user and her followers and the fact that the vast majority of the user's tweets focused on comedy and not on cancer or other medical topics, we excluded this account from our analysis.) A detailed analysis of the remaining 51 accounts was subsequently conducted following their extraction from the dataset.

Review of the relationships between users

Using the mentionmapp website [21], which enabled us to search for relationships between users on Twitter, we examined the presence and extent of specific relationships between Twitter users. This site graphically displays the number of tweets created most recently by a specific user prior to a search, as well as the relationship that exists between that user and other users (i.e., referring to sending a reply in the form of "@user name" on Twitter one or more times). This secondary search was conducted on December 4, 2011. As the technical capabilities of this Twitter-centric search engine have yet to be clarified by the site's operators, the period available to send replies that can be detected by a mentionmapp search is unknown.

Review of user-generated Twitter content

We extracted from our dataset the user account with the greatest number of followers from the accounts of breast cancer patients, who made up the largest population of Twitter users studied here. We subsequently used mentionmapp to extract the Twitter users who had a direct relationship with that primary user. In this way, we were able to extract the user accounts in which a direct relationship was found with the user who had the largest number of followers, as observed by one or more replies being sent. The number of tweets of such accounts per day was analyzed using Whotwi, a tool that displays the number of tweets per day or time zone, as based on an analysis of the most recent 600 tweets of individual accounts [22]. Among these accounts, the account that had the largest number of tweets per day was extracted for further analysis.

The contents of the tweets among the users who tweeted a reply one or more times to the extracted user are described using Bettween, a tool that enables retroactive searching of tweets among users [23]. Furthermore, tweets among cancer patients were also searched in the same manner using the Bettween Search instrument.

The Whotwi and Bettween searches began on December 11, 2011. The Whotwi search was completed this same day, and the Bettween search was carried out over a period of 7 days.

This study was approved by the Ethics Committee at Yamagata University Faculty of Medicine.

Results

Characteristics of user accounts

Characteristics of the extracted 51 "power accounts" that had 500 or more followers are shown in Table 1. As previously noted, the term "breast cancer" appeared more frequently than other cancer term in these users' profiles (n=13). The ratio of males to females in the "power accounts" was 1:1. The Kanto region, which includes the Japanese capital of Tokyo and several other major metropolitan areas, was listed as the home location for almost half of the studied user accounts (n=23). Of the 51 "power accounts," over half (n=27) of users disclosed their real names, while almost half (n=21) displayed a personal photograph in their profile. The number of tweets per day for the top 5 types of cancer of user accounts is shown in Figure 3. The median of the average number of tweets per day for breast cancer, leukemia, colon cancer, cancers of the uterus and malignant lymphoma was 2.12, 3.79, 3.21, 3.79 and 2.00, respectively, with corresponding ranges of 0.03–14.6, 0.03–16.2, 0.14–13.1, 0.57–22.3 and 0.13–10.7.

User connectedness

As previously noted, we opted to exclude from our analysis the account of the Twitter user—a celebrity— who had the largest number of followers; the comedian who owned this account had breast cancer, and her Twitter feed was followed by 33,828 other users. The Twitter account of user0 with the second largest number of followers (2,463 followers) was selected for the previously described December 4, 2011, analysis of the relationship between users. The results of this analysis are shown in Figure 4. The 5 accounts with the most followers all belonged to patients with breast cancer; the remaining 3 accounts from the "Top 5" accounts were those with 1,593, 1,518 and 1,241 followers, respectively.

As shown in Figure 4, it was found that there were cancer patients among the followers of user0. Those followers included 3 breast cancer patients, 1 uterine cancer patient and 1 user who was believed to be a cancer patient. It was found that these cancer patients communicated with one another via tweets, revealing real-life examples of information exchanges among cancer patients via Twitter. Among the 5 "power accounts" with the greatest number of followers, the fourth-largest account also had a network of cancer patients on Twitter (data not shown).

Content of tweets

The user accounts of cancer patients among the 6 user accounts that had relationships with user0 (5.5 tweets per day) as shown in Figure 4 were these 5 accounts: user16, user17, user23, user24 and user27, showing tweet numbers of 44, 15, 16, unknown and 5.5, respectively,

Table 1 Characteristics of the accounts (followers > 500)

Variables		Numbers
Sex (male/female/unknown)		24/24/3
Patients (male/female/unknown)	Breast cancer	13 (1/12/0)
	Malignant lymphoma	10 (8/1/1)
	Leukemia	5 (2/3/0)
	Stomach cancer	5 (3/1/1)
	Uterine cancer	4 (0/4/0)
	Brain tumor	4 (4/0/0)
	Colon cancer	4 (2/1/1)
	Renal cancer	1 (1/0/0)
	Prostate cancer	1 (1/0/0)
	Thyroid cancer	1 (0/1/0)
	Lung cancer	1 (1/0/0)
	Bladder cancer	1 (1/0/0)
	Ovarian cancer	10/1/0
Area (male/female/unknown)	Hokkaido, Tohoku	1 (1/0/0)
	Kanto	23 (7/14/2)
	Chubu	11 (6/5/0)
	Kinki	8 (4/4/0)
	Chugoku	0
	Shikoku	0
	Kyushu, Okinawa	2 (1/1/0)
	Unknown	6 (5/0/1)
Identified by full name		27 (12/15/0) (52.9%)
Profile photograph of self		21 (11/10/0) (41.2%)
Contained link to any Web site		14 (9/5/0) (27.5%)
Link to own blog		22 (11/10/1) (43.1%)
Followers	Average	2079
	Median	1077
	Minimum	520
	Maximum	33828
Tweets	Average	5608
	Median	2370
	Minimum	44
	Maximum	44746
Tweets/day	Average	15.2
	Median	5.7
	Minimum	0.1
	Maximum	126.3

when the search was conducted. Because user24 was set as a non-public user, it was not possible to conduct a search of the user's tweets.

As a result of our investigation into the contents of the tweets by user16, who had 44 tweets (the largest number) per day, with another 12 users (who were believed to have a relationship with this user, as shown in Figure 4), the contents were classified into categories such as greetings ("good morning,""good night"); daily conversations or chats ("I did so and so today"); and conversations concerning cancer treatments ("I am going to the hospital today." The total number of tweets for each category was as follows: 176 for greetings, 139 for daily conversations or chats, and 24 for conversations concerning cancer treatments. The contents of the exchanged tweets about cancer treatments through the network shown in Figure 4 are shown in Table 2. These tweets represented psychological encouragement (12 tweets), greetings when visiting the hospital or reports on the outpatient ward (10 tweets), tweets concerning physical condition (6 tweets) and advice for treatment (2 tweets).

Discussion

This study indicated that Twitter could be a valuable medium for sharing information among cancer patients. A total of 51 Japan-based cancer patients with Twitter accounts were determined by our study to be influential Twitter users as based on their having 500 or more Twitter followers. Although this study examined a considerably smaller sample of influential Twitter users (n=51) than did a previous United States-based study of the "power accounts" of influential tweeting physicians (n=260) [12], our research revealed that cancer patients can empower themselves by tweeting information about their own medical condition and treatment and by providing a forum for the discussion of specific topics.

The breakdown of influential accounts was found to be in the order of breast cancer, leukemia, colon cancer, cancer of the uterus and malignant lymphoma; this differs significantly from the order of cancer prevalence in Japan, in which the top 5 types of cancer are, in descending order: stomach cancer, lung cancer, colon cancer, breast cancer and liver cancer [19]. We found it interesting that the cancer prevalence of our influential users and the general population were so dissimilar. We expect that this discrepancy is associated closely with the widespread Internet usage of the younger population, which made up a disproportionate percentage of our studied Twitter users. Compared with other cancers in our study, breast cancer was seen most in women in their late 30s to early 40s. The Internet usage rate of Japanese women in this age range is as high as 95% [24]; we believe that this high Internet literacy confirms our findings.

