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PREVENTIVE MEDICAL SERVICES NOT COVERED BY PUBLIC HEALTH INSURANCE AT DAIKO MEDICAL CENTER IN JAPAN, 2004–2011

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ABSTRACT

Preventive medical services not covered by public health insurance started in the Daiko Medical Center of Nagoya University in June, 2004. Those services included: 1) *Helicobacter pylori* (*H. pylori*) diagnosis and eradication treatments, for which *CYP2C19* genotyping was introduced in November 2005; 2) smoking cessation support with genotype tests of *CYP1A1* Ile462Val, *GSTM1* present/null, *GSTT1* present/null, and *NQO1* Pro187Ser; 3) advice on alcohol consumption with genotype tests of *ADH* Arg47His and *ALDH2* Glu487Lys; 4) advice on folate-associated diseases with a genotype test of *MTHFR* C677T; 5) advice on a tumor marker CA19-9 with genotype tests of *Lewis* and *Secretor* genes; and 6) raloxifene prescription aimed to prevent breast cancer for high-risk postmenopausal women. A total of 683 patients visited the Center until it closed in March 2011. Those given diagnoses and eradication treatments for *H. pylori* numbered 567, followed by 44 for smoking cessation support, 35 for advice on folate-associated diseases, 26 for advice on alcohol consumption, 8 for CA19-9, and 3 for raloxifene prescription. Around 2004, public interest in *H. pylori* was relatively high, but thereafter patient numbers dropped markedly. The Center closed in March 2011 due to the reduction in patient visits. Our unique trial showed that continuing to provide uninsured preventive services at a clinic was difficult in Japan without the affiliation of hospitals/clinics providing medical services covered by public health insurance.

Key Words: Uninsured preventive service, *Helicobacter pylori*, Genotype tests

INTRODUCTION

The Daiko Medical Center opened as a restructured clinic succeeding the Nagoya University Branch Hospital in 1996 on the Daiko Campus. In June, 2004, preventive medical services not covered by public health insurance began for eradication treatments of *Helicobacter pylori* (*H. pylori*), smoking cessation support, advice on alcohol consumption, folate-associated diseases and a tumor marker CA19-9 with genotype tests, as well as chemoprevention for breast cancer with raloxifene. At that time, we expected that a substantial number of citizens might seek those preventive medical services.

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Since those services are not covered by public health insurance in Japan, all the attendant costs have to be paid by patients, whereas only 30% of the costs are charged to patients in cases of medical services covered in Japan. Six years and 10 months after its start, the Center closed in March of 2011 due to the limited number of visitors seeking preventive services. This article describes our challenges in providing uninsured preventive medical services at the Center. We report the number of patients according to each service, the reason for eradication treatment visits, and the final outcome of eradication treatments. Since the reports on uninsured health services in Japan were very scarce, some documentation on the Center's performance was thought to be meaningful.

SUBJECTS AND METHODS

Subjects

Patients who visited the Daiko Medical Center from June, 2004 to March, 2011 were tracked according to the following medical services received: 1) *H. pylori* diagnosis and eradication treatments, for which *CYP2C19* genotyping was introduced from November 2005[1,2]; 2) smoking cessation support with genotype tests for *CYP1A1* Ile462Val, *GSTM1* present/null, *GSTT1* present/null, and *NQO1* Pro187Ser[3]; 3) advice on alcohol consumption with genotype tests of *ADH* Arg47His and *ALDH2* Glu487Lys[4,5]; 4) consultation on folate-associated diseases with a genotype test of *MTHFR* C677T[6]; 5) consultation on a tumor marker CA19-9 with genotype tests of *Lewis* and *Secretor* genes[7]; and 6) raloxifene prescription to prevent breast cancer for high-risk postmenopausal women.[8] The genotype methods were described in our previous papers.[1-3,5-7,9]

