Comparison of Self-Reported Diagnosis of Connective Tissue Disease with Medical Records in Female Health Professionals

The Women's Health Cohort Study

Elizabeth W. Karlson, I-Min Lee, Nancy R. Cook, JoAnn E. Manson, Julie E. Buring, and Charles H. Hennekens

To compare self-report of connective tissue disease (CTD) with medical records, subjects were selected from 395,543 female health professionals with and without breast implants who reported CTD on mailed questionnaires from 1992 to 1995. The authors identified 220 women with breast implants (exposed) who self-reported CTD and a random sample of 879 women without breast implants (unexposed) who also self-reported CTD, matched by age and date of diagnosis. Medical records were reviewed using classification criteria from the American College of Rheumatology or other published criteria. After up to three requests and a telephone call, 27.7% of the women provided consent for medical record review. Exposed women appeared somewhat more likely (33.2% vs. 26.3%, p = 0.04) to provide consent. Using medical record reviews for 90% of the women who provided consent, confirmation rates of definite CTD were similar among the exposed and unexposed (22.7% vs. 24.0%, p = 0.83). This study demonstrates the difficulty of obtaining consent for medical record review of CTD reported to have occurred years ago in women with and without breast implants. Confirmation rates were low but were similar in exposed and unexposed. Despite the fact that the study had low participation rates, the data suggest that relative risk estimates for any definite CTD among women with breast implants compared with women without breast implants would be similar in analyses of self-reported or medical record-confirmed cases.

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breast implants; connective tissue diseases; medical records; women

In recent years, concern has been raised that breast implants may pose health hazards, including increased risk of connective tissue diseases. We tested this hypothesis using retrospective data from a very large cohort of female health professionals in the Women's Health Cohort Study (1). Self-reported data were compared between women with breast implants and women without breast implants. We found a relative risk of 1.24 (95 percent confidence interval (CI) 1.08, 1.41) for any connective tissue disease among women with breast implants.

It is unclear how valid are self-reports of connective tissue diseases. In previous studies of self-reports of rheumatoid arthritis, the diagnosis was confirmed in 31 percent of male and female respondents to a large postal survey and in 21 percent of older women enrolled in a study of osteoporosis (2, 3). In another large cohort study, self-reports of physician-diagnosed connective tissue diseases by female registered nurses were confirmed in 10 percent of cases (4). Further, it is of interest to evaluate whether women with breast implants might overreport connective tissue diseases. Therefore, in the present investigation, we compared self-reports of connective tissue diseases with medical records among female health professionals with and without breast implants in the Women's Health Cohort Study.

MATERIALS AND METHODS

Study subjects

The Women's Health Cohort Study consists of 426,774 female health professionals who completed
questionnaires in response to enrollment mailings for the Women's Health Study, a randomized, double-blind, placebo-controlled 2 × 2 factorial trial of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer among 39,876 female health professionals (including nurses, physicians, and dentists), aged 45 years and older (5, 6). Between September 1992 and May 1995, letters of invitation to participate in the trial and questionnaires that inquired about sociodemographics, life-style habits, and medical history were sent to 1.75 million female health professionals in the United States and Puerto Rico. Women were asked to return the enrollment questionnaire, regardless of whether they were willing or eligible to participate in the trial. By August 1, 1995, 426,774 women, aged 18 to 99 years, had returned enrollment questionnaires. These respondents formed the Women's Health Cohort Study (1).

In the Women's Health Cohort Study, 231 women reported any connective tissue disease (rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polymyositis/dermatomyositis, Sjogren's syndrome, or other connective tissue disease including mixed), that occurred between 1962 and 1991, and a history of breast implant exposure that occurred before the disease onset (1). We excluded 11 women who were taking part in our ongoing randomized trials (Women's Health Study or Women's Antioxidant Cardiovascular Study). For each of the remaining 220 women, we randomly selected four women from the Women's Health Cohort Study who also reported a diagnosis of connective tissue disease (1962–1991), but who reported no history of breast implants, silicone injections, or paraffin injections. We also excluded from the unexposed group 186 women who were taking part in the same ongoing randomized trials. The unexposed women (without breast implants) were matched to exposed women (with breast implants), according to age (in 5-year categories) and reported date of connective tissue disease diagnosis (1962–1967, 1968–1972, … 1988–1991). Since the original report, no woman had died in the exposed group but one woman had died in the unexposed group. This left 220 exposed and 879 unexposed women available for the present study.