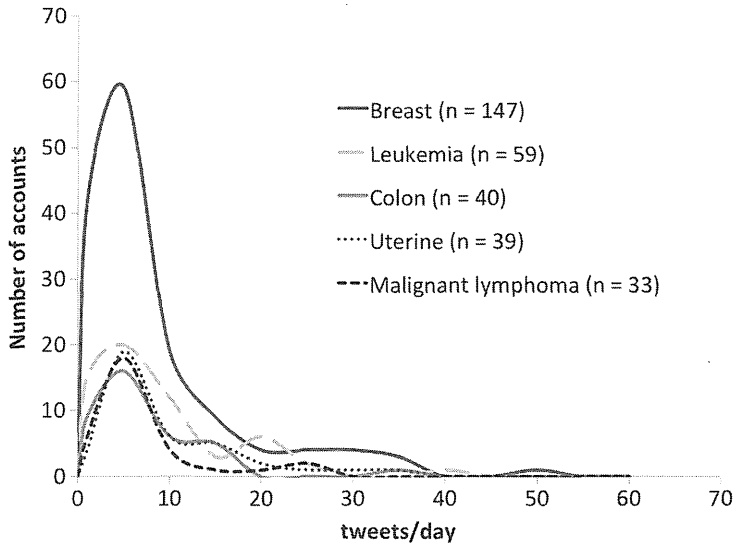

Figure 3 Average number of tweets and number of users per day for Twitter users' 5 most prevalent types of cancer.

Furthermore, while malignant lymphoma or leukemia is a disease with lower numbers of affected people, we found users with these types of cancer to be highly influential in terms of their Twitter connections. This may be a result of the background in which the treatments for leukemia or malignant lymphoma are mainly centered on chemotherapy, with a long treatment period, indicating that treatment for the disease affects the daily life of these patients for a prolonged period. These patients are thus also more likely to have more opportunities over an extended period of time to engage in timely discourse about their individual conditions and treatment.

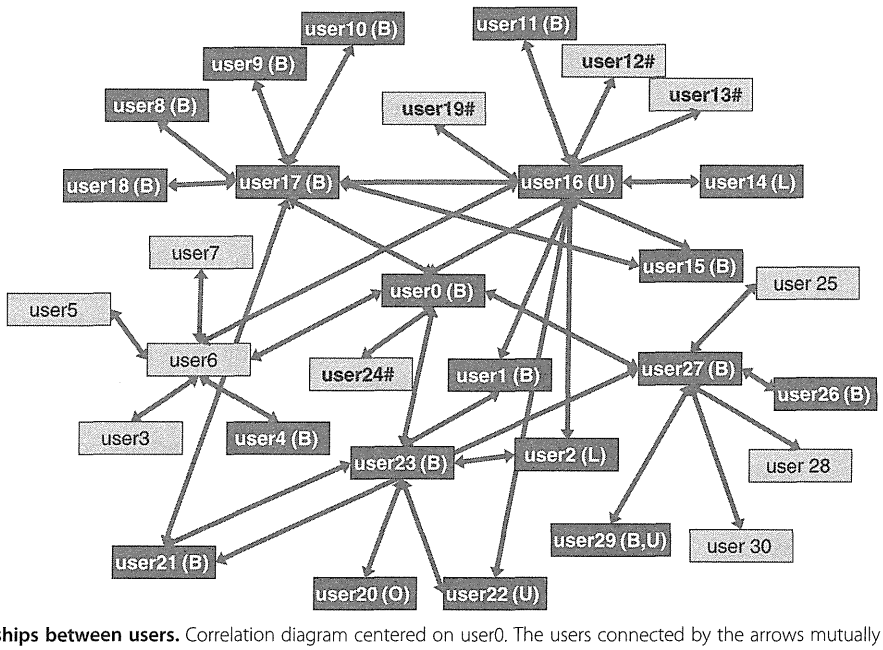

Figure 4 Relationships between users. Correlation diagram centered on user0. The users connected by the arrows mutually sent one or more replies. The search was conducted to incorporate friends' friends. userXX(outlined) : cancer patients. Users who listed their specific type of cancer in their profiles. (B): breast cancer, (L): lung cancer, (O): ovarian cancer, (U): cancer of the uterus. userXX#: Users who are believed to be cancer patients judging from their tweets, although no disease names were described in the profiles (because of descriptions of terms such as anticancer drugs, routine examinations, CT, contrast dyes, bone scintigrams). userXX: Other users.

Table 2 Conversations regarding treatment*

Conversation 1 (psychological encouragement)	user18	I cleared the blood test ♪ but because of a concerning observation above my collarbone (I have had it for 3 years) that I feel has gotten a bit bigger, I had to take an echo test. (>_<)
	user17	Glad to hear that you cleared the test!
	user18	Dear (user17), thank you ♪, now the echo test. . . Wish me luck(^^)
Conversation 2 (psychological encouragement)	user14	Dear (user16), thank you. The medication was effective and I was able to confirm the shrunken CT image. So I think I am ready for chemotherapy. (^O^)/
	user16	Once it turns out to be effective, we feel we'll be able to take it further. Let's do this!!
Conversation 3 (psychological encouragement)	user16	You don't have to try hard. Just keep yourself in good physical condition for now, so you're ready for the operation next year.After completing treatment, you can come back.
	user16	Dear (user15), keep it up.
	user15	Dear (user16), good morning. (*⌒-⌒*)o ♪ I took a day off from work today.~(¯∇¯;)
	user15	Thank you. (^-^)v I will just take a day off to relax and refresh myself. (*⌒-⌒*)o
	user16	Be careful not to catch a cold.
	user15	Dear (user16), thank you for your kindness as usual. (*´∇`*)
Conversation 4 (report on hospital visit)	user16	Dear (user12), be careful when you visit the hospital.
	user12	Thank you. I am off to the hospital. (*^o^*)
Conversation 5 (conversation regarding physical constitution)	user19	Good morning!! I still have some pain 1 week after the operation. Strangely, my left arm which I broke some years ago hurts. Why?
	user16	Because the weather is terrible today, my scar hurts, too.
	user19	Hi sister, good morning! Well, you, too! It's my first time to experience an old wound hurting. Having various pains here and there is confusing (laughing), ha-ha.
	user16	It also hurts just before it starts to rain. Because I have keloid diathesis and my wound is rather wide and mounted, with adhesion, it really hurts when I have intestinal movements. It is really painful when I have diarrhea, but now I am used to it.
	user17	Dear (user19), good morning (^_^). My cut wound from a year ago has been hurting me since yesterday. Although I can bear the pain if I just moan, apparently there are many people who feel pain from old wounds when the weather gets cold. I hate it. Let's keep ourselves warm.
	user19	Dear (user17), good morning. Wow, you, too, dear (user17)! I guess the cold weather does have an effect, after all. Let's keep ourselves warm so that we can heal, everybody. Keep it up today, too.
Conversation 6 (report on hospital visit)	user11	Dear (user16), good evening. Here is your aunt to talk about nice things. (Laughing) It's nice. I feel like drinking tonight. . . but I will have a gynecological exam tomorrow for the first time in 6 months. Because they will collect my blood as well, I will leave that until tomorrow so I have something to look forward to. d(⌒-⌒)
	user16	Don't miss it.
	user11	I will meet with my favorite attending physician for the first time in 6 months. I'm really looking forward to it. d(⌒-⌒)!
	user16	Me, too. With CT and check-up, there will be two hospital visits this month.
	user11	Just like this year's year-end tax adjustment? For both of us. . . I will have a gynecological exam tomorrow, too, and the year-end lymph care adjustment the day after tomorrow. (laughing)
Conversation 7 (report on hospital visit)	user11	Dear (user16), good morning. Today is the last lymph care of the year ♪ I am wearing order-made new stockings and feeling great, ready to leave for the doctor's office. d(⌒-⌒)!
	user16	Have a nice day.
Conversation 8 (report on hospital visit)	user16	Dearest (user22), good luck with your bone scintigraphy, RT @(user22): Good morning, everybody, today is the day for the bone scintigraphy~~ .
Conversation 9 (psychological encouragement)	user7	Dearest △△, good morning (^_^)/I totally understand your feelings. Me too, when I was receiving radiotherapy treatment, I really felt depressed whenever I went down the steps, because I felt like I was being told every time "cancer patients are this way?"

