

Supplementary Materials

Supplementary table 1 contains ecological, observational and interventional studies addressing specific external exposures in PCa.

Author, Year	Country	Study Design	Population	Exposure	Findings	Observations
Korc, 2017 (26)	USA	Meta-analysis	10 studies	Smoking	(+) PCa <sup>1</sup> risk: current vs. never smokers (RR <sup>2</sup> 1.66; 95%CI <sup>3</sup> 1.38-1.98); former vs. never smokers (RR 1.40; 95%CI 1.16-1.67); current vs. former smokers (RR 1.18; 95%CI 1.00-1.38)	
Kuzmickiene, 2012 (31)	Lithuania	Cohort	PCa cases (n=77)	Smoking	(+) PCa risk: higher smoking intensity >20 cigarettes/day (HR <sup>4</sup> 2.60; 95%CI 1.42-3.09); >30 pack-years (HR 2.24; 95%CI 1.12-4.49); age < 18 years (HR 2.29; 95%CI 1.11-4.70)	Adjusted for age, BMI <sup>5</sup> , education, and alcohol consumption
Wang, 2014 (32)	China	Case-control	Cases (n=307), controls (n=1,228)	Smoking	(+) PCa risk: current smokers (OR <sup>6</sup> 1.71; 95%CI 1.25-2.35); >20 cigarettes/day (OR 2.18; 95%CI 1.66-3.69)	
Heinen, 2010 (33)	The Netherlands	Cohort	PCa cases (n=520)	Smoking	(+) PCa risk: former smokers (HR 1.34; 95%CI 1.02-1.75), current smokers (HR 1.82; 95%CI 1.40-2.38); per increment of 10 years (HR 1.15; 95%CI 1.08-1.22); per 10 cigarettes per day (HR 1.08; 95%CI 0.98-1.19).	
Hassan, 2007 (25)	USA	Case-control	Cases (n=808), controls (n=808)	Smoking, Passive Smoking and Non-Cigarette Smoking	(+) PCa risk: Men: smoking and DM <sup>7</sup> (OR 3.6; 95%CI 1.8-7.2); smoking and FHPC <sup>9</sup> (OR 2.4; 95%CI 1.1-5.4). Women: smoking and DM (OR 9.3; 95%CI 2.0-44.1); smoking and FHPC (OR 10.1; 95%CI 2.2-45.9); (+) PCa risk: current smoking (OR 1.7; 95%CI 1.4-2.2); passive smoking (OR 1.7; 95%CI 1.03-2.6); cigar smoking (OR 2.2; 95%CI 1.0-4.7)	Adjusted for age, sex, ethnicity, history of DM, FH <sup>8</sup> of cancer, alcohol consumption, education level, and state of residency.
Antwi, 2016 (24)	USA	Case-control	Cases (n=817), controls (n=1,756)	Smoking	(+) PCa risk: former vs. never smokers (OR 1.29; 95%CI 1.07-1.54); current vs. never smokers (OR 3.40; 95%CI 2.28-5.07); high DII <sup>10</sup> score and current smokers (OR 4.79; 95%CI 3.00-7.65)	
Matsubayashi, 2011 (27)	Japan	Case-control	Cases (n=577), controls (n=577)	Smoking	(+) PCa risk: FH of Pca (OR 2.5; 95%CI 1.37-4.38); current smokers (OR 1.5; 95%CI 1.12-1.89); DM (OR 1.7; 95%CI 1.23-2.28); 3 factors combined (OR 10.1; 95%CI 1.25-81.32)	

Villeneuve, 2004 (41)	Canada	Case-control	Cases (n=583), controls (n=4,813)	Environmental Tobacco Smoke (ETS)	(+/-) PCa risk: ETS <sup>11</sup> exposure (OR 1.21; 95%CI 0.60-2.44)	Adjusted for age, sex, BMI, SES <sup>12</sup> and providence of residency
Lo, 2007 (38)	Egypt	Case-control	Cases (n=194), controls (n=194)	Passive Smoking	(+) PCa risk: passive smoking (OR 6.0; 95%CI 2.4-14.8); cigarette smoking (OR 4.5; 95%CI 1.9-10.7); cigarette and non-cigarette smokers (OR 7.8; 95%CI 3.0-20.6).	Adjusted for age, sex and area of residence
Korc, 2017 (26)	USA	Meta-Analysis	10 studies	Alcohol Consumption	(+) PCa risk: Heavy vs. never drinkers (RR 1.29; 95%CI 1.20-1.38); heavy vs. light drinkers (RR 1.36; 95%CI 1.02-1.80)	
Lu, 2006 (46)	China	Case-control	Cases (n=119), controls (n=238)	Alcohol Consumption	(+) PCa risk: Heavy drinkers (>20 cup-years) (OR 3.68; 95%CI 1.60-8.44)	
Genkinger, 2009 (43)	USA	Meta-Analysis	14 studies	Alcohol Consumption	(+) PCa risk: heavy drinkers (>30g/day) (RR 1.22; 95%CI 1.03-1.45); alcohol consumption in females (RR 1.41; 95%CI 1.07-1.85)	Adjusted for smoking, history of DM, energy intake and age.
Klein, 2013 (45)	USA	Pooled Analysis	Cases (n=3,349), controls (n=3,654)	Alcohol Consumption	(+) PCa risk: heavy drinkers (>3 drinks/day) (OR 1.45; 95%CI 1.19-1.76)	
Brand, 2009 (34)	USA	Pooled Analysis	2 cohorts (CIRF and UMPCR)	Alcohol Consumption	(+) PCa risk: current vs. never drinkers; current drinkers were diagnosed at significantly younger age than never drinkers (65yrs vs.70 - CIRF; 60yrs vs. 65yrs- UMPCR)	
Hassan, 2007 (37)	USA	Case-Control	Cases (n=808), controls (n=808)	Alcohol Consumption	(+) PCa risk: heavy drinkers (>60 mL/day) (OR 1.6; 95%CI 1.1-2.5)	Adjusted for age, sex, ethnicity, smoking, history of DM, FH of PCa, history of pancreatitis, education level, and state of residency
La Torre, 2014 (220)	Italy	Case-Control	Cases (n=80), controls (n=392)	Alcohol Consumption	(+) PCa risk: alcohol consumption (OR 2.25; 95%CI 1.30-3.89); alcohol consumption and hypercholesterolemia (OR 5.11; 95%CI 2.66-9.82); alcohol consumption and DM (OR 3.31; 95%CI 1.50-7.32)	Adjusted for work activity, DM and ever smoking
Naudin, 2018 (48)	EPIC Study	Cohort	PCa cases (n=1,283)	Alcohol Consumption	(+) PCa risk: heavy drinkers (>60g/day)(HR 1.77; 95%CI 1.06-2.95); beer consumption (>40g/day)(HR 1.58; 95%CI 1.97-2.34); spirits consumption (>10g/day)(HR 1.41; 95%CI 1.93-2.94)	Only in men
Gupta, 2010 (44)	USA	Case-Control	Cases (n=532), controls (n=1,701)	Alcohol Consumption	(+) PCa risk: heavy drinkers (22-35 drinks/week)(OR 2.2; 95%CI 1.1-4.0); (>35 drinks/week)(OR 2.6; 95%CI 1.6-7.5)	Adjusted for age, energy intake, BMI, ethnicity, smoking, DM, and physical activity

