Hormone replacement therapy and incident arthritis

Kathryn Wilkins

Abstract

Objectives
This article provides estimates of the incidence of arthritis between 1994/95 and 1996/97 among women aged 38 or older. It also examines the association between hormone replacement therapy (HRT) and a new diagnosis of arthritis by 1996/97.

Data source
The data are from the household component of the National Population Health Survey, conducted by Statistics Canada. Results are based on a sample of 2,673 female respondents who reported that they did not have arthritis in 1994/95. This sample, when weighted, represents 4.3 million women.

Analytical techniques
Two-year incidence of arthritis was estimated using weighted bivariate frequencies. Associations of arthritis with HRT use and numerous covariates were examined using multivariate logistic regression.

Main results
In the two years between 1994/95 and 1996/97, about 8% of women (338,600) aged 38 or older were newly diagnosed with arthritis. The odds of incident arthritis for current HRT users who had used hormones for five years or longer were twice as high as for non-users. These results persisted even after controlling for potential confounders including age, number of medical visits, and body mass index.

Keywords
estrogen replacement therapy, incidence, longitudinal studies, health surveys

Author
Kathryn Wilkins (613-951-1769; wilkkat@statcan.ca) is with the Health Statistics Division at Statistics Canada, Ottawa K1A 0T6.

Arthritis is a major cause of pain, long-term disability, activity restriction and medication use.[1-3] Its etiology is not fully understood. However, it is known that osteoarthritis—the most common form of the disease—develops more frequently in women than men beginning at midlife,[4] and the risk is higher among women who have undergone surgical removal of their ovaries.[5]

Although numerous studies have addressed possible hormonal influences on the development of osteoarthritis, the results of these studies are contradictory.[5-14] In recent years, reports on the possible role of hormone replacement therapy (HRT) in preventing osteoarthritis have appeared. Curiously, in some studies that hypothesized and reported a "protective" effect of HRT, the associations observed were not statistically significant.[5,7,8,14] Other studies did find significantly lower prevalence of osteoarthritis among HRT users than among non-users, but the cross-sectional design of the research limits the interpretation of the findings.[9,10] Yet another study reported no association between HRT and osteoarthritis, once the confounding effects of obesity and health care utilization were controlled.[11]

Data source

This article is based on Statistics Canada's National Population Health Survey (NPHS). The NPHS, which began in 1994/95, collects information about the health of the Canadian population every two years.[15,16] It covers household and institutional residents in all provinces and territories, except persons living on Indian reserves, on Canadian Forces bases, and in some remote areas. The NPHS has both a longitudinal and a cross-sectional component. Respondents who are part of the longitudinal component will be followed for up to 20 years.

Individual data are organized into two files: General and Health. Socio-demographic and some health information was obtained for each member of participating households. These data are found in the General file. Additional, in-depth health information was collected for one randomly selected household member. The in-depth health information, as well as the information in the General file pertaining to that individual, is found in the Health file.

Among households in the longitudinal component, the person providing in-depth health information about himself or herself for the Health file was the randomly selected person for the household in cycle 1 and was usually the person who provided information on all household members for the General file in cycle 2.

The 1994/95 provincial, non-institutional sample consisted of 27,263 households, of which 88.7% agreed to participate in the survey. After the application of a screening rule to keep the sample representative, 20,725 households remained in scope.[17] In 18,342 of these households, the selected person was aged 12 or older. Their response rate to the in-depth health questions was 96.1%, or 17,626 respondents. Of these 17,626 randomly selected respondents, 14,786 were eligible members of the NPHS longitudinal panel, along with 468 persons for whom only general information was collected. And 2,022 of the 2,383 randomly selected respondents under age 12 were also eligible. Thus, 17,276 respondents were eligible for re-interview in 1996/97. Interviews of the remaining respondents were sponsored by provincial governments that elected to enlarge the sample size in their province for cycle 1 only. These respondents were not followed up.

A response rate of 93.6% was achieved for the longitudinal panel in 1996/97. Of these 16,168 respondents, 15,670 provided full information; that is, general and in-depth health information for both cycles of the survey.

