

Supplementary Table S4. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of esophageal cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	<i>P</i>_{Heterogeneity}^a	<i>I</i>² (%)	<i>P</i>_{Difference}^b
Testosterone					
Study design					
Cohort study	3	1.06 (0.89-1.27)	0.291	17.6	0.076
Nested case-control study	2	0.60 (0.36-0.99)	0.924	0.0	
Sex					
Male	5	1.01 (0.77-1.32)	0.076	50.0	0.921
Female	3	0.91 (0.66-1.25)	0.465	0.0	
Postmenopausal women (only)	2	0.92 (0.63-1.33)	0.279	21.6	
Histology					
Adenocarcinoma	3	0.86 (0.62-1.20)	0.221	31.9	0.628
Squamous cell carcinoma	1	1.14 (0.43-3.08)	0.046	74.9	
Mixed	2	1.12 (0.92-1.36)	0.519	0.0	
Follow-up time (years)					
Mean/median<10	3	1.01 (0.81-1.28)	0.107	42.6	0.543
Mean/median≥10	2	0.85 (0.55-1.31)	0.370	0.0	
Free testosterone					
Study design					
Cohort study	2	0.93 (0.71-1.21)	0.128	41.6	0.632
Nested case-control study	1	0.74 (0.37-1.48)	-	-	
Sex					
Male	3	0.99 (0.79-1.25)	0.296	18.9	0.364
Postmenopausal women	2	0.74 (0.42-1.31)	0.153	46.8	
Histology					
Adenocarcinoma	2	0.85 (0.65-1.12)	0.558	0.0	0.887
Squamous cell carcinoma	1	0.72 (0.22-2.36)	0.041	76.2	
Mixed	1	0.98 (0.64-1.50)	0.134	55.4	
Estradiol					
Study design					
Cohort study	1	1.23 (0.81-1.87)	0.954	0.0	0.985
Nested case-control study	2	1.24 (0.81-1.90)	0.738	0.0	
Sex					
Male	3	1.24 (0.92-1.68)	0.985	0.0	0.835
Postmenopausal women	1	0.92 (0.07-12.09)	-	-	
Histology					
Adenocarcinoma	3	1.23 (0.90-1.67)	0.983	0.0	0.850
Squamous cell carcinoma	1	1.38 (0.47-4.05)	-	-	
Follow-up time (years)					
Mean/median<10	2	1.21 (0.85-1.71)	0.988	0.0	0.798
Mean/median≥10	1	1.33 (0.74-2.39)	-	-	
Sex hormone-binding globulin					

Study design					
Cohort study	2	1.16 (0.99-1.35)	0.955	0.0	0.286
Nested case-control study	2	0.86 (0.54-1.37)	0.809	0.0	
Sex					
Male	4	1.10 (0.94-1.29)	0.863	0.0	0.602
Postmenopausal women	2	1.23 (0.86-1.76)	0.629	0.0	
Histology					
Adenocarcinoma	3	1.05 (0.82-1.34)	0.794	0.0	0.633
Squamous cell carcinoma	1	1.45 (0.80-2.63)	0.486	0.0	
Mixed	1	1.14 (0.94-1.38)	0.972	0.0	
Follow-up time (years)					
Mean/median<10	3	1.14 (0.98-1.33)	0.960	0.0	0.348
Mean/median≥10	1	0.82 (0.44-1.53)	-	-	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a *P* value in Cochran's *Q* test.

^b *P* value in the test of subgroup difference.

