

**Supplementary Table S1. Characteristics of studies included in the meta-analysis**

| First author                       | Year | Country       | Study design              | Study period   | Follow-up (years)    | Sample size                | Baseline age (years)   | Males (%)                     | Sex hormones                                | Primary outcome |
|------------------------------------|------|---------------|---------------------------|--|----------------------|----------------------------|--|-------------------------------|---|-----------------|
|                                    |      |               |                           |  |                      | N (case/control, or event) |  |                               |   |                 |
| Ming-Whei Yu <sup>1</sup>          | 1993 | China         | Nested case-control study | Taiwan community-based study (1984-1990)                     | 6, mean 4.6          | 175 (35/140)               | HBsAg-negative:<br>Cases: 58.3±9.8<br>Controls: 60.1±8.8<br>HBsAg-positive:<br>Cases: 59.2±9.2<br>Controls: 58.6±8.9 | All men (100)                 | Testosterone                                | HCC             |
| Jian-Min Yuan <sup>2</sup>         | 1995 | China         | Nested case-control study | Shanghai male residents cohort (1986-1993)                   | 7, mean 5.3          | 486 (76/410)               | 45-64  | All men (100)                 | Testosterone                                | HCC             |
| Nathalie Ganne-Carrie <sup>3</sup> | 1997 | France        | Cohort study              | HCC screening study in males with cirrhosis (1987-1992)      | 5, mean 3.2          | 101 cirrhosis (HCC: 29)    | 56.3±10.5  | All men (100)                 | SHBG  | HCC             |
| Anthony J. Alberg <sup>4</sup>     | 2000 | United States | Nested case-control study | Washington County serum bank and cancer registry (1974-1991) | 17, mean 9           | 234 (117/117)              | ≤44 (8.5%)<br>45-54 (30.8%)<br>55-64 (35.0%)<br>≥65 (25.6%)  | Cases: 41.9<br>Controls: 41.9 | DHEA, DHEAS                                 | CC              |
| Keitaro Tanaka <sup>5</sup>        | 2000 | Japan         | Cohort study              | Japan cirrhosis cohort in                                    | 10, mean 5.1, median | 46 cirrhosis (HCC: 20)     | Median 56  | All men (100)                 | Testosterone, free testosterone, estradiol, | HCC             |

|                                |      |               |                           |  |                                     |  |  |                      |  |             |
|--------------------------------|------|---------------|---------------------------|--|-------------------------------------|--|--|----------------------|--|-------------|
|                                |      |               |                           | Kyushu University Hospital (1985-1995)                               | 4.4                                 |  |  |                      | SHBG, testosterone: estradiol ratio                                  |             |
| Ming-Whei Yu <sup>6</sup>      | 2001 | China         | Nested case-control study | Taiwan male HBV carriers cohort study (1988-2000)                    | 12, mean 4.8 (time to diagnosis)    | 357 (119/238)  | Cases: 50.6±9.3<br>Controls: 50.3±9.0  | All men (100)        | Testosterone, estradiol, testosterone/estradiol ratio                | HCC         |
| Marc J. Gunter <sup>7</sup>    | 2008 | United States | Case-cohort study         | Women's Health Initiative Observational Study (1993-2004)            | 11, mean 6.4                        | 1,247 (438/809)  | Cases: 65.93±7.2<br>Subcohort: 62.78±7.5   | Postmenopausal women | Estradiol  | CRC         |
| Tess V. Clendenen <sup>8</sup> | 2009 | United States | Nested case-control study | New York University Women's Health Study (1985-2003)                 | 18, median 10.7 (time to diagnosis) | CRC: 441 (148/293)<br>Colon cancer: 372 (125/247)<br>Rectal cancer: 69 (23/46) | Cases: median 60.4<br>Controls: median 60.4  | Postmenopausal women | Estrone, estradiol, SHBG   | CC, RC, CRC |
| Jennifer H Lin <sup>9</sup>    | 2013 | United States | Nested case-control study | NHS (1976-2008), WHS (1992-2008), HPFS (1986-2008), and PHSII (1997- | 32, 16, 22, 11                      | 1158 men (439/719)<br>730 postmenopausal women (293/437)                       | Men (cases: 67.2±8.6<br>controls: 66.7±8.6)<br>Women (cases: 62.7±5.8<br>controls: 62.2) | 1158 (61.33)         | Estrone, estradiol, testosterone, SHBG, estradiol/testosterone ratio | CRC         |

