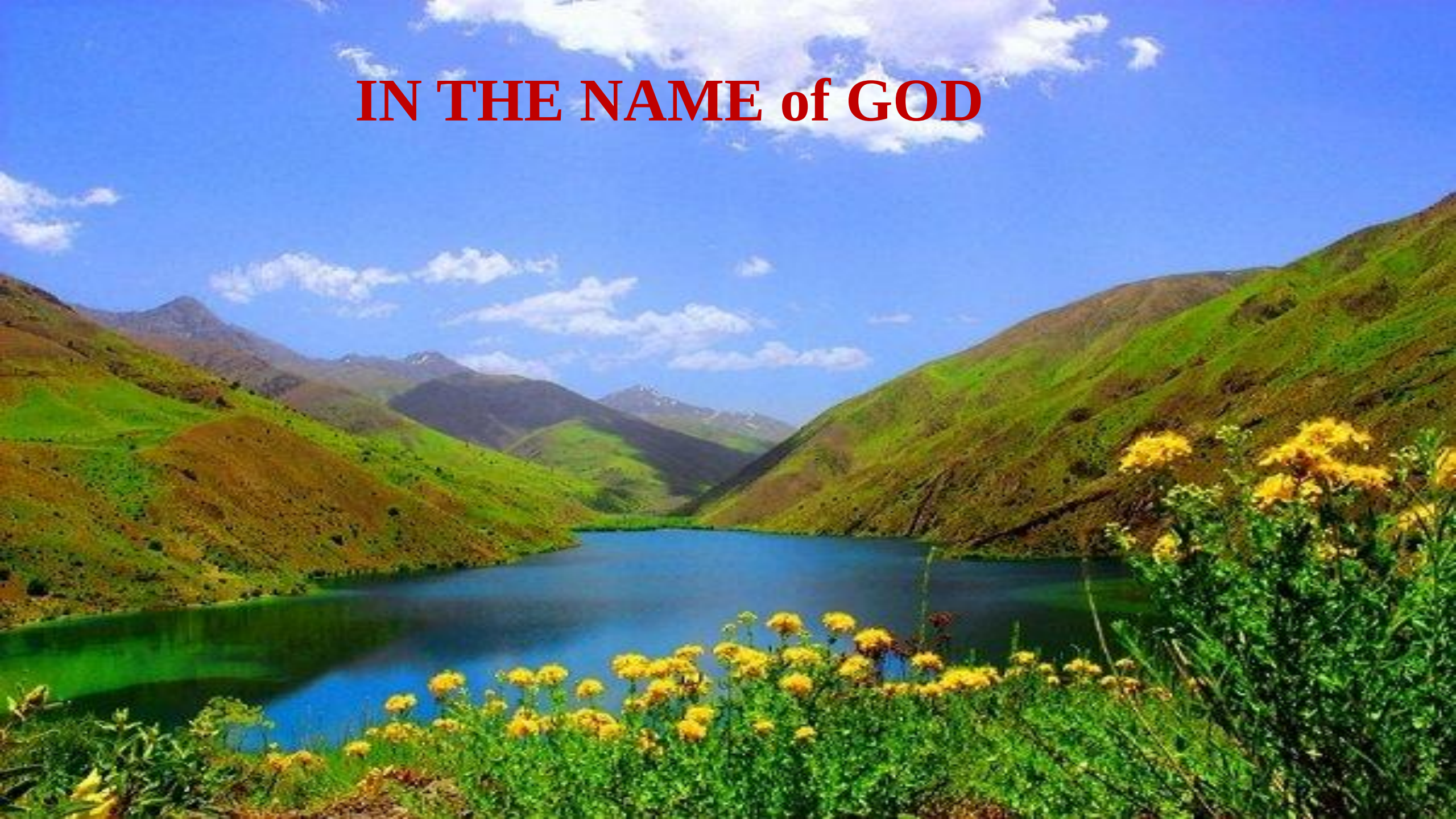
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Associations of Intrapancreatic Fat Deposition With Incident Diseases of the Exocrine and Endocrine Pancreas: A UK Biobank Prospective Cohort Study

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INTRODUCTION: **To investigate whether increased intrapancreatic fat deposition (IPFD) heightens the risk of diseases of the exocrine and endocrine pancreas.**

METHODS: **A prospective cohort study was conducted using data from the UK Biobank. IPFD was quantified using MRI and a deep learning–based framework called nnUNet. The prevalence of fatty change of the pancreas (FP) was determined using sex- and age-specific thresholds. Associations between IPFD and pancreatic diseases were assessed with multivariate Cox-proportional hazard model adjusted for age,**

INTRODUCTION

Intrapancreatic fat deposition (IPFD) is the diffuse presence of fat within the pancreas (1). In contrast to the liver, which stores fat exclusively in lipid droplets within liver cells, IPFD involves a variety of cells, including endocrine cells, acinar cells, adipocytes, and others (2,3). IPFD can occur through either lipid droplet accumulation inside cells or the substitution of functional cells with adipocytes.

Although a small amount of fat usually exists in the pancreas of healthy individuals, excessive IPFD leads to fatty change of the pancreas (FP) (4). The prevalence of FP varies greatly between published studies, ranging from 8.4% to 35.0% (5–9); 1 reason for this might be the retrospective analyses of imaging databases that collect data from large tertiary referral centers, which may not represent the general population and involve various noninvasive imaging techniques such

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INTRODUCTION

- Intrapancreatic fat deposition (**IPFD**) is the diffuse presence of fat within the pancreas. In contrast to the liver, which stores fat exclusively in lipid droplets within liver cells, IPFD involves a variety of cells, including endocrine cells, acinar cells, adipocytes, and others.
- IPFD can occur through either lipid droplet accumulation inside cells or the substitution of functional cells with adipocytes.

