Ethnic and geographic variations in the incidence of pancreatitis and post-pancreatitis diabetes mellitus in New Zealand: a nationwide population-based study

Sayali A Pendharkar, Juby Mathew, Jinfeng Zhao, John A Windsor, Daniel J Exeter, Maxim S Petrov

ABSTRACT

AIM: To determine the incidence of acute pancreatitis (AP), chronic pancreatitis (CP), and post-pancreatitis diabetes mellitus (DP) in New Zealand, and the effect of ethnic and geographic variations.

METHODS: Data were collected from all district health boards in New Zealand by the Ministry of Health (Manatū Hauora). Diagnosis of AP, CP and DP was determined by the International Classification of Diseases-10 codes. Incidence rates per 100,000 population per year were calculated using incident AP, CP and DP cases as the numerator, and the adult resident population of New Zealand as the denominator. Poisson distribution was used to estimate 95% confidence intervals. The district health board domicile codes and corresponding incidence rates were used to map geographical variations for AP, CP and DP.

RESULTS: On average, 2,072 new cases of AP, CP and DP were diagnosed in New Zealand every year. The crude incidence of AP was 58.42 [57.55, 59.30], CP - 3.97 [3.74, 4.20], and DP - 7.95 [7.62, 8.27] per 100,000 population per year. Māori had the highest incidence of AP (95.21 [91.74, 98.68] per 100,000 population per year), CP (6.27 [5.37, 7.16] per 100,000 population per year), and DP (18.23 [16.71, 19.76] per 100,000 population per year). Incidence of AP and DP was at least 1.8 and 2.6 times higher in Māori than New Zealand Europeans in every age group, and incidence of DP was at least 1.9 times higher in Pacific people than New Zealand Europeans in every age group. Auckland/Northland had the highest incidence of AP (135.25 [134.82, 135.68] per 100,000 population), and CP (9.03 [8.60, 9.46] per 100,000 population), while Lakes/Waikato had the highest incidence of DP (20.64 [20.21, 21.07] per 100,000 population) in New Zealand.

CONCLUSIONS: New Zealanders have a very high incidence rate of AP, with Māori having the highest reported incidence of AP worldwide. There is a significant geographic variation in incidence of pancreatic diseases, with the Upper North Island having the highest incidence rates of AP, CP and DP in the country. Future high-quality studies are required to understand the mechanisms of pancreatitis and DP in order to develop preventive and therapeutic strategies that would benefit New Zealanders in general and Māori in particular.

Inflammatory diseases of the pancreas are common worldwide and pose a substantial burden on healthcare systems. The global incidence of acute pancreatitis (AP) is 33.7 per 100,000 population per year, whereas the global incidence of chronic pancreatitis (CP) is 9.6 per 100,000 population per year. In the USA alone, pancreatitis results in more than 800,000 visits to hospitals and costs more than $2.6 billion. Further, while burden of type 1 and type 2 diabetes mellitus has long been acknowledged worldwide and in New Zealand, post-pancreatitis diabetes mellitus (DP) has only gained attention recently. In particular, a nationwide population-based study from Taiwan showed that patients after AP have a 2.5 times higher risk of developing...
newly diagnosed diabetes mellitus than individuals in the general population.\textsuperscript{14} The risk of diabetes appears to be independent of the degree of mechanical destruction of the pancreas,\textsuperscript{15,16} suggesting that patients with pancreatitis are at increased risk of developing DP regardless of pancreatitis severity.

Although research on pancreatitis has been conducted in New Zealand and Australia for years, it was limited to single-centre studies only.\textsuperscript{17-20} These studies typically had a small sample size, and were prone to selection and participation bias, including underrepresentation of minorities and underserved populations, particularly the Māori. Further, the recent comprehensive systematic review and meta-analysis on the global burden of diseases of the pancreas showed that large population-based data on incidence of acute and chronic pancreatitis are available for every World Health Organization (WHO) region except for Australasia and Africa.\textsuperscript{3} Given that Māori and Pacific people are at an increased risk of developing chronic metabolic diseases,\textsuperscript{21-23} population-based studies, particularly nationwide studies, are essential for determining the true incidence of diseases, effect of covariates and pattern of healthcare utilisation, as they have large sample size and lack of selection and participation bias.

