**Supplemental Digital Content 1: search strategy**

**MEDLINE**

1. (pancreatic neoplasm/)
2. (pancrea\*.mp. OR pancreas/)
3. (carcinoma\*.mp. OR exp neoplasm/ OR cancer/ OR neoplas\*.mp. OR exp carcinoma/ OR adenocarcinoma\*.mp. OR adenoma\*.mp. OR tumo?r\*.mp. OR malignan\*.mp.)
4. (clinical risk factor\*.mp. OR sex\*.mp. OR gender.mp. OR ethnic\*.mp. OR race\*.mp. OR smoking/ OR smok\*.mp. OR tobac\*.mp. OR cigar\*.mp. OR alcohol drinking/ OR alcohol\*.mp. OR obesity/ OR body mass index.mp. OR BMI.mp. OR diabetes.mp. OR chronic pancreatitis\*.mp. OR height\*.mp. OR waist-hip\*.mp. OR health data.mp. OR electronic clinical record\*.mp. OR electronic health record\*.mp. OR medical record\*.mp. OR clinical record\*.mp. OR lifestyle risk factor\*.mp. OR clinical database\*.mp.)
5. (risk score.mp. OR "Sensitivity and specificity"/ OR sensitivity.mp. OR specificity.mp. OR predictive value of tests/ OR prediction\*.mp. OR predictive value\*.mp OR predictive value\*.mp. OR receiver operating characteristic curve\*.mp. OR ROC curve\*.mp. OR area under curve\*.mp. OR "area under curve"/ OR area under the curve\*.mp. OR AUC.mp. OR C statistic\*.mp. OR discriminat\*.mp. OR reclassif\*.mp. OR absolute risk\*.mp. OR brier\*.mp. OR lorenz curves.mp.)
6. 2 AND 3
7. 1 OR 6
8. 4 AND 5 AND 7
9. limit 8 to humans
10. limit 9 to reviews
11. 9 NOT 10

**EMBASE**

1. (pancreatic neoplasm/)
2. (pancrea\*.mp. OR pancreas/)
3. (carcinoma\*.mp. OR exp neoplasm/ OR cancer/ OR neoplas\*.mp. OR exp carcinoma/ OR adenocarcinoma\*.mp. OR adenoma\*.mp. OR tumo?r\*.mp. OR malignan\*.mp.)
4. (clinical risk factor\*.mp. OR sex\*.mp. OR gender.mp. OR ethnic\*.mp. OR race\*.mp. OR smoking/ OR smok\*.mp. OR tobac\*.mp. OR cigar\*.mp. OR alcohol drinking/ OR alcohol\*.mp. OR obesity/ OR body mass index.mp. OR BMI.mp. OR diabetes.mp. OR chronic pancreatitis\*.mp. OR height\*.mp. OR waist-hip\*.mp. OR health data.mp. OR electronic clinical record\*.mp. OR electronic health record\*.mp. OR medical record\*.mp. OR clinical record\*.mp. OR lifestyle risk factor\*.mp. OR clinical database\*.mp.)
5. (risk score.mp. OR "Sensitivity and specificity"/ OR sensitivity.mp. OR specificity.mp. OR predictive value of tests/ OR prediction\*.mp. OR predictive value\*.mp. OR receiver operating characteristic curve\*.mp. OR ROC curve\*.mp. OR area under curve\*.mp. OR "area under curve"/ OR area under the curve\*.mp. OR AUC.mp. OR C statistic\*.mp. OR discriminat\*.mp. OR reclassif\*.mp. OR absolute risk\*.mp. OR brier\*.mp. OR lorenz curves.mp.)
6. 2 AND 3
7. 1 OR 6
8. 4 AND 5 AND 7
9. limit 8 to humans
10. limit 9 to reviews
11. 9 NOT 10

