**Supplementary material 1. Search query**

The following search terms were used:

- PubMed: (intraductal papillary mucinous neoplasms[ti] OR pancreatic[ti]) AND (cost[ti] OR cost\*[ti] OR economic[ti] OR effectiveness[ti] OR utility[ti] OR utilities[ti] OR benefit[ti] OR benefits[ti] OR simulation[ti] OR microsimulation[ti] OR Markov[tw]) AND (early detection[tw] OR management[tw] OR surveillance[tw] OR screening[tw] OR natural history[tw] OR development[tw] OR progression[tw])

- Embase: ('intraductal papillary mucinous neoplasms':ti OR pancreatic:ti) AND (cost:ti OR cost\*:ti OR economic:ti OR effectiveness:ti OR benefit:ti OR benefits:ti OR utility:ti OR utilities:ti OR simulation:ti OR microsimulation:ti OR markov:ab,ti) AND (detection:ab,ti OR management:ab,ti OR surveillance:ab,ti OR screening:ab,ti OR 'natural history':ab,ti OR development:ab,ti OR progression:ab,ti)

- Cochrane: ('intraductal papillary mucinous neoplasms' OR pancreatic):ti AND ((cost OR cost\* OR economic OR effectiveness OR utility OR utilities OR benefit OR benefits OR simulation OR microsimulation OR Markov):ti OR (Markov):ab) AND ((detection OR management OR surveillance OR screening OR 'natural history' OR development OR progression):ti OR (detection OR management OR surveillance OR screening OR 'natural history' OR development OR progression):ab)

The search was filtered for studies from their inception till June 19th, 2022.

**Supplementary material 2.** **Data extraction form**

**Reviewer**

* Name:
* Date form completed:
* Final status (completed/on-going):
* Notes:

**Section A**: General Information

* Article title:
* Study number:
* First author(s):
* Corresponding author(s):
* Journal name:
* Year published:
* Location (country/city):
* Conflict of interest (Yes/No, Declared/Undeclared):
* Study registered or published protocol available (not stated/stated):
* Consideration of reporting guideline (e.g., CHEERS 2022):

**Section B: Study overview/design**

* Study objectives:
* (P) Study population:
* (I) Intervention evaluated (list all strategies evaluated):
* (C) Control (base case):
* (O) Outcomes Assessed (primary outcome, e.g., ICER estimated based cost to QALY gained):
* Model cycle frequencies (week/month/year):
* Methodological approach (prospective/retrospective observational study vs. model-based, hypothetical cohort study):
* Economic study design (cost-effectiveness analysis [CEA], cost-benefit analysis [CBA], cost-utility analysis [CUA], cost-minimization analysis [CMA], cost-consequences analysis [CCA], costs only, health outcomes only, budget impact analysis, others):
* Author conclusion (simplified):

**Section C1: Model Structure** (provide diagrams for base case and intervention strategies)

* Model detail
* Model type (static, dynamic):
* Rational for model structure (No/Yes, if Yes, specify):
* Software used:
* Structural assumptions (including analytic horizon and cycle length):
* Uncertainty
* Sensitivity analysis considered (one way, two way, multi-way, scenario analysis, threshold analysis, probabilistic/Monte Carlo simulations, others, none]):
* Parameter identification (no explanation given, all parameter varied, justification provided):
* Range specification (no explanation, literature review, expert opinion, using confidence interval, other justification):
* Model judgement by experts (No/Yes, if Yes, specify who? Why they are experts? Level of agreement?):
* Model comparison with literature (No/Yes, if Yes, specify reference):
* Source of data for parameter ranges

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| --- | --- | --- | --- | --- |
| Parameters used | Data source used (systematic review, RCT, expert opinion, others) | Actual parameters (w/ uncertainty range) | Types of data (epidemiologic, test accuracy/intervention characteristics/ effectiveness measures/outcomes, cost) | Notes and references |
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* Outcome Assessment (primary and secondary)

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| Outcomes assessed | Outcome definition and evaluation | Types of outcomes | Notes |
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**Section C2: Study design and methods for observation studies**

* Source of data for utilities

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| --- | --- |
| Data types | Check |
| 1. Direct utility assessment for the specific study from a sample either:  (a) of the general population, or  (b) with knowledge of the disease(s) of interest, or  (c) of patients with the disease(s) of interest |  |
| - Indirect utility assessment for the specific study from patient sample with disease(s) of interest, using a tool validated for the patient population |  |
| 2. Direct utility assessment from a previous study from a sample either: (a) of the general population, or (b) with knowledge of the disease(s) of interest, or (c) of patients with the disease(s) of interest |  |
| - Indirect utility assessment from a previous study from patient sample with disease(s) of interest, using a tool validated for the patient population |  |
| 3. Indirect utility assessment from a patient sample with disease(s) of interest, using a tool not validated for the patient population |  |
| - Patient preference values obtained from a visual analogue scale |  |
| 4. Delphi panels, expert opinion |  |
| 5. Not clearly stated |  |
| 6. Other:  Specify relevant data sources:  More than 1 data source per parameter?  Reasons for excluding data sources?  Evidence synthesis performed?  Calibration |  |

* Were QoL estimate derived? (Yes/No)
* Instruments used as validated tools (Rosser Index, Health Utilities Index [HUI], EQ-5D, Quality of Well Being [QWB], 15D, SF-36, SF-12, SF-6, other, not perform):
* Converted into utilities (No/ Yes, if Yes, report value set):
* Approach(s) for direct elicitation (Standard Gamble, VAS/rating scale, time trade-off, person trade-off, other, not perform):
* Combination of utility values with survival to form QALYs (Yes/No):
* If the study did not evaluate QoL empirically, but assessed CE based on QALY or DALYs, how did the study used their primary and secondary outcomes to evaluate HRQoL?

**Section C3: Economic details**

* Perspective of analysis (society, insurer/third party payer, patients and their family, healthcare system, healthcare provider, others, not specify):
* Types of costs included:

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| --- | --- | --- | --- | --- | --- |
| Direct cost | Check | Indirect cost | Check | Forgone cost | Check |
| Direct medical |  | Direct non-medical |  | Productivity losses |  |
| Direct treatment |  | Social care |  | Income forgone due to illness |  |
| In-patient |  | Social benefits |  | Income forgone due to death |  |
| Out-patient |  | Travel costs |  | Other |  |
| Day care |  | Caregiver out-of-pocket |  |  |  |
| Community healthcare |  | Criminal justice |  |  |  |
| Medication |  | Training of staff |  |  |  |
| Side effect cost |  | Other |  |  |  |
| Staff |  |  |  |  |  |
| Labs/diagnostic |  |  |  |  |  |
| Overhead |  |  |  |  |  |
| Capital equipment |  |  |  |  |  |
| Real estate |  |  |  |  |  |
| Other |  |  |  |  |  |

* Sources of data for costs:

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| --- | --- |
| Data source | Check |
| 1. Cost calculations based on reliable databases or data sources conducted for specific study – same jurisdiction |  |
| 2. Recently published cost calculations based on reliable databases or data sources – same jurisdiction |  |
| 3. Unsourced data from previous economic evaluation – same jurisdiction |  |
| 4. Recently published cost calculations based on reliable databases or data sources – different jurisdiction |  |
| 5. Unsourced data from previous economic evaluation – different jurisdiction |  |
| 6. Expert opinion |  |
| 7. Not stated |  |
| 8. Other:  Specify relevant data sources:  More than 1 data source per parameter?  Reasons for excluding data sources?  Evidence synthesis performed?  Calibration? |  |