McWilliams, 2016 (47)	USA	Meta-Analysis	8 Studies	Alcohol Consumption	(+) PCa risk: heavy drinkers (>26 g/day) EOPC <sup>13</sup> (OR 1.49; 95%CI 1.21-1.84); VEOPC <sup>14</sup> (OR 2.18; 95%CI 1.17-4.09)	Adjusted for FH of PCa, history of DM, sex, smoking, BMI, and study site
Lu, 2017 (238)	China	Meta-Analysis	32 Studies	Dietary Patterns	(-) Pca risk: highest category of healthy pattern (OR 0.86; 95%CI 0.77-0.95); (+) PCa risk: highest category of western-type diet (OR 1.24; 95%CI 1.06-1.45)	Healthy pattern: high intake of vegetables, fruits, whole grains, olive oil, fish, soy, poultry and low-fat dairy products. Western-type pattern: red and/or processed meat, refined grains, sweets, high-fat gravy and low intake of fruits and vegetables.
Antwi, 2018 (54)	USA	Meta-Analysis	11 Studies (PanScan and PanC4)	Dietary Patterns	(+) PCa risk: High DII score -Q5 vs. Q1 (OR 2.20; 95%CI 1.85-2.61)	
Antwi, 2016 (24)	USA	Case-Control	Cases (n=817), controls (n=1,756)	Dietary Patterns	(+) PCa risk: High DII score (OR 2.54; 95%CI 1.87-3.46); high DII score and DM (OR 6.03; 95%CI 3.00-7.65)); high DII score and smoking (OR 4.79; 95%CI 3.00-7.65)	
Shivappa, 2015 (56)	Italy	Case-Control	Cases (n=326), controls (n=652)	Dietary Patterns	(+) PCa risk: High DII score Q <sup>15</sup> vs. Q1 (OR 2.48; 95%CI 1.50-4.10)	
Larsson, 2012 (55)	Sweden	Meta-Analysis	11 Studies	Dietary Patterns	(+) PCa risk: 120g increase per day in red meat (RR 1.13; 95%CI 0.93-1.39); 50g per day increase in processed meat consumption (RR 1.19; 1.04-1.36)	
Ghadirian, 1995 (239)	Canada	Case-Control	Cases (n=179), Controls (n=239)	Dietary Patterns	(+) Pca risk: high salt consumption (RR 4.28; 95%CI 2.20-8.36); smoked meat (RR 4.68; 95%CI 2.05-10.69); dehydrated food (RR 3.10; 95%CI 1.55-6.22); fried food (RR 3.84; 95%CI 1.74-8.48); (-) Pca risk: food with no preservatives (RR 0.08; 95%CI 0.01-0.59); raw food (RR 0.28; 95%CI 0.10-0.75)	
Abdelrehim, 2018 (240)	Egypt	Case-Control	Cases (n=75), controls (n=149)	Dietary Patterns	(+) PCa risk: High DII (OR 9.88; 95%CI 2.56-38.1); vegetable intake (OR 0.24; 95%CI 0.07-0.85)	Adjusted for age, smoking, physical activity, mental stress and total energy intake
Zheng, 2018 (67)	USA	Cohort	PCa cases (n=328)	Dietary Patterns	No significant associations	
Zheng, 2019 (68)	USA	Cohort	PCa cases (n=2,824)	Dietary Patterns	No significant associations	
Mueller, 2010 (70)	Singapore	Cohort	PCa cases (n=140)	Soft drink and juice consumption	(+) PCa risk: >2 drinks/week (HR 1.87; 95%CI 1.10-3.25)	Adjusted for age, sex, ethnicity, year of interview, education, smoking,

Schernhammer, (86)	2005	USA	Cohort	PCa cases (n=379)	Soft drink and juice consumption	(+) PCa risk: >3 drinks/week (RR 1.57; 95%CI 1.02-2.41)	PA <sup>16</sup> , alcohol, added sugar and candy
Nothlings, 2007 (72)		USA	Cohort	PCa cases (n=434)	Soft drink and juice consumption	(+) PCa risk: Q4 vs. Q1- fructose (RR 1.35; 95%CI 1.02-1.80) and other sugars; juice and fruit intake (RR 1.37; 95%CI 1.02-1.84)	Adjusted for ethnicity, age at cohort entry, smoking status, pack-years of smoking, family history of pancreatic cancer, energy intake, intakes of red meat and processed meat, and BMI
Guertin, 2015 (9)		USA	Cohort	PCa cases (n=1,541)	Coffee consumption	No significant associations	
Bidel, 2013 (241)		Finland	Cohort	PCa cases (n=235)	Coffee consumption	No significant associations	
Turati, 2011 (74)		Italy	Pooled Analysis	Cases (n=688), controls (n=2,204)	Coffee and tea consumption	(+) Pca risk: coffee drinkers (OR 1.34; 95%CI 1.01-1.77) - no trend in risk associated to dose and duration / No associations for decaffeinated coffee or tea.	Adjusted for age, sex, center, year of interview, education, BMI, smoking, alcohol drinking, and DM
Banim, 2013 (75)		UK	Cohort	PCa cases (n=49)	Dietary Antioxidants	(-) PCa risk: Q4 vs. Q1 - vitamin C (HR 0.33; 95%CI 0.13-0.84); Selenium (HR 0.49; 95%CI 0.26-0.93), Vitamin E (HR 0.57; 95%CI 0.29-1.09)	
Lucas, 2016 (76)		Italy	Case-Control	Cases (n=326), controls (n=652)	Dietary Antioxidants	(-) Pca risk: Q3 vs. Q1 antioxidants (OR 0.61; 95%CI 0.39-0.94)	
Lin, 2005 (58)		Japan	Case-Control	Cases (n=109), Controls (n=109)	Dietary Antioxidants	(-) PCa risk: Q3 vs. Q1- Vitamin C (OR 0.45; 95%CI 0.22-0.94) / No associations found with Vitamin E	Adjusted for energy intake
Waterhouse, 2015 (77)		USA	Meta-Analysis	9 Studies	Vitamin D	(+) Pca risk: Dietary vitamin D - per 110 IU/day (OR 1.13; 95%CI 1.07-1.19); >230 vs <110 UI/day (OR 1.31; 95%CI 1.10-1.55)	
Stolzenberg-Solomon, 2009 (79)		Finland	Case-Control	Cases (n=184), Controls (n=368)	Vitamin D	No significant associations with serum Vitamin D / (+) PCa risk in patients with low estimated annual residential solar UVB exposure	
Stolzenberg-Solomon, 2010 (78)		USA	Meta-Analysis	8 Studies	Vitamin D	(+) PCa risk: High serum Vitamin D (>100 nmol/L)(OR 2.12; 95%CI 1.23-3.64)	
Chuang, 2011 (80)		European Prospective Investigation	Case-Control	Cases (n=463), Controls (n=463)	Folate Intake	No significant associations	