**Web of Sceince**

1. TS=(pancrea\* OR pancreatic\* OR pancreatic ductal\*)
2. TS=(cancer\* OR carcinoma\* OR neoplas\* OR malignan\* OR tumo$r\* OR adenocarcinoma\* OR adenoma\*)
3. TS=(clinical risk factor\* OR sex\* OR gender\* OR ethnic\* OR race\* OR smok\* OR tobac\* OR cigar\* OR alcohol drinking\* OR alcohol consumption\* OR alcohol\* OR obesity\* OR body mass index\* OR BMI\* OR diabetes\* OR chronic pancreatitis\* OR height\* OR waist-hip\* OR health data\* OR electronic clinical record\* OR electronic health record\* OR medical record\* OR clinical record\* OR lifestyle risk factor\* OR clinical database\*)
4. TS=(risk score\* OR "sensitivity and specificity" OR sensitivity OR specificity OR predictive value of test\* OR prediction\* OR predictive value\* OR receiver operating characteristic curve\* OR ROC curve\* OR area under curve\* OR area under the curve\* OR AUC OR C statistic\* OR discriminat\* OR reclassif\* OR absolute risk\* OR brier\* OR lorenz curve\*)
5. #1 AND #2 AND #3 AND #4
6. #1 AND #2 AND #3 AND #4 and Review Articles (Document Types)
7. #5 NOT #6

**Supplemental Digital Content 2.** Characteristics of the included prediction model studies within patients with chronic pancreatitis or pancreatic cyst.

WFUBMC, Wake Forest University Baptist Medical Centre; MHH, Memorial Hermann Hospital; BJCYH, Beijing Chaoyang Hospital; KPSC, Kaiser Permanente Southern California.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Study design** | **Setting** | **Outcome/Cases** | **Participants** | **Model performance** | |  |
| **Calibration** | **Discrimination using C-statistics** |  |
| **Risk prediction for individuals with chronic pancreatitis** | | | | | | | |
| **Zhao, 2020 (2)** | Retrospective cohort study | 1) WFUBMC 2) MHH 3) BJCYH | Pancreatic cancer within chronic pancreatitis patients | Development= 2,545 (14 cases) External validation= 415 (7 cases) | Not stated | Development/Validation: 0.82 (CI: 0.71 to 0.93)/0.73 (CI: 0.48 to 0.97) | |
| **Risk prediction model for individuals with pancreatic cyst** | | | | | | | |
| **Chen, 2020 (3)** | Retrospective cohort study | KPSC healthcare system in Southern California | PDAC or death with pancreatic cancer within the 3 years after the index date | Cohort: 7,819 Cases = 781 | Observed to predicted risk (bar chart) | 0.833 ± 0.008 | |
| **Hijioka, 2014 (4)** | Retrospective cohort study | Aichi Cancer Centre Hospital in Nagoya, Japan | Outcome was pancreatic carcinoma | Cohort: 126 Cases = 7 | Not stated | 0.865 | |
| **Chen, 2021 (5)** | Case-control study | Optum | Pancreatic cancer and controls matched for geographic region and enrolment period | Cases = 3,322  Controls = 53,152 | Not stated | 0.84 (95% CI, 0.83 to 0.85) | |

