

ABSENCE OF EXCESS BODY FATNESS

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2.2.17 Cancer of the urinary bladder

Cancer of the urinary bladder accounts for approximately 3% of all cancers and is the ninth most common cancer worldwide. The incidence of urinary bladder cancer in men is approximately 4 times that in women. The average age of diagnosis is after age 70 years. Globally, incidence rates are highest in Europe and North America and lowest in Asia and Latin America.

The strongest risk factor is smoking, as was established several decades ago ([IARC, 1986](#)). Compared with never-smokers, smokers have a 6-fold increase in the risk of developing urinary bladder cancer ([WCRF/AICR, 2015](#)). Other risk factors include occupational exposure to aromatic amines and polyaromatic hydrocarbons.

About 90% of urinary bladder cancers are transitional cell carcinoma; the remainder are squamous cell carcinoma, adenocarcinoma, and small cell carcinoma.

(a) Cohort studies

See Table 2.2.17a (web only; available at: <http://publications.iarc.fr/570>).

A total of 23 prospective cohorts were identified that evaluated associations between BMI and either urinary bladder cancer incidence (19 studies) ([Tulinius et al., 1997](#); [Nagano et al., 2000](#); [Tripathi et al., 2002](#); [Samanic et al., 2004, 2006](#); [Oh et al., 2005](#); [Rapp et al., 2005](#); [Cantwell et al., 2006](#); [Holick et al., 2007](#); [Reeves et al., 2007](#); [Jee et al., 2008](#); [Koebnick et al., 2008](#); [Larsson et al., 2008](#); [Prentice et al., 2009](#); [Andreotti et al., 2010](#); [Häggström et al., 2011](#); [Bhaskaran et al., 2014](#); [Roswall et al., 2014](#); [Song et al., 2014](#)) or urinary bladder cancer-related mortality (5 studies) ([Calle et al., 2003](#); [Batty et al., 2005](#); [Fujino et al., 2007](#); [Reeves et al., 2007](#); [Parr et al., 2010](#)) as the end-point. The large majority of these studies reported no significant association with urinary bladder cancer incidence or mortality.

Two studies did show a positive association between BMI and risk of urinary bladder cancer. The NIH-AARP cohort ([Koebnick et al., 2008](#)) reported significantly increased associations with overweight (RR, 1.16; 95% CI, 1.03–1.29), obesity I (RR, 1.23; 95% CI, 1.06–1.43), and obesity II (RR, 1.30; 95% CI, 1.04–1.63) in men and women combined, compared with normal weight; stratified analysis indicated that these positive associations were limited to men. The EPIC study ([Roswall et al., 2014](#)) found a small but significant association for BMI in men only (RR per 2 kg/m², 1.05; 95% CI, 1.02–1.08), with a strong dose–response relationship. Findings from the Iowa Women’s Health Study ([Tripathi et al., 2002](#)) demonstrated a statistically marginal inverse association between BMI and urinary bladder cancer incidence also in men only ($P_{\text{trend}} = 0.06$ after adjustments).

Almost all studies adjusted for smoking. Stratified analyses suggested that the associations were stronger in former smokers than in never-smokers. Four studies ([Calle et al., 2003](#); [Reeves et al., 2007](#); [Koebnick et al., 2008](#); [Bhaskaran et al., 2014](#)) specifically stratified by never versus ever smoking status and statistically tested for interactions. None of those interactions were significant.

Several studies reported on the associations between BMI and urinary bladder cancer in Asian populations ([Nagano et al., 2000](#); [Oh et al., 2005](#); [Fujino et al., 2007](#); [Jee et al., 2008](#); [Parr et al., 2010](#)). No pattern of difference compared with European or North American populations was noted.

From a large meta-analysis for the association between BMI and urinary bladder cancer risk, based on 22 prospective cohort studies, the summary risk estimate was 1.03 (95% CI, 0.97–1.09) ([WCRF/AICR, 2015](#)). Two additional meta-analyses, of 11 cohort studies ([Qin et al., 2013](#)) and 15 cohort studies ([Sun et al., 2015](#)), reported summary risk estimates of positive

associations between BMI and urinary bladder cancer. [These differences in part reflect variations in study inclusion. In the meta-analysis by [Sun et al., \(2015\)](#), the summary estimate may have been disproportionately influenced by an incorrect data extraction of risk estimates from the FINRISK study ([Song et al., 2014](#)).]

