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A Cost Benefit Analysis of AminoIndex™ Cancer Screening in Japan

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Abstract:

This article presents a cost benefit analysis of AminoIndex™ Cancer Screening (AICS) in Japan. AICS is a new cancer diagnosis method based on profiles of amino acids. The cost benefit analysis is performed on each type of cancer, each sex, and each age class. The results indicate that AICS is cost-beneficial mainly for 50-75 years old for screening of several types of cancer including stomach, lung, and colorectal cancer. AICS is also cost-beneficial for younger female for screening of uterine-ovarian cancer.

1. Introduction

Cancer is the most popular cause of death in Japan. In 2010, 29.5% of the Japanese people die from cancer. The reasons for this include lengthened life expectancies and changes in dietary habits. The prevention, early detection and treatment for cancer are becoming more and more important. Especially for early detection of cancer, cancer screening is known as one of the most effective ways. The government currently recommends cancer screening by distributing coupons and providing consultation services. Though there are evidences that show the current cancer screening is effective for early detection and decreasing death from cancer, there is still more needs for them. In addition, the current cancer screening is limited to several type of cancer.

Recently new technological progress leads to a new method of cancer screening: AminoIndex™ Cancer Screening (AICS). AICS is a new cancer diagnosis method based on profiles of amino acids. As shown in …, AICS is effective for early detection of cancer from a medical and scientific point of view. However, the economic effectiveness of AICS is still an open question. The economic effectiveness refers to the economic benefit of patients compared to the economic cost of patients. The economic effectiveness is important because the patients choose and demand a medical test by taking into account their benefit and cost. Therefore, whether they demand a medical test, or equivalently whether it contributes to the welfare of the people, depends on the economic effectiveness. This article gives a cost-benefit analysis of AICS and measures the economic effectiveness of AICS. Specifically, we can answer to the following questions: when should we take AICS? Who should take AICS? For what types of cancer is AICS effective? We also evaluate the current cancer screening.

This article is organized as follows. In section 2, we overview the technological aspect of AICS. Section 3 gives the cost-benefit analysis of AICS. Section 4 conducts sensitivity analysis. In section 5, we present the data source that we employ in our analysis. Section 6 concludes this article.

2. Technical Characteristics of AminoIndexTM Cancer Screening (AICS)

Various screening methods have been established for the cancers. For gastric cancer, both X-ray examination and endscope is used for screening. For lung cancer, both X-ray and sputum cytology is used. In other case, fecal occult blood examination for colorectal cancer, prostate specific antigen (PSA) for prostate cancer, mammography and clinical breast examination for breast cancer, and cytology for cervix cancer, are used generally, respectively. However, the high specificity of these methods means that subjects must undergo each screening examination separately, which can be expensive and time consuming. These examinations can also impose a physical and/or mental burden upon subjects, which can lead to avoidance. By contrast, the method described in the present study involves a relatively simple plasma assay and imposes a lower physical burden on subjects.

Several rapid advances have been made in easy-to-use cancer diagnosis methods based on profiles of metabolites using biological samples such as peripheral blood and urine. Among several metabolites, amino acids are among the most suitable candidates as their physiological characteristics. Especially, plasma free amino acids (PFAAs), which abundantly circulate as a medium linking all organ systems, would be the most favorable target because their profiles have been known to be altered by specific diseases including cancer[1,2)].

Additionally, analytical technologies have recently been developed to analyze amino acids with high accuracy by means of high-performance liquid chromatography (HPLC)–electrospray ionization (ESI)–mass spectrometry (MS).

Many studies have also reported changes in PFAA profiles in various diseases including cancer. However, despite evidence of a relationship between PFAA profiles and diseases, few studies have explored the use of PFAA profiles for practical diagnosis. Although PFAA profiles differ significantly between patients, the discriminating ability of the difference of concentration of single plasma amino acid was not sufficient for clinical use. To overcome this problem, we established the concept of the "AminoIndex technology", to compress multidimensional information from PFAA profiles into single dimension and maximize the differences between patients and controls (Figure 1)[3].

In general, multivariate discriminating function is inferred as described below;

1. *Multivariate analysis with variable selection;* usually, linear models such as linear regression analysis, logistic regression analysis, linear discrimination analysis, etc, are used according to the characteristics of the case and model. Variable selection is to be performed as stepwise variable selection, or model selection among all the possible combinations based on specific statistics such as Akaike Information Criterion (AIC), Area under Curve (AUC) of Receiver Operator Characteristics (ROC) curve, and so on.

2. *Cross validation;* then cross validation (CV) was performed to correct potential over-optimization for obtained model. For example, leave one out cross validation (LOOCV) is the most preferable method. In brief, one sample was omitted from the study data set, and the model was calculated for the remaining samples to estimate coefficients for each amino acid. The function values for the left-out sample were calculated based on the model. This process was repeated until every sample in the study data set had been left out once. Else, hold out method, or bootstrap method is also to be used.

Plasma samples were collected from approximately 200 patients from multiple institutes, each diagnosed with one of the following five types of cancer: lung, gastric, colorectal, breast, prostate, or gynecologic cancers, i.e. cervix, endometrial, and ovarian cancers, including early stage cancer patients. Patients were compared to five age- and gender-matched control groups. Index for each cancer was estimated by conducting with multivariate logistic regression analysis using plasma concentrations of amino acids as explanatory variables and presence (=1) or absence (=0) of cancer as objective variable, respectively[3].

After inferring of statistically most suitable models, the validities of the models were estimated using independent validation data set[4,5].

