Age at Natural Menopause and All-Cause Mortality: A 37-Year Follow-up of 19,731 Norwegian Women

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In a cohort of 19,731 Norwegian postmenopausal women, the authors analyzed relations between the age at natural menopause and all-cause mortality. A total of 18,533 women died during the 37 years of follow-up from 1961 to 1997. An inverse relation was found between the age at menopause and the all-cause mortality rate (p = 0.003). The strength of the association was moderate, however, with 1.6% (95% confidence interval: 0.6, 2.7) reduced mortality per 3 years’ increase in age at menopause. The impact appeared to be stronger in women with an attained age of less than 70 years (3.7% reduction in risk) than in women aged 80 years or more (1.0%). The inverse relation could not be explained by extreme mortality rates in women with very early (<40 years) or late (>55 years) menopause or by possible confounding variables like birth cohort, place of residence, occupational category (own or husband’s occupation), body mass index, age at menarche, and first and last delivery or parity. The smoking prevalence was low in the underlying population, and the use of hormone replacement therapy was very rare. The authors conclude that age at natural menopause is inversely related to all-cause mortality.

MATERIALS AND METHODS

During 1956–1959, information about reproductive factors was collected in personal interviews of women who participated in a screening program for breast cancer in the...
three counties of Vestfold, Nord-Trøndelag, and Aust-Agder. Vestfold and Aust-Agder are both situated in the southern part of Norway, south of the capital Oslo, whereas Nord-Trøndelag is in the central part of the country. All counties must be considered rural as 70, 72, and 89 percent of the female population aged 15 years or above in 1960 lived in rural areas in Vestfold, Aust-Agder, and Nord-Trøndelag, respectively. Two thirds of Norwegian women lived in rural areas in 1960 (11). A total of 63,090 women aged 32–74 years in January 1961 were included in this study. The information collected comprised, inter alia, age at menarche and menopause (if the woman was postmenopausal), number of full-term pregnancies, and ages at first and last delivery, as well as information about surgery on genital organs (e.g., oophorectomy). In particular, the women were asked about the age when the menstruation stopped, which was recorded as age at menopause. The screening procedures have been detailed elsewhere (5). A total of 22,151 women stated their age at menopause. In this group, 2,420 women also reported uni- or bilateral oophorectomy, other ovarian operations, hysterectomy, or unspecified operations on the womb. These women were excluded, leaving 19,731 women for analyses of the effects of natural menopause. This procedure has probably resulted in the exclusion of some women with a natural menopause but has hardly left many, if any, women with a surgical menopause in our data set.

Information on height and weight was available for 13,622 of the 19,731 women, derived from separate measurements made during the period 1963–1975 as part of a compulsory mass examination for tuberculosis. Body mass index was defined as weight (kg)/height (m)^2. Associations between age at menopause and reproductive and demographic factors recorded before the start of follow-up were explored in analyses with age at menopause as the dependent variable. Possible predictors for age at menopause were entered as categorical factors in an analysis of variance.

The official personal registration number served as a unique identification of each woman and made it possible to link our data about age at menopause (which occurred sometime before the screening in 1956–1959) to information on vital status and cause of death obtained from files kept at Statistics Norway, Oslo. Follow-up started on January 1, 1961, when the personal registration number was introduced. During the complete follow-up through 1997, 18,533 women died.

The relations between age at natural menopause and the total mortality rate were investigated in a Cox proportional hazards regression model using attained age (divided into 2-week periods) as the time variable. Women who were alive at the end of follow-up were censored on December 31, 1997, and women who emigrated were censored on the day they left Norway. In all analyses, we adjusted for birth cohort (1886–1889, 1890–1894, 1895–1899, 1900–1904, 1905–1909, 1910–1914, 1915–1926), county of residence and, as an indicator of social class (12), occupational group (own or husband’s occupation). Married housewives were assigned to the occupational class of their husbands.

Age at menopause was categorized into seven groups: aged 40 years or below, 41–43, 44–46, 47–49, 50–52, 53–55, and 56–60 years. Women aged 50–52 years were considered the reference category. However, when computing the p value for linear trend and mean change in mortality rate related to an increase in age at menopause by 3 years, we included age at menopause in the model as a continuous (1-year interval) variable. Body mass index was adjusted for in separate analyses restricted to women with information about height and weight and with follow-up starting January 1 of the year after the measurements were made.