Supplementary Table S5. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of gastric cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	<i>P</i>_{Heterogeneity}^a	<i>I</i>² (%)	<i>P</i>_{Difference}^b
Testosterone					
Study design					
Cohort study	2	1.19 (0.93-1.53)	0.993	0.0	0.105
Nested case-control study	2	0.74 (0.51-1.07)	0.494	0.0	
Sex					
Male	4	0.99 (0.73-1.34)	0.187	37.5	0.937
Female	2	1.12 (0.66-1.91)	0.990	0.0	
Postmenopausal women (only)	1	1.12 (0.62-2.02)	-	-	
Geographic area					
Asia	1	0.67 (0.42-1.07)	-	-	0.115
Non-Asia	3	1.14 (0.91-1.44)	0.928	0.0	
Anatomical subsite*					
Cardia	2	1.05 (0.74-1.51)	0.633	0.0	0.286
Non-cardia	2	0.82 (0.58-1.15)	0.421	0.0	
Mixed	2	1.19 (0.93-1.53)	0.993	0.0	
Follow-up time (years)					
Mean/median<10	2	1.12 (0.87-1.45)	0.689	0.0	0.333
Mean/median≥10	2	0.91 (0.57-1.43)	0.240	29.9	
Free testosterone					
Study design					
Cohort study	1	0.95 (0.70-1.29)	0.603	0.0	0.677
Nested case-control study	1	0.79 (0.44-1.42)	-	-	
Sex					
Male	2	0.88 (0.65-1.19)	0.685	0.0	0.636
Postmenopausal women	1	1.10 (0.59-2.05)	-	-	
Anatomical subsite*					
Cardia	2	0.82 (0.57-1.19)	0.608	0.0	0.708
Non-cardia	1	0.73 (0.40-1.33)	0.965	0.0	
Mixed	1	0.95 (0.70-1.29)	0.603	0.0	
Estradiol					
Study design					
Cohort study	1	1.09 (0.62-1.92)	-	-	0.815
Nested case-control study	2	0.88 (0.40-1.96)	0.025	80.2	
Geographic area					
Asia	1	1.29 (0.85-1.96)	-	-	0.522
Non-Asia	2	0.79 (0.42-1.49)	0.115	59.6	
Anatomical subsite*					
Cardia	2	0.86 (0.36-2.08)	0.063	71.0	0.874
Non-cardia	2	1.22 (0.82-1.81)	0.412	0.0	
Mixed	1	1.09 (0.62-1.92)	-	-	

Follow-up time (years)					
Mean/median<10	2	0.79 (0.42-1.49)	0.115	59.6	0.522
Mean/median≥10	1	1.29 (0.85-1.96)	-	-	
Sex hormone-binding globulin					
Study design					
Cohort study	1	1.26 (0.93-1.71)	0.365	0.0	0.534
Nested case-control study	2	1.52 (1.03-2.25)	0.517	0.0	
Sex					
Male	3	1.43 (1.10-1.85)	0.742	0.0	0.388
Postmenopausal women	1	0.97 (0.51-1.84)	-	-	
Geographic area					
Asia	1	1.71 (1.01-2.90)	-	-	0.431
Non-Asia	2	1.27 (0.97-1.67)	0.657	0.0	
Anatomical subsite*					
Cardia	2	1.37 (0.94-1.99)	0.982	0.0	0.630
Non-cardia	2	1.62 (1.06-2.49)	0.331	9.6	
Mixed	1	1.26 (0.93-1.71)	0.365	0.0	
Follow-up time (years)					
Mean/median<10	2	1.27 (0.97-1.67)	0.657	0.0	0.431
Mean/median≥10	1	1.71 (1.01-2.90)	-	-	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a *P* value in Cochran's *Q* test.

^b *P* value in the test of subgroup difference.

* The data for cardia, non-cardia and mixed of McMenamin 2021 were included simultaneously in the subgroup analysis of anatomical subsite.