The aim of this population-based study was to determine the incidence of AP, CP and DP in New Zealand using national-level health dataset, as well as investigate the effect of ethnicity and geographical location.

**Methods**

**Data source**

Data for this study were obtained from and prepared by New Zealand’s Ministry of Health Analytical Services Database (National Health Board, Ministry of Health, New Zealand). The dataset included information on patients’ age, sex, ethnicity, tenth revision International Classification of Diseases (ICD-10) codes and the hospital admitted to. All patients were anonymised by the Analytical Services for the purpose of this study. In line with the Ministry of Health guidelines, ethical review was not required for this study. No contact was made with the study population.

**Study population**

All New Zealand residents have a unique alpha-numeric code, the National Health Index, assigned at the very first contact with the health-care system. The population for this study (n=2,597,217) constituted registered patients admitted to a public hospital across New Zealand from 1\textsuperscript{st} January 2006 to 31\textsuperscript{st} October 2015 with the diagnosis of AP (ICD-10 K85.0, ICD-10 K85.1, ICD-10 K85.2, ICD-10 K85.3, ICD-10 K85.8, ICD-10 K85.9), CP (ICD-10 K86.0, ICD-10 K86.1) or DP (ICD-10 E-1364, ICD-10 E1365, and non-diabetic patients who had new diabetes mellitus ICD-10 codes after the date of AP or CP).\textsuperscript{24} All patients who had a prior principal or secondary diagnosis of acute or chronic pancreatitis or diabetes back to 1 January 2005 were excluded. Further, patients who had an initial principal or secondary diagnosis of CP, followed by a later diagnosis of AP, were excluded from those designated as having AP. In case of multiple admissions for a patient, data from only the very first admission were used, with duplicate entries excluded.

In this study, people less than 20 years of age (n=1117) were excluded from analyses, as non-adults according to the WHO guidelines.\textsuperscript{25} Age for all remaining patients was standardised according to the WHO standardised age groups.\textsuperscript{25}

Ethnic groups were categorised in line with Statistics New Zealand Census (2013)\textsuperscript{26} and prioritised in the following order: New Zealand European, Māori, Asian, Pacific people and other. The “other” category comprised of the following ethnic groups: Middle Eastern, African, Latin American, North American Indian, Mauritian, South African and those who did not identify with any ethnic group.

New Zealand district health boards (DHBs) were aggregated into seven broad regions from North to South according to the geographic location. The regions contained sufficient number of cases of AP, CP and DP to meaningfully map the geographical variations in crude incidence of AP, CP and DP per 100,000 population, and by ethnicity. Maps for incidence rates were created at the DHB region level using the Jenks classification, which groups similar values in each class and maximises the differences between
All maps were created using the ArcGIS 10.3.1 for Desktop (ESRI 2015. ArcGIS Desktop: Version 10.3.1.4959 Redlands, CA: Environmental Systems Research Institute).

Statistical analyses
Discrete variables were presented as counts. Percentage incidence and incidence rate per 100,000 population per year were determined using incident AP, CP, and DP cases as the numerator and the adult resident population of New Zealand at the start of the study period (2006), reported by Statistics New Zealand, as the denominator. These were calculated by ethnicity, geographical variation, age and sex. Poisson distribution was used to estimate 95% confidence intervals (CI). All analyses were conducted using SPSS for Windows Version 23 (SPSS Inc., Chicago, IL, USA).

Results
There were a total of 20,198 incident cases of AP, CP and DP. The annual incidence of AP was 58.42 [57.55, 59.30] per 100,000 population per year, CP - 3.97 [3.74, 4.20] per 100,000 population per year, and DP - 7.95 [7.62, 8.27] per 100,000 population per year. On average 1,721 people were newly diagnosed with AP, 117 with CP and 234 people with DP every year. Median (interquartile range) duration between an incident event of pancreatitis and DP was 25 (6–44) months.