Table 2 Conversations regarding treatment* *(Continued)*

Conversation 10 (advice on treatment)	user17	Dearest (user21), good morning. You are now being treated with Xeroda. It's been just a few days, right? Sorry if I am wrong but it may take some time for the drug to take effect.
	user21	Dear (user17), good morning! Oh, Xeroda. Well, if left for 2-and-a-half months without chemotherapy, that seems rational. (´;ω;`) Internal medicine apparently works slowly.(´;ω;`) It will take time, too. (´;ω;`)

*Japanese conversations were translated into English.

To better understand how cancer patients influence their followers via Twitter, direct investigation involving the use of a survey of cancer patients with Twitter accounts may be necessary in the future. Examining the distribution of user activities did not reveal any significant differences among the different types of cancer noted in users' profiles. On the other hand, our study showed that a smaller number of extremely active accounts existed for each type of cancer examined (Figure 3). Under the hypothesis that such small numbers of active users serve as the center of the patients' networks on social media, we investigated the connections related to the most active users. As a result, we were able to demonstrate that information was exchanged in real time among patients (Figure 4). Based on this finding, we were able to demonstrate for the first time that an information exchange network among patients via social media had already been established.

Of further interest to us is the content of the tweets exchanged among patients. Most of the examined tweets included details of daily life such as greetings or messages concerning treatments, and it was found that almost no medical information concerning cancer was exchanged; this went against our initial expectation that cancer patients would use Twitter to primarily discuss specific cancer-related news and medical information.

Our findings demonstrate that patients use Twitter as a tool of psychological support by being connected among patients, even though it is not a standard or face-to-face method of discussing such information. This observation may support the notion that Twitter plays a unique role that is different from similar-seeming Internet tools such as hospital websites in which patients primarily obtain medical information [2] or blogs in which patients can share their experiences [1]. We expect that as Twitter usage becomes more widespread in the coming years, there will be an attendant rise in the medium's importance to maintaining—and perhaps improving—public health [25]. However, the dissemination of Twitter among patients in the future may generate various methods of usage, making it necessary to continue careful observation in the future.

Twitter can be used not only with real names but also anonymously, which is often controversial. In our study, 53% of the accounts included the users' real names, and 41% of the accounts included personal pictures. Investigation into the Twitter accounts of physicians revealed that 78% of these accounts displayed the users' real names and personal pictures [12], indicating that anonymity is more preferred among patients than physicians. We expect that this discrepancy can be correlated to the fact that information about individuals' medical conditions is considered personal and confidential, and that revealing a Twitter account user's name could lead to the disclosure of potentially private medical details. Many people consider it necessary to maintain anonymity when sharing information through Twitter and other social media; such anonymity may be linked to Twitter's ability to maintain its relevance among the patient populations that use it.

Limitations

While this study demonstrated that a patient network via Twitter is in the process of being established, there remain several issues to be discussed. First, this study targeted only those Twitter users who described "cancer" either in Japanese Hiragana, Katakana or Kanji letters in their profiles. However, this does not mean that all users who were cancer patients included relevant disease names in their profiles; the absence of cancer details in user profiles could potentially exclude an unknown number of cancer patients from analysis.

Second, because of limitations in search tool performance, we were unable to conduct a large-scale comprehensive qualitative analysis. It is expected that the improvement of search-tool performance will enable larger-scale studies in the future.

Finally, future research into this field of study will need to clarify the types of information most often disseminated via social media. It has been reported that social media often include information that is not necessarily beneficial to the health of media users [26]. Furthermore, Chretien et al. (2011), who studied physicians' accounts on Twitter, stated that there existed, although rarely, some ethically problematic content, which could possibly violate the patient privacy [12].

Twitter and other forms of social media can prove quite useful in permitting the rapid and timely dissemination of health-related information. However, as social media continue to evolve, they will need to find ways to provide relevant health information without obstructing patient privacy or delivering inappropriate content.

Overcoming this point will be an important element in the dissemination of medical information via social media.

Conclusions

Twitter users with a variety of types of cancer have proved influential on their followers, as demonstrated through the information exchange engaged in by account owners and their followers. Twitter represents a timely and low-cost medium for cancer patients and others seeking information about specific medical conditions, but our study found that the majority of the tweets posted by the 51 users with "power accounts" focused on conversational details (e.g., greetings, cancer treatments) and psychological support rather than the expected medical news and information. Furthermore, Twitter will need to evolve further in order for patients to fully embrace the power of this social medium, as many people are reluctant to reveal personal details via their Twitter accounts. Our study has demonstrated that Twitter is a powerful medium capable of connecting cancer patients via the establishment of a patient network.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

YS and HN designed the study, provided the study materials, collected and assembled the data and wrote the manuscript. YS, HN, AH, LS, KO and AF analyzed and interpreted the data. All authors reviewed and approved the manuscript.

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ORIGINAL RESEARCH

Coverage of genomic medicine: information gap between lay public and scientists

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Abstract: The sharing of information between the lay public and medical professionals is crucial to the conduct of personalized medicine using genomic information in the near future. Mass media, such as newspapers, can play an important role in disseminating scientific information. However, studies on the role of newspaper coverage of genome-related articles are highly limited. We investigated the coverage of genomic medicine in five major Japanese newspapers (*Asahi*, *Mainichi*, *Yomiuri*, *Sankei*, and *Nikkei*) using Nikkei Telecom and articles in scientific journals in PubMed from 1995 to 2009. The number of genome-related articles in all five newspapers temporarily increased in 2000, and began continuously decreasing thereafter from 2001 to 2009. Conversely, there was a continuous increasing trend in the number of genome-related articles in PubMed during this period. The numbers of genome-related articles among the five major newspapers from 1995 to 2009 were significantly different ($P = 0.002$). Commentaries, research articles, and articles about companies were the most frequent in 2001 and 2003, when the number of genome-related articles transiently increased in the five newspapers. This study highlights the significant gap between newspaper coverage and scientific articles in scientific journals.

Keywords: coverage, personalized medicine, mass media, newspaper

Introduction

In the wake of the Human Genome Project,[1,2] which has mapped the entire human DNA sequence, genomic medical research has entered a new era. A working draft of the genome was announced in 2000 and the complete DNA sequence was announced in 2003. In particular, one of the major challenges for medical research in the first half of the 21st century is to develop preventive and therapeutic measures against various diseases by clarifying their relationships with respect to the patterns of human genetic variability.