	into Cancer and Nutrition (EPIC) study						
Stolzenberg-Solomon, 1999 (82)	Finland	Case-Control	Cases (n=126), Controls (n=247)	Folate Intake	(-) PCa risk: Q3 vs. Q1 – Folate (OR 0.45; 95%CI 0.24-0.82)		
Skinner, 2004 (207)	USA	Cohort	PCa cases (n=326)	Folate Intake	No significant associations	Adjusted for age, energy intake, smoking, BMI, DM, height.	
Gong, 2009 (81)	USA	Case-Control	Cases (n=532), Controls (n=1,701)	Folate Intake	(-) Pca risk: Q5 vs Q1 - Folate intake (OR 0.67; 95%CI 0.48-0.93)	Adjusted for age, sex, total energy intake, BMI, DM, and alcohol consumption	
Bradley, 2010 (223)	UK	Case-Control	Cases (n=1,141), Controls (n=7,954)	Nonsteroidal Anti-inflammatory Drugs	(-) PCa risk: Chronic NSAID <sup>17</sup> use (OR 0.78; 95%CI 0.62-0.97)		
Archibugi, 2017 (83)	Italy	Case-Control	Cases (n=408), Controls (n=816)	Nonsteroidal Anti-inflammatory Drugs	No significant associations		
Khalaf, 2018 (87)	USA	Pooled Analysis	PCa cases (n=1,112)	Nonsteroidal Anti-inflammatory Drugs	(-) Pca risk: regular use of aspirin in patients with DM (RR 0.71; 95%CI 0.54-0.94) / No other significant associations		
Schernhammer, 2004 (86)	USA	Cohort	PCa cases (n=161)	Nonsteroidal Anti-inflammatory Drugs	(+) PCa risk: chronic NSAID use (RR 1.58; 95%CI 1.03-2.43) / No associations related with dose	Adjusted for age, DM, smoking, physical activity and BMI– Only women in this analysis	
Coogam, 2000 (85)	USA	Cohort	PCa cases (n=504)	Nonsteroidal Anti-inflammatory Drugs	No significant associations		
Wang, 2013 (89)	China	Meta-Analysis	10 Studies	Hepatitis B Virus	(+)PCa risk: Chronic or inactive HBV <sup>18</sup> infection (OR 1.60; 95%CI 1.26-2.06)		
Xing, 2013 (88)	China	Meta-Analysis	10 Studies	Hepatitis B Virus and Hepatitis C Virus	(+) PCa risk: HBV infection (OR 1.28; 1.11-1.48); HCV <sup>19</sup> infection (OR 1.21; 95%CI 1.02-1.44)	*One study included in meta-analysis above	
Song, 2019 (90)	China	Cohort	PCa cases (n=504)	Hepatitis B Virus	(+) PCa risk: HBV infection (HR 1.65; 95%CI 1.03-2.65)		
Chang, 2014 (91)	China	Case-Control	Cases (n=585), Control (n=1,716)	Hepatitis B Virus and Hepatitis C Virus	No significant associations		

Tang, 2014 (92)	USA	Cohort	PCa cases (n=200)	Hepatitis B Virus	No significant associations	
Ai, 2015 (94)	China	Cohort	PCa cases (n=56)	Helicobacter Pylori	H. Pylori infection rate was 64% in the observation group vs. 47% in the control group	
Hirabayashi, 2019 (96)	Japan	Cohort	PCa cases (n=119)	Helicobacter Pylori	No significant associations	
Risch, 2014 (231)	China	Case-Control	Cases (n=761), Controls (n=794)	Helicobacter Pylori	No significant associations	
Risch, 2013 (231)	China	Meta-Analysis	24 Studies	Helicobacter Pylori	(+) PCa risk: H. Pylori infection – ABO group A, B and AB (OR 1.40 (95%CI 1.32-1.49); OR 1.38 (95%CI 1.16-1.64); OR 1.52 (95%CI 1.24-1.84), respectively)	
Lindkvist, 2008 (97)	Sweden	Cohort	PCa cases (n=87)	Helicobacter Pylori	No significant associations*	
De Martel, 2008 (95)	USA	Case-Control	Cases (n=104), Controls (n=597)	Helicobacter Pylori	No significant associations	
Chen, 2016 (98)	China	Cohort	PCa cases (n=)	Helicobacter Pylori	No significant associations	
Caygill, 1994 (103)	UK	Cohort	PCa cases (n=)	Typhoid and Paratyphoid Carriers	(+) Pca risk: chronic typhoid and paratyphoid carriers (OR 8.1)	
Gotland, 2020 (104)	Denmark	Cohort	PCa cases (n=)	Staphylococcus Aureus Bacteremia	(+) PCa risk: Staphylococcus aureus bacteremia (IRR 2.8; 95%CI 1.27-6.16)	
Fan, 2018 (101)	USA	Case-Control	Cases (n=121), Controls (n=371)	Oral Bacteria	(+) Pca risk: Porphyromonas gingivalis (OR 1.60; 95%CI 1.15-2.22) and Aggregatibacter actinomycetemcomitans (OR 2.20; 95%CI 1.16-4.18) / (-) Pca risk: Non-oral bacteria- Phylum Fusobacteria (OR 0.94; 95%CI 0.89-0.99) and its genus Leptotrichia (OR 0.87; 95%CI 0.79-0.95)	Adjusted for age, ethnicity, sex, BMI, smoking, alcohol intake, and DM
Michaud, 2013 (102)	European Prospective Investigation into Cancer and Nutrition (EPIC) study	Cohort	PCa cases (n=405)	Oral Bacteria	(+) Pca risk: porphyromonas gingivalis (OR 2.14; 95%CI 1.05-4.36) / (-) Pca risk: antibodies against non-pathogenic oral bacteria (OR 0.55; 95%CI 0.36-0.83)	
Michaud, 2007 (100)	USA	Cohort	PCa cases (n=216)	Periodontal Disease	(+) PCa risk: periodontal disease (RR 1.64; 95% CI 1.19-2.26)	Adjusted for age, smoking, profession, ethnicity, geographic location, physical activity, BMI,

