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Research Article

Diabetes and Pancreatic Cancer: Epidemiology, Temporality, Mechanisms, Biomarkers, and Opportunities for Earlier Detection

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Abstract

Background: Diabetes and pancreatic cancer have a bidirectional, time-dependent relationship. Long-standing type 2 diabetes mellitus (T2DM) may contribute to carcinogenesis, whereas new-onset diabetes can be an early manifestation of occult pancreatic ductal adenocarcinoma (PDAC).

Methods: This structured narrative review integrates systematic reviews, meta-analyses, prospective and pooled epidemiological studies, mechanistic investigations and screening guidance. Evidence was interpreted according to diabetes phenotype, exposure timing, outcome ascertainment and susceptibility to reverse causation. No new meta-analysis or formal risk-of-bias assessment was performed.

Results: A meta-analysis of 35 cohorts found an overall pancreatic-cancer relative risk of 1.94 (95% confidence interval 1.66–2.27), with the highest risk shortly after diabetes onset. In a landmark cohort of adults aged ≥50 years, 0.85% developed pancreatic cancer within three years of new diabetes. Prospective evidence supports increased risk with both recent and longer-standing diabetes, although excluding the immediate prediagnostic interval attenuates estimates. Glucose trajectories and weight loss are more informative for risk enrichment than isolated glycemic values. Candidate mechanisms include insulin resistance, inflammation and tumor-derived mediators that impair β-cell function. Clinical risk models and exosomal biomarkers remain distinct from proven screening interventions.

Conclusions: Diabetes should be interpreted by timing and phenotype. Later-life onset accompanied by unintentional weight loss or rapid glycemic deterioration warrants clinical attention. Routine pancreatic-cancer screening of all people with diabetes is unsupported; prospective evaluation of staged risk enrichment, biomarkers and selective imaging remains necessary.

Keywords: *Balinese Adat Law, Lokika Sanggraha, Clinical Forensic Medicine, Medicolegal Framework, Evidence-Based Justice.*

Introduction

Pancreatic cancer remains a malignancy in which incidence and mortality are unusually close. IARC estimates indicate more than 530,000 new cases and more than 490,000 deaths worldwide in 2024. These figures underscore the importance of diagnosis before advanced disease develops. PDAC is the dominant exocrine malignancy considered in the diabetes–pancreatic cancer literature. [1]

Diabetes is simultaneously common and heterogeneous. WHO estimates that 14% of adults ≥18 years were living with diabetes in 2022, making even a moderate association with pancreatic cancer potentially important at population scale. Yet diabetes is not a single exposure. Type 1 diabetes mellitus (T1DM) reflects autoimmune β-cell destruction; T2DM is characterized principally by insulin resistance with progressive β-cell dysfunction; and pancreatogenic or type 3c diabetes results from disease of the exocrine pancreas and includes diabetes related to chronic pancreatitis, pancreatic neoplasia and pancreatic surgery. [2, 3]

This distinction matters because pancreatic cancer and diabetes can be positioned on either side of the causal arrow. In one direction, obesity, insulin resistance, compensatory hyperinsulinemia, hyperglycemia, inflammation and associated metabolic disturbances could create a biological environment favorable to neoplastic initiation or progression. In the opposite direction, an occult pancreatic tumor can disrupt systemic glucose homeostasis before its anatomical consequences produce jaundice, pain or other classical manifestations. [4]

The epidemiology strongly suggests that both processes occur. Ben and colleagues' meta-analysis of 35 cohort studies found an overall RR of 1.94 but also showed a negative relationship between duration of diabetes and pancreatic-cancer risk, with the highest risk in diabetes diagnosed less than one year earlier. A review of pancreatic-cancer-associated diabetes reported that new-onset diabetes is associated with an approximately five- to eightfold short-term probability of pancreatic cancer diagnosis compared with the background population and that dysglycemia may precede cancer diagnosis by two to three years. These observations are difficult to explain exclusively through diabetes causing a new malignancy over a period of months; they strongly support reverse causation from preclinical cancer. [4, 5]

The central clinical challenge is therefore statistical as much as biological. New-onset diabetes is common, whereas pancreatic cancer remains uncommon; fewer than approximately 1% of unselected people with new-onset diabetes develop pancreatic cancer over the short term. Screening every newly diagnosed diabetic patient with computed tomography (CT), MRI or endoscopic ultrasonography (EUS) would consequently expose large numbers of people without cancer to cost, incidental findings and potential procedure-related harms. This low positive predictive value explains why diabetes is best conceived as a first-stage enrichment marker rather than a stand-alone screening indication. [6, 7]

The purpose of this review is to integrate epidemiology with temporality, diabetes classification, glycemic and endocrine biomarkers, biological mechanisms, diagnostic biases and current screening recommendations, with particular emphasis on which findings are sufficiently robust for clinical translation and which remain investigational.