Personalized medicine using genomic information, which takes into consideration the patient's genetic characteristics and history of environmental factors, is expected to catalyze the next generation of therapy, with the potential to provide preventive and curative interventions specific to each individual.[3,4] Full-fledged personalized medicine will successfully personalize disease prevention efforts based on the available knowledge of each patient's specific risk factors. It will also adopt patient-specific practices, including the selection of pharmacotherapy tailored to the variations in an individual's pharmacogenetic/pharmacogenomic profile and risk of adverse drug reactions. Thus, personalized medicine is anticipated to reduce disease morbidity and mortality and improve therapeutic effectiveness, as well as impact other aspects of

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medical care.[5–7] Since individual genomic information will be essential in fostering personalized medicine, lay people are required to possess accurate knowledge about genomic medicine – so-called "genomic literacy."[8]

The role of mass media in sharing information about medical sciences is uncertain. Several studies have highlighted the importance of news media as a source of information about medicine and health;[9–22] however, sharing of information about advanced science and medicine between academia and the mass media was reported as being difficult. Although the output of scientific papers increased by 15% between 1990 and 2001, with a total output over 650,000, fewer than 0.013%–0.34% of papers gained attention from the mass media.[23]

Given that newspaper coverage can include more information than other mass media such as television or radio, many medical professionals believe that newspapers are a suitable medium to disseminate information about genomic medicine;[9] however, since studies on newspaper coverage are limited, the role of print media remains uncertain. In Japan, we have a unique and large newspaper database (Nikkei Telecom) that covers all articles in the five major national newspapers. In this study, we investigated newspaper coverage of genomic medicine in Japan.

Methods

Objective of this study

To examine the number of articles related to genomic medicine and their reported contents published by the five major Japanese newspapers within a 15-year time period (from 1995 to 2009), which is the time period covered by the newspaper database.

Target newspapers

This study was directed at the five major newspapers in Japan (*Asahi*, *Mainichi*, *Yomiuri*, *Sankei*, and *Nikkei*). The total number of subscribers to these newspapers was 26 million per day in 2010, indicating that 48% of households subscribed to these five newspapers in Japan.[24]

Data extraction

We extracted the articles using a keyword search of the database Nikkei Telecom, which is the largest newspaper database in Japan. This database incorporates almost all newspapers issued in Japan, including every article in the five major newspapers since 1995.

First, using a thesaurus search of the Igaku Chuo Zasshi database (Japan Medical Abstracts by NPO Japan Medical Abstracts Society), we extracted Japanese terms related to the word "genome" in order to define the following keywords: genome, human genome, Human Genome Project, genomic medicine, personalized medicine, made-to-order medicine, and tailor-made medicine. The contents of articles from 2001, 2003, and 2009 were analyzed by two researchers who are medical providers (YS and HN). Given the large number of articles, several of them could not be checked to ensure that the content pertained to genomic medicine and other relevant topics. The above-mentioned newspapers were subsequently searched for articles that contained these Japanese keywords, and annual changes in the numbers of such articles and their contents were investigated.

To quantify the number of genome-related research articles in academic journals, we conducted a PubMed search using the same keywords as above in English, and included the term "individualized medicine." The terms "genome, human," "Human Genome Project," and "individualized medicine" were indexed as Medical Subject Headings (MeSH). We also conducted a PubMed search using these MeSH terms.

We defined the terms "genomic medicine," "personalized medicine," "made-to-order medicine," "tailor-made medicine," and "individualized medicine" as genomic medicine-related keywords. Genomic medicine-related newspaper articles that were published in 2001 and 2003 – when the number of genomic medicine-related articles increased temporarily – and 2009, the most recent year, were extracted and categorized according to their contents.

Statistical analysis

Differences in the numbers of articles among the five newspapers were tested by a two-way ANOVA (newspapers x year), followed by Tukey's multiple-comparison post hoc test. R version 2.15.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses.

Results

Total number of articles

The total number of articles published in the five major newspapers in Japan (*Asahi*, *Mainichi*, *Yomiuri*, *Sankei*, and *Nikkei*) averaged 1,140,000 per year, including 280,000 in *Asahi*, 310,000 in *Mainichi*, 280,000 in *Yomiuri*, 130,000 in *Sankei*, and 140,000 in *Nikkei*. Figure 1 shows the change in the total number of articles across the five major newspapers during the study period. While the number of published articles has

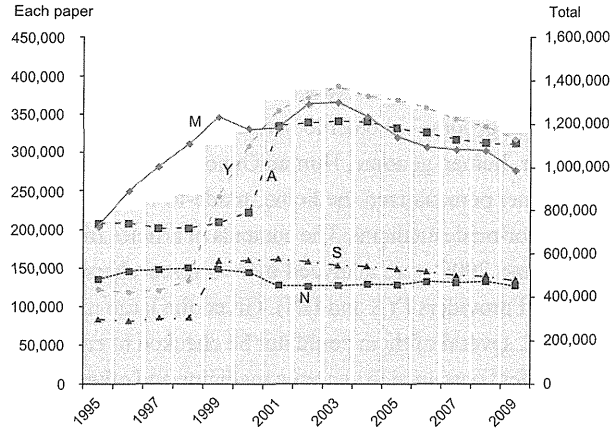

Figure 1 Total number of articles in five major newspapers.
Note: Bar: the five newspapers taken together.
Abbreviations: A, *Asahi*; M, *Mainichi*; Y, *Yomiuri*; S, *Sankei*; N, *Nikkei*.

increased since the early 1990s, there has been almost no change since 2000. Since 2000, the total number of articles published in the *Yomiuri*, *Asahi*, and *Mainichi* newspapers has been approximately three times that in *Nikkei* and *Sankei*.

Number of genome-related articles in the newspapers and genomic medicine-related scientific articles in PubMed

From 1995 to 2009, the total number of genome-related articles published in the five newspapers was 16,735, including 3019 in *Asahi*, 2583 in *Mainichi*, 3422 in *Yomiuri*, 3299 in *Sankei*, and 4412 in *Nikkei*. The numbers of articles containing the selected keywords in the five newspapers were: genome, n = 7518; human genome, n = 4063; Human Genome Project, n = 4310; made-to-order medicine, n = 425; tailor-made medicine, n = 336; genomic medicine, n = 69; and personalized medicine, n = 14.

Figure 2 shows the change in the number of genome-related articles published in the five major newspapers. The trends in the number of newspaper articles related to the human genome (Figure 2A) and the Human Genome Project (Figure 2B) were almost the same, while the number of articles related to the human genome, the Human Genome Project, and those containing genomic medicine-related keywords, temporarily increased in 2000 across all five major newspapers. Conversely, articles containing genomic-medicine-related keywords (Figure 2C) demonstrated a unique trend: in 2003, the number of genomic-medicine-related articles published in *Nikkei*, *Yomiuri*, and *Mainichi* temporarily increased.

Figure 2 also shows the change in the number of genome-related articles published in PubMed. The trends in the number of human genome- (Figure 2A) and genomic-medicine-related articles in PubMed (Figure 2C) were the same; the number of human genome- and genomic-medicine-

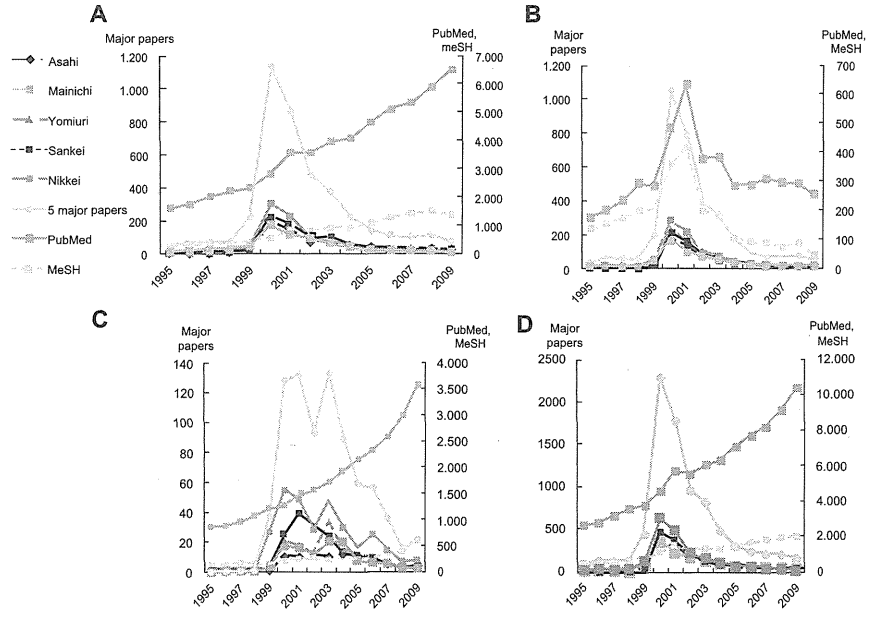

Figure 2 Number of genome-related articles in five major newspapers and genomic-medicine-related scientific articles in PubMed. (**A**) Articles related to human genome, (**B**) articles related to Human Genome Project, and (**C**) articles containing genomic medicine-related keywords in five major newspapers. A PubMed search using the following MeSH terms: "genome, human," "Human Genome Project," and "individualized medicine" was conducted in (**A–C**), respectively. The total number of articles related to (**A–C**) in the newspapers and PubMed are shown in (**D**).
Abbreviation: MeSH, Medical Subject Headings.