Supplementary Table S6. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of liver cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	<i>P</i>_{Heterogeneity}^a	<i>I</i>² (%)	<i>P</i>_{Difference}^b
Testosterone					
Study design					
Cohort study	4	1.96 (1.57-2.44)	0.357	9.2	0.792
Nested case-control study	5	2.33 (1.04-5.21)	0.000	83.6	
Sex					
Male	7	2.63 (1.65-4.18)	0.002	68.3	0.516
Female	3	1.46 (0.93-2.30)	0.104	55.8	
Postmenopausal women (only)	2	1.27 (0.81-2.00)	0.131	56.1	
Mixed	1	1.22 (0.42-3.54)	-	-	
Geographic area					
Asia	5	3.27 (1.57-6.83)	0.002	73.6	0.113
Non-Asia	4	1.62 (1.17-2.23)	0.051	54.7	
HBsAg status					
Negative	1	1.00 (0.40-2.50)	-	-	0.389
Positive	3	3.90 (1.43-10.64)	0.002	83.4	
Mixed	4	1.84 (0.77-4.40)	0.051	61.3	
Unspecified	2	1.93 (1.50-2.49)	0.291	19.7	
Adjustment for HBsAg status					
Yes	4	1.84 (0.77-4.40)	0.051	61.3	0.630
No	5	2.24 (1.54-3.26)	0.002	69.6	
Adjustment for anti-HCV positivity					
Yes	4	1.84 (0.77-4.40)	0.051	61.3	0.630
No	5	2.24 (1.54-3.26)	0.002	69.6	
Histology ^d					
Total liver cancer	3	1.65 (1.16-2.34)	0.031	62.3	0.122
Hepatocellular carcinoma	7	2.72 (1.52-4.87)	0.003	67.0	
Intrahepatic cholangiocarcinoma	1	0.56 (0.24-1.31)	-	-	
Follow-up time (years)					
Mean/median<10	6	2.55 (1.60-4.08)	0.001	72.1	0.267
Mean/median≥10	3	1.49 (0.99-2.25)	0.170	40.3	
Free testosterone					
Study design					
Cohort study	2	0.92 (0.53-1.60)	0.161	45.3	0.572
Nested case-control study	2	0.72 (0.46-1.14)	0.904	0.0	
Sex					
Male	2	0.80 (0.27-2.37)	0.260	21.3	0.783
Postmenopausal women	2	0.93 (0.59-1.48)	0.182	44.0	
Mixed	1	0.68 (0.24-1.93)	-	-	
Geographic area					
Asia	1	3.30 (0.20-54.45)	-	-	0.406

Non-Asia	3	0.82 (0.61-1.10)	0.337	11.1	
HBsAg status					
Mixed	3	0.75 (0.48-1.17)	0.572	0.0	0.734
Unspecified	1	0.87 (0.48-1.58)	0.093	64.6	
Adjustment for HBsAg status					
Yes	3	0.75 (0.48-1.17)	0.572	0.0	0.734
No	1	0.87 (0.48-1.58)	0.093	64.6	
Adjustment for anti-HCV positivity					
Yes	3	0.75 (0.48-1.17)	0.572	0.0	0.734
No	1	0.87 (0.48-1.58)	0.093	64.6	
Histology^d					
Total liver cancer	2	0.83 (0.57-1.20)	0.198	38.2	0.935
Hepatocellular carcinoma	3	0.73 (0.36-1.45)	0.549	0.0	
Intrahepatic cholangiocarcinoma	1	0.90 (0.38-2.13)	-	-	
Follow-up time (years)					
Mean/median<10	3	0.87 (0.58-1.33)	0.270	23.5	0.703
Mean/median≥10	1	0.73 (0.44-1.21)	-	-	
Estradiol					
Study design					
Cohort study	2	0.46 (0.16-1.31)	0.769	0.0	0.219
Nested case-control study	2	1.28 (0.83-1.98)	0.650	0.0	
Sex^c					
Male	3	0.95 (0.54-1.69)	0.362	1.6	0.778
Female	2	1.30 (0.72-2.34)	0.387	0.0	
Postmenopausal women (only)	1	1.42 (0.76-2.65)	-	-	
Mixed	1	0.55 (0.11-2.75)	-	-	
Geographic area					
Asia	2	0.82 (0.31-2.18)	0.168	47.3	0.710
Non-Asia	2	1.20 (0.58-2.45)	0.282	13.7	
HBsAg status					
Positive	1	1.16 (0.63-2.14)	-	-	0.872
Mixed	2	0.88 (0.26-2.94)	0.102	62.5	
Unspecified	1	0.55 (0.11-2.75)	-	-	
Adjustment for HBsAg status					
Yes	2	0.88 (0.26-2.94)	0.102	62.5	0.997
No	2	1.06 (0.60-1.87)	0.395	0.0	
Adjustment for anti-HCV positivity					
Yes	2	0.88 (0.26-2.94)	0.102	62.5	0.997
No	2	1.06 (0.60-1.87)	0.395	0.0	
Histology^e					
Total liver cancer	2	1.20 (0.58-2.45)	0.282	13.7	0.577
Hepatocellular carcinoma	4	1.21 (0.61-2.40)	0.238	29.0	
Intrahepatic cholangiocarcinoma	2	2.11 (0.25-18.03)	0.171	46.6	
Follow-up time (years)					