From previous analyses (1), we suspected that the effect of age at menopause on total mortality might be influenced by the attained age of the women. We therefore performed the analyses in three predetermined age groups: <70 years, 70–79 years, and 80 years or above. In addition, other analyses were carried out within subgroups defined by demographic and reproductive variables.

All analyses were performed using SAS software (13).

RESULTS

The mean and median ages at natural menopause in the women included in our analysis were 48.4 and 49 years, respectively. A total of 2.8 percent of the women stated that they had experienced menopause before the age of 40, and 1.6 percent had menopause after the age of 55 years. In the birth cohorts born before 1900, comprising almost exclusively women who were postmenopausal when the information was collected, the mean and median ages at menopause were 48.9 and 50 years, respectively. The mean age at start of follow-up was 61.8 (range, 34–74) years. Nearly 13 percent of the women were aged 54 years and below at the start of follow-up, 56 percent were aged 55–64 years, and 31 percent were aged 65–74 years. The mean follow-up period was 20.6 (range, 0–37) years.

Occupational group, county, ever been married, age at menarche, and parity were considered possible predictors for age at natural menopause. After adjustment for birth cohort and the other predictors considered, only minor (although statistically significant (p ≤ 0.005)) differences remained in the mean age at natural menopause between women in the separate occupational groups and counties and between women with different ages at menarche or different parity. The maximum contrast was a 0.6-year lower age at menopause in nulliparous women than in women with five deliveries. Having ever been married had no bearing on the age at menopause (p = 0.99).

In an analysis confined to women with two or more deliveries, we also included parity and ages at first and last delivery as possible predictors. Ever been married was omitted as a possible predictor, however, as very few never married women had two or more children. Among the variables related to reproduction, only age at last delivery was significantly related to age at menopause, with an adjusted 0.8-year later menopause in women with an age at last delivery of 40 years or above compared with women with a relatively young age at last delivery of less than 28 years (p < 0.001). A statistically significant linear positive relation between age at menopause and age at last delivery was also found in women born before 1900, with a difference in mean age at menopause between the extreme groups (≥40 years vs. <28 years) of 1.3 years.
In this cohort, 18, 19, and 16 percent of the deaths were caused by ischemic heart disease, stroke, and cancer, respectively (table 1). Other diseases caused 43 percent of the deaths, whereas violent deaths were rather uncommon. The cause of death was unknown for less than 1 percent of all deaths. This category occurred almost exclusively in the early parts of the follow-up, during 1961–1970.

Table 2 shows the relations between age at natural menopause and total mortality. The all-cause mortality rate was 45.5 per 1,000 person-years. An inverse relation was found in the overall cohort (\(p = 0.003\)). A 3-year increase in the age at menopause was associated with 1.6 percent reduction in total mortality (95 percent confidence interval: 0.6, 2.7). This corresponds to 6 percent reduced total mortality associated with a 12-year increase in age at menopause, assuming a linear relation.

We investigated in particular the association between age at natural menopause and total mortality within the attained age intervals of less than 70 years, 70–79 years, and 80 years or above. In all three age groups, an inverse linear relation was indicated, and in the two youngest age groups, the relation was statistically significant (\(p \leq 0.05\)). No statistical support was found for a U-shaped relation with an increased risk in women with a very late menopause. This was also the case among women aged less than 70 years (\(p = 0.48\) for a quadratic effect). The results presented in table 2 reflect a statistically nonsignificant tendency (\(p = 0.15\)) toward a stronger relation the younger the women were. However, as a whole, our data are also compatible with a uniform effect of age at menopause on total mortality in the postmenopausal years.

Mortality among women with very early (<40 years) or late (>55 years) menopause did not materially influence the results with age at menopause as a continuous variable. When these women were excluded from the analysis, the mean percentage of reduction in mortality associated with a 3-year increase in age at menopause was 1.7 percent (95 percent confidence interval: 0.4, 3.0). In the three different age groups (<70 years, 70–79 years, and 80 years or above), the mean reductions in mortality were 3.2 percent (95 percent confidence interval: –1.4, 7.6), 2.8 percent (95 percent confidence interval: 0.3, 5.1), and 1.0 percent (95 percent confidence interval: –0.6, 2.7), respectively.