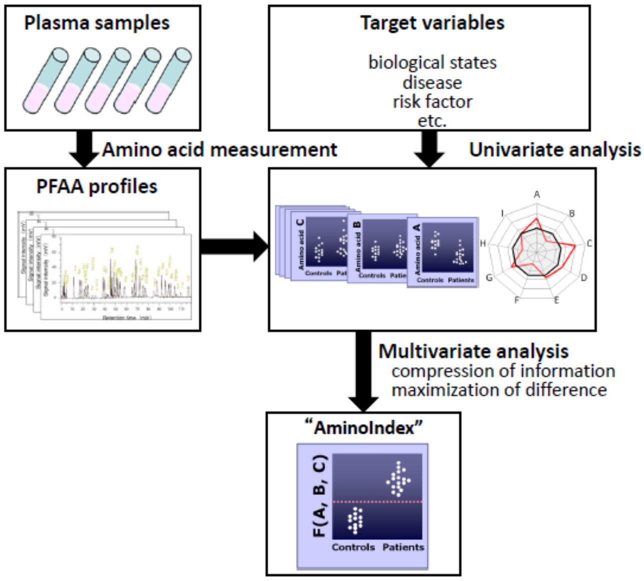

Figure 1. Concept of the "AminoIndex Technology"[3].

By means of validation, using independent validation data set, clinical characteristics of AICS test have been estimated. In general, performance of clinical assay is to be estimated by sensitivity, specificity, and positive predictive value (PPV). Conceptually, the result of clinical assay is categorized into four groups as shown, true positive, true negative, false positive, and false negative. Sensitivity is determined as the ratio of true positive to summation of true positive and false negative (A/A+B), specificity is determined as the ratio of true negative to summation of true negative and false positive (D/C+D), respectively. PPV is determined as the ratio of true positive to summation of true positive and false positive (A/A+C). Both sensitivity and specificity is not to be influenced the frequency of the patient of the subjects (prevalence, (A+B)/(A+B+C+D)) whereas PPV is to be influenced strongly by prevalence.

	With disease	Without disease
Test positive	True positive (A)	False positive (C)
Test negative	False negative (B)	True negative (D)

Sensitivitiesand at specificities are 80% and 95% for each cancer are as summarized below[4,5];

	Sensitivity at 80% specificity	**Sensitivity at 95% specicifity**
Gastric cancer	75%	51%
Lung cancer	73%	45%
Colorectal cancer	60%	41%
Prostate cancer	64%	32%
Breast cancer	47%	20%
Gynecologic cancer	80%	58%

For PPV estimation, prevalence is substituted the incidence rate data from “A Study of 21 Population-based Cancer Registries for the Monitoring of Cancer Incidence in Japan (MCIJ) Project” was used because there are no available prevalence data in Japan[6].

Besides those parameters, AICS test has noteworthy characteristics from the view point of early detection. Almost same sensitivity is observed regardless the cancer stage in AICS test while decrease of sensitivities for early stage cancer is broadly observed in existing method used in population-based screening. Early detection of cancer is one of the effective provision to decrease of the death from cancer for several cancer.

In summary, AICS test is simple, high-throughput and versatile method for early detection of several kinds of cancer.

3. Cost-Benefit Analysis

3-1. Overview of Our Method

Our analysis is based on the incremental cost-benefit analysis. The incremental cost-benefit analysis compares the increased cost and increased benefit when a new treatment would be taken in addition to a basic treatment, and evaluates the economic efficiency of the new treatment. In our case, we compares the increased cost and increased benefit when patients undergo AICS in addition to the normal cancer screening, and indicates whether AICS is efficient for patients to take in the economic sense.

For this purpose, we consider two scenarios:

(1) Patients undergo cancer screening.

(2) Patients undergo both cancer screening and AICS.

We estimate the cost and benefit in each scenario. C1 denotes the cost of case (1), and C2 denotes the cost of case (2). B1 denotes the benefit of case (1), and B2 denotes the benefit of case (2). Then, the incremental cost is defined as C1 – C2, and the incremental benefit is defined as B1 – B2. Then, we calculate the index of the economic efficiency of AICS when patients would take AICS in addition to the cancer screening.

Incremental Cost-benefit Ratio
= Incremental Benefit of AICS / Incremental Cost of AICS
= (B1 – B2) / (C1 – C2)

If the incremental cost-benefit ratio exceeds 1, we conclude that the case (2) is better than the case (1). In other words, AICS is desirable for patients to undergo. On the other hand, if the incremental cost-benefit ratio is lower than 1, we conclude that case (2) is worse than the case (1). In other words, AICS is not desirable for patients to undergo.

Note that our incremental cost-benefit analysis indicates whether AICS should be taken from patients' point of view, not from society's point of view. Our analysis is on the patients' decision for AICS, and hence only focuses on the patients' own payments and own benefit. However, we can alternatively consider other types of cost and benefit. For example, the national health insurance has to pay for the treatment of cancer, and the increased survival rate of patients give positive externality to the productivity of the whole economy. In our analysis, these social cost and benefit are not taken into account.

3-2. Action Trees

For the estimation of the cost and benefit in each scenario (C1, C2, B1, and B2), we need to clarify the actions that patients take in each scenario. We employ the action trees to illustrate what actions patients take and how each of C1, C2, B1, and B2 is measured.

The action tree for the patients with and without cancer in case (1) is shown in the figure 2. Patients are assumed to take these actions in case (1). We divide the patients into two types: "with cancer" and "without cancer".

