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Consensus statement

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Conceptual framework and expert guidance on intrapancreatic fat deposition: the Melbourne consensus

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Abstract

Intrapancreatic fat deposition (IPFD) has garnered appreciable attention across diverse medical disciplines amid the rising global burden of pancreatitis, pancreatic cancer and type 2 diabetes mellitus. Despite growing interest in the field, there remains no conceptual framework for it. To address this gap, 25 experts from 6 continents were brought together to develop guidance. Drawing on multiple peer-reviewed systematic reviews and applying an iterative, anonymous Delphi process, a consensus document was developed and ratified in Melbourne, Australia. The final document contains 58 recommendations — 30 reached unanimous agreement and 28 attained 90–99% agreement. The consensus formally defines fatty pancreas disorder (FPD) as a distinct pathological state, characterized by excessive IPFD that poses a risk to health. Assessment of IPFD is best performed with MRI. Expert-established diagnostic criteria enable identification and classification of FPD. Recognition of type 1 FPD (in individuals without excess body fat mass) and type 2 FPD (in individuals with excess body fat mass) is instrumental in gaining novel insights and tailoring preventive strategies to the individual. The Melbourne consensus is foundational in operationalizing the dissemination of new knowledge in the field, fostering intercontinental collaborations and, ultimately, addressing the global burden of diseases of the pancreas.

Sections

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Key points

- The morphological basis of intrapancreatic fat deposition (IPFD) is intrapancreatic adipocytes and lipid-rich inclusions in pancreatic cells, excluding focal fat masses.
- Low IPFD is physiological, and increases in IPFD can occur independently of body weight gain or hepatic fat accumulation.
- Fatty pancreas disorder (FPD) typically develops from cumulative lifetime exposure to diverse pancreatic insults, rendering attribution to a single cause less meaningful.
- FPD is best understood as an organ-specific pathological state that can predispose individuals to multiple disease trajectories, including pancreatic cancer, pancreatitis and type 2 diabetes mellitus, among others.
- MRI that measures fat content on a voxel-wise basis is the modality of choice for diagnosing FPD.
- Conventional endoscopic ultrasonography is not a valid modality for diagnosing FPD despite being commonly accessible to gastroenterologists.

Introduction

Fat within the pancreas was first documented in the scholarly literature in the 1860s[1]. Yet, for much of the time since, the phenomenon drew little interest from the medical community. This limited engagement can be partly attributed to the anatomical inaccessibility of the pancreas, which rendered it largely the domain of surgeons and pathologists. Furthermore, adipose tissue was long regarded as a biologically inert lipid reservoir[2]. It was not until the turn of the twenty-first century that nascent multidisciplinary interest in fat within the pancreas began to take shape — catalysed by advances in cross-sectional imaging. These developments enabled the non-invasive quantification of what had previously been a hidden fat depot in living individuals, curtailing the need for surgical specimens or post-mortem examinations[2]. Concurrently, a paradigm shift occurred in the understanding of adipose tissue[2], which came to be recognized as an active contributor to disease pathogenesis.

From early observations to the present day, the field has undergone a profound transformation. This progress has advanced understanding of population health, as shown by a 2025 meta-analysis of nearly 100,000 participants reporting that about 1 in 5 adults harbours excess fat within the pancreas[3]. Research on this topic has been conducted across all inhabited continents, reflecting substantial global engagement[4]. The annual number of original studies has steadily increased, showing more than a threefold growth over the past decade[4]. Moreover, contributions to the field have become highly multidisciplinary, with major input from gastroenterology, endocrinology, radiology, nutrition, physiology, epidemiology, oncology and pharmacology[4]. The breadth of stakeholders involved, alongside a growing body of literature summaries of variable rigour and epistemological depth, underscore the need for a global, multidisciplinary panel of subject-matter experts to develop a conceptual framework. Furthermore, given the conflicting evidence in the literature regarding many aspects of fat within the pancreas, leading guidance developed through the gold-standard consensus-building methodology is essential for informing clinical practice. Such a synthesis of collective expert knowledge worldwide is also well placed to standardize future investigations, facilitate the resolution of contentious issues, and guide the meaningful use of large-scale data on fat within the pancreas — now increasingly accessible through large biorepositories (for example, the UK Biobank, the German National Cohort)[5].

In this Consensus Statement, the basis for the study and clinical interpretation of fat within the pancreas is clearly set out. Particular emphasis is placed on the openness and inclusivity in identifying subject-matter experts and contributors, as well as on ensuring transparency and reproducibility in the consensus-building process.

Methods

The Global Intrapancreatic FaT (GIFT) Alliance served as the platform for the development of this consensus and was established to unite a global, multidisciplinary network of experts to advance the understanding of fat within the pancreas and to coordinate complementary basic, translational and clinical research with a view to accelerating scientific progress and informing clinical practice. The GIFT alliance convened a Steering Committee, chaired by M.S.P., that comprised distinguished experts (M.S.P., H.Y., G.L. and A.H.A.-M.), each bringing approximately a decade of experience in the field and a strong publication track record on the topic. They represented diverse disciplinary backgrounds, were drawn from four countries across three continents, and had not previously collaborated with one another. The Steering Committee was responsible for overseeing and coordinating the engagement of the broader Working Group. The Working Group consisted of core experts, including those on the Steering Committee, and collaborating members (Supplementary Table 1). Core experts participated in the rating and endorsement of statements during the consensus-building process, whereas collaborating members contributed additional perspectives without formal decision authority. The process was facilitated by an independent coordinator (Y.S.) with no prior collaborative relationships that might introduce potential bias. The coordinator organized meetings, managed logistical arrangements, oversaw scheduling, ensured data confidentiality, and managed the collection and presentation of Working Group input.

Following the 2024 ACCORD guideline[6], a structured, iterative feedback process designed to refine expert opinion towards convergence whilst minimizing bias — the Delphi method — was employed for the consensus-building process. Key elements included multidimensional systematic literature searches (Supplementary Table 2) and structured synthesis of relevant evidence provided to core experts at the outset, two rounds of anonymous rating exercises, a summary report incorporating controlled feedback prepared for each core expert and a moderated online meeting held between the rounds, as well as a face-to-face moderated meeting in Melbourne (Australia) that concluded the consensus-building process (Fig. 1). The Working Group was assembled using non-probability purposive and targeted sampling approaches to ensure equitable representation of core experts across disciplines, geographical regions and country income levels. The Chair formally announced the consensus-building process in person at Digestive Disease Week — the premier meeting for professionals worldwide working in gastroenterology, gastrointestinal surgery, endoscopy and related disciplines — in San Diego (USA) in 2025. During his invited lecture on fat within the pancreas, the Chair issued a call for participation and circulated an electronic expression of interest form via a QR code. In parallel, a bibliometric analysis of authors publishing on the

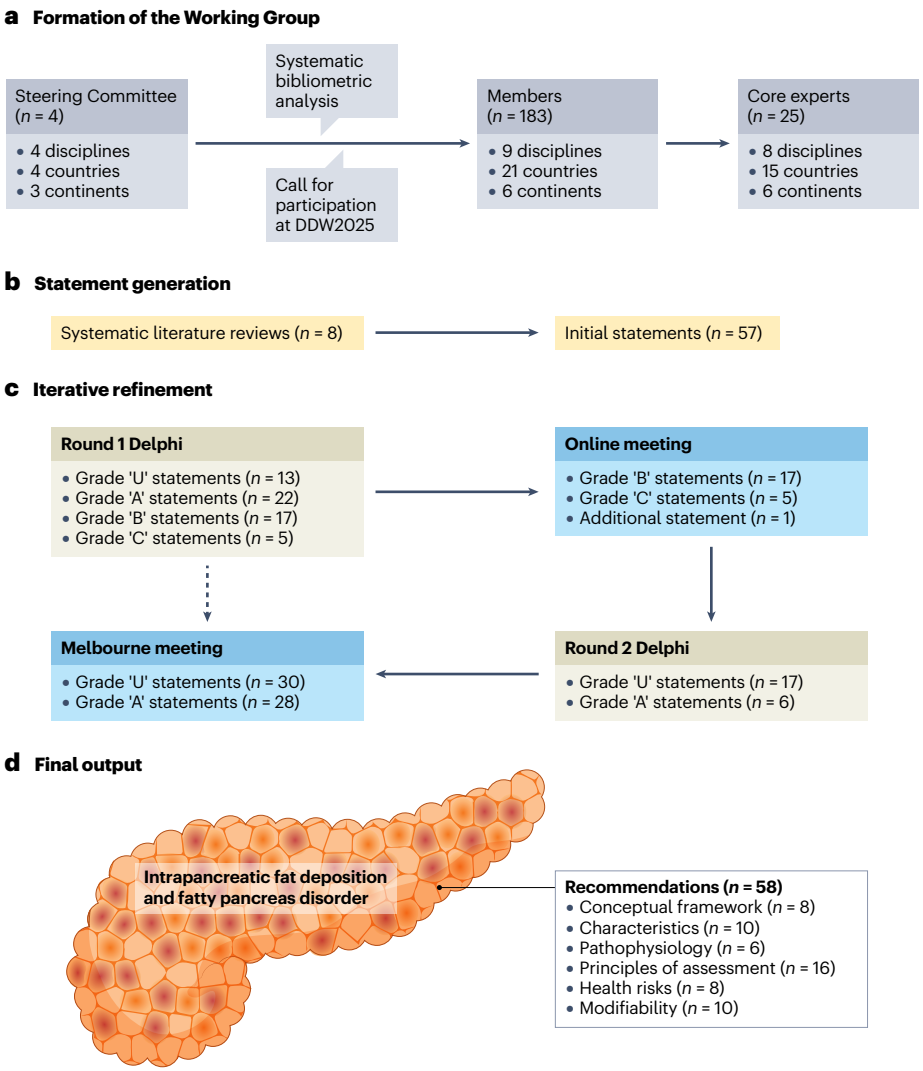

Fig. 1 | Delphi consensus-building process. A global Working Group was established through an open call for participation and a systematic bibliometric analysis (part **a**). Initial draft statements were then developed (part **b**). These statements underwent iterative refinement through two Delphi rounds and two meetings (part **c**). Ratings were anonymized and aggregated to determine the level of agreement, categorized as follows: 'U' for 100%; 'A' for 90–99%; 'B' for 78–89%; and 'C' for 67–77%. The final output comprised 58 recommendations organized across six domains (part **d**). DDW, Digestive Disease Week.

topic — across all disciplines — was conducted to systematically identify core experts and potential members of the Working Group[4]. To be eligible, core experts were required to be fluent in English and to have contributed to at least two studies related to fat within the pancreas, published in the previous 5 years or currently in progress. No more than two core experts from the same institution were permitted to ensure diversity of perspectives. A total of 25 experts were selected, in line with the panel size pre-specified in the consensus protocol, which was deemed appropriate to facilitate meaningful engagement and exchange of knowledge among core experts. These people were drawn from eight primary disciplines (Table 1), with several individuals contributing expertise across multiple areas. None of the core experts, including those on the Steering Committee, received remuneration or reimbursement for their participation.