Table 3 gives the results from the analyses within strata defined by a number of possible confounders and effect modifiers. The analyses confirm the results from the main analysis presented in table 2. No interactions were indicated, and the consistency of the weak inverse relation is striking, except possibly for occupational categories (\(p = 0.52\) for heterogeneity). The association between age at menopause and all-cause mortality hardly differed over birth cohorts (\(p\) value for linear trend = 0.92). The data may suggest a stronger inverse relation in multiparous women than in those

### TABLE 1. Main causes of deaths during a 37-year follow-up of 19,731 postmenopausal Norwegian women, 1961–1997

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>No. of deaths</th>
<th>% of all deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>3,353</td>
<td>18.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>3,561</td>
<td>19.2</td>
</tr>
<tr>
<td>Cancer</td>
<td>2,908</td>
<td>15.7</td>
</tr>
<tr>
<td>Other diseases</td>
<td>7,882</td>
<td>42.5</td>
</tr>
<tr>
<td>Violent deaths</td>
<td>678</td>
<td>3.7</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>151</td>
<td>0.8</td>
</tr>
<tr>
<td>All deaths</td>
<td>18,533</td>
<td>100</td>
</tr>
</tbody>
</table>

### TABLE 2. All-cause mortality according to age at menopause and attained age in 19,731 Norwegian women, 1961–1997

<table>
<thead>
<tr>
<th>Age at menopause (years)</th>
<th>All women</th>
<th>Women aged &lt;70 years</th>
<th>Women aged 70–79 years</th>
<th>Women aged ≥80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of women</td>
<td>No. of person-years</td>
<td>No. of deaths</td>
<td>MRR* CI†</td>
</tr>
<tr>
<td>≤40</td>
<td>1,054</td>
<td>22,594</td>
<td>926</td>
<td>1.06</td>
</tr>
<tr>
<td>41–43</td>
<td>1,267</td>
<td>27,596</td>
<td>1,132</td>
<td>1.02</td>
</tr>
<tr>
<td>44–46</td>
<td>2,823</td>
<td>60,531</td>
<td>2,595</td>
<td>1.05</td>
</tr>
<tr>
<td>47–49</td>
<td>5,135</td>
<td>109,849</td>
<td>4,783</td>
<td>1.01</td>
</tr>
<tr>
<td>50–52</td>
<td>6,917</td>
<td>138,382</td>
<td>6,623</td>
<td>1.00</td>
</tr>
<tr>
<td>53–55</td>
<td>2,217</td>
<td>43,073</td>
<td>2,158</td>
<td>0.97</td>
</tr>
<tr>
<td>56–60</td>
<td>318</td>
<td>5,368</td>
<td>316</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Mean reduction in mortality (%)*† | 1.6 (0.6, 2.7) | 3.7 (0.7, 3) | 2.2 (0.2, 4.2) | 1.1 (–0.3, 2.5) |

*p value for linear trend

* MRR, mortality rate ratio; CI, confidence interval.
† The mean reduction in mortality (in %) associated with a 3-year increase in age at menopause (95% confidence interval). Age at menopause included in the model as continuous (1-year interval) variable. Results are based on the Cox proportional hazards model and adjusted for attained age, county, occupational group, and birth cohort.

TABLE 3. Age at natural menopause and all-cause mortality within subgroups of the data set in a 37-year follow-up of 19,731 postmenopausal Norwegian women, 1961–1997

