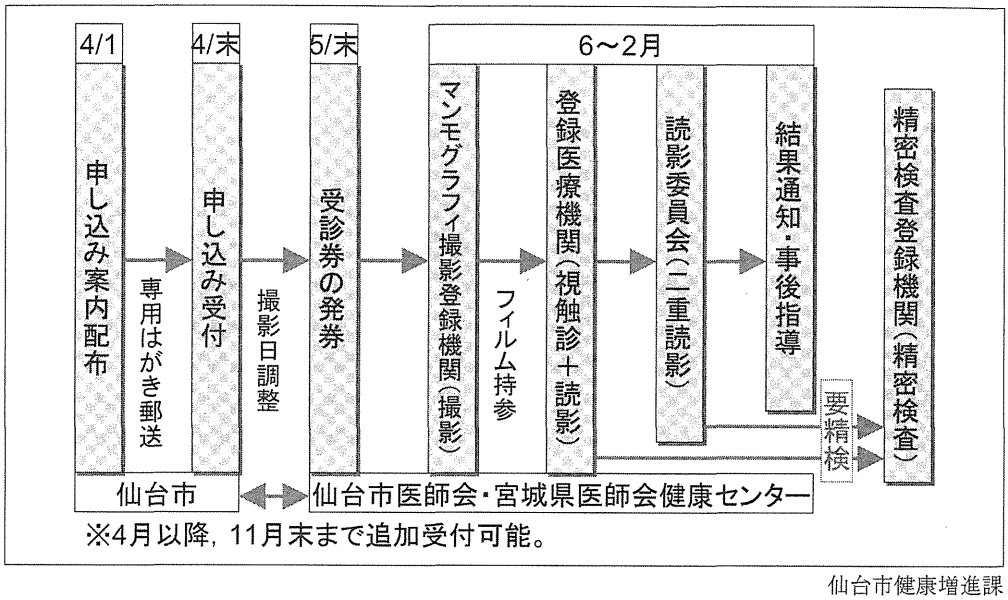
**表1.** 平成22年度乳がん検診実施概要

| | |
|---|---|
| 対　　象 | 40歳以上の女性　185,573人（前年度受診者を除く） |
| 申込期間 | 平成22年４月１日～平成22年11月30日 |
| 実施内容 | マンモグラフィ併用方式（問診，視診，触診，マンモグラフィ） |
| 実施期間 | 平成22年６月７日～平成23年２月28日<br>（ただし，マンモグラフィ撮影は平成23年２月12日まで） |
| 受診見込 | 40,500人 |

仙台市健康増進課




仙台市健康増進課

**図1.** 乳がん検診の流れ

**表2.** 平成21年度女性特有のがん検診推進事業（乳がん検診）年齢別利用者数

| | | 対象者数（人） | 利用者数（人） | 利用率（％） |
|---|---|---|---|---|
| 仙台市 | 40歳 | 7,698 | 1,583 | 20.6 |
| | 45歳 | 6,529 | 1,873 | 28.7 |
| | 50歳 | 6,515 | 1,256 | 19.3 |
| | 55歳 | 6,735 | 1,798 | 26.7 |
| | 60歳 | 8,319 | 2,193 | 26.4 |
| | 合計 | 35,796 | 8,703 | 24.3 |
| 宮城県 | | 81,421 | 24,519 | 30.1 |
| 全　国 | | 4,357,223 | 1,047,974 | 24.1 |

仙台市健康増進課

らに多いものと推測されます。

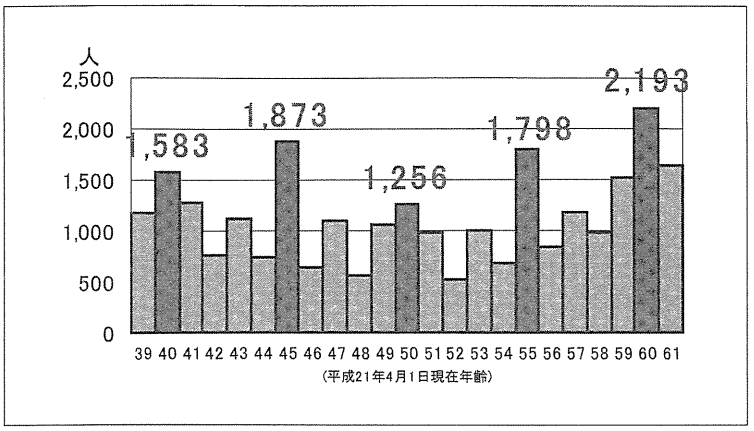
また，受診率は2.6％増加し，初めて40％を超えて40.7％に上昇しています。

**表3**は，国の事業報告の抜粋ですが，平成18年度から平成20年度にかけても，仙台市，宮城県の受診率はともに全国平均の約14％を２倍以上上回り，全国的にとても高い受診率で推移しています。

宮城県の平成21年度の受診率は，全体で36.2％でした。がん対策基本計画に示された受診率の目標50％の対象年齢は75歳未満と聞いています。75歳未満で受診率を推計すると，44.8％とかなり高い数値となり，さらに50歳未満で推計すると，42.3％とこちらも職域の受診者を加えると，実質的には50％を超えていると考えられます。

## Ⅲ．考　察

それでは，受診率の向上につながった取組みとして，検診体制の早期確立，受診増への体制強化，行政，




仙台市健康増進課

**図2.** 平成21年度乳がん検診年齢別受診者数(抜粋)

**表3.** 事業報告(平成18年度～平成20年度)抜粋

| | 仙台市 | | 宮城県 | | 全国 | |
|---|---|---|---|---|---|---|
| | 受診者数(人) | 受診率(%) | 受診者数(人) | 受診率(%) | 受診者数(人) | 受診率(%) |
| 平成20年度 | 33,656 | 38.1 | 71,763 | 35.0 | 1,792,176 | 14.7 |
| 平成19年度 | 34,543 | 30.8 | 82,044 | 31.7 | 1,892,834 | 14.2 |
| 平成18年度 | 31,724 | 29.0 | 78,169 | 32.1 | 1,631,811 | 12.9 |

平成19～21年度地域保健・健康増進(19年・20年は老人保健)事業報告の概況より

**表4.** 検診体制の早期確立期

| | |
|---|---|
| 昭和63年4月 | 視触診による乳がん検診開始 |
| 平成10年4月 | 仙台市医師会乳がん検診委員会 |
| 平成10年11月 | 仙台市のがん検診に関するあり方会議 |
| 平成11年1月 | 厚生省特別事業によるマンモグラフィ検診の実施 |
| 平成12年4月 | マンモグラフィ導入に関する協議 |
| 平成13年4月 | マンモグラフィ導入(50歳以上偶数年齢) |

仙台市健康増進課

医師会，大学等，専門機関等との定期的な連携の三点についてご紹介します。

1)検診体制の早期確立(表4)

まず，平成13年度からのマンモグラフィ導入以降の，年齢拡大に対応した検診体制について，関係機関と早期に確立できた点についてお話しします。

導入にあたり，平成10年11月，仙台市のマンモグラフィ併用検診の確立に多大なご協力をいただきました大内憲明教授をはじめとする東北大学，仙台市医師会の学識経験者を交えた，がん検診に関するあり方会議にて，マンモグラフィの必要性について検討しています。

平成11年の厚生省特別事業では，講習会を実施することで，かかりつけ医による適切な読影が可能であることを確認し，平成12年3月の国の指針改正を受けて，同年4月から仙台市医師会との具体的な協議に入りました。

医師会において読影医師の確保および育成のため，かかりつけ医を対象とした読影講習会の開催や撮影施設の確保など，準備を進める一方，早期からの仙台市医師会乳がん検診委員会における，行政，医師会，大学等，専門機関との連携が効を奏したことにより，初年度から13,022人の検診が実施できたと考えています。

2)受診者増への体制強化(表5)

次に，受診率アップには申し込み方法の簡易さが重要と考えます。本市では，各種がん検診と，生活習慣病健診を，世帯単位で一度に申し込みいただくため，平成11年度から申し込み案内を各家庭に全戸配布しています。

申し込み内容は電算処理し，延べ40万件以上の申し込みに対して，迅速に対象者を確認，受診券を作成し，

**表5.** 受診者数増への体制強化期

| | |
|---|---|
| 平成11年～ | 検診申し込み案内の全戸配布・受診券発行の電算処理化＝大量処理可能 |
| 平成17年4月 | 40歳以上に拡大，40歳～49歳偶数年齢対象 |
| 平成18年10月 | ピンクリボンフェスティバル開催(～継続中) |
| 平成21年10月 | 女性特有のがん検診推進事業(～継続中)※40，45，50，55，60歳対象 |

仙台市健康増進課

**表6.** 仙台市乳がん検診に関する会議等(仙台市医師会主催)

| |
|---|
| 精度管理委員会(年1回，1月) 委員7名 |
| 登録医療機関研修会(年2回，3月)120医療機関出席 |
| 精検医療機関・撮影施設との懇談会(年1回4月)40施設出席 |
| 読影研修会(年3回，4月)登録医療機関検診医が参加 |

