



Preventive health care, 1999 update:

3. Follow-up after breast cancer

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Abstract

Objective: To make recommendations to physicians who provide follow-up care for women who have been treated for early-stage breast cancer.

Options: Combination of blood tests, bone scans, liver echography and chest radiography for detection of distant disease; physical examination with or without mammography for detection of contralateral breast cancer; and physical examination with or without mammography for detection of ipsilateral recurrent disease after breast-conserving therapy.

Outcomes: Survival, disease recurrence and quality-of-life measures for distant disease, local recurrence of disease and disease in the contralateral breast.

Evidence: A MEDLINE search for relevant articles published between January 1966 and January 1998 with the MeSH terms "breast neoplasms" and "neoplasm recurrence" (local and distant) with limits to "human" was done. A subsequent MEDLINE search using the MeSH terms "breast neoplasms," "neoplasm recurrence," "local/diagnosis" and "mammography" was done to address issues of mammography. The literature search was reviewed by a medical librarian and 2 breast cancer specialists to ensure completeness.

Benefits, harms and costs: Breast cancer is the most common cancer in Canadian women and is the second leading cause of death after lung cancer. Even with early-stage breast cancer, recurrence after treatment for primary breast cancer is frequent. Traditionally, follow-up has been felt to facilitate early detection and improve survival. Randomized controlled trials (RCTs) have shown that routine screening (blood tests and diagnostic imaging) for distant disease does not alter survival or quality of life over routine physical examination. In an underpowered secondary analysis of RCT data, the detection of contralateral breast cancer did not affect survival. However, there have been no RCTs examining the role of mammography and physical examination and their effect on survival in the detection of contralateral breast cancer. The sensitivity and specificity of mammography after local excision and radiotherapy is unknown. There have been no RCTs examining the role of mammography or physical examination, or both, and their effect on survival in the detection of ipsilateral breast recurrence.

Values: The strength of evidence was evaluated using the methods of the Canadian Task Force on Preventive Health Care. A high value was placed on interventions that changed survival. When evidence was available, high value was also placed on interventions that affected quality of life.

Recommendations: There is good evidence not to include blood work and diagnostic imaging as part of screening for distant disease (grade E recommendation). There is no evidence to suggest that mammography decreases mortality by detecting ipsilateral disease in the conservatively treated breast; however, there is indirect evidence that it may be beneficial (grade C recommendation). There is no direct evidence to suggest that physical examination or mammography, or both, should be used to detect contralateral breast cancer; however, there is indirect evidence that it may be beneficial (grade C recommendation).

Validation: The findings of this analysis were reviewed through an iterative process by the members of the Canadian Task Force on Preventive Health Care.

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Education

Éducation

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Despite earlier detection of breast cancer and changes in breast cancer therapy, recurrence continues to be a problem. The disease recurs even in women with early disease (stage I disease [T1 (< 2 cm), N0, M0] or stage II disease [T1, N1, M0; T2 (2–5 cm), N0/N1, M0; or T3 (> 5 cm), N0, M0]) (recurrence rate 30%).¹ The rate of local recurrence after breast-conserving therapy (local excision and radiation) has been reported in randomized controlled trials (RCTs) to be 6% to 12% at 5 to 10 years.^{2–7} Women continue to be at risk for local recurrence for 20 years, and an ipsilateral recurrence develops in 1% to 2% of women every year.^{8,9} With mastectomy, local recurrence is less frequent (4%), but distant disease is more frequent.¹⁰ Regardless of local therapy (mastectomy or local excision and radiation), metastatic disease develops in 23% of women with stage I and II breast cancer.^{11,12} In addition to recurrent disease, women who have had breast cancer are at risk for cancer in the contralateral breast. After the first breast cancer, the risk of a new primary breast cancer is 3 to 5 times the risk of a first breast cancer.^{13,14} Large case series have shown a cumulative risk of contralateral breast cancer of 6% to 8%.^{15–18}

There is significant variation in both patient expectations and physician practice patterns in the follow-up of women with breast cancer. Early data from a British RCT suggest that women prefer less frequent follow-up,¹⁹ whereas data from a US survey suggest that women want very extensive investigations.²⁰ On the one hand, a recent US survey showed that the majority of oncologists would perform blood tests every 3 to 6 months (58%), annual chest radiography (52.1%) and annual mammography (95.9%).²¹ On the other hand, two UK surveys revealed that few breast cancer specialists (10% to 12%) would order blood tests, chest radiography or bone scans.^{22,23} In this guideline, the role of follow-up in improving survival and quality of life after breast cancer is evaluated to establish evidence-based guidelines.