Exposed and unexposed women were asked to sign a consent form for review of their medical records pertaining to the diagnosis of connective tissue disease and to complete a questionnaire on symptoms and signs of connective tissue diseases, atypical connective tissue diseases, and fibromyalgia. To increase participation rates, nonrespondents were mailed a second request and asked to complete the questionnaire, even if they chose not to provide consent for medical records. In a third mailing to nonrespondents, the questionnaire was shortened by approximately 60 percent to include only questions pertaining to the six connective tissue diseases listed above. A random sample of 100 nonrespondents to the three mailings (50 exposed, 50 unexposed) was telephoned to ascertain reasons for their nonparticipation. Of 64 women contacted, 18 stated no interest in the study, 31 reported that they had either never received the mailing or were planning to put their response in the mail, seven stated that their original self-report was not accurate, and eight were in litigation regarding breast implants (six of the latter women refused to participate for this reason). Of these 100 nonrespondents, 31 subsequently returned completed questionnaires after follow-up telephone calls. The reasons for nonparticipation did not differ by breast implant status (data not shown).

Confirmation of connective tissue disease by medical records

Medical records concerning the self-reported diagnosis were requested for all women who signed the consent form. Medical records were copied by a research assistant who blinded the data by eliminating all exposure information, any references to breast cancer, silicone or other types of breast implants, as well as any localized breast symptoms and breast examinations. Thus, both exposed and unexposed women had portions of their medical record covered, and reviewers were blinded to exposure. Records were reviewed independently by two board-certified rheumatologists. Disagreements regarding presence or absence of specific criteria were reviewed by an independent third reviewer (EWK), and all three rheumatologists reached consensus regarding all diagnoses. The date of the first symptom as well as the date of diagnosis were recorded. The specific diagnosis made by the subject's physician was recorded, in addition to whether this physician was a member of the American College of Rheumatology (ACR). Each reviewer recorded their opinion of the diagnosis based on the medical record review, regardless of presence/absence of specific criteria, and whether this diagnosis was possible or definite. If the medical record contained inadequate information regarding classification criteria, further medical records were requested from the subject's other physicians until all potential sources of evaluation were exhausted.

Definite connective tissue disease was defined according to ACR criteria for rheumatoid arthritis and systemic lupus erythematosus (7, 8), preliminary ACR criteria for scleroderma (9), and items from published studies of classification criteria for polymyositis or dermatomyositis, Sjogren's syndrome, and mixed connective tissue disease (10–12). Criteria for rheumatoid
arthritis were four out of seven ACR criteria, with a positive rheumatoid factor (RF) defined as ≥1:40, and radiographic changes typical for rheumatoid arthritis (7).

The criteria for systemic lupus erythematosus were four out of 11 criteria used by the ACR, validated in 1982 (8): malar rash, discoid rash, photosensitivity, oral ulcers, inflammatory arthritis, serositis (pleuritis, pericarditis), renal disorder (proteinuria, cellular casts), neurologic disorder (seizures, psychosis), hematologic disorder (hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia), immunologic disorder (positive tests for lupus erythematosus prep, anti-Smith antibody, anti-double-stranded DNA antibody, false positive serologic test for syphilis, or anti-cardiolipin antibody), and positive anti-nuclear antibody (ANA), defined as ≥1:40.

The criteria for scleroderma included: one major criterion (proximal scleroderma) or ≥2 minor criteria (sclerodactyly, digital pitting scars or loss of substance from the finger pad, or bibasilar pulmonary fibrosis) (9).

The criteria for polymyositis or dermatomyositis were proximal muscle weakness, an elevated muscle enzyme (creatinine phosphokinase), and a muscle biopsy demonstrating inflammatory myositis (10).

The criteria for Sjogren’s syndrome were dry eyes and dry mouth and at least one positive serologic test (ANA, RF, or the Sjogren’s syndrome antibodies anti-SSA(Ro) or anti-SSB(La)) (11).

Classification of mixed connective tissue disease was based on a positive serologic test (anti-ENA >1:10,000 or anti-UI RNP antibodies) and three out of four of the following: synovitis as defined by the rheumatoid arthritis algorithm (see above), Raynaud’s phenomenon, myositis as defined by the polymyositis/dermatomyositis algorithm (see above), and acrosclerosis (12).