A comprehensive summary of relevant literature was compiled (Supplementary Tables 3–10), drawing on a series of systematic reviews conducted by the core experts. Based on this evidence base, the Steering Committee developed an initial set of 57 statements on fat within the pancreas, addressing 6 key domains: conceptual framework, characteristics, pathophysiology, principles of assessment, health risks and modifiability. Each core expert received an information pack that included the evidence summary, full texts of the systematic reviews and supporting references. Two rounds of online rating exercises were then administered via SurveyMonkey (San Mateo, California, USA) and distributed to all 25 core experts. Responses to each statement were measured using a nine-point Likert scale: 1 (strongly disagree), 2 (disagree), 3 (moderately disagree), 4 (somewhat disagree), 5 (neither agree nor disagree), 6 (somewhat agree), 7 (moderately agree), 8 (agree) and 9 (strongly agree). Consensus was defined as a rating of 7–9 by a supermajority (that is, at least 67% of panellists)[7]. Agreement was further classified into four grades: unanimous consensus (100%; labelled as 'U'), strong consensus (between 90% and 99%; 'A'), moderate consensus (between 78% and 89%; 'B') and minimal consensus (between 67% and 77%; 'C')[7]. All responses were submitted securely and confidentially, with panellist identities accessible only to the non-voting coordinator. Both rounds of the Delphi process included an optional comment box beneath each statement, enabling panellists to justify their ratings and suggest revisions. In addition, Round 1 included a general comments

Table 1 | Roles of members of the Working Group

Full name	Country/ territory	Primary area of expertise	Role
Reda Albadawy	Egypt	Gastroenterology	Core Expert
Laure Alexandre-Heymann	France	Endocrinology and metabolism	Core Expert
Ahmad H. Al-Mrabeh	UK	Endocrinology and metabolism	Core Expert Steering Committee
Danijela Budimir Mršić	Croatia	Imaging science and radiology	Core Expert
Cristina Cadenas-Sanchez	Spain	Endocrinology and metabolism	Core Expert
Ethem Turgay Cerit	Türkiye	Endocrinology and metabolism	Core Expert
Saurabh Chawla	USA	Gastroenterology	Core Expert
Giuseppe Della Pepa	Italy	Endocrinology and metabolism	Core Expert
Xiaowu Dong	China	Gastroenterology	Core Expert
Tsuyoshi Hamada	Japan	Gastroenterology	Core Expert
Zhiyin Huang	China	Gastroenterology	Core Expert
Juyeon Ko	South Korea	Nutrition and dietetics	Core Expert
Idoia Labayen	Spain	Physiology	Core Expert
Tuo Li	China	Endocrinology and metabolism	Core Expert
Xiaoyu Li	China	Gastroenterology	Core Expert
Yutong Liu	New Zealand	Nutrition and dietetics	Core Expert
Guotao Lu	China	Gastroenterology	Core Expert Steering Committee
Claudio Luchini	Italy	Pathology	Core Expert
Hiroki Oyama	Japan	Gastroenterology	Core Expert
Maxim S. Petrov	New Zealand	Surgery	Core Expert Steering Committee Chair
Sunitha Priya	India	Physiology	Core Expert
Susanne Rospleszcz	Germany	Epidemiology	Core Expert
Yan Shen	China	Pharmacology	Coordinator
Matheus Souza	Brazil	Gastroenterology	Core Expert
John Virostko	USA	Imaging science and radiology	Core Expert
Hajime Yamazaki	Japan	Epidemiology	Core Expert Steering Committee

Names are listed alphabetically. The Steering Committee comprised four distinguished experts and was led by the Chair. The Working Group included all Steering Committee members, the remaining 21 core experts, the non-voting coordinator and 157 collaborating members. A list of collaborating members and their affiliations appears at the end of the paper.

section, allowing panellists to reflect on the consensus-building process more broadly and propose new statements.

Following completion of Round 1 of the Delphi process, each core expert received a personalized report comparing their individual ratings with the overall panel results. The report presented the mean and standard deviation for each statement, the percentage of panellists assigning each rating from 1 to 9, and the corresponding agreement grade ('U', 'A', 'B' or 'C'). An online meeting of the panel, moderated by the Chair, was held on 6 June 2025 in two separate sessions to accommodate panellists across 16 time zones. During the meeting, 22 statements that had not reached the 'U' or 'A' grades were discussed, along with the corresponding free-text comments submitted by panellists for each statement. Additionally, one new statement proposed through feedback was considered in detail. Following the group consultation, the Steering Committee revised several statements (with all modifications documented to ensure transparency and traceability) and incorporated the new one. These 23 statements were subsequently included in Round 2 of the Delphi process, which followed the same format and rating criteria as in Round 1. After each round, the Steering Committee considered minor edits proposed by the panellists to statements graded 'U' or 'A'. Where necessary, semantic and formatting adjustments were made to enhance clarity and coherence, provided these changes did not alter the original meaning. The level of evidence for the consensus statements was assessed using the Oxford Centre for Evidence-Based Medicine framework[8]. Evaluation categories were defined based on the content of each statement, and evidence was ranked according to study design, with systematic reviews and well-designed primary studies assigned higher levels. Evidence was categorized from Level 1 (highest) to Level 5 (lowest)[8].

The in-person meeting of the Working Group, moderated by the Chair and with an option for online participation, was held on 19 September 2025 in Melbourne, Australia, concurrent with the 2025 World Congress of Gastroenterology and the annual meeting of the International Association of Pancreatology. During this Working Group meeting, the final versions of the consensus statements were reviewed, discussed as needed and formally adopted. Additionally, the Chair organized a dedicated symposium for all conference attendees, featuring presentations delivered by core experts to raise public awareness of the consensus topics and disseminate the published evidence. Awareness among the public was also enhanced through a dedicated article on Medscape[9], a prominent online resource for medical professionals.

Attainment of consensus across Delphi rounds

Expert panel composition and consensus convergence

The panel comprised experts (11 women, 14 men) representing six continents: Europe ($n = 8$), Africa ($n = 1$), Asia ($n = 11$), Oceania ($n = 2$), North America ($n = 2$) and South America ($n = 1$). Panellists were drawn from all of the top 10 countries identified in the bibliometric analysis of published research on the topic[4] as well as from additional countries beyond this list. On average, panellists had 4 years of experience conducting research on the topic and had co-authored three relevant studies. Other professional characteristics are summarized in Table 2.

All panellists completed both rounds of the Delphi process, achieving a 100% response rate. The proportion of statements that panellists rated as 'strongly agree', 'agree' or 'moderately agree' (thereby meeting the a priori agreement threshold required for consensus) increased from 61% in Round 1 to 100% in Round 2. The average rating assigned by the panel increased from 8.10 ± 1.32 in Round 1 to 8.39 ± 0.88 in Round 2 (mean ± standard deviation), with the Round 2 average incorporating both statements re-evaluated during that round and those carried forward from Round 1. Changes within specific domains were as follows: conceptual framework (from 8.35 ± 1.27 in Round 1 to 8.55 ± 0.83 in Round 2); characteristics (from 7.89 ± 1.57 in Round 1 to 8.52 ± 0.81 in Round 2); pathophysiology (from 8.17 ± 1.30 in Round 1 to 8.39 ± 0.90 in Round 2); principles of assessment (from 8.33 ± 1.11 in Round 1 to

8.47 ± 0.83 in Round 2); health risks (from 8.03 ± 1.22 in Round 1 to 8.26 ± 0.88 in Round 2); and modifiability (from 7.99 ± 1.29 in Round 1 to 8.26 ± 0.92 in Round 2). Detailed statement-level ratings are provided in Supplementary Tables 11–16.

Domain 1: conceptual framework

Domain 1 defines lipids interspersed within the pancreas, excluding membrane-bound lipids that are integral to cellular architecture (Table 3). It refers to mobile lipids that are part of a dynamic process of lipid deposition within the pancreas over the life course[2]. This process resembles geological sedimentation, whereby particles settle gradually and diffusely over time, embedding themselves subtly within a landscape. With time, this sedimentation can reshape and transform the landscape. This analogy underscores the aptness of the term 'intrapancreatic fat deposition' (IPFD), conveying the gradual and diffuse build-up of lipids within the pancreas throughout life — analogous to sedimentation processes occurring within, for example, a geological basin. First introduced in 2019 through a series of original studies conducted as part of the COSMOS programme[10], IPFD has since gained broad use. Formulated during the current consensus-building process, the companion term to IPFD — 'fatty pancreas disorder' (FPD) — denotes excessive IPFD. IPFD and FPD are not interchangeable, as they represent distinct entities. IPFD is a continuous measure of lipid content within the pancreas, with values spanning a spectrum from those observed in healthy individuals to levels that may precede (or coexist with) pancreatic disease[2]. By contrast, FPD is a categorical construct representing a structural alteration of the pancreas that poses a health risk — analogous to how obesity is defined by the World Health Organization. FPD represents a distinct, organ-specific pathological state that can evolve into multiple diseases of the pancreas. The Working Group carefully considered whether this entity fulfils generally accepted criteria for a disease state[11]. Disease is typically defined by the presence of symptoms, signs and/or objectively measured alterations in organ function — features that can be variably present or absent in individuals with FPD. Although adverse health outcomes can develop in some individuals, progression is not inevitable[2]. Accordingly, excessive IPFD alone was considered to define a pathological state of the pancreas, supporting its conceptualization as a 'disorder' rather than a 'disease'. Caution is warranted against overly permissive characterization of the mere presence of (excessive) fat within the pancreas as a disease, as this designation would carry an unacceptably high risk of overdiagnosis and associated burdens for patients, clinicians and health-care systems[7,11].

Not all fat observed in the pancreas qualifies as IPFD. IPFD is understood as a diffuse process that explicitly excludes focal fat within the pancreas[2]. This distinction is important because the most encountered, although still exceedingly rare, focal fat masses involving the pancreas, such as lipomas and liposarcomas, typically originate in the retroperitoneum and secondarily involve the pancreas through mass effect[12]. When they do arise within the pancreas itself, they represent a classic neoplastic process[12]. Lipomas are benign, encapsulated neoplasms consisting of mature adipocytes. These masses do not arise from lipid deposition in the pancreas over time but rather from the proliferation of adipocytes[2]. Liposarcomas are malignant neoplasms composed of immature adipocytes (lipoblasts), characterized by increased mitotic activity and the presence of tumour necrosis — features that are absent in lipomas[13]. Furthermore, some neoplasms originating from pancreatic cells (for example, pancreatic ductal adenocarcinoma (PDAC), pancreatic neuroendocrine tumours) can be associated with focal fat resulting from secondary processes, including but not limited to fatty metaplasia within the neoplasm and entrapment of adjacent adipose tissue resulting from invasive growth[14,15]. Fat located in or immediately adjacent to these neoplasms is not considered IPFD.