**Supplemental Digital Content 3.** List of predictors assessed in each study.

|  |  |  |
| --- | --- | --- |
| **Study ID** | **Predictors assessed** | **Number of variables included vs. considered** |
| **Risk prediction model for the general population** | | |
| **Colditz, 2000 (6)** | **Cigarette smoking, family history of PC, vegetables, type 2 diabetes, chronic pancreatitis.** Also mentioned including genetic, environmental, nutritional, lifestyle factors, and major illnesses that are established or likely causes of the different cancers assessed. | **5**/not clear |
| **Galeotti, 2021 (7)** | **Smoking, diabetes, PRS (rs13303010 rs351365 rs2816938 rs3790844 rs1486134 rs9854771 rs2736100 rs2853677 rs2736098 rs35226131 rs401681 rs17688601 rs73328514 rs6971499 rs172310 rs2941471 rs10094872 rs1561927 rs8176746 rs505922 rs10991043 rs7310409 rs9581943 rs9543325 rs8028529 rs7190458 rs4795218 rs11655237 rs1517037 rs16986825)** | **3**/3 |
| **Hippisley-Cox, 2015 (8)** | **Age**, **chronic pancreatitis**, **BMI**, **smoking**, **previous breast cancer**, **previous renal cancer (for women), previous blood cancer (for men)**, **Townsend deprivation score**, **type 2 diabetes**, type 1 diabetes, family history of cancer, alcohol, ethnicity, deprivation, manic depression or schizophrenia, antipsychotics, hormone replacement therapy, oral contraceptive, previous diagnoses of other cancer, and peptic ulcer | **7**/18 |
| **Kachuri, 2020 (9)** | **Age, sex, BMI, smoking status, cigarette pack-years, family history of cancer (prostate, breast, lung, or bowel), PRS (rs13303010 rs2816938 rs3790844 rs1486134 rs9854771 rs2736098 rs35226131 rs401681 rs17688601 rs73328514 rs6971499 rs2941471 rs10094872 rs10991043 rs505922 rs9581943 rs9543325 rs7190458 rs4795218 rs7214041 rs1517037 rs16986825).** | **7**/7 |
| **\*Kim, 2004 (10)** | **Vegetable intakes, current cigarette smoking, and diabetes.** | **3**/3 |
| **Kim, 2020 (11)** | **BMI, waist to hip ratio, physical activity, diabetes, proinsulin, adiponectin, IL6, Total BCAA, weighted genetic risk factors: rs13303010, rs10919791, rs2816938, rs1486134, rs9854771, rs2736098, rs31490, rs35226131, rs78417682, rs17688601, rs6971499, rs2941471, rs10094872, rs1561927, rs687289, rs9581943, rs9543325, rs7190458, rs4795218, rs11655237, rs1517037, and rs16986825** | **30**/30 |
| **Klein, 2013 (12)** | **Cigarette smoking, diabetes > 3 year, family history of PC, heavy alcohol use, BMI, non-O ABO genotype, 3 genetic factors (rs3790844, rs401681, rs9543325).** | **8**/8 |
| **Muhammad, 2019 (13)** | **Age, vigorous exercise, moderate exercise, family history of PC, BMI, sex, emphysema, asthma, stroke, coronary heart disease, angina pectoris, heart attack, other heart disease, ulcer, alcohol consumption, other cancer, hypertension, ethnicity, diabetes, and smoking.** | **20**/20 |
| **Nakatochi, 2018 (14)** | Age, sex, height, weight, BMI, **cigarette smoking, family history of PC,** 61 SNPs (**rs13303010, rs12615966, rs657152, rs9564966, rs16986825,** rs12029406, rs4465241, rs10919791, rs2816938, rs3790844, rs3790843, rs2689154, rs962856, rs1486134, rs6711606, rs1427593, rs12478462, rs6736997, rs9854771, rs6537481, rs2736098, rs401681, rs31490, rs2255280, rs9502893, rs9363918, rs4269383, rs3016539, rs17688601, rs7779540, rs6464375, rs6973850, rs7832232, rs2941471, rs10088262, rs1561927, rs10974531, rs10991043, rs2417487, rs687289, rs505922, rs630014, rs12413624, rs708224, rs7310409, rs1182933, rs9554197, rs9581943, rs1585440, rs9573163, rs4885093, rs9543325, rs2039553, rs4924935, rs225190, rs2257205, rs1517037, rs372883, rs1547374, rs450960, rs5768709) | **7**/68 |