Methods

This manuscript is a structured narrative evidence review, rather than a registered systematic review or de novo meta-analysis. Searches targeted PubMed/MEDLINE-indexed publications and primary journal, governmental, cancer-registry and guideline sources. No lower publication-date limit was imposed; landmark earlier studies and evidence available through September 2026 were prioritized. Bibliographic details and cited recommendations were checked during revision.

Search concepts included combinations of: pancreatic cancer, pancreatic ductal adenocarcinoma, diabetes mellitus, type 1 diabetes, type 2 diabetes, pancreatogenic diabetes, type 3c diabetes, new-onset diabetes, diabetes duration, fasting glucose, HbA1c, insulin, C-peptide, hyperinsulinemia, oxidative stress, inflammation, extracellular vesicles, exosomes, adrenomedullin, population attributable fraction, risk prediction, END-PAC, screening and surveillance. Reference chaining from major reviews was used to identify older primary studies.

Priority was given to systematic reviews and meta-analyses, prospective cohorts, pooled analyses, objectively measured glycemia, explicit diabetes duration and adjustment for age, smoking and body mass index. Extracted information included design, population, exposure definition, temporal interval, adjusted effect estimates and uncertainty. Mechanistic evidence was distinguished as experimental, translational or observational; meta-analytic estimates were not recomputed.

The review did not use duplicate independent selection or a formal risk-of-bias instrument. Heterogeneous definitions of new-onset diabetes and incomplete longitudinal metabolic data limit comparison.

Retrospective classification cannot reliably separate conventional T2DM from tumor-induced diabetes. The synthesis is therefore interpretive and does not claim exhaustive retrieval or a pooled causal estimate.

Results

Epidemiology and temporal patterns

The most reproducible finding across decades of observational research is that diabetes and pancreatic cancer co-occur more often than expected. In the 2011 cohort meta-analysis by Ben et al., 35 studies produced a pooled pancreatic-cancer RR of 1.94 (95% CI 1.66–2.27). Heterogeneity was high (I^2 = 93.6%), and shorter diabetes duration was associated with progressively greater risk, which is a major warning against treating 1.94 as a homogeneous causal estimate.

The distinction is demonstrated well by the Pancreatic Cancer Cohort Consortium. Elena et al. pooled 1,621 pancreatic adenocarcinoma cases and 1,719 matched controls from 12 prospective cohorts. Importantly, people diagnosed with diabetes within two years of cancer diagnosis were excluded. Under this design, diabetes was associated with only a 40% increase in risk (OR 1.40, 95% CI 1.07–1.84). Risk was strongest for diabetes of 2–8 years' duration (OR 1.79, 95% CI 1.25–2.55) and absent statistically at ≥9 years (OR 1.02, 95% CI 0.68–1.52) in that particular pooled analysis. This does not prove that long-standing diabetes is harmless; rather, it demonstrates how estimates vary with population, exposure definition, insulin biology, competing mortality and analytic exclusion of the prediagnostic period.

Later prospective analyses continue to support persistent risk beyond the immediate prediagnostic interval. In the Nurses' Health Study and Health Professionals Follow-up Study, Yuan et al. reported an age-adjusted HR of 2.97 (95% CI 2.31–3.82) for recent-onset diabetes and 2.16 (95% CI 1.78–2.60) for longer-standing diabetes compared with no diabetes. The combination of recent diabetes and weight loss was particularly informative, supporting the clinical observation that metabolically atypical diabetes differs from ordinary weight-gain-associated T2DM.

The risk curve around pancreatic cancer diagnosis is asymmetric. Long-standing diabetes conveys a modest background excess risk, while diabetes beginning within approximately three years before cancer diagnosis is enriched for tumor-associated dysglycemia. Chari et al. demonstrated that 0.85% of people ≥50 years with newly developed diabetes were diagnosed with pancreatic cancer within three years, with more than half of cancer diagnoses occurring during the first six months. Reviews subsequently estimated that new-onset diabetes carries an approximately five- to eightfold short-term enrichment for pancreatic cancer compared with background rates.