仙台市健康増進課

自宅へ送付する仕組みを築いています。

また，平成17年度の40歳以上への対象者拡大時には，約8,000人の受診者増に対応するため，撮影期間の終わりを11月から2月に変更し，期間を拡大のほか，マンモグラフィ専用の撮影診療所を整備しています。

さらに平成18年度から開催中のピンクリボンフェスティバルによる受診啓発，昨年度からの無料クーポン券の配布による受診者数の増加，これらにも撮影可能枠の拡大，期間延長などの柔軟な対応により，希望者全員が受診できる態勢を維持しています。

3)行政，医師会，大学等専門機関との定期的な連携

次に，市民ニーズを把握する，われわれ行政の情報を共有し，検診に生かすために行う，定期的な医師会や大学，専門機関との連携についてご紹介します(**表6**)。

医師会の乳がん検診精度管理委員会では，翌年度の実施概要の説明，市民からの苦情内容や改善策などを報告，検討しています。

それから，約120の医療機関が参加する登録医療機関研修会では，事業報告および事業計画，検診の流れを説明して，本市検診への協力をお願いしています。

さらに，精検医療機関および撮影施設の医師，放射線技師との懇談会でも，同様に継続した協力依頼と，事務手続きの改善等の意見交換を行っています。可能なものについては，当該年度から反映するようにしています。

ほか，東北大学の先生方による登録医療機関を対象にした，読影研修会が年に3回開催されています。これらの定期的な連携については，仙台市医師会のバックアップによるところが非常に大きく，関係機関と情報が共有されることで，よりよい検診体制と市民の受診環境の向上につながっています。

## Ⅳ．今後の課題とまとめ

今後，仙台市が受診率50%を達成するには，毎年5万人の受診者を要すると推定されます。受診者増に必要なこととして，第1に無料クーポン券の事業が継続できることです。昨年度実施時は，初回受診者数が全体で約3,800人増加して，今後も定期的な受診者となることを期待しています。

事業継続できた場合，3年後の平成25年度には，約46,000人の受診者に達する見込みと考えています。

また，未受診者への啓発も重要と考えて，市政広報番組やパブリシティ，ピンクリボンフェスティバルを活用した，広く市民への受診啓発，それから乳がん検診に協力的な企業との連携により，行政に関心の薄い層への受診啓発にも力を入れたいと思います。

さらに，定期的な検診受診を促進するため，多様な申し込み方法，受付方法の確立が必要であり，インターネットやショッピングセンターでの受付など，市民の生活に合った方法を提供していくことが必要と考えています。

最後に，従来から健康福祉行政は市民の健康を守ることを一番に考えていました。関係機関と綿密な連携と信頼関係を築いてきたことが，今後のさらなる受診率の向上につながるものと考えています。

**大貫** 佐竹先生，どうもありがとうございました。仙台市の取り組みについてお話しいただきました。では，佐竹先生，また後ほどよろしくお願いいたします。

最後のご発表になります。「日本乳がんピンクリボン運動が実践した検診率アップのためのプログラム」ということで，NPO法人J.POSHの松田先生，よろしくお願いいたします。

原　著 ● Original Article

# 乳癌死ひとりを回避するのに必要な日本人女性のマンモグラフィ検診必要対象者数

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雑賀公美子[1,2)]　斎藤　博[2)]　大内　憲明[3)]　祖父江友孝[1)]

**要旨**：2009年に米国予防医学専門委員会(U.S. Preventive Services Task Force; USPSTF)は乳癌検診ガイドラインを改訂し，40～49歳の定期的な乳癌マンモグラフィ検診については，個人ごとに利益と不利益を勘案して判断することを勧めるとした。この理由の1つとして，メタアナリシスの結果から40～69歳のすべての年齢階級においてマンモグラフィ検診による乳癌の死亡率減少効果はあると判断できるものの，1人の乳癌死亡を回避するのに必要な検診対象者数(the Number Needed to Invite; NNI)は，50～69歳に比べて40～49歳の間で大きいことを挙げた。しかし，USPSTFの推計はランダム化比較試験のそれぞれの観察年数の違いを考慮しておらず，40歳代のNNIを過大評価しているため，観察年数の違いを考慮したNNIを推計し直した上で，日本のNNIを推計することを目的とした。NNIの推計方法はUSPSTFの推計と同様の方法を用いたが，日本にはNNIを算出するために必要なマンモグラフィ受診勧奨群と未勧奨群の累積死亡率の絶対差や相対リスクの情報がないため，受診率の低い日本人女性の死亡率は，欧米のマンモグラフィ未受診勧奨群の死亡率と同様と仮定し，相対リスクはUSPSTFによるメタアナリシスの結果を用いた。日本人女性のNNIとUSPSTFが報告したNNIを比較すると，40～59歳では同様の値であったが，60～69歳の日本人のNNIはUSPSTFの報告の約2倍であった。エビデンスに基づいた推奨グレードを決定するには，マンモグラフィ受診における利益と不利益の実測を行った上で，利益と不利益のバランスを検討することに加え，数理モデル等による評価研究も必要である。

**索引用語**：NNI，米国予防医学専門委員会(USPSTF)，乳癌検診ガイドライン

## 緒　言

米国予防医学専門委員会(U.S. Preventive Services Task Force; USPSTF)は，乳癌検診ガイドラインにおいて，2002年版では40歳以上のすべての女性に対して定期的なマンモグラフィを推奨していた(推奨レベルB)が，2009年のガイドライン改訂において，40歳代については個人ごとに利益と不利益を勘案して受診の判断を行うことを勧めるとした(推奨レベルC)[1)]。推奨レベルの変更の理由としては，乳癌ランダム化比較試験のメタアナリシスの結果，マンモグラフィを行うことで乳癌の死亡率減少効果は明らかであるものの，1人の乳癌死亡を回避するために必要な検診対象者数(the Number Needed to Invite; NNI)は，50歳以上に比べて40歳代でかなり大きいことが挙げられた[2,3)]。USPSTFの研究結果では，NNIの算出を行うメタアナリシスにランダム化比較試験の観察年数の違いが考慮されておらず，年齢が若いほど観察年が短く，NNIが過大評価(死亡減少効果は過小評価)されることが考えられるため，観察年数を考慮したNNIの算出を試みた結果，40歳代と50歳代の差は小さくなることを報告した[4)]。USPSTFの報告は欧米のデータに基づいた判断であるため，日本における推奨は可能な限り日本のデータに基づいて決定すべきである。そこで，本研究では，USPSTFの結果の一部を用い，日本での40～69歳の年齢階級別NNIを算出し，USPSTFによる米国のNNIと比較することを目的とした。

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## 1. 対象および方法

1人の乳癌死亡を回避するために必要な検診対象者数(NNI)を算出するためには，マンモグラフィ受診勧奨群と未勧奨群それぞれの累積死亡率の絶対差が必要となる。米国予防医学専門委員会(USPSTF)の計算では，ランダム化比較試験のメタアナリシスにより，40～69歳の10歳年齢階級別累積死亡率(観察年数は各研究における観察期間)を用いている。日本ではランダム化比較試験が行われていないため，可能な限り日本のデータを用いて受診勧奨群と未勧奨群の累積死亡率を推計する必要がある。本研究では，40歳以上の5歳年齢階級別乳癌死亡率(2008年人口動態統計)を用い，40～49歳，50～59歳，60～69歳の女性を10年，15年，20年観察した場合の累積死亡率をマンモグラフィ未受診群の乳癌死亡率($r_{c\_JPN}$)として算出した。この際に用いた全死亡率も2008年人口動態統計の報告値を用いた。

$$r_{c\_JPN}=r_a+\sum_{t=1}^{T-1}\left\{ {}_{a-t}r_{a-t}\prod_{k=a}^{a-t-1}(1-{}_{all}r_k)\right\}$$

ここで，$r_a$ を $a$ 歳の女性の乳癌死亡率，${}_{all}r_a$ を $a$ 歳の女性の全死亡率，$T$ を観察年数(10, 15, 20年)とする。さらに，マンモグラフィ受診勧奨群の累積死亡率($r_{i\_JPN}$)は，2009年に米国予防医学専門委員会(USPSTF)が行った同様の方法でメタアナリシスを行い算出したマンモグラフィ受診勧奨群と未勧奨群の相対リスク($r_i/r_c$)を用いて推計した。

$$r_{i\_JPN}=r_{c\_JPN}\times\frac{r_i}{r_c}$$

相対リスクの算出には，2009年にUSPSTFがメタアナリシスに用いた8試験それぞれの相対リスク(RR)，受診勧奨群と未勧奨群の対象数，観察人年および乳癌死亡数を用いた[5~10]。ただし，観察人年については40～49歳におけるGothenbergの試験[8]の観察人年は不明であったため，平均観察年(12年)に対象数を乗じたものを観察人年として用いた。50～59歳におけるCNBSS-2の試験[11]はUSPSTFのNNIの算出を行った論文内[3]において引用文献の誤植があったため，今回の解析には使用していない。メタアナリシスを行い相対リスクの算出に用いたモデルは，2009年のUSPSTFが用いたベイズのランダム効果モデルと同様である[3]。ベイズの推定にはWinBUGS version1.4[12]を用いた。