INTRODUCTION

- Although a small amount of fat usually exists in the pancreas of healthy individuals, excessive IPFD leads to **fatty change of the pancreas** (FP).
- **The prevalence of FP** varies greatly between published studies, ranging from **8.4%** to **35.0%**; 1 reason for this might be the ***retrospective analyses*** of imaging databases that collect data from large tertiary referral centers, which may ***not represent the general*** population and involve ***various*** noninvasive ***imaging*** techniques such as ultrasonography, endoscopic ultrasound, computed tomography, and magnetic resonance imaging (MRI).

INTRODUCTION

- FP, or excessive IPFD, may disrupt normal pancreatic function and elevate the risk of diabetes mellitus (**DM**), acute pancreatitis (**AP**), chronic pancreatitis (**CP**), and pancreatic cancer (**PC**)

- The advancement of ***chemical shift MRI technology*** has enabled quantitative evaluation of fat content in tissues, thereby mitigating the impact of incomplete diagnostic criteria for FP . The large-scale, prospective cohort of the UK Biobank and standardized chemical shift MRI examinations provide an opportunity for further exploration into the above-mentioned issues.

- In this study, we initially conducted a **prospective cohort study** involving a population from the **UK Biobank** to investigate the prevalence of FP, then explored the association between IPFD and the occurrence of pancreatic diseases

METHODS

Study design and participants

Study design and participants

- A prospective cohort study
- **Outcomes:**
- diseases of the exocrine and endocrine pancreas (including acute pancreatitis(**AP**), pancreatic cancer (**PC**), **DM**, and other **pancreatic diseases**)
- **Exposure** was determined by IPFD level.
- **Covariates** included variables such as *age*, *sex*, *ethnicity*, *body mass index* (BMI), *waist circumference*, *hip circumference*, ***Townsend deprivation index***, *smoking* status, *alcohol* consumption, and *disease history*.

Exclusion criteria

- (i) without follow-up data
- (ii) missing baseline data
- (iii) history of pancreatic disease
- (iv) time from enrollment ,1 year
- (v) IPFD values exceeding 3 times the interquartile range

MRI examination

- In our study, we used the MRI examination time point (the time of IPFD measurement) as the baseline. However, for some participants, certain variables such as Townsend deprivation index, smoking, and drinking status were missing during the MRI examination. In such cases, we used data recorded before the MRI examination (information collected at initial registration of the participant into the UK Biobank) to fill in these missing values. Subsequently, participants who still had missing data were excluded from the analysis. After exclusion, **42,599 eligible** participants were included for further analysis (Figure 1).

Townsend index

- The **Townsend index** is a measure of material deprivation within a population. It was first described by sociologist Peter Townsend in 1988.
- The measure incorporates four variables:

- Unemployment (as a percentage of those aged 16 and over who are economically active);
- Non-car ownership (as a percentage of all households);
- Non-home ownership (as a percentage of all households); and
- Household overcrowding.

The UK Biobank is a large database of more than 500,000 participants recruited from the general population

July2014 to January 2023

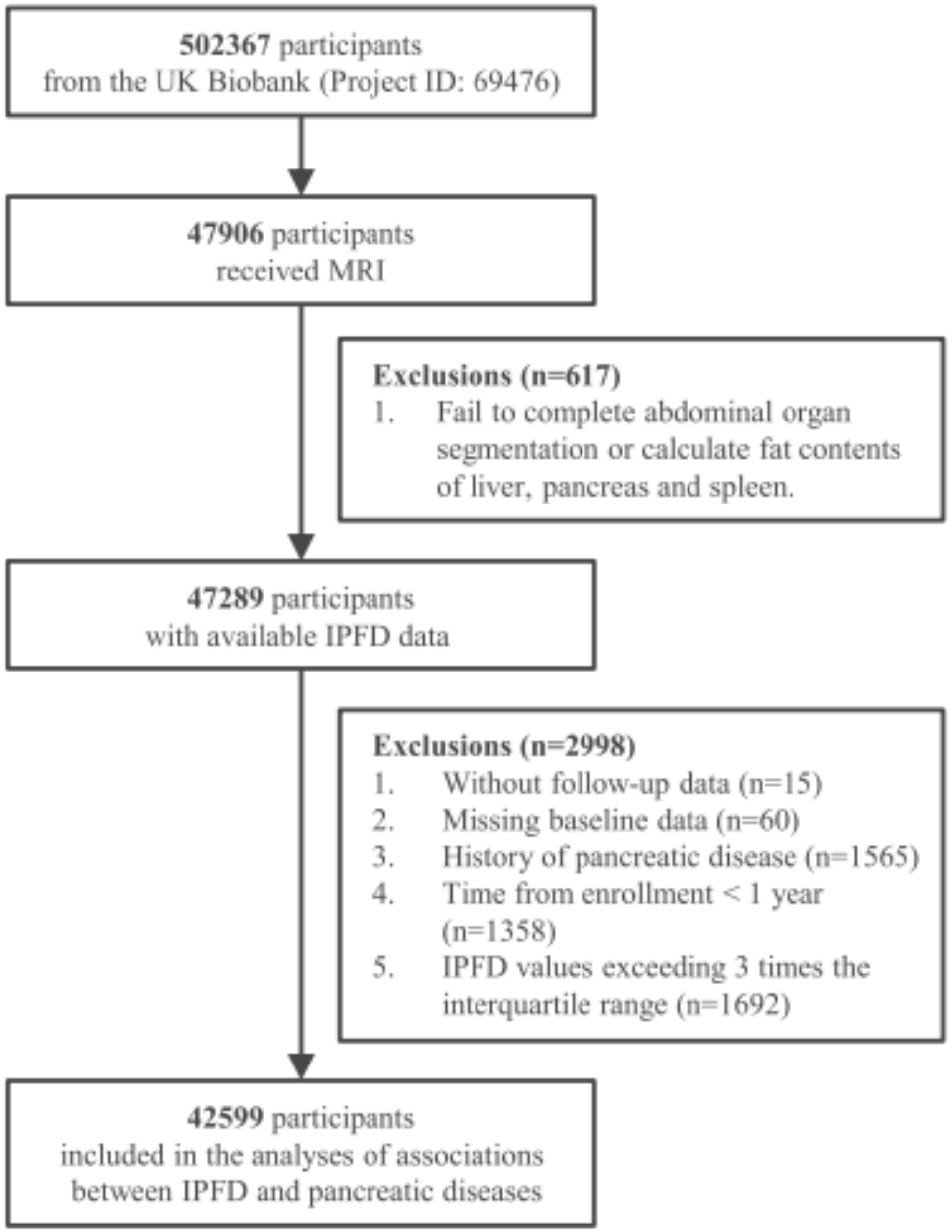

Figure 1. Flowchart of the study. IPFD, intrapancreatic fat deposition; MRI, magnetic resonance imaging.

