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Vaginal Estrogen Therapy Use and Survival in Females With Breast Cancer

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IMPORTANCE Genitourinary syndrome of menopause can be treated with vaginal estrogen therapy. However, there are concerns about the safety of vaginal estrogen therapy in patients with breast cancer.

OBJECTIVE To determine whether the risk of breast cancer–specific mortality was higher in females with breast cancer who used vaginal estrogen therapy vs females with breast cancer who did not use hormone replacement therapy (HRT).

DESIGN, SETTING, AND PARTICIPANTS This cohort study analyzed 2 large cohorts, one each in Scotland and Wales, of females aged 40 to 79 years with newly diagnosed breast cancer. These population-based cohorts were identified from national cancer registry records from 2010 to 2017 in Scotland and from 2000 to 2016 in Wales and were followed up for breast cancer–specific mortality until 2020. Females were excluded if they had a previous cancer diagnosis (except nonmelanoma skin cancer). Data analysis was performed between August 2022 and August 2023.

EXPOSURE Use of vaginal estrogen therapy, including vaginal tablets and creams, was ascertained from pharmacy dispensing records of the Prescribing Information System for the Scotland cohort and from general practice prescription records for the Wales cohort.

MAIN OUTCOMES AND MEASURES The primary outcome was time to breast cancer–specific mortality, which was obtained from national mortality records. Time-dependent Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs for breast cancer–specific mortality, comparing vaginal estrogen therapy users with HRT nonusers and adjusting for confounders, including cancer stage and grade.

RESULTS The 2 cohorts comprised 49 237 females with breast cancer (between 40 and 79 years of age) and 5795 breast cancer–specific deaths. Five percent of patients with breast cancer used vaginal estrogen therapy after breast cancer diagnosis. In vaginal estrogen therapy users compared with HRT nonusers, there was no evidence of a higher risk of breast cancer–specific mortality in the pooled fully adjusted model (HR, 0.77; 95% CI, 0.63-0.94).

CONCLUSIONS AND RELEVANCE Results of this study showed no evidence of increased early breast cancer–specific mortality in patients who used vaginal estrogen therapy compared with patients who did not use HRT. This finding may provide some reassurance to prescribing clinicians and support the guidelines suggesting that vaginal estrogen therapy can be considered in patients with breast cancer and genitourinary symptoms.

Supplemental content

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Many females with breast cancer experience symptoms of genitourinary syndrome of menopause,[1] such as vaginal itchiness, burning, pain with sexual activity, and urinary incontinence. These symptoms may be precipitated by endocrine treatments and contribute to noncompliance with endocrine therapy.[2] Vaginal estrogen therapy is an effective treatment for genitourinary syndrome of menopause.[3] Trials have shown increased recurrence in patients with breast cancer who received systemic hormone replacement therapy (HRT).[4] A recent trial observed a small increase in serum estradiol with use of a vaginal estradiol tablet (10 µg).[5]

There have been no large randomized clinical trials of vaginal estrogen therapy in patients with breast cancer that are powered to investigate recurrence or mortality,[6] and observational studies have been limited by small sample size[7,8] and unavailable confounders.[9] A recent observational Danish study showed no increase in recurrence in patients with breast cancer who received vaginal estrogen therapy aside from a subgroup who received both vaginal estrogen therapy and aromatase inhibitors.[10] Consequently, in this study, we investigated vaginal estrogen therapy and breast cancer-specific mortality in 2 large cohorts. We aimed to determine whether the risk of breast cancer-specific mortality was higher in females with breast cancer who used vaginal estrogen therapy vs females with breast cancer who did not use HRT.

Key Points

Question Do females with breast cancer who use vaginal estrogen therapy, such as tablets or creams, have a higher risk of breast cancer–specific mortality?

Findings In this cohort study of 49 237 females with breast cancer, there was no evidence of an increase in early breast cancer–specific mortality with use of vaginal estrogen therapy compared with no hormone replacement therapy use after breast cancer diagnosis.

Meaning Findings of this study may provide some reassurance to clinicians and support the guidelines suggesting that vaginal estrogen therapy can be considered in patients with breast cancer and genitourinary symptoms if nonhormonal treatments were unsuccessful.