related articles continuously increased. On the other hand, the number of articles related to the Human Genome Project (Figure 2B) showed a unique trend: the number of articles related to the Human Genome Project increased temporarily in 2001. The total number of articles containing all genome-related keywords are shown in Figure 2D.

The numbers of genome-related articles that were published among the five major newspapers from 1995 to 2009 were significantly different ($P = 0.002$). Table 1 shows the comparison between the newspapers. Differences between *Nikkei* and *Asahi* ($P = 0.04$), and *Nikkei* and *Mainichi* ($P = 0.001$) were statistically significant.

Contents of genomic medicine-related articles published in newspapers

We investigated the contents of articles published in 2000, when the working draft of the genome was announced, and in 2003, when the complete genome was reported. We also investigated the contents of relevant articles published in 2009, the most recent year available in the database. The number of genomic medicine-related articles was 132 in 2001, 133 in 2003, and 21 in 2009. The contents of genomic medicine-related articles in the newspapers and changes in content over the years are shown in Table 2. Commentary articles, articles about research, and articles about companies were most frequently published in 2001 and 2003 (86 articles in 2001 and 88 articles in 2003), when the number of genome-related articles transiently increased across the five newspapers.

Discussion

The present study shows that newspaper coverage about genomic medicine is usually transient. The number of such articles substantially, though temporarily, increased in 2001 (Figure 2). This is probably due to the fact that reports from the Human Genome Project were covered as one of the topics during this time period. In contrast, the rapid decrease after the transient increase in genome-related articles indicated that detailed information about genomic medicine is not currently reported in newspapers. In contrast, the number of scientific articles about genomes or personalized medicine using genomic information that were found in PubMed has continuously increased, indicating that constant research and advances in genomic medicine have been occurring. This contrast reveals that there has been an information gap about genomic medicine as indicated in the findings noted between the mass media and scientists, and as described in other areas of advanced science.[23] This gap might interfere with the dissemination of knowledge pertaining to genomic medicine, which may affect the conduct of related medical practices in the near future.

Table 1 Comparison of the number of genome-related articles in the five major newspapers*

	Asahi	Yomiuri	Nikkei	Mainichi	Sankei
Asahi	NA	–	–	–	–
Yomiuri	0.83	NA	–	–	–
Nikkei	0.04	0.35	NA	–	–
Mainichi	0.71	0.15	0.001	NA	–
Sankei	0.92	1.00	0.24	0.23	NA

Note: *P-values are shown.
Abbreviations: NA, not applicable; *P*, probability level.

As previously reported, one characteristic feature of newspaper reporting on scientific issues is that only part of the subject matter is emphasized due to a poor balance in the number of news reports when compared to the number of scientific articles available.[9,10] This would appear to be related to the amount of time it takes to discuss medical issues and to the fact that public interest drops when more detailed information or discussions appear. This is believed to be a structural problem inherent to the media, particularly with newspapers, which target the general public and report on a wide range of fields. This structural problem has already been recognized as an "issue attention cycle" in the United States, which was first described by Downs in 1972.[11] This cycle has been observed and reported in relation to other medical issues, such as childhood obesity.[12] In this cycle, public attention to a single issue is rarely sustained over an extended period, even in the case of critically important, unresolved problems. Scientists should be aware of this structural problem with mass media when they share information with the public. In this study, we did not investigate how much information is shared about other scientific topics; it would be worthwhile to investigate the newspaper coverage of these topics as well. In addition, the actual newspaper format might also have affected the results. Further, the influence of whether or not the newspaper carries a regular science section or employs science editors also needs to be considered when analyzing our results.

Although this study provided important information on the newspaper coverage of genomic medicine, the following issues still remain to be discussed. First, this study focused only on mass media. These days, the internet plays an increasingly important role in medical practice; information on the adverse effects of an anticancer drug, for example, was shared mainly by internet media such as blogs, homepages, and mail magazines between physicians, patients, pharmaceutical

Table 2 Contents of genome-medicine related articles in the five major newspapers in Japan

Classification	Detailed classification 2001	n	Detailed classification 2003	n	Detailed classification 2009	n
Commentary	Tailor-made medicine	12	Glossary	4	Gender-specific medicine	1
	Glossary	8	Tailor-made medicine	4	Nanotechnology and new medical devices	1
	Genes, SNPs, and gene therapy	6	Announcement of sequencing of the complete human genome	2		
	Genomic drug discovery	5	Meaning and benefits of deciphering the human genome	2		
	Regenerative medicine	3	Biochips	2		
	Structural problems in bioscience research	2	Allergy genes	2		
	Post-genome	2	Tailor-made medicine in dentistry	1		
	Personalized drug administration	2	Ten-year general strategy against cancer	1		
	Bioinformatics	1	Amyotrophic lateral sclerosis and tailor-made medicine	1		
	Anticancer drug sensitivity tests	1	Diabetes and tailor-made medicine	1		
	Future predictions	1	"Chronotherapy," in which adverse effects are decreased with time of day medicine is taken	1		
	Genetic discrimination	1	Advanced cancer screening	1		
	Comparison of accuracy with Celera Genomics	1	Explanation of advanced medicine	1		
			Use of genetic information	1		
Articles on research	Herceptin	7	Gene bank (project to provide medicine suited to individual genetic information)	11	Creation of muscular dystrophy patient genetic information database	2
	DNA chip development	4	Bipolar disorder and tailor-made medicine	5	Development of pathological diagnosis center	1
	ES cells	2	Lecture meeting guide	3	iPS cells	1
	Celera Genomics research	2	International standardization of databases	2	Researcher profile	1
	HIV and tailor-made medicine	2	Cancer society conferences	2	Hepatitis C and tailor-made medicine	1
	DNA vaccine	2	Researcher profile	2	New blood concentration analysis methods (theophylline, etc)	1
	Irinotecan	2	Industry-government-academia joint projects	2	Drug design	1
	Discovery of epilepsy gene	2	Completion of genome sequencing and future significance	2	Genes related to hepatitis B	1
	Bronchial asthma and tailor-made medicine	2	Memory and genetic mutations	2		
	Human genome SNP identification	1	Predicting efficacy of rheumatism drugs using genes	1		
	Genetic diagnosis of chronic fatigue syndrome	1	Predictions of survival following lung cancer surgery	1		
	High blood pressure gene	1	Diabetes drugs and SNP	1		
	Industry-government-academia collaboration	1	Kazusa Akademia Park, a biotechnology center in Chiba Prefecture	1		
	Esophageal cancer and anticancer drugs	1	Bioventures originating at universities	1		
	Development of gene analysis systems	1	New drug development and start of clinical trials	1		
	Tailor-made medicine for atomic bomb survivors	1	Establishment of specialized courses	1		
	Hepatitis C research	1	Regenerative medicine	1		
	Methods of detecting individual differences in genetic information	1	Protein analysis	1		