							height, cholecystectomy, NSAIDs, and baseline teeth number
Gerlovin, 2019 (99)	USA	Cohort	PCa cases (n=78)	Periodontal Disease		No significant associations	
Bosetti, 2013 (109)	Italy	Meta-Analysis	10 Studies	Peptic Disease	Ulcer	No significant associations	Adjusted for study, study center (for multicenter studies), age, sex, race/ethnicity, education, body mass index, tobacco smoking, alcohol drinking, history of diabetes, and history of pancreatitis.
Bao, 2010 (105)	USA	Cohort	PCa cases (n=274)	Peptic Disease	Ulcer	(+) Pca risk: gastric ulcer (RR 1.83; 95%CI 1.13-2.97)	Adjusted for age, smoking, DM, BMI, PA
Luo, 2007 (106)	Sweden	Cohort	PCa cases (n=)	Peptic Disease	Ulcer	(+) Pca risk: gastric ulcer (SIR <sup>21</sup> 1.5; 95%CI 1.1-2.0); duodenal ulcer (SIR 1.6; 95%CI 1.1-2.1)	
Ko, 2007 (242)	USA	Case-Control	Cases (n=532), Controls(n=1,701)	Peptic Disease	Ulcer	(+) Pca risk: duodenal ulcer (OR 2.3; 95%CI 1.1-4.6)	
Lo, 2007 (38)	Egypt	Case-Control	Cases (n=194), Controls (n=194)	Occupational Exposures		(+) Pca risk: Pesticide exposure (OR 2.6; 95%CI 0.97-7.2)	Adjusted for age, sex and residence
Kauppinen, 1995 (120)	Finland	Case-Control	Cases (n=595), Controls (n=1,622)	Occupational Exposures		(+) Pca risk: Ionizing radiation (OR 4.3; 95%CI 1.6-11.4); inorganic dust containing silica (OR 2.0; 95%CI 1.2-3.5)	
Hoppin, 2000 (114)	USA	Case-Control	Cases (n=108), Controls (n=82)	Occupational Exposures		(+) Pca risk: Pesticide exposure (Q3 vs Q1)(OR 4.2; 95%CI 1.8-9.4)	
Antwi, 2015 (118)	USA	Case-Control	Cases (n=2,092), Controls (n=2,353)	Occupational Exposures		(+) Pca risk: pesticides (OR 1.21; 95%CI 1.02-1.44); asbestos (OR 1.54; 95%CI 1.23-1.92); benzene (OR 1.70; 95%CI 1.23-2.35); chlorinated hydrocarbons (OR 1.63; 95%CI 1.32-2.02)	Self-reported and adjusted for age, sex, smoking, history of DM, BMI, and education.
Kachuri, 2017 (119)	Canada	Cohort	PCa cases (n=500)	Occupational Exposures		(+) Pca risk: Pesticide Exposure- women (HR 1.36; 95%CI 1.07-1.72)	Adjusted for age, province of residence, and education level
Andreotti, 2009 (111)	USA	Cohort	PCa cases (n=93)	Occupational Exposures		(+) Pca risk: Pesticide Exposure (OR 3.0; 95%CI 1.3-7.2)	
Gandini, 2005 (201)	Italy	Meta-Analysis	14 Studies	Allergies		(-) Pca risk: Allergies (RR 0.82; 95%CI 0.68-0.99); Atopy (RR 0.71; 95%CI 0.64-0.80)	
Cotterchio, 2014 (200)	Italy	Case-Control	Cases (n=345), Controls (n=1,285)	Allergies		(-) Pca risk: Hay fever (OR 0.68; 95%CI 0.52-0.89); Dust/Mold Allergy (OR 0.49; 95%CI 0.31-0.78); Animal Allergy (OR 0.68; 95%CI 0.46-0.99)	Adjusted for age
Dai, 1995 (243)	China	Case-Control	Cases (n=108), Controls (n=275)	Allergies		(-) Pca risk: Allergies (0.60; 95%CI 0.40-1.0)	Adjusted for age, sex, smoking and income

Gomez-Rubio, (202)	2015	Spain	Case-Control / Meta-Analysis	Cases (n=1,297), Controls (n=1,024) / 10 Studies	Allergies	(-) PCa risk: Asthma (OR 0.64 (95% 0.47-0.88); metaOR 0.73 (95% 0.59-0.89); long-standing asthma (>17yrs; OR 0.39 (95%CI 0.24-0.65)) / Nasal allergy (OR 0.66 (95%CI 0.52-0.83); metaOR 0.60 (95%CI 0.50-0.72)	
Anderson, 2009 (199)		Canada	Case-Control	Cases (n=422), Controls (n=312)	Allergies	(-) PCa risk: Allergies (OR 0.40; 95%CI 0.26-0.59)	Adjusted for age
Eppel, 2007 (203)		Canada	Case-Control	Cases (n=276), Controls (n=378)	Allergies	(-) PCa risk: Allergies (OR 0.43; 95%CI 0.29-0.63)	Adjusted for age

PCa, pancreatic cancer; <sup>2</sup>RR, relative risk; <sup>3</sup>CI, confidence interval; <sup>4</sup>HR, hazard ratio; <sup>5</sup>BMI, body mass index; <sup>6</sup>OR, odds ratio; <sup>7</sup>DM, diabetes mellitus; <sup>8</sup>FH, family history; <sup>9</sup>FHPC, family history of pancreatic cancer; <sup>10</sup>DII, dietary inflammatory index; <sup>11</sup>ETS, environmental tobacco exposure; <sup>12</sup>SES, socioeconomic status; <sup>13</sup>EOPC, early-onset pancreatic cancer; <sup>14</sup>VEOPC, very early-onset pancreatic cancer; <sup>15</sup>Q, quartile; <sup>16</sup>PA, physical activity; <sup>17</sup>NSAID, non-steroidal anti-inflammatory drugs; <sup>18</sup>HBV, hepatitis B virus; <sup>19</sup>HCV, hepatitis C virus; <sup>21</sup>SIR, standardized incidence ratio.

**Supplementary table 2 contains ecological, observational and interventional studies addressing internal exposures in PCa.**

Author, Year	Country	Study Design	Population	Exposure	Findings	Observations
Risch, 2012 (231)	USA	Meta-analysis	22 studies	ABO Group	(+) PCa <sup>1</sup> risk: Compared to group O, ABO group A (OR <sup>2</sup> 1.40; 95%CI 1.28-1.53); ABO group B (OR 1.19; 95%CI 1.05-1.35); ABO group AB (OR 1.29; 95%CI <sup>3</sup> 1.10-1.51)	(+) Risk PCa in endemic populations for CagA-positive H. Pylori associated with ABO group A
Antwi, 2018 (54)	USA	Meta-Analysis	11 studies (PanC4 and PanScan consortiums)	ABO Group	(+) PCa risk: non-O groups in PanC4 studies (OR 1.28; 95%CI 1.13-1.44); non-O groups in PanScan studies (OR 1.36; 95%CI 1.07-1.75)	Both adjusted for age, sex, race, personal history of DM <sup>4</sup> , family history of PCa, BMI <sup>5</sup> , and smoking
Li, 2018 (162)	China	Case-Control	Cases (n=264), controls (n=423)	ABO Group	(+) Pca risk: ABO group A (OR 2.13; 95%CI 1.41-3.22); ABO group AB (OR 2.38; 95%CI 1.31-4.32)	Adjusted for sex, age, family history of PCa, smoking, history of DM, chronic pancreatitis, hepatitis B infection, and alcohol intake.
Risch 2010 (230)	USA	Case-Control	Cases (n=373), Controls (n=690)	ABO Group	(+) PCa risk: Non-O-blood group (OR1.37; 95%CI 1.02-1.83)	Adjusted for age, sex, and smoking
Wolpin, 2010 (232)	USA	Meta-Analysis	12 Studies	ABO Group	(+) PCa risk: Compared to OO, subjects with AO and AA (ORs of 1.33 (95% CI, 1.13-1.58) and 1.61 (95% CI, 1.22-2.18)); subjects with BO and BB (ORs of 1.45 (95% CI, 1.14-1.85) and 2.42 (1.28-4.57)); Non-O + Smoking (OR 2.68; 95%CI 2.03-3.54)	