Methods

Before performing a literature search, we developed the fol-

lowing inclusion criteria: women must have had stage I to III infiltrating ductal adenocarcinoma of the breast; there was no clinical evidence of distant disease at the time of diagnosis; when appropriate, adjuvant therapy, if received, was described; and the women were followed up for at least 5 years.

On consultation with a medical librarian, we performed a MEDLINE search of the English-language literature from January 1966 to January 1998 combining the MeSH headings “breast neoplasms” and “neoplasm recurrence” (local and distant), with limits to “human.” To determine the sensitivity of mammography after local excision, we performed a MEDLINE search from 1966 to 1998 combining the MeSH headings “breast neoplasms,” “neoplasm recurrence,” “local/diagnosis” and “mammography.” Reference lists of retrieved articles were reviewed. Two breast cancer specialists were then consulted to ensure the completeness of the literature search.

The evidence was reviewed systematically using the method of the Canadian Task Force on Preventive Health Care (formerly the Canadian Task Force on the Periodic Health Examination).²⁴ The task force of expert clinician/methodologists from a variety of medical specialties used a standardized evidence-based method for evaluating the effectiveness of this intervention (Appendix 1). Procedures to achieve adequate documentation, consistency, comprehensiveness, objectivity and adherence to the task force method were maintained at all stages during review development, the consensus process and beyond.

Manoeuvres

Distant disease

Follow-up for distant disease has included physical examination, blood tests (complete blood count, liver function tests, and determination of calcium and creatinine levels)^{25,26} and diagnostic imaging (chest roentgenography, bone scan and liver ultrasonography).^{11,25,26}

Local recurrence

There is no method to detect occult local recurrence in a woman after mastectomy. Therefore, local recurrence is

Table 1: Reported sensitivity and specificity of mammography and physical examination for detecting local recurrence of breast cancer

Investigator	Sensitivity, %		Specificity, %	
	Mammography	Physical examination	Mammography	Physical examination
Stomper et al ^{27*}	61 (14/23)	65 (15/23)	59 (13/22)	23 (5/22)
Dershaw et al ^{28*}	70 (7/10)	70 (7/10)	39 (7/18)	17 (3/18)
Dershaw et al ^{29†}	67 (29/43)	58 (25/43)	—	—
Fowble et al ^{30†}	50 (33/66)	29 (19/66)	—	—
Haffty et al ^{31†}	74 (23/31)	74 (23/31)	—	—
Orel et al ^{32,33*}	55 (21/38)	66 (25/38)	60 (12/20)	30 (6/20)
Hassell et al ^{34*}	38 (9/24)	71 (17/24)	60 (15/25)	24 (6/25)
Ciatto et al ^{35†}	59 (47/80)	75 (77/102)	—	—

*Studies examined biopsy specimens (benign and malignant) of women who had biopsy, mammography and physical examination findings recorded in their chart.

†Studies examined the method of detection in women with recurrence.



detected by physical examination and consists of abnormalities in the incision site or the surrounding skin.

After breast-conserving treatment, local recurrence may be detected by physical examination or mammography, or both. Following surgery and radiation, there are significant changes in the sensitivity and specificity of mammography and physical examination, which have been reported only in case-control and cohort studies (Table 1). Although these studies are plagued with small and highly selected samples, it is evident that 35% to 64% of women who have biopsy of the conserved breast are found to have benign disease, and recurrence is often missed on mammography (25% to 50%) or physical examination (25% to 42%).²⁷⁻³⁵ There are no prospective studies addressing the sensitivity and specificity of mammography or physical examination, or both, for the ipsilateral conserved breast.