To most appropriately reflect its morphological composition, it is important to recognize that IPFD comprises several distinct compartments (Fig. 2). In the human pancreas, these include intrapancreatic adipocytes, which can be located both within the pancreatic stroma separating the lobules (interlobular adipocytes) and inside the lobules themselves (intralobular adipocytes)[16]. This distinction is important because pancreatic lobules are considered the fundamental structural units of the pancreatic parenchyma. Other IPFD compartments are intracellular in nature and include lipid droplets situated within the cytoplasm of acinar cells and endocrine cells of the islets of Langerhans. Their presence in the human pancreas was first documented in 1981 using lipid-specific stains and confirmed by electron microscopy[17]. This finding has since been corroborated by numerous human studies over the ensuing decades[18–20]. Lipid droplets are also a hallmark of pancreatic stellate cells in their quiescent state. Furthermore, acinar-to-adipocyte transdifferentiation in the pancreas has been observed in preclinical studies[21–23]; however, it has not yet been documented in humans. Collectively, these compartments highlight the intricate and heterogeneous lipid architecture within the pancreas. In addition to the compartments of IPFD, it is also important to recognize the main lipid classes present. Direct biochemical analyses of lipid composition in human pancreatic tissue have shown that triacylglycerols are the predominant lipid class in the organ, with oleic acid (a monounsaturated fatty acid) as the most abundant constituent and palmitic acid (a saturated fatty acid) next in abundance[24,25]. Other lipid classes present in much smaller amounts include cholesteryl esters and free fatty acids, barring phospholipids (as structural membrane lipids are not considered part of the definition of IPFD). Additional lipid esters involved in IPFD include retinyl esters, which are formed from retinol (vitamin A) and are primarily stored in pancreatic stellate cells in their quiescent state[2], although their overall presence is minor.

Table 2 | Professional backgrounds of the core experts

Characteristic		*n* (%)
Medical degree (MD or equivalent)	Yes	18 (72)
	No	7 (28)
Master's degree	Yes	20 (80)
	No	5 (20)
PhD degree	Yes	18 (72)
	No	7 (28)
Primary area of expertise/specialty	Endocrinology and metabolism	6 (24)
	Gastroenterology	9 (36)
	Other	10 (40)
Primary sector of employment	Academia/Education	19 (76)
	Health care	6 (24)
Country of employment, by income level	Lower-middle income	2 (8)
	Upper-middle income	7 (28)
	High income	16 (64)

Data were obtained through a self-administered questionnaire. Income level was classified according to the World Bank country classification for the 2024–2025 period.

Table 3 | Summary of recommendations

Number	Statement	Consensus grade	Level of evidence
Domain 1: conceptual framework			
1.1	IPFD refers to the lipid content of the pancreas (excluding structural lipids in membranes) that is typically diffusely distributed throughout the organ	U	NA
1.2	IPFD is multifaceted and principally consists of intrapancreatic adipocytes, lipid-rich inclusions in non-cancerous pancreatic cells or a combination of both	U	NA
1.3	Intrapancreatic adipocytes refer to mature adipocytes residing within the pancreas, specifically in the interlobular spaces and the lobules	A	NA
1.4	Lipid-rich inclusions refer to cytoplasmic lipid droplets within acinar cells, endocrine cells and pancreatic stellate cells	U	NA
1.5	Visceral adipose tissue surrounding the pancreas — sometimes referred to as 'peripancreatic fat' — does not constitute IPFD	A	NA
1.6	Focal fat within the pancreas — irrespective of its origin — does not constitute IPFD	U	NA
1.7	FPD is a structural alteration of the pancreas, characterized by excessive IPFD, that poses a risk to health	U	NA
1.8	While FPD constitutes a distinct pathological state, IPFD is a continuous measure of lipid content within the pancreas	A	NA
Domain 2: characteristics			
2.1	Low IPFD is a physiological constituent of the human pancreas	A	1
2.2	In individuals without a genetic predisposition, IPFD begins to build up physiologically during puberty, particularly as body mass increases	A	3
2.3	IPFD generally increases with advancing age in adults	U	1
2.4	IPFD is generally higher in male individuals than in female individuals	U	1
2.5	IPFD is influenced by behavioural, environmental and genetic factors	U	2
2.6	IPFD cannot be entirely explained by BMI alone	U	1
2.7	IPFD cannot be entirely explained by waist circumference alone	A	1
2.8	IPFD cannot be entirely explained by hepatic fat content alone	U	1
2.9	Intraday and intraweek variations in IPFD are typically low in magnitude	U	3
2.10	Variations in IPFD across the head, body and tail of the pancreas are typically low in magnitude — particularly when body fat mass and demographics are taken into account	A	2
Domain 3: pathophysiology			
3.1	FPD represents an insidious morphological change in the pancreas arising from cumulative exposures to a broad range of insults to the pancreas (for example, heavy alcohol consumption, tobacco smoking, poor dietary habits, cardiometabolic factors) over the lifespan	U	NA
3.2	FPD has a dynamic role in pancreatic allostasis by eliciting multiple complex responses that remodel the pancreatic microenvironment, alter cellular architecture and function, and promote lipotoxicity, inflammation and fibrosis	A	NA
3.3	The differential modulation of the 'secretome' from IPFD compartments and variable activation of intercellular crosstalk could influence the development of the initial pancreatic disease	U	NA
3.4	Intra-organ crosstalk, combined with the spatial proximity of IPFD compartments, could explain the frequent sequential emergence of pancreatic diseases	U	NA
3.5	FPD is not necessarily a manifestation of obesity and could involve different pathogenic mechanisms — as well as differing health risks and responses to intervention — in individuals with and without obesity	U	NA
3.6	The presence or absence of excess body fat mass could serve to delineate distinct types of FPD	A	NA
Domain 4: principles of assessment			
4.1	In living individuals, IPFD can be identified through pathological evaluation of pancreatic tissue — obtained during surgery or biopsy — but is most commonly assessed using non-invasive imaging modalities	A	3
4.2	When pathological evaluation is indicated, a multimodal approach, including histology, histochemistry, immunohistochemistry and, if available, electron microscopy, should be employed to fully characterize the compartments of IPFD	A	5
4.3	Magnetic resonance is the most robust imaging modality for in vivo quantification of IPFD	U	2
4.4	Quantitative magnetic resonance measurements of IPFD should be performed using techniques that characterize voxel-wise fat content, rather than relying on single-voxel spectroscopic methods	A	3
4.5	Unenhanced MRI is sufficient to quantify IPFD, making contrast unnecessary for this purpose	A	2
4.6	MRI holistically measures mobile lipids across all IPFD compartments	A	1
4.7	IPFD on MRI should be quantified as the proportion of fat protons relative to the sum of fat and water protons, expressed as a percentage	A	5

Table 3 (continued) | Summary of recommendations

Number	Statement	Consensus grade	Level of evidence
Domain 4: principles of assessment (continued)			
4.8	If MRI is unavailable, unenhanced CT can be used for in vivo quantification of a surrogate measure of IPFD — pancreatic attenuation — provided its use is appropriate to the clinical context	U	2
4.9	Transabdominal ultrasonography and endoscopic ultrasonography cannot quantify IPFD but might suggest the presence of FPD, which requires confirmation by MRI	U	3
4.10	If quantification of IPFD or its surrogate measure involves pancreas segmentation, manual outlining of the organ on MRI or CT should currently be considered the gold standard	A	1
4.11	If quantification of IPFD or its surrogate measure on MRI or CT does not involve pancreas segmentation, a mean value should be calculated from three regions of interest placed in the head, body and tail on representative cross-sectional images that capture each of these three parts	A	5
4.12	Regions of interest selected for IPFD quantification on MRI or CT must exclude visceral adipose tissue, the main pancreatic duct, cystic lesions and tumours	A	5
4.13	At present, no universally applicable absolute normal values for IPFD can be recommended	U	3
4.14	FPD can be identified using an absolute comparison, provided that the 95% reference interval for IPFD values in healthy individuals is available in the given setting	A	5
4.15	Relative comparison of IPFD values — using cutoffs such as the upper quartile on MRI — may indicate the presence of FPD within a given population	U	5
4.16	Absolute comparison of IPFD values is applicable in both clinical and research settings, whereas relative comparison is limited to research contexts	U	5
Domain 5: health risks			
5.1	FPD poses an increased risk of acute pancreatitis	U	2
5.2	FPD poses an increased risk of post-endoscopic retrograde cholangiopancreatography pancreatitis	U	2
5.3	FPD poses an increased risk of non-hereditary chronic pancreatitis	A	2
5.4	FPD poses an increased risk of sporadic pancreatic cancer	A	1
5.5	FPD poses an increased risk of postoperative pancreatic fistula	A	1
5.6	FPD poses an increased risk of type 2 diabetes mellitus	U	1
5.7	FPD poses an increased risk of post-pancreatitis diabetes mellitus	U	4
5.8	FPD poses an increased risk of cystic fibrosis-related diabetes	A	4
Domain 6: modifiability			
6.1	IPFD is amenable to both surgical and non-surgical interventions (provided they are apposite to the clinical context), although the effectiveness of these approaches might differ between individuals with and without excess body fat mass	A	3
6.2	Metabolic bariatric surgery is a surgical intervention that can reduce IPFD	U	2
6.3	Non-surgical interventions that can reduce IPFD include dietary modification, exercise training and pharmacological treatment	U	2
6.4	Reduction of IPFD can be achieved through diets with energy restriction (for example, a very-low-energy diet, a low-energy diet)	A	2
6.5	Reduction of IPFD might be achieved with diets without energy restriction — by improving nutrient quality (for example, a Mediterranean-style diet, a carbohydrate-reduced high-protein diet)	A	2
6.6	Reduction of IPFD might be achieved through exercise training, delivered as either moderate-intensity continuous aerobic activity or sprint interval training	A	2
6.7	Reduction of IPFD can be achieved using newer glucose-lowering medications with pleiotropic effects (for example, glucagon-like peptide 1 receptor agonists, sodium-glucose cotransporter 2 inhibitors)	U	1
6.8	Reduction of IPFD following effective interventions is typically proportional to baseline IPFD	A	1
6.9	Reduction of IPFD following effective interventions typically requires several months to manifest	U	1
6.10	Reduction of IPFD through effective interventions might underlie the prevention, interception or remission of both diseases of the exocrine pancreas and diseases of the endocrine pancreas	U	5

Agreement was classified as 'U' for unanimous consensus (100%) and 'A' for strong consensus, defined as 90–99% agreement. Levels of evidence were assessed using the Oxford Centre for Evidence-Based Medicine framework for statements addressing testable clinical claims, with 1 representing the highest level and 5 the lowest. Theoretical constructs, including the conceptual framework and proposed pathophysiology, were not assigned levels of evidence. FPD, fatty pancreas disorder; IFPD, intrapancreatic fat deposition; NA, not applicable.