Mean/median<10	3	0.85 (0.45-1.61)	0.311	14.3	0.452
Mean/median≥10	1	1.42 (0.76-2.65)	-	-	
Testosterone/estradiol ratio					
Study design					
Cohort study	1	25.40 (3.10-208.11)	-	-	0.206
Nested case-control study	2	0.96 (0.62-1.49)	0.427	0.0	
Sex					
Male	2	4.58 (0.23-92.64)	0.006	86.8	0.622
Postmenopausal women	1	0.81 (0.44-1.49)	-	-	
Geographic area					
Asia	2	4.58 (0.23-92.64)	0.006	86.8	0.622
Non-Asia	1	0.81 (0.44-1.49)	-	-	
HBsAg status					
Positive	1	1.16 (0.61-2.21)	-	-	0.748
Mixed	2	3.89 (0.13-112.40)	0.002	89.5	
Adjustment for HBsAg status					
Yes	2	3.89 (0.13-112.40)	0.002	89.5	0.748
No	1	1.16 (0.61-2.21)	-	-	
Adjustment for anti-HCV positivity					
Yes	2	3.89 (0.13-112.40)	0.002	89.5	0.748
No	1	1.16 (0.61-2.21)	-	-	
Histology ^d					
Total liver cancer	1	0.81 (0.44-1.49)	-	-	0.539
Hepatocellular carcinoma	3	2.64 (0.71-9.78)	0.022	73.9	
Intrahepatic cholangiocarcinoma	1	0.34 (0.10-1.16)	-	-	
Follow-up time (years)					
Mean/median<10	2	4.58 (0.23-92.64)	0.006	86.8	0.622
Mean/median≥10	1	0.81 (0.44-1.49)	-	-	
Sex hormone-binding globulin					
Study design					
Cohort study	3	2.00 (1.14-3.51)	0.033	65.6	0.874
Nested case-control study	2	2.23 (1.02-4.87)	0.176	45.5	
Sex					
Male	3	2.09 (0.78-5.64)	0.038	69.5	0.495
Postmenopausal women	2	1.58 (1.09-2.29)	0.793	0.0	
Mixed	1	3.86 (1.32-11.29)	-	-	
Geographic area					
Asia	1	0.20 (0.02-2.00)	-	-	0.171
Non-Asia	4	2.15 (1.56-2.97)	0.160	39.2	
HBsAg status					
Mixed	4	2.21 (0.92-5.27)	0.035	65.2	0.733
Unspecified	1	1.95 (1.34-2.82)	0.171	46.7	
Adjustment for HBsAg status					
Yes	3	1.61 (0.55-4.76)	0.064	63.7	0.714

No	2	2.21 (1.41-3.45)	0.096	57.3	
Adjustment for anti-HCV positivity					
Yes	3	1.61 (0.55-4.76)	0.064	63.7	0.714
No	2	2.21 (1.41-3.45)	0.096	57.3	
Histology ^d					
Total liver cancer	2	1.95 (1.52-2.49)	0.317	13.1	0.362
Hepatocellular carcinoma	4	2.92 (1.19-7.14)	0.095	52.9	
Intrahepatic cholangiocarcinoma	1	1.23 (0.44-3.44)	-	-	
Follow-up time (years)					
Mean/median<10	4	2.20 (1.34-3.63)	0.042	59.6	0.700
Mean/median≥10	1	1.67 (0.95-2.94)	-	-	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: anti-HCV, antibody to hepatitis C virus; CI, confidence interval; HBsAg, hepatitis B surface antigen; OR, odds ratio.