This analysis of hormone replacement therapy (HRT) and subsequent diagnosis of arthritis is based on longitudinal data from the household component of the first (1994/95) and second (1996/97)

cycles of the NPHS for the 10 provinces. The data were weighted to reflect the sample design, adjustments for non-response, and post-stratification. The findings are based on female respondents who did not have arthritis/rheumatism and were aged 38 or older in 1994/95, and for whom complete data were provided in both interviews. The resulting sample was 2,673, weighted to represent 4.3 million women (see Appendix Table A).

Analytical techniques

With data from the longitudinal file, cross-tabulations were used to estimate disease incidence. Multiple logistic regression was used to model the relationships between HRT and self-report of physician-diagnosed incident arthritis/rheumatism in women who were aged 38 or older in 1994/95. The lower age limit for this article was specified as 38 because by 1996/97 women this age would have entered the perimenopausal period, generally defined as beginning at age 40.[18] To account for survey design effects, standard errors and coefficients of variation were estimated with the bootstrap technique.[19,20]

HRT was considered according to duration of use before the cycle 2 interview. (Because duration of HRT use was collected in 1996/97, but not in 1994/95, only data from the cycle 2 interview were used for information on HRT.) A variable for HRT use of five years or longer was included in the regression model. The reference category for this variable was not using HRT.

The analysis incorporated factors observed in previous research to be associated with the development or diagnosis of arthritis, as well as others noted to arise as a consequence of this disease. Most variables in multiple logistic regression modelling of incident arthritis were based on data collected in 1994/95. They included age, smoking history, level of physical activity, self-reported health, and body mass index. A variable for the frequency of contacts with a physician was based on data collected in 1996/97. Frequency of contacts was measured as the reported number of visits to a family doctor or general practitioner in the 12 months before the cycle 2 interview. The variable was categorized as 0 to 2 visits or 3 or more visits.

A household member other than the selected longitudinal respondent could provide information about chronic conditions, including arthritis/rheumatism. To account for possible effects of the information source on the report of incident arthritis, a variable for proxy reporting (whether the data in either cycle were reported by the respondent to whom they pertain, or by another household member) was included in the multiple regression model, but the results are not shown.

An opposing viewpoint posits that because HRT prevents bone loss, and higher bone mass is associated with an increased risk of osteoarthritis in older women, HRT may actually *increase* the risk. In the United States, a case-control study indicated that women with osteoarthritis were significantly more likely to be taking HRT than those without the disease,[21] and a cross-sectional study showed that women with osteoarthritis who were using HRT had significantly worse joint deterioration than did women who were not using HRT.[12] As well, a population-based, longitudinal study in the United States recently reported a positive association between HRT and incident arthritis.[6] This investigation's prospective design, together with the observation of a positive gradient in risk of incident arthritis with length of HRT use, enhances the plausibility of its findings. Nonetheless, evidence of a positive association between HRT and osteoarthritis is still limited.

Altogether, there is no consistency in findings on the association of HRT with arthritis, and certainly no consensus on whether HRT is beneficial, harmful or immaterial in the development of this chronic and potentially debilitating disease. The availability of longitudinal data from the first two cycles (1994/95 and 1996/97) of the National Population Health Survey (NPHS) provides the relatively rare opportunity to study hormone replacement therapy in relation to incident arthritis (see *Methods*, *Limitations* and *Definitions*). The NPHS collects information on a variety of health-related, behavioural and socio-demographic characteristics, so the analysis can control for the effects of factors known to be confounders of the HRT–arthritis relationship.