Measurement of intrapancreatic fat and fat content of liver and spleen

- 2 steps.
- organ segmentation
- Initially, we performed organ segmentation using an organ autosegmentation model based on nnUNet
- After organ segmentation, the fat content of the pancreas and liver was calculated using the following formula: fat/(fat + water) X 100%.

Table 1. Baseline characteristics of participants grouped by quintiles of IPFD

	All (N = 42,599)	Quintiles of IPFD					*P* value
		Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	
Follow-up time (yr)	4.61 (3.77 to 5.98)	4.6 (3.77 to 5.84)	4.66 (3.81 to 6.11)	4.68 (3.81 to 6.06)	4.63 (3.77 to 6)	4.52 (3.67 to 5.84)	<0.001
Age	65 (58 to 70)	61 (56 to 68)	63 (57 to 69)	65 (58 to 70)	66 (60 to 71)	67 (61 to 72)	<0.001
Sex (male)	19,855 (46.61)	2,232 (26.2)	3,265 (38.32)	4,074 (47.82)	4,811 (56.47)	5,473 (64.24)	<0.001
Ethnicity (White)	39,285 (92.22)	7,781 (91.34)	7,793 (91.47)	7,823 (91.83)	7,917 (92.92)	7,970 (93.54)	<0.001
BMI	25.73 (23.41 to 28.54)	23.17 (21.54 to 25.15)	24.62 (22.79 to 26.8)	25.83 (23.81 to 28.21)	27.11 (24.89 to 29.75)	28.39 (25.99 to 31.28)	<0.001
Waist circumference	87 (79 to 96)	77.5 (72 to 84)	83 (76 to 90)	88 (80 to 94)	92 (85 to 99)	96 (89 to 103)	<0.001
Hip circumference	100 (95 to 105)	96 (92 to 100)	98 (94 to 103)	100 (95 to 105)	101 (97 to 107)	103 (99 to 109)	<0.001
Central obesity	29,240 (68.64)	3,136 (36.81)	4,943 (58.02)	6,179 (72.53)	7,138 (83.78)	7,844 (92.07)	<0.001
TDI	−2.61 (−3.88 to −0.5)	−2.57 (−3.9 to −0.48)	−2.61 (−3.92 to −0.46)	−2.59 (−3.85 to −0.45)	−2.63 (−3.9 to −0.52)	−2.63 (−3.83 to −0.59)	0.540
Tobacco smoking							<0.001
Never	26,694 (62.66)	5,880 (69.02)	5,588 (65.59)	5,302 (62.24)	5,068 (59.48)	4,855 (56.98)	
Previous	14,442 (33.9)	2,420 (28.41)	2,645 (31.04)	2,915 (34.22)	3,089 (36.26)	3,373 (39.59)	
Current	1,463 (3.43)	219 (2.57)	287 (3.37)	302 (3.55)	363 (4.26)	292 (3.43)	
Heavy alcohol consumption							0.286
Never	1,336 (3.14)	284 (3.33)	267 (3.13)	263 (3.09)	249 (2.92)	273 (3.2)	
Previous	1,378 (3.23)	308 (3.62)	259 (3.04)	276 (3.24)	282 (3.31)	253 (2.97)	
Current	39,885 (93.63)	7,927 (93.05)	7,994 (93.83)	7,980 (93.67)	7,989 (93.77)	7,994 (93.83)	

Table 1. Baseline characteristics of participants grouped by quintiles of IPFD

	All (N = 42,599)	Quintiles of IPFD					*P* value
		Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	
Hypertension	5,609 (13.17)	541 (6.35)	776 (9.11)	1,116 (13.1)	1,397 (16.4)	1,779 (20.88)	<0.001
Dyslipidemia	2,604 (6.11)	221 (2.59)	334 (3.92)	506 (5.94)	662 (7.77)	881 (10.34)	<0.001
History of gallstones	1,537 (3.61)	187 (2.2)	229 (2.69)	302 (3.55)	364 (4.27)	455 (5.34)	<0.001
Lipid-lowering drugs	3,239 (7.6)	565 (6.63)	605 (7.1)	619 (7.27)	707 (8.3)	743 (8.72)	<0.001
Glucose-lowering drugs	589 (1.38)	33 (0.39)	61 (0.72)	109 (1.28)	157 (1.84)	229 (2.69)	<0.001
IPFD (%)	7.72 (6.22 to 10.5)	5.28 (4.8 to 5.63)	6.5 (6.22 to 6.78)	7.72 (7.39 to 8.11)	9.7 (9.07 to 10.5)	14.97 (12.91 to 18.3)	<0.001
Liver fat content (%)	4.79 (4.32 to 5.96)	4.3 (4.01 to 4.68)	4.55 (4.21 to 5.05)	4.81 (4.38 to 5.7)	5.25 (4.62 to 6.86)	5.95 (4.85 to 8.67)	<0.001
Spleen fat content (%)	5.45 (4.85 to 6.5)	4.9 (4.52 to 5.43)	5.21 (4.75 to 5.85)	5.5 (4.93 to 6.47)	5.89 (5.14 to 7.18)	6.22 (5.32 to 7.99)	<0.001
Pancreatic disease	782 (1.84)	56 (0.66)	73 (0.86)	140 (1.64)	173 (2.03)	340 (3.99)	<0.001
Exocrine disease	143 (0.34)	17 (0.2)	17 (0.2)	26 (0.31)	25 (0.29)	58 (0.68)	<0.001
Acute pancreatitis	55 (0.13)	7 (0.08)	7 (0.08)	8 (0.09)	6 (0.07)	27 (0.32)	<0.001
Pancreatic cancer	52 (0.12)	4 (0.05)	6 (0.07)	11 (0.13)	7 (0.08)	24 (0.28)	<0.001
Other	65 (0.15)	7 (0.08)	9 (0.11)	12 (0.14)	14 (0.16)	23 (0.27)	0.018
Endocrine disease	659 (1.55)	42 (0.49)	56 (0.66)	118 (1.39)	151 (1.77)	292 (3.43)	<0.001
Diabetes mellitus	636 (1.49)	36 (0.42)	51 (0.6)	113 (1.33)	149 (1.75)	287 (3.37)	<0.001
Other	38 (0.09)	9 (0.11)	5 (0.06)	9 (0.11)	4 (0.05)	11 (0.13)	0.327