^a *P* value in Cochran's *Q* test.

^b *P* value in the test of subgroup difference.

^c The data for male, female, mixed of Ahmed 2023 were included simultaneously in the sex subgroup analysis of estradiol.

^d The data for liver cancer, hepatocellular carcinoma, and intrahepatic cholangiocarcinoma of Petrick 2020 were included simultaneously in the subgroup analysis of histology.

^e The data for liver cancer, hepatocellular carcinoma, and intrahepatic cholangiocarcinoma of Petrick 2020 and Ahmed 2023 were included simultaneously in the histology subgroup analysis of estradiol.

Supplementary Table S7. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of pancreatic cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	$P_{\text{Heterogeneity}}^a$	I^2 (%)	$P_{\text{Difference}}^b$
Testosterone					
Sex ^c					
Male	2	1.11 (0.77-1.60)	0.742	0.0	0.503
Female	2	0.75 (0.50-1.14)	0.756	0.0	
Mixed	1	0.99 (0.72-1.36)	-	-	
Follow-up time (years)					
Mean/median<10	1	0.99 (0.72-1.36)	-	-	0.648
Mean/median≥10	1	0.82 (0.50-1.35)	0.460	0.0	
Free testosterone					
Sex ^c					
Male	1	1.15 (0.74-1.79)	-	-	0.619
Female	1	0.58 (0.33-1.02)	-	-	
Mixed	1	0.89 (0.63-1.26)	-	-	
Estradiol					
Sex ^d					
Male	1	2.82 (0.20-39.76)	-	-	0.912
Female	1	0.32 (0.08-1.28)	-	-	
Mixed	1	0.43 (0.13-1.42)	-	-	
Free estradiol					
Sex ^d					
Male	1	0.67 (0.38-1.18)	-	-	-
Female	1	0.68 (0.46-1.01)	-	-	
Sex hormone-binding globulin					
Sex ^c					
Male	1	1.16 (0.72-1.87)	-	-	0.953
Female	1	1.22 (0.70-2.13)	-	-	
Mixed	1	1.18 (0.82-1.70)	-	-	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a P value in Cochran's Q test.

^b P value in the test of subgroup difference.

^c The data for male, female, and mixed of Peila 2020 were included simultaneously in the subgroup analysis of sex.

^d The data for male, female, and mixed of Ahmed 2023 were included simultaneously in the subgroup analysis of sex.

Supplementary Table S8. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of colorectal cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	$P_{\text{Heterogeneity}}^a$	I^2 (%)	$P_{\text{Difference}}^b$
Testosterone					
Study design					
Cohort study	5	0.94 (0.86-1.02)	0.907	0.0	0.813
Nested case-control study	4	1.04 (0.75-1.46)	0.006	72.0	
Sex					
Male	6	0.88 (0.80-0.97)	0.530	0.0	0.057
Female	5	1.12 (0.90-1.40)	0.116	45.9	
Postmenopausal women (only)	3	1.35 (0.98-1.86)	0.214	35.0	
Geographic area					
Asia	1	2.10 (1.11-3.97)	-	-	0.041
Non-Asia	8	0.93 (0.86-1.01)	0.370	7.8	
Follow-up time (years)					
Mean/median<10	3	0.93 (0.85-1.02)	0.661	0.0	0.722
Mean/median≥10	6	1.01 (0.81-1.26)	0.038	53.0	
Free testosterone					
Study design					
Cohort study	3	0.99 (0.90-1.08)	0.999	0.0	0.647
Nested case-control study	3	1.11 (0.76-1.62)	0.054	65.7	
Sex					
Male	3	0.97 (0.87-1.07)	0.474	0.0	0.288
Female	3	1.13 (0.89-1.42)	0.161	45.3	
Postmenopausal women (only)	2	1.29 (0.99-1.70)	0.368	0.0	
Geographic area					
Asia	1	1.63 (0.92-2.89)	-	-	0.166
Non-Asia	5	0.99 (0.91-1.08)	0.504	0.0	
Follow-up time (years)					
Mean/median<10	3	0.99 (0.90-1.08)	0.999	0.0	0.647
Mean/median≥10	3	1.11 (0.76-1.62)	0.054	65.7	
Dehydroepiandrosterone					
Sex*					
Male	2	1.11 (0.83-1.49)	0.817	0.0	0.582
Female	2	0.87 (0.65-1.18)	0.941	0.0	
Postmenopausal women (only)	1	0.87 (0.63-1.20)	-	-	
Mixed	1	0.84 (0.43-1.64)	-	-	
Follow-up time (years)					
Mean/median<10	1	0.84 (0.43-1.64)	-	-	0.739
Mean/median≥10	2	0.98 (0.78-1.24)	0.301	6.4	
Estrone					
Study design					
Nested case-control study	5	1.03 (0.76-1.39)	0.004	71.1	0.837