* Price year:
* Currency used:
* Inflation rate (No/Yes, if Yes, specify):
* Discounting (No/Yes, if Yes, specify):

**Figure S1.** Model structures implemented to simulate the natural history of PCNs

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**Table S1.** CHEERS checklist evaluation for economic evaluation studies

| **Checklist item** | **Faccioli et al., 2022** | **Schwartz et al., 2022** | **Bicu et al., 2021** | **Wang et al., 2021** | **Kumar et al, 2021** | **Lobo et al., 2020** | **Kowada et al., 2020** | **Sharib et al., 2020** | **Morelli et al., 2019** | **Corral et al., 2019** | **Rosenkrantz et al., 2018** | **Aronsson et al., 2018** | **Joergensen et al., 2016** | **Bruenderman et al., 2015** | **Das et al., 2015** | **Ghatnekar et al., 2013** | **Huang et al., 2010** | **Das et al., 2009** | **Rubenstein et al., 2007** | **Lim et al., 2005** | **Rulyak et al., 2003** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Title | PR | FR | PR | FR | FR | PR | FR | FR | FR | FR | PR | FR | FR | FR | PR | PR | PR | FR | FR | FR | FR |
| Abstract | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR |
| Background and objectives | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR | FR | FR |
| Health economic analysis plan | NR | NR | NR | PR | NR | NR | NR | PR | NR | FR | PR | NR | NR | NR | PR | NR | NR | PR | NR | NR | NR |
| Study population | FR | FR | NR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | NR | FR | FR | FR | FR | FR | FR |
| Setting and location | NR | FR | NR | NR | NR | NR | NR | NR | NR | NR | FR | NR | NR | PR | NR | FR | NR | NR | NR | FR | NR |
| Comparators | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR |
| Perspective | PR | FR | FR | FR | FR | NR | FR | NR | NR | FR | NR | NR | NR | NR | FR | FR | FR | FR | FR | NR | FR |
| Time horizon | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR | PR | NR | FR | FR | FR | FR | NR | FR |
| Discount rate | NR | FR | NR | FR | FR | NR | FR | FR | NR | FR | FR | FR | FR | NR | FR | NR | FR | FR | FR | NR | FR |
| Selection of outcomes | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR |
| Measurement of outcomes | FR | FR | FR | FR | FR | FR | NR | FR | FR | FR | FR | FR | FR | FR | NR | FR | FR | FR | FR | FR | FR |
| Valuation of outcomes | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR | FR | NR | FR | FR | FR | FR | FR | FR |
| Measurement and valuation of resources and costs | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR | FR | PR | FR | FR | FR | FR | FR | FR |
| Currency, price date, and conversion | PR | PR | PR | PR | FR | NR | FR | FR | PR | FR | FR | FR | FR | NR | FR | FR | FR | FR | FR | PR | FR |
| Rationale and description of model | FR | FR | FR | FR | FR | FR | FR | FR | NA | FR | NA | FR | NA | NA | FR | FR | FR | FR | FR | NA | FR |
| Analytics and assumptions | FR | FR | PR | FR | FR | FR | FR | FR | NA | FR | NA | FR | NA | NA | PR | FR | FR | FR | FR | NA | FR |
| Characterizing heterogeneity | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | FR | NR | NR | NA | NR |
| Characterizing distributional effects | NR | NR | NR | NR | NR | NR | NR | NR | FR | NR | FR | NR | NR | FR | NR | NR | FR | NR | NR | NA | NR |
| Characterizing uncertainty | FR | FR | FR | FR | FR | FR | FR | FR | NA | FR | NA | FR | NA | NA | FR | FR | FR | FR | FR | NA | FR |
| Approach to engagement with patients and others affected by the study | NA | NA | NA | NA | NA | NA | NA | NA | PR | NA | PR | NA | NR | NR | NA | NA | NA | NA | NA | NA | NA |
| Study parameters | FR | FR | FR | FR | FR | FR | FR | FR | NA | FR | NA | FR | NA | NA | FR | FR | FR | FR | FR | FR | FR |
| Summary of main results | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR |
| Effect of uncertainty | FR | FR | FR | FR | FR | FR | FR | FR | NA | FR | NA | FR | NA | NA | FR | FR | FR | FR | FR | NA | NR |
| Effect of engagement with patients and others affected by the study | NA | NA | NA | NA | NA | NA | NA | NA | NR | NA | NR | NA | NR | NR | NA | NA | NA | NA | NA | NA | NA |
| Study findings, limitations, generalizability, and current knowledge | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR |
| Source of funding | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | NR | FR | NR | NR |
| Conflicts of interest | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | FR | NR | NR |