Contralateral breast cancer

The screening characteristics of physical examination with or without mammography have been examined only in the Canadian National Breast Screening Study, in which women aged 50 to 59 years without breast cancer were randomly assigned to yearly physical examination or to yearly physical examination and mammography.^{36,37} The sensitivity and specificity of physical examination were 75% to 100% and 75% to 85% respectively.³⁸ The corresponding values for mammography and physical examination were 81% to 88% and 96.5% to 99.9%.³⁷

Effectiveness of detection and treatment

Distant disease

The role of follow-up in detecting distant disease has been studied in a secondary analysis of 5 RCTs and in 2 RCTs (Table 2).

Survival

Crivellari and colleagues²⁵ found that among 241 744 blood tests, 6% of the 52% of women with recurrent disease had an elevated alkaline phosphatase level at some point before the metastasis was detected. In the GIVIO RCT, the investigators compared the outcome of women with stage I or II breast cancer who had intensive or conservative clinical follow-up and found that intensive follow-up did not improve the overall survival of the women with recurrent disease (death rate 18% with conservative follow-up and 20% with intensive follow-up).²⁶

Rosselli Del Turco and associates¹¹ compared the 5-year survival rates for women randomly assigned to intensive versus conservative follow-up and found that, although relapse-free survival was shorter in the intensive follow-up group, there was no significant difference in the 5-year death rate between the 2 groups (18.6% v. 19.5%). Interestingly, some women without metastatic symptoms after breast cancer surgery who were assigned to conservative follow-up had diagnostic tests; however, the number of tests in this group (444) was significantly smaller than

Table 2: Data from randomized controlled trials examining the role of follow-up in the detection of distant disease

Investigator	Subjects	Intervention	Follow-up	Results	Quality of evidence
Rosselli Del Turco et al ¹¹	11 Italian centres, 1243 women < 70 yr of age who received diagnosis of T1-3, N0-1, M0 breast cancer < 6 mo earlier	1. Conservative: PE and mam. every 6 mo 2. Intensive: as above, plus chest radiography and bone scan every 6 mo Equal numbers received chemotherapy or hormonal therapy or both	5 yr; 0.4% loss to follow-up	Local recurrence: 7.9% conservative v. 8.8% intensive ($p > 0.05$) Distant disease: 20.1% conservative v. 26.4% intensive ($p > 0.05$) Death: 19.5% conservative v. 18.6% intensive ($p > 0.05$)	RCT (level I)
Crivellari et al ²⁵	4105 patients enrolled in 1978-1985	Relapse before or after abnormal blood test result (ALP, SGOT, GGT, bilirubin, calcium, creatinine) every 3 mo for 2 yr, then every 6 mo for 3 yr	3 RCTs with 13-yr follow-up, 2 RCTs with 9-yr follow-up	6% of patients had abnormal ALP level at least 6 mo before relapse	Secondary analysis of 5 RCTs (level II)
GIVIO Investigators ²⁶	26 Italian centres, 1320 women < 70 yr of age who received diagnosis of T1-T3, N0-1, M0 breast cancer < 6 wk earlier	1. Conservative: PE every 6 mo, mam. yearly 2. Intensive: as above, plus chest radiography every 6 mo, bone scan yearly, liver ultrasonography yearly Standardized protocol for adjuvant therapy	Median follow-up of 71 mo; 9% loss to follow-up	Locoregional recurrence: 18.4% conservative v. 15.9% intensive ($p > 0.05$) Distant disease: 19.1% conservative v. 19.4% intensive ($p > 0.05$) Death: 18% conservative v. 20% intensive ($p > 0.05$)	RCT (level I)

Note: PE = physical examination, mam. = mammography, ALP = alkaline phosphatase, SGOT = serum glutamic oxaloacetic transaminase, GGT = gamma-glutamyl transpeptidase.



the number in the intensive follow-up group (8060).