**Continued…**

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| --- | --- | --- |
| **Study ID** | **Predictors assessed** | **Number of variables included vs. considered** |
| **Pang, 2017 (15)** | **Smoking**, **alcohol consumption**, **family history of PDAC**, **chronic pancreatitis**, **cholecystectomy**, **diabetes**, **total cholesterol**, **high-density lipoprotein-cholesterol**, medical history of gastritis, cholelithiasis, weight, height, gallbladder polyps, hypertension, fasting blood glucose, albumin/globulin ratio, alanine transaminase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, alpha-L-fucosidase, triglycerides, and low-density lipoprotein-cholesterol. | **8**/23 |
| **Risch, 2015 (16)** | **Jewish ancestry**, **ABO blood group**, **history of diabetes mellitus**, **history of pancreatitis**, **cigarette smoking**, **regular use of PPIs**, BMI, H. pylori CagA seropositivity, regular use of H2RAs, regular use of antacids. | **6**/10 |
| **Salvatore, 2021 (17)** | **Age, sex, smoking status, drinking status, BMI, PheRS (diseases of pancreas; secondary malignant neoplasm of digestive systems; cancer of other lymphoid, histiocytic tissue; cholelithiasis with other cholecystitis; genital prolapse; colon cancer; gingival and periodontal diseases; cerebral artery occlusion, with cerebral infarction; obesity; plexus disorders; respiratory failure, insufficiency, arrest; diseases of spleen; type 1 diabetes; ventral hernia; other disorders of intestine; fracture of tibia and fibula; other symptoms referable to back; tachycardia NOS; lymphadenitis; asthma; mastodynia; otalgia; disorders of other cranial nerves; coagulation defects; occlusion and stenosis of precerebral arteries; dysphagia; other disorders of male genital organs; nontoxic nodular goiter; fracture of vertebral column without mention of spinal cord injury; lipoma); PRS (used 18 genetic variants, name not clear).** | **7**/7 |
| **Yu, 2016 (18)** | **Age**, **height**, **BMI**, **duration of smoking, amount of smoking per day**, **drinking habit**, **fasting blood and urine glucose levels**, previous disease history (hepatitis, diabetes, and any other cancer), eating habits (bland, moderate, spicy, or salty), meal preference (meat vs. vegetables), frequency of meat intake, amount of alcohol consumed at a time, year of smoking cessation, physical activity, systolic and diastolic blood pressure, total cholesterol. | **7**/16 |
| **Yu, 2020 (19)** | **miRNA-25, CA19-9, CEA, CA125, TBIL, age, and sex** | **7**/7 |
| **Risk prediction model for individuals with history of diabetes** | | |
| **Badrick, 2017 (20)** | **Sex, age, smoking status, BMI, weight loss, alcohol consumption, government office region, and index of multiple deprivation.** | **8**/8 |
| **Boursi, 2017 (21)** | **Age, BMI, change in BMI, smoking, use of PPI, anti-diabetic medications, levels of HbA1C, cholesterol, haemoglobin, creatinine, alkaline phosphatase.** Also assessed other risk factors as well as variables related to glucose metabolism (54 candidate variables in total). These predictors included anthropometric variables, lifestyle factors, medical comorbidities, medications, and laboratory studies. | **12**/54 |
| **Boursi, 2021 (22)** | **Age, BMI, PPI use, total cholesterol, low-density lipoprotein, alanine aminotransferase and alkaline phosphatase.** Also assessed other risk factors as well as variables related to glucose metabolism (49 candidate variables in total). These predictors included anthropometric variables, lifestyle factors, medical comorbidities, medications and laboratory studies. | **7**/49 |

**Continued…**

|  |  |  |
| --- | --- | --- |
| **Study ID** | **Predictors assessed** | **Number of variables included vs. considered** |
| **\*Chen, 2020 (23)** | **Change in weight, change in blood glucose, and age at onset of diabetes.** | **3**/3 |
| **Hsieh, 2018 (24)** | **Age, sex, acute pancreatitis, chronic pancreatitis, gallstone, cholecystectomy, cirrhosis, COPD, hepatitis B, hepatitis C, hypertension, hyperlipidaemia, obesity, Charlson comorbidity index, retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular disease, metabolic, change in adapted Diabetes Complication Severity Index score per year, statin, insulin, sulfonylureas, metformin, other antidiabetic drugs, and thiazolidinediones.** | **28**/28 |
| **Lee, 2012 (25)** | **Age, weight change, BMI, familial history of diabetes,** sex, use of tobacco, alcohol intake, fasting insulin, fasting C-peptide, fasting glucose. | **4**/10 |
| **Munigala, 2015 (26)** | **Age,** **smoking,** **history of obesity, chronic pancreatitis, gallstone disease,** race, sex. | **5**/7 |
| **Sharma, 2018 (27)** | **Change in weight, change in blood glucose, and age at onset of diabetes.** | **3**/3 |
| **Risk prediction model for individuals with gastrointestinal (and other) symptoms** | | |
| **Appelbaum, 2021 (28)** | **4150 diagnosis codes in addition to the patient sex, age, and ethnicity.** | **4153**/4153 |
| **Baecker, 2019 (29)** | **Age, sex, year of diagnosis, ethnicity, influenza vaccine, acute pancreatitis, chronic pancreatitis, abdominal pain,** **diabetes mellitus**, **weight loss/anorexia/cachexia**, **dyspepsia/gastritis/peptic ulcer disease**, **jaundice**, **gallbladder disease**, fatigue, itching/pruritis, depression, nausea and/or vomiting, digestive problems, chest pain, acute cholecystitis, and oesophageal reflux. | **12**/20 |
| **\*Collins, 2013 (30)** | **Age**, **smoking status**, **type 2 diabetes**, **chronic pancreatitis**, **abdominal pain**, **abdominal distension (female only)**, **appetite loss, weight loss,** **dysphagia (male only)**, **constipation (male only).** | **9**/9 |
| **De Icaza, 2009 (31)** | **Tobacco habits,** **jaundice,** **abnormal glucose metabolism,** **CA 19-9,** **ultrasound,** **computed tomography,** **endoscopic retrograde cholangiopancreatography,** family history (any cancer; PC; chronic pancreatitis; and diabetes mellitus), alcohol, dyspepsia, DM and pancreatitis, abdominal pain, weight loss, tiredness, nausea, vomiting, change in bowel habits, fever, depression, pyrosis, steatorrhea, endoscopic ultrasound. | **7**/22 |
| **Hippisley-Cox, 2012 (32)** | **Age**, **smoking status**, **type 2 diabetes**, **chronic pancreatitis**, **abdominal pain**, **abdominal distension (female only)**, **appetite loss, weight loss,** **dysphagia (male only)**, **constipation (male only)**, previous diagnosis of cancer apart from PC, alcohol, deprivation, BMI, diarrhoea, tiredness, itching, and anaemia. | **9**/17 |
| **Hippisley-Cox, 2012 (33)** | **Age**, **smoking status**, **type 2 diabetes**, **chronic pancreatitis**, **abdominal pain**, **abdominal distension (female only)**, **appetite loss, weight loss,** **dysphagia (male only)**, **constipation (male only), indigestion, and heartburn.** | **11**/11 |