Fees for each service

As a general rule, fees for insured medical services are fixed throughout Japan by the government, with 30% of them being charged to the patient. On the other hand, the fees for uninsured medical services can be set by each medical facility, with patients having to pay 100% of the fees. In our Center, the fees for a particular service are arranged to be the same as the corresponding fees when provided as a medical service covered by public health insurance, as described in the fee schedule. Accordingly, the actual fees our patients had to pay at the Center were about three times (100% vs. 30% of the fee) higher than those under public health insurance. For example, the first visit for an *H. pylori* infection diagnosis (a serum anti-*H. pylori* antibody test and a urea breath test) cost about 16,000 yen, which would only be about 4,800 yen under public health insurance. In cases where the eradication was successful, the total costs came to about 30,000 yen for three visits; a diagnosis at the first visit, medication at the second visit, and a test after the medication at the third visit. For other services, about 2,900 yen at the first visit and about 1,300 yen at the second visit or thereafter were charged as the basic rate. Patients were not charged for any genetic tests that we ourselves conducted at the Center.

Statistical analysis

The percentage differences between two groups were examined by a chi-square test. Statistical analysis and tabulation were performed using Stata/MP 11 software (StataCorp LP, Texas, USA).

RESULTS

From June, 2004 to March, 2011, 683 subjects (293 males and 390 females) visited the Daiko Medical Center. Among them, 26 individuals sought two or more of the six services. Table 1 shows the total number of patients according to the preventive service to be 683. Among them, eighty-three percent visited for diagnosis and eradication treatments for *H. pylori*.

The reasons patients visited for *H. pylori* diagnosis and eradication treatments are shown in Table 2. Multiple selections were allowed from the items listed in the questionnaire. The most frequent reason was *H. pylori* infection diagnosed at other facilities (45.1%), followed by gastrointestinal symptoms (36.5%), family history of gastric cancer (20.3%), and anxiety aroused by TV programs featuring *H. pylori* (18.2%). Significant differences in the percentage between males and females were observed for items regarding *H. pylori* infection diagnosed at other facilities (χ^2=5.84, p=0.016), past diagnosis of gastric ulcer and/or duodenal ulcer (χ^2=4.44, p=0.035), and urticaria (χ^2=4.36, p=0.037).

Table 1 Number of patients according to preventive services received, who visited the Daiko Medical Center from June, 2004 to March, 2011

Preventive service	Male (age)	Female (age)	Total (age)
Eradication treatment for *H. pylori*	235 (19–78)	332 (19–80)	567 (19–80)
Smoking cessation support	32 (27–82)	12 (16–58)	44 (16–82)
Genotyping for metabolism of folate	11 (27–65)	24 (22–67)	35 (22–67)
Genotyping for metabolism of alcohol	13 (28–71)	13 (18–47)	26 (18–71)
Genotyping for metabolism of tumor maker CA19-9	2 (41–77)	6 (42–82)	8 (41–82)
Chemoprevention for breast cancer	—	3 (47–53)	3 (47–53)
Total	293 (19–82)	390 (16–82)	683 (16–82)

Table 2 Reasons for visits for *H. pylori* diagnosis and eradication treatments (listed by percentage)

Reason*	Male N=235	Female N=332	Total N=567
H. pylori infection diagnosed at other facilities**	39.1	49.4	45.1
Eradication failure at other clinics	13.2	12.7	12.9
Past diagnosis of gastric ulcer and/or duodenal ulcer**	16.6	10.5	13.1
Gastrointestinal symptoms	33.2	38.9	36.5
Surgical history of gastric cancer	1.7	3.0	2.5
Family history of gastric cancer	17.4	22.3	20.3
Thrombocytopenic purpura	0.4	1.5	1.1
Urticaria**	0.9	3.6	2.5
Other diseases	4.3	3.9	4.1
Anxiety aroused from television program on *H. pylori*	20.0	16.9	18.2
Advice of a family member	17.4	18.4	18
Other reasons	21.3	20.5	20.8
No particular reason	1.1	2.1	2.3

* Two or more reasons for visits were allowed.
** Significant difference between males and females (p<0.05)

Figure 1 shows the number of patients visiting for *H. pylori* diagnosis and eradication treatments between June, 2004 and March, 2011. Around 2004, public interest in *H. pylori* infection was generally high; TV programs, newspaper articles, and public lectures on *H. pylori* were relatively common. The opening of our *H. pylori* clinic was reported in the press on July 16, 2004. However, patients at the Center decreased, possibly due to reduced public interest and/or the increased opportunity for *H. pylori* eradication under public health insurance. Between June, 2009 and May, 2010, we enrolled 5,172 participants in a cohort study at the Daiko Medical Center.[10] In that study, a free urinary *H. pylori* antibody test was provided. Among the participants with a positive test, 112 sought *H. pylori* eradication at the Center, making 2009 the patient peak (Fig. 1). From then on, there were no incentives to encourage people to seek *H. pylori* diagnosis and treatments at the Center, resulting in a drastic reduction in 2011.