The GIVIO investigators, using a similar protocol, compared the overall survival of 1220 women with stage I to III breast cancer who received intensive follow-up of physical examination, mammography and diagnostic imaging.²⁶ Asymptomatic metastases were identified in 31% of the patients in the intensive follow-up group and in 21% of those in the conservative follow-up group. There was a difference of 1 month in the detection of distant metastasis between the 2 groups, and there was no difference in overall survival or length of survival between the 2 groups.

Quality of life

As a component of the GIVIO trial, the quality of life in the intensive and conservative follow-up groups was compared.²⁶ The health-related quality-of-life assessment was found to have good psychometric properties, and no difference was found in quality of life at 6, 12, 24 or 60 months between the 2 groups. Thus, although there were no negative consequences of screening, the evidence does not suggest that intensive follow-up improves quality of life.

Local recurrence

The survival of women with a local recurrence following

local excision has been examined carefully in RCTs (Table 3). In all RCTs, follow-up for the detection of ipsilateral disease has included frequent physical examination and mammography. In this context, despite higher rates of local recurrence, no differences have been found in the survival of women with stage I or II breast cancer treated with either mastectomy or local excision and radiotherapy after 6 and 12 years of follow-up.^{2,7} Although associated with higher local recurrence rates, local excision without radiotherapy has not been shown to increase death rates in 5 RCTs with 5 to 12 years of close follow-up for local recurrence.²⁻⁶ One cohort study has also shown no differences in survival between women who do and those who do not manifest local recurrences after 5 and 10 years.³⁹ In addition, a meta-analysis using individual data for 9709 patients from 10 RCTs comparing various surgical therapies with or without radiotherapy showed that, despite higher local recurrence rates with local excision, overall survival was not affected.⁴⁰ In summary, local recurrence, if managed appropriately, does not appear to affect overall survival.

Because survival does not appear to be affected by local recurrence after breast-conserving therapy in a research setting, it becomes important to evaluate the methods used to detect local recurrence. Although follow-up in the 5 RCTs comparing various surgical treatments with or without radiotherapy was almost complete (0.1% to 1% of sub-

Table 3: RCTs with level I evidence examining local recurrence and survival after breast-conserving surgery

Author	Subjects	Intervention	Follow-up	Results
Van Dongen et al ⁷	902 women, 734 < 71 yr of age with stage I-II disease enrolled at multiple centres in 1980-1986	Mast. v. BCT (50 Gy RT)	"Standard regimen" Median 6 yr, minimum 5 yr	Actuarial 8-yr survival: 73% mast. v. 71% BCT (p = 0.71) Local recurrence: 9% mast. v. 15% BCT
Veronesi et al ⁵	567 women with stage I and II disease (T ≤ 4 cm) enrolled in Italy in 1988-1989	Quad. v. quad. and 50 Gy + 10 Gy boost RT	1. PE and mam. (? frequency) Minimum 5 yr	Actuarial survival: 96% quad. v. 97% quad. + RT
Liljegren et al ³	381 women with stage I disease enrolled in Sweden in 1981-1988	Lump. v. BCT (54 Gy RT)	1. PE every 4 mo for 3 yr then every 6 mo thereafter 2. Mam. yearly Median 65 mo, minimum 5 yr	Local recurrence: 18.4% lump. v. 2.3% BCT 5-yr actuarial survival: 91% lump. v. 90.3% BCT
Clark et al ⁴	837 women with stage I, negative margins, enrolled in Ontario in 1984-1989	Lump. v. BCT (40 Gy whole breast and 12.5 Gy boost to primary site)	1. PE every 3 mo for 2 yr then every 6 mo 2. Mam. yearly Median 7.6 yr, minimum 5 yr	Local recurrence: 33.5% lump. v. 10.6% BCT 5-yr actuarial survival: 24% lump. v. 21% BCT
Fisher et al ²	2163 women with stage I and II disease enrolled in Canada and United States in 1976-1984	Mast. v. lump. v. BCT	1. PE every 3 mo for 3 yr then every 6 mo* 2. Chest radiography every 6 mo 3. CBC every 3 mo for 1 yr 4. Mam. yearly Mean 12 yr	Local recurrence: 35% lump. v. 10% BCT 12-yr survival: 62% mast. v. 60% lump. v. 62% BCT
Forrest et al ⁶	585 women with T 0-4 cm, N0 disease < 70 yr of age receiving adjuvant therapy enrolled in Scotland in 1985-1991	Lump. v. BCT	1. PE (? frequency) 2. Mam. yearly Median 5.7 yr	Local recurrence: 24.5% lump. v. 5.8% BCT Survival hazard ratio 0.67-1.44

Note: Mast. = mastectomy; BCT = breast-conserving therapy (lumpectomy and radiotherapy); RT = radiotherapy; quad. = quadrantectomy; lump. = lumpectomy, no radiotherapy; CBC = complete blood count.