The timeline should not be interpreted as a deterministic progression. The overwhelming majority of people developing ordinary T2DM within this time window do not have pancreatic cancer. The clinical value of timing lies in changing the prior probability enough to justify a second risk-stratification step, not in making diabetes itself a cancer diagnosis.

Objectively dating diabetes onset is important because clinical diagnosis may lag behind abnormal glycemia. The prospective study by Chari and colleagues identified 18,838 adults aged ≥50 years with glycemically defined new-onset diabetes, reinforcing the feasibility of studying the metabolic interval before cancer diagnosis. Such cohorts improve temporal ascertainment but do not themselves establish a benefit from screening.

Table 1 summarizes selected epidemiological studies. Relative risks (RRs), hazard ratios (HRs), odds ratios (ORs), incidence-rate ratios (IRRs) and observed-to-expected ratios are not interchangeable; differences in populations and time windows preclude direct causal comparison. The glucose and population-attributable-fraction studies are discussed below.

Table 1. Selected epidemiological evidence.

Study	Design and exposure	Main finding
Ben 2011	Meta-analysis of 35 cohorts; diabetes	RR 1.94 (95% CI 1.66–2.27); highest risk within one year of diabetes onset.
Chari 2005	Population cohort; 2,122 adults ≥50 with new diabetes	18 cancers within three years (0.85%); observed/expected ratio 7.94 (4.70–12.55).
Elena 2013	12 prospective cohorts; diabetes <2 years before cancer excluded	OR 1.40 (1.07–1.84); duration 2–8 years: 1.79 (1.25–2.55); ≥9 years: 1.02 (0.68–1.52).
Yuan 2020	Two prospective US cohorts; duration and weight change	Age-adjusted HR: recent diabetes 2.97 (2.31–3.82); long-standing diabetes 2.16 (1.78–2.60).
Liao 2015	Nine prospective studies; fasting glucose	Rate ratio 1.14 (1.06–1.22) per 10 mg/dL increase.
Chuang 2025	Taiwan cohort; 80,186 with and 152,323 without diabetes	Adjusted IRR 1.77 (1.51–2.09); PAF 12.9% (7.9–18.6%).

Diabetes phenotypes

T2DM has the strongest evidence base because it is common and because the metabolic phenotype overlaps biologically with several established pancreatic-cancer determinants. The association persists after statistical adjustment for BMI and smoking in many cohorts, although residual confounding remains possible. T1DM is less well studied. A 2018 meta-analysis comprising 15 observational studies and approximately 1.9 million participants found overall cancer risk increased in T1DM and found pancreatic cancer among the sites with a statistically significant increase; however, site-specific estimates were based on fewer events and substantial between-study heterogeneity.

Type 3c diabetes deserves special emphasis because of under-recognition. It refers to diabetes secondary to pancreatic exocrine disease, including chronic pancreatitis, pancreatic cancer, cystic fibrosis and pancreatic resection. Unlike classic T2DM, the phenotype can combine deficient insulin secretion with deficient glucagon secretion, pancreatic exocrine insufficiency and malnutrition. In patients with pancreatic cancer, the term overlaps with cancer-associated diabetes, although not every patient with PDAC-related new-onset hyperglycemia has the advanced exocrine destruction traditionally associated with pancreatogenic diabetes. The paraneoplastic phenotype may therefore begin before major structural pancreatic destruction is clinically evident.

Glycemic and endocrine biomarkers

Liao and colleagues combined nine prospective studies with 2,408 pancreatic-cancer cases. Each 10 mg/dL (0.56 mmol/L) increase in fasting glucose was associated with a rate ratio of 1.14 (95% CI 1.06–1.22). This graded association extends below the diagnostic threshold for diabetes, but does not establish that lowering glucose prevents pancreatic cancer.

A meta-analysis published online in 2024 and in print in 2025 estimated an adjusted effect size of 1.40 (95% CI 1.23–1.59) for prediabetes compared with normoglycemia. Because dysglycemia is common and nonspecific, these findings do not justify pancreatic imaging of everyone with prediabetes.

The biomarker findings reinforce a trajectory-based rather than threshold-based approach. Fasting glucose has a continuous relationship with risk, and HbA1c can help reconstruct recent glycemic deterioration, but neither provides cancer specificity. Insulin and C-peptide are mechanistically attractive but analytically difficult because concentrations change with fasting status, duration of diabetes, β-cell reserve, renal function and treatment. The prospective C-peptide literature illustrates this complexity: fasting insulin and C-peptide were not clearly associated with pancreatic cancer in one major analysis, whereas non-fasting C-peptide showed a positive relationship.