相対リスクおよびNNIの算出は，メタアナリシスに用いるランダム化比較試験の観察年数を考慮しない場合(累積死亡率の分母を対象者数で計算)と考慮する場合(死亡率の分母を人年で計算)の二通りで行った。NNIは，1人の乳癌死亡を回避するために受診勧奨

**表1.** メタアナリシスに用いた

| 試験，年 | 受診勧奨群 ベースライン年 | フォローアップ年 | 死亡数 | 対象者数 | 人年* |
|---|---|---|---|---|---|
| 40～49歳 | | | | | |
| Health Insurance Plan of Greater New York, 1986 | 1963 | 12.2 | 64 | 13,740 | 192360 |
| Canadian National Breast Screening Study-1, 2002 | 1980 | 11.2 | 105 | 25,214 | 282606 |
| Gothenburg Breast Screening trial, 2003 | 1982 | 12.0 | 34 | 11,724 | 140688 |
| Stockholm, 2002 | 1981 | 14.3 | 34 | 14,303 | 203000 |
| Malmo, 2002 | 1976-1978 | 13.3 | 53 | 13,568 | 184000 |
| Swedish Two-County trial(Kopparberg), 1995 | 1977 | 13.0 | 22 | 9,582 | 124566 |
| Swedish Two-County trial(Ostergotland), 2002 | 1977 | 16.8 | 31 | 10,285 | 172000 |
| Age trial, 2006 | 1991 | 10.7 | 105 | 53,884 | 578390 |
| 50～59歳 | | | | | |
| Canadian National Breast Screening Study-2, 2002 | 1980 | 11.0 | 107 | 19,711 | 216133 |
| Gothenburg Breast Screening trial, 2003 | 1982 | 12.9 | 40 | 10,112 | 130000 |
| Stockholm, 2002 | 1981 | 13.7 | 25 | 15,946 | 217000 |
| Malmo, 2002 | 1976-1978 | 18.1 | 88 | 9,285 | 168000 |
| Swedish Two-County trial(Kopparberg), 1995 | 1977 | 13.0 | 34 | 11,728 | 152464 |
| Swedish Two-County trial(Ostergotland), 2002 | 1977 | 16.1 | 53 | 12,011 | 194000 |
| 60～69歳 | | | | | |
| Malmo, 2002 | 1976-1978 | 15.5 | 46 | 7,520 | 117000 |
| Swedish Two-County trial(Ostergotland), 2002 | 1977 | 14.3 | 64 | 11,573 | 166000 |

*：40～49歳のGothenberg試験は，person-yearsが不明であったため，フォローアップ年に試験の参加者数を乗じて算出

が必要な対象者数であり，マンモグラフィ受診勧奨群と未勧奨群の累積死亡率の差の逆数で表せる。観察年数を考慮しない場合の累積死亡率には観察期間内の死亡数を観察開始時の対象者数で除したものを用い，観察年数を考慮する場合の累積死亡率には，観察人年を考慮した死亡率(死亡数/対象人年)に観察年数を乗じたものを用いる。ここでの観察年数とは，1乳癌死亡を回避するためにT年観察を続けると仮定した場合に受診勧奨が必要な対象者数を定義することを意味し，死亡率にTを乗じることで累積死亡率となる。NNIの推計は，日本の40～49歳，50～59歳，60～69歳の女性を10年，15年，20年観察した状況設定のもとで行った。

## 2. 成　績

**表1**にメタアナリシスに用いたランダム化比較試験の詳細を示した。40～49歳を対象とした試験はもっとも多く8件，50～59歳が6件，60～69歳が2件であった。また試験が行われた国は，米国が1件[5]，カナダが1件[6,11]，スウェーデンが5件[7~9]，英国が1件[10]であった。平均フォローアップ期間は40～49歳を対象とした試験では10.7年から16.8年，50～59歳では11年から18.1年，60～69歳では14.3年から15.5年であり，同じ年齢階級であっても試験によってフォローアップ年は6～7年異なった。マンモグラフィ受診未勧奨群に対する受診勧奨群の相対リスクは50～59歳，60～69歳では観察年数を考慮した相対リスクと考慮しない相対リスクではすべての試験においてあまり違いはないが，40歳代では少しばらつきが見られた。

**表2**にメタアナリシスによって算出した相対リスクおよび検診必要対象者数(NNI)を示す。本研究において，USPSTFと同様の方法を用いて再計算した結果は，USPSTFの論文に掲載されていた値[3]とほぼ同様の結果を示した。観察年数を考慮しない相対リスクと観察年数を考慮した相対リスクはほぼ同じであり，40～49歳で15%，50～59歳代で18%，60～69歳で32%の死亡率減少効果があると推計された。NNIについては観察年を何年と仮定するかによって異なり，観察年数が10年，15年，20年と長くなるほどNNIは小さくなる。観察年数を考慮しない場合のNNIは，USPSTFの算出(再計算)で40～49歳が1,908人，50～59歳が1,229人であり，40歳代と50歳代には679人の差がある。しかし，観察年数を考慮したところ，この差は10年観察で691人，15年観察で460人，20年観察では345人であり，観察年数を考慮することで差が小さくなることが示された。

USPSTFの報告は欧米のNNIを推計したものであるため，観察年数を考慮したNNIを日本の推計値と

ランダム化比較試験(USPSTF論文)

| Control Group | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 死亡率(1万人対) | 死亡率(1万人年対) | 死亡数 | 対象者数 | 人年* | 死亡率(1万人対) | 死亡率(1万人年対) | 相対リスク(追跡期間中) | 相対リスク |
| 4.7 | 3.3 | 108 | 25,216 | 282575 | 4.3 | 3.8 | 1.09 | 0.87 |
| 4.2 | 3.7 | 108 | 25,216 | 282575 | 4.3 | 3.8 | 0.97 | 0.97 |
| 2.9 | 2.4 | 59 | 14,217 | 170604 | 4.1 | 3.5 | 0.70 | 0.70 |
| 2.4 | 1.7 | 13 | 8,021 | 117000 | 1.6 | 1.1 | 1.47 | 1.51 |
| 3.9 | 2.9 | 66 | 12,279 | 160000 | 5.4 | 4.1 | 0.73 | 0.70 |
| 2.3 | 1.8 | 16 | 5,031 | 65403 | 3.2 | 2.4 | 0.72 | 0.72 |
| 3.0 | 1.8 | 30 | 10,459 | 176000 | 2.9 | 1.7 | 1.05 | 1.06 |
| 1.9 | 1.8 | 251 | 106,956 | 1149380 | 2.3 | 2.2 | 0.83 | 0.83 |
| 5.4 | 5.0 | 105 | 19,694 | 216042 | 5.3 | 4.9 | 1.02 | 1.02 |
| 4.0 | 3.1 | 67 | 15,997 | 206000 | 4.2 | 3.3 | 0.94 | 0.95 |
| 1.6 | 1.2 | 24 | 8,421 | 118000 | 2.9 | 2.0 | 0.55 | 0.57 |
| 9.5 | 5.2 | 90 | 9,322 | 168000 | 9.7 | 5.4 | 0.98 | 0.98 |
| 2.9 | 2.2 | 34 | 5,557 | 72241 | 6.1 | 4.7 | 0.47 | 0.47 |
| 4.4 | 2.7 | 54 | 11,495 | 185000 | 4.7 | 2.9 | 0.94 | 0.94 |
| 6.1 | 3.9 | 72 | 7,515 | 116000 | 9.6 | 6.2 | 0.64 | 0.63 |
| 5.5 | 3.9 | 83 | 10,862 | 155000 | 7.6 | 5.4 | 0.72 | 0.72 |

**表2.** 年齢階級別マンモグラフィ未受診勧奨群の受診勧奨群に対する相対リスクおよび検診必要対象者数

| 年齢 | RR(95%信頼区間) | 1乳がん死亡を回避する検診必要対象者数(95%CI)：USPSTF | 1乳がん死亡を回避する検診必要対象者数(95%CI)：日本 |
|---|---|---|---|
| USPSTFによる報告値[1] | | | |
| 40～49 | 0.85( 0.75－ 0.96) | 1904( 929－ 6378) | |
| 50～59* | 0.86( 0.75－ 0.99) | 1339( 322－ 7455) | |
| 60～69 | 0.68( 0.54－ 0.87) | 377( 230－ 1050) | |
| 観察年数の調整なしの推計値(USPSTFで推計された方法) | | | |
| 40～49 | 0.85( 0.75－ 0.96) | 1908( 957－ 7339) | 1836( 1099－ 6069) |
| 50～59 | 0.83( 0.69－ 0.99) | 1229( 299－ 7490) | 1207( 627－ 6329) |
| 60～69 | 0.68( 0.54－ 0.87) | 388( 64－ 4438) | 728( 500－ 1771) |
| 観察年数調整ありの推計値 | | | |
| フォローアップ10年を仮定 | | | |
| 40～49 | 0.85( 0.75－ 0.96) | 2399( 1195－ 8550) | 2638( 1565－ 8468) |
| 50～59 | 0.82( 0.69－ 0.98) | 1708( 452－10215) | 1734( 907－ 9032) |
| 60～69 | 0.68( 0.53－ 0.86) | 520( 36－ 2907) | 1018( 700－ 2385) |
| フォローアップ15年を仮定 | | | |
| 40～49 | | 1599( 797－ 5700) | 1758( 1043－ 5645) |
| 50～59 | | 1139( 302－ 6810) | 1156( 604－ 6021) |
| 60～69 | | 347( 24－ 1938) | 678( 467－ 1590) |
| フォローアップ20年を仮定 | | | |
| 40～49 | | 1199( 598－ 4275) | 1319( 782－ 4234) |
| 50～59 | | 854( 226－ 5107) | 1124( 588－ 5856) |
| 60～69 | | 260( 18－ 1453) | 509( 350－ 1192) |

*Canadian National Breast Screening Study－2を含む6試験.