Methods

We obtained data from the Prescribing Information System for the cohort in Scotland[11] and from the SAIL Databank for the cohort in Wales.[12] The SAIL Databank Information Governance Review Panel and the Privacy Advisory Committee of the National Health Service National Services Scotland approved this cohort study. Informed consent was not required as the data were deidentified prior to analysis. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Population-based cohorts of females aged 40 to 79 years with newly diagnosed breast cancer (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision [ICD-10]* code C50) were identified from cancer registries in Scotland from 2010 to 2017 and in Wales from 2000 to 2016. Patients who were previously diagnosed with other invasive cancers (except nonmelanoma skin cancer) were excluded.

Exposure, Outcome, and Covariates

Medication use was ascertained from general practitioner (GP) prescribing records for patients in Wales or from pharmacy dispensing records for patients in Scotland. Vaginal estrogen therapy (mainly estriol creams and estradiol tablets) and systemic HRT (including estrogen- or tibolone-containing products) were identified using the British National Formulary classification.[13] The primary outcome of time to breast cancer-specific mortality was identified from national mortality records (an underlying cause of death for *ICD-10* code C50) until June 2019 in Scotland and until June 2020 in Wales.

Cancer registry records provided stage, grade, treatment (radiotherapy, chemotherapy, or surgery), and, in Scotland, hormone receptor status. Tamoxifen, aromatase inhibitor, and other medication used were identified from prescribing or dispensing records. Charlson Comorbidity Index, anemia, and hysterectomy or oophorectomy were determined from GP diagnoses and hospital admissions in Wales and from hospital admissions alone in Scotland. Deprivation (defined as poverty level in an area) was based on the Index of Multiple Deprivation and the areas were categorized into fifths, with the highest fifth indicating the least deprived area. The GP records provided smoking status and body mass index data in Wales only.

Statistical Analysis

In the primary analysis (eFigure in Supplement 1), patients were followed up from 6 months after cancer diagnosis to breast cancer-specific mortality and censored, according to whichever occurred first, on death from other causes, end of mortality follow-up, or end of GP records in Wales and date of emigration in Scotland. The exposure was modeled as a single time-varying variable, with a lag of 6 months, into the following hierarchical categories: systemic HRT (with or without vaginal estrogen therapy), vaginal estrogen therapy alone, and no HRT. Analyses were conducted by number of prescriptions and separately for higher-dose vaginal estrogen therapy (consisting of 25-µg estradiol tablets).

Time-dependent Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs by exposure, adjusting for age, year, deprivation level, cancer treatment (surgery, chemotherapy, and radiotherapy), tamoxifen or aromatase inhibitor use (as time-varying covariates with 6-month lags), Charlson Comorbidity Index (before diagnosis), anemia (before diagnosis), other medication use (including statins, aspirin, metformin, and oral contraceptives before diagnosis), hysterectomy or oophorectomy (anytime up to 6 months after diagnosis), and cancer stage and grade. Where missing, cancer stage

Table 1. Patient Characteristics by Hormone Replacement Therapy (HRT) Use After Diagnosis