Case-cohort study	1	1.13 (0.73-1.75)	-	-	
Sex					
Male	2	1.06 (0.84-1.34)	0.815	0.0	0.945
Postmenopausal women	5	1.04 (0.69-1.57)	0.002	76.9	
Estradiol					
Study design					
Cohort study	4	1.01 (0.86-1.19)	0.402	0.0	0.454
Nested case-control study	6	0.95 (0.77-1.17)	0.157	35.5	
Case-cohort study	2	1.28 (0.74-2.22)	0.103	62.3	
Sex					
Male	5	0.99 (0.85-1.14)	0.477	0.0	0.969
Female	8	1.04 (0.82-1.31)	0.055	49.2	
Postmenopausal women (only)	7	1.04 (0.78-1.38)	0.035	55.6	
Geographic area					
Asia	1	2.28 (0.77-6.75)	-	-	0.180
Non-Asia	11	1.00 (0.88-1.15)	0.181	26.9	
Follow-up time (years)					
Mean/median<10	4	1.12 (0.87-1.45)	0.099	52.2	0.392
Mean/median≥10	8	0.97 (0.81-1.15)	0.244	22.5	
Free estradiol					
Study design					
Cohort study	1	1.02 (0.77-1.36)	0.567	0.0	0.471
Nested case-control study	3	0.78 (0.51-1.20)	0.010	78.1	
Sex					
Male	2	0.93 (0.73-1.18)	0.933	0.0	0.682
Female	3	0.83 (0.50-1.37)	0.005	81.2	
Postmenopausal women (only)	2	0.71 (0.33-1.52)	0.004	87.8	
Follow-up time (years)					
Mean/median<10	1	1.02 (0.77-1.36)	0.567	0.0	0.471
Mean/median≥10	3	0.78 (0.51-1.20)	0.010	78.1	
Estradiol/testosterone ratio					
Study design					
Cohort study	1	1.19 (0.90-1.58)	0.643	0.0	0.866
Nested case-control study	2	1.07 (0.49-2.35)	0.000	89.2	
Sex					
Male	2	1.59 (0.79-3.22)	0.016	82.7	0.484
Female	3	0.91 (0.55-1.48)	0.021	74.2	
Postmenopausal women (only)	2	0.74 (0.34-1.60)	0.021	81.3	
Follow-up time (years)					
Mean/median<10	1	1.19 (0.90-1.58)	0.643	0.0	0.866
Mean/median≥10	2	1.07 (0.49-2.35)	0.000	89.2	
Progesterone					
Study design					
Nested case-control study	4	0.96 (0.81-1.14)	0.940	0.0	0.431