**Continued…**

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| --- | --- | --- |
| **Study ID** | **Predictors assessed** | **Number of variables included vs. considered** |
| **Hippisley-Cox, 2013 (34)** | **Chronic pancreatitis, type2 diabetes, smoking status, abdominal pain, appetite loss, dysphagia, hematemesis, indigestion, venous thrombo-embolism, weight loss, constipation, Townsend score,** abdominal distension, haematuria, haemoptysis, haematospermia, heartburn, neck lump, night sweats, rectal bleeding, testicular pain, testicular lump, back pain Bruising, change in bowel habit, constipation, cough, diarrhoea, dyspnoea, fever, headache, hesitancy, impotence, itching, nausea, nocturia, poor stream, tiredness, urgency, urinary dribbling, urinary frequency, urinary incontinence, urinary retention, age, alcohol intake, BMI, prior cancer, family history of gastrointestinal cancer, family history of prostate cancer, COPD, type 1 diabetes, and anaemia. | **12**/51 |
| **Hippisley-Cox, 2013 (35)** | **Chronic pancreatitis, type2 diabetes, smoking status, abdominal pain, appetite loss, dysphagia, hematemesis, indigestion, venous thrombo-embolism, weight loss, change in bowel habit**,constipation, Townsend score, abdominal distension, haematuria, haemoptysis, haematospermia, heartburn, neck lump, night sweats, rectal bleeding, testicular pain, testicular lump, back pain, bruising, constipation, cough, diarrhoea, dyspnoea, fever, headache, hesitancy, impotence, itching, nausea, nocturia, poor stream, tiredness, urgency, urinary dribbling, urinary frequency, urinary incontinence, urinary retention, age, alcohol intake, BMI, prior cancer, family history of gastrointestinal cancer, family history of prostate cancer, COPD, type 1 diabetes, and anaemia. | **11**/51 |
| **Lu, 2006 (36)** | **Age, sex, alcohol consumption, smoking, diabetes, high meat consumption, family history of PC, chronic pancreatitis, cholelithiasis history, cholecystitis history, anorexia, epigastric pain, weight loss, jaundice,** marriage status, acute pancreatitis, cholecystectomy, back ache, hypogastralgia, abdominal pain, and skin itch. | **14**/21 |
| **Malhotra, 2021 (37)** | **Cardiovascular diseases, hypertension, migratory thrombophlebitis, abdominal pain, jaundice, gastrointestinal conditions, constipation, oesophago-gastric problems, irritable bowel syndrome, diverticular disease, pancreatitis, abdominal mass, odynophagia, gallbladder diseases, flatulence, oral problems, xerostomia, inflammatory bowel disease, stomatitis, halitosis, glossodynia, steatorrhoea, back pain, rheumatoid arthritis, pruritis, on opioids, on antiplatelets, on HRT, on NSAIDS, Diabetes, polydipsia, hyperlipidaemia, kidney problems, urinary problems, gynaecological conditions, endometriosis, fibroids, dysmenorrhoea, anaemia, atopic diseases, auto-immune diseases, mumps, insomnia, hypersomnia, family history of breast cancer, Peutz-Jeghers syndrome, familial atypical multiple mole melanoma, weight loss, fatigue/malaise, anorexia, anxiety/depression, weakness, fever, obesity, disturbances in smell/taste, ever smoker, and ever heavy drinker.** | **57**/57 |
| **Stapley, 2012 (38)** | **Abdominal pain,** **weight loss,** **Nausea/ vomiting,** **back pain, constipation, diarrhoea, malaise, jaundice, new-onset diabetes,** abnormal liver function, low haemoglobin, and raised inflammatory markers. | **9**/12 |