Characteristic	Patients in Scotland, No. (%)			Patients in Wales, No. (%)		
	No HRT	Systemic HRT	Only vaginal estrogen therapy	No HRT	Systemic HRT	Only vaginal estrogen therapy
Age, y						
40-49	4207 (17)	32 (15)	184 (14)	3491 (17)	49 (14)	184 (15)
50-59	7444 (29)	86 (39)	455 (34)	6143 (30)	153 (45)	411 (34)
60-69	8231 (32)	71 (33)	436 (32)	6685 (32)	104 (31)	394 (33)
70-79	5506 (22)	29 (13)	281 (21)	4423 (21)	32 (9)	206 (17)
Year of diagnosis						
2000-2004	0	0	0	4795 (23)	139 (41)	443 (37)
2005-2009	0	0	0	6030 (29)	94 (28)	422 (35)
2010-2014	15 674 (62)	155 (71)	1045 (77)	6967 (34)	86 (25)	270 (23)
2015-2017	9714 (38)	63 (29)	311 (23)	2950 (14)	19 (6)	60 (5)
Deprivation level						
First fifth: most deprived area	5580 (22)	44 (20)	342 (25)	3387 (16)	70 (21)	158 (13)
Fifth fifth: least deprived area	4240 (17)	38 (17)	202 (15)	4634 (22)	73 (22)	313 (26)
Hysterectomy or oophorectomy[a]						
Before or at cancer diagnosis	1034 (4)	23-28 (11)[b]	50-55 (4)[b]	1476 (7)	41 (12)	87 (7)
After cancer diagnosis	740 (3)	<5[b]	53 (4)	1092 (5)	33 (10)	110 (9)
Select comorbidity, any time before diagnosis						
COPD	1413 (6)	24 (11)	90 (7)	781 (4)	23 (7)	33 (3)
Diabetes	1760 (7)	12 (6)	101 (7)	1653 (8)	21 (6)	77 (6)
CKD	250 (1)	<5[b]	16 (1)	1093 (5)	8 (2)	48 (4)
Anemia	480 (2)	<5[b]	33 (2)	1135 (5)	18 (5)	55 (5)
Medication use, any time before diagnosis						
Statin	6254 (25)	59 (27)	361 (27)	4920 (24)	69 (20)	263 (22)
Aspirin	3742 (15)	35 (16)	213 (16)	3360 (16)	53 (16)	174 (15)
Metformin	1302 (5)	8 (4)	73 (5)	1054 (5)	18 (5)	54 (5)
Oral contraceptive	1666 (7)	13 (6)	83 (6)	1841 (9)	23 (7)	90 (8)
Hormone receptor status						
ER-positive	21287 (84)	171 (78)	1136 (84)	NA	NA	NA
PR-positive	14340 (57)	136 (62)	706 (52)	NA	NA	NA
ERBB2-positive	3581 (14)	25 (12)	198 (15)	NA	NA	NA
Cancer stage						
1	11 150 (44)	119 (55)	710 (52)	8475 (41)	179 (53)	554 (46)
2	9513 (38)	70 (32)	490 (36)	6812 (33)	80 (24)	331 (28)
3	1903 (8)	9 (4)	65 (5)	1698 (8)	8-18[b]	45-55[b]
4	1183 (5)	7 (3)	21 (2)	378 (2)	<10[b]	<10[b]
Missing data	1639 (7)	13 (6)	70 (5)	3379 (16)	61 (18)	255 (21)
Cancer grade						
1	3204 (13)	39 (18)	214 (16)	3120 (15)	66 (20)	224 (19)
2	11 899 (47)	105 (48)	680 (50)	9390 (45)	155 (46)	535 (45)
3	8827 (35)	59 (27)	406 (30)	5205 (25)	60 (18)	266 (22)
Missing data	1458 (6)	15 (7)	56 (4)	3027 (15)	57 (17)	170 (14)
Cancer treatment						
Surgery	21 257 (84)	196 (90)	1234 (91)	18 699 (90)	304 (90)	1110 (93)
Chemotherapy	9393 (37)	67 (31)	465 (34)	1500 (7)	26 (8)	85 (7)
Radiotherapy	10 726 (42)	95 (44)	650 (48)	6030 (29)	63 (19)	315 (26)
Hormonal treatment use, any time after diagnosis						
Tamoxifen	13 864 (55)	109 (50)	725 (54)	12 721 (61)	196 (58)	690 (58)
Aromatase inhibitor	12 191 (48)	115 (53)	769 (57)	8722 (42)	164 (49)	648 (54)

Abbreviations: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ER, estrogen receptor; *ERBB2*, erb-b2 receptor tyrosine kinase 2 (formerly *HER2*); NA, not available; PR, progesterone receptor.

[a] Hysterectomy or oophorectomy in the following periods: before cancer or at cancer diagnosis (anytime up to 6 months after cancer diagnosis) and after cancer diagnosis (>6 months after cancer diagnosis).

[b] Range is shown to maintain statistical disclosure control.