Case-cohort study	1	1.19 (0.77-1.84)	-	-	
Sex					
Male	1	0.90 (0.68-1.19)	-	-	0.490
Postmenopausal women	4	1.03 (0.85-1.25)	0.895	0.0	
Geographic area					
Asia	1	0.94 (0.43-2.05)	-	-	0.909
Non-Asia	4	0.99 (0.84-1.16)	0.752	0.0	
Sex hormone-binding globulin					
Study design					
Cohort study	4	0.99 (0.86-1.15)	0.140	45.2	0.928
Nested case-control study	6	1.02 (0.75-1.39)	0.002	70.9	
Sex					
Male	5	0.89 (0.80-0.98)	0.591	0.0	0.295
Female	6	1.16 (0.91-1.49)	0.020	62.6	
Postmenopausal women (only)	5	1.17 (0.81-1.69)	0.011	69.2	
Geographic area					
Asia	1	0.94 (0.56-1.58)	-	-	0.826
Non-Asia	9	1.02 (0.86-1.21)	0.002	65.9	
Follow-up time (years)					
Mean/median<10	3	0.98 (0.83-1.16)	0.084	59.6	0.753
Mean/median≥10	7	1.04 (0.79-1.38)	0.004	66.5	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a *P* value in Cochran's *Q* test.

^b *P* value in the test of subgroup difference.

*The data for male, female, and mixed of Alberg 2000 were included simultaneously in the sex subgroup analysis of dehydroepiandrosterone.

Supplementary Table S9. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of colon cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	<i>P</i>_{Heterogeneity}^a	<i>I</i>² (%)	<i>P</i>_{Difference}^b
Testosterone					
Study design					
Cohort study	3	0.93 (0.83-1.05)	0.350	8.6	0.947
Nested case-control study	2	0.93 (0.65-1.33)	0.099	63.2	
Sex					
Male	3	0.86 (0.75-0.97)	0.481	0.0	0.281
Female	3	1.03 (0.90-1.19)	0.646	0.0	
Postmenopausal women (only)	1	1.12 (0.82-1.53)	-	-	
Follow-up time (years)					
Mean/median<10	2	0.93 (0.77-1.13)	0.098	63.5	0.949
Mean/median≥10	3	0.94 (0.78-1.13)	0.356	7.5	
Free testosterone					
Study design					
Cohort study	2	1.00 (0.89-1.13)	0.474	0.0	0.955
Nested case-control study	2	0.99 (0.66-1.48)	0.068	69.9	
Sex					
Male	2	0.92 (0.79-1.07)	0.326	0.0	0.797
Female	2	1.09 (0.93-1.27)	0.433	0.0	
Postmenopausal women (only)	1	1.21 (0.89-1.65)	-	-	
Follow-up time (years)					
Mean/median<10	2	1.00 (0.89-1.13)	0.474	0.0	0.955
Mean/median≥10	2	0.99 (0.66-1.48)	0.068	69.9	
Dehydroepiandrosterone					
Sex*					
Male	2	1.11 (0.83-1.49)	0.817	0.0	0.530
Female	2	0.87 (0.65-1.18)	0.941	0.0	
Postmenopausal women (only)	1	0.87 (0.63-1.20)	-	-	
Mixed	1	0.84 (0.43-1.64)	-	-	
Follow-up time (years)					
Mean/median<10	1	0.84 (0.43-1.64)	-	-	0.739
Mean/median≥10	2	0.98 (0.78-1.24)	0.301	6.4	
Estrone					
Sex					
Male	1	1.09 (0.80-1.49)	-	-	0.880
Postmenopausal women	3	0.94 (0.40-2.23)	0.000	90.6	
Estradiol					
Study design					
Cohort study	2	0.98 (0.75-1.29)	0.278	14.9	0.482
Nested case-control study	3	0.77 (0.48-1.23)	0.007	79.6	
Sex					

