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Meta-analysis

Pancreatic fat and the risk of future dysglycemia: a systematic review and meta-analysis

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Abstract

Context **Pancreatic fat has emerged as a metabolically relevant ectopic fat depot, but its longitudinal association with future dysglycemic outcomes remains incompletely defined.**

Objective **This study aims to evaluate the longitudinal association of pancreatic fat with incident type 2 diabetes (T2D) and glycemic progression, with exploratory narrative synthesis of evidence in lean populations.**

Data Sources **PubMed, Embase, Web of Science, and the Cochrane Library were searched from inception to March 1, 2026.**

Study Selection **Longitudinal observational studies assessing pancreatic fat at baseline and reporting subsequent incident T2D, glycemic progression, or both were included.**

Data Extraction **Two reviewers independently screened studies and extracted data. Methodological quality was assessed using the Newcastle–Ottawa Scale.**

Data Synthesis **Ten studies were included. In the primary binary meta-analysis (5 studies), higher pancreatic fat burden was associated with incident T2D (pooled effect estimate, 2.56; 95% CI, 1.27-5.14; $I^2 = 93.3\%$). Exclusion of 1 influential ultrasound-based study attenuated heterogeneity while preserving the association (pooled effect estimate, 1.45; 95% CI, 1.23-1.73; $I^2 = 10.2\%$). A separate continuous analysis (3 studies) also supported an association with incident T2D (1.17; 95% CI, 1.04-1.32; $I^2 = 79.2\%$), although exposure scales were not directly comparable. Pancreatic fat was also associated with glycemic progression (2 studies; 1.96; 95% CI, 1.10-3.48; $I^2 = 73.2\%$). Exploratory lean-population evidence was limited to 2 analytical contexts, synthesized narratively, and directionally consistent with the overall findings.**

Conclusion **Pancreatic fat was associated with adverse future glycemic outcomes across multiple analytical contexts. These findings support pancreatic fat as a potentially meaningful imaging-derived marker of future dysglycemia, while suggesting that heterogeneity is partly explained by differences in exposure ascertainment.**

Keywords pancreatic fat, fatty pancreas, type 2 diabetes, glycemic progression, systematic review, meta-analysis

Type 2 diabetes (T2D) is a major and growing global health challenge, and identifying early markers of future glycemic deterioration remains an important clinical priority (1, 2). Beyond general adiposity, ectopic fat deposition has emerged as a metabolically relevant feature of dysglycemia (3). In recent years, pancreatic fat has attracted increasing attention as one such ectopic fat depot, with accumulating evidence suggesting that it may carry metabolic relevance beyond conventional anthropometric measures alone (4, 5).

However, the clinical significance of pancreatic fat remains incompletely defined. Prior studies have linked pancreatic fat to adverse metabolic phenotypes, including insulin resistance, metabolic syndrome, and diabetes-related traits (6-8). Much of this literature, however, has been cross-sectional, limiting inference about temporal direction and clinical relevance (9, 10). Although previous reviews have summarized pancreatic fat in relation to metabolic or pancreatic disease outcomes, its longitudinal relationship with future dysglycemia has not been

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specifically synthesized. Whether pancreatic fat provides information beyond broader adiposity and related ectopic fat depots, including hepatic fat and visceral adipose tissue, also remains uncertain.

More recently, longitudinal cohort studies have begun to examine whether pancreatic fat is associated with future glycemic outcomes, including incident T2D and glycemic progression (11-14). These studies have reported variable findings and have differed substantially in how pancreatic fat was defined, including ultrasound-based categorical assessment, direct imaging-derived binary definitions, continuous quantitative imaging metrics, and phenotype-derived exposure patterns (11-14). This heterogeneity underscores the need for a synthesis that separates analytical layers and explicitly accounts for differences in exposure definitions.

We therefore conducted a systematic review and meta-analysis of longitudinal studies evaluating pancreatic fat in relation to future dysglycemic outcomes. The present study was designed to extend prior reviews by focusing specifically on longitudinal evidence for incident T2D and glycemic progression, summarizing lean-population evidence as an exploratory narrative component, and using a prespecified framework to interpret heterogeneity arising from differences in exposure ascertainment, overlapping cohorts, and analytical parameterization.

Materials and methods

Search strategy and study selection

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and AMSTAR 2 guidance (15, 16). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42023420370).

A comprehensive literature search was performed in PubMed, Embase, Web of Science, and the Cochrane Library from database inception to March 1, 2026, using terms related to pancreatic steatosis or fatty pancreas, T2D or dysglycemia, and longitudinal cohort designs. The full search strategies for all databases, including database-specific search dates and search strings, are provided in the Supplementary Methods (17).