First, consider the patients with cancer. The patients take the cancer screening. The cancer screening test shows positive or negative. If it is positive, they undergo a detailed examination. The examination can detect both early and advanced cancer. When the cancer is detected at the early stage, the patients take unserious treatment and survival rate is relatively high. Note that, on the other hand, the cancer screening can show false negative. If it is (false) negative, they do not undergo a detailed examination. No examination can not detect early cancer, and in a while patients are found to have advanced cancer. When the cancer is at the advanced stage, the patients take serious treatment and survival rate is relatively low.

Second, consider the patients without cancer. The patients take the cancer screening. The cancer screening test shows positive or negative. Note that there can be false positive in the cancer screening. If it is (false) positive, they undergo a detailed examination. If it is negative, they do not undergo a detailed examination. However, whichever they undergo examination or not, they are found to have no cancer, and receive no treatment.

Positive	Exam
Negative	No Exam

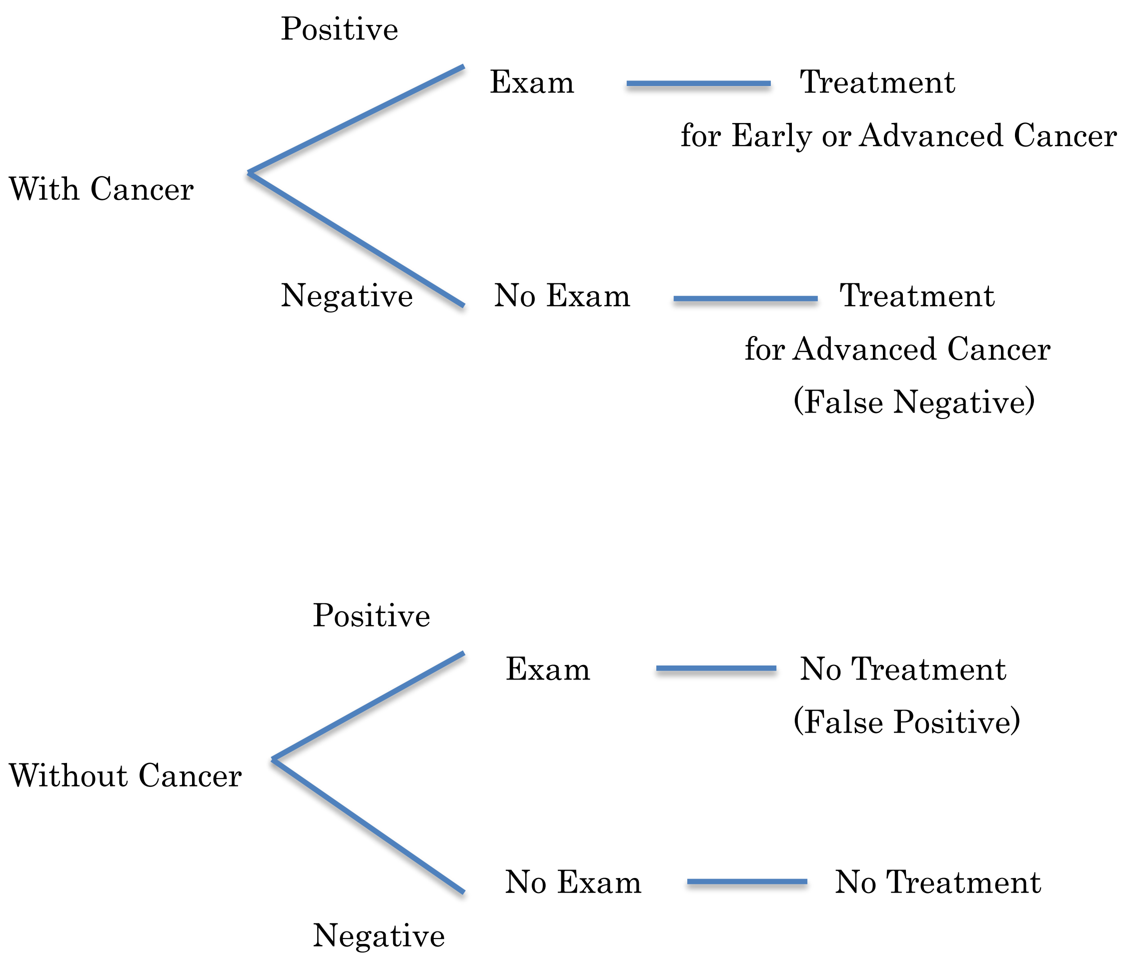

Figure 2. Action Tree in the Case (1)

The action tree for the patients with and without cancer in case (2) is shown in the figure 3. First, consider the patients with cancer. The patients take both the cancer screening and AICS. The cancer screening and AICS are positive or negative respectively. If at least one of them is positive, they undergo a detailed examination. The examination can detect both early and advanced cancer. When the cancer is detected at the early stage, the patients take unserious treatment and survival rate is relatively high. Note that, on the other hand, the cancer screening and AICS can show false negative. If both of them are (false) negative, they do not undergo a detailed examination. No examination can not detect early cancer, and in a while patients are found to have advanced cancer. When the cancer is at the advanced stage, the patients take serious treatment and survival rate is relatively low. It should be noted that the possibility of cancer detection in the case (2) is calculated as follows:

Possibility of Cancer Detection = Incidence Rate ×
{1 – (1 - Sensitivity) × (1 – AICS Sensitivity) }.