Acute pancreatitis
The study cohort included 16,753 incident cases of AP, of whom 8,063 (47.65%) were men. The incidence rate of AP in the different ethnic groups is shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Incidence of acute pancreatitis, chronic pancreatitis and post-pancreatitis diabetes mellitus by ethnicity.</th>
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</thead>
<tbody>
<tr>
<td>Incident cases</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Acute pancreatitis</strong></td>
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<tr>
<td>NZ European</td>
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<tr>
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<tr>
<td>Asian</td>
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<td>Pacific people</td>
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<tr>
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<td>Asian</td>
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<tr>
<td>Pacific people</td>
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<tr>
<td>Other</td>
</tr>
<tr>
<td><strong>Post-pancreatitis diabetes mellitus</strong></td>
</tr>
<tr>
<td>NZ European</td>
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<td>Māori</td>
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<tr>
<td>Asian</td>
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<tr>
<td>Pacific people</td>
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<tr>
<td>Other</td>
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</tbody>
</table>
Figure 1: Distribution of population incidence of acute pancreatitis per 100,000 per year by age and ethnicity.

Table 2: Incidence ratios of acute pancreatitis, chronic pancreatitis and post-pancreatitis diabetes mellitus in Māori and Pacific People compared to New Zealand Europeans.

<table>
<thead>
<tr>
<th>Demographic factors</th>
<th>Māori</th>
<th>Pacific People</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AP</td>
<td>CP</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
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</tr>
<tr>
<td>20–24</td>
<td>2.04</td>
<td>1.61</td>
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<tr>
<td>25–29</td>
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<td>≥75</td>
<td>3.14</td>
<td>3.66</td>
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</tr>
<tr>
<td>Men</td>
<td>1.83</td>
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<tr>
<td>Women</td>
<td>2.08</td>
<td>1.94</td>
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</table>

**Abbreviations**: AP, acute pancreatitis; CP, chronic pancreatitis; DP, post-pancreatitis diabetes mellitus; N/E, not estimable.

**Footnote**: The incidence ratios for AP, CP and DP were calculated by dividing the incidence rate of Māori and Pacific People by the incidence rate of Europeans for each pancreatic disease.
Māori had a significantly higher overall incidence of AP at 95.21 [91.74, 98.68] per 100,000 population per year, than both New Zealand European at 60.22 [59.05, 61.39] per 100,000 population per year, and New Zealanders altogether at 57.84 [56.97, 58.72] per 100,000 population per year (p<0.05) (Table 1). Although the overall incidence of AP was observed to increase with increasing age in all ethnic groups (Figure 1), Māori were more likely to develop AP than New Zealand Europeans in every age group, ranging from 1.75 times higher in the 35–39 group to 3.14 times higher in the ≥75 group (Table 2). Pacifi c people had overall incidence of AP at 54.28 [50.37, 58.19], which was not significantly different from both New Zealand Europeans and all New Zealanders. However, in those aged ≥50 years, Pacifi c people were consistently more likely to develop AP than New Zealand Europeans, ranging from 1.13 times in the 60–64 group to 2.62 in the ≥75 group (Table 2).

Chronic pancreatitis

The study cohort included 1,143 incident cases of CP, of whom 671 (58.30%) were men. The incidence rate of CP in the different ethnic groups is shown in Table 1.

Māori had a significantly higher incidence rate of CP at 6.27 [5.37, 7.16] per 100,000 population per year, than both New Zealand Europeans and all New Zealanders at 4.36 [4.05, 4.68] per 100,000 population per year and 3.95 [3.72, 4.18] per 100,000 population per year, respectively (p<0.05). Although no significant overall change in incidence of CP with increasing age was observed in any of the ethnic groups (Figure 2), Māori were more likely to develop CP than New Zealand Europeans among people older than 40, ranging from 1.5 times higher in the 45–49 group to 3.66 times higher in the ≥75 group (Table 2). Pacifi c people had overall incidence of CP at 1.92 [1.18, 2.65], which was significantly lower than both New Zealand Europeans and all New Zealanders.

Figure 2: Distribution of population incidence of chronic pancreatitis per 100,000 per year by age and ethnicity.
Post-pancreatitis diabetes mellitus

The study cohort included 2,302 incident cases of DP, of whom 1,462 (63.51%) were men. The incidence rate of DP in the different ethnic groups is shown in Table 1. Both Māori and Pacific people had a significantly higher incidence of DP at 18.23 [16.71, 19.76] per 100,000 population per year, and 17.04 [14.84, 19.23] per 100,000 population per year, respectively, than New Zealand Europeans at 6.56 [6.17, 6.95] per 100,000 population per year (p < 0.05). Increase in incidence of DP was significantly associated with increasing age in New Zealand Europeans, Māori and Pacific people (Figure 3). Māori were more likely to develop DP than New Zealand Europeans in every age group, ranging from 3.23 times higher in the 55–59 group to 13.84 times higher in the 25–29 group (Table 2). Pacific people were also more likely to develop DP than New Zealand Europeans in every age group, ranging from 1.90 times in the 45–49 group to 6.86 in the ≥75 group (Table 2).