The purpose of this article is to improve understanding of the association between HRT and the subsequent development of arthritis, using population-based data that represent women aged 38 or older residing in Canadian households. This issue is especially important given the substantial number of Canadian women using hormones. Cross-sectional data from the NPHS show that nearly 1 million women aged 40 or older (15%) were using HRT in 1996/97, up from close to 800,000
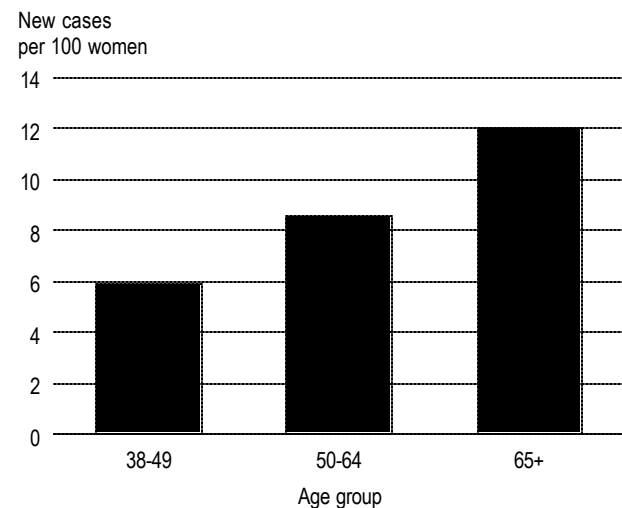
(13%) in 1994/95. And among those aged 50 to 64, more than one-quarter (28%) reported HRT use in 1996/97 (data not shown).

One in twelve developed arthritis

Among women aged 38 or older who did not have arthritis/rheumatism at the time of the NPHS cycle 1 interview in 1994/95, an estimated 8% (338,600) had been diagnosed with the disease by the time of their cycle 2 interview in 1996/97. Two-year incidence rates rose sharply with age; for women aged 65 or older, the rate was twice that for women aged 38 to 49 (Chart 1). Because the NPHS questionnaire asks simply if a respondent has "arthritis or rheumatism," it is not possible to differentiate between specific disorders such as rheumatoid arthritis and osteoarthritis. However, prevalence studies show that osteoarthritis is by far the most common form of the disease[4] (see also *Arthritis and rheumatism*).

The rate of incident arthritis differed significantly with three characteristics studied: age, number of physician visits and years of HRT use (Table 1). As expected, the two-year incidence rate was significantly higher among women aged 65 or older than among 38- to 49-year-olds. Not surprisingly,

Chart 1
Two-year incidence rate of arthritis/rheumatism, women aged 38 or older in 1994/95, by age group, household population, Canada excluding territories

New cases
per 100 women

Data source: 1994/95 and 1996/97 National Population Health Survey, longitudinal sample, Health file

a new diagnosis of arthritis was more frequent among those who consulted physicians more often. Among women who had visited a general practitioner or their family doctor three or more times during the 12 months before the cycle 2 interview, 13 per 100 received a new diagnosis of arthritis sometime in the two-year interval. In contrast, the rate was 5 per 100 women who reported none or fewer than three doctor visits.

The two-year incidence rate of arthritis was also significantly high for long-term HRT users (five years or more), but only in comparison with women who reported less than five years of use. Among long-term users, 13 per 100 had been newly

diagnosed by 1996/97, compared with 8 per 100 who were not HRT users. But because of the small sample size for long-term HRT use, the difference in these two rates is not statistically significant.

Long-term HRT linked to arthritis
Age, doctor visits and long-term HRT use tend to be related. Yet even after controlling for age and other potential confounders, the odds of incident arthritis among long-term HRT users were twice as high as for non-users (Table 2).

This analysis focussed on women who reported in 1994/95 that they did not have arthritis. Of these, women who reported HRT use of five years or more

Table 1
Two-year incidence rate of arthritis/rheumatism, women aged 38 or older in 1994/95, by selected characteristics, household population, Canada excluding territories

Characteristics	New cases per 100 women
Age group in 1994/95†	
38-49	5.9
50-64	8.6
65+	12.0‡
Self-reported health in 1994/95	
Good/Very good/Excellent	7.7
Fair/Poor	10.9§
Physician visits in past 12 months, 1996/97	
0-2	4.8
3+	12.7††
Smoking status in 1994/95	
Occasionally/ None	8.1
Daily	7.5§
Physical activity level in 1994/95	
Moderate/Active	7.9
Inactive	7.8
Body mass index in 1994/95	
Lower 2 tertiles (< 26.48)	7.1
Upper tertile (≥ 26.48)	9.8
Years of hormone replacement therapy as of 1996/97†	
None	7.8
< 5	4.9‡‡
5+	13.3§§

