Supplementary Table S2. Adjusted or matched covariates and sex hormone measurement methods of studies included in the meta-analysis

First author	Year	Adjusted covariates	Matched covariates	Source of controls	Blood sample type	Sex hormone measurement methods
Ming-Whei Yu[1]	1993	HBsAg carrier status, positivity of serum anti-HCV, cigarette smoking, alcohol drinking, past liver disease history, and dietary habits	Age, date of questionnaire interview and blood collection, and residential township	Cancer-free control	Serum	RIA
Jian-Min Yuan[2]	1995	Duration of cigarette smoking	Age, time of blood sample collection, and neighborhood of residence	Cancer-free control	Serum	RIA
Nathalie Ganne-Carrie[3]	1997	Age, serum bilirubin and albumin	-	Cirrhosis	Serum	Solid-phase assay
Anthony J. Alberg[4]	2000	-	Age, sex, and race	Cancer-free control	Serum	RIA
Keitaro Tanaka[5]	2000	Age, years since LC diagnosis, department, hospitalization status, heavy drinking history, albumin, aspartate aminotransferase, and AFP, the serostatus of HBsAg and anti-HCV, and other hormonal parameters	-	Cirrhosis	Serum	RIA (testosterone, free testosterone, estradiol), time-resolved fluoroimmunoassay (SHBG)
Ming-Whei Yu[6]	2001	Age at recruitment, the time of blood draw, ethnicity, years of education, cigarette smoking, alcohol consumption, history of chronic liver disease, BMI, and other hormone-related factors	Date of blood collection and year of birth	HBV carriers	Plasma	Competitive immunoassay that uses direct chemiluminescent technology (testosterone), RIA (estradiol)
Marc J. Gunter[7]	2008	Age, smoking, ethnicity, physical activity,	-	Subcohort	Serum	Immunodiagnostic assay

		waist circumference, use of NSAIDs in the preceding year, alcohol consumption, family history of colorectal cancer, history of colonoscopy, insulin, free IGF-I and HT/E2				
Tess V. Clendenen[8]	2009	BMI at enrollment, age, date of blood donation	Age, date of blood donation	Cancer-free control	Serum	RIA (estrone, estradiol), two-site immunometric chemiluminescent assay (SHBG)
Jennifer H Lin[9]	2013	Age at blood draw, study cohort, fasting status, and time for the blood draw, physical activity, family history of colorectal cancer in a first-degree relative, history of colorectal polyps, smoking status, current alcohol consumption, and screening examination, BMI, C-peptide levels	Age, fasting status, and time of day of blood draw (NHS were not matched to controls)	Cancer-free control	Plasma	LC-MS/MS (estrone and estradiol in men and women and testosterone in women), EI (SHBG in men and women and testosterone in men)
Annekatrin Lukanova[10]	2014	BMI, smoking, ethanol at baseline, HBsAg/anti-HCV, diabetes, liver damage (a score based on albumin, bilirubin, AST, ALT, GGT, and AP concentrations outside normal range)	Recruitment center, sex, age, date, fasting status, and time of the day at blood collection; Women were additionally matched for menopausal status and exogenous hormone use at blood donation	Cancer-free control	Plasma	RIA (testosterone), immunoradiometric assay (SHBG)
D. D Ørsted[11]	2014	Smoking status, cumulative smoking,	-	Same cohort	Plasma	Immunochemical assay

		BMI, alcohol consumption, level of education, and level of income for both men and women; For women, parity, menopausal status, oral contraceptive use, and HRT were also adjusted for				
Roni T. Falk[12]	2015	Clinic site, trial participation status, age at blood collection, and total BMD	-	Subcohort	Serum	LC-MS/MS
Neil Murphy[13]	2015	Waist circumference, alcohol consumption, family history of colorectal cancer, physical activity, smoking status, NSAID use, insulin, free IGF-1, and CRP	Age, ethnicity, HT assignments, DM assignments, and CaD assignments	Cancer-free control	Serum	RIA (estrone, estradiol, progesterone), two-site chemiluminescent immunoassay (SHBG)
Yi X. Chan[14]	2017	Age, BMI, smoking status, physical activity, alcohol intake, diabetes mellitus, HDL, TG, and history of prevalent cancer	-	Same cohort	Plasma	LC-MS/MS (testosterone, DHT, estradiol), chemiluminescent immunoassays (LH, SHBG)
Yi X. Chan[15]	2018	Age, marital status, occupation, smoking, alcohol consumption, leisure time physical activity, BMI, and diabetes	-	Same cohort	Serum	LC-MS/MS (testosterone, DHT, estradiol), chemiluminometric immunoassay (LH), enzyme immunometric assay with chemiluminescent substrate (SHBG)
Nagisa Mori[16]	2019	BMI, smoking status, alcohol consumption, physical activity	Age, area code, population size of the area, season of blood collection, year of blood	Cancer-free control	Plasma	Electrochemiluminescence (estradiol, progesterone, testosterone), chemiluminescence enzyme

