quo, defined as HbA_{1c} testing only at SHC visits and conventional opportunistic screening in clinics; and 2) HbA_{1c} testing at SMOs as a complement to the status quo. We calculated the respective costs and effects of these scenarios, and the difference between costs and effectiveness was compared. That is, we calculated incremental cost-effectiveness ratios (ICERs; cost per QALYs) over the lifetime analytic horizon as the primary end point of the cost-effectiveness analysis. ICERs were defined as follows:

$$\text{ICER} = \frac{\text{Incremental cost}}{\text{Incremental effectiveness}}$$

$$= \frac{\text{Cost HbA}_{1c} \text{ testing at SMOs} - \text{Cost status quo}}{\text{Effectiveness HbA}_{1c} \text{ testing at SMOs} - \text{Effectiveness status quo}}$$

Model outcomes were analyzed using TreeAge Pro 2016 (TreeAge Software, Inc., Williamstown, MA).

RESULTS

Base-Case Analysis

The total cost per individual for those individuals 40–74 years of age was

estimated to be USD 4,951 (JPY 495,053) for HbA_{1c} testing at SMOs, compared with USD 5,478 (JPY 547,775) for the status quo scenario. QALYs were estimated to be 17.996 for HbA_{1c} testing at SMOs compared with 17.975 for the status quo. Therefore, the total gain in QALYs was greater, and the total cost was lower for HbA_{1c} testing at SMOs compared with the status quo. Thus, this cost-effectiveness analysis showed that, compared with the status quo, introducing HbA_{1c} testing in SMOs is more effective and less costly, which means cost saving with improved QALYs for the population 40–74 years of age (Table 2). We conducted a subgroup analysis by each age group and assumed the participant cohort to be 40–74 years of age (in 5-year increments). The largest outcome gain in QALYs was estimated to be among individuals 60–64 years of age. The introduction of HbA_{1c} testing at SMOs remained dominant in all age groups from 40 to 74 years (Table 2). We also conducted a subgroup analysis focusing on the participant cohort as specific age groups in those participants 40–74 years of age (in 5-year increments) (Supplementary Table 2).

Stability of Cost-effectiveness

Sensitivity analysis is commonly used for handling uncertainty. Figure 2A shows the results of one-way sensitivity analysis for the top 10 variables that effect ICER, depicted as tornado diagrams. The parameters that have a potential effect on ICER could differ depending on the variable. Each transition probability for progression to ESRD among individuals with type 2 diabetes with and without treatment for type 2 diabetes affected the ICERs. ICER was sensitive to the utility of ESRD and to each probability for death because of ESRD among both male and female participants.

Figure 2B shows the results of probabilistic sensitivity analyses by depicting 1,000 ICERs produced by Monte Carlo simulations. HbA_{1c} testing in SMOs was estimated to cost less and gain more in 63.8% of simulations. This was also estimated to be cost-effective in 90.6% of simulations, including dominant cases, which were under the threshold of USD 50,000 (JPY 5,000,000) per QALY gained; 97.7% of simulations, including dominant cases, were under the threshold of USD 100,000 (JPY 10,000,000) per QALY. Figure 2C shows scatter plots of

Table 2—Results of cost-effectiveness analysis

Age of target population		Cost (\$ and ¥)	Incremental cost (\$ and ¥)	Effectiveness (QALYs)	Incremental effectiveness (QALY)	ICER([\$/ and ¥]/QALY)*
Age 40–74 years	Status quo†	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs‡	\$4,951 ¥495,053	–\$527 –¥52,722	17.996	0.0203	Cost less, gained more
Age 40–44 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,407 ¥540,718	–\$71 –¥7,057	17.977	0.0021	Cost less, gained more
Age 45–49 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,418 ¥541,769	–\$60 –¥6,007	17.977	0.0019	Cost less, gained more
Age 50–54 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,392 ¥539,164	–\$86 –¥8,612	17.978	0.0030	Cost less, gained more
Age 55–59 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,393 ¥539,281	–\$85 –¥8,494	17.979	0.0032	Cost less, gained more
Age 60–64 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,379 ¥537,919	–\$99 –¥9,856	17.980	0.0041	Cost less, gained more
Age 65–69 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,396 ¥539,615	–\$82 –¥8,160	17.979	0.0037	Cost less, gained more
Age 70–74 years	Status quo	\$5,478 ¥547,775		17.975		
	HbA _{1c} testing at SMOs	\$5,432 ¥543,239	–\$45 –¥4,536	17.978	0.0022	Cost less, gained more