Continuous values were presented as median (interquartile range), and categorical variables were presented as counts (percentages).
BMI, body mass index; IPFD, intrapancreatic fat deposition; TDI, Townsend deprivation index.

Diagnosis and definition

- All diseases were **diagnosed** based on the **International Classification of Diseases**, Ninth and Tenth Revisions with specific coding
- According to the division of age limited by **World Health Organization**, individuals were categorized as **middle-aged** (younger than 65 years) and **elderly** (aged 65 years and older).
- **Central obesity** was defined as meeting one of the following criteria: for ***males***, ***waist circumference ≥ 90*** cm or **waist-to-hip ratio ≥ 0.9**, or **waist-to-height ratio ≥ 0.5**, and
- for **females**, waist circumference ≥ 80 cm or waist-to-hip ratio ≥ 0.85, or waist-to-height ratio ≥ 0.5.

Diagnosis and definition

- The **determination of FP** was derived from the sex- and age-specific **95th percentile upper limit of IPFD in the general population** .
- After excluding participants with a BMI of 25 or higher, central obesity, current or past histories of smoking and alcohol intake, hypertension, and lipid metabolism disorders, 8.01% for females aged 45–54 years, 11.03% for females aged 55–64 years, 11.70% for females aged 65 years and older, 11.96% for males aged 45–54 years, 15.77% for males aged 55–64 years, and 12.43% for males aged 65 years and older were used as the **standard upper limit values for IPFD**.

Statistical analysis

- Continuous variables that conform to a normal distribution were presented as mean 6 SD. Intergroup comparisons of normally distributed data involved using t tests for 2 groups or 1-way ANOVA for multiple groups. Non-normally distributed data were represented by the median (quartile range) (M (P25, P75)), and the Mann–Whitney U test or Kruskal–Wallis H test was used for intergroup comparison. Categorical variables were analyzed using the x2 test, with the Fisher exact test used when deemed necessary. Standard differences in baseline data were assessed between individuals who underwent MRI examinations and those who did not

Statistical analysis

- All analyses were performed using R software version 4.2.2 and GraphPad Prism 8.0.2. A 2-sided P value of ≤ 0.05 was designated statistically significant

RESULTS

Characteristics of the study population

- After the initial exclusion step, 42,599 eligible participants were included for further analysis (Figure 1). Of these**, 7,607** (**17.86%**) participants had **FP** according to the sex- and age-specific 95th percentile upper limit of IPFD in healthy participants.

Figure 2 presents comparisons of IPFD and the prevalence of FP between sexes and ages. A trend of increasing FP prevalence was observed with advanced age in both males and females

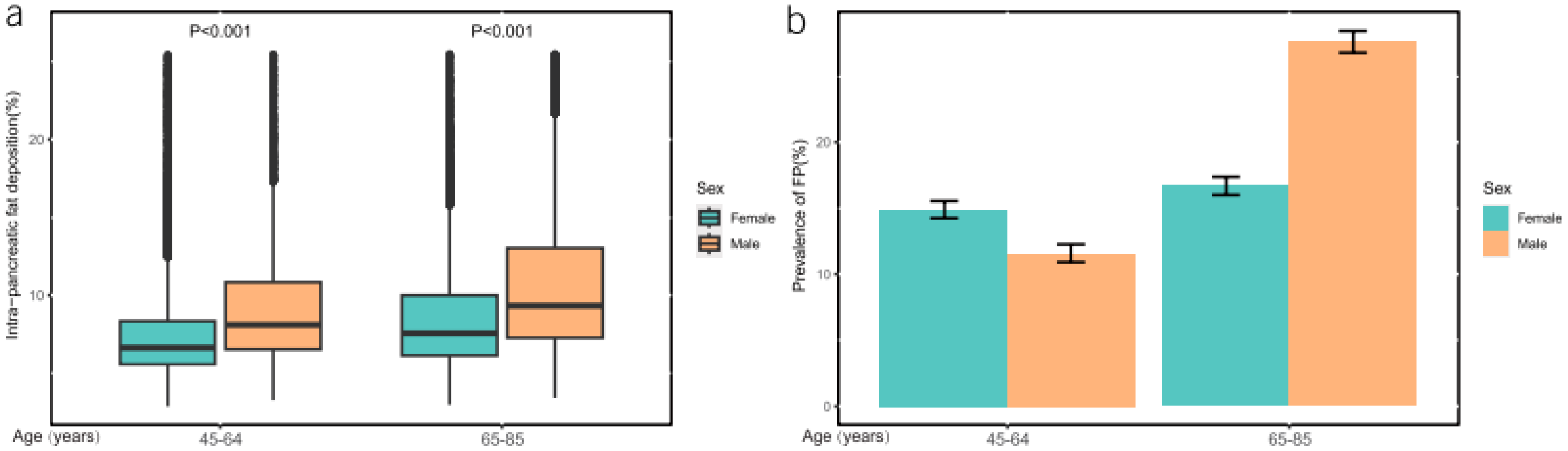

Figure 2. Distribution of IPFD (**a**) and the prevalence of FP (**b**) by sex and age. The boxes represented medians with interquartile ranges (**a**) or proportions (**b**). The whiskers represented 1.5 × interquartile ranges (**a**) or confidence interval (**b**). FP, fatty change of the pancreas; IPFD, intrapancreatic fat deposition.