|                                    |      |                    |                           |  |                                    |                  |   |                      |  |   |
|------------------------------------|------|--------------------|---------------------------|--|------------------------------------|------------------|---|----------------------|--|---|
|                                    |      |                    |                           | 2008)  |                                    |                  | ±5.5)                                       |                      |  |   |
| Annekatriin Lukanova <sup>10</sup> | 2014 | European countries | Nested case-control study | EPIC (1992-2006)                                     | 14, median 4.7 (time to diagnosis) | 372 (125/247)    | Median 60.6                                 | 253 (68)             | Testosterone, free testosterone, SHBG                          | HCC                                       |
| D. D Ørsted <sup>11</sup>          | 2014 | Denmark            | Cohort study              | Copenhagen City Heart Study (1981–2009)              | 28, median 22                      | 8,771 (1,949)    | 20-94                                       | 4,453 (50.77)        | Testosterone   | Any cancer (including EC, GC, LC, PC, CC) |
| Roni T. Falk <sup>12</sup>         | 2015 | United States      | Case-cohort study         | B~FIT (1992-2004)                                    | 12, median 10.3                    | 688 (187/501)    | Cases: 69.8±5.6<br>Subcohort: 67.3±6.2      | Postmenopausal women | Estrone, estradiol   | CRC                                       |
| Neil Murphy <sup>13</sup>          | 2015 | United States      | Nested case-control study | Women's Health Initiative Clinical Trial (1993-2008) | 15                                 | 1,203 (401/802)  | Cases: median 66.0<br>Controls: median 66.0 | Postmenopausal women | Estrone, free estradiol, total estradiol, progesterone, SHBG   | CC, RC, CRC                               |
| Yi X. Chan <sup>14</sup>           | 2017 | Australia          | Cohort study              | Health in Men Study (2001-2013)                      | 12, median 9.1                     | 3,690 (CRC: 137) | 77.0±3.6                                    | All men (100)        | Testosterone, free testosterone, DHT, estradiol, LH, SHBG      | CRC                                       |
| Yi X. Chan <sup>15</sup>           | 2018 | Australia          | Cohort study              | Busselton Health Study (1994-2014)                   | 20                                 | 1574 (CRC: 48)   | 51.1±14.7                                   | All men (100)        | Testosterone, DHT, estradiol, LH, SHBG                         | Overall cancer, CRC                       |
| Nagisa Mori <sup>16</sup>          | 2019 | Japan              | Nested case-control study | JPHC Study Cohort II (1998-2012)                     | 14, mean 12                        | 546 (185/361)    | Cases: 60.0±5.8<br>Controls: 59.8±6.0       | Postmenopausal women | Estradiol, SHBG, progesterone, testosterone, free testosterone | CRC                                       |

|                                  |      |                |                           |  |                |   |                                       |                      |  |              |
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| Jessica L. Petrick <sup>17</sup> | 2019 | United States  | Nested case-control study | PLCO (1993-NA), ATBC (1985-NA), CPS-II (1982-NA) | Median 8.4     | 518 (259/259)                             | Cases: 62.0±6.6<br>Controls: 61.0±6.6 | All men (100)        | DHEA, androstenedione, testosterone, DHT, estrone, estradiol, SHBG, parent estrogens, testosterone: parent estrogens ratio, androstenedione: estrone ratio, testosterone: estradiol ratio, free testosterone, free DHT, free estradiol | EAC, GCA     |
| Jessica L. Petrick <sup>18</sup> | 2020 | United States  | Nested case-control study | Liver Cancer Pooling Project (1964-2010)         | 16-45          | 617 (191/426)                             | Cases: 62.8±7.2<br>Controls: 62.5±6.9 | Postmenopausal women | Estradiol, estrone, testosterone, DHEA, 4-androstenedione, 5-androstenediol, SHBG, free estradiol, free testosterone, testosterone/estradiol ratio, free testosterone/free estradiol, androstenedione/estrone                          | LC, HCC, ICC |
| Rita Peila <sup>19</sup>         | 2020 | United Kingdom | Cohort study              | UK Biobank (2006-2016)                           | 10, median 7.1 | 425,614 (CRC: 3,247; colon cancer: 2,376; | 40-69                                 | 206,508 (48.52)      | Testosterone, free testosterone, estradiol, free estradiol,  | CC, RC, CRC  |

|                                    |      |                |                           |                                      |                            |  |  |   |   |   |
|------------------------------------|------|----------------|---------------------------|--------------------------------------|----------------------------|--|--|---|---|---|
|                                    |      |                |                           |                                      |                            | rectal cancer:<br>871)                             |  |   | estradiol/testosterone<br>ratio, SHBG   |   |
| Rita Peila <sup>20</sup>           | 2020 | United Kingdom | Cohort study              | UK Biobank (2006-2016)               | 10, median<br>7.1          | 425,793<br>(pancreatic cancer: 225)                | 40–69                                  | Pancreas cancer (59.4)<br>Noncases (46.4) | Total testosterone, free testosterone, SHBG   | PC  |
| Shao-Hua Xie <sup>21</sup>         | 2020 | Norway         | Nested case-control study | Janus Serum Bank Cohort (1970s-2016) | 41, mean<br>24.4           | 488 (244/244)                                      | Cases: 42.2±7.2<br>Controls: 42.1±4.1  | All men (100)                             | SHBG, DHEAS, FSH, LH, prolactin, testosterone, 17-OH progesterone, progesterone, estradiol, androstenedione, testosterone: estradiol ratio, free testosterone index | EAC   |
| Terry Cheuk-Fung Yip <sup>22</sup> | 2020 | China          | Cohort study              | CDARS (2000-2017)                    | 17, median<br>10.7         | 928 CHB patients with DM (HCC: 83)                 | 53.5 ± 10.9                            | All men (100)                             | Testosterone  | HCC   |
| Una C. McMenamin <sup>23</sup>     | 2021 | United Kingdom | Cohort study              | UK Biobank (2006-2016)               | 10                         | 366,605 (EAC: 376; ESCC: 108; GC: 333; CRC: 2,868) | 40–69                                  | 219,425 (59.85)                           | Testosterone, free testosterone, estradiol, SHBG  | EAC, ESCC, GC (cardia or non-cardia), CC, RC, CRC |
| Kara A. Michels <sup>24</sup>      | 2021 | United States  | Case-cohort study         | B~FIT (1992-2004)                    | 12, mean<br>10.2 (SD: 2.2) | 682 (187/495)                                      | Cases: 70.0±5.6<br>Subcohort: 67.2±6.2 | Postmenopausal women                      | Pregnenolone, progesterone, progesterone: estradiol   | CRC   |
| Nagisa Mori <sup>25</sup>          | 2021 | European       | Nested case-              | EPIC (1992-                          | Median 13.9                | 1,028 (512/516)                                    | EPIC                                   | Postmenopa                                | Estrone, estradiol, free  | CC  |