After duplicate removal, 2 reviewers independently screened records by title and abstract, and potentially eligible articles underwent full-text review by the same process. Disagreements were resolved through discussion with a third reviewer. Eligible studies were longitudinal observational studies, including retrospective or prospective cohort studies and case-cohort studies, that assessed pancreatic fat or fatty pancreas at baseline and reported subsequent incident T2D, glycemic progression, or both. For incident T2D analyses, studies were required to include participants without diabetes at baseline. Studies were excluded if they were cross-sectional only, limited to prevalent diabetes, conducted in animals, review articles, editorials, conference abstracts without usable data, non-peer-reviewed reports, Mendelian randomization studies, or duplicate reports without distinct analytical value. Studies were also excluded if pancreatic fat was not assessed at cohort baseline.

Data extraction and study framework

For each eligible study, 2 reviewers independently extracted data using a standardized form, and disagreements were resolved through discussion with a third reviewer. Extracted items included country or region, study design, source population, follow-up duration, sample size, baseline age, baseline body mass index (BMI), prevalence of fatty pancreas where available, imaging modality, exposure operationalization, outcome definition, effect measure, and covariate adjustment. When multiple models were reported, the most fully adjusted effect estimate was selected for the primary synthesis.

In addition to standard study characteristics, we prespecified a study framework to describe between-study differences in exposure ascertainment, outcome ascertainment, and covariate adjustment structure (Table S1) (17). Particular attention was given to whether the most fully adjusted model accounted for general adiposity, baseline glycemic status, liver fat or fatty liver, central or visceral adiposity, and lifestyle-related factors. Because the number of studies within each analytical layer was limited, these study-level features were summarized descriptively rather than examined using formal meta-regression.

Study quality assessment

The methodological quality of the included observational studies was assessed using the Newcastle–Ottawa Scale (NOS), which evaluates study selection, comparability, and outcome assessment (18). Two reviewers independently rated each study, and discrepancies were resolved by discussion when needed. Average scores across the 2 reviewers were used for the domain-specific and total NOS summaries presented in Table S2 (17).

Handling of overlapping cohorts

When multiple reports originated from the same underlying cohort or data source, only 1 effect estimate from that source was allowed to contribute to any single pooled analysis. The representative estimate was selected according to the prespecified analytical layer, the exposure parameterization most relevant to that layer, and the need to avoid duplicate contribution of the same source population. Different reports from the same cohort could therefore be used across separate analytical layers when they addressed different exposure representations or different outcome families, but they were not co-entered within the same pooled estimate. Details of cohort overlap governance and representative estimate selection are provided in Table S3 (17).

For the Japan Keijinkai cohort, Yamazaki 2022 was used in the primary binary analysis, Yamazaki 2020 in the main continuous analysis, and Yamazaki 2016 in continuous sensitivity analyses. For UK Biobank, Dong 2024 was used as the default representative study in the primary binary and main continuous analyses, whereas Wang 2025 and Cai 2026 were reserved for continuous sensitivity analyses rather than combined with Dong 2024. Within Chan 2022, the binary effect estimate was used in the primary binary meta-analysis and the continuous estimate in the

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continuous analysis. Within Hung 2018, the incident diabetes estimate contributed to the primary binary analysis and the glycemic progression estimate to the secondary outcome analysis. For Bi 2022, the main cohort effect was used in the primary binary analysis, whereas the lean subgroup estimate was reserved for narrative synthesis only.

Exposure ascertainment hierarchy and analytical layers

In this review, "pancreatic fat" was used as the umbrella term for imaging-detected fat accumulation within the pancreas. "Fatty pancreas" was used when referring to categorical or binary exposure definitions reported by individual studies, whereas "intrapancreatic fat deposition" was retained only when describing study-specific quantitative imaging metrics that used this terminology. The evidence base was organized according to a prespecified exposure ascertainment hierarchy comprising ultrasound-based categorical assessment, binary imaging-defined fatty pancreas, quantitative continuous imaging measures, and phenotype-derived binary exposure patterns. This framework was used to classify the included studies according to how pancreatic fat exposure was operationalized and to support interpretation of between-study heterogeneity arising from differences in exposure ascertainment. This hierarchy was not intended to imply equivalence among study-specific binary thresholds, but rather to make explicit the heterogeneity in exposure definitions across modalities and analytical parameterizations.

The analyses were structured into 4 analytical layers. First, the primary analysis evaluated binary or categorical pancreatic fat exposure in relation to incident T2D. This layer was designated as the primary analysis because binary or categorical pancreatic fat status was the most consistently reported exposure representation across longitudinal studies of incident T2D and most closely corresponded to a clinically interpretable classification of pancreatic fat status. However, because no universally accepted or validated threshold for high pancreatic fat exists, binary definitions were treated as study-specific exposure classifications rather than interchangeable biological cutoffs. Second, continuous-effect estimates for incident T2D were synthesized separately as supportive evidence because exposure scales were not directly comparable across studies. Third, a secondary analysis examined glycemic progression, defined as progression from normoglycemia or prediabetes to a worse glycemic category. Fourth, evidence in lean populations was synthesized narratively because the available studies arose from different analytical contexts and were not considered appropriate for pooled quantitative analysis.