			collection, and fasting time			immunoassay (SHBG)
Jessica L. Petrick[17]	2019	Age, race/ethnicity, study year of blood draw, parent study, education, smoking status, number of cigarettes per day, BMI, and diabetes	Study, age, race/ethnicity, year of blood draw, time of blood draw, and number of freeze-thaw cycles for available serum samples	Cancer-free control	Serum	GC-MS (sex hormones), EI (SHBG)
Jessica L. Petrick[18]	2020	Age, matching factors, BMI, smoke status, alcohol status, HBsAg, anti-HCV, diabetes, and current MHT use	Sex, cohort, age, race/ethnicity, and blood collection date	Same cohort	Serum/plasma	GC-MS/MS (sex hormones), EI (SHBG)
Rita Peila[19]	2020	Age, ethnicity, education, smoking status, pack-years, alcohol, BMI, waist circumference, diabetes status, red and processed meat consumption, CRP, IGF-1, calcium, folate, vitamin D, physical activity, family history of colorectal cancer, ever screened for colorectal cancer; plus previous use of HRT and menopausal status (women)	-	Same cohort	Serum	Chemiluminescent immunoassay
Rita Peila[20]	2020	Age at recruitment, sex, education, race, smoking status and pack-years, alcohol intake, and BMI	-	Same cohort	Serum	Chemiluminescent immunoassay
Shao-Hua Xie[21]	2020	Tobacco smoking, physical activity, BMI at baseline	Age, year of blood sample drawn, and health survey from where the	Cancer-free control	Serum	LC-MS (testosterone, 17-OH progesterone, and androstenedione),

			participants were recruited			immunoassays (others)
Terry Cheuk-Fung Yip[22]	2020	Baseline platelet, total bilirubin, alanine aminotransferase, age, cirrhosis, hypertension, albumin, INR, HBeAg positivity, time-weighted average HbA1c, use of metformin, sulfonylureas, insulin, statins, and antiviral therapy	-	CHB patients with DM	Serum	NA
Una C. McMenamin[23]	2021	Age at baseline, deprivation, smoking status, BMI, alcohol consumption (except EAC), diabetes, aspirin use, and statin use (CRC only)	-	Same cohort	Serum	Chemiluminescent immunoassay
Kara A. Michels[24]	2021	Age and BMI, clinic enrollment site, and enrollment arm in the original FIT trial	Age and clinical center	Subcohort	Serum	LC-MS/MS
Nagisa Mori[25]	2021	BMI, smoking status, physical activity, ever used hormone therapy, and alcohol consumption, estrone, estradiol, and testosterone for SHBG and vice versa	Age, study center, follow-up time since blood collection, time of day at blood collection, and fasting status	Cancer-free control	Plasma	LC-MS (sex hormones), Solid-phase "sandwich" enzyme-linked immunoassay (SHBG)
Eleanor L. Watts[26]	2021	Townsend deprivation score, education level, ethnic group, height, BMI, cigarette smoking, alcohol consumption, total physical activity, IGF-I, CRP, HbA1c. For postmenopausal women, additionally adjusted for past HRT use, past oral contraceptive pill use, parity and age at	-	Same cohort	Serum	Chemiluminescent immunoassay

		first birth, age at menarche, and age at menopause				
Zhikai Zhu[27]	2021	Age, smoking status, alcohol drinking, BMI, trial, and other related sex steroid hormones or SHBG	Age at start of pills, date of blood collection and trials	Cancer-free control	Serum	RIA, immunoassay
Justin Harbs[28]	2022	BMI, smoking status, physical activity, alcohol consumption; SHBG model additionally adjusted for levels of estradiol and testosterone	Study center, age at and date of blood sample	Cancer-free control	Plasma	LC-MS/MS (Sex hormones), enzyme-linked immunoassays kit (SHBG)
Muktar Ahmed[29]	2023	Age, sex, assessment centre, educational status, Townsend deprivation score, smoking, alcohol consumption, physical activity, and health diet score	-	Same cohort	Serum	Chemiluminescent immunoassay