JPY, ¥; USD, \$. *ICER (cost per QALY). †Status quo, defined as HbA_{1c} testing only at SHC visits and conventional opportunistic screening in clinics. ‡HbA_{1c} testing services available at SMOs.

the cost-effectiveness plane; 0% of simulations showed negative QALY gained.

CONCLUSIONS

This study assessed the cost-effectiveness of a new walk-in fingertip HbA_{1c}

testing strategy at SMOs in Japan, such as at community pharmacies. The results showed that HbA_{1c} testing services available at SMOs offer cost savings compared with the status quo of HbA_{1c} testing only at SHC visits and

conventional opportunistic screening in clinics.

We focused on walk-in fingertip HbA_{1c} testing for the early detection of diabetes through HbA_{1c} screening in a pharmacy setting, a unique point of this study. If

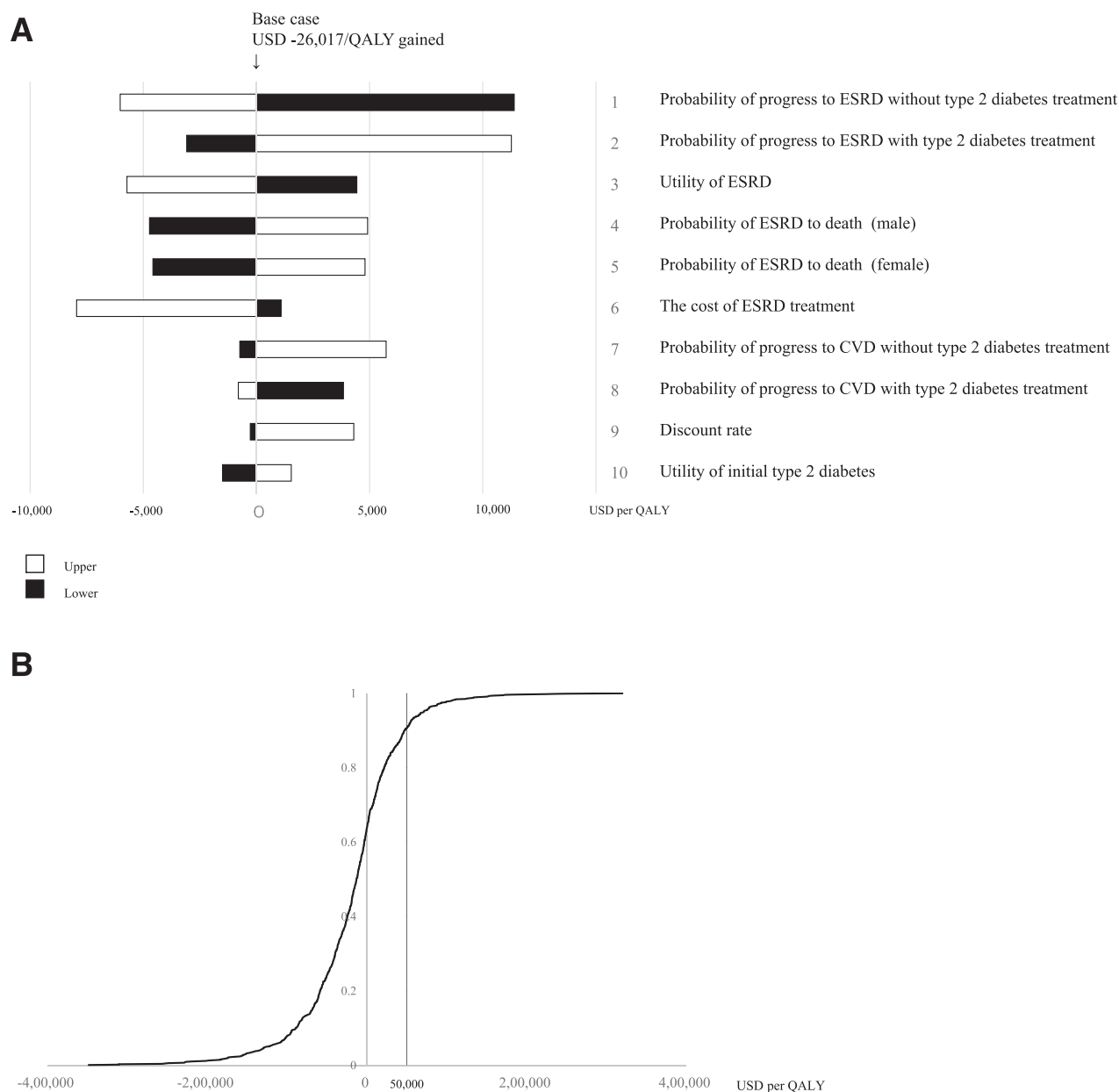


Figure 2—A: Sensitivity analysis: results of one-way sensitivity analysis. **B:** Sensitivity analysis: results of probabilistic sensitivity analyses. **C:** Sensitivity analysis: scatter plots of cost-effectiveness plane.

given the opportunity, some individuals who test positive in this setting would seek confirmatory testing and receive a diagnosis by a doctor, which could lead to earlier intervention. This study is different from other cost-effectiveness studies that have focused on type 2 diabetes screening strategies such as universal, community-based, targeted, and opportunistic screening conducted together with management for other diseases like hypertension (6,31). Complementary HbA_{1c} testing in SMOs could benefit the population who live far from the SHC or checkup sites or conventional opportunistic screening.

Based on the RADD Project background, we modeled walk-in fingertip HbA_{1c} testing in an SMO setting. In this model, we took the following points into account. First, the percentage of individuals who have never undergone routine SHC checkups was 21.2% on average (for individuals 40–74 years of age). Second, the proportion of individuals with HbA_{1c} level ≥ 6.0 mmol/mol among all participants (age range, 40–74 years) who had never had a health checkup was 32.8%. Therefore, $\sim 7\%$ ($21.2\% \times 32.8\%$) of participants newly learned that they possibly had type 2 diabetes in the pharmacy settings. There is an undiagnosed

population with type 2 diabetes of ~ 3.3 million in Japan (10). This model is generalized for the population who are unaware of walk-in fingertip HbA_{1c} testing besides a lack of access to SHC checkups.

We consider our results to be stable and robust since most simulations are under the threshold of USD 50,000 (JPY 5,000,000) per QALY gained. In one-way sensitivity analysis, this model was most sensitive to probabilities of transition from type 2 diabetes to ESRD with and without treatment for type 2 diabetes. The speed of the progress to ESRD by early detection of type 2 diabetes and intervention for effective management