(*Continued*)

Table 2 (*Continued*)

Classification	Detailed classification 2001	n	Detailed classification 2003	n	Detailed classification 2009	n
	Biotechnology and genomic medicine	1	Current status of anticancer agent use	1		
	Foundation of translational research centers	1				
	Researcher profile	1				
	Problems in bioscience research	1				
	MDR1 protein gene	1				
Articles on companies	Corporate collaboration and joint research	5	DNA chips	7	Corporate researcher profile	1
	DNA chips	4	Bioventures	3		
	Other businesses enter genome medicine market	2	Development of DNA synthesis and detection devices	2		
	Foreign manufacturers market new anticancer drugs in Japan	2	Business manager lectures	2		
	Establishment of corporate genome research center	2	Corporate restructuring	2		
	Bioventures	2	Research not advancing at genomic medicine information analysis center (Kobe)	2		
	Personnel rotation at Olympus	2	Corporate researcher profile	1		
	Comparison of drug industry in other countries and Japan	1	Gene function analysis system	1		
	Development of new drugs for lifestyle-related diseases	1	Gene analysis for type of leukemia	1		
	Start of gene analysis services	1	Establishment of corporate research organizations	1		
	Sales of genome data by Celera Genomics	1	Protein analyzers	1		
	Development of genetic information databases	1	Establishment of new research centers	1		
			SNP analysis for gastrointestinal drugs	1		
			Personnel rotation	1		
			Company president interviews	1		
			Growth strategy	1		
			Establishment of new companies	1		
Lecture presentations	Tailor-made medicine	8	Tailor-made medicine	13	General science	2
	Bioscience in general	3	Nanotechnology and bioscience	1	Bioscience	1
National strategy	Budget	3	Anti-cancer strategy	3	Medical Engineering Technology Industrial Strategy Consortium (METIS)	1
	Promotion of genomic medicine	2	Budget	2		
	Promotion of cooperation between medicine and engineering	2	Cooperative projects with nanotechnology ministries and agencies	1		
	Key government policies in each country	1				
	Proposed general plan of the Council for Science and Technology Policy, Cabinet Office	1				
	Financial support for advanced technologies	1				
Problems	Bioethics	4	Need for personal information protection in the field of medicine	2	Problems with insurance system	1
	Concerns about human cloning	3	New drug review	1		
	Lack of human cell samples	1	Lack of bioinformatics specialists	1		
	Sharing of genetic information	1	Cancer screening standardization	1		

(*Continued*)

Table 2 *(Continued)*

Classification	Detailed classification 2001	n	Detailed classification 2003	n	Detailed classification 2009	n
	Differences in way of thinking about bioethics in Japan and Western countries	1				
Book reviews	Newspaper feature articles	1	Post-genome	1	Hospice	2
	Problems of research in Japan	1	Individual differences in drug effectiveness	1		
	Full explanations of genome research	1				

companies, and governments.[25] We are planning future studies to investigate the roles these media play in the public dissemination of medical information. Social media, such as Twitter or Facebook, may also be worth investigating. Second, this study was limited to Japanese media. Media in English or other languages need to be investigated in future studies to determine how Japanese newspapers compare in terms of the reporting of genome-related articles. Third, only newspaper articles were included in this study. Significant differences in the coverage of medical issues have been reported between newspapers and television.[12] This is possibly because different types of media attract different audiences. Genomic medicine is not a major health issue that is on the minds of the general public, especially when compared to issues such as obesity, smoking, or cancers, which have been the subject matter of previous reports.[12,15,21,26–28] Therefore, highly limited space was probably available for the issue of genomic medicine on television, making it difficult to provide detailed results as to why this discrepancy in news coverage exists. Further investigations about the role of this media are warranted. Additionally, it would be worthwhile to investigate advertising related to genomic medicine in future studies. Fourth, it may actually be appropriate for the media to have reported less upon genomic medicine than scientific journals, given the current stage of this area of research. To date, there are very few health conditions that have shown relevant pharmacogenetic treatment models or preventive medical practices, so it is reasonable that there is a lack of coverage in the press. We could argue that this lack of coverage exhibits appropriate restraint by the press. Fifth, we did not conduct a direct comparison using statistical models due to the difference in methods of detecting articles; however, differences in the trends of newspaper coverage and the number of academic journals itself provided enough useful and important information in this study. Sixth, in the last several years, the rapid expansion of "next-generation" sequencing is making genomic medicine a true reality. While our data is derived from just before the "next-generation" era, it is extremely likely that another increase in coverage in the press is currently occurring, and this transition may have been occurring beginning in 2010. The revolution that is being wrought by new technologies that make high-throughput sequencing a financial and logistical reality in many contexts may be influencing the coverage by the mass media. This issue is worth investigating in future studies. Seventh, another possible limitation of this study is that journalists may have used more lay language, including words such as "family history" or "risk;" therefore, there may have been some oversight when extracting data from newspaper articles.

The optimal strategy in sharing information on genomic medicine between scientists, physicians, and the lay public via the media is uncertain. Schnoll et al reported that the publication of information regarding the use of spiral computed tomography for early lung cancer detection[27] did not increase the level of public awareness and interest, although lung cancer is one of the most important and widely mentioned cancers, with the general public having an intense interest in its prevention and detection.[11] In contrast, genomic medicine is less well known than is cancer among the general public, although genetic medicine is expected to play an important role in the future. Thus, it is more difficult to increase the general public's level of awareness and interest in this topic. Although an optimal strategy of disseminating this information is still unknown, Schnoll et al[27] provided an important clue. They showed that greater exposure of health news within magazines is related to greater awareness. Magazines can provide more detailed information in their health-related articles than newspapers. This kind of media can, potentially, also play an important role in communicating findings and information about genomic medicine. Internet media may also be a promising medium through which to present this information because there are no space constraints.

Conclusion

The present study revealed a significant gap in the amount of information being presented about genomic medicine between newspaper coverage and scientific articles in academic journals. Sharing information about genomic medicine is crucial for the facilitation of personalized medicine in the future. Hence, scientists and medical professionals need to be aware of the features and structural characteristics of mass media when they disseminate information to the public.

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Disclosure

The authors report no conflicts of interest in this work.

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ORIGINAL ARTICLE

Harms of screening mammography for breast cancer in Japanese women

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Abstract
Background The US Preventative Services Task Force assesses the efficacy of breast cancer screening by the sum of its benefits and harms, and recommends against routine screening mammography because of its relatively great harms for women aged 40–49 years. Assessment of the efficacy of screening mammography should take into consideration not only its benefits but also its harms, but data regarding those harms are lacking for Japanese women.
Methods In 2008 we collected screening mammography data from 144,848 participants from five Japanese prefectures by age bracket to assess the harms [false-positive results, performance of unnecessary additional imaging, fine-needle aspiration cytology (FNA), and biopsy and its procedures].
Results The rate of cancer detected in women aged 40–49 years was 0.28%. The false-positive rate (9.6%) and rates of additional imaging by mammography (5.8%) and ultrasound (7.3%) were higher in women aged 40–49 years than in the other age brackets. The rates of FNA (1.6%) and biopsy (0.7%) were also highest in women aged 40–49 years. However, they seemed to be lower than the rates reported by the Breast Cancer Surveillance Consortium (BCSC) and other studies in the US.
Conclusions The results, although preliminary, indicate the possibility that the harms of screening mammography for Japanese women are less than those for American women.