Effect harmonization

Hazard ratios (HRs) and odds ratios (ORs) were pooled on the log scale as a common relative risk metric. All effect estimates were harmonized so that greater pancreatic fat burden corresponded to higher risk of the relevant glycemic outcome. For CT attenuation–based studies, directional alignment was required because lower Hounsfield unit (HU) values indicate greater pancreatic fat burden. Accordingly, effect estimates were reoriented where necessary to ensure consistent interpretation of pooled effects across studies.

Statistical analysis

All meta-analyses were performed in R using the meta package (19). Pooled effect estimates were calculated using the generic inverse variance method. Random-effects models were fitted using the DerSimonian–Laird estimator for between-study variance with classic random-effects confidence intervals. Statistical heterogeneity was assessed using the I^2 statistic. Binary and continuous analyses for incident T2D were synthesized separately, and evidence in lean populations was summarized narratively rather than quantitatively. Influence diagnostics, including leave-one-out analysis, Baujat plots, Cook's distance, and studentized residuals, were used to evaluate influential studies in the primary binary meta-analysis (20). Prespecified sensitivity analyses examined the robustness of the primary binary findings after exclusion of influential studies and the robustness of the continuous analysis using alternative representative estimates from overlapping cohorts. Because each pooled analysis included only a small number of studies, formal assessment of publication bias or small-study effects was not performed.

Results

Study selection

The literature search identified 2689 records across the 4 databases. After removal of 870 duplicates, 1819 records remained for title and abstract screening. Of these, 1798 were excluded, and 28 reports underwent full-text review. Eighteen full-text articles were excluded for the following reasons: no longitudinal incident outcome (n = 15), not peer-reviewed (n = 1), Mendelian randomization design (n = 1), and pancreatic fat not assessed at cohort baseline (n = 1). Ultimately, 10 studies were included in the quantitative synthesis, with subsets contributing to the primary binary, continuous, and glycemic progression analyses according to the prespecified analytical framework (Fig. 1) (11-14, 21-26).

Study characteristics

The characteristics of the included studies are summarized in Table 1. The evidence base comprised longitudinal observational studies from East Asia and the United Kingdom, including cohorts from Japan, Taiwan, mainland China, Hong Kong, Korea, and UK Biobank. Study designs included retrospective cohorts, prospective cohorts, and a prospective case-cohort study. Follow-up duration ranged from approximately 3 to 11 years, and sample sizes ranged from several hundred participants to more than 40 000. Exposure ascertainment varied across studies and included ultrasound-based categorical assessment, CT attenuation, and MRI-derived pancreatic fat measures. Exposure definitions also differed, including binary definitions of fatty pancreas, continuous pancreatic fat metrics, quintile-based analyses, and phenotype-derived binary exposure patterns.

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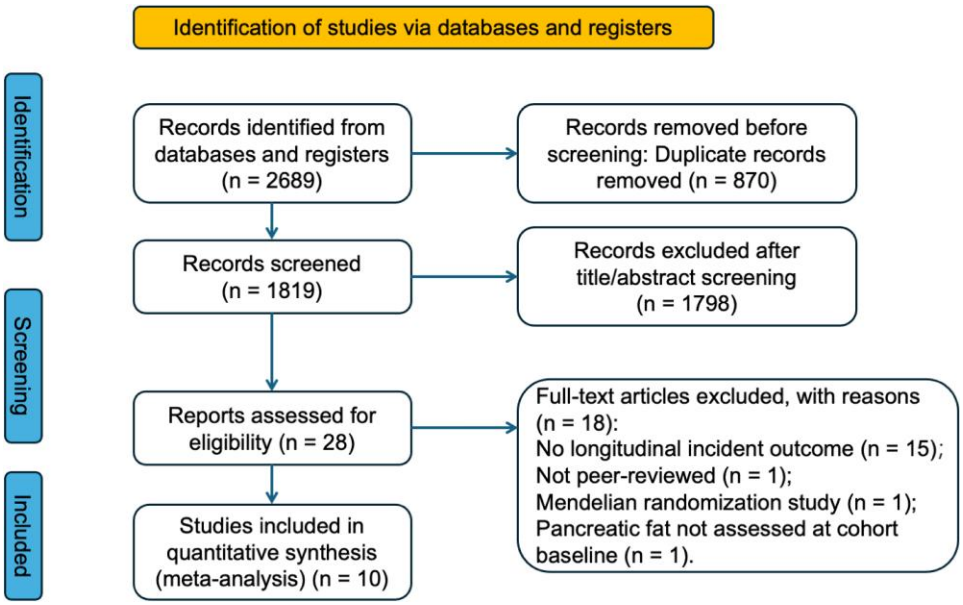

Figure 1 PRISMA flow diagram of study inclusion in the review.

Outcome ascertainment ranged from biochemical and medication-based definitions to registry- or ICD-based ascertainment. Additional details on exposure ascertainment, outcome ascertainment, and covariate adjustment are provided in Table S1 (17). Average NOS scores ranged from 8.0 to 9.0 across the included studies, consistent with generally good methodological quality, although differences in exposure ascertainment, outcome ascertainment, and covariate adjustment remained evident (Tables S1 and S2) (17).