<table>
<thead>
<tr>
<th></th>
<th>No. of person-years</th>
<th>No. of deaths</th>
<th>Mean reduction in mortality (%)&lt;sup&gt;*&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women</td>
<td>407,393</td>
<td>18,533</td>
<td>1.6 (0.6, 2.7)</td>
</tr>
<tr>
<td>Birth cohort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1886–1894</td>
<td>73,774</td>
<td>5,171</td>
<td>1.6 (–0.3, 3.5)</td>
</tr>
<tr>
<td>1895–1899</td>
<td>101,372</td>
<td>5,253</td>
<td>1.5 (–0.4, 3.5)</td>
</tr>
<tr>
<td>1900–1904</td>
<td>135,538</td>
<td>5,397</td>
<td>1.7 (–0.4, 3.8)</td>
</tr>
<tr>
<td>1905–1926</td>
<td>96,708</td>
<td>2,712</td>
<td>1.9 (–1.6, 5.2)</td>
</tr>
<tr>
<td>County</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nord-Trøndelag</td>
<td>129,792</td>
<td>6,096</td>
<td>0.3 (–1.7, 2.3)</td>
</tr>
<tr>
<td>Aust-Agder</td>
<td>95,069</td>
<td>4,380</td>
<td>2.9 (0.7, 5.1)</td>
</tr>
<tr>
<td>Vestfold</td>
<td>182,532</td>
<td>8,057</td>
<td>1.9 (0.3, 3.4)</td>
</tr>
<tr>
<td>Occupational category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professional, private enterprise</td>
<td>58,549</td>
<td>2,597</td>
<td>–0.8 (–3.8, 2.1)</td>
</tr>
<tr>
<td>Clerical work</td>
<td>43,479</td>
<td>1,855</td>
<td>2.1 (–1.6, 5.6)</td>
</tr>
<tr>
<td>Fishing, ship officers, crew</td>
<td>34,169</td>
<td>1,460</td>
<td>3.2 (–0.5, 6.7)</td>
</tr>
<tr>
<td>Farm and forestry work</td>
<td>98,038</td>
<td>4,551</td>
<td>2.5 (0.2, 4.7)</td>
</tr>
<tr>
<td>Industrial work</td>
<td>41,524</td>
<td>1,815</td>
<td>–0.1 (–3.9, 3.5)</td>
</tr>
<tr>
<td>Domestic and other work</td>
<td>73,903</td>
<td>3,367</td>
<td>2.0 (–0.6, 4.4)</td>
</tr>
<tr>
<td>Not specified</td>
<td>57,732</td>
<td>2,888</td>
<td>2.3 (–0.4, 4.8)</td>
</tr>
<tr>
<td>Age (years) at menarche†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;14</td>
<td>88,950</td>
<td>3,936</td>
<td>0.6 (–1.7, 2.8)</td>
</tr>
<tr>
<td>14</td>
<td>122,710</td>
<td>5,622</td>
<td>1.9 (–0.1, 3.9)</td>
</tr>
<tr>
<td>15</td>
<td>101,124</td>
<td>4,552</td>
<td>2.0 (–0.3, 4.3)</td>
</tr>
<tr>
<td>&gt;15</td>
<td>85,208</td>
<td>3,976</td>
<td>1.6 (–0.8, 3.9)</td>
</tr>
<tr>
<td>Parity†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>92,840</td>
<td>4,259</td>
<td>1.0 (–1.2, 3.2)</td>
</tr>
<tr>
<td>1–2</td>
<td>140,702</td>
<td>5,944</td>
<td>1.7 (–0.2, 3.6)</td>
</tr>
<tr>
<td>3–4</td>
<td>105,972</td>
<td>4,796</td>
<td>2.0 (–0.2, 4.2)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>57,453</td>
<td>3,032</td>
<td>2.4 (–0.4, 5.1)</td>
</tr>
<tr>
<td>Age (years) at first delivery‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women with information</td>
<td>283,237</td>
<td>12,705</td>
<td>1.5 (0.2, 2.9)</td>
</tr>
<tr>
<td>&lt;23</td>
<td>63,431</td>
<td>3,067</td>
<td>2.3 (–0.3, 4.9)</td>
</tr>
<tr>
<td>23–28</td>
<td>125,386</td>
<td>5,662</td>
<td>0.9 (–1.2, 2.8)</td>
</tr>
<tr>
<td>&gt;28</td>
<td>94,421</td>
<td>3,976</td>
<td>1.5 (–1.1, 4.1)</td>
</tr>
<tr>
<td>Age (years) at last delivery§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women with information</td>
<td>227,072</td>
<td>10,328</td>
<td>1.3 (–0.2, 2.8)</td>
</tr>
<tr>
<td>&lt;31</td>
<td>54,296</td>
<td>2,472</td>
<td>1.5 (–1.4, 4.2)</td>
</tr>
<tr>
<td>31–36</td>
<td>76,862</td>
<td>3,541</td>
<td>1.1 (–1.4, 3.6)</td>
</tr>
<tr>
<td>&gt;36</td>
<td>95,913</td>
<td>4,315</td>
<td>0.8 (–1.9, 3.4)</td>
</tr>
</tbody>
</table>

* The mean reduction in mortality (in %) associated with a 3-year increase in age at menopause (95% confidence interval). Age at menopause was included in the model as a continuous (1-year interval) variable. Results are based on the Cox proportional hazards model and are adjusted for attained age, county, occupational group, and birth cohort.
† Because of missing values, the number of women included in the analysis is somewhat lower than in the total analysis.
‡ In women with at least one delivery and information about age at first delivery.
§ In women with at least two deliveries and information about age at last delivery.
who had not given birth to a child, but no linear trend over
categories defined by parity could be established (p = 0.44).