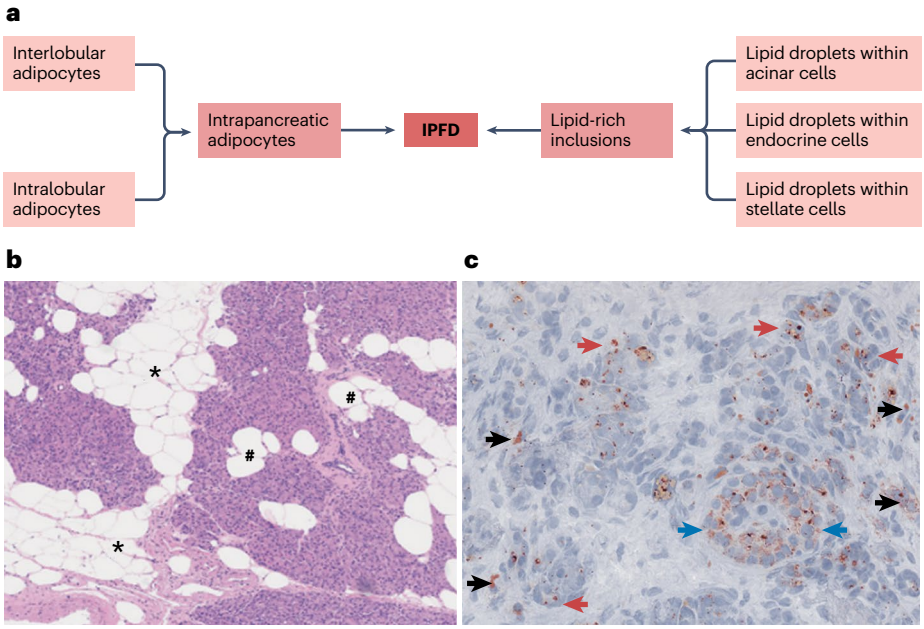

Fig. 2 | Compartments of IPFD in humans. Compartments of intrapancreatic fat deposition (IPFD) are shown conceptually (part **a**) and corroborated by representative histological specimens (parts **b** and **c**). In part **b**, both interlobular adipocytes (marked with an asterisk, *) and intralobular adipocytes (marked with a hash, #) are visible in human pancreatic tissue. The section was stained with haematoxylin and eosin and imaged at 4× magnification. In part **c**, lipid droplets within acinar cells (red arrows) appear as red signals contrasting with the surrounding acinar parenchyma in human pancreatic tissue. Lipid droplets within endocrine cells (blue arrows) are seen as red signals diffusely distributed within a human islet of Langerhans. Lipid droplets within stellate cells (black arrows), located at the periphery of acinar cell clusters, also appear as red signals. The section was stained with Oil Red O and imaged at 40× magnification. Images in parts **b** and **c** were obtained from prospectively collected pancreatic neck margin specimens and are provided courtesy of Claudio Luchini, University of Verona, Italy.

The complexity of IPFD necessitates careful attention to terminology, which should not be dismissed as a matter of personal preference. Several terms previously used in the literature were initially useful for distinguishing fat within the pancreas from other fat depots (thereby drawing scientific attention) but are now considered outdated or incomplete. In particular, the terms 'pancreatic steatosis' and 'steatotic disease' — borrowed from hepatology without sufficient adaptation — are overly simplistic and anachronistic, failing to capture the distinct morphological compartments of fat in the pancreas[2]. Etymologically derived from the Greek *στέαρ* (meaning 'fat' or 'tallow'), steatosis specifically denotes the accumulation of lipids within the cytoplasm of non-adipose cells[26,27]. When used in its correct semantic sense, the term becomes overly restrictive in the context of the pancreas as it fails to account for the presence of adipocytes. Similarly, 'fatty infiltration' is a limited term in the context of the pancreas as it implies the migration of adipocytes from surrounding visceral adipose tissue, yet lipid-rich inclusions within non-adipose cells arise through entirely different mechanisms[2]. Another adaptation from earlier hepatology literature is the term 'non-alcoholic fatty pancreas disease', derived from the historical nomenclature of non-alcoholic fatty liver disease. In hepatology, non-alcoholic fatty liver disease terminology has since evolved into metabolic dysfunction-associated steatotic liver disease, in part to reduce stigma and to better reflect underlying pathophysiology — considerations that are also relevant to pancreatology. This term is both stigmatizing and exclusionary. IPFD can result from multiple causes, rendering it impossible to isolate alcohol as a singular causative factor, particularly given the common coexistence of other risk factors such as smoking[28,29]. Moreover, this approach depends heavily on patient self-reporting of alcohol consumption, which is prone to under-reporting and recall bias. The term 'fatty pancreas' is succinct and conveys the idea but it is vague and, in standard English, always requires the article 'a' before it (since the organ is countable and singular). Another term, 'pancreatic lipomatosis', is a misnomer because the Greek suffix *-osis* denotes a pathological process, whereas IPFD is not inherently pathological. Furthermore, focal fat masses, such as lipomas, fall outside the definition of IPFD (as discussed in detail above). Last, omission of the prefix 'intra' before 'pancreatic' when referring to fat within the pancreas is discouraged, as this usage lacks specificity and could be misinterpreted by some as referring to peripancreatic fat[30,31]. The term IPFD explicitly excludes peripancreatic fat — a part of the extensive visceral adipose tissue depot — whose boundaries are not clearly and objectively delineated in humans[32]. In the same vein, 'interlobular' is recommended over 'extralobular' in describing adipocytes as the latter is variably used and might, in some usages, include peripancreatic fat.

Domain 2: characteristics

Domain 2 focuses on key considerations related to IPFD in health (Table 3). Evidence suggests that IPFD is more common in the normal pancreas than traditionally believed[2]. In a modern study involving 11 human cadaver donors (aged 13–58 years), native, non-decellularized pancreata contained 38 ± 3.6% lipids by dry weight (mean ± standard deviation)[33]. Even after homogenization and decellularization, the pancreata retained 3.9 ± 1.1% of their lipid content[33]. These findings align with an earlier autopsy study of 50 individuals (aged 12–82 years), which found that IPFD accounted for at least 3% of total pancreas weight and averaged 9.7 ± 6.5 g in lean individuals[34]. The largest autopsy study on the topic examined 394 consecutive individuals (aged 20–96 years) and found that all but one had detectable IPFD[35]. Furthermore, a study of 55 organ donors (aged 16–80 years) reported that all pancreata showed detectable IPFD on histological evaluation, with a minimum lipid content of 4.7%[36].

Investigations of IPFD in the paediatric population are understandably far fewer than those in adults[37]. In a cross-sectional CT study of 135 individuals, IPFD was detected in all 5-year age brackets from birth up to 20 years[38]. Furthermore, IPFD was substantially higher in the second decade of life, which might be partly due to the increase in parenchymal volume of the pancreas occurring during whole-body growth[38]. A longitudinal MRI study of 76 individuals (mean age

16 years) examined changes in IPFD over 2 years in relation to pubertal stage at baseline, comparing early versus advanced groups[39]. The study found that only the advanced pubertal maturity group (Tanner stages 4–5) developed a statistically significant increase in IPFD during follow-up[39]. Consistent with these findings, a study of human pancreas donors reported that lipid droplets within pancreatic cells tend to emerge during adolescence[20]. Taken together, these observations suggest that the hormonal changes during puberty might lead to the first notable build-up of IPFD during the human lifespan for most individuals, barring rare mutations (for example, in the genes encoding cystic fibrosis transmembrane conductance regulator, carboxyl-ester lipase or Shwachman–Bodian–Diamond syndrome protein) that lead to earlier-onset IPFD[40–42].

Throughout adulthood, various factors can contribute to the progressive build-up of IPFD, including tobacco smoking, heavy alcohol consumption and intake of ultra-processed foods, among others[43–46]. Notably, it is the cumulative exposures over time that drive this process, as IPFD remains largely stable over short timeframes with negligible diurnal and weekly variations[47]. Ageing itself contributes to increased IPFD, with population-based studies consistently showing that older adults (aged 65 years and above) tend to have higher levels of IPFD than younger individuals[48–51]. These studies also typically report higher levels of IPFD in men than in women, independent of BMI[50,52,53]. By contrast, variations in IPFD across the head, body and tail of the pancreas are largely attributable to BMI and demographic factors[49,54], and are occasionally reported only in studies with suboptimal IPFD measurement protocols or no adjustment for covariates. That said, IPFD might differ between the dorsal and ventral anlagen within the head of the pancreas (reflecting its embryological origin from two distinct buds)[34,55].

Historically, the entrenched view that IPFD is a consequence of general or central obesity — as measured by BMI or waist circumference — has stemmed from an overly simplistic belief that ectopic fat arises merely as a spillover of excess subcutaneous fat in individuals with sustained positive energy balance[2]. However, this perspective reflects a reductionist approach and fails to capture the multipronged nature of IPFD (Fig. 2). The current consensus emphasizes that IPFD is a distinct process, with excess body fat mass being only one of several contributing factors. Meta-analyses have consistently demonstrated a lack of statistically significant association between IPFD and BMI or waist circumference[3,56,57]. Moreover, individuals with comparable visceral adipose tissue can have markedly different IPFD[58,59]. The fat spillover narrative has also given rise to the common belief that hepatic fat and IPFD are inherently interconnected, despite evidence pointing to a more complex and context-dependent relationship[60–63]. There is notable incongruity in the literature, with some studies demonstrating a statistically significant association between fat in the liver and pancreas, whereas others find none[64–67]. A large 2024 study elegantly resolved this discrepancy by identifying the specific factors upon which the presence or absence of an association between hepatic fat and IPFD depends[68]. Typically, this association is observed in younger individuals without obesity with good cardiometabolic health but it becomes uncoupled in older adults or those with cardiometabolic risk factors or obesity[68].

Domain 3: pathophysiology

Domain 3 depicts FPD as a key early pathological alteration of the pancreas in response to overwhelming exposure to a wide array of factors (Table 3). This depiction aligns with a central tenet of the PANcreatic Diseases Originating from intRapancreatic fAt (PANDORA) hypothesis (*Pandōra* in Greek literally means 'all-gifted')[69,70]. FPD disrupts pancreatic architecture and triggers early lipotoxic injury, endoplasmic reticulum stress and low-grade inflammation according to data from cell and animal models[71,72]. These initial changes progressively evolve into classic pathological features of the pancreatic parenchyma such as acinar cell injury, ductal cell abnormalities and β-cell dysfunction[73,74]. Although these changes might remain subclinical for a period, they have the potential to culminate in overt pancreatic disease (Fig. 3). Importantly, FPD constitutes an early organ-specific pathological state rather than a late consequence of pancreatic disease. For example, de novo fat appearing upstream towards the tail due to an advanced PDAC obstructing the main pancreatic duct does not qualify as FPD.