Especially for patients with early stage, the possibility of cancer detection in the case (2) is calculated as follows:

Possibility of Early Stage Cancer Detection = Incidence Rate ×
{1 – (1 - Sensitivity × ratio of early stage cancer detected in existing screening) × (1 – AICS Sensitivity × ratio of early stage cancer detected in AICS) },

where ratio of early stage cancer detected in existing screening is determined by
http://ganjoho.jp/data/professional/statistics/odjrh3000000hwsa-att/cancer_survival(1993-2005).xls and ratio of early stage cancer detected in existing screening is assumed as 80%.

Second, consider the patients without cancer. The patients take both the cancer screening and AICS. The cancer screening and AICS are positive or negative respectively. Note that there can be false positive in the cancer screening and AICS. If at least one of them is (false) positive, they undergo a detailed examination. If both of them are negative, they do not undergo a detailed examination. However, whichever they undergo examination or not, they are found to have no cancer, and receive no treatment. It should be noted that the possibility of false positive in the case (2) is calculated as follows:

Possibility of False Positive =
（1－ Incidence Rate） × (1-Specificity × AICS Specificity)

CST ＼ AICS	AICS Positive	AICS Negative
Positive	Exam	Exam
Negative	Exam	No Exam

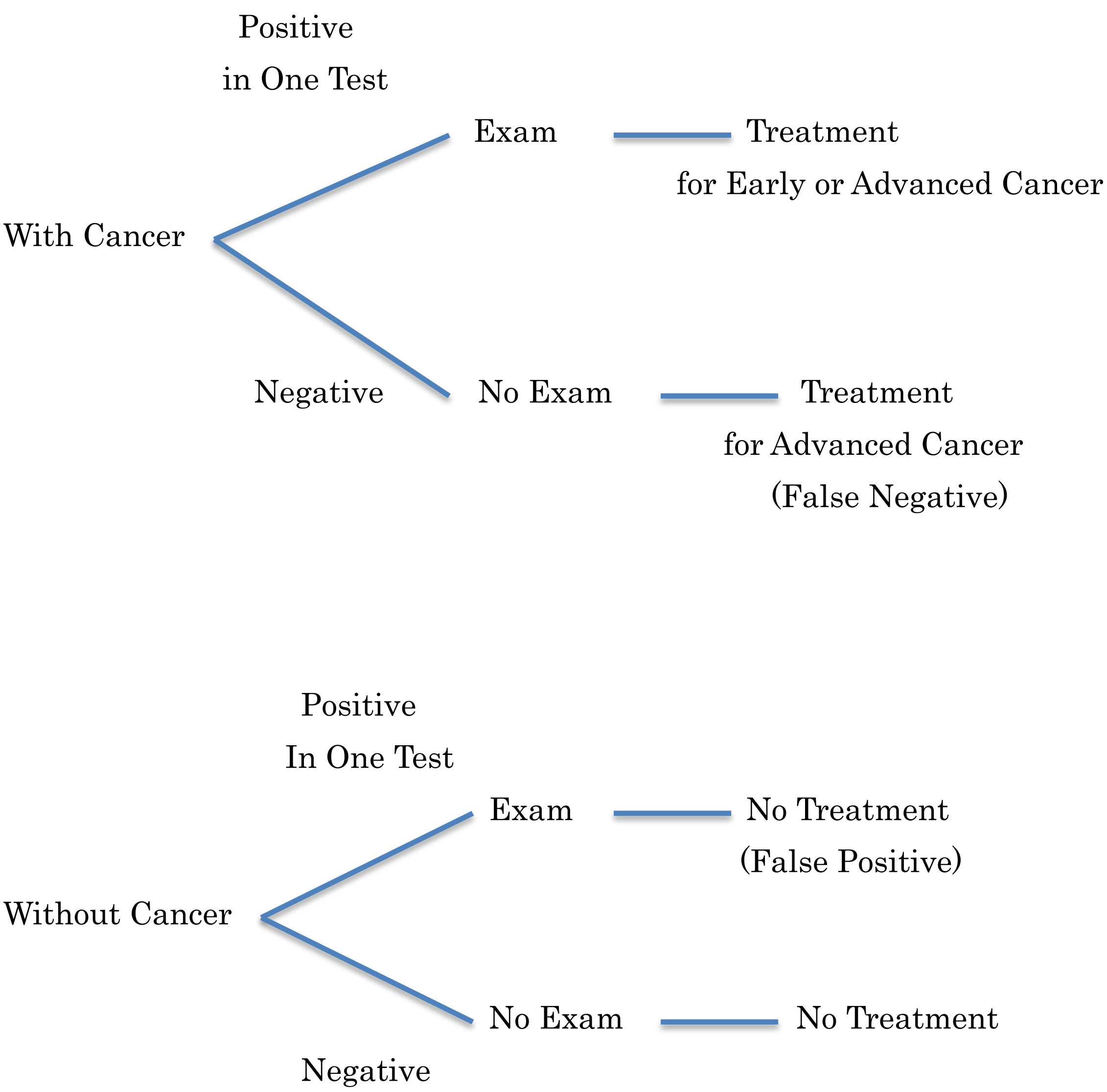

Figure 3. Action Tree in the Case (2)

In the following, we summarize the cost and benefit that derives from the action trees above.

3-3. Cost

The cost of case (1) consists of two parts: the fee of the cancer screening test and the fee of the examination. First, all of the patients pay for cancer screening. Second, if they are found positive, they undergo the examination, and additionally pay for it. If they are found negative, they do not pay any more. Note that there can be a case of false positive in which patients without cancer are found positive, and pay for the examination. In this case, the payment is just a cost that yields no benefit.