**Connective tissue disease screening questionnaire (CSQ)**

Participants were also asked to complete a validated screening questionnaire for symptoms/signs of connective tissue diseases (CSQ) as well as symptoms/signs regarding atypical connective tissue disease and fibromyalgia (13). This questionnaire made no mention of breast implants. The CSQ was developed to screen for potential cases from population studies (13). Thus, the questionnaire was designed to maximize sensitivity at the expense of specificity. The 30-item questionnaire asked for information regarding ever having symptoms of six connective tissue diseases: rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polymyositis/dermatomyositis, Sjogren’s syndrome, and mixed connective tissue disease. In a prior study, the CSQ had been mailed to 253 patients from an arthritis clinic, with a diagnosis of one of six connective tissue diseases confirmed by medical record review, and to 340 controls without connective tissue disease but with either non-articular rheumatism or general medical problems (13). Sensitivity for detecting any connective tissue disease ranged from 83 percent to 96 percent and specificity ranged from 83 percent to 93 percent.

An algorithm for identifying symptoms and signs consistent with potential connective tissue disease was designed based on ACR or published clinical criteria. Criteria for potential rheumatoid arthritis were four out of six of the following: morning stiffness for at least one hour and present for ≥6 weeks, swelling of ≥3 joints for ≥6 weeks, swelling of wrist, metacarpophalangeal, or proximal interphalangeal joints for ≥6 weeks, symmetric joint swelling, rheumatoid nodules, and positive test for rheumatoid factor (7). X-ray findings were not ascertained by questionnaire.

The potential diagnosis of systemic lupus erythematosus was based on four of 12 criteria including ten criteria from the 1982 revised ACR criteria (8): malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, proteinuria, seizures, hematologic disorder (anemia, leukopenia, low platelet count), and positive ANA. In addition, two criteria from the 1971 American Rheumatism Association criteria for systemic lupus erythematosus were included to improve sensitivity: alopecia and Raynaud’s phenomenon (cold sensitivity plus white, blue, or purple color changes of the fingers on exposure to cold) (14, 15). The two additional criteria were demonstrated by Tan et al. (8) to have good sensitivity for systemic lupus erythematosus but lower specificity in distinguishing systemic lupus erythematosus from other connective tissue disease (8). Markers of immunologic disorders including lupus erythematosus prep, anti-Smith antibody, anti-double stranded DNA antibody, and false positive serologic test for syphilis were not ascertained by questionnaire because we felt that most patients would not know the results of these laboratory tests.

The criteria for potential scleroderma included one major (skin thickening proximal to the metacarpophalangeal joints) or two or more minor (sclerodactyly, digital pitting scars or loss of substance from the finger pad, or pulmonary fibrosis) preliminary ACR criteria for scleroderma (9).

The criteria for potential polymyositis or dermatomyositis were two of the following four: muscle weakness for >3 months, upper extremity proximal muscle weakness for >3 months, lower extremity proximal muscle weakness for >3 months, or a history of an elevated muscle enzyme (creatinine phosphokinase). Electromyography and muscle biopsy results were not
Self-Reported Connective Tissue Disease Diagnosis

ascertained. This corresponds to two of Bohan’s four criteria for “probable polymyositis” (10).

The criteria for potential Sjogren’s syndrome were 1) dry eyes and dry mouth or 2) positive serologic tests (antinuclear antibody or rheumatoid factor) plus dry eyes or dry mouth. Lip biopsy, rose-bengal staining, and Schirmer’s test results were not ascertained. This algorithm included two of Fox’s four criteria (11). Fulfillment of both constitutes “probable Sjogren’s syndrome.”

The classification of potential mixed connective tissue disease was based on four out of five of the following: synovitis as defined by the rheumatoid arthritis algorithm (see above), hand edema, Raynaud’s phenomenon, myositis as defined by the polymyositis/dermatomyositis algorithm (see above), and acrosclerosis (12).