Keywords Breast cancer screening · Harm · Mammography

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Introduction

Recent years have seen increased awareness of the need for assessment of the efficacy of cancer screening on the basis of both its benefits and harms [1–5]. The US Preventative Services Task Force (USPSTF) [3, 4] reported their updated guidelines for screening mammography. They comprehensively assessed the efficacy of breast cancer screening in terms of the net benefit, which is the sum of benefits (mortality reduction) and harms (radiation exposure, pain, anxiety, over-diagnosis, and false-negative and false-positive mammography results). For women in their 40s and 50s, screening mammography had a 15 and 14% mortality reduction effect as the benefit in eight and six meta-analysis studies [3]. On the other hand, the harms (especially false-positive mammography, unnecessary additional imaging tests and histological examinations) were relatively greater in women aged 40–49 years when comparing the analyzed data [6–12] with the data of the Breast Cancer Surveillance Consortium (BCSC) [3]. The USPSTF thus recommended against routine screening mammography in women aged 40–49 years (grade C recommendation) [4]. That recommendation, however, has not escaped criticism [5]. That paper reevaluated the data that served as the basis for preparation of the USPSTF guidelines and argued that, for maximization of the survival results, it would be necessary to start screening once annually beginning from the age of 40 years [5].

On the other hand, in Japan, screening mammography, which was endorsed in 2000 for women aged 50 years and over, was expanded to cover women aged 40–49 years in 2004. However, at the time of that endorsement, data regarding the improvement in survival and the harms of screening mammography were not yet available. It will take considerable time to elucidate the improvement in survival, and a conclusion cannot be drawn at this time. Conversely, the harms of the technique can be investigated. Accordingly, the present study was designed to evaluate the harms of breast cancer screening by mammography in Japanese women. We studied the harms of screening mammography using the initial test data collected from five prefectures. The analyzed harms consisted of false-positive results, unnecessary additional imaging tests, and the need for biopsies and their procedures, which were compared with the US data.

Materials and methods

We collected community-based screening mammography data for 144,848 participants that had been recorded in fiscal 2008 in five prefectures—Gunma, Ibaraki, Fukui, Miyagi and Tokushima—with the support of the Japan Association of Breast Cancer Screening. Participants undergo—in principle—biennial screening mammography, based on the guidelines of the Japanese Ministry of Health, Labour and Welfare. Using a questionnaire, we inquired about the following items by age bracket (40–49, 50–59, 60–69, and 70 years or over): the number of participants, number recalled, number of responders and number of detected breast cancer cases. Recalls were defined as women who required further examinations after the initial screening. Responders were defined as women who were recalled after the initial screening because of a positive finding and actually presented for further examination. False-positive screenings were defined as the proportion of recalls except cases whose further examinations proved to be breast cancer.

We ascertained the methods used for additional imaging [mammography, ultrasound (US)] and interventions [cytological examination by fine-needle aspiration cytology (FNA) and histological examination] for women with or without breast cancer by age bracket. We used data from only four of those Japanese prefectures (Gunma, Ibaraki, Fukui and Miyagi) for analysis of the details of the further examinations [additional mammography, additional US, cytological examination by FNA and biopsy (any method)], because the data from Tokushima lacked adequate details.

Furthermore, we ascertained the details of biopsy, such as core-needle biopsy (CNB), vacuum-assisted biopsy

Table 1 Total data of this analysis of all five prefectures

Prefecture	Participants	Recalled		Responders		Cancer		PPV	False positive	
	(*n*)	(*n*)	(%)	(*n*)	(%)	(*n*)	(%)		(*n*)	(%)
Gunma	22,893	1,172	5.1	1,124	95.9	75	0.33	6.4%	1,097	4.8
Ibaraki	63,451	3,451	5.4	3,055	88.5	121	0.19	3.5%	3,330	5.2
Fukui	13,796	1,534	11.1	1,418	92.4	43	0.31	2.8%	1,491	10.8
Miyagi	32,847	3,066	9.3	3,036	99.0	115	0.35	3.8%	2,951	9.0
Tokushima	11,861	1,134	9.6	1,061	93.6	51	0.43	4.5%	1,083	9.1
Total	144,848	10,357	7.2	9,694	93.6	405	0.28	3.9%	9,952	6.9

PPV positive predictive value

(VAB) and open surgical biopsy (OSB), for each age bracket. CNB was defined as percutaneous histological examination using an 11, 14- or 16-gauge needle without aspiration. VAB was defined as percutaneous histological examination using a needle with aspiration by Mammotome® (Johnson & Johnson Ethicon Endo-Surgery, Inc., Cincinnati, OH) and Vacora® (BARD, Murray Hill, NJ, USA). Data from only three prefectures (Gunma, Ibaraki and Fukui) were used for analysis of the details of the histological examination methodology (CNB, VAB or OSB), because the data from Miyagi and Tokushima lacked sufficient detail.

Differences in the recall rate, response rate, cancer yields, positive predictive values, false positives, additional imaging (screening mammography, US), FNA and biopsy between ages 40–49 years and the other age brackets were statistically evaluated using the chi-square test. The Japanese data and BCSC data on the harms were also comparatively analyzed. Differences were regarded as significant if the two-sided P value was <0.05.

Results

Table 1 shows the region-specific data. The data obtained from the five prefectures and the age-specific data are summarized in Table 2. In women aged 40–49 years, the recall rate (9.9%) and false-positive rate (9.6%) were higher than in the other age brackets, with statistical significance ($p < 0.001$). The response rate for detailed examinations (92.2%) and the positive predictive value (2.8%) were slightly lower in the women in their 40s than in women in the other age brackets. Cancer detection rates in the 40s, 50s, 60s and above 70 were 0.28, 0.25, 0.24 and 0.43%, respectively.

Table 3 shows the data for the additional imaging and interventions performed in the four analyzed prefectures. The respective rates of performance of mammography, US, cytological examination (FNA) and biopsy (histological examination) as the detailed investigations were 4.0, 4.8, 0.9 and 0.4% among the total participants, and 5.8%, 7.3%, 1.6% and 0.7% in women aged 40–49 years. The rates of additional imaging, FNA and biopsy were significantly higher in the 40s than in the other age brackets ($p < 0.001$).

Table 4 presents the details of the information obtained by histological examinations (CNB, VAB and OSB) performed in Gunma, Ibaraki, Fukui and Miyagi prefectures. CNB, VAB and OSB were performed in 0.26, 0.08 and 0.04% of the total participants, respectively. Each of those rates was highest for women in their 40s: 0.38, 0.16 and 0.07%. Next, the Japanese and BCSC data on the harms were comparatively analyzed (Table 5) [3]. The harms in terms of false positivity and unnecessary additional

Table 2 Analysis by age bracket (data from all five prefectures)

Age Bracket	Participants	Recalled			Responders			Breast cancer cases (cancer yield)			PPV		False positives		
(years)	(*n*)	(*n*)	(%)	(*p*)	(*n*)	(%)	(*p*)	(*n*)	(%)	(*p*)	(%)	(*p*)	(*n*)	(%)	(*p*)
40–49	33,924	3,357	9.9		3,096	92.2		95	0.28		2.8		3,262	9.6	
50–59	43,144	3,051	7.1	$p < 0.001$	2,836	93.0	$p = 0.267$	107	0.25	$p = 0.388$	3.5	$p = 0.121$	2,944	6.8	$p < 0.001$
60–69	46,650	2,591	5.6	$p < 0.001$	2,461	95.0	$p < 0.001$	113	0.24	$p = 0.296$	4.4	$p < 0.01$	2,478	5.3	$p < 0.001$
70 -	21,130	1,358	6.4	$p < 0.001$	1,301	95.8	$p < 0.001$	90	0.43	$p < 0.05$	6.6	$p < 0.001$	1,268	6.0	$p < 0.001$
Total	144,848	10,357	7.2		9,694	93.6		405	0.28		3.9		9,952	6.9	

PPV positive predictive value

Table 3 Rates of additional imaging and interventions (data from four prefectures)