Abbreviations: AFP, α-fetoprotein; ALT, alanine aminotransaminase; anti-HCV, antibody to hepatitis C virus; AP, alkaline phosphatase; AST, aspartate aminotransaminase; BMD, bone mineral density; BMI, body mass index; CaD, calcium plus vitamin D; CHB, chronic hepatitis B; CRC, colorectal cancer; CRP, C-reactive protein; DHT, dihydrotestosterone; DM, diabetes mellitus; EAC, esophageal adenocarcinoma; EI, electrochemiluminescence immunoassay; FIT, Fracture Intervention Trial; GC-MS, gas chromatography-mass spectrometry; GC-MS/MS, gas chromatography selected reaction monitoring/tandem mass spectrometry assay; GGT, gamma-glutamyltransferase; HbA1c, glycated hemoglobin; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDL, high density lipoprotein; HRT, hormone replacement therapy; HT, hormone therapy; HT/E2, hormone therapy/estradiol; IGF-I, insulin-like growth factor-I; INR, international normalized ratio; LC, liver cancer; LC-MS, liquid chromatography-mass spectrometry; LC-MS/MS, liquid chromatography tandem mass spectrometry; LH, luteinizing hormone; MHT, menopausal hormone therapy; NA, not available; NHS, Nurses' Health Study; NSAID, nonsteroidal anti-inflammatory drug; RIA, radioimmunoassay; SHBG, sex hormone-binding globulin; TG, triglycerides; WHR, waist to hip ratio.

References

1. Yu MW, Chen CJ. Elevated serum testosterone levels and risk of hepatocellular carcinoma. Cancer Res 1993;53(4):790–4.
2. Yuan JM, Ross RK, Stanczyk FZ, et al. A cohort study of serum testosterone and hepatocellular carcinoma in Shanghai, China. Int J Cancer 1995;63(4):491–3.
3. Ganne-Carrie N, Chastang C, Uzzan B, et al. Predictive value of serum sex hormone binding globulin for the occurrence of hepatocellular carcinoma in male patients with cirrhosis. J Hepatol 1997;26(1):96–102.
4. Alberg AJ, Gordon GB, Hoffman SC, et al. Serum dehydroepiandrosterone and dehydroepiandrosterone sulfate and the subsequent risk of developing colon cancer. Cancer Epidemiol Biomarkers Prev 2000;9(5):517–21.
5. Tanaka K, Sakai H, Hashizume M, et al. Serum testosterone:estradiol ratio and the development of hepatocellular carcinoma among male cirrhotic patients. Cancer Res 2000;60(18):5106–10.
6. Yu MW, Yang YC, Yang SY, et al. Hormonal markers and hepatitis B virus-related hepatocellular carcinoma risk: a nested case-control study among men. J Natl Cancer Inst 2001;93(21):1644–51.
7. Gunter MJ, Hoover DR, Yu H, et al. Insulin, insulin-like growth factor-I, endogenous estradiol, and risk of colorectal cancer in postmenopausal women. Cancer Res 2008;68(1):329–37.
8. Clendenen TV, Koenig KL, Shore RE, et al. Postmenopausal levels of endogenous sex hormones and risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 2009;18(1):275–81.
9. Lin JH, Zhang SM, Rexrode KM, et al. Association between sex hormones and colorectal cancer risk in men and women. Clin Gastroenterol Hepatol 2013;11(4):419-424.e1.
10. Lukanova A, Becker S, Husing A, et al. Prediagnostic plasma testosterone, sex hormone-binding globulin, IGF-I and hepatocellular carcinoma: etiological factors or risk markers? Int J Cancer 2014;134(1):164–73.
11. Orsted DD, Nordestgaard BG, Bojesen SE. Plasma testosterone in the general population, cancer prognosis and cancer risk: a prospective cohort study. Ann Oncol 2014;25(3):712–8.
12. Falk RT, Dallal CM, Lacey JV, et al. Estrogen Metabolites Are Not Associated with Colorectal Cancer Risk in Postmenopausal Women. Cancer Epidemiol Biomarkers Prev 2015;24(9):1419–22.
13. Murphy N, Strickler HD, Stanczyk FZ, et al. A Prospective Evaluation of Endogenous Sex Hormone Levels and Colorectal Cancer Risk in Postmenopausal

Women. J Natl Cancer Inst 2015;107(10):djv210.