Data analysis

We compared the proportions providing consent for medical record review as well as those returning the CSQ among exposed and unexposed women who self-reported a connective tissue disease. The gold standard for confirmation of a self-reported connective tissue disease was confirmation by medical record review. A secondary analysis was performed to compare self-reported connective tissue disease with symptoms and signs reported on the CSQ which would be consistent with potential connective tissue disease. For the CSQ, blank forms were treated as missing; however, for individual item nonresponse, missing symptom information was treated as negative. Differences in diagnostic confirmation rates and symptom/sign rates among exposed and unexposed women were compared with chi-square tests or Fisher’s exact test.

For women with a definite connective tissue disease confirmed by medical record review, we compared the date of diagnosis reported on the enrollment questionnaire with the date documented in the medical record among exposed and unexposed women. We also calculated the time between the first symptom documented in the medical record and the date of diagnosis documented in the medical record for each group.

Finally, we recalculated the relative risk for any connective tissue disease associated with breast implants after adjustment for false positives (16). The previously observed relative risk estimate for self-reported connective tissue disease (1) was adjusted by confirmation rates in the sample reviewed by medical record. The 95 percent confidence interval for the adjusted log relative risk was obtained from the observed distribution over 1,000 bootstrap samples (17).

RESULTS

Response rates

After up to three mailings and a telephone call, only 73 (33.2 percent) of the 220 exposed women and 231 (26.3 percent) of the 879 unexposed women gave consent for medical record review (p = 0.04) (table 1). Consent rates overall varied from 25 percent in women with self-reported rheumatoid arthritis to 36.5 percent in women with self-reported Sjogren’s syndrome. Consent rates for the different connective tissue diseases did not differ significantly by exposure status, except for self-reported polymyositis/dermatomyositis where exposed women were more likely to give consent (10 (50 percent) vs. 13 (22 percent), p = 0.02). We obtained medical records for 66 (30 percent) of the exposed women and 208 (23.7 percent) of unexposed women (p = 0.05), representing 90 percent of women who gave consent in each group. We compared consent rates among women defined by age, menopausal status, education level, and smoking status (ever or never smoker) and found no significant differences. The only subgroup in which a significant difference emerged was a lower consent rate in postmenopausal unexposed women (23 percent vs. 30 percent of premenopausal women in this group, p = 0.04). Of 505 CSQs received, seven were blank and were treated as missing. We thus received the CSQ from 104 (47.3 percent) exposed women and 394 (44.8 percent) unexposed women (p = 0.51).

<table>
<thead>
<tr>
<th>TABLE 1. Response rates to request for consent to review medical records and to connective tissue disease screening questionnaire (CSQ), Women’s Health Cohort Study, 1992-1995</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Records requested</td>
</tr>
<tr>
<td>Consent to review records</td>
</tr>
<tr>
<td>Records received</td>
</tr>
<tr>
<td>CSQ received</td>
</tr>
</tbody>
</table>

* Records received from 90% of women who gave consent, overall and in each group.
Confirmation rates: medical record review

According to medical record review, definite connective tissue disease was confirmed in 22.7 percent of the exposed women and 24.0 percent of the unexposed women \((p = 0.83)\) (table 2). For individual connective tissue diseases, total medical record diagnosis confirmation rates varied widely according to individual disease, ranging from 1 percent for mixed connective tissue disease to 37.9 percent for Sjogren’s syndrome. The numbers of records reviewed varied from six records for scleroderma to 120 records for rheumatoid arthritis. Among the exposed women, rheumatoid arthritis was the most frequently confirmed diagnosis (range: 0 percent for Sjogren’s syndrome to 40.7 percent for rheumatoid arthritis). None of the women with breast implants who self-reported scleroderma consented to have their medical records reviewed. For some connective tissue diseases, the rate was based on very few medical records (e.g., Sjogren’s syndrome, five medical records). Of five medical records reviewed in women with breast implants, Sjogren’s syndrome was not confirmed in any, whereas, among those without breast implants, Sjogren’s syndrome was the most frequently confirmed diagnosis (range: 0 percent for polymyositis/dermatomyositis and mixed connective tissue disease to 45.8 percent for Sjogren’s syndrome). Polymyositis/dermatomyositis was not confirmed in any of the women without breast implants. For exposed and unexposed women, mixed connective tissue disease was confirmed infrequently among women who reported “other connective tissue disease including mixed” (0–3.7 percent). The confirmation rates between the exposed and unexposed women were similar and did not approach statistical significance, except for Sjogren’s syndrome (0 percent vs. 45.8 percent, \(p = 0.13\)).