**Table S2.** Summary of cost parameters in individual studies

| **Study**  **(cost unit)** | **Screening cost** | **Surgical and postoperative cost** | **Cancer non-surgical treatment cost** | **Palliative care** | **Patient cost** |
| --- | --- | --- | --- | --- | --- |
| Faccioli et al., 2022 (€) | Annual abdominopelvic CT: 106.23 |  |  |  |  |
|  | Annual abdominal MRI: 219.61 |  |  |  |  |
|  | Annual EUS: 739 |  |  |  |  |
|  | Annual CEUS: 70.50 |  |  |  |  |
| Schwartz et al., 2022 | CT: 203 (162-244)  EUS with biopsy: 277 (222-333) |  | Locoregional, resectable total direct treatment: 239,615 (222,924-256,337) | Monthly diabetes care: 298 (256-346) |  |
|  |  | Locoregional, unresectable total direct treatment: 229,617 (216,463-260,845) |  |  |
|  |  | Distant total direct treatment: 190,602 (180,454-200,745) |  |  |
| Bicu et al., 2021 ($) | Contrast-enhanced MRI: 492  18F-FDG-PET: 1,551 | Open pancreatoduodenectomy: 28,623 |  | Recurrence disease: 78,630 |  |
|  | Distal pancreatic resection: 13,900 |  | Readmission: 1,930 |  |
| Wang et al., 2021 ($) | MRI: 613 (570-680)  EUS/FNA: 1,231 (930-1,530)  Bleeding: 11,363 (10,230-12,500)  Pancreatitis: 10,384 (9,350-11,430) |  | Local cancer: 77,027 (69,320-84,730)  Regional cancer: 78,810 (70,930-86,690)  Distant cancer: 131,225 (118,100-144,350) | Diabetes: 4,149 (3,530-4,770) |  |
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| Kumar et al, 2021 ($) | EUS with 1-h anesthesia: 984.88 (886.39-1,083.37) | Lifetime pancreatectomy without associated cancer treatments: 19,935.56 (17,942.00-21,929.12) | Lifetime care for distant cancer: 56,562.94 (50,906.65-62,219.23)  Lifetime care for resectable cancer: 155,490.36 (139.941.32-171.039.40) | |  |
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| Lobo et al., 2020 ($) | MRI: 1,200 (+/- 20%)  EUS: 1,500 (+/- 20%) | Whipple procedure: 40,000 (+/- 20%) |  |  |  |
|  | Distal pancreatectomy: 25,000 (+/-20%) |  |  |  |
| Kowada et al., 2020 ($) | Abdominal US: 48.0 (40-100)  CT: 269.0 (130-600)  EUS: 130.4 (100-1,525)  MRI: 285.3 (140-700) |  | Treatment of stage I and II cancer: 46,250 (23,125-92,500)  Treatment of stage III cancer: 34,626 (17,313-69,252)  Treatment of stage IV cancer: 29,658 (14,829-59,316) |  |  |
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| Sharib et al., 2020 ($) | MRI: 3,471 (2,830-4,431) | Pancreatectomy: 109,528 (76,000-147,000)  Complication: 30,885 (17,000-37,000)  Annual diabetes care: 16,750 (9,600-25,000) | Metastatic treatment of cancer: 63,533 (30,000-112,500) | Annual healthcare: 7,150 (500-17,500) | End of life care: 45,052 (10,000-80,000) |
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| Morelli et al., 2019 (€) | US: 60  MRI: 480  Contrast-enhanced CT: 314  Contrast-enhanced MRI:  734 |  |  |  |  |
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| Corral et al., 2019 ($) | MRI/MRCP: 700 (0-700)  EUS (includes sedation, professional and facility fees, pathology cost): 1,525 (0-1,525) | Total preventive pancreatectomy: 15,505 (0-15,505)  Annual diabetes care: 11,764 (3,000-11,764) | Initial PC treatment (including diagnostic work up): 94,092 (50,000-150,000) | Subsequent care after initial treatment of PC annually up to 5 years: 11,697 (5,000-20,000) | Dying from terminal PC: 113,115 (75,000-150,000) |
|  | Dying from surgical complication: 47,565 (20,000-80,000) |
| Rosenkrantz et al., 2018 ($) | Abdominal MRI: 435.6  Abdominopelvic CT: 317.52  18F-FDG-PET: 1,928.5  EUS/FNA: 353.16 |  | Chemotherapy: 3,310.47 |  | Follow-up office visit: 73.93 |
| Aronsson et al., 2018 (€) | CT thorax + abdomen IV contrast: 321 (0-1,000)  MRI pancreas: 406 (0-1,000)  EUS: 1,246 (0-2,000) | Partial pancreatectomy: 14,766 (0-30,000)  Total pancreatectomy: 20,206 (0-40,000)  Remnant pancreatectomy: 14,766 (0-30,000)  Annual diabetes care: 2,332 (0-6,000) | Creon (annual consumption): 2,296  (0-4,000)  Oncological treatment: 7,800 (0-15,000) | Palliative care: 20,000 (0-40,000) | Appointment medical doctor: 170 (0-300) |
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| Bruenderman et al., 2015 ($) | MRI abdomen (with and without contrast): 587.92 (421.47-773.69)  MRCP: 71.45  MRI/MRCP: 659.37  CT abdomen (with and without contrast): 325.6 (324.78-426.51)  EUS: 307.23 (254.21-393.91)  EUS with 1 hour  anesthesia: 601.23 |  |  |  |  |
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| Das et al., 2015 ($) | CT/MRI: 1,000 (750-1,250)  EUS/FNA (including cost of sedation with monitored anesthesia care + CEA + cytology): 1,525 (675-2,675)  PathFinder TG Testing: 3,100 (2,500-5,000) | Pancreatic surgery: 40,000 (30,000-50,000) | Advanced malignancy treatment: 50,000 (37,500-62,500) |  |  |
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| Ghatnekar et al., 2013 (€) |  |  | Resectable PC (stage 0-IIB) (hospital-related costs): 20.633 |  |  |
|  |  |  | Locally advanced PC (stage III) (hospital-related costs): 15,455 |  |  |
|  |  |  | Metastatic PC (stage IV) (hospital-related costs): 16,783 |  |  |
| Huang et al., 2010 ($) | Annual MRI: 544 (250-1,500) | Pancreaticoduodenectomy: 61,807 (25,000-120,000)  Surgical complication: 23,709 (10,000-55,000)  Postoperative care: 6,858 (1,000-15,000) |  | Diabetes care: 12,131 (3,000-25,000)  Non-diabetes care: 5,263 (500-15,000) | Physical visit: 44 (10-100)  End-of-life: 32,547 (10,000-60,000) |
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| Das et al., 2009 ($) | EUS/FNA (including cytology and CEA estimation): 1,350 (+/-25%) | Pancreatic surgery: 40,000 (+/-25%) |  | Palliative care: 10,000 (+/-25%) |  |
|  | CR or MRI: 1,000 (+/-25%) |  |  |  |  |
| Rubenstein et al., 2007 ($) | EUS without FNA: 766 (383-1,531)  EUS/FNA: 1,065 (532-2,129) | Pancreatectomy: 15,505 (7,753-31,010)  Annual diabetes care: 11,674 (5,837-23,347) | Cancer diagnosis: 3,270 (1,635-6,540)  Treatment of local cancer: 30,564 (15,282-61,127)  Treatment of regional cancer: 23,548 (11,774-47,097)  Treatment of distant cancer: 14,415 (7,207-28,830) |  |  |
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| Lim et al., 2005 ($) | CT scan of abdomen and pelvis: 3,608  Triphasic CT scan of pancreas: 2,567  MRI of abdomen: 1,969  Transabdominal US: 785  EUS without FNA: 4,222  EUS with FNA: 4,614  ERCP: 2,855  ERCP with stent placement: 3,997  Fluid amylase: 56  Fluid CEA level: 119  Serum CA 19-9: 13  Cytology: 317 |  |  |  |  |
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| Rulyak et al., 2003 ($) | EUS: 596 (400-1,800)  ERCP: 740 (600-1,500)  ERCP complication: 3,687 (2,625-9,725) | Pancreatectomy: 36,627 (20,461-47,515)  Diabetes care: 11,195 (5,598-22,390) | PC care (direct cost): 23,384 (19,250-48,803)  PC care (indirect cost): 265,248 (116,046-464,184) |  |  |