The cost of case (2) consists of three parts: the fee of cancer screening test, the fee of AICS, and the fee of the examination. First of all, the patients undergo the cancer screening and AICS. They pay for both tests. Second, if one of the tests indicates positive, they undergo the examination, and additionally pay for it. Otherwise, they do not undergo the examination, and do not pay any more. In other words, the patients do not pay any more only if both tests are negative. Note that there can be a case of false positive in which patients without disease are found positive, and pay for the examination.

3-4. Benefit

As seen in section 3-2, we assume that the patients with cancer who do not undergo the examination are found to have advanced cancer. On the other hand, the patients with cancer who undergo the examination are found to have early or advanced cancer. To sum up, the cancer screening and AICS help them to detect early cancer through the examination.

The cancer screening and AICS leads to early detection of cancer, which benefit the patients in three ways: first, early detection of cancer reduces the direct treatment cost for cancer. This is because the treatment cost for early cancer is smaller than the treatment cost for advanced cancer. This direct treatment cost includes cost of hospitalization, cost of treatment including surgery, radiotherapy, and chemotherapy, and other medical cost such as dietary and recuperation. For example, the treatment cost of early lung cancer is 673855 JPY though that of advanced lung cancer is 2695421 JPY.

Second, early detection reduces indirect productivity loss from hospitalization and recess. In cancer treatment, patients need to be in hospital. This hospitalization period is shorter for early cancer than for advanced cancer. In addition, patients have to heal oneself at home after leaving hospital to return to business. Therefore, it is regarded as benefit for the patients. However, in a cost-benefit analysis, we should evaluate the benefit not in terms of time length, but in terms of money. As an approximation, by calculating average income multiplied by average work suspension period, we estimate income loss (productivity loss) that would be earned if patients would not be under recuperation. Early detection reduces hospitalization and work suspension period, and hence income loss, that would be caused by lost-worktime.

Third, early detection of cancer increases the survival rate of the patients. The survival rate of early cancer is higher than that of advanced cancer. For example, the survival rate of early (i.e. localized) lung cancer is 77.2%, though that of advanced lung cancer is 3.7 – 23.1% depending on metastasis. Then, how can we evaluate the increased survival rate of the patients from economics point of view? One approximation is the increase of life time income. If the patients could live shorter, they would lose more future income. In short, early detection of cancer reduces future income loss. We regard this as the third source of the benefit from the cancer screening and AICS.

In addition, the benefit is calculated according to

$$B_i = \sum_{t=1}^{T} \frac{Y_t}{(1+\rho)^t}$$

where Y_t denotes the income that would be lost when patients do not undergo AICS, ρ denotes the discount rate. In this article, we use apply ρ =0.04. To calculate this value, we need the data of average income for each sex and age class.

3-5. Results

We calculate the incremental cost-benefit ratio ((B1 – B2) / (C1 – C2)) for each kind of cancer, each age class, and each sex. It should be noted that if the incremental cost-benefit ratio exceeds 1, we conclude that AICS is desirable for patients to take. On the other hand, if the incremental cost-benefit ratio is lower than 1, we conclude that AICS is not efficient for patients to take.

The results are shown in the table 3 and figure 4. For 6 cancer, (B1 – B2) / (C1 – C2) > 1 for age over 50. For stomach cancer, (B1 – B2) / (C1 – C2) > 1 mainly for male over 50. For lung cancer, (B1 – B2) / (C1 – C2) > 1 mainly for male over 50. For colorectal cancer, (B1 – B2) / (C1 – C2) > 1 mainly for age over 55. For prostate cancer, (B1 – B2) / (C1 – C2) < 1 for all male age class. For breast cancer, (B1 – B2) / (C1 – C2) > 1 for all female age class. For uterine-ovarian Cancer, (B1 – B2) / (C1 – C2) > 1 for female 45-60.

These results indicate that AICS is desirable mainly for 50-75 years old for screening of several types of cancer including stomach, lung, and colorectal cancer. AICS is also desirable for younger female for screening of uterine-ovarian cancer.

All cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total	5304	7380	10731	11211	18673	14481	28879	15837	36721	15750	43858	16079	47457	17195	37396	16423
	Therapy	136	584	298	927	597	1189	1132	1397	1939	1549	3793	2104	5786	2600	8262	3267
	Opportunity	5136	6635	10363	10034	17918	13013	27433	14151	34348	13956	39475	13748	40831	14337	28130	12886
	Productivity	32	161	70	249	158	279	314	290	435	245	590	227	840	258	1004	270
Cost(C2-C1)	Total	22204	22664	22204	22666	22205	22668	22206	22669	22208	22669	22211	22669	22215	22670	22219	22670
	Screening	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900	18900
	Examination	3304	3764	3304	3766	3305	3768	3306	3769	3308	3769	3311	3769	3315	3770	3319	3770
(B2-B1)-(C2-C1)		-16900	-15284	-11473	-11455	-3532	-8188	6673	-6832	14513	-6919	21646	-6590	25242	-5475	15177	-6247
(B2-B1)/(C2-C1)		0.24	0.33	0.48	0.49	0.84	0.64	1.30	0.70	1.65	0.69	1.97	0.71	2.14	0.76	1.68	0.72