After adjustment for the confirmation rate for self-reported connective tissue disease of 22.7 percent for exposed women and 24 percent for unexposed women in the sample, the relative risk of connective tissue disease associated with breast implants would be 1.17 (95 percent CI 0.62, 1.90), compared with the previously reported relative risk of 1.24 (95 percent CI 1.08, 1.41) for the entire cohort that was calculated based on self-report (1).

Incomplete medical records

In 209 of 274 (76 percent) of the medical records obtained, there were insufficient criteria or detail to confirm a diagnosis of connective tissue disease. In our main analyses of confirmation rates according to medical record review, such women were considered as not having their self-reported connective tissue disease confirmed. However, in 13 (6.2 percent) of the 209 unconfirmed medical record reviews, both reviewers agreed that their clinical impression was a definite connective tissue disease (despite the lack of sufficient criteria); two were from the exposed women and 11 from the nonexposed women \((p = 0.74, \text{Fisher's exact test})\). Most of these women (85 percent) had been evaluated by rheumatologists who were members of the American College of Rheumatology. This includes five women who were diagnosed by their physicians with rheumatoid arthritis, four women with systemic lupus erythematosus, and four women with polymyositis. If these 13 women were to be added to the confirmed cases, the medical record confirmation rate for any connective tissue disease would become

<table>
<thead>
<tr>
<th>Self-reported diagnosis</th>
<th>Total (n = 274)</th>
<th>Women with breast implants (n = 66)</th>
<th>Women without breast implants (n = 208)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Records reviewed</td>
<td>Confirmed</td>
<td>%*</td>
<td>Records reviewed</td>
</tr>
<tr>
<td>Any CTD</td>
<td>274</td>
<td>65</td>
<td>23.7</td>
<td>66</td>
</tr>
<tr>
<td>RA†</td>
<td>120</td>
<td>43</td>
<td>35.8</td>
<td>27</td>
</tr>
<tr>
<td>SLE‡</td>
<td>48</td>
<td>10</td>
<td>20.8</td>
<td>10</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>6</td>
<td>1</td>
<td>16.7</td>
<td>0</td>
</tr>
<tr>
<td>PM/DM‡</td>
<td>23</td>
<td>1</td>
<td>4.4</td>
<td>10</td>
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<tr>
<td>Sjogren’s syndrome</td>
<td>29</td>
<td>11</td>
<td>37.9</td>
<td>5</td>
</tr>
<tr>
<td>Other CTD‡</td>
<td>102</td>
<td>1</td>
<td>1.0</td>
<td>27</td>
</tr>
</tbody>
</table>

* Percent of women self-reporting each diagnosis whose connective tissue disease was confirmed by medical record review.
† By Fisher’s exact test.
‡ RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; PM/DM, polymyositis/dermatomyositis; other CTD, other connective tissue disease including mixed.
§ No medical records were reviewed for women who self-reported scleroderma and who had breast implants.
25.8 percent among women with breast implants and 29.3 percent among those without breast implants \((p = 0.58)\). For rheumatoid arthritis, it would become 44.4 percent for women with breast implants and 38.7 percent for those without breast implants \((p = 0.59, \text{ Fisher's exact test})\); for systemic lupus erythematosus, 10.0 percent and 34.2 percent, respectively \((p = 0.24, \text{ Fisher's exact test})\); and for polymyositis/dermatomyositis 20.0 percent and 23.1 percent, respectively \((p = 1.00)\).

**Confirmation of self-reported date of connective tissue disease diagnosis**

Among women with definite connective tissue disease confirmed by medical record review, a significantly greater frequency of those with breast implants had a confirmed date of diagnosis in the medical record within one year of the self-reported date of diagnosis on the enrollment questionnaire compared with women without breast implants (100 percent vs. 65 percent, \(p = 0.008\)). Among the remaining 35 percent of women without breast implants, the interval between self-reported diagnosis and medical record diagnosis varied from 2 to 18 years (figure 1). Ninety-three percent of women with breast implants had the first symptom recorded in the medical record within one year of confirmed connective tissue disease diagnosis compared with 51 percent of women without breast implants \((p = 0.003)\). The 49 percent of remaining women without breast implants had their first symptom ranging from 2 to 16 years before connective tissue disease diagnosis (figure 2).