HbA1c and fasting glucose should consequently be considered longitudinal clinical measurements rather than tumor markers. An isolated abnormal result cannot determine whether dysglycemia reflects conventional T2DM, pancreatic disease or a transient metabolic disturbance. Reviewing earlier measurements helps distinguish genuinely recent onset from longstanding but previously unrecognized diabetes. Likewise, interpreting weight loss requires its timing and clinical context: intentional dietary change differs from progressive unexplained loss accompanying worsening glycemia. A coherent temporal pattern may increase suspicion, but no combination of these features establishes a cancer diagnosis without appropriate further investigation.

Mechanistic pathways

For long-standing T2DM, the most coherent causal model begins with insulin resistance. Compensatory hyperinsulinemia increases signaling through insulin receptors and interacts with the IGF system, potentially promoting proliferative and anti-apoptotic signaling through pathways including PI3K–AKT–mTOR. Obesity and T2DM also promote a chronic inflammatory environment involving cytokine signaling, adipokine imbalance and innate immune activation. Persistent hyperglycemia can enhance oxidative stress, reactive oxygen species generation and metabolic stress, providing plausible links to DNA damage and tumor-supportive signaling. These pathways are biologically credible but should not be interpreted as proof that glucose itself is the dominant causal agent; insulin resistance, adiposity, inflammation and glycemia are tightly correlated exposures.

PDAC-associated diabetes can involve systemic insulin resistance and β-cell dysfunction disproportionate to pancreatic tissue destruction. Aggarwal and colleagues identified increased adrenomedullin expression and demonstrated impaired glucose-stimulated insulin secretion in experimental systems. Javeed and colleagues subsequently showed that pancreatic-cancer-derived exosomes containing adrenomedullin entered β cells and inhibited insulin secretion; receptor blockade reversed the inhibitory effect in their models. These findings support a paraneoplastic mechanism but do not establish an accurate clinical screening assay.

This distinction predicts an important clinical paradox: ordinary T2DM frequently emerges in the setting of weight gain and metabolic syndrome, whereas occult-PDAC-associated diabetes may emerge despite unintentional weight loss. That paradox forms the biological and epidemiological foundation of the END-PAC model.

Risk models and population burden

Sharma and colleagues developed END-PAC using age at diabetes onset, change in glucose and change in weight. A score ≥3 achieved approximately 80% sensitivity and specificity in the discovery cohort. In the independent validation cohort, it identified seven of nine cancers, and cancer prevalence among patients scoring ≥3 was 3.6%. The small number of cancer outcomes and differences between derivation and validation performance require caution.

However, an 80%/80% test performs differently in a population where disease prevalence is approximately 1% than it does in a high-prevalence referral cohort. With a hypothetical 1% prevalence, 80% sensitivity and 80% specificity would generate roughly 0.8 true positives and 19.8 false positives per 100 tested, corresponding to a positive predictive value of only around 4%. This arithmetic illustrates why further biomarkers or imaging triage are required after a clinical risk score. Later models based on routine biochemical variables, health-record data and machine learning are being investigated, but external validation, transportability and demonstration of patient benefit remain incomplete.

In Taiwan, Chuang and colleagues compared 80,186 participants with diabetes with 152,323 without diabetes. The adjusted pancreatic-cancer IRR was 1.77 (95% CI 1.51–2.09), and the estimated population-attributable fraction (PAF) was 12.9% (95% CI 7.9–18.6%).

A PAF estimates the proportion of disease statistically attributable to an exposure under specified assumptions; it is not automatically the proportion preventable by treating diabetes.

Reverse causation is especially consequential for PAF interpretation: some diabetes classified as an exposure may already be a manifestation of cancer. Estimates also depend on population age, exposure prevalence and adjustment for shared risk factors. Combining a global adult prevalence with an historical pooled association would therefore not produce a reliable global causal PAF. A meaningful prevention estimate requires separation of long-standing diabetes from the prediagnostic metabolic interval.