比較すると，仮定する観察年数に関わらず，40歳代と50歳代のNNIは同程度であるが，60歳代の日本の推計値はUSPSTFの約2倍となった。

### 3. 考　察

検診必要対象者数(NNI)は，1人の乳癌死亡を回避するために何人にマンモグラフィ受診勧奨をする必要があるのかを表わし，値が小さいほど死亡減少効果が大きいと判断できる。米国予防医学専門委員会(USPSTF)は，定期的なマンモグラフィ受診勧奨の推奨年齢の下限を40歳から50歳に改訂した理由の1つに50歳代のNNIに比べて40歳代のNNIが大きいことを挙げたが，USPSTFによる試算では，用いたランダム化比較試験のそれぞれの観察年数が異なることを考慮していないため，40歳代のNNIと50歳代のNNIの差を過大評価している。

本研究結果より，日本のNNIは欧米と比べ，40～49歳および50～59歳は同様であるが，60～69歳で約2倍大きいことが推計された。これは，日本の60歳代の乳癌死亡率が欧米に比べ低いためであり，緑茶や大豆などの乳癌のリスクを下げる食品の摂取量が欧米人より多い日本人は閉経後の乳癌リスクが低いことが認められている[13]。WHO死亡データベースから日本，米国，英国，スウェーデンの2005年の年齢階級別乳癌死亡率(人口10万対)をみると，日本の死亡率は40～59歳では他国とそれほど変わらないが，60～64歳および65～69歳の日本の死亡率は，31.5，28.2であり，米国の62.1，71.2，英国の71.1，80.7，スウェーデンの60.7，60.9と比べると，ほぼ半分である[14]。NNI算出に用いたランダム化比較試験は，受診勧奨群と受診未勧奨群の乳癌累積死亡率を比較した試験であり，すべて欧米の試験である。日本ではランダム化比較試験が存在しないため，マンモグラフィ受診勧奨および未勧奨群それぞれの累積死亡率が不明である。本研究において，NNIを算出するために未勧奨群の累積死亡率を日本の乳癌女性の死亡率としたのは，日本のマンモグラフィ受診率は2007年の国民生活基礎調査によると20%と欧米に比べて低く[15]，欧米の未勧奨群におけるコンタミネーションの割合と同程度であると判断したからである。

本研究の限界は，日本のマンモグラフィ未勧奨群の受診勧奨群に対する死亡の相対リスクが欧米と同様で

あると仮定した点であり，もし日本における相対リスクが欧米より高ければNNIは本研究の推計より小さくなり，逆に欧米より低ければNNIは大きくなる。

USPSTFのガイドライン改訂には，マンモグラフィの登録データを集積した乳癌サーベイランス・コンソーシアム(Breast Cancer Surveillance Consortium: BCSC)からのマンモグラフィ受診に関する不利益の調査結果を根拠として用いている。BCSCのデータによると，1回のマンモグラフィにおいて進行癌を1件発見するのに必要な受診者，追加で画像診断を受ける必要のある受診者，生検を受ける必要のある受診者は，50歳代でそれぞれ294人，22人，3人，60歳代で200人，14人，2人であるのに対して40歳代では556人，47人，5人とかなり多いことが示されている[1)]。

その他にも米国のCancer Intervention and Surveillance Modeling Networkの調査グループが行った，さまざまな検診状況下での死亡率減少効果と偽陽性や不必要な細胞診の多さを試算した解析結果がある[15)]。この解析において，2年に1度のマンモグラフィを実施した場合，検診を実施しない場合に比べて，40～69歳の対象では16%，50～69歳の対象では15%と同程度の死亡率減少が認められたが，検診の不利益とされる偽陽性と不必要な細胞診は，女性1,000人あたり40～69歳の対象でそれぞれ1,250件と88件，50～69歳の対象で780件と55件であり，対象年齢の開始年齢を40歳から50歳にすることで37%減少することが試算された[16)]。すなわち，40歳代をマンモグラフィの受診推奨の対象年齢に含むことは，全体の死亡率減少効果よりも不利益が大きいことが示唆された。日本においても，今後不利益に関する調査およびさまざまな検診状況下での利益と不利益の効果の試算が必要と考える。

## 結　語

米国予防医学専門委員会(USPSTF)の2009年の乳癌検診ガイドラインの改訂のように，日本においてもマンモグラフィ検診の利益と不利益のバランスを考慮した推奨が必要である。本研究では，欧米のランダム化比較試験のメタアナリシスの結果から，マンモグラフィ受診勧奨群と未勧奨群の相対リスクが同様である場合，必要と考えられる検診対象者数を推計した。その結果，40歳代，50歳代については欧米と同程度であるが，欧米に比べ乳癌死亡率の低い60歳代では欧米の2倍の対象者数が必要であると推計された。今後，エビデンスに基づいた推奨グレードを決定するには，マンモグラフィ受診における利益と不利益の実測を行った上で，利益と不利益のバランスを検討することに加え，数理モデル等による評価研究も必要である。

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# The Number Needed to Invite (NNI) for Breast Cancer Mammography Screening in Japan

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In 2009, the US Preventive Services Task Force (USPSTF) recommended that the decision to start regular screening mammography (MMG) before the age of 50 years should be an individual one. They calculated the number needed to invite (NNI) to screening to prevent one death from breast cancer (BC) and concluded that the net benefit is smaller for women aged 40–49yr with its larger NNI than that for women aged 50–59yr. Estimating the NNI by age group is also important in Japan. There has been a need to estimate absolute differences in BC cumulative mortality between women with and without MMG. Since such data are unavailable, we assumed that BC mortality for Japanese women would be the same as that for women without MMG, and that the relative risks were the same as those reported by the USPSTF. Comparison of NNI in Japan with the USPSTF report yielded results that were similar for women aged 40–49yr and 50–59yr, whereas the NNI in Japan was double that reported by the USPSTF for women aged 60–69yr. In Japan, studies for evaluating the balance between the benefits and drawbacks of MMG are needed.

**Key words:** NNI, USPSTF, screening guideline

Breast Cancer
DOI 10.1007/s12282-012-0434-2

ORIGINAL ARTICLE

# Effect of screening mammography on cumulative survival of Japanese women aged 40–69 years with breast cancer

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Received: 9 October 2012 / Accepted: 29 November 2012


**Abstract**
*Background* The effectiveness of screening mammography (MMG) has mainly been demonstrated by studies in western countries. This study was conducted to evaluate cumulative survival and the risk of breast cancer death among Japanese women aged 40–69 years with screening-detected and interval breast cancer divided into three groups: MMG with clinical breast examination (CBE), CBE alone, and self-detection.
*Methods* By matching a list of 126,537 women (358,242 person-screenings) who participated in the Miyagi Cancer Society Screening program between 1 April 1995 and 31 December 2002 with the Miyagi Prefectural Cancer Registry, 429 MMG with CBE, 522 CBE, and 3,047 self-detected cases were included in this study. Follow-up was performed until the date of death or 31 December 2007. Survival was estimated by the Kaplan–Meier method. The Cox proportional hazards model was used to estimate hazard ratios (HR) and 95 % confidence intervals (CI) for breast cancer death.
*Results* Five-year survival for women in the MMG with CBE, CBE, and self-detection groups was 96.8, 92.7, and 86.6 %, respectively. The HR (95 % CI) for breast cancer death was 2.38 (0.72–7.94) among CBE-screened and 4.44 (1.42–13.89) among self-detected cases for women aged 40–49 years, but was 3.00 (1.63–5.50) among CBE-screened and 4.51 (2.69–7.56) among self-detected cases for women aged 50–69 years relative to cases screened by use of MMG with CBE.
*Conclusions* In terms of the survival and risk of breast cancer death, MMG with CBE may be more effective than MMG alone or self-detection for Japanese women aged 40–69 years.

**Keywords** Breast cancer · Mammography · Screening · Survival

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## Introduction

Breast cancer is one of the most common cancers worldwide. Among Japanese women, the age-standardized incidence of breast cancer has now risen to first place among all cancers, and it is increasing rapidly [1]. Furthermore, the age-specific incidence of breast cancer among Japanese women aged 45–49 years and mortality due to breast cancer among Japanese women aged 35–64 years are the highest for any type of cancer [1]. Therefore, screening mammography (MMG) is regarded as an important public health priority.