Table 2. Baseline characteristics of participants grouped by the presence or absence of FP

	All (N = 42,599)	FP		*P* value
		No (n = 34,992)	Yes (n = 7,607)	
Follow-up time (yr)	4.61 (3.77 to 5.98)	4.64 (3.79 to 5.99)	4.53 (3.68 to 5.91)	<0.001
Age	65 (58 to 70)	64 (58 to 70)	67 (60 to 72)	<0.001
Sex (male)	19,855 (46.61)	15,828 (45.23)	4,027 (52.94)	<0.001
Ethnicity (White)	39,285 (92.22)	32,170 (91.94)	7,115 (93.53)	<0.001
BMI	25.73 (23.41 to 28.54)	25.2 (23.03 to 27.76)	28.53 (26.05 to 31.57)	<0.001
Waist circumference	87 (79 to 96)	86 (77 to 93)	96 (88 to 103)	<0.001
Hip circumference	100 (95 to 105)	99 (94 to 104)	104 (99 to 110)	<0.001
Central obesity	29,240 (68.64)	22,293 (63.71)	6,947 (91.32)	<0.001
TDI	−2.61 (−3.88 to −0.5)	−2.62 (−3.9 to −0.49)	−2.59 (−3.8 to −0.53)	0.053
Tobacco smoking				<0.001
Never	26,694 (62.66)	22,302 (63.73)	4,392 (57.74)	
Previous	14,442 (33.9)	11,486 (32.82)	2,956 (38.86)	
Current	1,463 (3.43)	1,204 (3.44)	259 (3.4)	
Heavy alcohol consumption				0.051
Never	1,336 (3.14)	1,069 (3.05)	267 (3.51)	
Previous	1,378 (3.23)	1,151 (3.29)	227 (2.98)	
Current	39,885 (93.63)	32,772 (93.66)	7,113 (93.51)	

Table 2. Baseline characteristics of participants grouped by the presence or absence of FP

	All (N = 42,599)	FP		*P* value
		No (n = 34,992)	Yes (n = 7,607)	
Hypertension	5,609 (13.17)	4,058 (11.6)	1,551 (20.39)	<0.001
Dyslipidemia	2,604 (6.11)	1,872 (5.35)	732 (9.62)	<0.001
History of gallstones	1,537 (3.61)	1,092 (3.12)	445 (5.85)	<0.001
Lipid-lowering drugs	3,239 (7.6)	2,570 (7.34)	669 (8.79)	<0.001
Glucose-lowering drugs	589 (1.38)	388 (1.11)	201 (2.64)	<0.001
IPFD (%)	7.72 (6.22 to 10.5)	7.14 (5.97 to 8.75)	15.48 (13.11 to 18.78)	<0.001
Liver fat content (%)	4.79 (4.32 to 5.96)	4.68 (4.26 to 5.51)	5.86 (4.81 to 8.6)	<0.001
Spleen fat content (%)	5.45 (4.85 to 6.5)	5.34 (4.79 to 6.24)	6.2 (5.3 to 7.95)	<0.001
Pancreatic disease	782 (1.84)	499 (1.43)	283 (3.72)	<0.001
Exocrine disease	143 (0.34)	92 (0.26)	51 (0.67)	<0.001
Acute pancreatitis	55 (0.13)	30 (0.09)	25 (0.33)	<0.001
Pancreatic cancer	52 (0.12)	33 (0.09)	19 (0.25)	<0.001
Other	65 (0.15)	47 (0.13)	18 (0.24)	0.056
Endocrine disease	659 (1.55)	417 (1.19)	242 (3.18)	<0.001
Diabetes mellitus	636 (1.49)	399 (1.14)	237 (3.12)	<0.001
Other	38 (0.09)	29 (0.08)	9 (0.12)	0.468

Continuous values were presented as median (interquartile range), and categorical variables were presented as counts (percentages).
BMI, body mass index; FP, fatty change of the pancreas; IPFD, intrapancreatic fat deposition; TDI, Townsend deprivation index.

Associations of IPFD with pancreatic diseases

- Participants with higher IPFD levels had an elevated cumulative risk of developing pancreatic diseases (Table 3 and Figure 3).

Table 3. **Incidence density of diseases of the pancreas according to fat in the pancreas**

	Acute pancreatitis		Pancreatic cancer		Diabetes mellitus		All pancreatic diseases	
	Event	Incidence density (per 1,000 person-years)	Event	Incidence density (per 1,000 person-years)	Event	Incidence density (per 1,000 person-years)	Event	Incidence density (per 1,000 person-years)
All (n = 42,599)	55	0.263 (0.193–0.332)	52	0.248 (0.181–0.316)	636	3.057 (2.820–3.294)	782	3.764 (3.500–4.027)
Quintiles of IPFD								
Q1 (lowest) (n = 8,520)	7	0.168 (0.043–0.292)	4	0.096 (0.002–0.190)	36	0.864 (0.582–1.146)	56	1.345 (0.993–1.697)
Q2	7	0.164 (0.043–0.286)	6	0.141 (0.028–0.254)	51	1.200 (0.871–1.530)	73	1.720 (1.326–2.114)
Q3	8	0.189 (0.058–0.320)	11	0.260 (0.106–0.414)	113	2.689 (2.194–3.184)	140	3.334 (2.782–3.885)
Q4	6	0.143 (0.029–0.257)	7	0.167 (0.043–0.290)	149	3.581 (3.007–4.155)	173	4.163 (3.544–4.782)
Q5 (highest)	27	0.661 (0.412–0.911)	24	0.587 (0.352–0.822)	287	7.132 (6.310–7.954)	340	8.469 (7.573–9.365)
FP								
No (n = 34,992)	30	0.174 (0.112–0.236)	33	0.191 (0.126–0.256)	399	2.321 (2.094–2.549)	499	2.906 (2.652–3.161)
Yes (n = 7,607)	25	0.682 (0.415–0.949)	19	0.518 (0.285–0.751)	237	6.554 (5.722–7.386)	283	7.844 (6.934–8.754)

FP, fatty change of the pancreas; IPFD, intrapancreatic fat deposition.