*Follow-up protocol obtained by contacting the study coordinator where the protocol is described in procedure manual.



jects lost to follow-up), the follow-up protocol was documented clearly in only 3 of the trials.^{3,4,12} In these studies, follow-up consisted of frequent physical examination and yearly mammography. No investigators reported the rates of detection with mammography or physical examination, or both, by the physician separately, the stage of lesions detected by the 2 methods, or the differences in surgical therapy or survival based on the 2 methods. Many retrospective series showed that women (76% to 86%) identify their own local recurrences.^{8,13}

Two groups examined retrospectively the stage of the recurrence and method of detection. Abner and collaborators⁹ analysed a cohort of 1628 women treated for breast cancer between 1967 and 1985. Although the rates of compliance and loss to follow-up are unknown, the authors identified 163 women with ipsilateral recurrence. Histopathological study of 123 mastectomy specimens showed that 99 had invasive, 10 had microinvasive and 14 had non-invasive disease. The 5-year survival rate was significantly higher with noninvasive (including microinvasive) disease than with invasive disease. Although more noninvasive lesions were detected by mammography, as compared with physical examination, there was no significant difference in survival between women with palpable recurrences and those with unpalpable recurrences. Orel and coworkers³² analysed a cohort of 1636 women treated for stage I or II breast cancer and identified 83 women with local recurrence. Physical examination and mammographic information for 72 women showed that 47% had unpalpable le-

sions. The unpalpable lesions were statistically more likely to be an earlier stage than were the palpable lesions. However, there were no significant differences in the histologic grade of recurrence or the 5-year survival rate between women with palpable lesions and those with unpalpable lesions. Thus, despite some evidence to suggest that mammography detects earlier lesions or those with a more favourable prognosis, these studies do not show any improvement in the survival of women with lesions detected on mammography versus those detected by other means.

There is evidence suggesting that local recurrence can be cured. However, the effect of early detection is unknown. The studies examining the prognostic implications of detection method and stage of detection were retrospective and are subject to both lead and length time biases. The numbers lost to follow-up, referral biases and exclusion criteria were not described.

Contralateral breast cancer

Although screening for primary breast cancer has improved survival,⁴¹⁻⁴³ one cannot conclude that early detection of contralateral breast cancer will have the same effect. Early detection of contralateral breast cancer has never been the subject of an RCT (Table 4).

The effect of contralateral breast cancer on survival has been described in a secondary analysis of the National Surgical Adjuvant Breast Project Protocol No. 04, in which the survival of women after either a radical or mod-

Table 4: Results from studies examining contralateral (CL) breast cancer

Investigator	Subjects	Intervention	Follow-up	Results	Quality of evidence
Gutter ⁴⁴	3647 women with breast cancer during study period; 1323 had mam. follow-up	Introduction of mam.	Alberta Cancer Registry data	52 with CL breast cancer: 7 diagnosed before mam., 45 diagnosed after mam.	Historical cohort (level II-3) Co-occurred with the introduction of team approach to breast cancer
Senofsky et al ⁴⁵	A. 500 women with breast cancer before 1978 B. 557 women with breast cancer after 1977	Introduction of mam.	Chart audit	1969-1977: 37 with CL breast cancer 1978-84: 36 with CL breast cancer Earlier stage after 1977 stage O: 5.4% v. 33.3%; stage I: 48.6% v. 22.2%; stage II: 10.8% v. 29.6%; stage III: 21.6% v. 3.7%; stage IV: 13.5% v. 3.7%	Case-control (level II-3)
Mellink et al ¹⁴	A. 880 women with breast cancer undergoing PE and mam. B. 411 women with breast cancer undergoing PE	Mam. available in one county and not in another county	Cancer registry	24 with CL breast cancer Earlier tumour size at diagnosis: < 10 mm 35% v. 7% 14 with CL breast cancer	Prospective cohort (level II-2)
Fisher et al ¹⁰	1578 women with primary stage I or II breast cancer	Modified mast. v. modified mast. and RT v. radical mast.	PE and CBC every 3 mo for 2 yr then every 6 mo	66 with second breast cancer Second smaller than first (2.4 ± 1.5 cm v. 3.5 ± 1.8 cm) Survival not affected significantly	RCT (level II-1) Although RCT, examined cohort of women with CL disease



