

SUPPLEMENTARY DATA

Medication, disease and procedure codes used in this study

Medications: Anatomical Therapeutic Chemical classification system (ATC) codes:

Incretins:

DPP4 inhibitors:

Sitagliptin: A10BH01, A10BD07

Vildagliptin: A10BH02, A10BD08

Saxagliptin: A10BH03, A10BD10

Alogliptin: A10BH04, A10BD09

Linagliptin: A10BH05, A10BD11

GLP-1 receptor agonists:

Exenatide: A10BX04

Liraglutide: A10BX07

Other antihyperglycemic drugs:

Metformin: A10BA

Sulfonylureas: A10BB

Thiazolidinediones: A10BG

Insulin: A10A

Alfa-glucosidase inhibitors: A10BF

Combination products: A10BD other than A10BD07- A10BD11

Other oral antihyperglycemic drugs: A10BX other than A10BX04 or A10BX07

Other medications:

Nonsteroidal anti-inflammatory drugs (NSAIDs): M01A

Antiepileptics: N03

Azathioprine: L04AX01, L01BB02

Oral glucocorticoids: H02AB06, H02AB07, A07EA01, A07EA02, A07EA06

Lipid-lowering drugs including statins: C10, B04AB

Diseases and procedures: International Classification of Diseases, 8th revision (ICD-8) and 10th revision (ICD-10) codes, Danish National Board of Health surgical codes, and Nordic classification of surgical procedures codes:

Gallstone disease: ICD-8 codes 560.30, 574; ICD-10 codes K56.3, K80

Surgical procedures performed on the biliary tract (except procedures ≤ 10 days before the pancreatitis diagnosis to avoid reverse causality): surgical codes KJK, KTJK, 47320-48299, 92301 (gall bladder); KJL, KJTL, 48320-48895, 91920, 92305 (pancreas); KUJK, 91050-91059 (endoscopy of the biliary tract)

Obesity: ICD-8 code 277; ICD-10 codes E65-E66

Alcoholism-related diseases: ICD-8 codes 291, 303, 571.0, 979, 980; ICD-10 codes E24.4, F10.0-F10.9, G31.2, G62.1, G72.1, I42.6, K29.2, K70, T51, Z72.1, R78.0, K86.0, T500A, Z71.4; ATC code N07B B01 (disulfiram)

Any cancer (except first-time diagnoses ≤ 90 days before the pancreatitis diagnosis to avoid misdiagnosis bias): ICD-8 codes 140-207, 275.59; ICD-10 codes C00-C86, C88, C90-C96

Inflammatory bowel disease: ICD-8 codes 563.01, 569.04; ICD-10 codes K50, K51.0-K51.3

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Conditions included in the modified Charlson Comorbidity Index (CCI) score (diabetes, liver disease, and cancer categories controlled for separately):³⁰

Myocardial infarction: ICD-8 code 410; ICD-10 codes I21-I23

Congestive heart failure: ICD-8 codes 427.09, 427.10, 427.11, 427.19, 428.99, 782.49; ICD-10 codes I50, I11.0, I13.0, I13.2

Peripheral vascular disease: ICD-8 codes 440-445; ICD-10 codes I70-I74, I77

Cerebrovascular disease: ICD-8 codes 430-438; ICD-10 codes I60-I69, G45, G46

Dementia: ICD-8 codes 290.09-290.19, 293.09; ICD-10 codes F00-F03, F05.1, G30

Chronic pulmonary disease: ICD-8 codes 490-493, 515-518; ICD-10 codes J40-J47, J60-J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3

Connective tissue disease: ICD-8 codes 712, 716, 734, 446, 135.99; ICD-10 codes M05, M06, M08, M09, M30, M31, M32, M33, M34, M35, M36, D86

Peptic ulcer disease: ICD-8 codes 530.91, 530.98, 531-534; ICD-10 codes K22.1, K25-K28

Hemiplegy: ICD-8 code 344; ICD-10 codes G81, G82

Moderate-severe renal disease: ICD-8 codes 403, 404, 580-583, 584, 590.09, 593.19, 753.10-753.19, 792; ICD-10 codes I12, I13, N00-N05, N07, N11, N14, N17-N19, Q61

AIDS: ICD-10= B21-B24; ICD-8= 079.83

Diabetic complications (use of ICD-10 codes as available since 1994, and surgical codes):

Neurological complications: ICD-10 codes E104, E114, E144, G590, G632; Eye complications: ICD-10 codes E103, E113, E143, H340-H342, H280, H334, H450, H360, H540, H541, H544, H25, H268, H269, H430, H431, H438C, H439, H334A, H330, H335, KCKC10, KCKC15, KCKD65;

Renal complications: E102, E112, E142, I120, N083, N06, N17-N19, R809, BJFD2

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Supplementary Table 1. Descriptive characteristics and potential risk factors among pancreatitis case patients and population control subjects with incretin-based therapy