To control for the influence of reproductive variables, we
also performed a separate analysis with additional adjust-
ment for age at menarche, parity, and age at first delivery.
This analysis was restricted to 13,260 women with one or
more children and data about age at menarche and first
delivery. A total of 12,397 deaths were recorded during
276,673 person-years. The association between age at meno-
pause and total mortality was virtually unaffected by these
adjustments. Further adjustment for age at last delivery did
not influence the association.

In women with information about body mass index, we
found a 1.0 percent (95 percent confidence interval: –0.3,
2.4) reduction in mortality with an increase in age at natural
menopause of 3 years. Adjustment for body mass index (in
addition to the standard adjustments) did not influence the
association between age at menopause and total mortality
(estimated reduction, 1.0 percent (95 percent confidence
interval: –0.4, 2.3)).

**DISCUSSION**

We have previously presented the relations between age at
natural menopause and mortality from coronary heart
disease on the basis of the 1961–1989 follow-up of the same
cohort (1). In the present report, however, we extended our
follow-up to 1997 and focused on total mortality, as it has
been suggested that a young age at natural menopause is a
general indicator of premature aging (3). Our results support
this hypothesis but also indicate that the menopausal effect is
relatively moderate in strength.

The number of deaths in our study is considerably larger
than in earlier studies, 10 times that of the previously largest
one, the last follow-up of Californian Seventh-day Adventists (2).
The direction of the relation found by us is consist-
tent with results in previous studies (2, 7, 8, 10), but the
mortality rate ratio for women with late menopause (≥55
years) compared with women with premature menopause
(<40 years) may be weaker than estimates found previously
(2, 7, 10). One reason for this could be the very long follow-
up (1961–1997) with the large majority of the deaths occur-
ing in old age, when relations between age at menopause
and total mortality may be attenuated. Other explanations of
the weaker relation in our study should, however, also be
considered. For example, the distribution of causes of death
may differ between populations.

Our results are not conclusive with regard to whether the
effect of age at natural menopause is attenuated with
increasing age (1). Previous studies have suggested a
stronger inverse relation in women who were relatively
young at baseline, that is, in the first decades after meno-
pause (3, 7). If an attenuation of the relation does in fact take
place, this may simply reflect the longer time since a
premenopausal state characterized by, inter alia, high levels
of endogenous estrogen. With increasing age-related
mortality, the relative importance of each risk factor may
also be reduced. Although the difference in total mortality
with increasing age at natural menopause is moderate, a
reduction of 2.5 percent in the total mortality associated with
3 years’ increase in age at menopause in women aged less
than 80 years cannot be considered negligible on a popula-
tion level. The magnitude is comparable with the hypothe-
sical effects of eradication of cancer of the ovaries as a cause
of death, for example (accounting for 1.8 percent of the
deaths before the age of 80 years in this cohort). For the indi-
vidual woman, however, the reduction of the absolute mortality rate (six per 10,000 person-years) is probably of
marginal importance.

Our analyses did not include women who were premeno-
pausal at the time of screening. As women with an early
menopause therefore were overrepresented in the young
birth cohorts and as the total mortality rate was inversely
related to birth cohort, we adjusted for birth cohort in all
analyses, and we also carried out separate analyses restricted
to women born before 1894 and during 1895–1904 to verify
the overall results (table 3).

The prospective design of our study makes biased
reporting of age at menopause unlikely. However, there will
be some misclassification of age at menopause when it is
self-reported, and the misclassification may increase with
the time since menopause (14–16). In our study, the women
had been postmenopausal on an average of approximately 10
years when they reported age at menopause. The misclassifi-
cation of age at menopause must, however, be expected to be
mostly unrelated to the age-adjusted mortality. In view of
this misclassification, the inverse relation between age at
natural menopause and total mortality may be stronger than
we are able to demonstrate.

Many determinants have been suggested for age at meno-
pause, including for example genetic factors (17, 18), child-
hood cognitive function (19), and even a hypothetical male
(pheromonal) influence (20). Demographic variables (e.g.,
ever been married and low social class), reproductive
factors (e.g., late menarche, nulliparity, never used oral
contraceptives), and behavioral variables (e.g., smoking and
body mass index (both high and low)) have also been associ-
ated with early natural menopause (21, 22).