**Table S3.** Summary of model parameters other than costs in individual studies

| **Study** | **Diagnostic performance** | **Cut-off or proportion** | **Transition probability** | **Quality of life (utility)** | **Horizon and cycle length** |
| --- | --- | --- | --- | --- | --- |
| Faccioli et al., 2022 | Correct diagnosis: 0.85  CEUS sensitivity: 0.79-0.94  CEUS specificity: 0.76-0.99  CT sensitivity: 0.57-0.69  CT specificity: 0.63-0.83  MRI sensitivity: 0.75-0.82  MRI specificity: 0.94-0.96  EUS sensitivity: 0.78-0.83  EUS specificity: 0.91-0.95 | Location in head or neck of the pancreas: 0.5  Location in body or tail of the pancreas: 0.5  Proportion of mucinous cystic lesion/ branch-type IPMN at presentation: 0.65  Proportion of non-mucinous cystic lesions: 0.3 | Probability to have a benign pancreatic cyst: 0.10  Probability to have a malignant pancreatic cyst: 0.05  Annual probability of cystic lesion transitioning from asymptomatic to symptomatic state: 0.02  Probability that a benign cyst grows: 0.05  Probability of dying from an EUS/FNA: 0.0001  Probability of dying from a  malignant IPMN without treatment: 0.6 | Base case: 0.80  Annual decrease (aging): -0.01  Instant decrease (symptoms): -0.03  QoL of undergoing invasive surveillance: 0.73  QoL of undergoing non-invasive surveillance: 0.78  QoL of developing  malignant pancreatic cyst: 0.68 | 10-year horizon |
| Schwartz et al., 2022 | Fraction with END-PAC score ≤0: 0.484 (0.459-0.508)  END-PAC score sensitivity: 0.99 (0.95-1)  END-PAC score specificity: 0.488 (0.463-0.512)  END-PAC score positive predictive value: 0.016 (0.015-0.017)  END-PAC score negative predictive value: 1 (0.95-1) | Average age: 72 years (65-79 years)  Screen-detected PC cases: - Resectable: 0.4 (0.28-0.52) - Unresectable: 0.5 - Distant: 0.1 (0.07-0.13)  Clinically detected PC cases: - Resectable: 0.1 (0.09-0.11) - Unresectable: 0.38 (0.342-0.418) - Distant: 0.52 (0.468-0.572) | PC after first 3 years of new-onset diabetes: 0.82% (0.78-0.86%) | Before PC diagnosis: - Baseline: 0.92 (0.83-1.0) - No PC, positive screen: 0.81 (0.73-1.0)  After PC diagnosis: - Resectable PC, surgery to 6 months postsurgery: 0.78 (0.78-0.81) - Resectable PC, 6 months postsurgery to progression: 0.80 (0.62-0.80) - Unresectable PC, progression: 0.78 (0.70-0.85) - All PC, progression: 0.73 (0.62-0.80) | Lifetime horizon, monthly cycle |
| Bicu et al., 2021 | CT/MRI sensitivity (for risk factors predictive of malignancy): 0.809  CT/MRI specificity (for risk factors predictive of malignancy): 0.762  18F-FDG-PET sensitivity (for risk factors predictive of malignancy): 0.968  18F-FDG-PET specificity (for risk factors predictive of malignancy): 0.911 | Pre-test probability of malignant IPMN: 0.52  Average age at 18F-FDG-PET examination: 64.3 years  Proportion of pancreatic head resection vs. distal pancreatic resection: 0.78/0.21 | Risk of malignant transformation: 0.0223  Risk of death due to malignant IPMN: 0.027  Risk of death due to recurrent malignant IPMN: 0.283  Perioperative mortality in pancreatic surgery: 0.046  Probability of recurrence of malignant IPMN: 0.167  Reduction in risk of recurrence due to early detection by PET: 0.1 | QoL of patients with IPMN: 1  QoL of patients receiving IPMN resection: 0.818  QoL of patients with recurrence: 0.65  Long-term QoL of patients after IPMN resection: 0.896  Death: 0 | 15-year horizon, 1-year cycle length |
| Wang et al., 2021 | MRI and EUS/FNA sensitivity: 0.80 (0.56-0.9)  MRI and EUS/FNA specificity: 0.995 (0.90-1) | PDAC diagnosed at local stage: 0.3% (0.25-0.5%) | Bleeding after EUS/FNA: 0.001 (0.0009-0.0011)  Pancreatitis after EUS/FNA: 0.0044 (0.004-0.005) | Diabetes: 0.82 (0.77-0.92)  Pancreatitis: -0.0078 (-0.0014 to -0.018)  Bleeding: -0.0078 (-0.0014 to -0.018)  Local cancer: 0.729 (0.547-0.911)  Regional cancer: 0.732 (0.549-0.915)  Distant cancer: 0.72 (0.54-0.9) | Lifetime horizon (or until age 95), 3-month cycle length |
| Han et al., 2021 |  | Cut-offs for malignancy rates: <10%, 10%-35%, and >35%  Life expectancy duration:  20.8 years (aged 65), 12.7 years (aged 75), and 6.6 years (aged 85) | Survival rate (10 years)  Malignancy risk <10%  0.97 (age <65), 0.96 (age 65-75), 0.95 (age>75)  Malignancy risk 10-35%  0.97 (age,65), 0.95 (age 65-75), 0.92 (age>75)  Malignancy risk >35%  0.96 (age<65), 0.90 (age 65-75), 0.87 (age>75)  Surgical mortality: 0.002-0.05  Disease progression  Malignancy risk <10%  0.94 (no change), 0.04 (progression), 0.02 (death)  Malignancy risk 10-35%  0.95 (no change), 0.02 (progression), 0.03 (death)  Malignancy risk >35%  0.81 (no change), 0.19 (death) | Benign surveillance: 1  Malignant surveillance: 0.75-0.92  Perioperative complication: 0.51-0.94  Postoperative follow up (after 1 year): 1.0 |  |
| Koopmann et al., 2021 | Specificity of screening test (any pancreatic lesion): 0.9  Sensitivity of screening test: - Preinvasive stage low-grade dysplasia: 0.6 - Preinvasive stage intermediate-grade dysplasia:0.6 - Preinvasive stage high-grade dysplasia: 0.75 - Preclinical cancer stage I: 0.9 - Preclinical cancer stage II: 0.93 - Preclinical cancer stage III/IV: 0.99 | Lifetime PC risk: 7.5%  Mean duration of progression: - Preinvasive stage dysplasia: 3.33 years (progressive-only pathway) and 1.11 years (indolent included pathway) - Preclinical cancer stage I/II: 2 years (progressive-only pathway) and 0.66 year (indolent included pathway) - Preclinical cancer stage III/IV: 1 year (progressive-only pathway) and 0.33 year (indolent included pathway) - Estimated mean total preclinical: 14.3 years (progressive-only pathway) and 4.8 years (indolent included pathway)  Mean duration of indolent stages: - Preinvasive stage low-grade dysplasia: 7.08 years - Preinvasive stage intermediate-grade dysplasia: 11.78 years - Preinvasive stage high-grade dysplasia: 24.15 years | Treatment mortality: 3% |  | Pancreatic cancer lifetime risk horizon, annual and 5-year intervals |
| Kumar et al, 2021 | Normal index EUS in high-risk individuals: 0.607 (sd=0.0607)  Index EUS with findings that prompt surgery: 0.0812 (sd=0.00812)  Index EUS with findings that prompt surgery, and surgery finds premalignancy/ malignant lesion: 0.998 (0.9-1)  Missed lesion on index EUS: 0.05 (sd=0.025)  Second EUS (after indeterminate index EUS) finds a lesion: 0.05 (sd=0.025)  Future PDAC after normal index EUS: 0.03 (sd=0.015) | Lifetime PDAC in high-risk individuals: 0.096 (0.05-0.2) |  | Normal examination: 1 (0.99-1)  PDAC: 0.5 (sd=0.05)  Screen abnormal, but do not have cancer or undergo surgery: 0.99 (0.99-1)  Screen abnormal, undergo surgery and removal of high-grade lesion: 0.88 (sd=0.088)  Screen abnormal, undergo surgery, lesion identified is not high-grade: 0.88 (sd=0.088) | Lifetime horizon |