14. Chan YX, Alfonso H, Chubb SAP, et al. Higher Dihydrotestosterone Is Associated with the Incidence of Lung Cancer in Older Men. Horm Cancer 2017;8(2):119–26.

15. Chan YX, Knuiman MW, Divitini ML, et al. Lower Circulating Androgens Are Associated with Overall Cancer Risk and Prostate Cancer Risk in Men Aged 25-84 Years from the Busselton Health Study. Horm Cancer 2018;9(6):391–8.

16. Mori N, Sawada N, Iwasaki M, et al. Circulating sex hormone levels and colorectal cancer risk in Japanese postmenopausal women: The JPHC nested case-control study. Int J Cancer 2019;145(5):1238–44.

17. Petrick JL, Hyland PL, Caron P, et al. Associations Between Prediagnostic Concentrations of Circulating Sex Steroid Hormones and Esophageal/Gastric Cardia Adenocarcinoma Among Men. J Natl Cancer Inst 2019;111(1):34–41.

18. Petrick JL, Florio AA, Zhang X, et al. Associations Between Prediagnostic Concentrations of Circulating Sex Steroid Hormones and Liver Cancer Among Postmenopausal Women. Hepatology 2020;72(2):535–47.

19. Peila R, Arthur RS, Rohan TE. Sex hormones, SHBG and risk of colon and rectal cancer among men and women in the UK Biobank. Cancer Epidemiol 2020;69:101831.

20. Peila R, Arthur RS, Rohan TE. Association of Sex Hormones with Risk of Cancers of the Pancreas, Kidney, and Brain in the UK Biobank Cohort Study. Cancer Epidemiol Biomarkers Prev 2020;29(9):1832–6.

21. Xie SH, Ness-Jensen E, Rabbani S, et al. Circulating Sex Hormone Levels and Risk of Esophageal Adenocarcinoma in a Prospective Study in Men. Am J Gastroenterol 2020;115(2):216–23.

22. Yip TC, Wong GL, Chan HL, et al. Elevated testosterone increases risk of hepatocellular carcinoma in men with chronic hepatitis B and diabetes mellitus. J Gastroenterol Hepatol 2020;35(12):2210–9.

23. McMenamin UC, Liu P, Kunzmann AT, et al. Circulating Sex Hormones Are Associated With Gastric and Colorectal Cancers but Not Esophageal Adenocarcinoma in the UK Biobank. Am J Gastroenterol 2021;116(3):522–9.

24. Michels KA, Geczik AM, Bauer DC, et al. Endogenous Progestogens and Colorectal Cancer Risk among Postmenopausal Women. Cancer Epidemiol Biomarkers Prev 2021;30(6):1100–5.

25. Mori N, Keski-Rahkonen P, Gicquiau A, et al. Endogenous Circulating Sex Hormone Concentrations and Colon Cancer Risk in Postmenopausal Women: A Prospective Study and Meta-Analysis. JNCI Cancer Spectr 2021;5(6):pkab084.

26. Watts EL, Perez-Cornago A, Knuppel A, et al. Prospective analyses of testosterone and sex hormone-binding globulin with the risk of 19 types of cancer in men

and postmenopausal women in UK Biobank. Int J Cancer 2021;149(3):573–84.

27. Zhu Z, Chen Y, Ren J, et al. Serum Levels of Androgens, Estrogens, and Sex Hormone Binding Globulin and Risk of Primary Gastric Cancer in Chinese Men: A Nested Case-Control Study. Cancer Prev Res (Phila) 2021;14(6):659–66.

28. Harbs J, Rinaldi S, Gicquiau A, et al. Circulating Sex Hormone Levels and Colon Cancer Risk in Men: A Nested Case-Control Study and Meta-Analysis. Cancer Epidemiol Biomarkers Prev 2022;31(4):793–803.

29. Ahmed M, Mäkinen V-P, Lumsden A, et al. Metabolic profile predicts incident cancer: A large-scale population study in the UK Biobank. Metabolism 2023;138:155342.