Data source: 1994/95 and 1996/97 National Population Health Survey, longitudinal sample, Health file
† A critical value of 2.40 instead of 1.96 was used to account for multiple comparisons.
‡ Significantly higher than the rate for 38-49 age group
§ Coefficient of variation between 16.6% and 25.0%
†† Significantly higher than the rate for 0-2 physician visits (p £ 0.05)
‡‡ Coefficient of variation between 25.1% and 33.3%
§§ Significantly higher than the rate for < 5 years HRT

Table 2
Adjusted odds ratios for two-year incidence of arthritis/ rheumatism, women aged 38 or older in 1994/95, by selected characteristics, household population, Canada excluding territories

Characteristics	Odds ratio	95% confidence interval
Age group in 1994/95		
38-64†	1.0	…
65+	1.6*	1.0, 2.4
Self-reported health status in 1994/95		
Good/Very good/Excellent†	1.0	…
Fair/Poor	1.0	0.5, 1.8
Physician visits in past 12 months, 1996/97		
0-2†	1.0	…
3+	2.8*	1.9, 4.1
Smoking status in 1994/95		
Occasionally/None†	1.0	…
Daily	1.0	0.6, 1.6
Physical activity level in 1994/95		
Moderate/Active†	1.0	…
Inactive	1.0	0.7, 1.4
Body mass index in 1994/95		
Lower two tertiles† (BMI < 26.48)	1.0	…
Upper tertile (BMI ≥ 26.48)	1.3	0.9, 1.9
Years of hormone replacement therapy as of 1996/97		
None†	1.0	…
< 5	0.6	0.3, 1.2
5+	2.0*	1.0, 3.8

Data source: 1994/95 and 1996/97 National Population Health Survey, longitudinal sample, Health file
Notes: A variable for proxy-report was also entered into the model; the odds ratio is not shown. Analysis is based on a sample of 2,604; 69 were omitted from the analysis because of missing values. Because of rounding, some confidence intervals with 1.0 as the lower limit were significant.
*p £ 0.05
† Reference category, for which odds ratio is always 1.0
⋯ Not applicable

in 1996/97 would have been using HRT for at least three years when they were first interviewed in 1994/95. The association between HRT and arthritis was observed for these women, but not for women who had used HRT for shorter periods when compared with women who were not current users at the time of the 1996/97 interview.

The positive association between HRT and subsequent onset of arthritis, based on NPHS data, supports recent results from another longitudinal study conducted over a much longer time in the United States.[6] In that study, which was also based

Limitations

The National Population Health Survey (NPHS) asked simply about "arthritis or rheumatism," so it is not possible to differentiate specific types of arthritic disease. Because osteoarthritis is far more prevalent than any other arthritic condition (see *Arthritis and rheumatism*), the variables included in the analysis were selected on the basis of their reported associations with osteoarthritis.[3] However, if some covariates relate to osteoarthritis differently from the way they relate to other conditions that were reported as "arthritis or rheumatism," the observed association would be weakened. For example, if HRT were negatively associated with rheumatoid arthritis but positively associated with osteoarthritis, pooling all women with diagnoses of "arthritis/rheumatism" would dilute the positive association that existed between HRT and osteoarthritis.

For this analysis, self-reported medical diagnosis of arthritis or rheumatism in women who reported that they had not previously received such a diagnosis was defined as incident arthritis. A limitation of this definition is that self-selection may affect both the opportunity for diagnosis as well as the stage at which a disease is diagnosed. Therefore, the "incidence" of arthritis does not correspond to the actual onset of clinically detectable disease or appearance of symptoms for all women.

Since only cycle 2 data on HRT use were used for the analysis, women who had used HRT at any time and for any duration prior to the month before the cycle 2 interview and then had quit would have not been included among HRT users. This restriction likely resulted in misclassification of some women about their exposure to HRT (for example, 17% [82,655] of HRT users in cycle 1 reported not using HRT in cycle 2—data not shown), which would weaken the observed association between HRT and arthritis/rheumatism.