Primary meta-analysis of binary pancreatic fat exposure and incident type 2 diabetes

The primary binary meta-analysis included 5 studies: Hung 2018, Chan 2022, Bi 2022, Dong 2024, and Yamazaki 2022. Binary pancreatic fat exposure was associated with a significantly increased risk of incident T2D, with a pooled effect estimate of 2.56 (95% CI, 1.27-5.14; Fig. 2). Between-study heterogeneity was substantial ($I^2 = 93.3\%$). To further interpret this heterogeneity, we examined differences in exposure ascertainment and study influence. Across the included studies, binary exposure definitions were study-specific and spanned ultrasound-based categorical assessment, MRI-defined fatty pancreas, and a phenotype-derived binary exposure pattern (Fig. S1) (17). Within this framework, Bi 2022 belonged to the ultrasound-based categorical exposure class and defined fatty pancreas as a binary sonographic phenotype rather than a quantitative fat metric, whereas Yamazaki 2022 was categorized within the phenotype-derived binary exposure class. Influence diagnostics showed concordant findings, with leave-one-out analysis, Baujat plot, Cook's distance, and studentized residuals consistently identifying Bi 2022 as the principal contributor to between-study heterogeneity (Fig. S2) (17). In a prespecified sensitivity analysis excluding Bi 2022, the association remained statistically significant and heterogeneity was markedly attenuated (pooled effect estimate, 1.45; 95% CI, 1.23-1.73; $I^2 = 10.2\%$; Fig. S3) (17). By contrast, exclusion of Yamazaki 2022 did not materially reduce heterogeneity, and the pooled association remained significant (pooled effect estimate, 2.57; 95% CI, 1.16-5.72; $I^2 = 94.9\%$). Taken together, these findings suggest that Bi 2022 was an influential outlier and the principal driver of between-study heterogeneity, whereas the overall association was preserved across sensitivity analyses.

Supportive continuous analysis of pancreatic fat and incident type 2 diabetes

The continuous analysis included 3 representative studies: Yamazaki 2020, Chan 2022, and Dong 2024. Higher pancreatic fat burden was also associated with greater risk of incident T2D in this supportive analysis, with a pooled effect estimate of 1.17 (95% CI, 1.04-1.32; Fig. 3). Between-study heterogeneity remained substantial ($I^2 = 79.2\%$). This analysis was interpreted as supportive rather than co-primary evidence because the continuous exposure scales were not directly comparable across studies, including CT attenuation–based measures, MRI-derived pancreatic fat percentage, and quintile-based parameterizations of study-defined intrapancreatic fat deposition. Sensitivity analyses replacing the default representative estimates from overlapping cohorts with alternative eligible reports showed directionally consistent findings overall (Fig. S4) (17).

Secondary analysis of pancreatic fat exposure and glycemic progression

Two studies, Hung 2018 and Oh 2021, contributed to the glycemic progression analysis. Higher pancreatic fat burden was associated with increased risk of progression to a worse glycemic

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Table 1 Characteristics of included studies

Study	Country/ region	Design and population source	Follow-up, y	Sample size	Age at baseline	BMI at baseline	Pancreatic fat prevalence	Measurement modality	Exposure operationalization	Outcome focus	Outcome definition summary
Yamazaki 2016	Japan	Retrospective cohort; health checkup participants	5.06	813	51.8 ± 9.8	24.0 ± 3.3	NR	CT	Mean attenuation of pancreatic head/ body/tail; lower HU = more pancreatic fat	Incident T2D	FPG ≥ 126 mg/dL, HbA1c ≥ 6.5%, physician diagnosis, or diabetes medication
Hung 2018	Taiwan, China	Retrospective cohort; health examination cohort	3.17	8856	50.4 ± 12.2	23.8 ± 3.4	8.5%	Ultrasound	Increased pancreatic echogenicity vs no increased echogenicity	Incident T2D + glycemic progression	Incident diabetes at second visit; glycemic progression from normoglycemia/ prediabetes to worse glycemic state
Yamazaki 2020	Japan	Retrospective cohort; health examination cohort (lean-only analysis)	6.19	1478	52.0	<25	33.6%	CT	Continuous pancreatic attenuation; lower HU = more pancreatic fat	Incident T2D	FPG ≥ 126 mg/dL, HbA1c ≥ 6.5%, or diabetes medication
Oh 2021	Korea	Retrospective cohort; health screening cohort	5.9	1099	47.2 ± 10.6	23.5	40.6%	Ultrasound	4-point hyperechoic pancreas severity grading; moderate/ severe thresholds used	Glycemic progression	ADA 2014-based progression from normoglycemia or prediabetes to a worse glycemic category
Bi 2022	China	Retrospective cohort; health examination center	5	12 551	Non-FP 47.1 ± 14.3; FP 52.2 ± 12.9	Non-FP 24.7 ± 3.3; FP 27.8 ± 3.0	8.0%	Ultrasound	Fatty pancreas vs non-fatty pancreas by transabdominal ultrasound	Incident T2D	FPG ≥ 7.0 mmol/L or antidiabetic medication during follow-up
Chan 2022	Hong Kong, China	Prospective community population cohort	11.1	631	48 ± 11	22.6 ± 3.5	14.7%	MRI	Binary FP (>10.4%) and continuous pancreatic fat %	Incident T2D	HbA1c ≥ 6.5%, FPG ≥ 7.0 mmol/L, or antidiabetic medication
Yamazaki 2022	Japan	Prospective case-cohort study; health examination cohort	6.27	754	51 (43-59)	23.5 (21.6-25.8)	NR	CT	Phenotype-derived pancreatic steatosis cluster from CT-based fat distribution pattern	Incident T2D	FPG ≥ 126 mg/dL, HbA1c ≥ 6.5%, or antidiabetic medication
Dong 2024	United Kingdom	Prospective cohort; UK Biobank	4.61	42 599	65 (58-70)	25.7 (23.4-28.5)	17.9%	MRI	IPFD analyzed as binary fatty pancreas and continuous quintiles	Incident T2D	ICD-based diagnosis in UK Biobank follow-up