Wolpin, 2009 (155)	USA	Cohort	PCa cases (n=316)	ABO Group	(+) Pca risk: compared with group O- group A (HR <sup>6</sup> 1.32; 95%CI 1.02-1.72); group AB (HR 1.51; 95%CI 1.02-2.23); group B (HR 1.72; 95%CI 1.25-2.38)	Adjusted for age, BMI, PA <sup>5</sup> , smoking, history of DM.
Molina-Montes, 2018 (28)	Spain	Case-Control	Cases (n=1,431), Controls (n=1,090)	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (OR 1.24; 95%CI 1.01-1.52)	Adjusted for sex, age, family history of pancreatic cancer, history of smoking, DM, chronic pancreatitis, chronic hepatitis B infection, alcohol drinking, and ABO blood type.
Li, 2018 (162)	China	Case-Control	Cases (n=264), Controls (n=423)	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (OR 10.93; 95%CI 1.20-99.41)	Adjusted for age, sex, SES <sup>9</sup> , cardiovascular disease, smoking, other cancers, COPD <sup>7</sup> , BMI <sup>8</sup> , alcohol intake, and comorbidity index
Er, 2016 (153)	China	Cohort	PCa cases (n=114)	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (HR 2.53; 95%CI 1.96-3.26); poor glycaemic control (HR 3.61; 95%CI 1.34-9.78)	
Ben, 2011 (152)	China	Meta-Analysis	35 Studies	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (RR 1.94; 95%CI 1.66-2.27)	
Pang, 2017 (154)	China	Meta-Analysis	22 Studies	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (HR 1.87; 95%CI 1.48-2.37) with longer duration since diagnosis at higher risk; each 1mmol/L higher PG <sup>10</sup> (HR 1.12; 95%CI 1.04-1.21)	Adjusted for age, ethnicity, sex, alcohol intake, smoking, BMI, and FH <sup>11</sup> of PCa
Elena, 2013 (164)	USA	Meta-Analysis	12 Studies	Diabetes Mellitus	(+) Pca risk: Diabetes Mellitus (OR 1.40; 95%CI 1.07-1.84); risk was highest for duration 2-8 years (OR 1.79; 95%CI 1.25-2.55)	Adjusted for age, ethnicity, sex, alcohol intake, smoking, BMI, and FH of PCa
Song, 2015 (163)	China	Meta-Analysis	44 Studies	Diabetes Mellitus	(+) Pca risk: >2yrs Diabetes Mellitus (RR 1.64; 95%CI 1.52-1.78); >5yrs (RR <sup>12</sup> 1.58; 95%CI 1.42-1.75); >10yrs (RR .50; 95%CI 1.28-1.75)	
Bosetti, 2014 (169)	Italy	Meta-Analysis	15 Studies	Diabetes Mellitus	(+) Pca risk: >2 yrs Diabetes Mellitus (OR 1.90; 95%CI 1.72-2.09); >20 yrs (OR 1.30; 95%CI 1.03-1.63)	Adjusted for study, center (for multicenter studies), age, sex, race/ethnicity, education, body mass index, tobacco smoking, alcohol drinking, and history of pancreatitis.
Austin, 2013 (156)	USA	Case-Control	Cases (n=654), Controls (n=697)	Diabetes Mellitus	(+) Pca risk: first-degree FH of DM (OR 1.37; 95%CI 1.10-1.71); offspring with DM (OR 1.95; 95%CI 1.23-3.09)	Adjusted for sex, age, race, hispanic ethnicity
Ben, 2011 (152)	China	Case-Control	Cases (n=1,458), Controls (n=1,528)	Diabetes Mellitus	(+) Pca risk: >2yrs Diabetes Mellitus (OR 2.11; 95%CI 1.51-2.94); <2yrs Diabetes Mellitus (OR 4.43; 95%CI 3.44-5.72)	
Wang, 2006 (161)	USA	Case-Control	Cases (n=532), Controls (n=1,701)	Diabetes Mellitus	(+) Pca risk: history of Diabetes Mellitus (OR 1.5; 95%CI 1.1-2.1); 1-4 years (OR 2.4; 95%CI	

Setiawan, 2019 (160)	USA	Cohort	PCa cases (n=408)	Diabetes Mellitus	1.4-4.0), 5-9 yrs (OR 2.0; 95%CI 1.2-3.4); Insulin use (OR 6.8; 95%CI 3.7-12) (+) PCa risk: DM (HR 2.39; 95%CI 1.91-2.98); recent-onset DM (<3yrs of Pca) in latinors (HR 4.08; 95%CI 2.76-6.03) and in african americans (HR 3.38; 95%CI 2.30-4.98)	Adjusted for BMI, smoking, alcohol intake, and red meat intake
Tseng, 2017 (244)	China	Cohort	PCa cases (n=16)	Diabetes Mellitus	No significant associations	
Karp, 2019 (170)	UK	Cohort	Incretin Users (n=18,885)	Diabetes Mellitus	No significant associations	
Currie, 2009 (167)	UK	Cohort		Diabetes Mellitus	(+) PCa risk: insulin-based therapies (HR 4.63; 95%CI 2.64-8.10)	
Raz, 2014 (173)	USA	Randomized Controlled Trial	Drug (n=5), Placebo (n=12)	Diabetes Mellitus	No significant associations	
Buse, 2017 (171)	USA	Randomized Controlled Trial	Drug (n=9), Placebo (n=14)	Diabetes Mellitus	(-) PCa risk: Sitagliptin (DPP-4 <sup>13</sup> inhibitor) (0.66; 95%CI 0.28-1.51)	
Perrin, 2017 (157)	Israel	Cohort	PCa cases (n=54)	Gestational Diabetes	(+) PCa risk: Gestatinal Diabetes (RR 7.1; 95%CI 2.8-18.0) (+) PCa risk: Any pancreatitis (OR 3.42; 95%CI 1.98-5.91); Chronic Pancreatitis (OR 2.23; 95%CI 1.43-3.49) -- Pancreatitis >7 years before PCa diagnosis (OR 2.04; 95%CI 1.53-2.72); > 3 years before PCa diagnosis (OR 2.14; 95%CI 1.68-2.72); >1 year before PCa diagnosis (OR 3.42; 95%CI 1.87-2.86)	Adjusted for age at first birth and birth weight
Bansal, 1995 (186)	USA	Case-Control	Cases (n=2,639), Controls (n=7,774)	Pancreatitis	(+) PCa risk: Chronic pancreatitis (SIR 3.8; 95% CI 1.4-8.2); >1 episode of acute pancreatitis (SIR <sup>14</sup> 4.8; 95% CI 1.9-9.9)	
Ekbom, 1994 (179)	Sweden	Cohort	PCa cases (n=46)	Pancreatitis	(+) PCa risk: Chronic pancreatitis (SIR 19; 95%CI 5.2-48.8) (+) PCa risk: Pancreatitis >2yrs of PCa diagnosis (OR 2.71; 95%CI 1.96-3.74); within 2yrs of PCa diagnosis (OR 13.56; 95%CI 8.72-21.90); younger patients (<65yrs)+ history pancreatitis (OR 3.91; 95%CI 2.53-6.04) than older (>65yrs) + history pancreatitis (OR 1.68; 95%CI 1.02-2.76)	Adjusted for study, age, sex, ethnicity, education, BMI, smoking, alcohol intake and history of DM
Malka, 2002 (183)	France	Cohort	PCa cases (n=4)	Pancreatitis		
Duell, 2009 (213)	USA	Meta-Analysis	10 Studies	Pancreatitis		
Bracci, 2009 (187)	USA	Pooled Analysis	Cases (n=1,659), Controls (n=2,815)	Pancreatitis	(+) Pca risk: Pancreatitis (OR 7.2; 95%CI 4.0-13); patients <55 yrs (OR 9.9; 95%CI 3.5-28); < 3yrs	Adjusted for age, sex, ethnicity, smoking, alcohol intake, history of DM, and gallbladder disease