Because the data on use and duration of HRT, as well as incident arthritis, were collected from the same interview, there is some possibility of recall bias. That is, women who reported incident arthritis may have been more likely to report hormone use, or to report its initiation as occurring before the diagnosis of disease, compared with women who did not report arthritis. However, because the possible association between arthritis and HRT has not been widely publicized, and because the NPHS is a comprehensive survey that gathers data on a wide variety of health-related factors, the probability of such bias is likely quite small.

Because the NPHS does not collect information on menstrual status, the analysis focussed on women in the age group when the physiological changes associated with natural menopause begin.[18] However, the exclusion of younger women who had undergone surgical menopause, and the inevitable inclusion of women who had not yet completed menopause together with those who were postmenopausal somewhat impedes comparisons with other studies that dealt only with postmenopausal women.

In fact, by virtue of their age, most of the women in this analysis were perimenopausal or menopausal. However, the probable inclusion of some women who were not yet even perimenopausal, and who were therefore at lower risk of arthritis, would weaken the observed association between HRT and arthritis.

While body mass index (BMI) based on self-reports of height and weight was included as a variable in this analysis, the use of BMI for people older than 65 is not universally recommended. Because of the tendency for people to overstate their height, especially as they get older, the NPHS may underestimate the prevalence of overweight.[22] The effect would be to weaken the association between high BMI and the risk of arthritis.

The analysis was restricted to the NPHS household sample. Therefore, the results are not generalizable to the total population of women (7% of women aged 65 or older reside in long-term care facilities).[23]

Finally, the NPHS data are self- (or proxy-) reported, and the degree to which they are valid is unknown. In an effort to minimize reporting error in data related to chronic conditions (including arthritis/rheumatism), respondents were instructed to report only those conditions that had been "diagnosed by a health professional." When self-reported data on musculoskeletal symptoms from the US National Health and Nutrition Examination Survey I were compared with medical information, a high level of agreement was revealed.[24]

on self-reports of physician-diagnosed arthritis, but which focussed only on postmenopausal women, the risk of incident disease rose steadily with the duration of hormone use. A significant association

with incident arthritis was observed even for one year or less of HRT use, a finding that did not emerge in analysis of the NPHS, possibly because of a lack of statistical power due to the small sample size. With 4 to 10 years of use, the relative risk rose to 1.96 in the US study, a result remarkably similar to the odds ratio of 2.0 observed in the NPHS for women who had used HRT for five years or longer.

As expected, the NPHS data indicate that older age was significantly associated with incident arthritis. The odds of disease among women aged 65 or older were 1.6 times those for women aged 38 through 64. This is consistent with the long-observed pattern of increasing risk of arthritis with advancing age.

The odds of arthritis among women who had three or more contacts with a family doctor or general practitioner in the year before the cycle 2 interview were almost three times as high as for women who had fewer physician contacts. As other

Definitions

The National Population Health Survey (NPHS) asked, "Does . . . have any of the following long-term conditions that have lasted or are expected to last six months or more and that have been diagnosed by a health professional?" *Arthritis/rheumatism* was included in this list. As a validity check, respondents who were reported not to have arthritis/rheumatism in cycle 1, but who reported in cycle 2 that they had this disease, were asked the date of diagnosis. Those reporting a date before the cycle 1 interview were probed, "So you had arthritis/rheumatism prior to our last interview in [date of cycle 1 interview]?" After eliminating the 176 cases reported to have predated the cycle 1 interview, incident arthritis/rheumatism was ascertained by tabulating the number of respondents reporting in the cycle 2 interview that they now had the condition among those who had reported two years earlier that they did not.

Three *age groups* were established: 38 to 49, 50 to 64 and 65 or older (age in 1994/95). For multiple logistic regression modelling, the age groups 38 to 64 and 65 or older were used.

Self-reported health status for cycle 1 was classified as either good/very good/excellent or fair/poor.

Physician visits in past 12 months (1996/97) were also placed in two groups: 0 to 2 and 3 or more.

Smoking status in 1994/95 was categorized as less than daily, or daily smoking.

Physical activity level was based on a derived physical activity index and was categorized as moderate/active or inactive.

Body mass index (BMI), which is calculated by dividing weight in kilograms by height in metres squared, was categorized as within the lower two tertiles (a BMI of less than 26.48) or in the upper tertile (a BMI of 26.48 or more) in cycle 1.