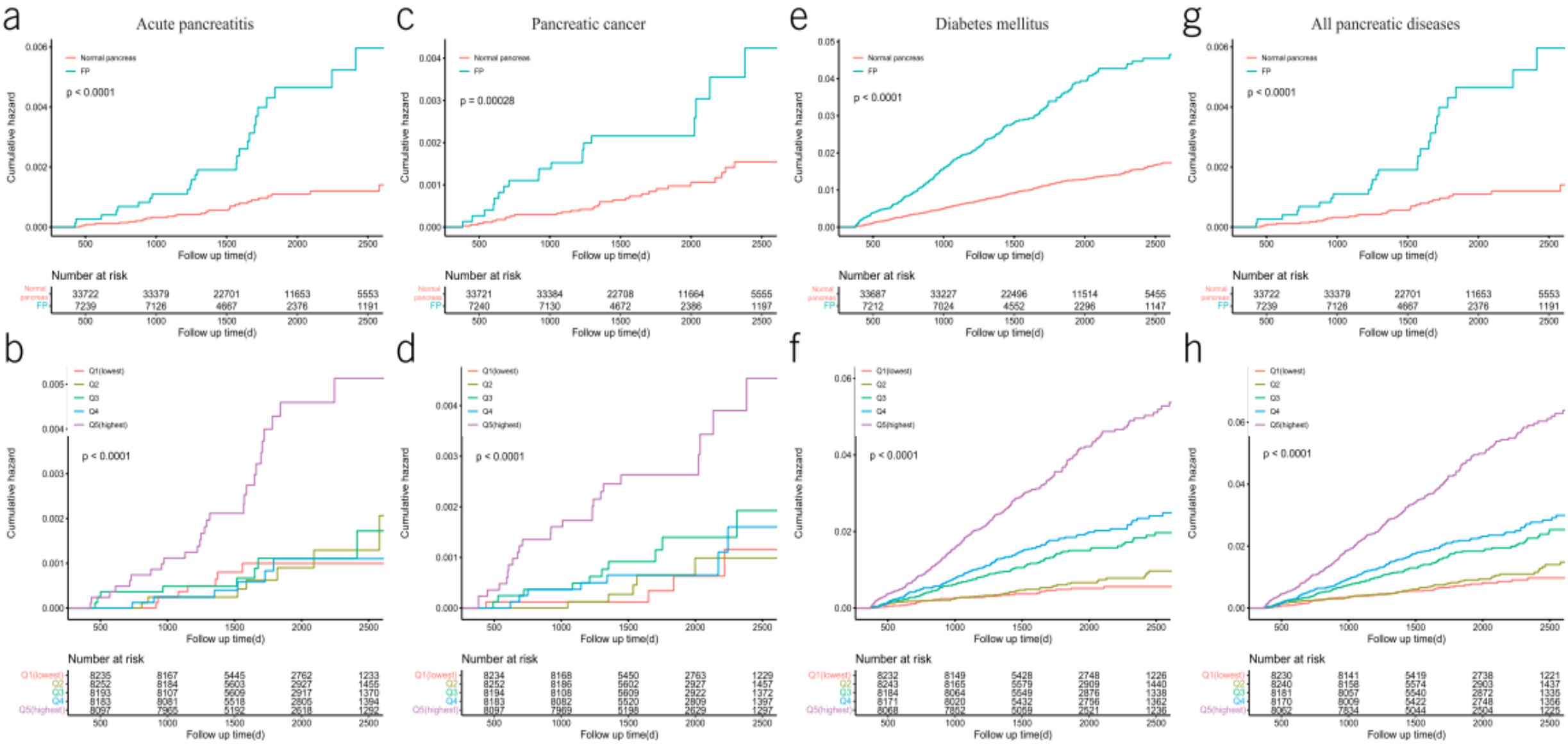

Figure 3. Kaplan-Meier estimates of acute pancreatitis (**a**, **b**), pancreatic cancer (**c**, **d**), diabetes mellitus (**e**, **f**), and all pancreatic diseases (**g**, **h**). FP, fatty change of the pancreas.