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **R2 (%)** | **D statistic** | **Sensitivity (%)** | **Specificity (%)**  **Supplemental Digital Content 4.** Risk prediction model discrimination and classification | **Positive predictive value (%)** | **Negative predictive value (%)** | **C-statistics** |
| **Risk prediction model for the general population** | | | | | | | |
| **Colditz, 2000 (6)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |
| **Galeotti, 2021 (7)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.63 (95% CI 0.59 to 0.67) |
| **Hippisley-Cox, 2015 (8)** | Male: 54.2 (CI: 51.8-56.5)  Female: 54.4 (52-56.8) | Male: 2.23 (2.12-2.33)  Female: 2.24 (2.13-2.35) | Male/female: 49.3/50 | Male/female: 90/90 | Not stated | Not stated | Male: 0.857 (CI: 0.847-0.867)  Female: 0.865 (CI: 0.855-0.875) |
| **Kachuri, 2020 (9)** | 43.9 | Not stated | Not stated | Not stated | Not stated | Not stated | 0.743 (standard error = 0.012) |
| **\*Kim, 2004 (10)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.71 (CI: 0.66-0.76) |
| **Kim, 2020 (11)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.62 |
| **Klein, 2013 (12)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.61 |
| **Muhammad, 2019 (13)** | Not stated | Not stated | Development/training: 87.3 (CI: 67-100)/80.7% (CI: 43-100) | Development/training: 80.8 (CI: 44-93)/80.7% (CI: 45-94) | Development/training: 0.1 (CI: 0.090.1)/0.086 (CI: 0.084-0.095) | Development/training: 99.997 (CI: 99.996-99.997)/99.995 (CI:99.993-99.996) | Development/training: 0.86±0.01/0.0.85±0.002 |
| **Nakatochi, 2018 (14)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.63 (CI: 0.60-0.66) |
| **Pang, 2017 (15)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |
| **Risch, 2015 (16)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |
| **Salvatore, 2021 (17)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.74 (95% CI: 0.72, 0.76) |
| **Yu, 2016 (18)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Male: 0.813 (CI: 0.800-0.826) Female: 0.804 (CI: 0.788-0.820) |
| **Yu, 2020 (19)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |
| **Risk prediction model for individuals with history of diabetes** | | | | | | | |
| **Badrick, 2017 (20)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.8034 |
| **Boursi, 2017 (21)** | Not stated | Not stated | 44.74 | 93.95 | 2.6 | Not stated | C-statistics: 0.82 (CI: 0.75-0.89)  Optimism of 0.0003 (95%CI -0.00574 to 0.00571) |
| **Boursi, 2021 (22)** | Not stated | Not stated | 66.53 | 54.91 | 0.26 | Not stated | 0.71 (95% CI, 0.67–0.75) |
| **\*Chen, 2020 (23)** | Not stated | Not stated | 62.6 | 78.5 | 2 | 99.7 | 0.75 |
| **Hsieh, 2018 (24)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | 0.727 (CI: 0.718-0.735) |
| **Lee, 2012 (25)** | Not stated | Not stated | 80.8 | 67.6 | 2.5 | 99.7 | Not stated |
| **Munigala, 2015 (26)** | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |
| **Sharma, 2018 (27)** | Not stated | Not stated | Development/training: 80/78 | Development/training: 80/85 | Not stated | Not stated | 0.87 |