Stomach cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total	2370	859	4456	1384	7403	1879	11515	2379	13793	2687	15650	3528	16583	4358	11637	4444
	Therapy	52	37	106	65	200	97	377	138	595	180	1182	356	1764	529	2324	741
	Opportunity	2306	818	4325	1313	7154	1772	11050	2228	13094	2493	14343	3152	14642	3798	9099	3664
	Productivity	11	4	25	7	49	10	89	14	104	15	125	20	177	31	214	39
Cost(C2-C1)	Total	5405	4460	5405	4460	5406	4460	5406	4460	5406	4461	5407	4461	5407	4461	5408	4461
	Screening	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780
	Examination	680	680	680	680	681	680	681	680	681	681	682	681	682	681	683	681
(B2-B1)-(C2-C1)		-3035	-3601	-949	-3076	1997	-2582	6109	-2081	8387	-1773	10243	-932	11176	-103	6229	-17
(B2-B1)/(C2-C1)		0.44	0.19	0.82	0.31	1.37	0.42	2.13	0.53	2.55	0.60	2.89	0.79	3.07	0.98	2.15	1.00

Lung cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total	1560	536	3788	1099	6662	1903	9917	2734	13180	3533	16023	4108	18109	4815	16128	4896
	Therapy	43	29	112	63	224	121	403	195	705	290	1229	419	1964	594	3228	810
	Opportunity	1517	507	3675	1036	6438	1782	9512	2538	12473	3242	14791	3688	16142	4221	12895	4085
	Productivity	0	0	0	0	1	0	2	0	2	0	3	0	4	1	6	1
Cost(C2-C1)	Total	5689	4744	5689	4744	5690	4744	5690	4745	5691	4745	5692	4745	5694	4746	5697	4746
	Screening	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780
	Examination	964	964	964	964	965	964	965	965	966	965	967	965	969	966	972	966
(B2-B1)-(C2-C1)		-4129	-4208	-1901	-3645	972	-2841	4226	-2011	7489	-1212	10331	-638	12415	70	10432	150
(B2-B1)/(C2-C1)		0.27	0.11	0.67	0.23	1.17	0.40	1.74	0.58	2.32	0.74	2.81	0.87	3.18	1.01	2.83	1.03

Colorectal cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total	1356	556	2405	828	4158	1564	6210	2083	7087	2512	8010	2947	7709	3316	5640	3494
	Therapy	40	32	76	51	148	105	266	157	400	219	783	383	1084	532	1459	779
	Opportunity	1297	517	2289	765	3929	1434	5802	1890	6530	2253	7041	2515	6390	2717	3902	2629
	Productivity	20	8	41	13	82	25	141	35	157	40	186	49	235	66	279	86
Cost(C2-C1)	Total	5685	4740	5685	4740	5686	4740	5686	4741	5686	4741	5687	4741	5688	4741	5688	4742
	Screening	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780	4725	3780
	Examination	960	960	960	960	961	960	961	961	961	961	962	961	963	961	963	962
(B2-B1)-(C2-C1)		-4329	-4184	-3280	-3912	-1527	-3176	524	-2658	1400	-2228	2323	-1794	2021	-1425	-48	-1248
(B2-B1)/(C2-C1)		0.24	0.12	0.42	0.17	0.73	0.33	1.09	0.44	1.25	0.53	1.41	0.62	1.36	0.70	0.99	0.74

Prostate cancer

Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total	17		82		450		1237		2662		4175		5056		3990	
	Therapy	1		4		26		85		239		599		974		1251	
	Opportunity	16		73		398		1069		2251		3300		3657		2234	
	Productivity	1		4		26		82		172		276		425		505	
Cost(C2-C1)	Total	5424		5424		5424		5424		5425		5425		5426		5427	
	Screening	4725		4725		4725		4725		4725		4725		4725		4725	
	Examination	699		699		699		699		700		700		701		702	
(B2-B1)-(C2-C1)		-5407	0	-5342	0	-4974	0	-4187	0	-2763	0	-1250	0	-370	0	-1436	0
(B2-B1)/(C2-C1)		0.00		0.02		0.08		0.23		0.49		0.77		0.93		0.74	

Breast cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total		1665		2378		1989		1804		1624		1423		1253		946
	Therapy		254		384		348		348		355		403		395		375
	Opportunity		1317		1850		1515		1337		1170		933		769		495
	Productivity		95		144		126		119		100		87		89		77
Cost(C2-C1)	Total		4475		4476		4475		4475		4475		4475		4475		4475
	Screening		3780		3780		3780		3780		3780		3780		3780		3780
	Examination		695		696		695		695		695		695		695		695
(B2-B1)-(C2-C1)		0	-2810	0	-2098	0	-2486	0	-2671	0	-2851	0	-3052	0	-3222	0	-3529
(B2-B1)/(C2-C1)			0.37		0.53		0.44		0.40		0.36		0.32		0.28		0.21

Uterine-ovarian cancer

Sex		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Age		40	40	45	45	50	50	55	55	60	60	65	65	70	70	75	75
Benefit(B2-B1)	Total		3763		5521		7145		6838		5393		4073		3453		2643
	Therapy		232		364		518		559		506		543		550		563
	Opportunity		3476		5071		6509		6158		4797		3460		2831		2013
	Productivity		54		86		118		121		90		70		71		67
Cost(C2-C1)	Total		4245		4246		4248		4248		4247		4247		4247		4246
	Screening		3780		3780		3780		3780		3780		3780		3780		3780
	Examination		465		466		468		468		467		467		467		466
(B2-B1)-(C2-C1)		0	-482	0	1275	0	2897	0	2590	0	1145	0	-173	0	-794	0	-1603
(B2-B1)/(C2-C1)			0.89		1.30		1.68		1.61		1.27		0.96		0.81		0.62