To determine use of *hormone replacement therapy (HRT)* in 1996/97, the NPHS asked: "In the past month, did you take hormones for menopause or aging symptoms?" Respondents who said "yes" were then asked: "What type of hormones are you taking?" (response options were estrogen only, progesterone only, both, neither) and "When did you start this hormone therapy?" Three categories were established: none, less than 5 years, and 5 or more years. Of women who reported in 1996/97 that they did take hormones, 91% specified use of estrogen, progesterone, or both (data not shown).

Arthritis and rheumatism

National Population Health Survey (NPHS) respondents were asked if they had "arthritis or rheumatism" diagnosed by a health professional. Although these terms apply to numerous clinically distinct conditions, the two most common arthritic disorders are osteoarthritis and rheumatoid arthritis. Estimates from cycle 1 of the NPHS indicate that among men and women aged 55 or older, the prevalence of arthritis or rheumatism in 1994/95 was 35%.[2] Information from survey data in the United States suggests that among people reporting physician-diagnosed arthritis or rheumatism, the ratio of rheumatoid arthritis to osteoarthritis varies from 1:23[24] to 1:15.[25]

The causes of both diseases are unclear. Osteoarthritis is a degenerative joint disease, characterized by deterioration of the joint cartilage, increases in the size of the bone at the margins, and changes in the synovial membrane. It is accompanied by pain and stiffness and occurs chiefly in older persons. Most frequently, it affects the lumbar spine, the hips, the hands and the knee.

Rheumatoid arthritis is a chronic inflammatory joint disease, usually affecting several joints. It may affect the tendons, ligaments, fascia and muscle and may also extend into the bone. Deformity develops in the late stages. Rheumatoid arthritis occurs in children as well as adults.[26]

researchers have noted, frequency of health care utilization may be related to HRT use as well as to arthritis. During their medical consultations about HRT, women taking these drugs might have a greater opportunity than non-users to receive a diagnosis of arthritis. Failure to account for this "detection bias" could confound any association between HRT and arthritis.[6,11,27] Nonetheless, the persistence of the positive association between long-term HRT use and arthritis, even after the effect of the number of physician contacts was controlled in the multiple logistic regression, strongly suggests an independent link between HRT and incident arthritis.

A positive association between high BMI and incident arthritis also emerged in unadjusted logistic regression analysis, although the designated significance level of $p < 0.05$ was not attained when the effects of other factors were considered (Table 2). The literature on the association of BMI with osteoarthritis is consistent, indicating a strong, positive link between higher levels of BMI and prevalence or incidence of disease.[7,28-37] Notably, all but one of these analyses are based on actual measures, rather than self-reports of height and weight. In the NPHS analysis, possible misclassification of respondents—specifically, categorizing people in lower BMI ranges than their actual physical measures would indicate—may have weakened the association between high BMI and arthritis.

Concluding remarks

In the current context of conflicting research results and confusion over the relationship of hormone replacement therapy with arthritis, this analysis adds to emerging evidence suggesting that long-term HRT use increases the risk of arthritis in middle-aged and older women. This association should be further examined in carefully controlled randomized clinical trials.

Because of the high prevalence and potentially disabling consequences of arthritis, identification of factors associated with its development is important. Prevention of even a small proportion of cases could have far-reaching consequences.

In recent years, numerous reports have documented the benefits of HRT, and data from the National Population Health Survey show that a substantial number of Canadian women are currently using HRT. The growing number of women who must make decisions about HRT use are entitled to the fullest information available about the risks as well as the advantages of this therapy. ●

References ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ●

1 Millar WJ. Chronic pain. *Health Reports* (Statistics Canada, Catalogue 82-003) 1996; 7(4): 47-53.

2 Wilkins K, Park E. Chronic conditions, physical limitations and dependency among seniors living in the community. *Health Reports* (Statistics Canada, Catalogue 82-003-XPB) 1996; 8(3): 7-15.

3 Badley EM. The effect of osteoarthritis on disability and health care use in Canada. *Journal of Rheumatology* 1995; 22 (suppl 43): 19-22.

