

**Appendix 1. Association of Log Serum Estradiol Levels While Taking Hormone Therapy With Demographic and Clinical Characteristics**

<b>Variable</b>	<b>Beta</b>	<b>Standard error</b>
Age* (years)	-0.0022	0.0041
Race/Ethnicity		
White, non-Hispanic	Reference	
African American, non-Hispanic	-0.0195	0.1049
Hispanic	0.0163	0.0895
Asian, non-Hispanic	0.0047	0.1022
Body mass index* (kg/m <sup>2</sup> )	0.0138	0.0044
Weight* (kg)	0.0020	0.0007
Time since menopause (years)	-0.0023	0.0038
Time since menopause* (years)	-0.0024	0.0038
Time since menopause		
Early postmenopause	Reference	
Late postmenopause	-0.0393	0.0549
Menopause type		
Natural	Reference	
Surgical	0.1808	0.0874
Menopause type		
Natural, early	Reference	
Natural, late	-0.0557	0.0576
Surgical, early	0.2783	0.1893
Surgical, late	0.1225	0.1005
Creatinine* (mg/dL)	0.1088	0.1470
Creatinine clearance* (ml/min)	0.0011	0.0009
Aspartate aminotransferase* (U/L)	-0.0004	0.0029
Alanine aminotransferase* (U/L)	-0.0011	0.0024
Fasting blood glucose* (mg/dl)	0.0020	0.0023

Sriprasert I, Kono N, Karim R, Hodis HN, Stanczyk FZ, Shoupe D, et al. Factors associated with serum estradiol levels among postmenopausal women using hormone therapy. *Obstet Gynecol* 2020;136.

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Smoking status*		
Never	Reference	
Past smoker	-0.1584	0.0561
Current smoker	-0.4013	0.0988
Alcohol use*		
None	Reference	
<1 drink per day	0.0353	0.0353
1-2 drinks per day	0.0899	0.0563
>2 drinks per day	0.5176	0.1153
Total weekly MET hours*	-0.0003	0.0005
Moderate + vigorous activity weekly hours*, tertiles		
0 - 2.60	Reference	
2.62 - 6.75	-0.0383	0.2682
6.80+	-0.0297	0.0306
Medications and supplements		
Lipid lowering medication*		
No	Reference	
Yes	0.0165	0.0455
Statin use*		
No	Reference	
Yes	0.0229	0.0474
Antihypertensive medication*		
No	Reference	
Yes	0.1093	0.0474
Calcium channel blocker*		
No	Reference	
Yes	0.0575	0.0922
Diabetes medication*		
No	Reference	
Yes	-0.0881	0.2145
Antifungal medication*		

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No	Reference	
Yes	-0.2170	0.0832
Anticonvulsant medication*		
No	Reference	
Yes	-0.1025	0.0821
Multivitamin use		
Never	Reference	
Took regularly in the past	-0.0260	0.0862
Take regularly now	-0.0558	0.0727
Vitamin E use		
Never	Reference	
Took regularly in the past	0.0985	0.0629
Take regularly now	0.0707	0.0761
Fish oil use		
Never	Reference	
Took regularly in the past	0.0907	0.0910
Take regularly now	0.0455	0.0621

Beta estimates and standard errors are from mixed effects linear model, adjusted for baseline serum estradiol level, follow-up visit and reduced estradiol dose indicator.

\*Time varying variable

**Appendix 2. Multivariable Association of Log-Transformed Estradiol Levels While Taking Hormone Therapy With Demographic and Clinical Characteristics Among Total Sample and by Postmenopausal**

**Strata**

Variable	Total analysis sample		Early postmenopause		Late postmenopause	
	Beta	Standard error	Beta	Standard error	Beta	Standard error
Body mass index (kg/m <sup>2</sup> )*	0.0149	0.0042	0.0108	0.0060	0.0179	0.0059
Smoking status*						
Never			Reference			
Past smoker	-0.1606	0.0547	0.2477	0.0826	-0.0768	0.0733
Current smoker	-0.3991	0.0973	0.4285	0.1241	-0.4191	0.1669
Alcohol use*						
None			Reference			
<1 drink per day	0.0406	0.0351	0.0162	0.0536	0.0541	0.0468
1-2 drinks per day	0.0952	0.0557	0.1124	0.0803	0.0640	0.0790
>2 drinks per day	0.5294	0.1143	0.8052	0.1623	0.2317	0.1614

Beta estimates and standard errors are from mixed effects linear model, adjusted for baseline serum estradiol level, follow-up visit and reduced estradiol dose indicator;

\*Time varying variable

### Appendix 3. Estimated Serum Estradiol Levels for Each Multivariable Model Determinant

Variable	Least square mean (pg/ml)	95% confidence interval (pg/ml)
Body mass index category	< 25 kg/m <sup>2</sup>	37.9
	25 to < 30 kg/m <sup>2</sup>	41.1
	≥ 30 kg/m <sup>2</sup>	43.2
Smoking status	Never	43.2
	Past smoker	36.9
	Current smoker	28.9
Alcohol use	None	39.0
	<1 drink per day	40.4
	1-2 drinks per day	42.7
	>2 drinks per day	65.5

Least square means are from mixed effects linear model, adjusted for baseline serum estradiol level, follow-up visit and reduced estradiol dose indicator