Randomized controlled trials (RCTs) conducted in western countries have clarified the effectiveness of MMG screening for women aged 40–69 years, and especially for

Published online: 14 December 2012

those aged 50–69 years [2]. Breast cancer screening by clinical breast examination (CBE) was introduced for Japan for women aged 30 years and over in 1987 in the absence of any evidence of its effectiveness [3]. Studies in Japan to evaluate the efficacy of screening using MMG with CBE compared with CBE alone revealed the former was superior to the latter in terms of sensitivity, specificity, and success of detection in women aged over 50 years [4, 5]. Based on the results of those studies, screening using MMG with CBE was endorsed in 2000 for women aged over 50 years, and in 2004 for those aged over 40 years. However, this initiative was based mainly on data obtained from RCTs of MMG screening in western countries [2]. The efficacy of screening using MMG with CBE for Japanese women was further examined by cost-effectiveness analysis based on actual screening data for those aged 40–49 years [6] and by a validation study of accurate false-negativity data for MMG with CBE screening [7]. Furthermore, our previous study revealed that the survival of women with MMG-detected breast cancer was superior to that of women with CBE-detected or self-detected breast cancer, especially for those aged 50–69 years, although the effectiveness of the screening program for women aged 40–49 years was not assessed at that time [8]. In relation to the effectiveness of the screening program, our previous study [8] may have included inherent bias, because it did not consider the presence of interval breast cancer [9], which may grow rapidly and have a poor outcome [10]. Therefore, to properly assess the effectiveness of MMG screening there is still a need to evaluate the survival and risks of breast cancer death among Japanese women aged 40 years and over with screening-detected and interval cancer [9].

For this purpose, this retrospective cohort study was conducted to clarify the efficacy of screening using MMG with CBE by investigating cumulative survival and the risk of breast cancer death among Japanese women aged 40–69 years with screen-detected and interval cancer by dividing them into groups according to the screening methods used (MMG with CBE, CBE alone, or self-detection) and stratifying the subjects according to age. Improvements in the survival of women with breast cancer and the risk of breast cancer death for MMG with CBE screening in comparison to CBE screening alone and self-detection were evaluated with reference to the Miyagi Prefectural Cancer Registry [11].

## Materials and methods

The Miyagi Cancer Society has performed breast cancer screening for women in Miyagi prefecture since 1989 [4, 5]. In brief, women aged 50 years and over living in Miyagi prefecture underwent annual single-view MMG with CBE in 32 registered communities; initially CBE only was provided in another 27 communities for breast cancer screening (Miyagi trial). Women aged 40 years and over underwent annual single-view MMG with CBE or CBE for breast cancer screening in 1995 and biennial single-view MMG with CBE or CBE for breast cancer screening between 1996 and 2004 [6]. The process of transition from CBE to MMG with CBE depended on the decision of each community and was gradual. Screening MMG was performed with CBE, and the mammograms were reviewed for each subject by two physicians at the Cancer Detection Center of the Miyagi Cancer Society. CBE is defined as inspection and palpation of breasts and regional lymph nodes by the attending physician at the screening. Women with any abnormal findings detected by MMG with CBE, or by CBE alone, were referred to community hospitals or followed up at the Cancer Detection Center of the Miyagi Cancer Society [4, 5]. All results of diagnostic examinations were reported by the hospitals that had performed the diagnostic MMG and/or ultrasonography (biopsy and/or surgical operation if necessary). Screening-detected cancer was defined as a case diagnosed pathologically within 6 months after a positive screening test (detected case) [7]. Interval cancers were defined as cases that were diagnosed as non-malignant at the primary screening but then clinically diagnosed as breast cancer during the interval until the next screening was conducted [7].

The end-point of this analysis was the cumulative survival of women with screening-detected and interval breast cancer (for women who underwent MMG with CBE, or CBE alone) and the survival of women with self-detected breast cancer, defined as topography code C50.0–C50.9 of the International Classification of Disease for Oncology, second edition (ICD-O-2) [12]. In the Miyagi Prefectural Cancer Registry, the relevant patients were abstracted from the medical records of the hospitals by a physician or trained medical records reviewer, except for patients reported directly to the registry by an institution. The clinical staging system was that of the Research Group for Population-Based Cancer Registration in Japan, among the methods used for detection. Lesions were classified into five stages (in situ, localized, lymph node metastasis, regional invasion, or distant metastasis) on the basis of information about tumor extension and metastasis to lymph nodes and distant sites [13]. This clinical staging system was available for breast cancer from 1 April 1995. Between that date and 31 December 2004, 6,134 cases of primary breast cancer were registered. The percentage of cases registered by death certificates only (DCO) for breast cancer was 2.82 % (178/6,134 primary breast cancers). DCO cases were excluded from the analysis.

Matching of records from the screening program database with the Miyagi Prefectural Cancer Registry was conducted with the aid of registry officials, using name, address, and date of birth to identify individuals. By matching the cancer registry with the Miyagi Cancer Society Screening program for a total of 126,537 subjects (358,242 person-screenings) from 1 April 1995 to 31 December 2002, 662 screening-detected cases and 289 interval breast cancer cases in patients aged 40–69 years were found and included in this analysis. Among the remaining 5,005 cases, 450 were excluded because they were entered in the Miyagi Prefectural Cancer Registry as having been detected by other screening programs, and a further 1,508 cases were excluded because age at diagnosis was under 40 or over 70 years. The remaining 3,047 cases, registered as having been detected by other methods, or those for which the details were unknown, for women aged 40–69 years, were regarded as having been self-detected. Thus, a final total of 3,998 cases were included in this analysis.

The numbers of women in the 40–49, 50–59, and 60–69-year age groups were 1,545, 1,270, and 1,183, respectively. The screening methods (MMG with CBE, and CBE alone) used for each cancer patient were confirmed from the breast cancer database of the Miyagi Cancer Society Screening program. Self-detection is defined as a patient finding a lesion by herself, the lesion being later diagnosed as breast cancer. Finally, we separated the subjects into three groups (429 screened by MMG with CBE, 522 screened by CBE alone, and 3,047 with self-detected lesions).

Follow-up was conducted for each of the subjects from the date of diagnosis of breast cancer until the date of death or the end of follow-up (31 December 2007), whichever occurred first. Patients who died from causes other than breast cancer were treated as censored cases. Patients for whom no information on death was available were regarded as alive at the end of the follow-up period. On the basis of these data, the association between type of screening method used and patient outcome was analyzed. Kaplan–Meier survival analysis was performed for each screening group. Differences between survival in the two groups were assessed statistically by use of the log-rank test. The Cox proportional hazards regression model was used to estimate the hazard ratios (HR) and 95 % confidence intervals (CI) for relative mortality risk in comparison with the MMG with CBE screened group [14]. All statistical analysis was performed by use of SAS version 9.3 (SAS, Cary, NC, USA). All reported $p$ values were two-sided, and differences were considered statistically significant at $p < 0.05$.

The study protocol was approved by the institutional review board of Tohoku University Graduate School of Medicine, the Miyagi Cancer Society, and the committee of the Miyagi Prefectural Cancer Registry. The study was conducted in accordance with the principles of the Declaration of Helsinki.

## Results

Four-hundred and twenty-nine cancers (10.7 %) were detected by MMG with CBE, 522 (13.1 %) by CBE alone, and 3,047 (76.2 %) were self-detected. Among the cancers, 1,545 (38.6 %), 1,270 (31.8 %), and 1,183 (29.6 %) occurred in women aged 40–49, 50–59, and 60–69 years, respectively. The proportion of interval cancer was higher in women screened by CBE alone (40.0 %; 209/522) than in those screened by use of MMG with CBE (18.6 %; 80/429) (Table 1).

Among cancers detected by MMG with CBE, 85 (19.8 %) were in situ, 248 (57.8 %) were localized, 68 (15.9 %) were lymph node metastases, 6 (1.4 %) were regional invasion, 2 (0.5 %) were distant metastases, and the stages of 20 patients (4.7 %) were unknown. Among cancers detected by CBE alone, 64 (12.3 %) were in situ, 273 (52.3 %) were localized, 68 (24.3 %) were lymph node metastases, 9 (1.7 %) were regional invasion, 12 (2.3 %) were distant metastases, and the stages of 37 patients (7.1 %) were unknown. Among 3,047 (76.2 %) self-detected cancers, 157 (5.2 %) were in situ, 1,324 (43.5 %)

**Table 1** Age distribution of the study subjects according to modality

| Modality | Age group (years), *N* | | | Total | | Median age (years) | SD |
|---|---|---|---|---|---|---|---|
| | 40–49 | 50–59 | 60–69 | *N* | % | | |
| MMG with CBE | 78 | 174 | 177 | 429 | 10.7 | 58.4 | 7.7 |
| MMG detected | 55 | 139 | 155 | 349 | | 59.1 | 7.6 |
| MMG interval | 23 | 35 | 22 | 80 | | 54.4 | 7.5 |
| CBE | 273 | 126 | 78 | 522 | 13.1 | 49.4 | 8.2 |
| CBE detected | 165 | 78 | 70 | 313 | | 49.2 | 8.1 |
| CBE interval | 108 | 48 | 53 | 209 | | 49.7 | 8.4 |
| Self-detection | 1,194 | 970 | 883 | 3,047 | 76.2 | 52.8 | 8.4 |
| Total | 1,545 | 1,270 | 1,183 | 3,998 | 100.0 | 53.0 | 8.4 |