Geographical variation in acute pancreatitis, chronic pancreatitis and post-pancreatitis diabetes mellitus

The Auckland/Waitemata/Northland region had the overall highest incidence of AP (135.25 [134.82, 135.68] per 100,000 population) and CP (9.03 [8.60, 9.46] per 100,000 population), while the Lakes/Waikato/Counties Manukau region had the overall highest incidence of DP (20.64 [20.21, 21.07] per 100,000 population) in New Zealand. By contrast, the Whanganui/Midcentral/Taranaki region had the overall lowest incidence of AP (42.80 [42.77, 42.88] per 100,000 population), while the Southland/Otago/South Canterbury region had the overall lowest incidence of CP (2.99 [2.91, 3.07] per 100,000 population) and DP (4.51 [4.44, 4.59] per 100,000 population) (Figures 4 and 5).

New Zealand Europeans in the Canterbury/West Coast/Nelson Marlborough region had the highest incidence of AP and CP (646.91 [646.06, 647.29], and 46.13 [45.30,
Figure 4: Geographic variation in incidence of pancreatitis and post-pancreatitis diabetes mellitus in New Zealand.

Figure 5: Incidence of acute pancreatitis, chronic pancreatitis, and post-pancreatitis diabetes mellitus, per 100,000 population by geographic regions.
Figure 6: Incidence of acute pancreatitis (A), chronic pancreatitis (B), and post-pancreatitis diabetes mellitus (C), per 100,000 population by geographic regions and ethnicity.
46.56] per 100,000 population, respectively) (Figures 6A and 6B), while those in the Wairarapa/Hutt/Capital and Coast region had the highest incidence of DP (68.40 [67.56, 68.82] per 100,000 population) (Figure 6C). Māori in the Lakes/Waikato/Counties Manukau region had the highest incidence of AP and DP (1102.29 [1101.92, 1102.36] and 234.03 [233.86, 234.20] per 100,000 population, respectively) (Figures 6A and 6C), while those in the Auckland/Waitemata/Northland region had the highest incidence of CP (64.83 [64.78, 64.88] per 100,000 population) (Figure 6B). Pacific people, from the Lakes/Waikato/Counties Manukau region, had the highest incidence of AP, CP and DP (591.04 [591.96, 591.30], 22.23 [21.24, 23.22], and 176.01 [175.65, 176.37] per 100,000 population, respectively) (Figure 6).

**Trends in incidence of acute pancreatitis, chronic pancreatitis and post-pancreatitis diabetes mellitus**

Incidence of AP increased significantly (p <0.05) from 2006 (41.27 [41.04, 41.51] per 100,000 population per year) to 2014 (76.81 [76.49, 77.13] per 100,000 population per year). The incidence of CP did not change significantly from 2006 to 2014 (5.26 [5.18, 5.35] per 100,000 population per year to 4.92 [4.84, 5.00] per 100,000 population per year in 2014). Post-pancreatitis diabetes mellitus significantly increased from 2006 (6.48 [6.39, 6.58] per 100,000 population per year) to 2014 (14.19 [14.05, 14.33] per 100,000 population per year) (Figure 7).

**Discussion**

A recent comprehensive systematic review and meta-regression showed that the global crude incidence of AP is 33.74 [23.33, 48.81] per 100,000 per year and CP - 9.62 [7.86, 11.78] per 100,000 per year. Findings from our study show, for the first time, that New Zealand sits at the higher end of the global spectrum with an incidence of 58.42 [57.55, 59.30] per 100,000 per year for AP, at par with North America, which has an incidence of 58.20 [56.90, 59.50] per 100,000 per year. By contrast, the crude incidence of CP in New Zealand sits at the lower end of the global spectrum and is 3.97 [3.74, 4.20] per 100,000 population per year compared to the higher incidence rate in Europe of 10.82 [8.12, 14.41] per 100,000 per year. This study is also first in the literature to determine the incidence of DP in a population-based dataset. The crude incidence rate of DP in New Zealand is 7.95 [7.62, 8.27] per 100,000 population per year.