Intrapancreatic adipocytes reside in close anatomical and functional proximity to acinar, ductal and islet cells, facilitating both direct cell–cell contact and bidirectional paracrine signalling[2,75,76]. Histological analyses of human pancreatic specimens indicate that increased IPFD is primarily driven by an increase in adipocyte number rather than cell size[16,19]. Both interlobular and intralobular adipocytes contribute to IPFD, with no marked difference observed between the two types[77]. Lipid droplets in acinar and endocrine cells are highly prevalent in the human pancreas. Notably, the largest and most comprehensive study of frozen pancreatic tissue to date, involving 100 patients undergoing pancreatic resection, reported their presence in 90% of individuals[77]. Furthermore, a statistically significant positive association was identified between the prevalence of lipid droplets in acinar cells and that in endocrine cells[77]. Similar findings were reported in a smaller study ($n = 55$) of donated non-diabetic human pancreata[36]. Although current evidence does not allow a definitive inference regarding the relative contribution of each individual IPFD compartment to FPD, available findings do suggest that all compartments participate in intra-organ crosstalk. This crosstalk likely actively remodels the pancreatic microenvironment by altering cellular interactions and promoting the release of bioactive lipid species (for example, free fatty acids, sphingolipids, ceramides and long-chain acylcarnitines), which in turn affect both the function and structure of pancreatic cells[78–85]. This lipotoxic milieu generated by FPD induces endoplasmic reticulum stress and mitochondrial dysfunction according to data from cell and animal models[69]. Prolonged exposure to this lipotoxic environment could induce low-grade inflammation, as evidenced by histological examinations showing macrophage infiltration within the pancreatic parenchyma of individuals with FPD[86]. This inflammatory cascade further exacerbates tissue injury and promotes alterations in cellular phenotype[87,88]. The spatial and temporal dynamics of biochemical signals derived from the IPFD compartments likely contribute to the vulnerability of pancreatic cells and modulate the trajectory of disease development[75,89]. These effects might be influenced by the proximity of these compartments to susceptible pancreatic cells and the local availability or type of bioactive lipids[90]. For example, a 2026 study demonstrated that intrapancreatic adipocytes are markedly closer to the islets of Langerhans in individuals with type 2 diabetes mellitus (T2DM) than in those without[91]. The IPFD compartments likely exhibit heterogeneous secretory profiles, releasing varying levels of adipokines, cytokines, chemokines and bioactive lipids that differentially modulate interactions among acinar, ductal, islet and stromal cells[92–94]. Thus, secretomes — the ensemble of bioactive molecules secreted by cells — originating from intralobular and interlobular adipocytes, as well as from other pancreatic cells containing

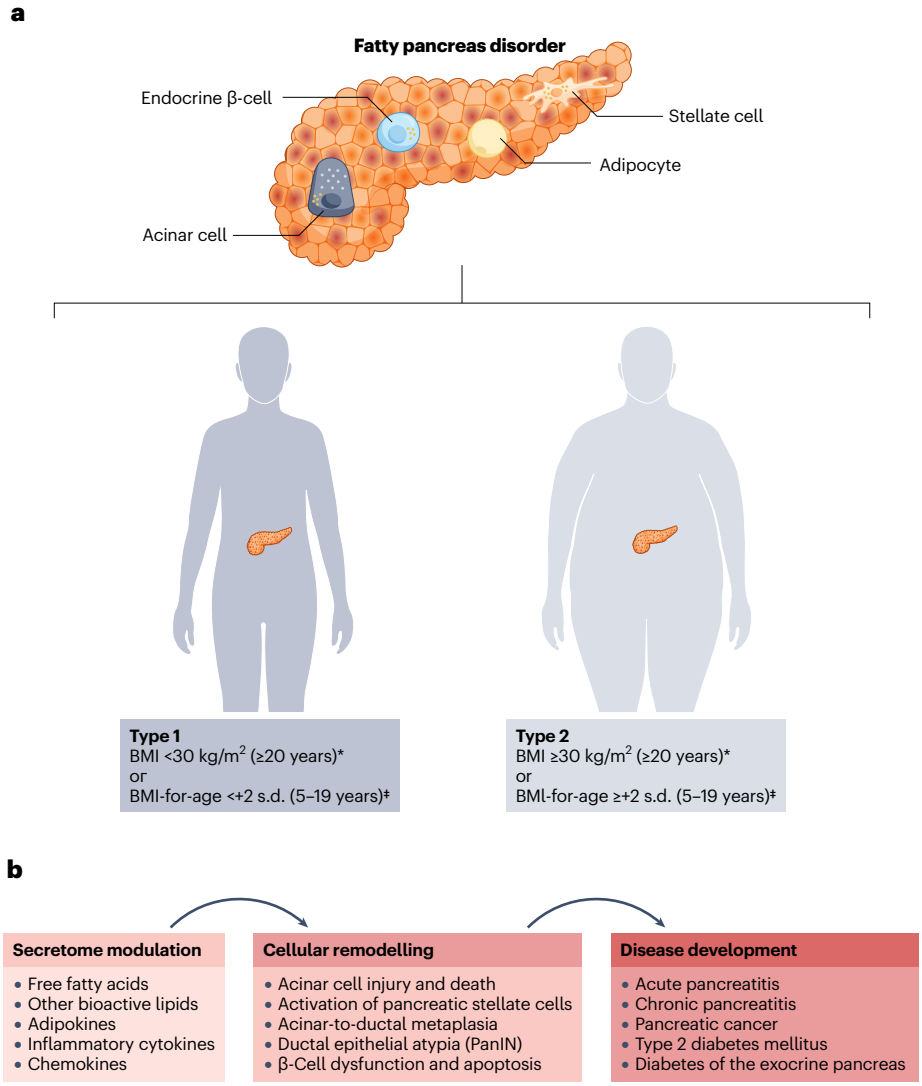

Fig. 3 | Typology of FPD and role in allostasis. Classification of fatty pancreas disorder (FPD) (part **a**) and its role in allostasis (part **b**). FPD is an organ-specific early pathological state that increases the risk of pancreatic diseases, rather than arising as a consequence of advanced pancreatic diseases. This notion aligns with allostasis — the active process by which the body, and specifically the pancreas, adapts to stressors by establishing a new physiological balance. Beyond simply storing neutral lipids, lipid droplets participate dynamically in lipid trafficking, signalling pathways and interactions with other organelles, thereby influencing pancreatic allostasis. Progressive intrapancreatic fat deposition (IPFD) drives time-dependent alterations in the 'secretome' (that is, the full range of bioactive molecules released by cells) of IPFD compartments. These secretome changes trigger structural and functional adaptations in pancreatic cells, collectively termed 'cellular remodelling'. Although transient remodelling can be adaptive, persistent or maladaptive remodelling contributes to the development of pancreatic diseases, including diabetes, pancreatitis and pancreatic cancer. Representative examples of cells and factors involved in pathophysiology are shown, including adipocyte and lipid droplets in acinar cells, pancreatic β-cells (serving as an example of endocrine cells in the pancreas) and stellate cells. Elements not related to IPFD are omitted. The specific mechanisms listed in part **b** are not exclusive to either type 1 or type 2 FPD. The development of specific pancreatic diseases might also require systemic factors (for example, infiltration of immune cells, insulin resistance, *KRAS* mutations). *When focusing primarily on adults of East, South and South-East Asian descent, obesity should be assessed using ethnicity-specific cut-off points. ‡When assessing children, obesity should be defined as a BMI greater than +2 s.d. above the World Health Organization growth reference median for age and sex. PanIN, pancreatic intraepithelial neoplasia.

lipid droplets, might have a crucial role in determining whether pancreatitis, pancreatic cancer or T2DM develops first.

Excess body fat mass is a major risk factor for FPD; however, FPD can develop regardless of general or visceral adiposity[58,95–97]. Furthermore, numerous studies focusing on individuals without adiposity have identified statistically significant associations of FPD with various diseases[87,98–101]. Additionally, FPD is frequently observed in conditions far removed from adiposity (for example, familial partial lipodystrophy)[102]. The current consensus holds that FPD can be broadly classified into two types: type 1, which develops in individuals without excess body fat; and type 2, which develops in individuals with excess body fat. Each type might involve different predominant

IPFD compartments and could be characterized by distinct pathophysiological mechanisms[103]. Type 2 FPD might represent a systemic overflow of lipid storage, chiefly driven by positive energy balance, overnutrition and obesity-driven insulin resistance. In this type of FPD, interlobular adipocytes could constitute the predominant IPFD compartment affected. By contrast, intralobular IPFD compartments (Fig. 2) might be more prominently involved in type 1 FPD. This form can coexist with insulin resistance, as individuals of normal weight can also exhibit insulin resistance[104]. However, current evidence is insufficient to determine the relative prevalence of insulin-sensitive versus insulin-resistant phenotypes within type 1 FPD[105], representing a priority for future research. Preliminary evidence suggests that potential mechanisms underlying type 1 FPD could also include activation of the mitochondrial unfolded protein response, impaired lipophagy, genetic susceptibility and environmental influences, although definitive causal pathways have yet to be established[90,106]. Overall, type 1 and type 2 FPD should be viewed as a provisional mechanistic construct rather than as mutually exclusive metabolic phenotypes at present.

Domain 4: principles of assessment

Domain 4 addresses the importance of appropriate IPFD quantification (Table 3). IPFD can be measured histologically from biopsy or surgical specimens, enabling characterization of individual IPFD compartments (Fig. 2). Importantly, beyond haematoxylin and eosin staining, additional techniques, such as histochemistry and immunohistochemistry and, when available, electron microscopy, are recommended for comprehensive assessment[77]. Although histological measurement provides detailed information, fine-needle biopsy or surgery should not be performed solely for the purpose of assessing FPD. Consequently, the assessment of FPD should preferentially rely on imaging modalities. Transabdominal ultrasonography and endoscopic ultrasonography (EUS) — the latter providing higher resolution but typically requiring sedation — can be used to suggest the presence of FPD when increased pancreatic echogenicity is observed (typically relative to an adjacent reference organ)[69]. However, MRI should be used for further evaluation when FPD is suspected as conventional ultrasonography-based assessments are highly operator-dependent and qualitative rather than quantitative, making them unsuitable for accurate evaluation of FPD[2,69]. Furthermore, EUS assesses the pancreas in a piecemeal, segmental manner, evaluating different anatomical portions of the organ from multiple internal vantage points rather than producing a whole-organ image in a single sweep (as is the case with cross-sectional imaging). It is appreciated that, in the gastroenterology setting, the use of EUS for the assessment of FPD might be appealing due to its wide availability and convenience. However, published data indicate that concordance between conventional EUS and cross-sectional imaging is limited[107,108]. In particular, 79% of individuals labelled as having FPD on EUS do not have it on MRI or CT[107]. This discrepancy increases to 94% when EUS is compared with MRI alone[108]. Although EUS can detect occult tumours not visible on MRI and identify subtle features of chronic pancreatitis, these advantages do not extend to the assessment of FPD. This limitation reflects the underlying physics of ultrasonography, which, unlike MRI, is not inherently suited to detecting lipid content within tissue[109]. A hyperechoic pancreas on EUS — defined relative to an adjacent reference organ — should not be interpreted as evidence of FPD, as echogenicity is influenced by multiple factors beyond the fat content of organs.