*MMG* mammography, *CBE* clinical breast examination

**Table 2** Cancer stages of the study subjects according to modality

| Modality | Stage | | | | | | | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | In situ | | Localized | | Lymph node metastasis | | Regional invasion | | Distant metastasis | | Unknown | | | |
| | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % |
| MMG with CBE | 85 | 19.8 | 248 | 57.8 | 68 | 15.9 | 6 | 1.4 | 2 | 0.5 | 20 | 4.7 | 429 | 10.7 |
| CBE | 64 | 12.3 | 273 | 52.3 | 127 | 24.3 | 9 | 1.7 | 12 | 2.3 | 37 | 7.1 | 522 | 13.1 |
| Self-detection | 157 | 5.2 | 1,324 | 43.5 | 851 | 27.9 | 197 | 6.5 | 213 | 7.0 | 305 | 10.0 | 3,047 | 76.2 |
| Total | 306 | 7.7 | 1,845 | 46.1 | 1,046 | 26.2 | 212 | 5.3 | 227 | 5.7 | 362 | 9.1 | 3,998 | 100.0 |

*MMG* mammography, *CBE* clinical breast examination

**Table 3** Cause of death of the study subjects according to modality

| Modality | Status | | | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Alive | | Breast cancer death | | Other cancer death | | Other causes | | | |
| | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % |
| MMG with CBE | 393 | 91.6 | 18 | 4.2 | 12 | 2.8 | 6 | 1.4 | 429 | 10.7 |
| CBE | 449 | 86.0 | 57 | 10.9 | 13 | 2.5 | 3 | 0.6 | 522 | 13.1 |
| Self-detection | 2,366 | 77.7 | 568 | 18.6 | 55 | 1.8 | 58 | 1.9 | 3,047 | 76.2 |
| Total | 3,208 | 80.2 | 643 | 16.1 | 80 | 2.0 | 67 | 1.7 | 3,998 | 100.0 |

*MMG* mammography, *CBE* clinical breast examination

were localized, 851 (27.9 %) were lymph node metastases, 197 (6.5 %) were regional invasion, 213 (7.0 %) were distant metastases, and the stages of 305 patients (10.0 %) were unknown (Table 2).

Among the patients whose cancers had been detected by MMG with CBE, 393 (91.6 %) were alive, 18 (4.2 %) died from breast cancer, 12 (2.8 %) died from other cancers, and 6 (1.4 %) died from other causes. Among patients whose cancers had been detected by CBE alone, 449 (86.0 %) were alive, 57 (10.9 %) died from breast cancer, 13 (2.5 %) died from other cancers, and 3 (0.6 %) died from other causes. Among the 3,047 patients whose cancers had been self-detected, 2,366 (77.7 %) were alive, 568 (18.6 %) died from breast cancer, 55 (1.8 %) died from other cancers, and 58 (1.9 %) died from other causes (Table 3).

The mean observation time for patients who had been screened using MMG with CBE was slightly shorter than that for patients who had been screened using CBE alone, or for patients with self-detected cancer. Five-year survival of breast cancer patients who had been screened by use of MMG with CBE, by CBE alone, and by self-detection was 96.8, 92.7, and 86.6 %, respectively. The corresponding 8-year survival was 94.9, 88.7, and 82.1 %, respectively (Table 4).

**Table 4** Survival of the study subjects according to modality

| Modality | Survival | | Mean observation time (month) | SD |
|---|---|---|---|---|
| | 5-year (%) | 8-year (%) | | |
| MMG with CBE | 96.8 | 94.9 | 86.1 | 29.5 |
| CBE | 92.7 | 88.7 | 94.8 | 36.6 |
| Self-detection | 86.6 | 82.1 | 96.9 | 39.8 |
| Total | 88.5 | 84.3 | 95.5 | 38.5 |

*MMG* mammography, *CBE* clinical breast examination

## Outcome and survival analysis according to detection method

Statistically significant differences in outcome and survival were observed between the patients screened by use of MMG with CBE and those screened by use of CBE alone ($p = 0.0008$), and those with self-detected cancers ($p < 0.0001$). The difference between the CBE screening and self-detection groups was significant ($p < 0.0001$) (Fig. 1).

## Mortality risk analysis according to detection method

Mortality risk of breast cancer was determined by age-adjusted risk analysis. Mortality risk among patients screened by CBE alone was 2.59-fold (95 % CI 1.52–4.41, $p = 0.0005$) and that among patients with self-detected cancers was 4.37-fold (95 % CI 2.73–6.99, $p < 0.0001$) higher than that among patients screened by MMG with CBE. The subjects were stratified into two age groups (40–49 years and 50–69 years) for statistical analysis of

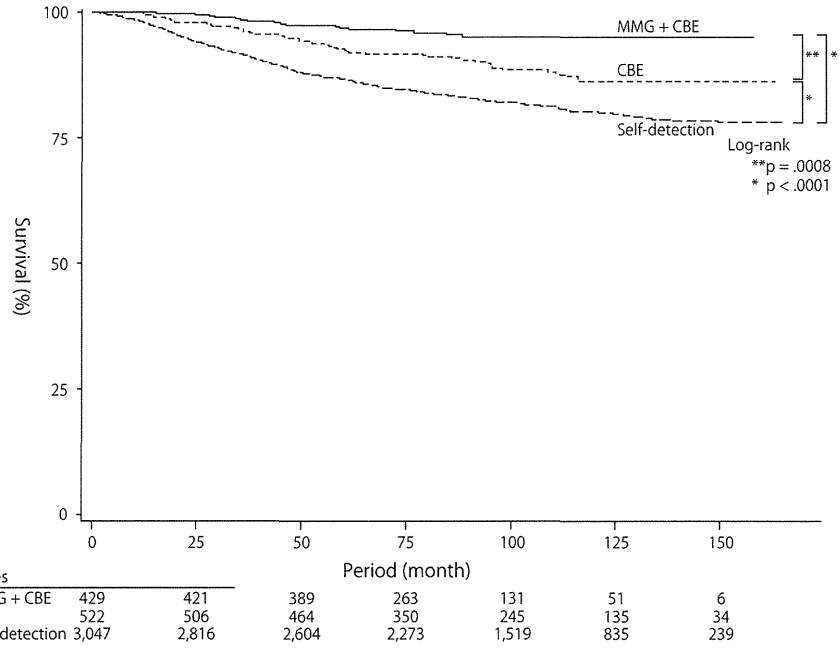


**Fig. 1** Kaplan–Meier survival curves for screening mammography (MMG) with clinical breast examination (CBE) (429 patients), CBE alone (522 patients), and self-detection (3,047 patients). Statistically significant differences were observed between the MMG with CBE group and the self-detection group ($p < 0.0001$), the CBE alone and self-detection groups ($p < 0.0001$), and the MMG with CBE and CBE alone groups ($p = 0.0008$)

**Table 5** Hazard ratio (HR) and 95 % confidence interval (CI) for the mortality risk of each group compared by screening mammography

| Age group | Modality | Cases | Person-years | Breast cancer death | HR | 95 % CI | *p* |
|---|---|---|---|---|---|---|---|
| All | MMG with CBE | 429 | 3,077.1 | 18 | 1.00 (reference)[a] | – | – |
| | CBE | 522 | 4,124.0 | 57 | 2.59 | 1.52–4.41 | 0.0005 |
| | Self-detection | 3,047 | 24,646.1 | 568 | 4.37 | 2.73–6.99 | <.0001 |
| 40–49 | MMG with CBE | 78 | 686.6 | 3 | 1.00 (reference) | – | – |
| | CBE | 273 | 2,145.5 | 23 | 2.38 | 0.72–7.94 | 0.16 |
| | Self-detection | 1,194 | 10,217.5 | 197 | 4.44 | 1.42–13.89 | 0.01 |
| 50–69 | MMG with CBE | 351 | 2,390.5 | 15 | 1.00 (reference) | – | – |
| | CBE | 249 | 1,978.5 | 34 | 3.00 | 1.63–5.50 | 0.0004 |
| | Self-detection | 1,853 | 14,398.6 | 371 | 4.51 | 2.69–7.56 | <.0001 |

*HR* hazard ratio, *CI* confidence interval, *MMG* mammography, *CBE* clinical breast examination

[a] Adjusted by age

mortality according to the detection method used. In the 40 to 49-year age group, mortality risk for CBE alone was 2.38-fold (95 % CI 0.72–7.94, $p = 0.16$) and that for self-detection was 4.44-fold (95 % CI 1.42–13.89, $p = 0.01$) higher than that for MMG with CBE. In the 50 to 69-year age group, however, the mortality risk for CBE alone was 3.00-fold (95 % CI 1.63–5.50, $p = 0.0004$) and that for self-detection was 4.51-fold (95 % CI 2.69–7.56, $p < .0001$) higher than that for MMG with CBE (Table 5).