Three studies evaluated the relationship between waist circumference and urinary bladder cancer risk. Two studies ([Tripathi et al., 2002](#); [Larsson et al., 2008](#)) found no significant association; the third study, based on the EPIC cohort ([Roswall et al., 2014](#)), found a small but significant association with waist circumference in men only (RR per 5 cm, 1.04; 95% CI, 1.01–1.08).

(b) Case-control studies

See Table 2.2.17b (web only; available at: <http://publications.iarc.fr/570>).

The four case-control studies that evaluated the relationship between BMI and urinary bladder cancer incidence ([Pelucchi et al., 2002](#); [Lin et al., 2010](#); [MacKenzie et al., 2011](#); [Attner et al., 2012](#)) found no significant associations.

References

- Andreotti G, Hou L, Beane Freeman LE, Mahajan R, Koutros S, Coble J, et al. (2010). Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort. *Cancer Causes Control*, 21(11):1759–75. doi:[10.1007/s10552-010-9603-9](https://doi.org/10.1007/s10552-010-9603-9) PMID:[20730623](https://pubmed.ncbi.nlm.nih.gov/20730623/)
- Attner B, Landin-Olsson M, Lithman T, Noreen D, Olsson H (2012). Cancer among patients with diabetes, obesity and abnormal blood lipids: a population-based register study in Sweden. *Cancer Causes Control*, 23(5):769–77. doi:[10.1007/s10552-012-9946-5](https://doi.org/10.1007/s10552-012-9946-5) PMID:[22467266](https://pubmed.ncbi.nlm.nih.gov/22467266/)
- Batty GD, Shipley MJ, Jarrett RJ, Breeze E, Marmot MG, Smith GD (2005). Obesity and overweight in relation to organ-specific cancer mortality in London (UK): findings from the original Whitehall study. *Int J Obes*, 29(10):1267–74. doi:[10.1038/sj.ijo.0803020](https://doi.org/10.1038/sj.ijo.0803020) PMID:[15997248](https://pubmed.ncbi.nlm.nih.gov/15997248/)
- Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L (2014). Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet*, 384(9945):755–65. doi:[10.1016/S0140-6736\(14\)60892-8](https://doi.org/10.1016/S0140-6736(14)60892-8) PMID:[25129328](https://pubmed.ncbi.nlm.nih.gov/25129328/)
- Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*, 348(17):1625–38. doi:[10.1056/NEJMoa021423](https://doi.org/10.1056/NEJMoa021423) PMID:[12711737](https://pubmed.ncbi.nlm.nih.gov/12711737/)
- Cantwell MM, Lacey JV Jr, Schairer C, Schatzkin A, Michaud DS (2006). Reproductive factors, exogenous hormone use and bladder cancer risk in a prospective study. *Int J Cancer*, 119(10):2398–401. doi:[10.1002/ijc.22175](https://doi.org/10.1002/ijc.22175) PMID:[16894568](https://pubmed.ncbi.nlm.nih.gov/16894568/)
- Fujino Y; Japan Collaborative Cohort Study for Evaluation of Cancer (2007). Anthropometry, development history and mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). *Asian Pac J Cancer Prev*, 8(Suppl):105–12. PMID:[18260709](https://pubmed.ncbi.nlm.nih.gov/18260709/)
- Hägström C, Stocks T, Rapp K, Bjørge T, Lindkvist B, Concin H, et al. (2011). Metabolic syndrome and risk of bladder cancer: prospective cohort study in the Metabolic Syndrome and Cancer Project (Me-Can). *Int J Cancer*, 128(8):1890–8. doi:[10.1002/ijc.25521](https://doi.org/10.1002/ijc.25521) PMID:[20568111](https://pubmed.ncbi.nlm.nih.gov/20568111/)
- Holick CN, Giovannucci EL, Stampfer MJ, Michaud DS (2007). Prospective study of body mass index, height, physical activity and incidence of bladder cancer in US men and women. *Int J Cancer*, 120(1):140–6. doi:[10.1002/ijc.22142](https://doi.org/10.1002/ijc.22142) PMID:[17036323](https://pubmed.ncbi.nlm.nih.gov/17036323/)
- IARC (1986). Tobacco smoking. *IARC Monogr Eval Carcinog Risk Chem Hum*, 38:1–421. Available from: <http://publications.iarc.fr/56>.
- Jee SH, Yun JE, Park EJ, Cho ER, Park IS, Sull JW, et al. (2008). Body mass index and cancer risk in Korean men and women. *Int J Cancer*, 123(8):1892–6. doi:[10.1002/ijc.23719](https://doi.org/10.1002/ijc.23719) PMID:[18651571](https://pubmed.ncbi.nlm.nih.gov/18651571/)
- Koebnick C, Michaud D, Moore SC, Park Y, Hollenbeck A, Ballard-Barbash R, et al. (2008). Body mass index, physical activity, and bladder cancer in a large prospective study. *Cancer Epidemiol Biomarkers Prev*, 17(5):1214–21. doi:[10.1158/1055-9965.EPI-08-0026](https://doi.org/10.1158/1055-9965.EPI-08-0026) PMID:[18483344](https://pubmed.ncbi.nlm.nih.gov/18483344/)
- Larsson SC, Andersson SO, Johansson JE, Wolk A (2008). Diabetes mellitus, body size and bladder cancer risk in a prospective study of Swedish men. *Eur J Cancer*, 44(17):2655–60. doi:[10.1016/j.ejca.2008.07.012](https://doi.org/10.1016/j.ejca.2008.07.012) PMID:[18707871](https://pubmed.ncbi.nlm.nih.gov/18707871/)
- Lin J, Wang J, Greisinger AJ, Grossman HB, Forman MR, Dinney CP, et al. (2010). Energy balance, the PI3K-AKT-mTOR pathway genes, and the risk of bladder cancer. *Cancer Prev Res (Phila)*, 3(4):505–17. doi:[10.1158/1940-6207.CAPR-09-0263](https://doi.org/10.1158/1940-6207.CAPR-09-0263) PMID:[20354165](https://pubmed.ncbi.nlm.nih.gov/20354165/)