We previously reported the *H. pylori* eradication rate for first-time treatments during the period before the introduction of a routine *CYP2C19* genotype test and during the period after its introduction.[2] Before the introduction, a first-line regimen (lansoprazole, clarithromycin, and amoxicilline) was prescribed for all first-time treatments. After the introduction, a second-line regimen (rabeprazole, metronidazole, and amoxicilline) was prescribed as a first-time treatment for those with *CYP2C19 *1*1* (rapid metabolizers), and a first-line regimen for the others. The final eradication rate was 80.0% (n=90) for the period before the test introduction, and 88.9% (n=144) for the period after it; the difference was marginally significant (χ^2=3.52, p=0.06), which was similar to a previous result (p=0.08).[2] The eradication rate was 100% (n=53) among those with *CYP2C19 *1*1* treated by the second-line regimen (Table 3).

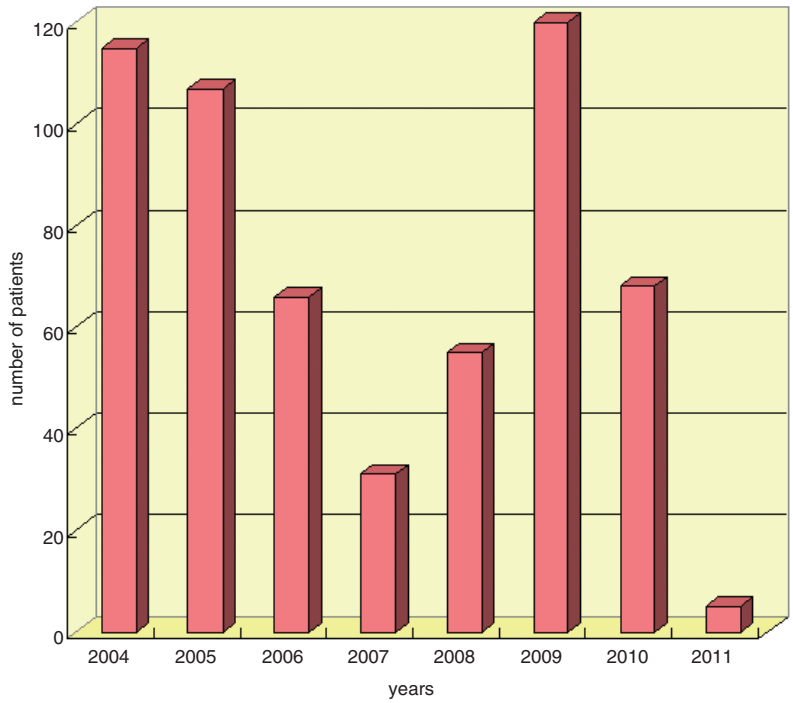

Fig. 1 Number of patients who visited the Center for *H. pylori* diagnosis and eradication treatments between June, 2004 and March 2011

Table 3 Eradication rate during periods without (June, 2004 to October, 2005) and with (November, 2005 to March, 2011) a routine genetic test for *CYP2C19*

Subjects	2004–2005	2005–2011			
	Untested n (%)	**1*1* n (%)	Other genotypes n (%)	Untested* n (%)	Total n (%)
Visited	198				296
Examined**	197 (100)				290 (100)
Infected	131 (66.5)	66	132	3	201 (69.3)
Treated	114	61	124	3	188
Succeeded***	72 (80.0)	53 (100.0)	74 (83.1)	1 (50.0)	128 (88.9)
Failed***	18 (20.0)	0 (0.0)	15 (16.9)	1 (50.0)	16 (11.1)
Not evaluated	24	8	35	1	44
Re-treated	12	0	14	1	15
Succeeded***	7 (87.5)	0	12 (92.3)	0	12 (92.3)
Failed***	1 (12.5)	0	1 (7.7)	0	1 (7.7)
Not evaluated	4	0	1	1	2