4 Kelsey JL, Hochberg MC. Epidemiology of chronic musculoskeletal disorders. *Annual Review of Public Health* 1988; 9: 379-401.

5 Dennison EM, Arden NK, Kellingray S, et al. Hormone replacement therapy, other reproductive variables and symptomatic hip osteoarthritis in elderly white women: A case-control study. *British Journal of Rheumatology* 1998; 37(11): 1198-1202.

6 Sahyoun NR, Brett KM, Hochberg MC, et al. Estrogen replacement therapy and incidence of self-reported physician-diagnosed arthritis. *Preventive Medicine* 1999; 28(5): 458-64.

7 Hart DJ, Doyle DV, Spector TD. Incidence and risk factors for radiographic knee osteoarthritis in middle-aged women: The Chingford Study. *Arthritis and Rheumatism* 1999; 42(1): 17-24.

8 Zhang Y, McAlindon TE, Hannan MT, et al. Estrogen replacement therapy and worsening of radiographic knee osteoarthritis: the Framingham Study. *Arthritis and Rheumatism* 1998; 41(10): 1867-73.

9 Spector TD, Nandra D, Hart DJ, et al. Is hormone replacement therapy protective for hand and knee osteoarthritis in women? The Chingford Study. *Annals of Rheumatic Disease* 1997; 56(7): 432-4.

10 Nevitt MC, Cummings SR, Lane NE, et al. Association of estrogen replacement therapy with the risk of osteoarthritis of the hip in elderly white women. Study of Osteoporotic Fractures Research Group. *Archives of Internal Medicine* 1996; 156(18): 2073-80.

11 Oliveria SA, Felson DT, Klein RA, et al. Estrogen replacement therapy and the development of osteoarthritis. *Epidemiology* 1996; 7(4): 415-9.

12 Sowers M, Hochberg M, Crabbe JP, et al. Association of bone mineral density and sex hormone levels with osteoarthritis of the hand and knee in premenopausal women. *American Journal of Epidemiology* 1996; 143(1): 38-47.

13 Samanta A, Jones A, Regan M, et al. Is osteoarthritis in women affected by hormonal changes or smoking? *British Journal of Rheumatology* 1993; 32(5): 366-70.

14 Hannan MT, Felson DT, Anderson JJ, et al. Estrogen use and radiographic osteoarthritis of the knee in women. The Framingham Osteoarthritis Study. *Arthritis and Rheumatism* 1990; 33(4): 525-32.

15 Statistics Canada. *National Population Health Survey, 1996/97. Household Component, User's Guide for the Public Use Microdata Files* (Statistics Canada, Catalogue 82-M0009GPE) Ottawa: Statistics Canada, 1998.

16 Swain L, Catlin G, Beaudet MP. The National Population Health Survey—its longitudinal nature. *Health Reports* (Statistics Canada, Catalogue 82-003) 1999; 10(4): 69-82.

17 Tambay J-L, Catlin G. Sample design of the National Population Health Survey. *Health Reports* (Statistics Canada, Catalogue 82-003) 1995; 7(1): 29-38.

18 Tierney LM Jr, McPhee SJ, Papadakis MA, eds. *Current Medical Diagnosis and Treatment*, 38th edition. Stamford, Connecticut: Appleton and Lange, 1999.

19 Rust KF, Rao JNK. Variance estimation for complex surveys using replication techniques. *Statistical Methods in Medical Research* 1996; 5: 283-310.

20 Rao JNK, Wu CFJ, Yue K. Some recent work on resampling methods for complex surveys. *Survey Methodology* (Statistics Canada, Catalogue 12-001) 1992; 18(2): 209-17.

21 Holbrook TL, Wingard DL, Barrett-Connor E. Self-reported arthritis among men and women in an adult community. *Journal of Community Health* 1990; 15(3): 195-208.

22 Health and Welfare Canada. *Canadian Guidelines for Better Weights* (Catalogue H39-134/1988E) Ottawa: Supply and Services Canada, 1988.

23 Tully P, Mohl C. Older residents of health care institutions. *Health Reports* (Statistics Canada, Catalogue 83-002) 1995; 7(3): 27-30.