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| Lobo et al., 2020 |  | Starting age: 55 years (50-60)  Proportion of male: 50%  Percent in head of the pancreas: 50%  Initial cyst size: 3-25 mm, 70% were <=10 mm  Presence of solid component: 0.75 (0.5-0.85) in patients with cancer, 0.01 (0.005-0.05) in patients without cancer | Cancer progression over 15-year horizon: 0.0175 (0.12% annually) (0.01-0.035)  Death from cancer: 0.05 (0.025-0.1) within 3 years, 0.2 (0.1-0.4) within 3-6 years, and 0.9 after 6 years  Benign growth rate: - 50% (+/-10%) for minimal linear growth, UNIF (0,0.04) mm per 6 months - 50% (+/-10%) for moderate linear growth, UNIF (0.04,0.06) mm per 6 months  Malignant growth rate:  - 30% (+/-10%) for slow linear growth, UNIF (0.15,0.25) mm per 6 months - 70% (+/-10%) for fast linear growth, UNIF (1.7,2.3) mm per 6 months  Pancreatic duct: dilation in 15% patients, increase of 0.25 mm per 6 months, starts growing up to 3 years before malignancy | Before cancer: 1.0  Early cancer: 0.9  Late cancer (after 1 year of cancer): 0.5  Postoperative: 0.95  Disutility for each EUS: 0.0048  One-time disutility for surgery: 0.27 | 15-year horizon, 6-month interval |
| Kowada et al., 2020 | Abdominal US sensitivity for PDAC diagnosis: 0.88 (0.86-0.9) | PC incidence in 50-year-old individuals in the general population: 0.00012 (0.00002-0.0014)  Relative risk of 3 individuals with first-degree relatives: 32.0 (10.2-74.7)  PC incidence in 50-year-old familial high-risk individuals: 0.0038 (0.0002-0.11) | Stage I and II cancer (resectable) without screening: 0.1 (0.05-0.2)  Stage III cancer (unresectable) without screening: 0.3 (0-0.5)  Stage IV cancer without screening: 0.6 (0.5-1.0)  Stage I and II cancer (resectable) with screening: 0.9 (0.7-1.0)  Stage III cancer (unresectable) with screening: 0.1 (0-0.2)  Mortality for stage I and II cancer: 0.21 (0.1-0.5)  Mortality for stage III cancer: 0.34 (0.1-0.5)  Mortality for stage IV cancer: 0.5 (0.1-0.7) | Healthy: 1  PC stage I and II: 0.834 (0.8-0.9)  PC stage III: 0.798 (0.7-0.9)  PC stage IV: 0.762 (0.7-0.8)  Death: 0 | Lifetime horizon, 1-year cycle |
|  | Abdominal US specificity for PDAC diagnosis: 0.94 (0.87-0.98) |  |
|  | CT sensitivity for PDAC diagnosis: 0.90 (0.87-0.93) |  |
|  | CT specificity for PDAC diagnosis: 0.87 (0.79-0.93) |  |  |
|  | EUS sensitivity for PDAC diagnosis: 0.91 (0.87-0.94) |  |  |
|  | EUS specificity for PDAC diagnosis: 0.86 (0.81-0.91) |  |  |  |
|  | MRI sensitivity for PDAC diagnosis: 0.93 (0.88-0.96) |  |  |  |
|  | MRI specificity for PDAC diagnosis: 0.89 (0.82-0.94) |  |  |  |  |
|  | PET sensitivity for PDAC diagnosis: 0.89 (0.85-0.93) |  |  |  |  |
|  | PET specificity for PDAC diagnosis: 0.70 (0.54-0.84) |  |  |  |  |
| Sharib et al., 2020 |  | Age: 60 years (40-90)  Present with a surgical indication (all comers): 0.43 (0.35-0.5) | Low-grade cystic lesions: 0.85 (0.5-1) - Present with surgical indication: 0.42 (0.1-0.65) - Develop surgical indication (annually): 0.02 (0-0.04) - Annual progression to high-grade dysplasia: 0.029 (0.005-0.2) - Annual progression to disseminated cancer (no surgery): 0.03 (0.01-0.13) per 5 years - Annual progression to disseminated cancer (after surgery): 0.028 (0.01-0.07) per 5 years  High-grade cystic lesions: 0.885 (0-0.2) - Present with surgical indication: 0.9 (0.75-0.95) - Develop surgical indication (annually): 0.386 (0.2-0.5) - Annual progression to invasive cancer: 0.3 (0.05-0.65) - Annual progression to disseminated cancer (no surgery): 0.455 (0.25-0.65) per 5 years - Annual progression to disseminated cancer (after surgery): 0.15 (0.05-0.3) per 5 years  Pancreatic cystic lesions with invasive cancer: 0.0615 (0-0.15) - Present with surgical indication: 0.92 (0.8-1) - Develop surgical indication (annually): 0.386 (0.2-0.5) - Annual progression to disseminated cancer (no surgery): 0.29 (0.15-0.5) per 5 years - Annual progression to disseminated cancer (after surgery): 0.53 (0.35-0.7) per 5 years  Long-term surgical complication: 0.318 (0.2-0.5)  Surgical mortality: 0.02 (0.01-0.1)  Temporary complication: 0.308 (0.2-0.5)  Mortality for disseminated pancreatic cancer: 0.9 (0.73-0.99) per year | Surgery disutility: -2.5% (-1.5% to -3.5%)  Surgical complication disutility: -2.5% (-1.5% to -3.5%)  Metastatic cancer: 0.69 (0.59-0.79)  Age-sex-matched utility: 1 (0.9-1) | Lifetime horizon, annual cycle |
| Corral et al., 2019 | EUS sensitivity in detecting abnormal lesions: 0.9 (0.74-0.92)  EUS specificity in detecting abnormal lesions: 0.9 (0.83-0.97)  MRI sensitivity in detecting abnormal lesions: 0.8 (0.68-0.92)  MRI sensitivity in detecting abnormal lesions: 0.8 (0.53-0.95) |  | Probability of local (resectable) stage PC detected without surveillance: 0.1 (0.05-0.2)  Probability of regional (un- or borderline resectable) stage PC detected without surveillance: 0.3 (0-0.5)  Probability of regional stage cancer detected during surveillance: 0.2 (0-0.2)  Probability of local stage cancer detected during surveillance: 0.75 (0-0.75)  Probability of long-term cure with local stage PC detected with surveillance: 0.1 (0.05-0.2)  Probability of healthy (average risk) person developing PC without surveillance: 0-0.0004  Probability of high-risk lesion with EUS surveillance; stage dependent: 0-0.0067 (stage <=1), 0.0013-0.0067 (stage >1)  Probability of low-risk lesion with EUS surveillance: 0.1 (0-0.1)  Probability of PC on EUS surveillance: 0-0.0038 (stage <=1), 0.008-0.0038 (stage >1)  Probability of abnormal EUS findings in high-risk patients undergoing EUS: 0.1 (0-0.2)  Probability of abnormal EUS findings in high-risk patients undergoing MRI: 0.1 (0-0.1)  Probability of dying from local stage PC: 0.1 (0.05-0.2)  Probability of dying from regional stage PC: 0.34 (0.1-0.5)  Probability of dying from advanced stage PC: 0.5 (0.1-0.7) | Patient undergoing MRI: 1 (0.98-1)  Patient undergoing EUS: 0.985 (0.95-0.985)  Patient undergoing PC treatment: 0.9 (0.75-0.95)  Healthy patient who is not undergoing surveillance: 0.98 (0.95-1)  DM: 0.98 (0.9-0.98) | Lifetime horizon, imaging interval-based cycle |
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| Peters et al., 2018 |  | Lifetime prevalence of PDAC: 1.13% in males and 1.06% in females  PDAC incidence in males: 0.11 (age 20-29), 0.56 (age 30-39), 3.67 (age 40-49), 15.44 (age 50-59), 38.44 (age 60-69), 65.22 (age 70-79) per 100,000 persons  PDAC incidence in females: 0.11 (age 20-29), 0.44 (age 30-39), 2.89 (age 40-49), 10.67 (age 50-59), 27.89 (age 60-69), 53.89 (age 70-79) per 100,000 persons  Proportion of PDAC diagnosed as localized disease: 8% in males and 10% in females  Proportion of PDAC diagnosed as regional disease: 27% in males and 28% in females  Proportion of PDAC diagnosed as distant disease: 56% in males and 50% in females  Proportion of PDAC diagnosed as unstaged disease: 9% in males and 12% in females  Proportion of PDAC from solid lesions: 90%  Lifetime risk of PDAC-associated death: 0.94% in males and 0.88% in females | PDAC mortality from detected localized disease (monthly probability of death): 0.0242 in males and 0.0228 in females  PDAC mortality from detected regional disease (monthly probability of death): 0.0393  PDAC mortality from detected distant disease (monthly probability of death): 0.0631  PDAC mortality from detected unstaged disease (monthly probability of death): 0.0522 |  | Lifetime horizon (or until age 100), 1-month cycle length |