	Acute pancreatitis cases with ever incretin-based therapy	Acute pancreatitis cases with ever GLP-1 receptor agonist use	Acute pancreatitis cases with ever DPP-4 inhibitor use	Population controls with any incretin-based therapy
Total	89 (100)	30 (100)	68 (100)	684 (100)
Gender:				
Male	57 (64.0)	17 (56.7)	44 (64.7)	454 (66.4)
Female	32 (36.0)	13 (43.3)	24 (35.3)	230 (33.6)
Age (years):				
18-39	4 (4.5)	3 (10.0)	1 (1.5)	6 (0.9)
40-59	27 (30.3)	10 (33.3)	21 (30.9)	184 (26.9)
60+	58 (65.2)	17 (56.7)	46 (67.7)	494 (72.2)
Previous hospital diagnoses:				
Gallstone disease	17 (19.1)	6 (20.0)	13 (19.1)	57 (8.3)
Obesity	26 (29.2)	13 (43.3)	16 (23.5)	145 (21.2)
Alcoholism-related dx	11 (12.4)	1 (3.3)	10 (14.7)	34 (5.0)
Inflammatory bowel disease	3 (3.4)	2 (6.7)	2 (2.9)	9 (1.3)
Any cancer (excl. new cancer ≤90 days to counteract misdiagnosis bias)	5 (5.6)	2 (6.7)	3 (4.4)	70 (10.2)
Procedures on biliary tract or pancreas (excl. procedures ≤10 days to avoid reverse causality)	12 (13.5)	5 (16.7)	9 (13.2)	47 (6.9)
Charlson Comorbidity Index:				
Low (0 point)	51 (57.3)	15 (50.0)	43 (63.2)	393 (57.5)
Medium (1-2 points)	32 (36.0)	12 (40.0)	22 (32.4)	242 (35.4)
High (≥3 points)	6 (6.7)	3 (10.0)	3 (4.4)	49 (7.2)
Preadmission drug use:				
Statins (ever)	73 (82.0)	29 (96.7)	52 (76.5)	593 (86.7)
Statins (≤100 days)	51 (57.3)	19 (63.3)	38 (55.9)	433 (63.3)
Oral glucocorticoids (ever)	19 (21.4)	9 (30.0)	12 (17.7)	88 (12.9)
Oral glucocorticoids (≤100 days)	4 (4.5)	1 (3.3)	4 (5.9)	24 (3.5)
Azathioprine (ever)	3 (3.4)	1 (3.3)	3 (4.4)	3 (0.4)
Azathioprine (≤100 days)	1 (1.1)	1 (3.3)	1 (1.5)	0 (0)
NSAIDs (ever)	72 (80.9)	25 (83.3)	54 (79.4)	483 (70.6)
NSAIDs (≤100 days)	23 (25.8)	9 (30.0)	14 (20.6)	104 (15.2)
Antiepileptics (ever)	10 (11.2)	3 (10.0)	7 (10.3)	56 (8.2)
Antiepileptics (≤100 days)	3 (3.4)	1 (3.3)	2 (2.9)	19 (2.8)

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Supplementary Table 2. Crude and adjusted acute pancreatitis ORs associated with ever incretin use among cases and control subjects with and without specific pancreatitis risk factors.

Characteristic	Adjusted* OR, incretin use vs. no use of any antidiabetic drug (95% CI)
Overall	0.95 (0.75-1.21)
Comorbidity index	
Low (0)	1.12 (0.82-1.54)
Medium (1-2)	0.91 (0.62-1.33)
High (3+)	0.48 (0.20-1.14)
Gallstone disease	
Present	0.76 (0.43-1.34)
Absent	1.01 (0.79-1.31)
Alcoholism-related conditions	
Present	1.19 (0.59-2.40)
Absent	0.93 (0.73-1.20)
Obesity	
Present	0.89 (0.57-1.40)
Absent	1.03 (0.78-1.35)
Inflammatory bowel disease	
Present	1.02 (0.22-4.79)
Absent	0.96 (0.76-1.22)
Any cancer	
Present	0.50 (0.20-1.26)
Absent	1.00 (0.78-1.28)
Oral glucocorticoids	
Current use	0.59 (0.19-1.82)
No current use	0.98 (0.77-1.24)
Azathioprine	
Current use	†
No current use	0.95 (0.75-1.20)
Lipid-lowering drugs	
Current use	0.86 (0.64-1.17)
No current use	1.15 (0.80-1.65)
Antiepileptics	
Current use	0.63 (0.18-2.28)
No current use	0.97 (0.76-1.23)
NSAIDs	
Current use	0.97 (0.60-1.59)
No current use	0.95 (0.73-1.25)

* Odds ratios adjusted by logistic regression analysis for age, sex, and previous diagnoses of gallstone disease, alcoholism-related conditions, obesity, inflammatory bowel disease, or any cancer; for 3 levels of the Charlson Comorbidity Index score; and for current use of oral glucocorticoids, azathioprine, lipid-lowering drugs, antiepileptics, or NSAIDs (except when stratified by variable).

† Data could not be modelled because of too few exposed subjects