

# INTRODUCTION

- The incidence of esophageal cancer (EC) has • risen in recent decades and tends to be more common in men than women. Yet, the reasons behind this pattern remain unclear. It has been hypothesized that female sex hormones, mainly estrogen, are protective against EC.
- Previous studies have shown that the use of hormone replacement therapy (HRT) reduces the risk of colorectal cancer, but it is associated with an increased risk of gastroesophageal reflux disease, breast, endometrial and ovarian cancers.
- AIM: To investigate the association between HRT and the risk of esophageal adenocarcinoma (AC) and squamous cell carcinoma (SCC) in post-menopausal women.

## METHODS

- **Databases:** Embase, PubMed/MEDLINE, and Google Scholar
- Eligible studies: Retrospective cohort and case-control studies including post-menopausal women who either received HRT or not
- **Primary endpoint:** Association between HRT use and various types of EC
- **Software used:** Review Manager 5.4 software

### The Association Between Hormone Replacement Therapy and The Incidence of Esophageal Cancer in Post-Menopausal Women: A Systematic Review and Meta-Analysis.

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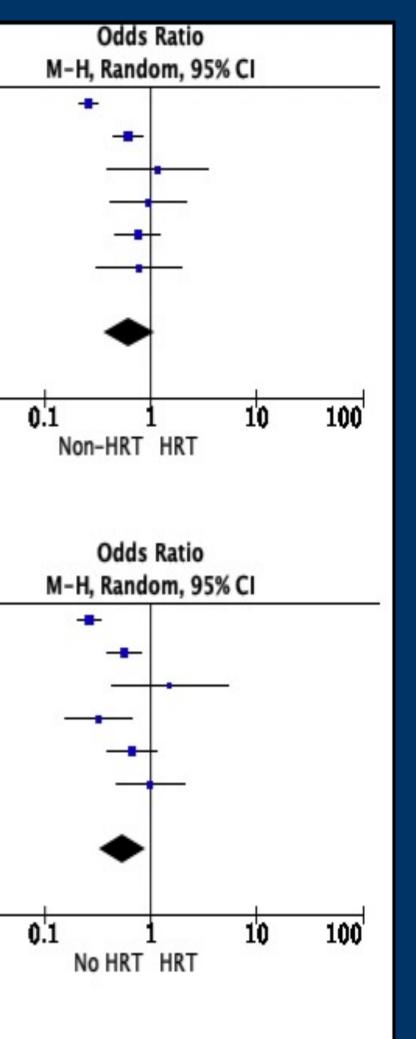
	HF	HRT No		HRT		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	
Shao-Hua Xie et al 2021	95	297059	598	485418	21.1%	0.26 [0.21, 0.32]	2021	
Brusselaers et al 2016	46	290186	224	870165	20.3%	0.62 [0.45, 0.85]	2016	
Meron et al 2014	7	51851	6	51851	11.9%	1.17 [0.39, 3.47]	2014	
Bodelon et al 2011	14	97702	9	60031	14.6%	0.96 [0.41, 2.21]	2011	
Freedman et al 2010	30	106964	33	89132	18.6%	0.76 [0.46, 1.24]	2010	
Undblad et al 2006	5	350	53	2899	13.6%	0.78 [0.31, 1.96]	2006	
Total (95% CI)		844112		1559496	100.0%	0.63 [0.36, 1.11]		
Total events	197		923					
Heterogeneity: Tau <sup>2</sup> = 0.33	7; Chi <sup>2</sup> =	39.29, df	= 5 (P <	: 0.00001);	l <sup>2</sup> = 87%	i		0.01
Test for overall effect: Z =	1.61 (P -	0.11)						V.VI
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	HF	RT	No	HRT		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	
Shao-Hua Xie et al 2021	68	297032	416	485238	21.6%	0.27 [0.21, 0.34]	2021	
Brusselaers et al 2016	33	290186	174	870165	20.3%	0.57 [0.39, 0.83]	2016	
Meron et al 2014	6	51851	4	51851	9.3%	1.50 [0.42, 5.32]	2014	
Bodelon et al 2011	11	95754	21	59091	15.4%	0.32 [0.16, 0.67]	2011	
Freedman et al 2010	24	106958	30	89129	18.1%	0.67 [0.39, 1.14]	2010	
Undblad et al 2006	8	353	66	2912	15.3%	1.00 [0.48, 2.10]	2006	
Total (95% CI)		842134		1558386	100.0%	0.54 [0.33, 0.90]		
Total events	150		713					
Heterogeneity: $Tau^2 = 0.25$ Test for overall effect: Z =	-	-	= 5 (P <	: 0.0001);	<sup>2</sup> = 82%			0.01

FIGURE 1: Forest plots showing the association between hormone and the incidence of esophageal adenocarcinoma (A) or squamo

- progesterone HRT
- progesterone therapy compared to estrogen only HRT
- affecting the association

The use of hormone replacement therapy in post-menopausal women was associated with a decreased risk of esophageal squamous cell carcinoma but not adenocarcinoma. In addition, combined estrogen and progesterone therapy was associated with a greater reduction in the risk of esophageal SCC compared to estrogen only therapy.





e replacement therapy use	
ous cell carcinoma (B).	

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A. Outcome	utcome Subgroup		OR [95% CI]	P-value	Test for Subgroup Differences P (I <sup>2</sup> %)	
AC	AC Estrogen only		0.59 [0.29, 1.21]	0.15		
	Estrogen	+ Progesterone	0.54 [0.32, 0.90]	0.02		-
SCC Estrogen only		ogen only	0.52 [0.31, 0.89]	0.02	.02 0.03 (78.9	
	Estrogen	+ Progesterone	0.27 [0.20, 0.36]	<0.00001		
В.						
Variables		Rate of Esopha	geal OR [	OR [95% CI] P-		
			Cancer (/100	0)		
Duration of	f HRT Use	<10 years	0.142	0.65 [(	0.35, 1.23]	0.19
		≥ 10 years	0.270			
Status of HRT Use		Past Users	0.212	1.18 [/	0.57, 2.44]	0.66
		Current Users	0.193			
Menarche Onset		Early (< 12 years)	0.529	1.46 [/	0.84, 2.53]	0.18
		Late (≥ 15 years)	0.235			
Menopaus	se Onset	Early (<45 years)	0.243	0.99 [/	0.23, 4.17]	0.99
	-	Late (≥ 55 years)	0.319			
Age at Fi	rst Birth	Early (<20 years)	0.511	1.08 [/	0.52, 2.23]	0.84
-		Late (≥ 30 years)	0.273			

TABLE 1: (A) Subgroup analysis investigating the association between different types of hormone replacement therapy (HRT) and the risk of either subtype of esophageal cancer (B) Evaluation of influencing factors affecting the association between HRT use and the risk of esophageal cancer

6 studies involving 2,403,608 post-menopausal women who either received HRT or not were included in the pooled analysis No statistically significant association between HRT use and esophageal AC (OR=0.63, P=0.11) with similar risk in estrogen only or estrogen +

Significantly reduced risk of esophageal SCC in patients receiving HRT (OR=0.54, P=0.02) that is more pronounced with combined estrogen +

The duration (> or < 10 years), status of HRT use (past or current users), age of menarche, menopause, and first birth were not confounding variables

## CONCLUSION