Male	2	0.90 (0.73-1.11)	1.000	0.0	0.665
Female	3	0.83 (0.46-1.52)	0.002	83.3	
Postmenopausal women (only)	2	0.69 (0.29-1.66)	0.002	89.1	
Follow-up time (years)					
Mean/median<10	2	0.98 (0.75-1.29)	0.278	14.9	0.482
Mean/median≥10	3	0.77 (0.48-1.23)	0.007	79.6	
Free estradiol					
Study design					
Cohort study	1	1.04 (0.65-1.67)	0.154	50.9	0.482
Nested case-control study	3	0.69 (0.37-1.29)	0.000	88.8	
Sex					
Male	2	0.89 (0.69-1.14)	0.680	0.0	0.609
Female	3	0.77 (0.35-1.71)	0.000	90.6	
Postmenopausal women (only)	2	0.59 (0.19-1.82)	0.000	93.7	
Follow-up time (years)					
Mean/median<10	1	1.04 (0.65-1.67)	0.154	50.9	0.482
Mean/median≥10	3	0.69 (0.37-1.29)	0.000	88.8	
Estradiol/testosterone ratio					
Study design					
Cohort study	1	1.18 (0.74-1.88)	0.150	51.7	0.830
Nested case-control study	1	1.06 (0.75-1.50)	-	-	
Sex					
Male	1	0.94 (0.61-1.45)	-	-	0.862
Female	2	1.21 (0.86-1.71)	0.240	27.7	
Postmenopausal women (only)	1	1.06 (0.75-1.50)	-	-	
Follow-up time (years)					
Mean/median<10	1	1.18 (0.74-1.88)	0.150	51.7	0.830
Mean/median≥10	1	1.06 (0.75-1.50)	-	-	
Sex hormone-binding globulin					
Study design					
Cohort study	2	1.00 (0.80-1.24)	0.116	59.6	0.691
Nested case-control study	3	1.17 (0.72-1.93)	0.010	78.3	
Sex					
Male	2	0.89 (0.76-1.04)	0.721	0.0	0.551
Female	3	1.26 (0.89-1.79)	0.032	70.9	
Postmenopausal women (only)	2	1.41 (0.68-2.92)	0.010	84.8	
Follow-up time (years)					
Mean/median<10	2	1.00 (0.80-1.24)	0.116	59.6	0.691
Mean/median≥10	3	1.17 (0.72-1.93)	0.010	78.3	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a *P* value in Cochran's *Q* test; ^b *P* value in the test of subgroup difference.

* The data for male, female, and mixed of Alberg 2000 were included simultaneously in the sex subgroup analysis of dehydroepiandrosterone.

Supplementary Table S10. Subgroup analysis of prediagnostic circulating sex hormones levels and risk of rectal cancer

Study characteristics	Number of studies	Pooled OR (95% CI)	$P_{\text{Heterogeneity}}^a$	I^2 (%)	$P_{\text{Difference}}^b$
Estradiol					
Study design					
Cohort study	1	0.86 (0.61-1.20)	0.848	0.0	0.461
Nested case-control study	1	1.44 (0.63-3.29)	-	-	
Sex					
Male	1	0.87 (0.61-1.24)	-	-	0.603
Postmenopausal women	2	1.14 (0.60-2.19)	0.372	0.0	
Follow-up time (years)					
Mean/median<10	1	0.86 (0.61-1.20)	0.848	0.0	0.461
Mean/median≥10	1	1.44 (0.63-3.29)	-	-	
Sex hormone-binding globulin					
Study design					
Cohort study	2	0.95 (0.80-1.13)	0.721	0.0	0.229
Nested case-control study	1	3.02 (1.31-6.96)	-	-	
Sex					
Male	1	0.93 (0.76-1.14)	-	-	0.361
Female	2	1.62 (0.55-4.75)	0.016	82.6	
Postmenopausal women (only)	1	3.02 (1.31-6.96)	-	-	
Follow-up time (years)					
Mean/median<10	2	0.95 (0.80-1.13)	0.721	0.0	0.229
Mean/median≥10	1	3.02 (1.31-6.96)	-	-	

Note: Expressed as pooled OR and 95% CI comparing the highest with the lowest tertiles of sex hormone levels.

Abbreviations: OR, odds ratio; CI, confidence interval.

^a P value in Cochran's Q test.

^b P value in the test of subgroup difference.