**Continued…**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **R2 (%)** | | **D statistic** | **Sensitivity (%)** | **Specificity (%)** | **Positive predictive value (%)** | **Negative predictive value (%)** | **C-statistics** |
| **Risk prediction model for individuals with gastrointestinal (and other) symptoms** | | | | | | | | |
| **Appelbaum, 2021 (28)** | | Not clear | Not clear | Not clear | Not clear | Not clear | Not clear | External validation:  0.68 (95% CI: 0.65-0.71) |
| **Baecker, 2019 (29)** | | Not stated | Not stated | 95-98 | 16.17-27.84 | Not stated | Not stated | C-statistics: 0.683 (CI: 0.680-0.687) Optimism-corrected C-statistics: 0.682 (CI: 0.678-0.686) |
| **\*Collins, 2013 (30)** | | Male/female: 66.6 (CI: 64.1-69.2)/60.0 (CI: 56.6-63.5) | Male/female: 2.89 (CI: 2.72-3.07)/2.51 (CI: 2.32-2.70) | Male/female: 63.8/74.3 | Male/female: 99/90.1 | Male/female: 0.2/0.2 | Male/female: 100/100 | Males/females: 0.92 (CI: 0.91-0.93)/0.89 (CI: 0.87-0.90) |
| **De Icaza, 2009 (31)** | | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | No stated |
| **Hippisley-Cox, 2012 (32)** | | Male/female: 62.0 (CI: 59.1-64.8)/58.7 (CI: 55.4-61.9) | Male/female: 2.61 (CI: 2.45-2.77)/2.44 (CI: 2.27-2.60) | 62.4 | 91.1 | 0.6 | 100 | Male/female: 0.87 (CI: 0.85-0.88)/0.84 (CI: 0.82-0.86) |
| **Hippisley-Cox, 2012 (33)** | | Male/female: 64/62 | Male/female: 2.7/2.6 | Not stated | Not stated | Not stated | Not stated | Males/females: 0.86/0.84 |
| **Hippisley-Cox, 2013 (34)** | | Not stated | Not stated | 70.1% | 90 | 0.4 | 100 | 0.89 (CI: 0.87-0.91) |
| **Hippisley-Cox, 2013 (35)** | | Not stated | Not stated | 67.9% | 90 | 0.4 | 100 | 0.87 (CI: 0.85-0.89) |
| **Lu, 2006 (36)** | | Not stated | Not stated | 88.9% | 97.6 | Not stated | Not stated | 0.981 |
| **Malhotra, 2021 (37)** | | Not stated | Not stated | ≤ 60 years old = 72.5  > 60 years old = 65.1 | ≤ 60 years old = 59  > 60 years old = 57 | ≤ 60 years old = 40  > 60 years old = 32.5 | ≤ 60 years old = 72.2  > 60 years old = 83.6 | ≤ 60 years old = 0.66  > 60 years old = 0.61 |
| **Stapley, 2012 (38)** | | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated | Not stated |

PC, pancreatic cancer; BMI, body mass index; PDAC, pancreatic ductal adenocarcinoma; COPD, chronic obstructive pulmonary disease; PPI, proton pump inhibitor; PRS, polygenic risk score; PheRS, phenotype risk score; HRT, hormone replacement therapy. Bold writing indicates predictors included in the final model. D statistic is a measurement of risk differences between the low- and high-risk group, where higher values suggest better discrimination (1).