Table 2. Vaginal Estrogen Therapy Use After Diagnosis and Breast Cancer–Specific Mortality

Analysis	No. of events	Person-years	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)[a]	*P* value	Fully adjusted HR (95% CI)[b]	*P* value
Pooled								
No HRT	5624	285 342	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Systemic HRT	51	3894	0.75 (0.57-0.98)	.04	0.90 (0.63-1.28)	.56	0.98 (0.68-1.40)	.90
Only vaginal estrogen therapy	120	11437	0.66 (0.55-0.80)	<.001	0.72 (0.60-0.86)	<.001	0.77 (0.63-0.94)	.01
1-4 Vaginal estrogen therapy prescriptions	105	9374	0.70 (0.58-0.85)	<.001	0.75 (0.62-0.92)	.005	0.81 (0.67-0.99)	.04
≥5 Vaginal estrogen therapy prescriptions	15	2062	0.49 (0.30-0.82)	.007	0.55 (0.32-0.97)	.04	0.57 (0.34-0.96)	.03
Lower-dose vaginal estrogen therapy	92-97[c]	9098	0.65 (0.53-0.80)	<.001	0.71 (0.55-0.93)	.01	0.77 (0.56-1.07)	.12
Higher-dose vaginal estrogen therapy[d]	23-28[c]	2339	0.69 (0.39-1.21)	.20	0.78 (0.53-1.15)	.22	0.81 (0.55-1.21)	.31
Scotland								
No HRT	2293	115 520	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Systemic HRT	15	859	0.91 (0.55-1.51)	.72	1.14 (0.69-1.90)	.61	1.26 (0.73-2.16)	.41
Only vaginal estrogen therapy	45	3979	0.65 (0.48-0.88)	<.001	0.78 (0.58-1.05)	.10	0.88 (0.65-1.19)	.40
Wales								
No HRT	3331	169 822	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Systemic HRT	36	3035	0.69 (0.49-0.95)	.03	0.78 (0.56-1.09)	.15	0.86 (0.61-1.21)	.38
Only vaginal estrogen therapy	75	7458	0.67 (0.53-0.85)	.001	0.68 (0.54-0.86)	.001	0.71 (0.56-0.90)	.005

Abbreviations: HR, hazard ratio; HRT, hormone replacement therapy; NA, not applicable.

[a] Model was adjusted for age, year, deprivation level, cancer treatment (surgery, radiotherapy, and chemotherapy), tamoxifen use (as time-varying covariate), aromatase inhibitor use (as time-varying covariate), Charlson Comorbidity Index (before diagnosis), anemia (before diagnosis), medication use (before diagnosis: statin, aspirin, metformin, and oral contraceptives), and hysterectomy or oophorectomy (before or at diagnosis).

[b] Model included variables in adjusted model as well as imputed cancer stage and grade using multiple imputation.

[c] Range is shown to maintain statistical disclosure control.

[d] Higher-dose vaginal estrogen therapy consisted of 25-µg estradiol tablets, and lower dose consisted of all other vaginal estrogen therapy.

and grade were imputed using multiple imputation with chained equations. Estimates were calculated within each cohort and pooled using random-effects meta-analysis models. The eMethods in Supplement 1 provide further details.

Two-sided $P < .05$ indicated statistical significance. Data analysis was performed between August 2022 and August 2023, using Stata, version 16/17 (StataCorp LLC).

Results

The 2 cohorts comprised 49 237 females with breast cancer (between 40 and 79 years of age) and 5795 breast cancer-specific deaths, with a median (IQR) duration of follow-up of 8 (5-12) years in the Wales cohort and 5 (3-7) years in the Scotland cohort. Overall, 5% of females (2551) used vaginal estrogen therapy after diagnosis and 1% (556) received systemic HRT.

Patient characteristics are shown in **Table 1** and the eTable and eResults in Supplement 1. **Table 2** shows there was no evidence of higher breast cancer-specific mortality in those who used vaginal estrogen therapy compared with those who used no HRT. A small decrease in mortality was found with vaginal estrogen therapy in the pooled fully adjusted model (HR, 0.77; 95% CI, 0.63-0.94). This estimate was similar in patients with 5 or more prescriptions (HR, 0.57; 95% CI, 0.34-0.96) and with higher-dose therapy (HR, 0.81; 95% CI, 0.55-1.21). **Table 3** shows that the associations were similar in most sensitivity analyses. In particular, no increased risks were observed after restricting the model to females with estrogen receptor-positive breast cancer (HR, 0.88; 95% CI, 0.62-1.25) or females using aromatase inhibitors (HR, 0.72; 95% CI, 0.58-0.91). The eResults in Supplement 1 provide additional description of findings.