The inverse relation was a consistent finding in most of the
subgroups of our material, thus suggesting that confounding
by factors potentially affecting age at menopause was not a
significant problem. This conclusion is also supported by
results from our analyses with adjustment for body mass
index and by analyses with adjustment for parity and age at
menarche and at first delivery (as well as last delivery).

Smoking is the behavioral factor that has most consistently
been found to be related to early menopause, as it lowers the
age at menopause by 1–2 years (21, 23, 24) and increases
death rates of several major causes such as coronary heart
disease and cancer. Considering the relatively weak relation
between age at menopause and total mortality and the impact
of smoking on total mortality also in Norway (25), smoking
may be suggested as a likely confounder.

Unfortunately, no information was available about smoking
habits of the individual women in our study. However, a large majority of the women in the birth cohorts
considered were nonsmokers, and the mean number of cig-
arettes per day in women who smoked was much lower than
in men (26, 27). From the national data presented by
Rønneberg et al. (26), we have estimated the smoking prev-
Menopause in Norwegian women aged 45–49 years in the birth cohorts included. The age interval, 45–49 years, was selected as the relevant age group because current, but not former, smoking is associated with earlier age at menopause (21, 22). The mean smoking prevalence was estimated at not more than 15 percent (26). Smoking prevalence among women in our cohort, living predominantly in rural parts of the country, was lower than in Norway in general (26, 27).

If our results were explained by smoking, we would expect a very weak or no relation in women born before 1895 because, in this group of women, the smoking prevalence when they were aged 45–49 years was hardly higher than 5 percent and probably lower (26). As shown in table 3, the mean reduction in mortality associated with 3 years’ change in age at menopause was 1.6 percent (95 percent confidence interval: −0.3, 3.5 percent); that is, the point estimate was the same as in the complete data set. Moreover, by adjusting for birth cohort and occupational group (and in some analyses for parity and age at first and last delivery), we have to some extent also adjusted for smoking, because birth cohort is particularly correlated with smoking prevalence. However, we recognize that there may be residual confounding by smoking in our analysis and that our overall risk estimates may therefore still be biased.

Hormone replacement therapy could have introduced both misclassification with regard to age at menopause and possible confounding, if there were any associations between age at natural menopause and use of hormone replacement therapy and if such therapy influenced total mortality. However, hormone replacement therapy was very uncommon for women in this cohort. We have excluded all women who reported surgery, such as uni- or bilateral oophorectomy, that may have been followed by prescription of estrogens. Hormone therapy for perimenopausal complaints (e.g., heat flashes) was very seldom used in Norway in the late 1950s and was uncommon during follow-up (1, 28). Ninety-nine percent of the women included in our analysis were born before 1912; that is, they were 50 years or older when estrogen medication for use in peri- and postmenopausal years was introduced in Norway. Thus, because of the birth year of the women, the prevalence of hormone replacement therapy in the women included in the analyses is without doubt very low, if not nearly zero. For similar reasons, the use of oral contraceptives does not represent a relevant confounder in our analysis.

A low age at natural menopause may in some women reflect clinical or subclinical medical conditions that may influence the mortality of the women. For example, a recent study demonstrated reduced age at natural menopause in women with diabetes mellitus type I (29). We have not made any effort to exclude these women from the analysis as we have studied the net effect of age at natural menopause on all-cause mortality. The hypothesis tested is that an early menopause is related to increased mortality, but it is clear that this hypothesis must be a crude simplification because it is well known that a low age at menopause reduces the risk of the most frequent cancer among Norwegian women, breast cancer (5, 6). The opposite is true for the risk of osteoporosis (30) (reflected in hip fracture mortality in our population (31)) and probably for coronary heart disease mortality (1, 2, 4). However, as coronary heart disease mortality rates are much higher than the mortality caused by breast cancer (32), the net result is an inverse relation. In order to get a more comprehensive picture of why an early menopause increases the mortality of some major causes of death and reduces the mortality of others, it may be necessary to study the determinants of age at natural menopause in more detail and to explore relations between age at menopause and cause-specific mortality. Nevertheless, establishing the relation between age at natural menopause and total mortality is a natural starting point for such an endeavor.

In summary, our very long follow-up study of 19,731 women with a natural menopause demonstrates an inverse relation of moderate strength between age at natural menopause and total mortality, and it suggests that this relation is stronger the younger the women are. The association was found consistently in stratified analysis and could not be explained by available information about possible confounders. Thus, women who experience an early natural menopause are subject to a slightly increased mortality.

REFERENCES