* Untested for *CYP2C19* before prescription
** Examined for *H. pylori* infection
***The parencethese shows rates excluding those unevaluated

The second most frequent patients (6.4%) were 43 smokers (and one former smoker) who sought cessation support, including a nicotine patch or genotyping related to their susceptibility to carcinogens. From May 31, 2008, when the nicotine patch became available at pharmacies without a prescription, the role of the Center diminished as a result. Moreover, smoking cessation support (including the prescription of a novel medicine, varenicline) under public health insurance started in May 8, 2008. Among 44 patients, 35 requested genotyping. In the follow-up of 25 smokers who agreed with a questionnaire survey three months after their first visit, nine participants out of 16 responders (36.0% out of 25 smokers) reported quitting at the time of their response.

The demand for genotyping of alcohol metabolism was small; most were from those who cannot drink alcoholic beverages to confirm their genotype of *ALDH2* Glu487Lys. The great majority of those who sought *MTHFR* C677T genotyping were patients and their families with oral clefts, or parents with a spina bifida child. In those cases, a specialist (teaching staff) together with a licensed midwife attended them throughout the process. Those who visited the Center for *Lewis* and *Secretor* genotyping were patients with elevated CA19-9, all of whom had *Le* allele and *sese* genotype. There were three for breast cancer chemoprevention. Two of them actually sought raloxifene after an explanation of its effect, but the prescription was given for only one time.

DISCUSSION

In Japan, medical services not covered by public health insurance are occasionally provided for cosmetic surgery, normal childbirth, private special consultation, some dental services, etc. Uninsured health services are often regarded as inappropriate, and are only provided to make money off of ineffective or unevaluated treatments. However, *H. pylori* eradication was one of the exceptions. The Japanese Society for *Helicobacter* Research approved uninsured medications for *H. pylori* eradication, and listed the medical facilities providing them on their homepage

(http://www.jshr.jp/). Although the number of patients treated in this framework has not been reported, the number at the Daiko Medical Center seemed to our knowledge to be one of the highest in Japan.

The reasons to visit the Center were mainly the past-positive tests of *H. pylori* without subsequent eradication treatment, and gastrointestinal symptoms with no occasion for *H. pylori* tests. At that time, *H. pylori* diagnosis and eradication were covered by public health insurance only for those with current peptic ulcers. Accordingly, hospitals or clinics could not usually provide such services for those without current peptic ulcers under the public health insurance system. In addition, uninsured medical service in hospitals/clinics providing insured medical service might result in a mixed practice (Kongou Shinryou, in Japanese), which is prohibited in Japan under financial penalties. Since the Daiko Medical Center did not provide insured medical services, we were free from any criticism or penalties regarding so-called mixed practice.

The influence of *CYP2C19* genotype on *H. pylori* eradication has been well documented.[1,11,12] The improvement of the eradication success rate for first-time treatment through a genetic test for *CYP2C19* at the Center was reported in our previous paper.[2] Since the report was on those who visited the Center until August 2010, the final results were added to this paper. Although the improved eradication success rate was still marginally significant (p=0.06), there seemed to be a possibility that the introduction of a genetic test would improve the success rate of those receiving eradication treatments for the first time.

Concerning genetic tests, the introduction to medical/preventive practice is still controversial.[13-15] However, in our trial, we found no problems related to genetic testing; no cases needed genetic counseling, as experienced in previous studies.[16-18] The responses of those who seek genetic tests for reasons unrelated to disease severity might differ from responses of those seeking help for severe diseases. A distinction in the approach between genetic tests of useful polymorphisms and those for severe hereditary diseases seemed to be necessary.

We expected that there would continue to be a large demand for the six services at the Center. However, even for *H. pylori* eradiation services, which were relatively popular among people, the demand did not continue. The Center's services might have been expensive for ordinary persons, although there were no available data on this issue. A lingering challenge is that preventive services are not covered by public health insurance in Japan. Other trials will be needed to find optimal conditions for medical/preventive services not covered, and to provide novel medical services which people can seek even if they are not covered.

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