Discussion

In these large, contemporary population-based breast cancer cohorts, there was no evidence that vaginal estrogen therapy was associated with increased risk of early breast cancer-specific mortality. The null finding is similar to results of a Danish study involving 8461 patients with breast cancer that observed no association between vaginal estrogen therapy and cancer recurrence (adjusted HR, 1.08; 95% CI, 0.89-1.32).[10] However, the Danish study observed a 39% increase in recurrence in users of both vaginal estrogen therapy and aromatase inhibitors.[10] We did not study recurrence, but we observed no evidence of an increase in breast cancer-specific mortality in this subgroup. Additionally, a case-control study showed no association between vaginal estrogen therapy and breast cancer recurrence (identified from GP records) among tamoxifen users but did not adjust for cancer stage.[9] Two small cohort studies found no increase in cancer recurrence in patients with breast cancer

Table 3. Sensitivity Analyses for the Association Between Vaginal Estrogen Therapy Use and No Hormone Replacement Therapy (HRT) After Cancer Diagnosis

Analysis	No HRT events (person-years), No.	Vaginal estrogen therapy events (person-years), No.	HR (95% CI)		
			Unadjusted	Adjusted[a]	Fully adjusted[b]
Main analysis	5624 (285 342)	120 (11 437)	0.66 (0.55-0.80)	0.72 (0.60-0.86)	0.77 (0.63-0.94)
With 1-y lag	5132 (262 441)	104 (10 202)	0.67 (0.55-0.81)	0.72 (0.59-0.87)	0.77 (0.63-0.94)
With 2-y lag	3932 (21 8204)	76 (8046)	0.63 (0.42-0.95)	0.72 (0.57-0.90)	0.75 (0.60-0.95)
Restricted to age 55-79 y at diagnosis	3880 (187 722)	86 (7745)	0.67 (0.54-0.83)	0.76 (0.61-0.95)	0.82 (0.63-1.07)
Including age 18-79 y at diagnosis	6062 (299 018)	121 (11 725)	0.64 (0.53-0.77)	0.69 (0.57-0.82)	0.74 (0.61-0.90)
Restricted to cancer stage I-III	3551 (243 892)	90 (9329)	0.73 (0.59-0.90)	0.75 (0.60-0.92)	0.80 (0.65-0.99)
New HRT[c]	5046 (233 546)	68 (6572)	0.66 (0.52-0.84)	0.70 (0.55-0.90)	0.76 (0.59-0.97)
Adjusting for prior HRT	5624 (285 342)	120 (11 437)	0.66 (0.55-0.80)	0.77 (0.64-0.92)	0.81 (0.67-0.98)
ER-positive breast cancer[d]	1516 (98 591)	35 (33,66)	0.69 (0.49-0.97)	0.83 (0.59-1.16)	0.88 (0.62-1.25)
ER-negative breast cancer[d]	732 (15 438)	10 (579)	0.53 (0.28-0.98)	0.55 (0.29-1.03)	0.68 (0.36-1.28)
Stratifying entire cohort[e]					
No tamoxifen or aromatase inhibitor	1752 (60 805)	21 (2207)	0.51 (0.33-0.78)	0.56 (0.36-0.86)	0.67 (0.43-1.04)
Tamoxifen only	595 (88 062)	14 (3433)	0.86 (0.51-1.48)	0.89 (0.52-1.53)	1.01 (0.52-1.95)
Aromatase inhibitor, with or without tamoxifen	3277 (13 6474)	85 (5797)	0.68 (0.54-0.84)	0.70 (0.57-0.87)	0.72 (0.58-0.91)
Stratifying only vaginal estrogen therapy users[f]					
No tamoxifen or aromatase inhibitor	5624 (285 342)	21 (2207)	0.61 (0.37-1.01)	0.58 (0.36-0.94)	0.68 (0.35-1.33)
Tamoxifen only	5624 (285 342)	14 (3433)	0.26 (0.15-0.43)	0.33 (0.20-0.56)	0.41 (0.21-0.79)
Aromatase inhibitor, with or without tamoxifen	5624 (285 342)	85 (5797)	0.94 (0.76-1.17)	0.98 (0.79-1.22)	0.99 (0.79-1.24)
Adjusting for cancer stage and grade, complete case[g]	3788 (231 575)	88 (8886)	0.71 (0.54-0.93)	0.72 (0.54-0.94)	0.82 (0.66-1.01)
Additionally adjusting for smoking status and BMI, multiple imputation[g]	3331 (169 822)	75 (7458)	0.67 (0.53-0.85)	0.68 (0.54-0.86)	0.73 (0.57-0.92)
Breast cancer as any cause of death	6489 (285 342)	144 (11 437)	0.68 (0.58-0.80)	0.73 (0.62-0.86)	0.77 (0.65-0.92)
Cardiovascular death	919 (285 342)	42-47 (11 437)	0.80 (0.30-2.11)	0.77 (0.28-2.15)	0.78 (0.28-2.16)
All-cause mortality	9612 (285 342)	290 (11 437)	0.73 (0.58-0.91)	0.78 (0.69-0.88)	0.80 (0.71-0.90)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ER, estrogen receptor; HR, hazard ratio.