Fernandez, 1995 (181)	Spain	Case-Control	Cases (n=362), Controls (n=1,408)	Pancreatitis	after diagnosis of pancreatitis (OR 29; 95%CI 12-71); 3-10yrs (OR 2.6; 95%CI 1.5-5.6). (+) Pca risk: Pancreatitis (RR 5.7; 95% CI 2.9-11.4); >5yrs after diagnosis of pancreatitis (RR 6.9; 95%CI 2.4-21.4); patients <60 yrs (RR 8.3; 95%CI 3.6-20.1)	Adjusted for age and sex
Talamini, 1999 (189)	Italy	Cohort	PCa cases (n=14)	Pancreatitis	(+) Pca risk: >4 yrs after diagnosis of pancreatitis (SIR 18.4; 95%CI 10-30); pancreatitis within 4yrs (SIR 13.3; 95%CI 6.4-24.5) (+) PCa risk: Chronic pancreatitis (HR 11.8; 95%CI 7.1-18.4); patients who continued to drink alcohol after pancreatitis diagnosis (HR 5-07; 95%CI 1.13-22.73) / (-) PCa risk: patients who received surgery (HR 0.11; 95%CI 0.01-0.80)	Adjusted for age and sex
Ueda, 2013 (190)	Japan	Cohort	PCa cases (n=19)	Pancreatitis	(+) PCa risk: Pancreatitis (SIR 2.8; 95%CI 2.5-3.2); pancreatitis diagnosed within 4 years (SIR 5.0; 95%CI 4.1-6.1); 5-9 yrs (SIR 2.5; 95%CI 2.0-3.1); >10 yrs (SIR 1.5; 95%CI 1.1-2.0)	Surgery: drainage operation or resection of pancreas
Karlson, 1997 (188)	Sweden	Cohort	PCa cases (n=472)	Pancreatitis	(+) PCa risk: Chronic pancreatitis (SIR 26.3; 95%CI 19.9-34.2)	Risk declined with time, except for patients with alcohol use after pancreatitis diagnosis
Lowenfels, 1993 (182)	USA	Cohort	PCa cases (n=56)	Pancreatitis	(+) PCa risk: Pancreatitis (OR 3.4; 95%CI 1.7-6.8)	Adjusted for age and sex
Fernandez, 1996 (127)	Italy	Case-Control	Cases (n=362), Controls (n=1,408)	Pancreatitis	(+) PCa risk: Surgery for pancreatitis (HR 3.71; 95%CI 1.05-6.37)	Adjusted for sex, area of residence, education, smoking, high meat intake, high fruit intake, and FH of PCa
Zheng, 2019 (245)	China	Cohort	PCa cases (n=12)	Pancreatitis	(+) PCa risk: higher age at menarche (HR 1.17; 95%CI 1.04-1.32) / (-) PCa risk: Use of HRT <sup>15</sup> (HR 0.48; 95%CI 0.23-1.00); Estrogen-only (HR 0.22; 95%CI 0.05-0.90)	Adjusted for age, smoking, alcohol consumption and BMI
Andersson, 2018 (210)	Sweden	Cohort	PCa cases (n=110)	Hormonal and Reproductive Factors	(-) PCa risk: Multiparity >4 births (OR 0.46; 95%CI 0.26-0.85)	
Lucenteforte, 2011 (206)	Italy	Pooled Analysis	Cases (n=285), Controls (n=713)	Hormonal and Reproductive Factors	(-) PCa risk: Multiparity >5 births (HR 0.58; 95%CI 0.34-0.98)	Adjusted for smoking, BMI, history of DM, and height
Skinner, 2003 (207)	USA	Cohort	PCa cases (n=243)	Hormonal and Reproductive Factors		