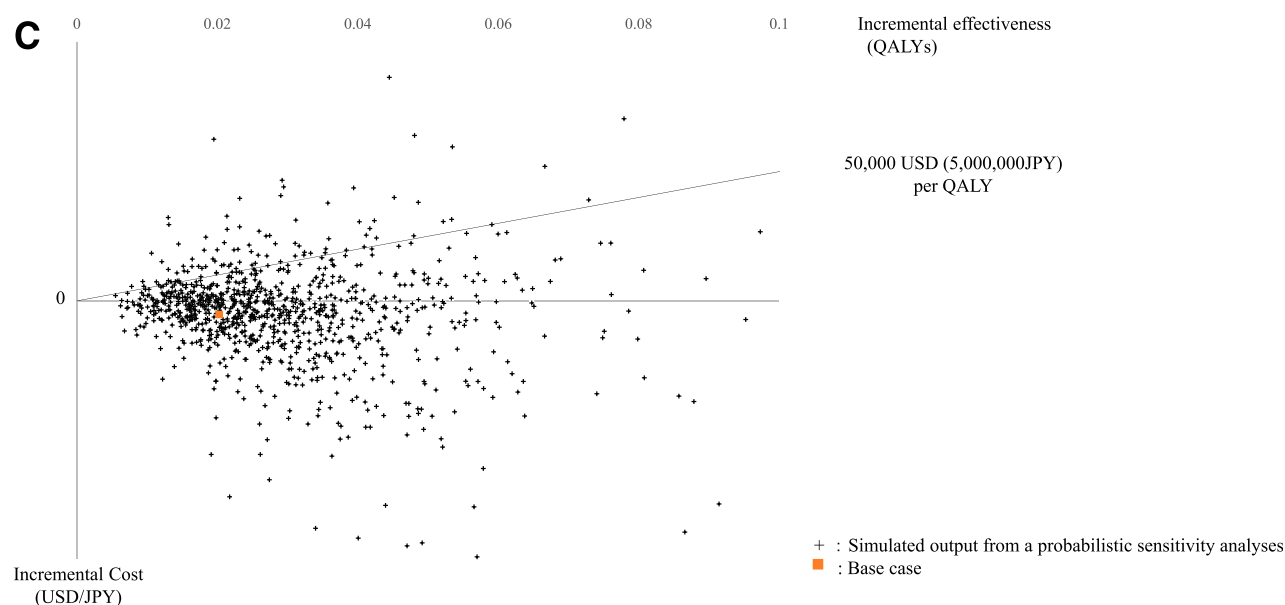


Figure 2—Continued.

to delay to ESRD could affect the ICER results (32). The probability for death because of ESRD was also a sensitive parameter to ICER. However, the crude death rate has remained stable at between 9.2% and 10.2% for the last 20 years (33).

Our results will be useful to managers of pharmacies or other health institutions and/or to policy makers in local government. Local policies, such as the subsidy program in Adachi Ward, Tokyo, for HbA_{1c} testing services provided in 10 pharmacies as SMOs since April 2015, are worth consideration. The similar subsidy programs are currently implemented in Mihara-city, Hiroshima, and Gyoda-city, Saitama, as well. Our results also have implications for policy makers in foreign countries that use community pharmacies for diabetes risk assessment programs (9).

This study has several limitations that must be considered when interpreting the results. First, the model in this study is a simplified economic model. We input four major complications of type 2 diabetes and considered each as a single item in the model. However, the consequences of type 2 diabetes vary in the real world, including the complications used in the model. Additionally, we simplified the definition of CVD to include coronary heart disease and stroke in the model. The cost was also determined using the same assumption (21). Second, although the effect of treatment on type 2 diabetes would depend upon treatment uptake, types, and adherence,

we assumed a population with 100% adherence to treatment in the model. The ICER may be biased as either lower or higher when participants stop medication. Whereas the effectiveness is overestimated, costs might be either lower or higher. Third, it is quite difficult to identify the transition probability of each complication for the population of individuals who did not undergo testing. Therefore, those transition probabilities were estimated using sequential/serial data, such as checkup data. Additionally, the possibility of multiple complications may not have been excluded from the probabilities. Fourth, the utility weight was estimated as higher, at 9 years for treated case patients and 5 years for untreated case patients (23,24). This estimation of a 4-year gap might be an underestimated outcome; however, this gap affected the outcomes slightly. Fifth, testing HbA_{1c} does not always provide a robust method for screening for type 2 diabetes. However, we considered that it was a suitable method in the pharmacy setting because of convenience. Finally, we should consider the different progression of type 2 diabetes at a timing of SMO testing as heterogeneity. The effect of treatment for type 2 diabetes, that is, the transition probability of complications, could differ depending on the baseline. However, there are no data identifying the exact duration of type 2 diabetes, especially for patients who have never undergone testing or received

medication. The base case was assumed using results from national surveys, such as the National Health and Nutrition Survey, and/or those from retrospective/prospective research surveys in Japan.

In summary, this study suggests that the introduction of HbA_{1c} testing in SMOs can be justified as an efficient use of finite health resources. Therefore, introducing opportunistic HbA_{1c} testing at SMOs that are mostly in community pharmacy settings is worth consideration by pharmacy managers and programs subsidized by local governments.

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