[a] Model was adjusted, except where otherwise stated, for age, year, deprivation level, cancer treatment (surgery, radiotherapy, and chemotherapy), tamoxifen use (as time-varying covariate), aromatase inhibitor use (as time-varying covariate), Charlson Comorbidity Index (before diagnosis), anemia (before diagnosis), medication use (before diagnosis: statin, aspirin, metformin, and oral contraceptives), and hysterectomy or oophorectomy (anytime before or up to 6 months after diagnosis).

[b] Fully adjusted model consisted of, except where otherwise stated, variables in the adjusted model as well as imputed cancer stage and grade using multiple imputation.

[c] Restricted to individuals who were not receiving HRT before breast cancer diagnosis.

[d] Scotland only.

[e] Stratifying entire cohort by endocrine therapy use (eg, vaginal estrogen therapy users who were not receiving tamoxifen or aromatase inhibitor were compared with HRT nonusers not receiving tamoxifen or aromatase inhibitors).

[f] Stratifying only vaginal estrogen therapy users by endocrine therapy use, and hence the comparison group comprised all HRT nonusers in each analysis (eg, vaginal estrogen therapy users who were not receiving tamoxifen or aromatase inhibitor vs all HRT nonusers).

[g] Wales only.

who received vaginal estrogen therapy,[7,8] but both studies included fewer than 10 recurrences in the exposed group. A recent Swedish case-control study showed no increase in breast cancer-specific mortality in patients with breast cancer who used estrogen but did not distinguish between vaginal or systemic estrogen.[14]

In the absence of trials of vaginal estrogen therapy in breast cancer, the findings of this study provide some reassurance that patients with breast cancer who received vaginal estrogen therapy were not at a markedly higher risk of breast cancer-specific mortality and appear to support national guidelines suggesting that vaginal estrogen therapy can be considered for genitourinary symptoms if nonhormonal treatments are unsuccessful.[3,15] The systemic HRT associations were examined for completeness but should not be a factor in clinical decisions given the wide CIs and previous trial observations of increased risks of recurrence with systemic HRT.[4]

Strengths and Limitations

Strengths of this study were the large population-based cohorts with up to 20 years of follow-up with linked prescribing or dispensing records, which eliminated recall bias and captured all HRT prescriptions. However, the study had limitations, including our inability to confirm medication adherence. The duration of follow-up did not allow the investigation of later breast cancer-specific mortality, and thus further research with extended follow-up is recommended. We adjusted

for many important confounders, including cancer stage and grade and, in a sensitivity analysis, body mass index and smoking status, but we could not rule out residual confounding from poorly recorded or unavailable variables, such as physical activity and menopausal status.[3] Estrogen receptor status of the tumor was not complete, but results were similar in endocrine therapy users, who have estrogen receptor–positive disease. Moreover, patients who received treatment for genitourinary syndrome of menopause may have lower estradiol levels and/or better compliance to endocrine therapies and thus have lower breast cancer–specific mortality.

Conclusions

In this large cohort study, there was no evidence of increased early breast cancer–specific mortality in females with breast cancer who received vaginal estrogen therapy compared with females with breast cancer who had no HRT. This finding may provide some reassurance to prescribing clinicians and support the guidelines suggesting that vaginal estrogen therapy can be considered in patients with breast cancer and genitourinary symptoms if nonhormonal treatments are unsuccessful.

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