**Connective tissue disease symptoms and signs according to the CSQ**

In secondary analyses using the CSQ, criteria for any one of the six connective tissue diseases were found more frequently in women with breast implants (78.8 percent) than in women without breast implants (66.0 percent) \((p = 0.01)\) (table 3). The mean numbers
of symptoms/signs of connective tissue disease among women with and without breast implants were 11.4 and 9.5, respectively ($p = 0.003$). For individual connective tissue diseases overall, presence of criteria on the CSQ varied widely according to individual disease, ranging from 12.4 percent for mixed connective tissue disease to 78.2 percent for systemic lupus erythematosus. Symptom/sign criteria for systemic lupus erythematosus and mixed connective tissue disease were found by CSQ more frequently in women with breast implants than in women without breast implants (100 percent vs. 73 percent, $p = 0.03$; 27.9 percent vs. 7.7 percent, $p = 0.001$, respectively).

**DISCUSSION**

In the Women's Health Cohort Study, we found self-reported connective tissue diseases to be infrequently confirmed by medical record review; this did not differ by breast implant status. Among six connective tissue diseases that were previously self-reported by female health professionals on a postal questionnaire, we found an overall rate of confirmation by medical record review of 23.7 percent. None of the confirmation rates for individual connective tissue disease was impressive. The highest confirmation rate was 37.9 percent for Sjogren's syndrome, followed by 35.8 percent for rheumatoid arthritis and 20.8 percent for systemic lupus erythematosus. Medical record confirmation rates for polymyositis/dermatomyositis, scleroderma, and mixed connective tissue disease were much lower.

Further, we found that symptoms of systemic lupus erythematosus and mixed connective tissue disease, in women who self-reported these specific diagnoses, were more frequent among women with breast implants than women without breast implants. Analysis of the mean number of connective tissue disease symptoms on the CSQ showed slightly more symptoms in the exposed women compared with the nonexposed women. The CSQ was developed as a screening tool for identifying potential cases of connective tissue disease in large population studies and was not meant to
diagnose connective tissue disease. Further, the CSQ asks about ever having symptoms, and was not restricted to the time frame covered by the self-report of CTD. The gold standard for confirmation of self-reported connective tissue disease generally has been regarded to be medical record review. We found no significant difference in confirmation rates for these diseases by careful medical record review. This suggests that exposed women may be more aware of connective tissue disease symptoms; however, evaluation by their physicians does not substantiate all of the symptoms as classic connective tissue disease symptoms.

When we compared self-reported date of diagnosis on the enrollment questionnaire with date of diagnosis in the medical record, we observed a different pattern of presentation among exposed and unexposed women. The date agreed within one year for all exposed women for whom we obtained medical records but the self-reported date varied from 1-18 years later in the unexposed women. In addition, connective tissue disease symptoms in the exposed women were more frequently documented in the medical record within one year of connective tissue disease diagnosis, but showed a larger spread over time in the unexposed women. This pattern suggests that the exposed women or their physicians may have been more heightened to the possibility of connective tissue disease symptoms and more likely to pursue an evaluation leading to a prompt diagnosis, while in the unexposed women the pattern is more typical, with connective tissue disease symptoms preceding diagnosis by a number of years.

The comparison of self-reported and medical record confirmation of connective tissue disease has been assessed in other reports. In a postal survey of 5,886 randomly selected individuals (2), 33 (31 percent) of 158 self-reports of physician-diagnosed rheumatoid arthritis were confirmed. Confirmation criteria were either inclusion of the subject in a national registry or examination by a rheumatologist and blood tests. Another study of 2,424 older women enrolled as controls in an osteoporosis study (3) had 127 self-reports of physician-diagnosed rheumatoid arthritis. For 26 (21 percent) of these self-reports, rheumatoid arthritis was confirmed either by a questionnaire for ACR criteria completed by the participant's physician or by radiographic changes on hand X-rays consistent with rheumatoid arthritis. Our confirmation rate for rheumatoid arthritis (35.8 percent) was higher than the rates reported by these studies, possibly reflecting better health knowledge among female health professionals regarding this common connective tissue disease than in the general public.