## Discussion

Several trials have been conducted to evaluate the effectiveness of MMG screening in western countries [2], on the basis of the relative risk of breast cancer death for women aged 40–69 years, and especially for those aged 50–69 years. Our previous study revealed that the survival of women aged over 50 years whose breast cancers had been detected by MMG was superior to that of women whose cancers had been detected by CBE alone or by self-examination; although the effectiveness of MMG for detecting breast cancer in women aged 40–49 years could not be evaluated by age-stratified analysis [8], there may have been some bias for screening-detected breast cancers, which may grow slowly and have a better prognosis [9]. In this retrospective cohort study of Japanese women aged 40–69 years, we evaluated whether the efficacy of screening using MMG with CBE was superior to that using CBE alone or to self-detection by investigating the

cumulative survival of women with screening-detected and interval cancer by reference to the Miyagi Prefectural Cancer Registry, one of the oldest and most reliable population-based cancer registries in Japan [11]. As in western countries, RCTs are required for evaluation of the effectiveness of MMG [15], but in Japan this is not realistic because many women have been included in the MMG program through studies to evaluate the efficacy of MMG [4–8] and because of endorsement by the Ministry of Health, Labour and Welfare in 2000. Therefore, this retrospective cohort study is one of the best recent attempts to clarify whether MMG is able to reduce breast cancer mortality in Japan.

Here we found that 5-year survival was over 90 % for women whose cancers had been detected by MMG with CBE, and by CBE alone. Survival of women who had been screened by use of MMG with CBE was significantly better than that of women who had been screened by use of CBE alone, or whose cancers had been self-detected. One possible reason for this better survival was the lower proportion of interval cancers in the group screened by use of MMG with CBE (18.6 %; 80/429) than in the group screened by use of CBE alone (40.0 %; 209/522). A previous study demonstrated that interval cancers tended to be more advanced, less well differentiated, and included a significantly higher proportion of triple-negative cancers, thus resulting a poorer outcome than for screening-detected and self-detected cancers [10]. In this study, the proportion of early, in situ, or localized, breast cancers was higher in the MMG with CBE group (77.6 %; 333/429) than in the CBE alone (64.6 %; 337/522) and self-detection (48.6 %; 1,481/3,047) groups. On the other hand, the proportion of advanced breast cancers, which are thought to be directly related to breast cancer death, was lower in women screened by use of MMG with CBE than in other groups. The proportion of breast cancer deaths was also lower in the MMG with CBE group (4.2 %) than in the CBE alone (10.9 %) and self-detection (18.6 %) groups. In the MMG with CBE group, age tended to be higher and mean observation time shorter than that in the CBE alone and self-detection groups; therefore, there was a possibility that the MMG with CBE group had a higher proportion of deaths from other causes. The proportion of deaths from other cancers and other causes in the MMG with CBE group (4.2 %; 18/429) was similar to that in the CBE alone (3.1 %; 16/522) and self-detection (3.7 %; 113/3,047) groups. Our observation period might have been sufficient because the three Kaplan–Meier curves were parallel at the end of follow-up; therefore, other causes of death might not have distorted the results. Ten-year survival might be almost the same as 8-year survival, because the three survival curves were almost horizontal after 96 months. The different clinical stages and pathological features of cancers in the MMG with CBE group might have resulted in the lower proportion of breast cancer deaths, which may be the presupposition of the declining mortality.

In the 40 to 49-year age group, the risk of breast cancer death among women screened by use of CBE alone was 2.38-fold higher than that among women screened by use of MMG with CBE, but this was not statistically significant (95 % CI 0.72–7.94, $p = 0.16$). The mortality risk in the self-detection group was significantly higher than that in the MMG with CBE group. In the 50 to 69-year age group, the mortality risk for women screened using CBE alone or self-detection was significantly higher than that in the MMG with CBE group. A meta-analysis of major MMG trials in western countries [2] found that MMG was effective in all age groups, but especially for woman aged 50 years and over. Our findings are consistent with those in that study, indicating that screening using MMG with CBE is more effective than self-detection for reduction of breast cancer mortality among women aged 40–69 years, and especially those aged 50–69 years.

The efficacy of MMG may be lower for women aged 40–49 years, for whom breast density is higher [7]. One approach for overcoming this weakness of MMG was evaluated in the "Japan Strategic Anti-cancer Randomized Trial (J-START)", which evaluated the effectiveness of MMG with ultrasound for breast cancer screening in comparison with mammography alone for women aged 40–49 years [16].

This study had both limitations and strengths. First, it was vulnerable to a variety of bias because of comparison of survival. Breast cancer screening presumably reduces mortality by detecting breast cancer and thus enabling a patient to be treated appropriately at an earlier stage. Differences in mortality risk between groups screened by use of MMG with CBE, CBE alone, and self-detection were presumably caused by the effect of MMG with CBE in reducing mortality and bias, for example self-selection bias (healthy screenee bias). However, the proportion of deaths from other cancers and other causes in the MMG with CBE group was almost the same as that in the CBE alone group and in the self-detection group, even though age tended to be higher in the MMG with CBE group. Therefore, any such bias might have been too small to distort the results. Second, we speculated whether lead time bias could cause these differences in survival [9]. However, the Kaplan–Meier survival curves for the three groups screened using these methods did not cross over, despite of our long observation period; it is, therefore, assumed that the effect of this bias on survival would have been too small to have affected the results.

One of the strengths of our study was that it was able to evaluate the effectiveness of MMG with CBE for women aged 40–49 years by analysis of mortality risk in different

age groups. Our previous study was unable to evaluate the effectiveness of MMG for women aged 40–49 years, for whom breast cancer incidence and mortality would be high in Japan [1], by analysis of mortality risk by age groups [8], because there were no deaths among patients whose cancers had been detected by MMG with CBE and the number of patients in this age group was small. Second, the quality of CBE and reading of MMG were controlled. The screening program was performed by registered surgeons who were approved by the committee for breast cancer screening of the Miyagi Cancer Society as having sufficient experience in general surgery, including the treatment of breast cancer. Statistically significant differences in survival were observed between self-detection and CBE alone, and between self-detection and MMG (Fig. 1). In comparison with self-detection, survival was significantly better for women whose cancers had been detected by CBE alone or by MMG with CBE. The difference in survival between the self-detection and CBE groups was larger than that between the CBE alone and MMG with CBE groups. This implies that the quality of CBE conducted by registered physicians was well controlled. It can be said that MMG with CBE is better than quality controlled CBE alone, although CBE is, of course, better than self-detection. Third, the Miyagi Prefectural Cancer Registry is one of the earliest and most accurate population-based cancer registries in Japan [11]. Therefore, the quality of the data is regarded as sufficiently reliable.

In conclusion, this analysis, conducted by reference to the population-based cancer registry in Miyagi, Japan and which included screening-detected and interval cancers, revealed that by screening using MMG with CBE it is possible to reduce breast cancer mortality from the perspective of survival and risk of breast cancer death among women aged 40–69 years in Japan. To reduce future breast cancer mortality in Japan, national screening by use of MMG with CBE should be increased. Currently, the prevalence of screening using MMG with CBE is 32.1 % (2005) in Miyagi Prefecture [17], as opposed to 60.8 % (2003) in the United States and 69.5 % (2005) in the United Kingdom [18]. This means there is still a higher proportion of self-detected cases in Japan. The only sure indicator of the effectiveness of MMG screening will be a decline in breast cancer mortality; before this can occur the problem of low screening must be addressed. Invitation to MMG screening for each eligible woman might effectively increase the amount of screening, as reported elsewhere [19].

**Acknowledgments** This work was supported by KAKENHI, including Grant-in-Aid for Scientific Research (C) (24590781), Grant-in-Aid for Young Scientists (A) (24689032), and the 3rd Term Comprehensive Control Research for Cancer (H23-Sanjigan-shitei-002) from the Ministry of Health, Labour and Welfare, Japan.

**Conflict of interest** The authors have no conflict of interest.

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Sugawara et al. BMC Research Notes 2012, 5:699
http://www.biomedcentral.com/1756-0500/5/699

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RESEARCH ARTICLE Open Access

# Cancer patients on Twitter: a novel patient community on social media

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## Abstract

**Background:** Patients increasingly turn to the Internet for information on medical conditions, including clinical news and treatment options. In recent years, an online patient community has arisen alongside the rapidly expanding world of social media, or "Web 2.0." Twitter provides real-time dissemination of news, information, personal accounts and other details via a highly interactive form of social media, and has become an important online tool for patients. This medium is now considered to play an important role in the modern social community of online, "wired" cancer patients.

**Results:** Fifty-one highly influential "power accounts" belonging to cancer patients were extracted from a dataset of 731 Twitter accounts with cancer terminology in their profiles. In accordance with previously established methodology, "power accounts" were defined as those Twitter accounts with 500 or more followers. We extracted data on the cancer patient (female) with the most followers to study the specific relationships that existed between the user and her followers, and found that the majority of the examined tweets focused on greetings, treatment discussions, and other instances of psychological support. These findings went against our hypothesis that cancer patients' tweets would be centered on the dissemination of medical information and similar "newsy" details.

**Conclusions:** At present, there exists a rapidly evolving network of cancer patients engaged in information exchange via Twitter. This network is valuable in the sharing of psychological support among the cancer community.

**Keywords:** Breast cancer, Breast neoplasms, Internet, Leukemia, Social media, Twitter messaging, Web 2.0

## Background

Health-focused websites have become an increasingly valuable information source for cancer patients in recent years, with such patients seeking details about treatment options for their specific condition as well as about general cancer information [1-3]. These websites provide a means of communication for patients and their families that is more convenient and less expensive than that provided by traditional face-to-face patient-serving health organizations [2]. In a previous study, we suggested that patient-authored web logs (or "blogs") represent a unique form of information delivery as they provide useful personal insights about cancer treatment that are unlike the information often conveyed by healthcare providers through face-to-face interactions and standard media [1]. Such patient-centric sites are also becoming a valuable source of personalized health information for the increasingly "wired" cancer-patient communities across the globe.