(*continued*)

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Table 1 Continued

Study	Country/ region	Design and population source	Follow-up, y	Sample size	Age at baseline	BMI at baseline	Pancreatic fat prevalence	Measurement modality	Exposure operationalization	Outcome focus	Outcome definition summary
Wang 2025	United Kingdom	Prospective cohort; UK Biobank	4.2	22 703	Reported separately by sex	Reported separately by sex	NR	MRI	Continuous IPFD using PRESCO algorithm; sex-specific analyses	Incident T2D	ICD-10 code E11 from linked records
Cai 2026	United Kingdom	Prospective cohort; UK Biobank	6.27	25 547	64 (58-70)	25.8 (23.4-28.7)	NR	MRI	Continuous IPFD/ pancreatic PDFF from deep learning–derived abdominal MRI traits	Incident T2D	UK Biobank registry-based non-insulin-dependent diabetes outcome

Age and BMI are reported as mean ± SD or median (IQR), as provided in the original studies.
Abbreviations: BMI, body mass index; CT, computed tomography; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HU, Hounsfield units; IPFD, intrapancreatic fat deposition; MRI, magnetic resonance imaging; NR, not reported; PDFF, proton density fat fraction; T2D, type 2 diabetes.

category, with a pooled effect estimate of 1.96 (95% CI, 1.10-3.48; Fig. 4). Between-study heterogeneity was moderate to substantial ($I^2 = 73.2\%$). These findings suggest that the association of pancreatic fat with adverse glycemic outcomes may extend beyond overt incident T2D to earlier dysglycemic progression.

Narrative evidence in lean populations

Exploratory evidence in lean populations was synthesized narratively rather than quantitatively because the available studies arose from different analytical contexts and used non-comparable exposure definitions. In the lean-only CT-based cohort reported by Yamazaki 2020, greater pancreatic fat burden was associated with higher risk of incident T2D (adjusted OR, 1.32; 95% CI, 1.06-1.63, per 10 HU lower pancreatic attenuation). In addition, the lean subgroup analysis from Bi 2022 showed a directionally concordant association, although the estimate was very large and imprecise (adjusted HR, 40.342; 95% CI, 8.733-186.363). Although quantitative synthesis was not appropriate, the available evidence suggests that pancreatic fat may have metabolic relevance even in lean individuals.

Discussion

In this systematic review and meta-analysis, pancreatic fat was associated with adverse future glycemic outcomes across several analytical layers (Fig. 5). The clearest signal came from the primary binary analysis, in which higher pancreatic fat burden was associated with a significantly increased risk of incident T2D. The continuous analysis pointed in the same direction, although the underlying exposure scales were not directly comparable. The pattern also extended beyond overt incident diabetes to glycemic progression. Exploratory evidence in lean populations was more limited and was synthesized narratively rather than quantitatively, but it was directionally consistent with the overall findings. Taken together, these observations suggest that pancreatic fat may be better understood as an imaging-derived marker of future dysglycemia than simply another cross-sectional correlate of metabolic dysfunction.