Lo, 2007 (38)	Egypt	Case-Control	Cases (n=194), Controls (n=194)	Hormonal and Reproductive Factors	(-) PCa risk: Long period of lactation (OR 0.2; 95%CI 0.1-0.9)	Adjusted for age, sex and residence
Zhang, 2010 (208)	USA	Case-Control	Cases (n=284), Controls (n=1,096)	Hormonal and Reproductive Factors	(+) PCa risk: Older age at first pregnancy >30 yrs (OR 2.0; 95%CI 1.1-3.3); Oral contraceptive use >10 yrs (OR 1.0; 95%CI 1.0-4.0) (-) PCa risk: Multiparity >3 births (OR 0.22; 95%CI 0.07-0.65); Oral contraceptive use (OR 0.36; 95%CI 0.13-0.96) / (+) PCa risk: Older age at pregnancy >30 yrs (OR 3.78; 95%CI 1.02-14.06)	Adjusted for age, study center, year of interview, and ethnicity
Kreiger, 2001 (205)	Canada	Case-Control	Cases (n=52), Controls (n=233)	Hormonal and Reproductive Factors	(+) PCa risk: Older age at menopause >45 (OR 1.80; 95%CI 1.2-2.8); Never use of oral contraceptives of HRT (OR 11.5; 95%CI 3.5-38.1)	Adjusted for smoking
Duell, 2005 (213)	USA	Case-Control	Cases (n=241), Controls (n=818)	Hormonal and Reproductive Factors	(+) PCa risk: Early menarche (OR 3.07; 95%CI 1.35-7.0)	
Bueno de Mesquita, 1992 (211)	The Netherlands	Case-Control	Cases (n=176), Controls (n=487)	Hormonal and Reproductive Factors	(-) PCa risk: Early age at first birth (OR 0.5; 95%CI 0.3-0.9); (+) PCa risk: early menarche (OR 1.9; 95%CI 1.0-3.6)	
Fernandez, 1995 (212)	Italy	Case-Control	Cases (n=133), Controls (n=377)	Hormonal and Reproductive Factors	(-) PCa risk: age at first birth (OR per 5 years 0.90; 95%CI 0.83-0.97);	
Karlsson, 1998 (209)	Sweden	Case-Control	Cases (n=1,015), Controls (n=5,073)	Hormonal and Reproductive Factors		Adjusted for age, sex, race, residential areas, smoking, tea drinking, mental pressure, family history of pancreatic cancer, diabetes, gallstone, pickle consumption, and vegetable consumption.
Zheng, 2016 (130)	China	Case-Control	Cases (n=323), Controls (n=323)	Obesity	(+) PCa risk: Obesity (BMI ≥30)(OR 1.77; 95%CI 1.22-2.57)	
Stolzenberg-Solomon, 2013 (215)	USA	Cohort	PCa cases (n=2,122)	Obesity	(+) PCa risk: Overweight/Obesity (BMI ≥25) (HR 1.06; 95%CI 1.02-1.09); overweight/obesity and DM (HR 1.18; 95%CI 1.05-1.30)	Adjusted for sex, smoking and energy-adjusted total fat
Larsson, 2007 (216)	Sweden	Meta-Analysis	21 Studies	Obesity	(+) PCa risk: per 5kg/m <sup>2</sup> increase in BMI (RR 1.12; 95%CI 1.06-1.17); men (RR 1.16; 95%CI 1.05-1.28); women (RR 1.10; 95%CI 1.02-1.19)	
Berrington, 2003 (214)	UK	Meta-Analysis	14 Studies	Obesity	(+) PCa risk: Obesity (BMI ≥30) (RR 1.19; 95%CI 1.10-1.29)	

Klein, 2013 (45)	USA	Case-Control	Cases (n=3,349), Controls (n=3,654)	Obesity	(+) PCa risk: Obesity (BMI $\geq$ 30) (OR 1.26; 95%CI 1.09-1.45)	
Jiao, 2010 (217)	USA	Meta-Analysis	7 Studies	Obesity	(+) PCa risk: per 5kg/m <sup>2</sup> increase in BMI (RR 1.12; 95%CI 1.05-1.19); overweight (RR 1.13; 95%CI 1.03-1.23) and obesity (RR 1.19; 95%CI 1.05-1.35)	Adjusted for age and sex
Arslan, 2010 (165)	USA	Case-Control	Cases (n=2,170), Controls (n=2,209)	Obesity	(+) Pca risk: BMI Q4 vs Q1 (OR 1.33; 95%CI 1.12-1.58); men Q4 vs Q1 (OR 1.33; 95%CI 1.04-1.69); women Q4 vs Q1 (OR 1.34; 95%CI 1.05-1.70)	
McWilliams, 2016 (47)	USA	Meta-Analysis	8 Studies	Obesity	(+) PCa risk: Obesity (BMI $\geq$ 30) (OR 1.28; 95%CI 1.08-1.52)	Adjusted for FH of DM, sex, smoking, alcohol intake, and study site
Noor, 2016 (218)	UK	Cohort	PCa cases (n=88)	Physical Activity	No associations with overall PA / (-) PCa risk: patients <60yrs with high PA (HR 0.27; 95%CI 0.07-0.99)	
Rosato, 2011 (221)	Italy	Cohort	PCa cases (n=326)	Metabolic Syndrome	(+) PCa risk: Metabolic Syndrome (OR 2.13; 95%CI 1.01-4.49)	
Inoue, 2009 (229)	Japan	Cohort	PCa cases (n=1,858)	Metabolic Syndrome	(+) PCa risk: Metabolic Syndrome (HR 1.99; 95%CI 1.00-3.96)	Adjusted for age, smoking, study area, alcohol intake, serum cholesterol
Kabat, 2018 (219)	USA	Cohort	PCa cases (n=156)	Dyslipidaemias	(-) PCa risk: High HDL Q4 vs. Q1 (HR 0.52; 95%CI 0.32-0.85)	Adjusted for age, smoking, alcohol intake, BMI, physical activity, aspirin use, education, and ethnicity
La Torre, 2014 (220)	Italy	Case-Control	Cases (n=80), Controls (n=392)	Dyslipidaemias	(+) PCa risk: High TC (OR 5.05; 95%CI 2.94-8.66)	Adjusted for sex, age, smoking and alcohol consumption
Kirkegard, 2020 (227)	Denmark	Cohort	PCa cases (n=153)	Statin Use	No significant associations	Adjusted for age, sex, SES and comorbidity index score
Chiu, 2011 (225)	China	Case-Control	Cases (n=190), Controls (n=760)	Statin Use	No significant associations	Adjusted for DM, chronic pancreatitis, number of hospitalizations, and use of other lipid-lowering drugs
Cui, 2012 (226)	China	Meta-Analysis	16 Studies	Statin Use	No significant associations	
Bradley, 2010 (223)	UK	Case-Control	Cases (n=1,141), Controls (n=7,954)	Statin Use	No significant associations	Adjusted for smoking, BMI, alcohol, history of chronic pancreatitis, use of other drugs (steroids and HRT), DM and prior cancer
Carey, 2013 (224)	UK	Case-Control	Cases (n=252), Controls (n=504)	Statin Use	No significant associations	Adjusted for smoking and DM