Attendant to the continuing rise in social media ("Web 2.0") participation and the resulting proliferation of user-generated online content, the public can thus potentially play a larger role in all stages of knowledge translation, including information generation, filtering and amplification. As with the Internet itself, social media outlets run the gamut of just about every imaginable scope and size, with Twitter, a free social-networking and micro-blogging service launched in 2006, taking the lead as a method of disseminating exceptionally brief online messages to a potentially global audience; Twitter enables its millions of users to send and read each other's "tweets," or short messages limited

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to 140 characters, with the users themselves determining whether their tweets can be read by the general public or restricted to preselected "followers." Followers of a specific Twitter user can view or respond to tweets online or via smart phones and other handheld devices, allowing for a nearly instantaneous dialogue between the user and his or her followers. The service has more than 190 million registered users worldwide and processes about 55 million tweets per day [4]. The Twitter service started in Japan in 2008; at present, there are more than 10.2 million active Twitter accounts registered in the country [5].

A recent health-focused analysis of the American "Twitter stream" revealed that a substantial proportion of tweets contain general chatter, user-to-user conversations that are only of interest to the parties involved, links to interesting pieces of news or self-promotion or unwanted "junk" messages (i.e., spam) [4]. Yet despite its high level of noise, the Twitter stream does contain useful information. Many recent news events or scientific issues have been documented and discussed via Twitter directly from users at the site in real time [6].

As tweets are often sent on location via smart phones and other handheld platforms,they convey more immediacy with interactivity than other websites or blogs [4]. In addition, healthcare providers and medical researchers are increasingly using Twitter for a variety of purposes related to patient care and treatment, including sharing clinical news with patients and discussing case studies with fellow physicians [7-11]. A recent *JAMA* letter showed that physicians frequently use Twitter to share medical information, with nearly half of the studied tweets being devoted to the discussion of health topics; the authors found that physicians' rapid and timely dissemination of such information via Twitter could potentially positively influence public health in a variety of ways [12].

Recent research has also shown that Twitter may also be a useful medium for patients, who use Twitter to exchange medical information and discuss various aspects of their individual illness; although detailed information about patients' use of Twitter for such purposes has yet to be fully studied, it has been shown that some patients with breast cancer, chronic kidney disease, diabetes and inflammatory bowel disease have used Twitter for the purpose of sharing information about these conditions [13-18].

Twitter is an interactive, real-time medium that can be used at a relatively low cost in terms of users' initial and ongoing monetary investment and in the time, effort and expertise required for use. Furthermore, as has been described above, Twitter has been effectively used in recent years for the dissemination of medical news and advice, as well as the delivery of "personal stories" related to a number of health topics. As a result, Twitter can be considered to have the potential to play an important role in modern social communities, including online communities consisting of "wired" cancer patients. However, the research conducted to date regarding the role of social media in influencing cancer patients remains very limited. In this study, we examine recent Twitter usage in Japan and evaluate its role in the lives of today's "wired" cancer patients.

## Methods

### Search of cancer Patients' Twitter accounts

A search was conducted of every publicly available user profile on Twitter in Japan. We began this search by reviewing all user accounts in which the names of cancers were described in the user's Twitter profile. The cancer names used in our search were obtained in accordance with the Foundation for Promotion of Cancer Research's 2010 report on Japanese cancer rates [19]. The terms searched were: breast cancer, leukemia, colon cancer, rectal cancer, colorectal cancer, cancers of the uterus, malignant lymphoma, brain tumor, stomach cancer, lung cancer, thyroid cancer, ovary cancer, kidney cancer, prostate cancer, esophagus cancer, bladder cancer, liver cancer, oral cancer, pharyngeal cancer, gallbladder cancer, cholangiocarcinoma, laryngeal cancer, skin cancer and multiple myeloma. These names were searched using both the Japanese Katakana writing system and Chinese characters.

The website used for the profile search was the "16 (one-six) Profile Search β Version for Twitter" [20], which enabled us to search, in addition to users' Twitter profiles, the number of follows, followers, tweets, lists, registered dates and last-posted dates. The search was conducted over a total of 5 days in the spring and summer of 2011: March 27, 28 and 29; April 3; and July 12. Following the methodology used by Chretien et al. (2011) [12], we then extracted from our dataset of cancer profiles only those user accounts that had 500 or more followers; we considered these to be "power accounts," as they had each developed a relatively robust Twitter following.

Our search of Japanese Twitter profiles that included the cancer terminology noted above yielded a total of 731 user accounts, of which 466 profiles belonged to cancer patients and were included in our initial review. The remaining 265 cancer profiles were excluded from our initial analysis because they belonged to persons and organizations who were not patients themselves (Figure 1).

Among the initial 731 user accounts that included cancer terminology, breast cancer was listed in user profiles most frequently (n=147), followed by leukemia (n=59), colon/rectal/colorectal cancer (n=40) and uterine cancer (n=39). Those patients who listed multiple

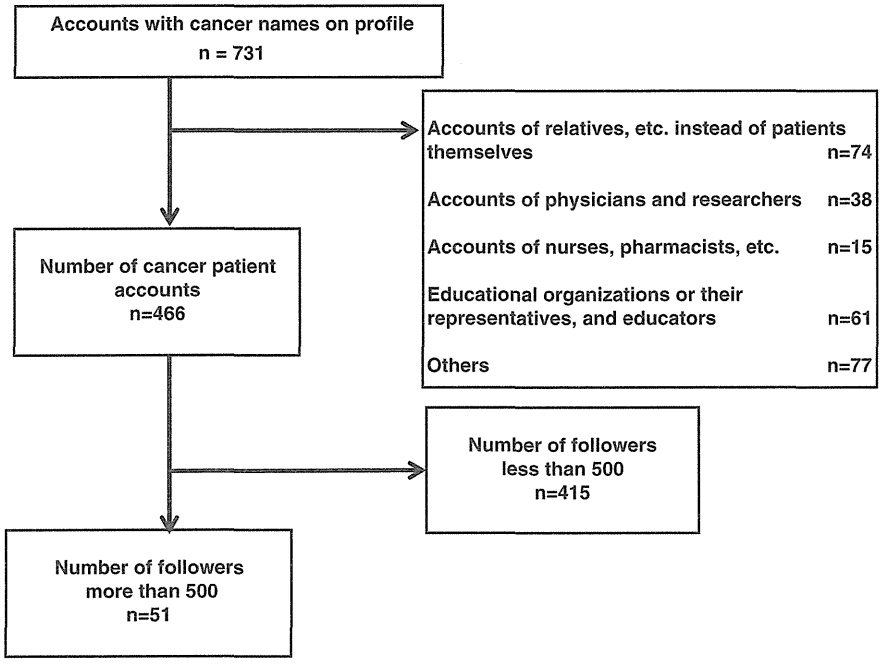


**Figure 1** Extraction of cancer patient accounts.

cancers in their Twitter profiles were counted separately (Figure 2).

Fifty-two Twitter accounts with the relevant cancer descriptions in their profiles met the criterion established by Chretien et al. (2011) [12] required for being "power accounts and were considered by us to be influential accounts because of their wide reach. (The account with the most followers belonged to a comedian with breast cancer; because of the user's celebrity status, the difficulty of adequately tracking tweets between the

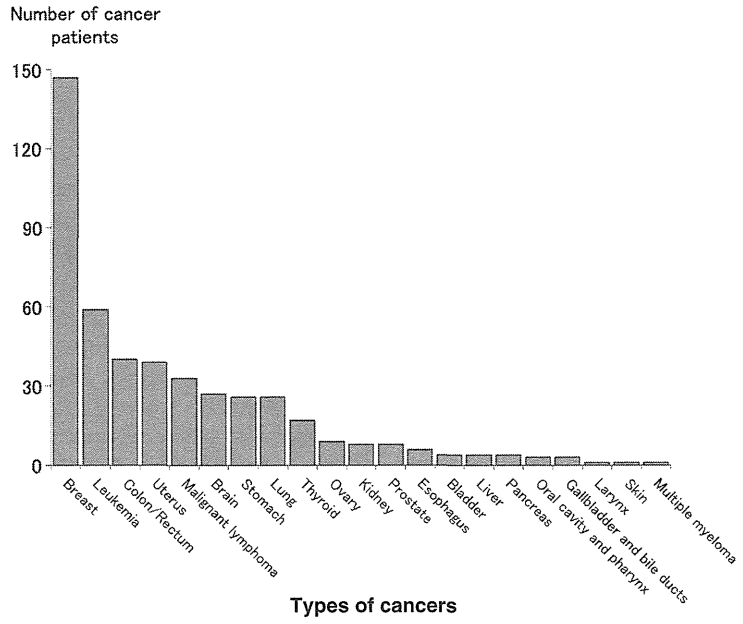


**Figure 2 Number of accounts by type of cancer.** Number of accounts of self-identified cancer patients, with cancer names described in their profiles. In the case of multiple cancers, each cancer was counted.