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| Aronsson et al., 2018 | BD-IPMN diagnostic accuracy: 0.85 (0.7-1.0) | Surgical candidate: age below 80 years  Benign other: 0.10 (0-0.2)  Cancer: 0.05 (0-0.1)  Location in head or neck of the pancreas: 50%  Location in body or tail of the pancreas: 50% | Detected at follow-up: 0.90 (0.6-1)  Resectable if found at follow-up: 0.75 (0.16-0.9)  Resectable if symptomatic patient: 0.16 (0-0.3)  Recurrence rate: 0.25 (0-0.4)  Survival unresectable/recurred (metastatic): 0.0  Turning symptomatic: 0.5 (0.1-1)  Unresected "resectable" turning metastatic: 0.5 (0.1-1)  Mortality partial pancreatectomy: 0.02 (0-0.1)  Mortality total pancreatectomy: 0.03 (0-0.1)  Mortality remnant pancreatectomy: 0.03 (0-0.1)  Diabetes following partial pancreatectomy: 0.22 (0-0.3)  Diabetes following total pancreatectomy: 1.0 | Base-case 65 year old: 0.808 (0.7-1)  Annual decrease: -0.01  Undergoing surveillance: no decrease  Surgical consequence (<1 year/cycle post surgery): -0.10 (-0.2-0)  1-year post partial pancreatectomy: no decrease  Post total pancreatectomy: -0.05 (-0.1-0)  Diabetes mellitus: -0.05 (-0.1-0)  Symptoms: -0.03 (-0.1-0)  Palliative: -0.25 (-0.4-0) | 35-year horizon, 1-year cycle |
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| Hu et al., 2018 |  |  | Annual progression rate from worrisome to high-risk: 0.05  Annual progression rates from worrisome to invasive: 0.01 (node-positive: 0.006, metastatic: 0.004)  Surgical staging:  Resection for worrisome BD-IPMN - Benign/high-grade dysplasia: 0.795 - High-grade dysplasia: 0.114 - Invasive cancer: 0.106 Resection for high-risk BD-IPMN - Benign: 0.315 - High-grade dysplasia: 0.385 - Invasive cancer: 0.257  Five-year overall survival: - Resected noninvasive: 0.87 - Resected invasive: 0.39 - Unresectable cancer: <0.01 - Baseline population: 0.70  Five-year recurrence-free survival: - Resected noninvasive: 0.98 - Resected invasive: 0.36  Surgical outcome: Pancreaticoduodenectomy - 30-day mortality: 0.024 - Pancreatic leak: 0.134 - Delayed gastric emptying: 0.18 Distal pancreatectomy - 30-day mortality: 0.017 - Pancreatic leak: 0.259 | Resected non-invasive/surveillance: 1.0  BD-IPMN, high-risk stigmata: 0.9  Resected invasive: 0.8  Unresectable cancer: 0.7  Perioperative recovery: -0.25  Pancreatic leak: -0.50  Delayed gastric emptying: -0.40  Chemotherapy: -0.04  Progression to high-risk stigmata: -0.06  Progression to cancer: -0.12 | 20-year horizon, 3-month cycle |
| Cucchetti et al., 2016 |  | Mean tumor doubling time: 109.8 days (76.5-143 days)  Mean tumor size at  diagnosis: - Stage IA: 1.4 cm (1.1-1.6 cm) - Stage IB: 2.4 cm (2.1-2.6 cm) - Stage IIA: 3.1 cm (2.8-3.4 cm) - Stage IIB: 3.3 cm (3.1-3.4 cm) - Stage III: 4.3 cm (4.1-4.5 cm) - Stage IV: 4.7 cm (4.5-4.8 cm) | 5-year survival after pancreatic resection: - Stage IA: 31.4% (21.7-41.1%) - Stage IB: 27.2% (18.9-35.5%) - Stage IIA: 15.7% (13.4-21.0%) - Stage IIB: 7.7% (5.0-10.4%) - Stage III: 6.8% (2.5-11.1%) - Stage IV: 2.8% (0-5.7%)  5-year survival without pancreatic  resection: - Stage IA: 3.8% (0-10.2%) - Stage IB: 3.4% (0-8.8%) - Stage IIA: 2.4% (0-5.6%) - Stage IIB: 2.0% (0-5.3%) - Stage III: 1.8% (0-4.1%) - Stage IV: 0.6% (0-1.2%) |  | Lifetime horizon |
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| Pandharipande et al., 2015 | MRI screening sensitivity: 0.56  MRI screening specificity: 0.97 | Biologic pathway to PDAC: cystic (10%) and solid (90%)  Prevalence of imaging-detected cysts (IPMN): - Cyst prevalence: 4.6% - High-risk lesions: 6% - Low-risk lesions: 94% | Surgical mortality: 2% |  | Lifetime horizon (or until age 99), 1-year cycle length |
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| Pandharipande et al., 2015 | MRI screening sensitivity: 0.56  MRI screening specificity: 0.97 | Relative risk of PDAC: - Primary cohort: 3.5 - 1 first-degree relative: 4.5 - 2 first-degree relative: 6.4 - >=3 first-degree relative: 32.0 | Surgical mortality: 1% |  | Lifetime horizon (or until age 100), 1-year cycle length |
| Das et al., 2015 | MRI/CT sensitivity in differentiating mucinous from non-mucinous cysts: 0.7 (0.5-1)  CEA + cytology sensitivity in differentiating mucinous from non-mucinous cysts: 0.8 (0.5-1)  CEA + cytology specificity in differentiating mucinous from non-mucinous cysts: 0.65 (0-0.8)  PathFinder TG + CEA + cytology sensitivity in differentiating mucinous from non-mucinous cysts: 0.68 (0.5-0.8)  PathFinder TG + CEA + cytology specificity in differentiating mucinous from non-mucinous cysts: 0.9 (0.7-0.95)  PathFinder sensitivity in distinguishing aggressive from non-aggressive cysts: 0.82 (0.7-0.9)  PathFinder specificity indistinguishing aggressive from non-aggressive  cysts: 0.85 (0.7-0.9) | Proportion of non-mucinous cystic lesions: 0.3 (0.1-0.6)  Proportion of mucinous cystic lesion/branch-type IPMN:  - Benign: 0.65 (0-1.0) - Borderline: 0.20 (0-1.0) - Malignant: 0.15 (0-1.0) | Annual probability of asymptomatic mucinous cystic lesion/side-branch IPMN transitioning from asymptomatic to symptomatic state:  - Cysts <=3 cm: 0.02 (0-0.05) - Cysts >3 cm: 0.1 (0.01-0.15)  Annual probability of benign mucinous cystic lesion/branch type IPMN transitioning from benign to malignant state:  - Cysts <=3 cm: 0.025 (0-0.5) - Cysts >3 cm: 0.05 (0-0.5)  Annual probability of malignant cysts transitioning from asymptomatic to symptomatic state: 0.25 (0-1.0)  Perioperative mortality (years): 3 (1-15)  Annual mortality from invasive malignant cysts: 0.1 (0-0.5) | Normal health states: 1.0  Incidental cystic lesion: 1.0 (0.75-1)  Symptomatic cystic lesion: 0.95 (0.7-1)  Postoperative state: 0.95 (0.7-1)  Early cancer: 0.9 (0.68-1)  Advanced cancer: 0.5 (0.38-1) | Lifetime horizon, 1-year cycle |
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| Ghatnekar et al., 2013 | Sensitivity of proteomic test for PC diagnosis: 0.88  Specificity of proteomic test for PC diagnosis: 0.85  Sensitivity of screening test: 0.95  Specificity of screening test: 0.95 | PC incidence corresponding to relatives among familial PC and >65 years old: 35% |  | Resectable PC (stage 0-IIB): 0.834  Locally advanced PC (stage III): 0.798  Metastatic PC (stage IV): 0.762 | Lifetime horizon, annual cycle length |
|  | PC incidence corresponding to Swedish general population aged 72: 0.046% |  |  |
|  | PC incidence corresponding Swedish general population aged 60: 0.026% |  |  |