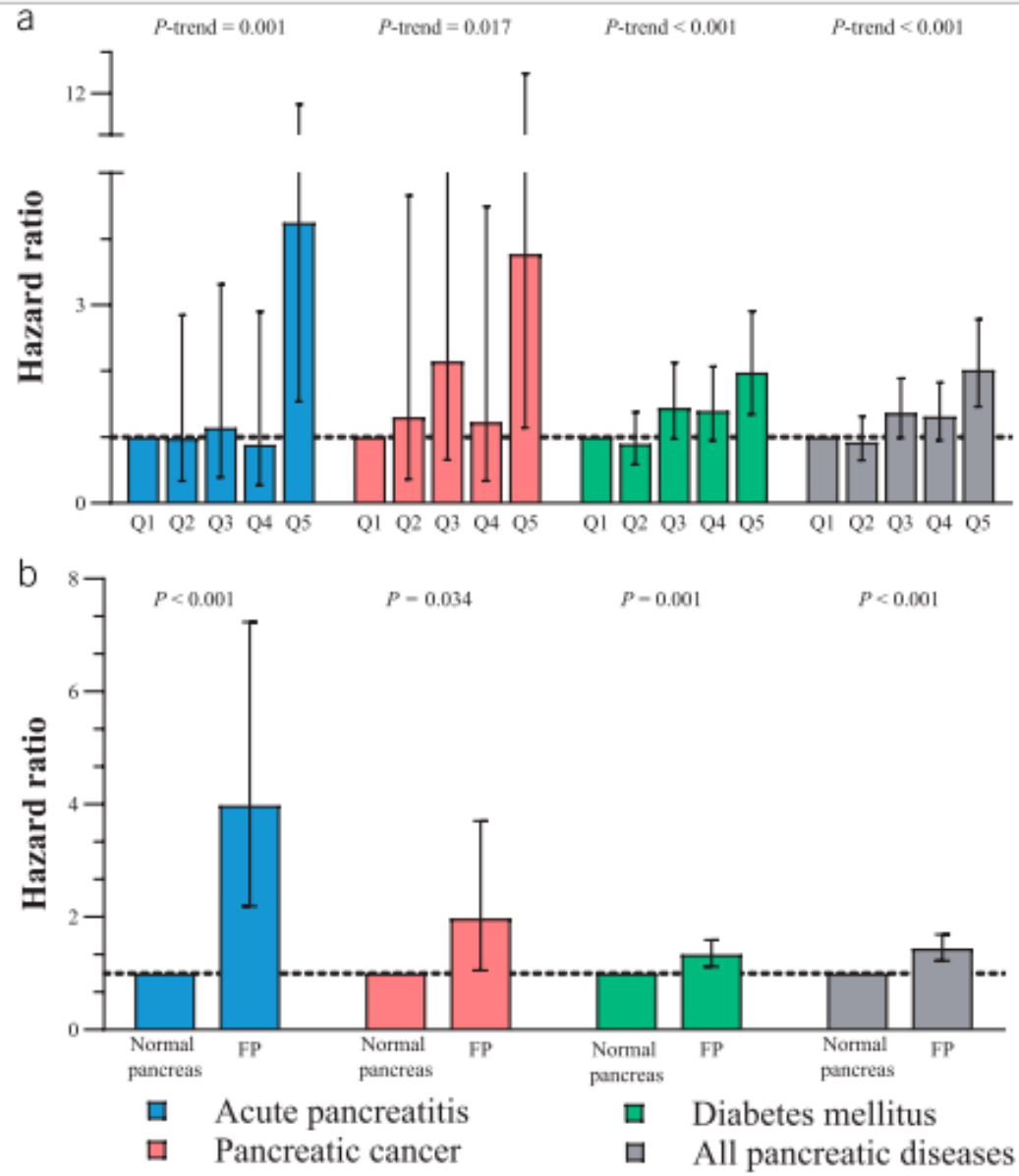

Figure 4. Cox regression model of the association between IPFD and all pancreatic diseases, DM, AP, and PC. (**a**) Participants were grouped by IPFD quintiles. Q1–Q5 represented the quintiles of IPFD, and individuals in the lowest quintile of IPFD (Q1) were used as the reference group. (**b**) Participants were grouped by FP diagnosis. Data presented as hazard ratio (95% CI), adjusted with model 2 for age, sex, ethnicity, BMI, central obesity, smoking and drinking status, hypertension, dyslipidemia, liver fat content, and spleen fat content. AP, acute pancreatitis; BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; FP, fatty change of the pancreas; IPFD, intrapancreatic fat deposition; PC, pancreatic cancer.