Table 3. The Results of Cost-Benefit Analysis

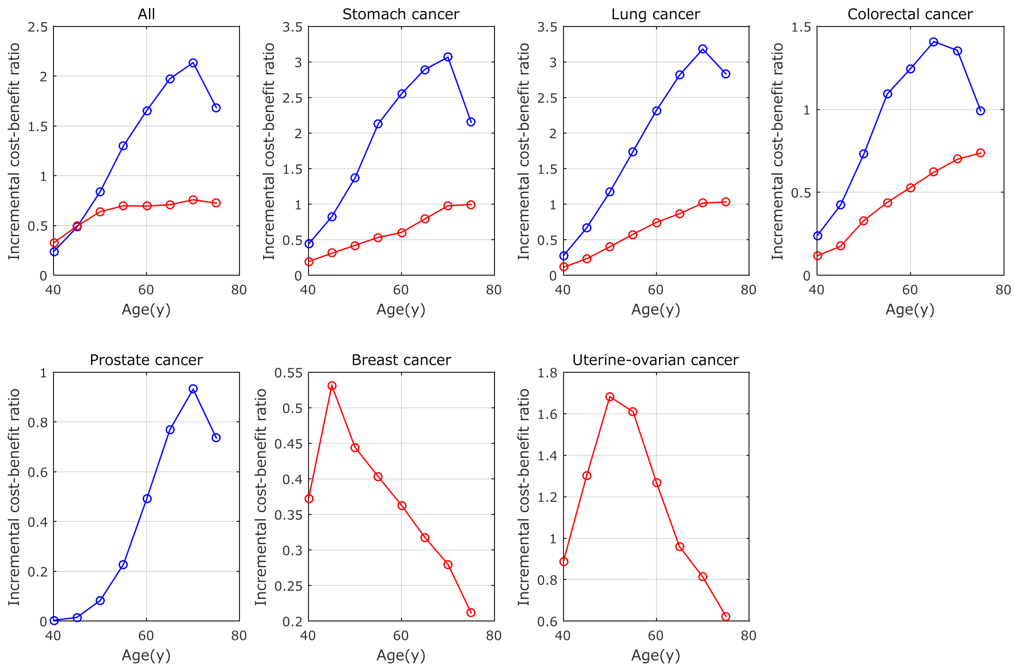

Figure 4. The Results of Cost-Benefit Analysis

4. Sensitivity Analysis

We conduct sensitivity analysis in two ways: first, we vary discount rate from 0.01% to 10.00%. The results are presented in Figure 5. The higher the discount rate is, the lower the cost-effective ratio is. This is because the large part of benefit comes from increased survival rate of patients that is measured by estimating future income. The benefit of future income becomes lower if the discount rate becomes higher.

Second, we substitute individual income for family income. So far, we have employed individual income in the estimation. Women's benefit (value of life) is measured by women's income, and men's benefit (value of life) is measured by men's income. As a result, women's value of life is lower than men's value of life, because the women's income is lower than men's income. This is not reasonable in some cases. For example, some married women save work time in order to do housework and childcare. The value of life should reflect the value of housework and childcare, which is quite difficult in the estimation. One way to deal with this problem is that we regard one half of family income (that is the average income of men and women at the same age class) as the each individual's income. Then, the results of our analysis are summarized in Figure 6.