Age (years)	Participants	Further evaluation of responders											
		Additional MMG			Additional US			FNA			Biopsy[a]		
	(*n*)	(*n*)	(%)[b]	(*p*)	(*n*)	(%)[b]	(*p*)	(*n*)	(%)[b]	(*p*)	(*n*)	(%)[b]	(*p*)
40–49	31,323	1,813	5.8		2,298	7.3		503	1.6		215	0.7	
50–59	40,199	1,728	4.3	$p < 0.001$	2,003	5.0	$p < 0.001$	359	0.9	$p < 0.001$	160	0.4	$p < 0.001$
60–69	42,789	1,304	3.0	$p < 0.001$	1,521	3.6	$p < 0.001$	204	0.5	$p < 0.001$	105	0.2	$p < 0.001$
70–	18,676	522	2.8	$p < 0.001$	586	3.1	$p < 0.001$	83	0.4	$p < 0.001$	78	0.4	$p < 0.001$
Total	132,987	5,367	4.0		6,408	4.8		1,149	0.9		558	0.4	

MMG Mammography, *US* ultrasound, *FNA* fine-needle aspiration cytology

[a] Number of cases undergoing histological examination

[b] % of participants

Table 4 Rates of each type of biopsy (data from three prefectures)

Age (years)	Participants	Type of biopsy								
		CNB			VAB			OSB		
	(*n*)	(*n*)	(%)[a]	(*p*)	(*n*)	(%)[a]	(*p*)	(*n*)	(%)[a]	(*p*)
40–49	25,159	95	0.38		39	0.16		17	0.07	
50–59	30,526	80	0.26	$p < 0.05$	26	0.09	$p < 0.05$	13	0.04	$p = 0.206$
60–69	32,491	49	0.15	$p < 0.001$	12	0.04	$p < 0.001$	9	0.03	$p < 0.05$
70–	11,964	34	0.28	$p = 0.153$	4	0.03	$p < 0.001$	4	0.03	$p = 0.196$
Total	100,140	258	0.26		81	0.08		43	0.04	

CNB Core-needle biopsy, *VAB* vacuum-assisted biopsy, *OSB* open surgical biopsy

[a] % of participants

imaging and biopsy were greatest for women in their 40s in Japan, but less than in the BCSC in all age brackets. In addition, the cancer detection rate per 1,000 screened in Japanese women aged 40–49 years was 2.8, which was slightly higher than the 2.6 recorded in the BCSC data.

Discussion

The USPSTF recommended against routine screening mammography in women aged 40–49 years [4]. As background to that recommendation, in terms of the benefit, screening mammography in the 40s results in 15% mortality reduction, and it was acknowledged to have a benefit in eight RCT meta-analyses. However, in terms of the harms, the BCSC data indicated that they (especially false positivity, unnecessary additional imaging and biopsy) were relatively greater for women in their 40s [4].

In this study, as well, the harms in terms of false positivity and performance of unnecessary additional imaging and biopsy were greatest for Japanese women in their 40s, but less than in the BCSC in all age brackets. Thus, screening mammography appears to be less harmful in Japan than in the US. In a report from the US [13], the relative proportions of biopsy performed using CNB, VAB and OSB were 23.2, 40.0 and 36.8% for women as a whole, and 25.3, 40.4 and 34.2% for women aged 40–49 years, respectively. That study found that the proportion of OSB has declined by the year, but it remains at approximately 30%. Figure 1 illustrates, per 1,000 screened women in their 40s, the estimated numbers of additional imaging, FNA, biopsy and its procedures, false positives and detected cancers. The number of biopsy procedures was calculated from the data for three prefectures in Japan and from the data of the US report [13]. As biopsy procedures, the respective numbers of CNB, VAB and OSB are approximately 3.8, 1.6 and 0.7 per 1,000 screened women in Japan, and 2.4, 3.8 and 3.2 in the US. These data suggest that once US women in their 40s go for screening, they undergo more biopsies and OSBs than in Japan. Based on these results, in addition to the lower rates of false positives, additional imaging and biopsy, the invasiveness of biopsy is lower in Japan. Accordingly, we speculate that the harms of breast cancer screening in women in their 40s are less in Japan than in the US. The costs associated with CNB, VAB and OSB in Japan are 19,300, 55,800 and

Table 5 Comparison of the data from the BCSC and this study

	Source	Age bracket (years)			
		40–49	50–59	60–69	70–
Outcomes per screening round (per 1,000 screened)					
False-positive mammogram	BCSC[a]	97.8	86.6	79.0	68.8
	This study[b]	96.2	68.2	53.1	60.1
Additional imaging	BCSC[a]	84.3	75.9	70.2	64.0
	This study[c]	73.4	49.8	35.5	31.4
Biopsy	BCSC[a]	9.3	10.8	11.6	12.2
	This study[c]	6.9	4.0	2.5	4.2
Screening-detected breast cancer[d]	BCSC[a]	2.6	4.7	6.5	7.9
	This study[b]	2.8	2.5	2.4	4.3

[a] Data from BCSC (Breast Cancer Surveillance Consortium) were cited from Ref. [3]

[b] Calculated from Table 2

[c] Calculated from Table 3

[d] Including invasive cancer and DCIS

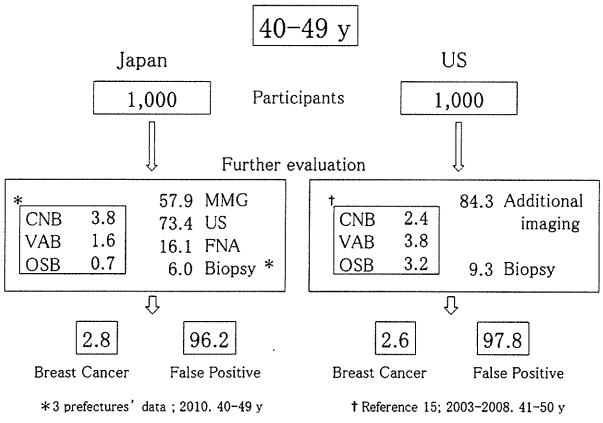

Fig. 1 The estimated numbers of additional imaging, FNA, biopsy and its procedures, false positives and detected cancers per 1,000 screened women in their 40s

65,600 Yen (including the pathological diagnosis fee), respectively, which are only 1/8 to 1/18 of the costs in the US [13]. We need to evaluate the harms of screening in consideration of the different economic circumstances between the countries. The benefit of screening can be assessed by a single measure of the decrease in mortality. With regard to its harms, however, the weight of each criterion differs by country, region, economic status and personal values. An overall net benefit should be decided upon, accounting for all the above factors.

One of the limitations of this study was that our data were taken from only 5 of the 47 prefectures in Japan. The participating prefectures had been conducting breast cancer screening for a long period, and their data can be assumed to be relatively accurate. However, analysis of larger data sets for the whole nation will be necessary before any firm conclusions can be drawn about the net benefit of breast cancer screening for Japanese women. A second limitation is that we did not focus on the other harms of breast cancer screening, such as psychological harm, over-diagnosis, radiation exposure and false-negative results. Psychological harm is said to be transient [14]. Over-diagnosis tends to occur mainly in older women, and methods for calculating it are not well established. Radiation exposure resulting from screening mammography might itself cause breast cancer, but the risk appears negligible [3].

We conclude that the major harms, consisting of false-positive results, unnecessary additional imaging, and the need for biopsy and its invasiveness, are greatest in women in their 40s undergoing breast cancer screening mammography in Japan, but they seemed to be less than those reported by the BCSC and other studies in the US. In the future, it will be necessary to compile more data regarding the mortality reduction and the accompanying harms in order to prove the efficacy of screening mammography in Japanese women age 40–49 years.

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