ified radical mastectomy with or without radiotherapy for stage I or II breast cancer was compared.^{10,46} In a secondary analysis, Fisher and colleagues⁴⁷ reported on the incidence and survival of women in whom contralateral breast cancer developed. In the project, follow-up of all women, regardless of randomization, included frequent physical examination of the contralateral breast. Of the 1578 women, 4.2% manifested a contralateral breast cancer at 10 years. The metachronous contralateral cancers were smaller than the primary breast cancer (2.4 cm [standard deviation 1.5 cm] v. 3.5 cm [standard deviation 1.8 cm]). Although the possibility of a type II error exists, there was no difference in survival between the women with and those without contralateral breast cancer after 10 years of follow-up.

The role of mammography in the detection of contralateral breast cancer in women who have been previously treated for breast cancer has been examined in 3 retrospective studies. Two studies looked at the frequency of contralateral breast cancer in cohorts of women treated for breast cancer before and after the implementation of mammography for routine follow-up.^{44,45} An increased incidence of both synchronous and metachronous contralateral breast cancer was found after the routine use of mammography. In the third study a cohort of women in a county where both physical examination and mammography were performed was compared with a cohort of women in a county where only physical examination was performed.¹⁴ Although the frequency of contralateral breast cancer was identical in the 2 counties, more recurrences were stage I in the women from the county where screening included mammography. All 3 studies contain many methodologic flaws, and the authors did not report the survival rates for women followed before and after the routine use of mammography.

Recommendations

Of the Canadian Task Force on Preventive Health Care (Table 5)

- There is good evidence from well-designed RCTs that there is no difference in survival or quality of life with laboratory or diagnostic screening as compared with physical examination for distant disease.^{11,26} Therefore, laboratory or diagnostic screening, or screening with both methods, for distant disease is not indicated (grade E recommendation).
- Ipsilateral recurrence after breast-conserving therapy was not shown to affect survival in RCTs comparing various surgical and radiotherapy treatments in which follow-up included frequent physical examination and mammography of all women (level I).²⁻⁷ However, the unique role of early detection in the ipsilateral breast by physical examination and mammography is unknown (grade C recommendation).
- There is some evidence (level II-3^{44,45} and level II-2¹⁴) that mammography of the contralateral breast identifies second primary cancers at an earlier stage than does physical examination. However, in an underpowered secondary analysis of an RCT comparing radical mastectomy with modified mastectomy and radiation, contralateral breast cancer, when detected by physical examination, was not shown to affect survival at 10 years (level II-2).⁴⁷ Screening with yearly mammography and physical examination has been included in the protocols of RCTs and is recommended by experts (level III). Although there is indirect evidence suggesting that there may be a clinical benefit, there is no direct evidence to support the inclusion or exclusion of the manoeuvre in the follow-up of women with breast cancer (grade C recommendation).