Discussion

Causality and limitations

The evidence supports a bidirectional model rather than the simplistic proposition that “diabetes causes pancreatic cancer.” The magnitude of association is greatest when diabetes begins immediately before cancer diagnosis, declines as the diabetes–cancer interval lengthens, but in several datasets remains above baseline well beyond the likely occult-cancer period. That combination is exactly what would be expected if two processes coexist: a moderate etiologic effect of metabolic disease and a much stronger short-term effect of pancreatic cancer causing diabetes. [4, 5, 8, 9]

At the same time, simply excluding recent diabetes may remove clinically useful information. From an etiological perspective, the first two or three years may be a source of bias. From an early-detection perspective, that same interval is the signal of greatest interest. Research studies must therefore distinguish two separate questions: “Does diabetes cause pancreatic cancer?” and “Can diabetes identify people who already harbor occult pancreatic cancer?” The appropriate exposure definitions and exclusion periods are almost opposite for these two questions. [4, 10]

Detection bias creates an additional problem. A person newly diagnosed with diabetes may have more medical consultations, laboratory testing and abdominal imaging, increasing the probability of finding an otherwise silent tumor. Conversely, a patient with nonspecific cancer symptoms may undergo blood testing that simultaneously detects hyperglycemia. Observational studies relying on administrative diagnostic codes therefore risk conflating biological temporality with patterns of healthcare utilization. Prospective cohorts with stored blood, repeated glucose measurements and cancer-registry follow-up are methodologically preferable for understanding true temporal sequence. [8, 10]

Misclassification bias is especially relevant to type 3c diabetes. Adults who develop diabetes in middle or older age are frequently assumed to have T2DM, even when exocrine pancreatic pathology is present. This may contaminate “T2DM” epidemiological categories with pancreatogenic disease and further inflate apparent causal relationships. Type 3c should be considered particularly when diabetes coexists with chronic pancreatitis, pancreatic abnormalities, pancreatic surgery, exocrine insufficiency or unexplained nutritional/weight abnormalities. [3]

Exosomes offer a biologically appealing possibility because they might provide a molecular “fingerprint” distinguishing tumor-induced dysglycemia from ordinary metabolic diabetes. The adrenomedullin findings supply proof-of-concept that a pancreatic tumor can communicate remotely with islet cells. Yet a mechanistic mediator is not automatically a useful screening biomarker. A successful assay must show reproducible pre-analytical handling, analytical validity, adequate sensitivity for stage I/II disease, very high specificity in millions of people with ordinary dysglycemia, and ultimately evidence that using the assay reduces late-stage disease or mortality. [18]

Absolute risk must remain visible when communicating these findings. An almost eightfold observed-to-expected ratio in the landmark new-onset-diabetes cohort corresponded to fewer than one cancer per hundred participants over three years. Conversely, a low absolute probability does not make progressive unexplained symptoms clinically unimportant. The purpose of enrichment is to identify a subgroup in whom the likely benefit of investigation outweighs its burdens. Relative associations should therefore be presented alongside population characteristics, follow-up duration and absolute event counts whenever available. [6, 16]

Clinical interpretation and investigation

The USPSTF recommends against screening asymptomatic average-risk adults for pancreatic cancer, concluding that evidence of benefit is insufficient and potential harms are at least moderate; it also notes that no validated biomarker is sufficiently accurate for population screening. Diabetes alone should therefore not lead automatically to CT, MRI, EUS or CA19-9 screening. [20]

Diagnostic investigation of symptoms is different from screening asymptomatic populations. NICE recommends considering urgent direct-access CT, or urgent ultrasound if CT is unavailable, in adults aged ≥60 years with weight loss and new-onset diabetes. This is a symptom-based diagnostic recommendation, not a universal imaging indication for new diabetes. [21]

For selected individuals with substantial inherited or familial pancreatic-cancer risk, the CAPS Consortium supports specialist surveillance using MRI/magnetic resonance cholangiopancreatography (MRCP) and EUS. New-onset diabetes in a high-risk individual should prompt additional investigation. Eligibility, timing and follow-up should be determined within an experienced multidisciplinary program. [22]

Table 2 summarizes these distinctions. Its practical framework combines guidance for average-risk adults, symptom-based investigation, inherited-risk surveillance and recognition of pancreatogenic diabetes; it is not a newly validated universal algorithm. [3, 7, 20, 21, 22]

Table 2. Clinical interpretation of diabetes patterns.