24 LaPlante MP. *Data on Disability from the National Health Interview Survey 1983-1985: An InfoUse Report*. Washington, DC: US National Institute on Disability and Rehabilitation Research, 1988.

25 Cunningham LS, Kelsey JL. Epidemiology of musculoskeletal impairments and associated disability. *American Journal of Public Health* 1984; 74: 574-9.

26 Wyngaarden JB, Smith LH, Jr., eds. *Cecil Textbook of Medicine*, 17th edition. Philadelphia: W.B. Saunders Co., 1985.

27 Felson DT, Nevitt MC. Editorial. Estrogen and osteoarthritis: How do we explain conflicting study results? *Preventive Medicine* 1999; 28: 445-8.

28 Felson DT, Zhang Y, Hannan MT, et al. Risk factors for incident radiographic knee osteoarthritis in the elderly: the Framingham Study. *Arthritis and Rheumatism* 1997; 40(4): 728-33.

29 Manninen P, Riihimaki H, Heliovaara M, et al. Overweight, gender and knee osteoarthritis. *International Journal of Obesity and Related Metabolic Disorders* 1996; 20(6): 595-7.

30 Sahyoun NR, Hochberg MC, Helmick CG, et al. Body mass index, weight change, and incidence of self-reported physician-diagnosed arthritis among women. *American Journal of Public Health* 1999; 89: 391-4.

31 Oliveria SA, Felson DT, Cirilla PA, et al. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999; 10 (2): 161-6.

32 Slemenda C, Heilman DK, Brandt KD, et al. Reduced quadriceps strength relative to body weight: A risk factor for knee osteoarthritis in women? *Arthritis and Rheumatism* 1998; 41(11): 1951-9.

33 Vingård E, Alfredsson L, Malchau H. Lifestyle factors and hip arthrosis. A case referent study of body mass index, smoking and hormone therapy in 503 Swedish women. *Acta Orthopaedica Scandinavica* 1997; 68 (3): 216-20.

34 Hochberg MC, Lethbridge-Cejku M, Scott WW Jr, et al. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: Data from the Baltimore Longitudinal Study of Aging. *The Journal of Rheumatology* 1995; 22(3): 488-93.

35 Felson DT, Zhang Y, Anthony JM, et al. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. *Annals of Internal Medicine* 1992; 116(7): 535-9.

36 Bagge E, Bjelle A, Edén S, et al. Factors associated with radiographic osteoarthritis: Results from the population study of 70-year-old people in Göteborg. *The Journal of Rheumatology* 1991; 18(8): 1218-22.

37 Hartz AJ, Fischer ME, Bril G, et al. The association of obesity with joint pain and osteoarthritis in the HANES data. *Journal of Chronic Diseases* 1986; 39(4): 311-9.

Appendix

Table A

Distribution of selected characteristics, women aged 38 or older in 1994/95, household population, Canada excluding territories, 1994/95 to 1996/97

	Sample size	Estimated population†	
		'000	%
Total	**2,673‡**	**4,257**	**100**
Age group in 1994/95			
38-49	1,196	2,063	49
50-64	810	1,345	32
65+	667	849	20
Self-reported health status in 1994/95			
Good/ Very good/ Excellent	2,390	3,853	91
Fair/ Poor	283	404	10
Physician visits in past 12 months, 1996/97			
0-2	1,527	2,536	60
3+	1,134	1,699	40
Smoking status in 1994/95			
Occasionally/ None	2,078	3,393	80
Daily	592	853	20
Physical activity level in 1994/95			
Moderate/ Active	955	1,459	35
Inactive	1,669	2,692	65
Body mass index in 1994/95			
Lower 2 tertiles (<26.48)	1,829	2,924	69
Upper tertile (≥ 26.48)	844	1,333	31
Years of hormone replacement therapy as of 1996/97			
None	2,280	3,608	85
< 5	224	377	9
5+	163	262	6

Data source: *1994/95 and 1996/97 National Population Health Survey, longitudinal sample, Health file*

† Percentages may not add to 100% because of rounding.

‡ Detail may not add to total as data were missing for some variables.