Subgroup and sensitivity analyses

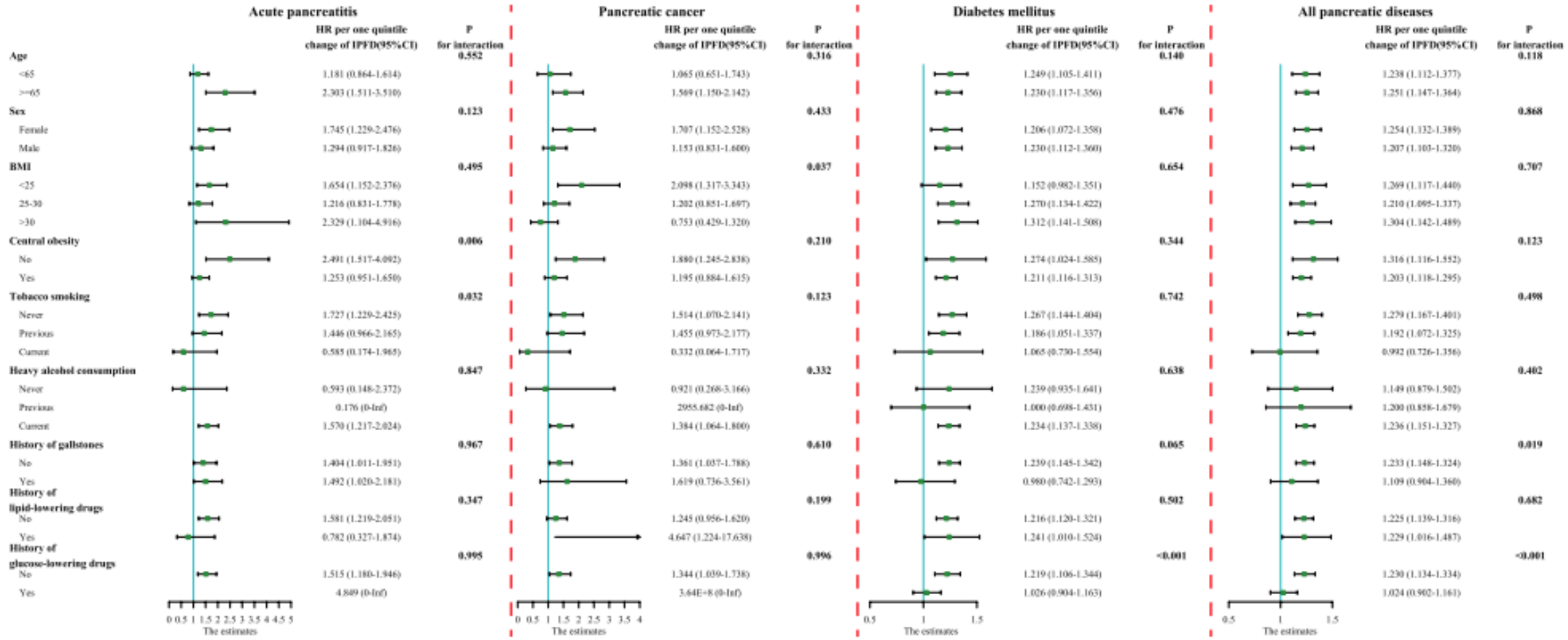

Figure 5. Subgroup analysis for the association between IPFD and AP, PC, DM, and all pancreatic diseases. Data presented as hazard ratio (95% CI), adjusted with model 2 for age, sex, ethnicity, BMI, central obesity, smoking and drinking status, hypertension, dyslipidemia, liver fat content, and spleen fat content. AP, acute pancreatitis; BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; FP, fatty change of the pancreas; PC, pancreatic cancer.

Subgroup and sensitivity analyses

- **Subgroup analyses** were conducted according to age, sex, BMI, central obesity, smoking and drinking status, history of gallstones, and the use of lipid-lowering or glucose-lowering drugs (Figure 5). Compared with participants with **central obesity**, IPFD had a higher HR for AP in participants without central obesity (P for interaction 5 **0.006**). There was no interaction between a history of gallstones and IPFD in relation to any specific pancreatic disease; however, it had a significant interaction with all pancreatic diseases. In the **sensitivity analysis,** the results remained consistent for **AP** and **DM** but exhibited instability for PC

DISCUSSION

- This is currently the largest prospective, population-based study on clinical relationships of increased IPFD.
- **The prevalence** of **FP** was **17.86%** in a population of 42,599 participants from the UK Biobank, a database collection from the general population. Fat in the pancreas was significantly associated with the development of new-onset diseases of the exocrine and endocrine pancreas.

- In addition, we used a deep learning–based method of abdominal organ segmentation (nnUNet) to automatically calculate the average IPFD for the entire pancreas.
- However, this region of interest–based approach has its limitations because it may introduce **selection bias** and may not fully reflect overall changes in the pancreas. In addition, this method relies heavily on **manual operations**, making it challenging to apply in large-scale studies. **By contrast**, the use of **nnUNet**, a deep learning–based tool, offers several advantages for measuring IPFD. **First**, it allows for **automated segmentation** of the pancreas, minimizing the potential bias introduced by **manual delineation**. **Second**, nnUNet has demonstrated **high accuracy** in segmentation tasks and has been widely adopted in various research fields

- Considering the **distinct sex differences in IPFD**, we used **sex** and **age-specific upper limit of normal**, resulting in an FP prevalence of 17.86%. To date, only a few studies have reported the distribution of IPFD and the prevalence of FP in the general population.

- The most reliable data were from MRI examinations of 685 **Hong Kong** adults , using the 95th percentile of IPFD in healthy individuals as the upper limit of normal, with an FP prevalence of 16.1%, similar to our results. In the same age group, males have higher levels of IPFD. When using sex- and age-specific thresholds as diagnostic criteria, **both sexes show an increasing trend with age**.

- In another **meta-analysis** covering 11 cohorts (including 12,675 individuals), the prevalence of **FP** in populations with various **metabolic disorders** can reach **33%**. With the increasing prevalence of metabolic disorders such as obesity and dyslipidemia, the **incidence** rate **of FP** may also **gradually increase** .

- Our study was the first prospective longitudinal cohort to investigate the association between increased IPFD and risk of AP in the general population.

- This study also found a consistent association between elevated IPFD and an **increased risk** of **DM**, consistent with previous studies

limitations in this study

- First, the UK Biobank database, in itself, has certain limitations, including a **limited response rate to recruitment** invitations (approximately 5%), which may introduce potential self-selection bias among the study participants. It is important to acknowledge that most participants who were enrolled were predominantly **white** and **older than 45 years**. Further studies on clinical relationships of increased IPFD with pancreatic diseases should be conducted in populations of different ages and ethnicities to gain a more comprehensive understanding of its distribution in the population.

limitations in this study

- In addition, ICD codes were used for diagnosis; however, they were primarily designed for billing and administrative purposes and may be subject to miscoding because of human error. Second, the median follow-up time in this study was only 4.61 years (interquartile range 3.77–5.98 years), which may not be sufficient to fully demonstrate the impact of IPFD. Thirdly, the IPFD data in this study were based on a single time point. One study showed that short-term training can effectively reduce ectopic fat in the pancreas and exercise training may therefore reduce the risk of type 2 diabetes .

- Fortunately, the UK Biobank is a long-term follow-up population

- FP is a common pancreatic disorder. Fat in the pancreas is an independent risk factor for diseases of both the exocrine pancreas and endocrine pancreas.

WHAT IS KNOWN

- ✓ Increased intrapancreatic fat deposition (IPFD) is common in general population.
- ✓ There is a paucity of longitudinal cohort studies investigating the relationship between fatty change of the pancreas (FP) and acute pancreatitis (AP), pancreatic cancer (PC), and diabetes mellitus (DM).

WHAT IS NEW HERE

- ✓ Prevalence of FP in the large population-based cohort was 17.86%.
- ✓ Increasing IPFD by 1 quintile raised the risk of AP by 51.3%, PC by 36.5%, and DM by 22.1%.
- ✓ FP independently increased the risks of AP by 298.2%, PC by 97.6%, and DM by 33.7%.