MRI is the preferred modality for quantifying IPFD as it affords unparalleled soft tissue contrast compared with other imaging modalities and has shown high accuracy and strong agreement with histologically measured IPFD[110,111]. MRI quantifies IPFD by calculating the proportion of fat protons relative to the combined signal from fat and water protons. As such, this modality captures not only lipids stored in intrapancreatic adipocytes but also cytoplasmic lipid droplets within other pancreatic cells, providing a holistic assessment of IPFD[69,111]. MRI protocols for quantifying IPFD are often similar to those used for the assessment of hepatic fat and are presumed to have the same reproducibility to hepatic measures across both 1.5 T and 3.0 T MRI scanners[112,113]. However, because the pancreas is smaller, breath-hold acquisition or correction for respiratory motion is essential[2,69]. Furthermore, spatial resolution must be sufficient to exclude the main pancreatic duct and vessels from analysis; resolutions of 2.5 mm in-plane with 5 mm slice thickness can be achieved within a single breath-hold, although higher resolution is preferred (for example, 2 × 2 × 3 mm). CT offers a range of attenuation-based approaches for approximating IPFD, such as measuring pancreatic attenuation (in Hounsfield units) relative to splenic attenuation. Unenhanced CT is recommended, as intravenous iodine contrast leads to increased Hounsfield unit values. This modality demonstrates reasonable agreement with both histology and MRI in assessing IPFD[59,114,115], supporting its use for IPFD evaluation when MRI is unavailable. Due to concerns about radiation exposure, performing CT prospectively solely for IPFD assessment is not recommended. However, because CT is widely available and frequently performed in hospital settings for other clinical indications, retrospective scans can be opportunistically used for IPFD assessment[114,116,117]. Overall, imaging methods for IPFD measurement have evolved over the past two decades (particularly in published interventional studies). Earlier studies mainly relied on single-voxel spectroscopic techniques and CT whereas more recent studies have predominantly utilized MRI.

In both MRI-based and CT-based assessments, manual measurement remains the current gold standard for quantifying IPFD[118]. The current consensus recommends obtaining measurements from three regions of interest in the pancreas — the head, body and tail — and using their average as a representative value of overall IPFD. This averaged IPFD demonstrates greater repeatability than a single region of interest, likely due to the sampling variability inherent to single-point measurements[119]. Each region of interest is recommended to have an area of at least 100 mm^2, provided that it can be placed within the pancreatic parenchyma, with care taken to avoid surrounding visceral fat, the main pancreatic duct and any visible pathological lesions[49,120–122]. One earlier study manually assessed IPFD in more than 2,000 individuals, demonstrating the feasibility of large-scale manual evaluation[100]. Machine learning-based organ recognition platforms have enabled scalable, automated quantification of IPFD[5,50]. However, full implementation remains premature, as a 2026 meta-analysis reported a pooled Dice similarity coefficient of only 82% between automated IPFD quantification and the ground truth, radiologist-performed measurements[123]. Furthermore, a 2025 original study showed that the presence of FPD makes automated pancreas segmentation less accurate[124]. This finding is consistent with earlier work that showed that pancreas segmentation errors using machine learning-based models are more pronounced in patients with pancreatic pathology compared with those with a normal pancreas[125]. In addition, agreement in IPFD measurements varies across field strengths, vendors, image acquisition parameters (for example, number of echo times, sequence) and post-processing techniques (for

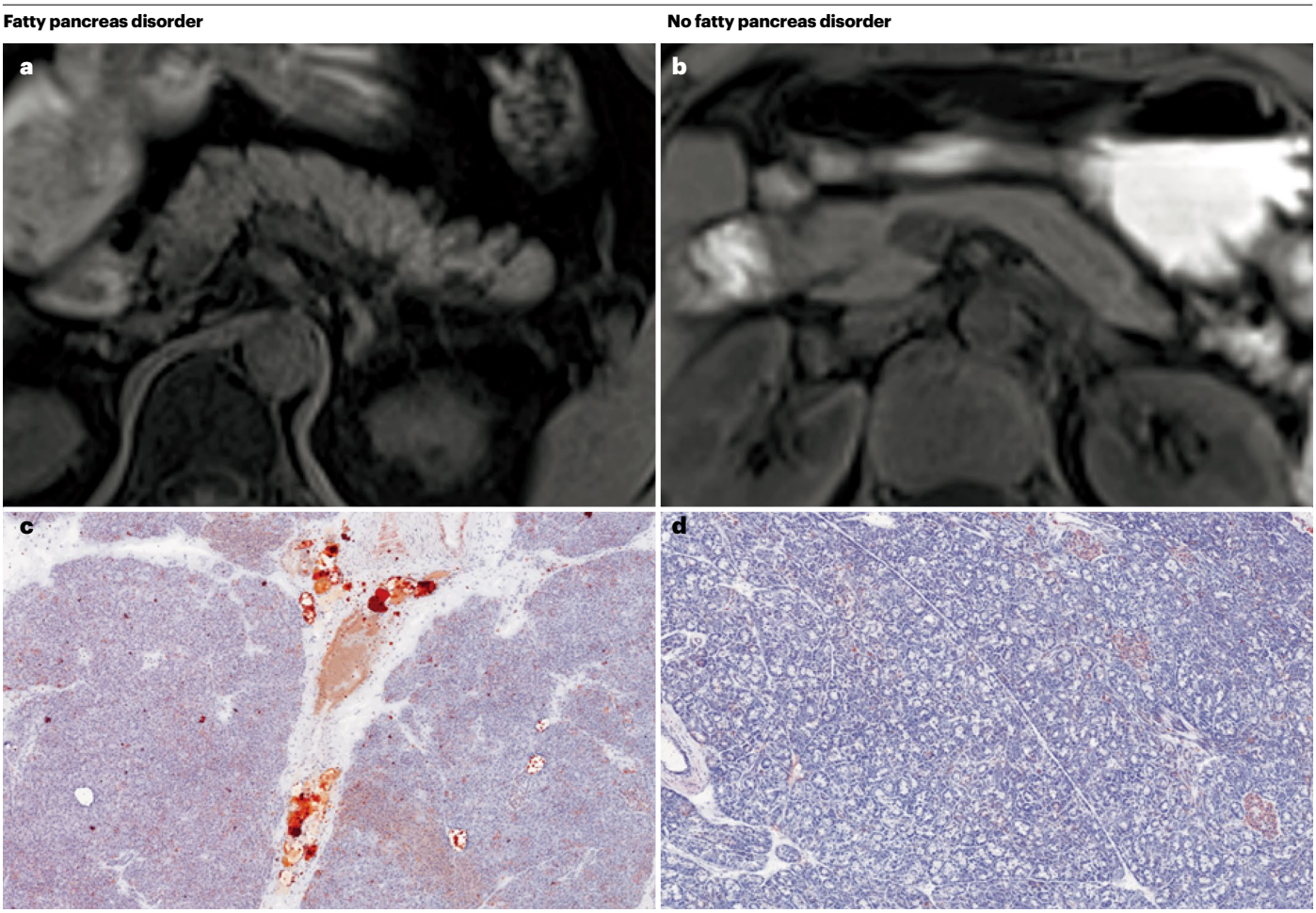

Fig. 4 | Representative examples of individuals with and without fatty pancreas disorder. MRI-based (parts **a** and **b**) and histological (parts **c** and **d**) assessments of the pancreas are shown. Fatty pancreas disorder was defined as intrapancreatic fat deposition values exceeding the cohort-specific upper quartile in both MRI-based and histological assessments, with full cohort details reported elsewhere[77,144]. The studies received approval from the institutional ethics committees of the University of Tokyo (Japan) and the University of Verona (Italy), as detailed in the original publications[77,144], with images used and informed consent obtained in accordance with the approved study protocols.

example, noise bias correction algorithms)[126–128]. The Working Group deliberated extensively on the possibility of a single, fixed MRI cut-off for the universal diagnosis of FPD. Although such a cut-off would be ideal, the current evidence does not support its establishment — a decision unanimously reached by all experts. This decision reflects a commitment to scientific rigour and to advancing the field by highlighting a critical research priority rather than prematurely committing to a single numerical cut-off that is unlikely to withstand the test of time. There was strong agreement among experts that identifying FPD using either an absolute approach (based on the 95% reference interval for IPFD values in healthy individuals) or a relative approach (for example, the upper quartile of MRI-derived IPFD values within a given population) represents a pragmatic step towards establishing a fixed cut-off (Fig. 4). Initially applied in commonly cited large IPFD studies more than a decade ago, the two methods have since endured over time[48,129].

In establishing a single, evidence-based cut-off for the universal diagnosis of FPD with the use of cross-sectional imaging, it will be important to reliably define reference intervals for IPFD using methodologies consistent with Clinical and Laboratory Standards Institute guidelines[130]. This approach includes appropriate handling of outliers, assessment of data distribution and the application of suitable statistical methods to determine the upper reference limit (Supplementary Figure 1). In addition, identifying IPFD thresholds associated with clinically meaningful outcomes will be important. Specifically, in large-scale imaging cohorts, the incidence of pancreatic diseases (such as pancreatic cancer) could be examined across fine increments of IPFD (for example, 2% intervals), along with corresponding 95% confidence intervals. However, even in currently available large-scale imaging studies, the number of incident pancreatic disease cases remains limited[50,51], making it difficult to generate stable estimates of incidence and confidence intervals across such fine IPFD strata. Larger-scale imaging-based epidemiological studies are therefore warranted. From a measurement standardization perspective, the selection of a robust and reproducible quantitative imaging parameter is a prerequisite for implementing such distribution-based and outcome-based

thresholding approaches[131]. Proton density fat fraction, a quantitative imaging parameter typically expressed as a percentage, is typically measured using multi-echo chemical-shift-encoded MRI and is currently regarded as the most promising metric for assessing IPFD. In this context, the work of the Quantitative Imaging Biomarkers Alliance (organized by the Radiological Society of North America) provides a valuable model as it has established standardized approaches for voxel-level fat fraction assessment in the liver[132]. A systematic body of work focused on pancreatic proton density fat fraction will be critical to advancing a universal diagnostic framework for FPD.