**Supplemental Digital Content 5.** PROBAST Results.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Participants** | **Predictors** | | **Outcome** | **Analysis** | **Overall** |
| **Model development studies** | | | | | | |
| ***Badrick, 2017*** *(20) A) Risk of bias B) Applicability* | Unclear Low | Unclear Low | | Low Low | High N/A | High Low |
| ***Baecker, 2019*** *(29) A) Risk of bias B) Applicability* | High Low | High Low | | Low Low | Unclear N/A | High Low |
| ***Boursi, 2017*** *(21) A) Risk of bias B) Applicability* | Low Low | Low Low | | High Low | High N/A | High Low |
| ***Boursi, 2021*** *(22)*  A) Risk of bias B) Applicability | Low  Low | Low  Low | | Low  Low | High  N/A | High  Low |
| ***Colditz, 2000*** *(6) A) Risk of bias B) Applicability* | Unclear Unclear | Unclear Low | High High | | High N/A | High High |
| ***De Icaza, 2009*** *(31) A) Risk of bias B) Applicability* | High High | High High | | High Low | High N/A | High High |
| ***Galeotti, 2021*** *(7)*  A) Risk of bias B) Applicability | High  Unclear | Unclear  Unclear | | Unclear  Unclear | High  N/A | High  Unclear |
| ***Hippisley-Cox, 2012*** *(32) A) Risk of bias B) Applicability* | Low Low | Low Low | | Low Low | Low N/A | Low Low |
| ***Hippisley-Cox, 2012*** *(33) A) Risk of bias B) Applicability* | Low Low | Low Low | | Low Low | Low N/A | Low Low |
| ***Hippisley-Cox, 2013*** *(34) A) Risk of bias B) Applicability* | Low High | Low Low | | Low High | Low N/A | Low High |
| ***Hippisley-Cox, 2013*** *(35) A) Risk of bias B) Applicability* | Low High | Low Low | | Low High | Low N/A | Low High |
| ***Hippisley-Cox, 2015*** *(8) A) Risk of bias B) Applicability* | Low Low | Low Low | | Low High | Low N/A | Low High |
| ***Hsieh, 2018*** *(24) A) Risk of bias B) Applicability* | High Low | Low Low | | High Low | High N/A | High Low |
| ***Kachuri, 2020*** *(9)*  A) Risk of bias B) Applicability | Low  Low | Low  Low | | Low  Low | High  N/A | High  Low |
| ***Kim, 2020*** *(11)*  A) Risk of bias B) Applicability | High  Low | Low  Low | | Unclear  Low | High  N/A | High  Low |
| ***Klein, 2013*** *(12) A) Risk of bias B) Applicability* | High High | High Low | | Unclear High | High N/A | High High |

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| **Study ID** | **Participants** | **Predictors** | **Outcome** | **Analysis** | **Overall** |
| ***Lee, 2012*** *(25) A) Risk of bias B) Applicability* | High Low | High Low | High Low | High N/A | High Low |
| ***Lu, 2006*** *(36) A) Risk of bias B) Applicability* | Low Low | High Low | Low Low | High N/A | High Low |
| ***Malhotra, 2021*** *(37)*  A) Risk of bias B) Applicability | High  Low | High  Low | High  Low | High  N/A | High  Low |
| ***Muhammad, 2019*** *(13) A) Risk of bias B) Applicability* | Unclear Unclear | High Low | High High | High N/A | High High |
| ***Munigala, 2015*** *(26)*  A) Risk of bias  B) Applicability | High  Low | High  Low | High  Low | High  N/A | High  Low |
| ***Nakatochi, 2018*** *(14) A) Risk of bias B) Applicability* | High Low | High Low | High Low | High N/A | High Low |
| ***Pang, 2017*** *(15) A) Risk of bias B) Applicability* | High Low | High Low | High Low | High N/A | High Low |
| ***Risch, 2015*** *(16) A) Risk of bias B) Applicability* | High Low | High Low | Unclear Low | High N/A | High Low |
| ***Stapley, 2012*** *(38)*  A) Risk of bias  B) Applicability | High  Low | High  High | High  Low | High  N/A | High  High |
| ***Yu, 2020*** *(19)*  A) Risk of bias B) Applicability | High  Low | Unclear  Low | Unclear  Unclear | High  N/A | High  Unclear |
| **Model development with external validation study** | | | | | |
| ***Appelbaum, 2021*** *(28)*  A) Risk of bias B) Applicability | High  Low | High  Low | High  Low | High  N/A | High  Low |
| ***Salvatore, 2021*** *(17)*  A) Risk of bias B) Applicability | Unclear  Unclear | Low  High | High  High | Unclear  N/A | High  High |
| ***Sharma, 2018*** *(27) A) Risk of bias B) Applicability* | High Low | Low Low | High Low | High N/A | High Low |
| ***Yu, 2016*** *(18) A) Risk of bias B) Applicability* | High Low | Low Low | Low Low | High N/A | High Low |

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| **Study ID** | **Participants** | **Predictors** | **Outcome** | **Analysis** | **Overall** |
| **Model validation studies** | | | | | |
| ***Chen, 2020*** *(23) A) Risk of bias B) Applicability* | Low Low | Low Low | Low Low | High N/A | High Low |
| ***Collins, 2013*** *(30) A) Risk of bias B) Applicability* | Low Low | Low Low | Low Low | Low N/A | Low Low |
| ***Kim, 2004*** *(10) A) Risk of bias B) Applicability* | High Low | Low Low | High High | High N/A | High High |

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