|                                |      |                    |                           |                                 |                                 |                  |   |                 |  |   |
|--------------------------------|------|--------------------|---------------------------|---------------------------------|---------------------------------|------------------|---|-----------------|--|---|
|                                |      | countries          | control study             | NA), NSHDS (1985-NA)            |                                 |                  | (Cases: 62.0±5.4<br>Controls: 61.9±5.4)<br>NSHDS<br>(Cases: 60.4±2.1<br>Controls: 60.3±2.0) | usal women      | estradiol, testosterone, free testosterone, estradiol-to-testosterone ratio, androstenedione, DHEA, progesterone, SHBG       |   |
| Eleanor L. Watts <sup>26</sup> | 2021 | United Kingdom     | Cohort study              | UK Biobank (2006-2016)          | 10, mean 7.0                    | 304,720 (15,151) | Men:56.13±8.22<br>Postmenopausal women: 60.15±5.29  | 182,608 (59.93) | Testosterone, free testosterone, SHBG  | 19 types of cancer (including EC, EAC, GC, LC, PC, CC, RC, CRC) |
| Zhikai Zhu <sup>27</sup>       | 2021 | China              | Nested case-control study | NIT (1991-2006)                 | 15, median 12.25                | 656 (328/328)    | Median 56.0   | All men (100)   | Androstenedione, testosterone, free and bioavailable testosterone, estradiol, estrone, free and bioavailable estradiol, SHBG | Non-cardia GC   |
| Justin Harbs <sup>28</sup>     | 2022 | European countries | Nested case-control study | EPIC (1992-NA), NSHDS (1985-NA) | Median 10.6 (time to diagnosis) | 1,380 (690/690)  | Cases: median 58.0,<br>Controls: median 57.7  | All men (100)   | Estrone, estradiol, free estradiol, testosterone, free testosterone, androstenedione, DHEA, progesterone, SHBG               | CC  |

|                            |      |                |              |                        |                    |                     |  |                   |  |                          |
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| Muktar Ahmed <sup>29</sup> | 2023 | United Kingdom | Cohort study | UK Biobank (2006-2016) | 10, median<br>3.87 | 290,888<br>(21,973) | 39–49 years:<br>67,723 (23.3),<br>50–59 years:<br>97,865 (33.6),<br>60–73 years:<br>125,300 (43.1) | 138,327<br>(47.6) | Testosterone, free<br>testosterone, estradiol,<br>free estradiol, SHBG | LC, HCC,<br>ICC, PC, CRC |
|----------------------------|------|----------------|--------------|------------------------|--------------------|---------------------|--|-------------------|--|--------------------------|

**Abbreviations:** ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; B-FIT, Breast and Bone Follow-up to the Fracture Intervention Trial; CC, colon cancer; CDARS, Clinical Data Analysis and Reporting System; CHB, chronic hepatitis B; CPS-II, Cancer Prevention Study II Nutrition Cohort; CRC, colorectal cancer; DHEA, dehydroepiandrosterone; DHEAS, dehydroepiandrosterone sulfate; DHT, dihydrotestosterone; DM, diabetes mellitus; EAC, esophageal adenocarcinoma; EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; EPIC, European Prospective Investigation into Cancer and Nutrition; FSH, follicle-stimulating hormone; GC, gastric cancer; GCA, gastric cardia adenocarcinoma; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; HPFS, Health Professional Follow-up Study; ICC, intrahepatic cholangiocarcinoma; JPHC, Japan Public Health Center-based Prospective Study; LC, liver cancer; LH, luteinizing hormone; NA, not available; NHS, Nurses' Health Study; NIT, Linxian Nutrition Intervention Trial; NSHDS, Northern Sweden Health and Disease Study; PC, pancreatic cancer; PHSII, Physicians' Health Study II; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; RC, rectal cancer; SHBG, sex hormone-binding globulin; WHS, Women's Health Study.

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