Table 5: Recommendations of the Canadian Task Force on Preventive Health Care

Manoeuvre	Effectiveness	Level of evidence*	Recommendation*
Blood work and diagnostic imaging	Screening blood work, chest radiography, liver echography and bone scans do not improve survival	RCTs ^{11,26} (I)	Blood work and diagnostic imaging should not be done as part of screening for distant disease (grade E recommendation)
Follow-up for local recurrence	Sensitivity and specificity of mammography and physical examination are unknown. ²⁷⁻³⁵ Local recurrence when detected by frequent follow-up has not been shown to affect mortality. ²⁻⁷ Role of physical examination or mammography, or both, in detecting local recurrence is unknown	Expert opinion (III) from follow-up protocols of RCTs comparing mastectomy with or without radiotherapy	There is no evidence to suggest that mammography decreases mortality by detecting ipsilateral disease in the conservatively treated breast; however, there is indirect evidence that it may be beneficial (grade C recommendation)
Follow-up for contralateral breast cancer	Sensitivity and specificity of physical examination or mammography, or both, are similar to those in general population. ³⁶⁻³⁸ However, because all RCTs have had frequent follow-up for contralateral cancer, its role in affecting survival is unknown	Expert opinion (III) from follow-up protocols of RCTs comparing mastectomy with or without radiotherapy and data from general population	There is no direct evidence to suggest that physical examination or mammography, or both, should be used to detect contralateral breast cancer; however, there is indirect evidence that it may be beneficial (grade C recommendation)

*See Appendix 1 for definitions of the levels of evidence and grades of recommendations.



Of other bodies

There are no other evidence-based guidelines for appropriate follow-up after breast cancer. Under the auspices of the Italian Ministry of Health and the Italian Research Council, an Italian group of stakeholders met in 1994 and recommended that yearly mammography and physical examination every 3 months be done for the first 2 years, yearly mammography and physical examination every 6 months be done for the next 3 years, and yearly mammography and physical examination be done thereafter.⁴⁸ Within Canada, a consensus document recommended frequent physical examination and yearly mammography,⁴⁹ although the authors acknowledged that their recommendations were extrapolated from findings in the general population. Thus, the proposed guidelines differ with respect to the strength of recommendations concerning the role of mammography and physical examination in the follow-up of local recurrence and contralateral breast cancer.

The recommendations for screening with mammography in the general population⁵⁰ cannot be extrapolated to women who have had breast cancer because all RCTs examining screening have excluded women with previous breast cancer. Although large RCTs²⁻⁵ and a meta-analysis of 16 000 women⁴⁰ have not shown an increase in death rates with local recurrence, frequent follow-up of the ipsilateral breast and contralateral breast have been part of the follow-up protocol. In addition, although inadequately studied, contralateral breast cancer has not been shown to affect survival. Therefore, although frequent physical examination and mammography have been used in the protocols of RCTs and is recommended by experts, there is no direct evidence to illustrate that early detection of local recurrence or contralateral breast cancer, or both, improves survival in women after breast cancer.

Research agenda

Although new therapies are studied extensively with RCTs, follow-up has not been subjected to the same rigorous examination. As we become more sophisticated in designing RCTs and as therapy for local recurrence evolves, other outcomes may be important in assessing the effectiveness of physical examination with or without mammography. Recurrences detected on mammography may be more amenable to local therapy than those detected by physical examination. Defining the role of follow-up in improving survival will increase our understanding of breast cancer. In addition, evaluating the effect of follow-up on quality of life is an important aspect of health care delivery to women that requires further research.

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Appendix 1: Canadian Task Force on Preventive Health Care levels of evidence and grades of recommendations

Levels of evidence

- I Evidence from at least one well-designed randomized controlled trial
- II-1 Evidence from well-designed controlled trials without randomization
- II-2 Evidence from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group
- II-3 Evidence from comparisons between times or places with or without the intervention; dramatic results from uncontrolled studies could be included here
- III Opinions of respected authorities, based on clinical experience; descriptive studies or reports of expert committees

Grades of recommendations

- A Good evidence to support the recommendation that the condition or manoeuvre be specifically considered in a periodic health examination (PHE)
- B Fair evidence to support the recommendation that the condition or manoeuvre be specifically considered in a PHE
- C Insufficient evidence regarding inclusion or exclusion of the condition or manoeuvre in a PHE, but recommendations may be made on other grounds
- D Fair evidence to support the recommendation that the condition be specifically excluded from a PHE
- E Good evidence to support the recommendation that the condition or manoeuvre be specifically excluded from a PHE