With respect to systemic lupus erythematosus, one study of 4,304 women recruited by random-digit dialing (18) found 15 women who self-reported this disease. Systemic lupus erythematosus was confirmed in 2 of 6 women for whom medical records could be reviewed. Our confirmation rate for systemic lupus erythematosus was 20.8 percent but we also had difficulty obtaining medical records for review.

A major limitation of the present study is the difficulty obtaining consent for the review of medical records. Twenty-eight percent gave permission to obtain medical records and we successfully traced medical records for 90 percent. Contrary to expectation, women with breast implants gave consent more frequently than did women without breast implants. This suggests that the subject studied was not a deterrent to providing consent. The Nurses' Health Study had less difficulty obtaining consent for medical record review (4). This may be because participants had been followed bienni-

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**TABLE 3. Symptoms of potential connective tissue diseases (CTD) from a CTD screening questionnaire (CSQ) in women who self-reported CTD, Women's Health Cohort Study, 1992-1995**

<table>
<thead>
<tr>
<th>Self-reported diagnosis</th>
<th>Total (n = 498)</th>
<th>Women with breast implants (n = 104)</th>
<th>Women without breast implants (n = 394)</th>
<th>p value</th>
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<td></td>
<td>CSQ reviewed</td>
<td>Potential CTD</td>
<td>%*</td>
<td>CSQ reviewed</td>
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<tr>
<td>Any CTD</td>
<td>489</td>
<td>342</td>
<td>68.7</td>
<td>104</td>
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<td>RA‡</td>
<td>216</td>
<td>109</td>
<td>50.5</td>
<td>45</td>
</tr>
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<td>SLE‡</td>
<td>78</td>
<td>61</td>
<td>78.2</td>
<td>15</td>
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<tr>
<td>Scleroderma</td>
<td>16</td>
<td>8</td>
<td>50.0</td>
<td>3</td>
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<tr>
<td>PM/DM†</td>
<td>37</td>
<td>16</td>
<td>48.7</td>
<td>13</td>
</tr>
<tr>
<td>Sjogren's syndrome</td>
<td>52</td>
<td>38</td>
<td>73.1</td>
<td>10</td>
</tr>
<tr>
<td>Other CTD‡</td>
<td>185</td>
<td>23</td>
<td>12.4</td>
<td>43</td>
</tr>
</tbody>
</table>

* Percent of women self-reporting each diagnosis who have potential connective tissue disease symptoms for that diagnosis on a CSQ.
† By Fisher's exact test.
‡ RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; PM/DM, polymyositis/dermatomyositis; other CTD, other connective tissue disease including mixed.
ally for 14 years in an ongoing prospective cohort study. In contrast, subjects in the Women's Health Cohort Study responded to an invitation to participate in a randomized trial of aspirin and vitamin E and were encouraged to return the enrollment questionnaire even if they had no further interest in participating. Subjects may have been unwilling to participate in the present study because they were either ineligible or unwilling to take part in the trial. Another important limitation was the low response rate (46 percent) to the CSQ. However, at the same time, we asked women from the Women's Health Cohort Study to respond to an invitation to participate in another substudy of secondary prevention of cardiovascular disease (19) and the response rate to that study was comparable with that in the present study. Therefore, it is unlikely that the subject matter of the present study (connective tissue diseases) proved a deterrent to response. Because of the low participation rate and the small proportion of women who provided consent for medical record review, it is unclear how valid might be the findings in regard to confirmation of self-reported connective tissue disease among women with and without breast implants.

Finally, we were unable to assess the possibility of surveillance bias in the exposed women. Surveillance bias could occur if there is more complete ascertainment of connective tissue disease cases in exposed women, or a greater degree of under diagnosis of connective tissue diseases in unexposed women. This possibility appears to be less likely since we only included cases of connective tissue disease reported to be diagnosed before 1992 when the use of breast implants was limited by the Food and Drug Administration and when widespread publicity regarding the potential health hazards of breast implants surfaced.

In conclusion, this study demonstrates the difficulty of obtaining medical records to validate self-reports of connective tissue disease diagnoses that may have occurred years ago. We observed confirmation rates to be low but similar in women with and without breast implants. Given the limitations outlined, the findings of this study comparing self-reported connective tissue disease with medical records support our previously estimated relative risk of connective tissue disease associated with breast implants calculated based on self-reports of disease (1).

ACKNOWLEDGMENTS

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REFERENCES