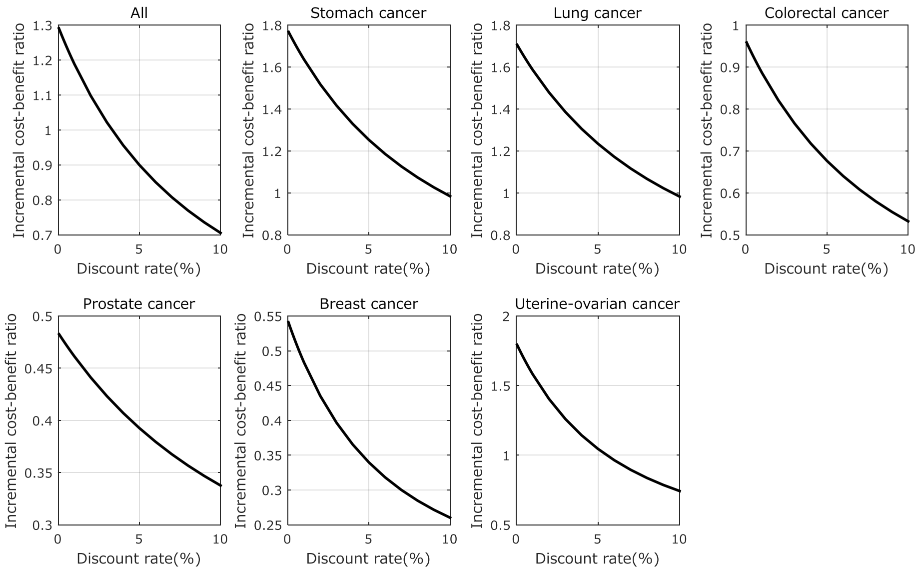

Figure 5. Sensitivity Analysis of Discount Rate

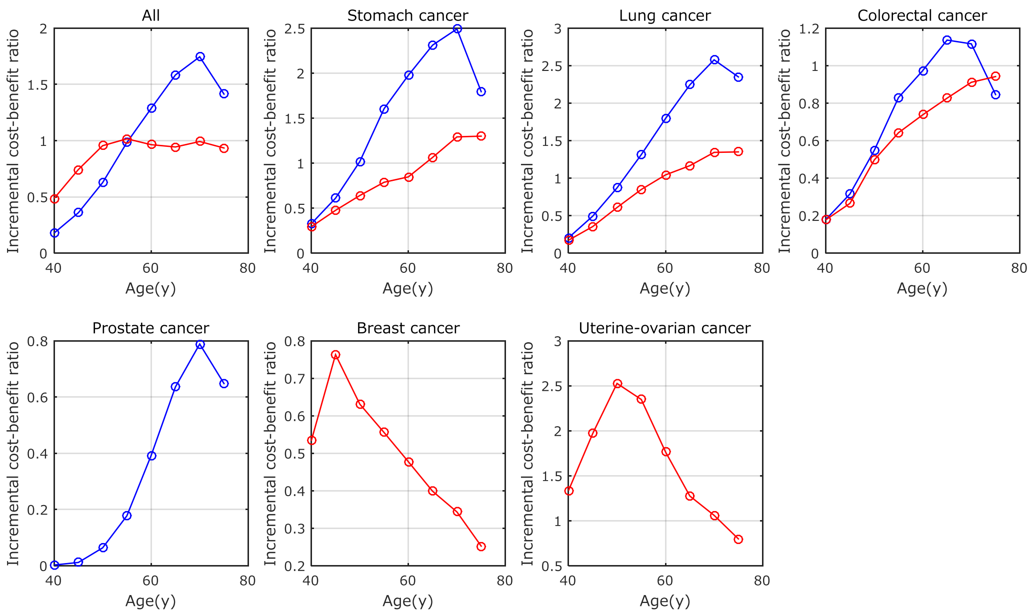

Figure 6. Sensitivity Analysis of Income Adjustment between Sexes

5. Statistics

In this section, we present the source of the data that we employ in the cost-benefit analysis.

The data of population in each generation is taken from National Census in 2010 of Statistics Bureau of Japan (http://www.e-stat.go.jp/SG1/estat/NewList.do?tid=000001039448). The data of average income in each generation is taken from Minkan-Kyuyo-Jittai-Tokei-Chosa in 2012 of National Tax Agency Japan (https://www.nta.go.jp/kohyo/tokei/kokuzeicho/minkan2011/pdf/000.pdf). The data of average mortality is taken from Abridged Life Table in 2012 of Ministry of Health, Labour and Welfare (http://www.mhlw.go.jp/toukei/saikin/hw/life/life11/dl/life11-11.xls). The cancer incidence rate in each generation is taken from Center for Cancer Control and Information Services, National Cancer Center, Japan (http://ganjoho.jp/data/professional/statistics/odjrh3000000hwsa-att/cancer_incidence(1975-2010).xls). The survival rate of cancer patients is taken from Monitoring of Cancer Incidence in Japan - Survival 2003-2005 Report (http://ganjoho.jp/data/professional/statistics/odjrh3000000hwsa-att/cancer_survival(1993-2005).xls). The consultation rate of cancer screening is calculated from the reports of Ministry of Health, Labour and Welfare (http://ganjoho.jp/data/professional/statistics/odjrh3000000hwsa-att/City_Cancer_Screening_Rate(2006-2010).xlsx and http://www.mhlw.go.jp/stf/houdou/2r9852000001igt0-att/2r9852000001iguh.pdf). For gastric cancer, colorectal cancer, breast cancer, and cervical cancer, the sensitivity and specificity of cancer screening is taken from research papers of Daido Life Welfare Foundation (http://www.daido-life-welfare.or.jp/research_papers/19/welfare_34.pdf). For lung cancer and prostate cancer, the sensitivity and specificity of cancer screening is taken from Cancer Screening and Management Division, Research Center for Cancer Prevention and Screening, National Cancer

Center (http://canscreen.ncc.go.jp/pdf/guideline/guide_lung070111.pdf and http://canscreen.ncc.go.jp/pdf/guideline/zenritsusenguide/zenritsusenguide.pdf). The cost of cancer screening, Workup and Treatment for early and advanced cancer are research report estimated by Industrial Growth Platform Inc.(Tokyo, Japan) based on following web sources; http://www.mhlw.go.jp/bunya/kenkou/gan_kenshin.html, http://www.ganchiryohi.com/ , and http://www.it-sui.com/cancer-treat-cost/, and hearing survey. Costs of hospitalization and therapy are taken from National Census in 2014 of Statistics Bureau of Japan (http://www.e-stat.go.jp/SG1/estat/GL08020103.do?_xlsDownload_&fileId=000006864950&releaseCount=1). Average hospitalization days is taken from the reports of Ministry of Health, Labour and Welfare (http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/dl/toukei.xls). The period of lost worktime is taken from reports of Bureau of Social Welfare and Public Health of Tokyo Metropolitan Government (http://www.fukushihoken.metro.tokyo.jp/iryo/iryo_hoken/gan_portal/soudan/ryouritsu/handbook.files/kisochishiki.pdf).

6. Conclusions

This article investigates economic efficiency of AminoIndex™ Cancer Screening (AICS) in Japan. The results indicate that, from patients' point of view, AICS is cost-beneficial mainly for 50-75 years old for screening of several types of cancer including stomach, lung, and colorectal cancer. AICS is also cost-beneficial for younger female for screening of uterine-ovarian cancer.

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