Domain 5: health risks

Domain 5 describes the implications of FPD for both diseases of the exocrine pancreas and diseases of the endocrine pancreas (Table 3), aligning with the predictions of the PANDORA hypothesis[69,70,133]. Initial links between FPD and acute pancreatitis in humans were reported in isolated autopsy studies[134,135]. These early observations were subsequently substantiated by a concerted series of MRI studies conducted within the COSMOS programme[10]. One study (n = 201) demonstrated that, when compared with healthy individuals as controls, both individuals with acute pancreatitis and those with chronic pancreatitis had statistically significantly higher IPFD (even after adjustment for BMI and other covariates)[136]. Notably, the magnitude of IPFD was comparable between the acute pancreatitis and chronic pancreatitis groups[136]. Another study demonstrated that each 1% higher IPFD was significantly associated with more than a 1.3-fold increased risk of a first attack of acute pancreatitis (even after adjustment for BMI and other covariates)[137]. Importantly, this elevated risk was not attributable to hypertriglyceridaemia[137]. More robust evidence emerged from a large prospective MRI cohort study, which demonstrated that individuals with FPD had a 3.9-fold significantly higher risk of developing acute pancreatitis than those without FPD in the general population (even after adjustment for BMI and other covariates)[50]. This association was further strengthened by a subsequent Mendelian randomization study, which established a causal relationship between FPD and acute pancreatitis: a one standard deviation increase in IPFD conferred a 1.4-fold significantly increased risk of acute pancreatitis (even after adjustment for visceral adipose tissue)[138]. Similarly, a one standard deviation increase in IPFD led to a 1.6-fold significantly increased risk of chronic pancreatitis. Importantly, Mendelian randomization did not support reverse causation of either acute pancreatitis or chronic pancreatitis on IPFD[133,138]. Consistent with these findings, clinical cohorts of individuals with chronic pancreatitis have consistently demonstrated higher IPFD than individuals without chronic pancreatitis, in both adult and paediatric populations[139,140]. In the context of post-endoscopic retrograde cholangiopancreatography pancreatitis, a 2025 meta-analysis of four studies demonstrated that FPD identified on pre-procedural CT scans was associated with a 3.7-fold significantly increased risk of developing the condition[141]. However, since the primary studies included patients with both biliary and pancreatic indications, it remains to be established whether this association is valid in individuals without underlying pancreatic diseases.

The link between FPD and sporadic pancreatic cancer has been reported across multiple clinical studies. The first systematic review on the topic, published in 2020 and including 13 studies, found that individuals with pancreatic cancer had a 2.8-fold higher likelihood of having FPD than individuals without pancreatic cancer[142]. The latest systematic review, published in 2025 and encompassing 23 studies, similarly reported a 3.2-fold increased likelihood in individuals with pancreatic cancer than in those without pancreatic cancer[143]. In both meta-analyses, FPD was present in more than half of individuals with pancreatic cancer, with reported prevalences of 52% and 54%, respectively[142,143]. Similarly, in a 2025 case–control study nested within a large prospective cohort of individuals with intraductal papillary mucinous neoplasm (the most common macroscopic precursor of pancreatic cancer), 47% of individuals with carcinoma concomitant with intraductal papillary mucinous neoplasm had FPD[144]. Furthermore, baseline FPD was associated with a 4.6-fold significantly increased risk of developing PDAC concomitant with intraductal papillary mucinous neoplasm over a follow-up period of up to 12 years (even after adjustment for BMI and other covariates). By contrast, no statistically significant association was observed between FPD and the risk of PDAC arising directly from intraductal papillary mucinous neoplasm[144]. Additionally, the most common pancreatic premalignant lesion, pancreatic intraepithelial neoplasia, was found to be significantly associated with FPD in a 2015 cross-sectional study[145]. The most compelling evidence to date implicating FPD in the causal pathway of pancreatic carcinogenesis comes from a Mendelian randomization study, which demonstrated that a 1-standard-deviation increase in IPFD was associated with a 1.5-fold significantly higher risk of pancreatic cancer[70,95]. Furthermore, analysis of a large institutional database found no statistically significant association between FPD and extra-pancreatic cancers (including malignancies with established obesity risk)[146], suggesting that FPD has a unique role in pancreatic cancer development. As pancreatic cancer is potentially curable only through surgical resection, FPD is clinically important not only as a factor posing a higher risk of cancer development but also as a clinically significant and independent predictor of a common postoperative complication, pancreatic fistula[147].

Statistically significant associations between FPD and T2DM have been demonstrated in several high-quality longitudinal cohort studies. These studies showed that FPD independently contributed to the risk of developing T2DM (even after adjustment for BMI, hepatic fat and other covariates). Dong et al. reported that FPD was associated with a 34% higher risk of diabetes over a medium follow-up of 4.6 years[50]. Chan et al. showed that individuals with FPD had an 81% higher risk of developing T2DM over a mean follow-up of 11.1 years; furthermore, each 1% increase in IPFD was associated with a 7% increase in diabetes risk[148]. The association of FPD with T2DM was also observed specifically in longitudinal cohort studies of individuals without obesity[100,149]. Beyond T2DM, FPD could also contribute to the risk of secondary diabetes that arises as a sequela of diseases such as pancreatitis and cystic fibrosis[150,151]. These subtypes of diabetes fall under the umbrella of diabetes of the exocrine pancreas, which is increasingly recognized as a distinct and underdiagnosed type of diabetes[152–154]. Studies in individuals with acute pancreatitis and chronic pancreatitis showed that the prevalence of FPD was significantly higher in those with post-pancreatitis diabetes mellitus (PPDM) than in those without it[155,156]. Moreover, in individuals with PPDM without obesity, IPFD had a stronger correlation with indices of insulin resistance than other fat depots[157]. Studies in individuals with cystic fibrosis found that FPD was significantly more prevalent in those with cystic fibrosis-related diabetes than in those without it[158,159]. Research on secondary diabetes, particularly concerning IPFD, is markedly limited compared with that on T2DM, underscoring the need to strengthen the evidence base in this area.

Although the holistic prevention paradigm in pancreatology was first introduced in 2019 in the context of pancreatitis[160], emerging evidence has since positioned FPD as a central element in extending this framework to encompass all major pancreatic diseases (Fig. 5).

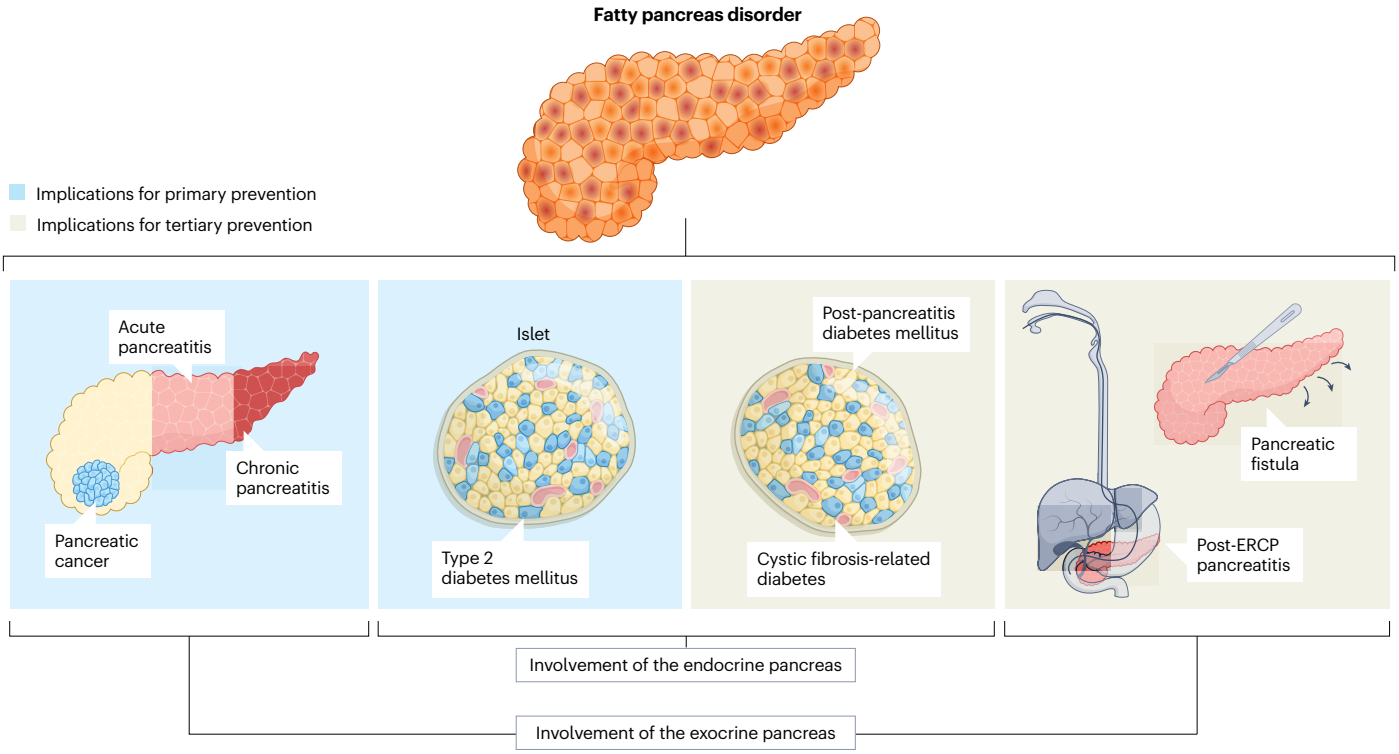

Fig. 5 | Fatty pancreas disorder as a risk to pancreas health. Fatty pancreas disorder is a potentially modifiable state relevant to both primary prevention (by reducing the risk of disease onset) and tertiary prevention (by mitigating complications and long-term sequelae) across a spectrum of diseases involving both the exocrine pancreas and endocrine pancreas. Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis refers to pancreatitis that develops following ERCP, particularly in patients undergoing the procedure for underlying pancreatic diseases.

Reversal of FPD might facilitate primary prevention by lowering the risk of developing pancreatic diseases, such as T2DM, acute pancreatitis and pancreatic cancer, in the general population. Reversal of FPD might also play a part in tertiary prevention by reducing the incidence of post-procedural complications (such as pancreatic fistula) and mitigating long-term sequelae (such as PPDM). Meanwhile, understanding the role of reversal of FPD in secondary prevention — focused on reducing disease severity (for example, severity of acute pancreatitis) and preventing progression in established pancreatic diseases — is likely to become an emerging priority in the years ahead.