- MacKenzie T, Zens MS, Ferrara A, Schned A, Karagas MR (2011). Diabetes and risk of bladder cancer: evidence from a case-control study in New England. *Cancer*, 117(7):1552–6. doi:[10.1002/cncr.25641](https://doi.org/10.1002/cncr.25641) PMID:[21425156](https://pubmed.ncbi.nlm.nih.gov/21425156/)
- Nagano J, Kono S, Preston DL, Moriwaki H, Sharp GB, Koyama K, et al. (2000). Bladder-cancer incidence in relation to vegetable and fruit consumption: a prospective study of atomic-bomb survivors. *Int J Cancer*, 86(1):132–8. doi:[10.1002/\(SICI\)1097-0215\(20000401\)86:1<132::AID-IJC21>3.0.CO;2-M](https://doi.org/10.1002/(SICI)1097-0215(20000401)86:1<132::AID-IJC21>3.0.CO;2-M) PMID:[10728607](https://pubmed.ncbi.nlm.nih.gov/10728607/)
- Oh SW, Yoon YS, Shin SA (2005). Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. *J Clin Oncol*, 23(21):4742–54. doi:[10.1200/JCO.2005.11.726](https://doi.org/10.1200/JCO.2005.11.726) PMID:[16034050](https://pubmed.ncbi.nlm.nih.gov/16034050/)
- Parr CL, Batty GD, Lam TH, Barzi F, Fang X, Ho SC, et al.; Asia-Pacific Cohort Studies Collaboration (2010). Body-mass index and cancer mortality in the Asia-Pacific Cohort Studies Collaboration: pooled analyses of 424,519 participants. *Lancet Oncol*, 11(8):741–52. doi:[10.1016/S1470-2045\(10\)70141-8](https://doi.org/10.1016/S1470-2045(10)70141-8) PMID:[20594911](https://pubmed.ncbi.nlm.nih.gov/20594911/)
- Pelucchi C, La Vecchia C, Negri E, Dal Maso L, Franceschi S (2002). Smoking and other risk factors for bladder cancer in women. *Prev Med*, 35(2):114–20. doi:[10.1006/pmed.2002.1061](https://doi.org/10.1006/pmed.2002.1061) PMID:[12200095](https://pubmed.ncbi.nlm.nih.gov/12200095/)
- Prentice RL, Shaw PA, Bingham SA, Beresford SA, Caan B, Neuhauser ML, et al. (2009). Biomarker-calibrated energy and protein consumption and increased cancer risk among postmenopausal women. *Am J Epidemiol*, 169(8):977–89. doi:[10.1093/aje/kwp008](https://doi.org/10.1093/aje/kwp008) PMID:[19258487](https://pubmed.ncbi.nlm.nih.gov/19258487/)
- Qin Q, Xu X, Wang X, Zheng XY (2013). Obesity and risk of bladder cancer: a meta-analysis of cohort studies. *Asian Pac J Cancer Prev*, 14(5):3117–21. doi:[10.7314/APJCP.2013.14.5.3117](https://doi.org/10.7314/APJCP.2013.14.5.3117) PMID:[23803089](https://pubmed.ncbi.nlm.nih.gov/23803089/)
- Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, et al. (2005). Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. *Br J Cancer*, 93(9):1062–7. doi:[10.1038/sj.bjc.6602819](https://doi.org/10.1038/sj.bjc.6602819) PMID:[16234822](https://pubmed.ncbi.nlm.nih.gov/16234822/)
- Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; Million Women Study Collaboration (2007). Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ*, 335(7630):1134. doi:[10.1136/bmj.39367.495995.AE](https://doi.org/10.1136/bmj.39367.495995.AE) PMID:[17986716](https://pubmed.ncbi.nlm.nih.gov/17986716/)
- Roswall N, Freisling H, Bueno-de-Mesquita HB, Ros M, Christensen J, Overvad K, et al. (2014). Anthropometric measures and bladder cancer risk: a prospective study in the EPIC cohort. *Int J Cancer*, 135(12):2918–29. doi:[10.1002/ijc.28936](https://doi.org/10.1002/ijc.28936) PMID:[24771290](https://pubmed.ncbi.nlm.nih.gov/24771290/)
- Samanic C, Chow WH, Gridley G, Jarvholm B, Fraumeni JF Jr (2006). Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control*, 17(7):901–9. doi:[10.1007/s10552-006-0023-9](https://doi.org/10.1007/s10552-006-0023-9) PMID:[16841257](https://pubmed.ncbi.nlm.nih.gov/16841257/)
- Samanic C, Gridley G, Chow WH, Lubin J, Hoover RN, Fraumeni JF Jr (2004). Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control*, 15(1):35–43. doi:[10.1023/B:CACO.0000016573.79453.ba](https://doi.org/10.1023/B:CACO.0000016573.79453.ba) PMID:[14970733](https://pubmed.ncbi.nlm.nih.gov/14970733/)
- Song X, Pukkala E, Dyba T, Tuomilehto J, Moltchanov V, Männistö S, et al. (2014). Body mass index and cancer incidence: the FINRISK study. *Eur J Epidemiol*, 29(7):477–87. doi:[10.1007/s10654-014-9934-z](https://doi.org/10.1007/s10654-014-9934-z) PMID:[24997743](https://pubmed.ncbi.nlm.nih.gov/24997743/)
- Sun JW, Zhao LG, Yang Y, Ma X, Wang YY, Xiang YB (2015). Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. *PLoS One*, 10(3):e0119313. doi:[10.1371/journal.pone.0119313](https://doi.org/10.1371/journal.pone.0119313) PMID:[25803438](https://pubmed.ncbi.nlm.nih.gov/25803438/)
- Tripathi A, Folsom AR, Anderson KE; Iowa Women's Health Study (2002). Risk factors for urinary bladder carcinoma in postmenopausal women. The Iowa Women's Health Study. *Cancer*, 95(11):2316–23. doi:[10.1002/cncr.10975](https://doi.org/10.1002/cncr.10975) PMID:[12436437](https://pubmed.ncbi.nlm.nih.gov/12436437/)
- Tulinus H, Sigfússon N, Sigvaldason H, Bjarnadóttir K, Tryggvadóttir L (1997). Risk factors for malignant diseases: a cohort study on a population of 22,946 Icelanders. *Cancer Epidemiol Biomarkers Prev*, 6(11):863–73. PMID:[9367058](https://pubmed.ncbi.nlm.nih.gov/9367058/)
- WCRF/AICR (2015). Continuous Update Project Report. Diet, nutrition, physical activity and bladder cancer. Washington (DC), USA: American Institute for Cancer Research. Available from: <https://www.wcrf.org/sites/default/files/Bladder-Cancer-2015-Report.pdf>.