

# Reduced risk of breast cancer-related mortality associated with use of estrogen-progestin therapy in older women

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## BACKGROUND

- **Estrogen-progestin therapy (EPT)** is associated with a reduced risk of **breast cancer-related mortality (BCM)**
- EPT use has been associated with many factors related to favorable prognosis in observational studies
- However, the WHI trial reported EPT use to be associated with an increased risk of advanced stage and larger tumor size
- In this study, we examined
  - the risk of death associated with pre-diagnostic use of EPT
  - the extent to which this reflects differences in mammography screening or tumor biology
  - the presence of effect modification

## METHODS

Cohort of 1,911 post-menopausal women diagnosed with invasive breast cancer at ages 45-79 from 1993-1999

- Derived from three previous population-based case-control studies of incident breast cancer in Western Washington state
- Participants completed detailed histories of their lifetime use of hormone therapy, including EPT use
- Were followed for a mean of 10.3 years
- Cox proportional hazards models

## RESULTS

- Use of EPT was associated with a reduction in BCM (Table 1)
  - Differences in BCM risk were statistically significant by age ( $p=0.04$ )
  - Risks did not differ substantially by duration or recency
- Mammography screening was strongly associated with EPT use (Figure 1)
  - Overall, the percentage of women who underwent mammographic screening differed between EPT users (94.7%) and never users (69.8%;  $p<0.001$ )
  - The mean time between diagnosis and a woman's last mammogram was:
    - 21.3 months for non-users
    - 5.3 months for former EPT users
    - 2.6 months for current EPT users

Figure 1. Mammographic screening and EPT Use

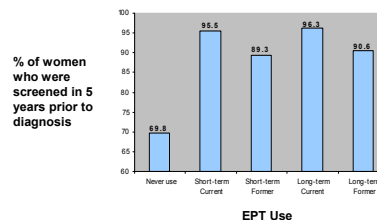


Table 1. Risk of dying from breast cancer in relation to EPT use, stratified by age

EPT use	All women		< 65 years				≥ 65 years				p-value				
	HR	95% CI	Alive/cens. (n=602)		BC death (n=124)		Alive/cens. (n=1026)		BC death (n=159)						
			n	%	n	%	n	%	n	%		HR	95% CI		
Never use	1.00	(ref)	121	(79.6)	31	(20.4)	1.00	(ref)	317	(83.9)	61	(16.1)	1.00	(ref)	0.04
Ever use	0.72	(0.50-1.03)	269	(84.1)	51	(15.9)	1.03	(0.60-1.79)	245	(91.4)	23	(8.6)	0.45	(0.26-0.80)	
Short term use	0.65	(0.40-1.05)	124	(85.5)	21	(14.5)	0.90	(0.47-1.72)	70	(89.7)	8	(10.3)	0.42	(0.18-0.97)	
Current	0.62	(0.34-1.13)	87	(87.0)	13	(13.0)	0.80	(0.38-1.70)	32	(88.9)	4	(11.1)	0.44	(0.13-1.47)	
Former	0.69	(0.37-1.29)	37	(82.2)	8	(17.8)	1.10	(0.48-2.54)	38	(90.5)	4	(9.5)	0.42	(0.15-1.19)	
Long-term use	0.76	(0.51-1.14)	145	(82.9)	30	(17.1)	1.15	(0.63-2.12)	175	(92.1)	15	(7.9)	0.47	(0.25-0.90)	
Current	0.72	(0.47-1.10)	137	(84.0)	26	(16.0)	1.09	(0.58-2.05)	156	(92.9)	12	(7.1)	0.44	(0.22-0.88)	
Former	0.95	(0.40-2.22)	8	(72.7)	3	(27.3)	1.25	(0.36-4.33)	19	(86.4)	3	(13.6)	0.67	(0.20-2.27)	

All models control for age, study, stage, treatment, and mammography history; p-value testing the difference of ever to never users in < 65 year olds vs. ≥ 65 year olds

- EPT use was associated with tumor characteristics
  - Among all women, EPT use was inversely associated with poorly differentiated tumors
  - Among older women, EPT use was associated with grade and histology (Table 2), but not ER, PR status, tumor stage or size

Table 2. Relationship between EPT use and tumor characteristics among older women

EPT	Tumor Characteristics					
	n	%	n	%	OR	95% CI
EPT	<i>Ductal</i> (n=800)		<i>Lob/Mix</i> (n=232)		1.00	(ref)
	Never	266	(60.5)	59		
Ever	174	(39.5)	62	(51.2)	1.68	(1.07-2.65)
EPT	<i>Well/Mod</i> (n=703)		<i>Poor/Undiff</i> (n=373)		1.00	(ref)
	Never	219	(54.2)	132		
Ever	185	(45.8)	64	(32.7)	0.57	(0.38-0.85)

All models control for age, study, and mammography history

## DISCUSSION

- This study adds to the growing literature indicating that pre-diagnostic EPT use is associated with a decreased risk of BCM, at least among older women
- The associations with tumor characteristics persisted beyond adjustment for screening
  - indicating that biologic mechanisms may underlie the relationship between EPT use and reduced risk of death

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