The substantial heterogeneity in the primary binary analysis should be interpreted in the context of how pancreatic fat was defined across studies. The binary evidence base did not represent a single uniform exposure construct, and the primary analysis should not be interpreted as applying a universal threshold for “high” pancreatic fat. Rather, binary definitions were study-specific and spanned ultrasound-based categorical assessment, direct imaging-defined binary exposure, and phenotype-derived binary exposure patterns. Seen in that light, the heterogeneity is not just a statistical inconvenience; it reflects meaningful differences in modality, threshold selection, exposure ascertainment, and analytical context. Within this framework, Bi 2022 belonged to the ultrasound-based categorical class and was consistently identified by leave-one-out analysis, Baujat plot, Cook's distance, and studentized residuals as the principal contributor to between-study heterogeneity. The unusually large effect estimate in Bi 2022 may partly reflect the nature of its exposure definition. In that study, fatty pancreas was diagnosed by transabdominal ultrasonography as a binary

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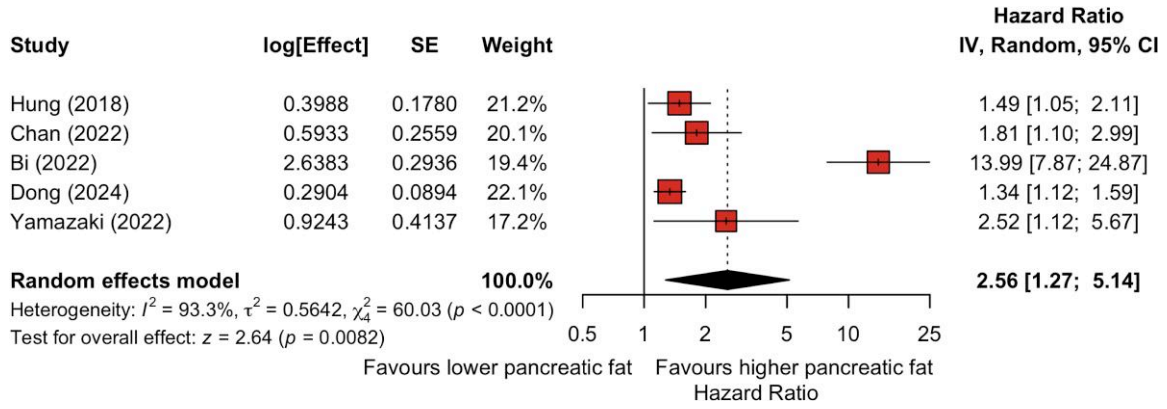

Figure 2 Primary meta-analysis of binary pancreatic fat exposure and incident type 2 diabetes.

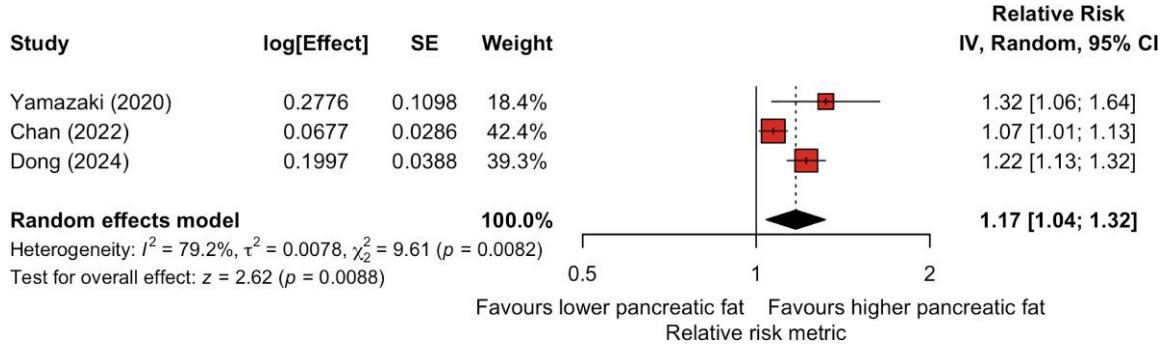

Figure 3 Supportive meta-analysis of continuous pancreatic fat exposure and incident type 2 diabetes.

sonographic phenotype based on increased pancreatic echogenicity rather than as a quantitative fat metric. This qualitative classification may have captured a more clinically apparent or advanced phenotype of pancreatic steatosis than the broader spectrum of fat accumulation represented by CT- or MRI-derived measures. This interpretation is supported by the markedly adverse baseline metabolic profile of participants with fatty pancreas in Bi 2022, but should remain cautious given the limited number of incident T2D events and incomplete reporting of some T2D-specific covariates. At the same time, the overall association did not disappear when that study was excluded. Heterogeneity fell markedly, but the pooled effect remained significant. By contrast, exclusion of Yamazaki 2022 did not materially change heterogeneity. This pattern supports a balanced interpretation: the primary binary signal was not driven solely by a single influential study, yet the variability across studies was real and was partly related to differences in how pancreatic fat exposure was operationalized.