Domain 6: modifiability

Domain 6 summarizes evidence that IPFD is modifiable and responsive to a variety of interventions (Table 3). Only evidence from human studies is considered below. Dietary interventions — both with and without energy restriction — have been the most extensively studied with respect to their effects on IPFD. Hypocaloric approaches, in particular very-low-energy diets and moderately energy-restricted diets, were shown to reduce IPFD. Two studies investigating very-low-energy diets of 600 kcal with macronutrient compositions of 46% carbohydrates, 33% protein and 20% fat (CH46|P33|F20) and 700 kcal (CH43|P34|F20) in 11 and 30 individuals with T2DM reported statistically significant absolute reductions in IPFD of 1.8%[161] and up to 0.8%[162] after 2 months of the diets, respectively. Notably, the magnitude of IPFD reduction did not correlate with BMI ($r = 0.01$)[161]. In a primary care-led weight management programme, participants with T2DM who followed a low-energy diet of approximately 850 kcal per day (CH59|P26|F13) for up to 5 months achieved a statistically significant absolute reduction of at least 0.7% in IPFD at 5 months, remaining at that level throughout the weight maintenance phase (up to 24 months)[163]. When the energy restriction goal was to maintain a daily deficit of at least 500 kcal per day or to induce a 6–10% weight loss, IPFD was significantly reduced by 0.3–8.4% through a balanced diet (CH62|P14|F24)[164], a conventional diabetes diet (CH50|P17|F33)[165] or low-carbohydrate diet (CH30|P30|F40)[165,166]. IPFD reduction might also be achieved through improvements in diet quality, independent of energy restriction. Trials demonstrating significant reductions in IPFD by 1.6–1.7% have included a carbohydrate-reduced high-protein diet (CH30|P30|F40)[167] and a Mediterranean-style multifactorial diet rich in polyunsaturated fatty acids, monounsaturated fatty acids, fibre, polyphenols and antioxidants (CH39|P18|F43)[168]. In addition, studies using food frequency questionnaires have reported a lower risk of FPD associated with adherence to the Dietary Approaches to Stop Hypertension diet (which is rich in fresh fruits, vegetables, whole grains and low-fat dairy)[169], as well as higher intake of dietary starch and partial substitution of saturated fat with monounsaturated fat[170,171].

Several exercise-based interventions have been shown to reduce IPFD, primarily among sedentary individuals aged 40–65 years. These interventions included moderate-intensity aerobic training (three sessions per week at 60–70% of maximum heart rate or maximal oxygen uptake)[172,173], sprint interval training[173] as well as a combination of strength and endurance training (equivalent to 4 h of intensive exercise per week)[174]. Glucose-lowering medications with pleiotropic effects

might also reduce IPFD[175]. A 2026 meta-analysis of eight randomized controlled trials (six of which included participants with T2DM only) reported a statistically significant 1.5% greater reduction in IPFD with glucose-lowering medications compared to their respective control groups[176]. When breaking down by specific medication classes, significant reductions in IPFD were observed with glucagon-like peptide 1 receptor agonists (−1.6%) and sodium-glucose cotransporter 2 inhibitors (−1.4%). These reductions were accompanied by marked improvements in glycated haemoglobin levels[177–179]. Notably, a sustained treatment duration seemed to be necessary, as statistically significant reductions in IPFD were observed only with medications administered for 3–6 months. The magnitude of IPFD reduction was significantly correlated with baseline IPFD ($r = 0.87$) but not with baseline weight ($r = 0.15$) or with changes in weight ($r = 0.01$)[176]. Although glucagon-like peptide 1 receptor agonists were once linked to an increased risk of acute pancreatitis, subsequent robust data suggest that these safety concerns might be less pronounced[180]. Newer dual glucagon-like peptide1–glucose-dependent insulinotropic polypeptide receptor agonists seem to be associated with acute pancreatitis very rarely[181]; however, their effects on IPFD reduction have not yet been investigated[175].

Bariatric procedures are an effective intervention for reducing IPFD. A 2025 meta-analysis reported a significant absolute reduction of 3.9% in IPFD from before to after metabolic bariatric surgery (predominantly, sleeve gastrectomy)[57]. Substantial reductions in IPFD were typically first observed at 3 months after surgery, which tended not to markedly change during the subsequent follow-up until 12 months (or more) after surgery. This finding suggests that the process of reducing IPFD is gradual, takes time and has limits. FPD reversal following surgery was observed in 7 of 13 (54%) patients[182]. Furthermore, IPFD was significantly reduced to the level of lean healthy individuals as controls[183,184]. The magnitude of IPFD reduction was significantly correlated with baseline IPFD ($r = 0.72$) but not with baseline weight ($r = -0.10$)[57]. Additionally, the above-mentioned meta-analysis showed that reductions in IPFD from before to after bariatric surgery brought about a statistically significant 42% reduction in the frequency of diabetes mellitus — effectively indicating diabetes remission[57]. Furthermore, a 2025 prospective cohort study of 31 individuals with impaired glucose tolerance and 18 with normal glucose tolerance prior to sleeve gastrectomy showed that, 3 months after surgery, IPFD reduction was significantly greater in the impaired glucose tolerance group[185].

Although several interventions described earlier demonstrate statistically significant reductions in IPFD, the magnitude of these changes and their translation into clinically meaningful and patient-centred outcomes remain uncertain across diverse populations and care settings. Future studies should, therefore, prespecify clinically meaningful effect sizes, systematically evaluate the relationship between changes in IPFD and relevant clinical endpoints, and further elucidate underlying mechanisms beyond weight loss alone to better inform interpretation and guide clinical application.

Strengths and limitations

It is important to recognize that agreement between individuals can be expressed in multiple ways. The Delphi method is widely regarded as the gold standard for consensus building, particularly in medical and health sciences, when applied with methodological rigour. Its key features include the synthesis of evidence shared with participants at the outset, multiple rounds of structured input, feedback between rounds (including summaries of group responses), iterative revision towards convergence and the anonymity of responses[186]. The work presented here constitutes an informed consensus on the topic developed using a true Delphi process, meeting all of these criteria and providing transparent documentation of changes in ratings across rounds (Supplementary Tables 11–16). Transparency was further enhanced by the independent management of the rating process and its summarization by the non-voting coordinator. Initial diversity of opinions is reflected empirically in Round 1 of this consensus-building process, in which 61% of statements met the pre-specified agreement threshold. Through controlled feedback and iterative refinement, consensus was ultimately achieved for all statements. By contrast, a single-round effort (such as a survey) captures a snapshot of opinions at a single point in time, without opportunities for revision and feedback-driven convergence over time. Although high levels of agreement can be observed, a single-round effort does not actively build consensus. Morevover, this limitation can be further compounded in the absence of structured anonymity, whereby variations in participant communication styles and respondent seniority can influence responses.

One of the major strengths of this consensus-building process was its intercontinental approach, with no single continent predominating. Core experts, with gender balance ensured, were drawn from all inhabited continents and included representatives not only from high-income countries but also from lower-middle-income and upper-middle-income nations, promoting diverse perspectives and fostering inclusivity in the development of guidance on IPFD[4]. Moreover, face-to-face engagements undertaken as part of this process took place across both the Northern and Southern Hemispheres. Another strength of this consensus-building process is its egalitarian model and open call for participation, irrespective of society affiliation. Although individual Working Group members currently hold affiliations with more than a dozen societies (often in leadership roles), such societal affiliations were not a prerequisite for participation. A further strength was the deep expertise within the panel. The conceptual framework and guidance presented in this document were developed by individuals with content-specific knowledge of IPFD, complemented by broader experience in classic pancreatic diseases. The medical expertise literature underscores that such subject-matter knowledge is a fundamental prerequisite for generating reliable and trustworthy guidance[187]. Given that IPFD expertise is not confined to gastroenterology[4], the panel was intentionally highly multidisciplinary in composition. Additionally, the consensus-building process was grounded in a rigorous and reproducible synthesis of the available evidence. At the outset, eight systematic reviews were conducted and published in peer-reviewed journals[3,57,123,176,188–191], providing a comprehensive foundation to inform deliberations and recommendations. While the present work was undergoing extensive and rigorous peer review, a separate effort was published in the *United European Gastroenterology Journal*[192]. This publication was geared towards a clinical audience and represents a single-round effort capturing responses to 22 questions related to fat within the pancreas, most of which were provided by respondents without active involvement in this field of research.

The consensus-building process was not without limitations. The 25 selected panellists did not represent all experts in the field. Although there is no universally accepted standard for panel size, the pre-specified number of 25 aligns with the average used in previous Delphi studies[6,193]. Another limitation was the consensus threshold: setting it at 67% might have underestimated the degree of expert disagreement on more nuanced statements[194]. However, this threshold was established a priori and, ultimately through iterative refinement, all statements reached strong agreement levels exceeding 90%, providing

reassurance that the guidance is based on well-supported evidence. In addition, formal society endorsement was not sought. Nevertheless, participants at conferences organized by several major gastroenterology and pancreatology societies contributed during dedicated sessions, facilitating broader engagement from the field. Fluency in English was a prerequisite for participation to ensure effective knowledge exchange. This requirement might have limited the involvement of non-English-speaking experts. To support broader global uptake, future efforts could include translation and cross-cultural adaptation of the current consensus recommendations into other languages[195]. Last, input from patient associations was not obtained at this stage; however, their contributions are expected to be incorporated in future updates as awareness of the burden of FPD increases among the general public[186,194]. It is also envisaged that subsequent iterations will include a broader range of stakeholders, including those not actively engaged in research within the scope of this consensus.

Conclusions

Knowledge of fat within the pancreas over the past one and a half centuries, once based on fragmented observations[1], has evolved into a more cohesive framework[69]. Beyond the simplistic notion of intrapancreatic adipocytes alone, lipid droplets within acinar cells of the human pancreas (first reported nearly half a century ago[17]), as well as in other non-adipose pancreatic cells[196], are now well documented in clinical studies and are increasingly recognized as key contributors to pancreatic allostasis[197,198]. The field has also advanced to the point where it is now clear that diffuse and focal fat within the pancreas arise from distinct processes, have different clinical implications and should not be conflated. Physiological when present in small amounts, diffuse fat becomes a health risk when excessive. Specifically, FPD has emerged as a key player and promising target in efforts aimed specifically at the prevention, interception or remission of diseases of the pancreas. Comprehensive guidance across several key domains was developed collaboratively by a global, multidisciplinary panel of subject-matter experts. The Melbourne consensus formally defined the field using a true Delphi process, providing unambiguous, state-of-the-art recommendations on FPD and laying the groundwork for a future with a markedly reduced burden of acute pancreatitis, chronic pancreatitis, PDAC and T2DM[199]. As knowledge continues to evolve, these recommendations will require updates. Nevertheless, they currently serve as the cornerstone for high-quality research and evidence-based clinical practice in the years to come.

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Author contributions

M.S.P. chaired the consensus-building process. M.S.P., H.Y., G.L. and A.H.A.-M. prepared the initial draft of the manuscript. All authors contributed to the consensus recommendation discussions, critically revised the manuscript and approved the final version.

Competing interests

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The Global Intrapancreatic FaT (GIFT) Alliance

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