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| Huang et al., 2010 | IAP 2006 Guideline sensitivity in detecting malignancy: 0.99 (0.65-1.0)  IAP 2006 Guideline specificity in detecting malignancy: 0.25 (0.1-0.5) | Symptoms of invasive cancer: 0.78 (0.5-1.0)  Symptoms of non-invasive IPMN (adenoma, dysplasia/CIS): 0.66 (0.4-0.9)  Cancer resectability in patients with missed invasive cancer: 0.56 (0.25-0.8)  Cancer resectability in patients with diagnosed invasive cancer: 0.80 (0.5-1.0) | Probability of malignancy (CIS and invasive cancer): 0.15 (0.01-0.5)  Probability of malignancy being invasive: 0.41 (0.15-0.8)  Perioperative mortality of pancreaticoduodenectomy: 0.046 (0.01-0.1)  Perioperative morbidity of pancreaticoduodenectomy: 0.35 (0.2-0.65)  Annual probability of recurrence for invasive cancer: 0.29 (0.15-0.4)  Annual probability of adenoma transitioning to dysplasia/CIS: 0.0293 (0.005-0.2)  Annual probability of dysplasia/CIS transitioning to invasive cancer: 0.305 (0.05-0.65)  Annual progression of symptoms in noninvasive IPMN: 0.1 (0.01-0.2)  Annual probability of developing indication for resection: 0.04 (0-0.1) | Post-Whipple procedure: 1.0 (0.7-1.0)  Unresectable cancer: 0.69 (0.3-0.8)  Diabetes: 0.88 (0.6-1.0)  Penalty toll for pancreaticoduodenectomy (4 weeks): -0.3 (-0.6 to -0.1)  Penalty toll for surgical complications (4 weeks): -0.3 (-0.6 to -0.1) | Lifetime horizon, 6-month cycle |
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| Weinberg et al., 2010 | Sensitivity of CT in detecting malignant IPMN: 0.8 (0.5-1)  Specificity of CT in detecting benign IPMN: 0.99 (0.5-1)  Sensitivity of EUS/FNA in detecting malignant IPMN: 0.86 (0.5-1)  Specificity of EUS/FNAin detecting benign IPMN: 0.99 (0.5-1) | Benign cyst: 9%  Benign BD-IPMN: 89% (size<1 cm), 86% (1<size<2 cm), 79% (2<size<3 cm), 70% (size≥3 cm)  Malignant BD-IPMN: 1% (size<1 cm), 3% (1<size<2cm), 11% (2(size<3 cm), 20% (size≥3 cm)  PC with cyst: 1%  Benign to malignant transformation per year: 0.001% (size<1 cm), 1% (1<size<2 cm), 1.7% (2<size<3 cm), 3% (size≥3 cm) | Benign cyst growth: 0.035 (0-0.1)  Chronic complications after pancreaticoduodenectomy: 0.194 (0.06-0.3)  Perioperative complications after pancreaticoduodenectomy: 0.412 (0.3-0.6)  Death with a recurrent PC after surgical resection: 0.9 (0.3-0.9)  Developing symptoms with a benign cyst: 0.05 (0.01-015)  Developing symptoms with a benign IPMN: 0.05 (0.01-0.15)  Developing symptoms with unrecognized malignant IPMN: 0.95 (0.8-1)  Dying from adjuvant chemotherapy: 0.002 (0-0.01)  Dying from an EUS/FNA: 0.0001 (0-0.002)  Dying from a malignant IPMN without treatment: 0.6 (0.4-0.8)  Dying from PC without treatment: 0.9 (0.8-1)  Dying from a pancreaticoduodenectomy: 0.064 (0.01-0.2)  Malignant IPMN found in the do nothing strategy is operable: 0.15 (0-0.2)  Malignant IPMN will return after pancreaticoduodenectomy: 0.17 (0-0.6)  PC will return after pancreaticoduodenectomy: 0.24 (0-0.6)  PC found in the do nothing strategy is operable: 0.1 (0.01-0.3) | Chemotherapy for malignant IPMN or PC: 0.62 (0.4-0.9)  Chronic complications from pancreaticoduodenectomy: 0.65 (0.4-0.9)  Perioperative complications from pancreaticoduodenectomy: 0.5 (0.4-0.9)  Developing inoperable malignant IPMN or PC: 0.65 (0.4-0.9)  Undergoing invasive surveillance: 0.98 (0.5-1)  Undergoing noninvasive surveillance: 0.98 (0.5-1)  Having been cured of cancer without any complications: 0.99 (0.5-1)  Developing recurrent malignant IPMN or PC: 0.68 (0.4-0.8)  Undergoing a PD with no complications: 0.98 (0.5-1) | 20-year horizon, annual cycle length |
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| Das et al., 2009 | Cross-sectional imaging accuracy in differentiating serous and mucinous cystic neoplasm/branch-type IPMN: 0.7 (0.5-1.0)  EUS/FNA + CEA + cytology accuracy: 0.8 (0.5-1.0) | Proportion of non-mucinous cystic lesions: 0.3 (0.1-0.6)  Proportion of mucinous cystic lesion/branch-type IPMN at presentation:  - Benign: 0.65 (0-1.0) - Borderline: 0.20 (0-1.0) - Malignant: 0.15 (0-1.0) | Annual probability of benign mucinous cystic lesion/branch-type IPMN transitioning from asymptomatic to symptomatic state:  - Cysts ≤3 cm: 0.02 (0-0.05) - Cysts >3 cm: 0.1 (0.01-0.15)  Annual probability of benign mucinous cystic lesion/branch-type IPMN transitioning from benign to malignant state:  - Cysts ≤3 cm: 0.025 (0-0.5) - Cysts >3 cm: 0.05 (0-0.5)  Annual probability of malignant cysts transitioning from asymptomatic to symptomatic state: 0.25 (0-1.0)  Annual probability of malignant cysts transitioning to advanced malignancy without treatment: 0.25 (0-1.0)  Perioperative mortality: 0.03 (0.01-0.15)  Annual mortality from invasive malignant cysts: 0.1 (0-0.5)  Annual mortality from advanced pancreatic malignancy: 0.9 (0.25-1.0) | Normal health states: 1.0 (+/-25%)  Incidental cystic lesion: 1.0 (+/-25%)  Symptomatic cystic lesion: 0.95 (+/-25%)  Postoperative state: 0.95 (+/-25%)  Early cancer: 0.9 (+/-25%)  Late cancer: 0.5 (+/-25%) | Lifetime horizon, 1 year cycle |
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| Rubenstein et al., 2007 | Sensitivity of EUS without FNA: 0.72 (0.5-0.9)  Specificity of EUS without FNA: 0.6 (0.45-0.75)  Sensitivity of EUS with FNA: 0.54 (0.25-0.81)  Specificity of EUS with FNA: 0.99 (0.82-1) | Standardized incidence ratio for cancer in 1st degree relatives <65 years old compared to general population: 15.8 (4.31-40.4)  Standardized incidence ratio for cancer in 1st degree relatives ≥65 years old compared to general population: 7.4 (2.97-15.2)  Proportion of 1st degree relatives who are susceptible to cancer: 0.5 (0.05-1)  Proportion of cancers that are local without surveillance: 0.08 (0.075-0.085)  Proportion of cancers that are local with surveillance: 0.5 (0.08-0.071)  Proportion of non-local cancers that have distant metastases: 0.67 (0.65-0.68)  Age at which prophylactic total pancreatectomy is performed: 45 years (45-75 years)  Mortality ratio of diabetes compared to general population: - Ages 45-49 years: 2.7 (1.2-6.1) - Ages 50-64 years: 1.9 (1.4-2.5) - Ages ≥65 years: 1.8 (1.5-2.3) | Mortality from local cancer: 0.839 (0-1)  Mortality from regional cancer: 0.93 (0.928-1)  Mortality from distant cancer: 0.984 (0.975-1)  Mortal complication from EUS without FNA: 0.0023% (0.0004-0.0129%)  Mortal complication from EUS with FNA: 0.0204% (0.0036-0.8406%)  Mortal operative complication from prophylactic total pancreatectomy: 0.05 (0.001-0.2) | Asymptomatic without cancer or pancreatectomy: 1.0 (0-1.0)  Diabetes: 0.88 (0.43-1.0)  One-time postoperative toll for recuperation: 0.125 (0-0.50) | Lifetime horizon (or until age 90), 1-year cycle length |
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| Rulyak et al., 2003 | EUS sensitivity: 0.9 (0.5-1) | Prevalence of dysplasia: 0.2 (0.01-0.5) | Probability that EUS will be normal: 0.34 (0.1-0.75) |  | Lifetime horizon |
|  | ERCP sensitivity: 0.9 (0.5-1) |  | Probability of progression to PC given that dysplasia is present: 0.9 (0.75-1) |  |  |
|  |  |  | Probability of developing PC in the absence of dysplasia: 0.01 (0-0.2) |  |  |
|  |  |  | Probability of ERCP complication (pancreatitis): 0.051 (0.003-0.082) |  |  |
|  |  |  | Operative mortality with total pancreatectomy: 0.03 (0.01-0.05) |  |  |