Why pancreatic fat may matter specifically, rather than simply mirroring overall obesity, remains an important question. One plausible explanation is that pancreatic fat reflects organ-specific ectopic fat topography rather than total adiposity alone, an idea that is increasingly supported by broader work on depot-specific fat distribution and metabolic risk (4, 27). In that sense, the pancreas is not merely another passive storage site. Contemporary reviews have emphasized that pancreatic fat accumulation may have distinct metabolic implications within the broader landscape of ectopic fat biology (5). Intrapancreatic fat is anatomically proximate to the endocrine compartment and may therefore reflect a local milieu relevant to β-cell dysfunction, lipotoxic stress, paracrine signaling, and impaired insulin secretion (4, 6-8). Prior imaging and metabolic studies have also linked pancreatic fat to insulin resistance and altered β-cell function, lending biological plausibility to a pancreas-specific contribution to dysglycemia (6-8). At the same time, the direction of this relationship is unlikely to be simple. Longitudinal evidence has shown that prediabetes predicts future pancreatic fat accumulation, indicating that the relationship may not be unidirectional and that pancreatic fat may also be a manifestation of ongoing dysglycemia (28). Taken together, the available evidence is most consistent with pancreatic fat as a biologically meaningful ectopic fat marker situated within a broader network of metabolic dysfunction, rather than as an isolated or definitively causal lesion.

A related issue is whether the observed association is merely a proxy for broader adiposity, hepatic steatosis, or visceral adipose tissue. This question has remained difficult to resolve in part because much of the earlier literature linking pancreatic steatosis to metabolic dysfunction was cross-sectional rather than longitudinal (9). Several of the stronger longitudinal studies adjusted for BMI or obesity-related measures, and some further accounted for fatty liver, liver fat content, central obesity, or other fat-distribution variables (12-14, 21). In particular, Chan et al reported that the association between fatty pancreas and incident diabetes persisted despite adjustment for BMI, central obesity, and concomitant fatty liver, supporting the view that pancreatic

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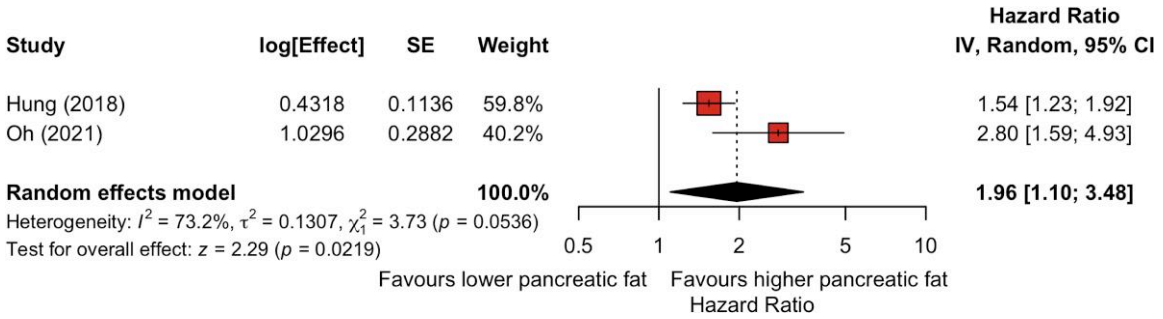

Figure 4 Meta-analysis of pancreatic fat exposure and glycemic progression.

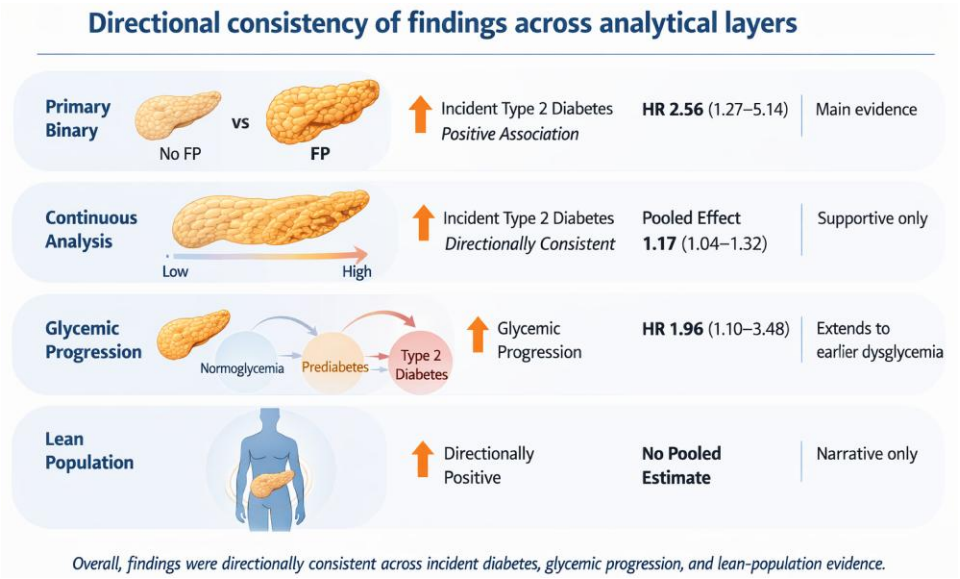

Figure 5 Integrative overview of the association between pancreatic fat and future glycemic outcomes across analytical layers. Summary schematic integrating the main findings across the analytical layers of the present review. The primary binary analysis showed a significant association between pancreatic fat and incident type 2 diabetes; the continuous analysis showed a directionally consistent supportive association; the secondary analysis supported an extension toward earlier glycemic progression; and the available evidence in lean individuals was directionally positive but was synthesized narratively rather than quantitatively.