Archibugi, 2017 (83)	Italy	Case-Control	Cases (n=408), Controls (n=816)	Statin Use	(-) PCa risk: Statin use (OR 0.61; 95%CI 0.43-0.88)	Adjusted for age, sex, BMI, FH of Pca, history of CP <sup>18</sup> , DM, smoking, alcohol use
Molina-Montes, 2018 (28)	Spain	Case-Control	Cases (n=1,431), Controls (n=1,090)	Family History of PCa	(+) PCa risk: FH of PCa (OR 3.88; 95%CI 2.96-9.73)	Adjusted for age, ethnicity, calendar year of questionnaire cycle, smoking, history of DM, BMI, physical activity, alcohol intake, and regular multivitamin use
Hamada, 2019 (132)	USA	Cohort	PCa cases (n=452)	Family History of PCa	(+) PCa risk: FH of PCa (HR 2.79; 1.28-6.07)	Adjusted for age, sex, education and smoking status
Schulte, 2016 (131)	Australia	Case-Control	Cases (n=591), Controls (n=646)	Family History of PCa	(+) PCa risk: FH of PCa (OR 2.20; 95%CI 1.16-4.19)	Adjusted for age, sex, ethnicity, residential area, smoking, tea consumption, BMI, DM, gallstones, pickle and vegetable consumption
Zheng, 2016 (130)	China	Case-Control	Cases (n=323), Controls (n=323)	Family History of PCa	(+) PCa risk: FH of PCa (OR 1.23; 95%CI 1.11-3.70)	
Paiella, 2019 (128)	Italy	Cohort	PCa cases (n=187)	Family History of PCa	(+) PCa risk: FH of PCa (OR 2.7; 95%CI 1.1-6.4)	
Matsubayashi, 2011 (27)	Japan	Case-Control	Cases (n=577), Controls (n=577)	Family History of PCa	(+) PCa risk: FH of PCa (OR 2.5; 95%CI 1.37-4.38)	
Fernandez, 1996 (127)	Italy	Case-Control	Cases (n=362), Controls (n=1,408)	Family History of PCa	(+) Pca risk: FH of PCa (OR 4.7; 95%CI 1.5-15.1)	Adjusted for age, area of residence and education
Schenk, 2001 (126)	USA	Case-Control	Cases (n=247), Controls (n=420)	Family History of PCa	(+) PCa risk: FH of PCa (RR 2.49; 95%CI 1.32-4.69)	Adjusted for age, ethnicity, smoking, and history of DM
Zhan, 2013 (125)	China	Case-Control	Cases (n=196), Controls (n=233)	Family History of PCa	(+) PCa risk: FH of PCa (OR 16.75; 95%CI 2.12-132.05)	
McWilliams, 2016 (47)	USA	Meta-Analysis	8 Studies	Family History of PCa	(+) EOPC <sup>19</sup> risk: FH of PCa (OR 2.53; 95%CI 1.77-3.61) / (+) VEOPC <sup>20</sup> risk: FH of PCa (OR 2.88; 95%CI 1.04-7.99)	
Fernandez, 1994 (123)	Spain	Case-Control	Cases (n=362), Controls (n=1,408)	Family History of PCa	(+) PCa risk: FH of PCa (RR 3.0; 95%CI 1.4-6.6)	

Klein, 2003 (133)	USA	Cohort	PCa cases (n=19)	Family History of PCa	(+) PCa risk: One first-degree relative (SIR 4.5; 95%CI 0.54-16.3); Two first-degree relatives (SIR 6.4; 95%CI 1.8-16.4); three or more first-degree relatives (SIR 32.0; 95%CI 10.4-74.7)	Adjusted for age, sex, and race
Sollie, 2019 (176)	UK	Cohort	PCa cases (n=286)	Inflammatory Markers	(+) PCa risk: High haptoglobin (HR2.23; 95%CI 1.72-2.88); CRP <sup>21</sup> (HR 1.32; 95%CI 1.00-1.74); leukocytes (HR 2.20; 95%CI 1.52-3.18)	Adjusted for age, gender, education, CCI and serum glucose
Grote, 2012 (177)	Germany	Case-Control	Cases (n=455), Controls (n=455)	Inflammatory Markers	(+) PCa risk: TNF-a <sup>22</sup> Q4 vs. Q1 (OR 1.97; 95%CI 1.02-3.79) in women / No other associations	
Moran, 2012 (136)	UK	Cohort	PCa cases (n=220)	Genetic Factors	(+) PCa risk: BRCA2 (RR 4.1; 95%CI 1.9-7.8) / No significant associations with BRCA1	
Bannon, 2018 (138)	USA	Cohort	PCa cases (n=584)	Genetic Factors	(+) EOPC risk: BRCA1 and BRCA2 (OR 1.93; 95%CI 1.03-3.70)	
Mersch, 2015 (137)	USA	Cohort	PCa cases (n=23)	Genetic Factors	(+) PCa risk: BRCA2 (SIR 21.7; 95%CI 13.1-34.0) / No significant associations with BRCA1	
Roberts, 2012 (140)	USA	Case-Control	Cases (n=166), Controls (n=190)	Genetic Factors	(+) PCa risk: ATM mutation (4/166 vs. 0/190, Fisher's Exact Test P=0.046)	
Lynch, 2005 (143)	USA	Cohort	PCa cases (n=19)	Genetic Factors	(+) PCa risk: BRCA1 and BRCA2	
Giardiello, 2000 (146)	USA	Meta-Analysis	6 Studies	Genetic Factors	(+) PCa risk: Peutz-Jeghers Syndrome (STK11 mutation) (RR 132; 95%CI 44.261)	
Rebours, 2008 (149)	France	Cohort	PCa cases (n=200)	Genetic Factors	(+) PCa risk: PRSS1 mutation (OR 87; 95%CI 42-113)	Adjusted for age and sex
Howes, 2003 (148)	UK	Cohort	PCa cases (n=418)	Genetic Factors	(+) PCa risk: PRSS1 mutation (OR 44; 95%CI 8-88)	
Vasen, 2000 (144)	The Netherlands	Cohort	PCa cases (n=15)	Genetic Factors	(+) PCa risk: Familial atypical multiple mole melanoma (CDKN2A mutation) (OR 17; 95%CI 13-30)	

Kastrinos, 2009 (246)	USA	Cohort	PCa cases (n=147)	Genetic Factors	(+) PCa risk: Lynch syndrome (MLH1, MSH2, MSH6 mutations)(RR 3.7; 95%CI 1.45-5.88)
Aarnio, 1999 (151)	Finland	Cohort	PCa cases (n=360)	Genetic Factors	(+) PCa risk: Lynch Syndrome (MSH2, MLH1, PMS1, PMS2 or MSH6)(SIR 4.5; 95%CI 1.0-13)
Tada, 2006 (233)	Japan	Cohort	PCa cases (n=197)	Cystic Lesions	(+) PCa risk: Pancreatic cystic lesions (SIR 22.5; 95%CI 11.0-45.3)
Matsubara, 2012 (234)	Japan	Case-Control	Cases (n=116), Controls (n=1,226)	Cystic Lesions	(+) PCa risk: Pancreatic cystic lesion ( OR 10.27; 95%CI 6.76-15.73); Size >10mm (OR 4.71; 95%CI 2.21-10.69)

<sup>1</sup>PCa, pancreatic cancer; <sup>2</sup>OR, odds ratio; <sup>3</sup>CI, confidence interval; <sup>4</sup>DM, diabetes mellitus; <sup>5</sup>PA, physical activity; <sup>6</sup>HR, hazard ratio; <sup>7</sup>COPD, chronic obstructive pulmonary disease; <sup>8</sup>BMI, body mass index; <sup>9</sup>SES, socioeconomic status; <sup>10</sup>PG, plasma Glucose; <sup>11</sup>FH, family history; <sup>12</sup>RR, relative risk; <sup>13</sup>Dipeptidyl peptidase-4; <sup>14</sup>SIR, standardized incidence ratio; <sup>15</sup>HRT, hormone replacement therapy; <sup>16</sup>HDL, HDL-cholesterol; <sup>17</sup>TC, total cholesterol; <sup>18</sup>CP, chronic pancreatitis; <sup>19</sup>EOPC, early-onset pancreatic cancer; <sup>20</sup>VEOPC, very early-onset pancreatic cancer; <sup>21</sup>CRP, C-reactive protein; <sup>22</sup>TNF-a, tumour necrosis factor alfa.

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