Presentation	Interpretation and response
Stable long-standing T2DM without concerning symptoms	Maintain usual diabetes care; diabetes alone does not justify routine pancreatic imaging.
New diabetes in later life without other warning features	Review previous glucose/HbA1c values, weight, symptoms and family history. Most patients do not have pancreatic cancer.
New or worsening diabetes with unexplained weight loss or pancreatic symptoms	Prompt diagnostic assessment is appropriate; follow local referral pathways.
Age ≥60 with weight loss and new-onset diabetes	NICE: consider urgent direct-access CT, or urgent ultrasound if CT is unavailable.
New diabetes in an inherited/ familial high-risk individual	Arrange additional specialist assessment within the pancreatic surveillance program.
Diabetes with pancreatitis, pancreatic surgery or exocrine insufficiency	Consider type 3c diabetes and assess pancreatic disease, nutrition and exocrine function.

Clinical recommendations should also avoid a common therapeutic inference: observational associations between particular glucose-lowering drugs and pancreatic-cancer incidence do not establish anticancer efficacy. Confounding by indication, disease duration, immortal-time bias, obesity, renal function and changes in therapy after cancer-associated metabolic deterioration can distort drug–cancer associations. Diabetes therapy should therefore be selected primarily for glycemic, cardiovascular, renal, nutritional and patient-specific indications rather than as an unproven method of pancreatic-cancer chemoprevention.

These distinctions also affect how clinical pathways should be evaluated. A pathway initiated because a patient has weight loss and new diabetes is diagnostic case finding; a scheduled program for an asymptomatic person with a qualifying inherited risk is surveillance. Testing all otherwise asymptomatic people with diabetes would constitute a much broader screening strategy. Evidence supporting one setting cannot simply be transferred to the others, because pretest probability, competing disease, downstream investigations and the balance of benefit and harm differ. Clear eligibility criteria are essential when interpreting reports of diagnostic yield. [20, 21, 22]

Research priorities

Several important data gaps prevent stronger recommendations. First, there is no universally accepted biological definition distinguishing pancreatic-cancer-induced diabetes from conventional T2DM. Second, prediction models require broader prospective validation across ethnicity, sex, healthcare systems and diabetes ascertainment methods. Third, exosomal and multi-omic biomarkers need standardized laboratory methods and blinded prospective validation before imaging. Fourth, the optimal definition of “rapid glycemic deterioration” remains unsettled. Fifth, evidence relating T1DM specifically to PDAC remains much thinner than evidence for T2DM. Sixth, PAF estimates do not adequately separate causal diabetes from cancer-induced diabetes. Most importantly, randomized or carefully designed prospective intervention studies have not yet shown that screening patients selected primarily by new-onset diabetes reduces pancreatic-cancer mortality. [10, 13, 16, 18, 19, 20]

Future studies should specify the date and laboratory definition of diabetes onset before evaluating prediction. They should report missing historical weight or glucose measurements, treatment changes and alternative causes of metabolic deterioration, rather than assuming that complete retrospective records represent routine practice. Risk models need assessment in populations distinct from those used for development, with calibration as well as discrimination reported. A model that ranks patients correctly may still overestimate their absolute risk and generate excessive imaging when applied in a different healthcare system. [10, 16, 19]

For circulating or extracellular-vesicle biomarkers, the relevant comparison is not simply patients with established PDAC versus healthy volunteers. Validation should include people with ordinary diabetes and benign pancreatic disease, using specimens obtained before diagnostic imaging whenever possible. Prospective evaluation should measure false-positive investigations, invasive procedures, unnecessary treatment and patient burden alongside cancer detection. An apparent improvement in survival from diagnosis alone can reflect earlier timing of diagnosis; outcome studies should therefore assess stage distribution and mortality rather than relying exclusively on longer observed survival. [3, 18, 20]

Conclusion

Diabetes and pancreatic cancer are linked through overlapping metabolic, paraneoplastic and pancreatic-disease pathways. Long-standing T2DM is associated with a moderate increase in risk, while later-life new-onset diabetes may signal an existing occult tumor. The timing of diabetes, weight trajectory and speed of glycemic deterioration are therefore more informative than diabetes status alone.

Routine screening of all people with diabetes is not supported. Clinical practice should distinguish stable metabolic disease from concerning symptoms and from inherited-risk surveillance. The most promising research strategy combines longitudinal clinical risk assessment with validated biomarkers and selective imaging. Demonstrating acceptable harms, an earlier stage at diagnosis and ultimately improved patient outcomes remains necessary before broad implementation.

Conflict of Interest

The authors declare no conflict of interest.

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