fat may capture a dimension of metabolic risk not fully explained by conventional anthropometric measures alone (12). Similar attempts to account for broader adiposity or hepatic fat were also evident in other cohorts (14, 21). Even so, the degree of true independence remains unresolved. Adjustment depth varied substantially across studies, baseline glycemic status was not handled uniformly, and in some reports, relevant adiposity- or liver-related covariates were either incompletely specified or incorporated differently across analytical models. Moreover, some data-driven exposure definitions, such as phenotype-derived fat-distribution clusters, do not permit straightforward interpretation of pancreatic fat independent of liver fat or visceral adiposity (13). The negative finding reported by Yamazaki et al after adjustment for BMI, liver attenuation, and alcohol intake further underscores that this issue is not settled (21). These findings do not require viewing pancreatic fat as either an entirely independent depot or merely a surrogate of generalized adiposity. A more plausible interpretation is that pancreatic fat may represent one component of a broader ectopic adiposity phenotype, while still carrying organ-specific information relevant to dysglycemia. Thus, the current evidence suggests that pancreatic fat is not reducible to a simple surrogate of obesity, fatty liver, or visceral adiposity, but its independent etiologic role beyond other ectopic fat depots remains to be clarified.

The clinical implications of these findings should be interpreted with caution. Our results do not support routine population-wide screening for pancreatic fat specifically for diabetes prediction. That would go well beyond the available evidence. A more realistic implication is that pancreatic fat may serve as an imaging-derived marker of elevated metabolic risk when it is identified incidentally on abdominal imaging performed for other reasons (29). In that setting, it may provide additional clinical context alongside established metabolic risk factors and other ectopic fat depots, such as hepatic fat and visceral adipose tissue. This is especially relevant because the pattern observed here was not confined to incident T2D alone, but extended to earlier glycemic deterioration and remained directionally compatible in lean individuals. Even so, an important

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question remains unresolved: whether pancreatic fat offers meaningful predictive information beyond conventional risk markers, general adiposity, and liver fat. That will require prospective studies designed for risk prediction rather than association alone. It will also be important to clarify whether pancreatic fat can be reduced through lifestyle interventions such as dietary modification or exercise and whether such changes are accompanied by measurable improvement in glycemic risk (30-32).

This review should also be interpreted in light of several strengths and limitations. It focused on longitudinal evidence, used a prespecified strategy to manage overlapping cohorts, and analyzed binary, continuous, glycemic progression, and lean-population evidence in separate but complementary analytical layers. Those design choices improved interpretability and helped avoid forced synthesis across fundamentally different exposure representations. Still, several limitations deserve emphasis. First, heterogeneity in the primary binary analysis was high, and 1 ultrasound-based categorical study exerted substantial influence on the pooled estimate. Second, the number of studies within each analytical layer was limited, which reduced precision and restricted more formal exploration of heterogeneity. Third, continuous exposure measures were not directly comparable across studies, so the continuous synthesis should be regarded as supportive rather than co-primary evidence. Fourth, the depth of covariate adjustment was not uniform. Several studies adjusted for adiposity, liver fat or fatty liver, central adiposity, lifestyle-related factors, or baseline glycemic status, but these features were not incorporated consistently across the evidence base. Finally, the lean-population evidence was limited and heterogeneous, and observational data cannot establish causality. Even with these constraints, the convergence of findings across distinct analytical layers supports pancreatic fat as a potentially meaningful marker of future dysglycemia.

In conclusion, the available longitudinal evidence suggests that pancreatic fat is associated with future dysglycemia across several analytical contexts, including incident T2D, glycemic progression, and, more tentatively, lean populations. Although heterogeneity in exposure ascertainment and study design remains important, the overall pattern supports pancreatic fat as a potentially meaningful imaging-derived marker of metabolic risk rather than a purely incidental finding. Future studies should clarify its incremental predictive value beyond established metabolic risk markers and determine whether modification of pancreatic fat through lifestyle or other interventions translates into measurable glycemic benefit.

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Author contributions

X.L. and Y.C. conceived and designed the study. J.Y. and X.Z. performed the literature search, screened the studies, and extracted the data. J.Y., X.Z., and L.L. conducted the statistical analyses, prepared the figures, and interpreted the data. J.Y. drafted the manuscript. X.Z., L.L., Z.Z., and C.T. critically revised the manuscript for important intellectual content. X.L. and Y.C. supervised the study. Y.C. obtained funding. All authors read and approved the final manuscript.

Disclosures

The authors have nothing to disclose.

Data availability

All data analyzed in this systematic review and meta-analysis were extracted from previously published studies. The extracted study-level data supporting the findings of this article are included in the article and the supplementary materials deposited in Zenodo (17). Additional analytic datasets used for the meta-analyses are available from the corresponding author upon reasonable request.

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