**Table S4.** Incremental cost-effectiveness ratios and cost differences of management strategies in economic evaluation studies

| **Strategy** | | | **Comparator** | | | **ICER/ delta cost** | **Study** | **Subgroup** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Cost** | **Effectiveness** |  | **Cost** | **Effectiveness** |
| **Guideline-based** | | | | | | | | |
| IAP 2017 | € 1,537.27 | 12.54 QALYs | Annual contrast-based EUS | € 705 | 13.57 QALYs | Dominated | Faccioli et al., 2022 | BD-IPMN/MCN <1 cm |
| Italian consensus | € 828.22 | 13.37 QALYs | Annual contrast-based EUS | € 705 | 13.57 QALYs | Dominated | Faccioli et al., 2022 | BD-IPMN/MCN <1 cm |
| IAP 2017 | € 1,756.88 | 11.32 QALYs | Annual contrast-based EUS | € 1,480.50 | 11.59 QALYs | Dominated | Faccioli et al., 2022 | BD-IPMN/MCN <1 cm |
| Italian consensus | € 1,663.95 | 11.46 QALYs | Annual contrast-based EUS | € 1,480.50 | 11.59 QALYs | Dominated | Faccioli et al., 2022 | BD-IPMN/MCN <1 cm |
| ACG and European guidelines | € 8,847.10 | 9.2 QALYs | Annual contrast-based EUS | € 3,684.71 | 9.7 QALYs | Dominated | Faccioli et al., 2022 | MCN 3-4 cm |
| European guideline | € 2,196.00 | 12.59 QALYs | Annual contrast-based EUS | € 1,301.44 | 13.46 QALYs | Dominated | Faccioli et al., 2022 | SCN <4 cm |
| Italian consensus | € 1,662.40 | 13.4 QALYs | Annual contrast-based EUS | € 1,301.44 | 13.46 QALYs | Dominated | Faccioli et al., 2022 | SCN <4 cm |
| IAP 2017 | $ 16,825 | 13.90 QALYs | AGA 2015 | $ 8,938 | 13.93 QALYs | Dominated \* | Lobo et al., 2020 |  |
| Radiologist recommendation | $317-$491 | - | ACR recommendation | $344-$528 | - | No difference | Rosenkrantz et al., 2018 |  |
| **CT-based** | | | | | | | | |
| Single 18F-FDG-PET/CT | $ 104,842 | 8.48 QALYs | Single CT/MRI | $ 106,424 | 8.37 QALYs | Dominant | Bicu et al., 2021 |  |
| Single CT | $ 11,275 | 17.4882 QALYs | Single abdominal US | $ 11,035 | 17.4875 QALYs | Dominated | Kowada et al., 2020 |  |
| Single PET | $ 11,731 | 17.4878 QALYs | Single abdominal US | $ 11,035 | 17.4875 QALYs | Dominated | Kowada et al., 2020 |  |
| **MRI-based** | | | | | | | | |
| Single MRI | $ 11,286 | 17.4892 QALYs | Single abdominal US | $ 11,035 | 17.4875 QALYs | 214,488 $/QALY | Kowada et al., 2020 |  |
| US-restricted MRI | $ 366.4 | - | European evidenced-based MRI | $ 1158.9 | - | $ -792.5 \* | Morelli et al., 2019 |  |
| **EUS-based** | | | | | | | | |
| Single EUS | $ 11,139 | 17.4885 QALYs | Single abdominal US | $ 11,035 | 17.4875 QALYs | 101,026 $/QALY | Kowada et al., 2020 |  |
| Single EUS/FNA + CEA + resect if operable | $23,337 | 10.73 QALYs | Resect if operable | $ 13,200 | 9.66 QALYs | 11,394 $/QALY | Das et al., 2009 |  |
| **No screening/surveillance** | | | | | | | | |
| No screening | $ 23,189 | 17.4532 QALYs | Single abdominal US | $ 11,035 | 17.4875 QALYs | Dominated | Kowada et al., 2020 |  |
| Wait-and-watch (after single cross-sectional imaging) | $ 18,883 | 10.34 QALYs | Resect if operable | $ 13,200 | 9.66 QALYs | 9,474 $/QALY | Das et al., 2009 |  |

\* Incremental cost-effectiveness ratios were calculated based on cost and effectiveness of strategies in original studies.

Dominated: the strategy listed is less effective and more expensive than the compared strategy

Dominant: the strategy listed is more effective and less expensive than the compared strategy

IAP, International Association of Pancreatology; ACG, American College of Gastroenterology; CT, computed tomography; 18F-FDG-PET, flourine-18 fluorodeoxyglucose positron emission tomography; PET, positron emission tomography; MRI, magnetic resonance imaging; US, ultrasound; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; CEA, carcinoembryonic antigen; QALY, quality-adjusted life year; AGA, American Gastroenterological Association; ACR, American College of Radiology; ICER, incremental cost-effectiveness ratio; BD-IPMN, branch duct intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; SCN, serous cystic neoplasm.