In New Zealand, the annual incidence of AP is 1.7 times higher in New Zealand than in the world in general and two times
higher than in Europe in particular. This is indicative of the immense AP-related costs and associated burden likely posed on New Zealand’s healthcare system. While data on cost of treating AP is not available in New Zealand, the direct costs of hospitalisation for AP in the USA exceeded $2.6 billion in 2003. In addition, older patients as well as patients in urban and teaching hospitals had higher costs per hospitalisation, based primarily on longer length of hospitalisation. Further, a steady increase in the incidence of and hospitalisations due to AP worldwide has been reported over the past 3–4 decades. A similar trend was observed in New Zealand, with findings from our study showing that the incidence of AP has nearly doubled since 2006, and it is likely attributed to increased prevalence of metabolic disorders. An interaction between defective glucose and lipid metabolism and abdominal adiposity is thought to increase the risk of developing AP. Evidence suggests that hyperglycaemia, hypertriglyceridaemia and abdominal or general adiposity significantly increase the risk of developing AP. Nonetheless, evidence on impact of obesity on AP is variable and difficult to determine.

Diabetes continues to increase and is a significant national and global concern. In the US, it is the seventh leading cause of mortality, and poses a considerable socioeconomic burden. Accumulating evidence shows that diabetes after either AP or CP presents a unique pathophysiology, and is not an uncommon clinical entity. Findings from our recent meta-analysis show that nearly 40% of patients after just one episode of AP develop new pre-diabetes or diabetes, while nearly 80% of DP is attributed to CP. However, diabetes in general is often undiagnosed with type 2 diabetes undiagnosed in 30–50% of New Zealand’s population. In light of the evidence that DP is often under- and mis-diagnosed as type 2 diabetes, it is reasonable to suggest that at least 30–50% of DP is undiagnosed in New Zealand. Findings from our study show that DP is an increasingly significant problem in New Zealand, with incidence rate having more than doubled over the last decade, and it requires clinical attention, correct diagnosis, and appropriate preventive and therapeutic measures.

Incidence of AP, CP and DP differs in various ethnic groups. Findings from our study show that Māori are not only 1.6 times, 1.5 times and 2.8 times more likely to develop AP, CP and DP, respectively, than New Zealand Europeans, but also have the highest reported incidence of AP in the world (95.21 [91.74, 98.68] per 100,000 population per year). A recent systematic review and meta-analysis of high-quality population-based studies on risk factors for pancreatic diseases showed that tobacco use, high BMI and heavy alcohol consumption are the three most perilous risk factors for developing pancreatitis. Compared with non-smokers, smokers are 1.7 times more likely to develop a pancreatic disease. Current smokers are at a 20% higher risk of developing a pancreatic disease compared with ex-smokers. Tobacco use is a leading risk factor for detrimental health worldwide. New Zealand is characterised by marked discrepancy in smoking prevalence between Māori and non-Māori population (33% versus 14% of New Zealand Europeans). The Māori population has over twice as high all-cause mortality rates as the non-Māori population, with the non-Māori population living on average 7.3 years longer than the Māori population. Compared with alcohol non-consumers, alcohol consumers are at a 1.12 times higher risk of developing disease of the exocrine pancreas. Heavy drinkers (≥4 drinks per day) have a 40% increase in risk of developing a pancreatic disease compared to non-heavy alcohol users. Alcohol consumption is another major cause of mortality, disease and injury globally. Internationally, alcohol consumption alone causes 2.7 million deaths annually. In New Zealand, 5.4% of deaths in people aged less than 80 years are attributed to alcohol, with Māori having 2.5 times higher death rate attributable to alcohol than non-Māori. In light of this evidence, it is not surprising that Māori have the highest incidence of pancreatitis and DP in the country. High quality studies are now needed to investigate factors protective against pancreatitis and DP and develop preventive strategies, particularly among Māori.

This study also brings to the forefront the geographic variation and confirmation of significant difference in the incidence
of pancreatic diseases between the north and the south of the country. Northern New Zealand is 2.7 times, 3 times and 4.75 more likely to develop AP, CP and DP, respectively, than southern New Zealand. The pattern persisted when stratified by ethnicity, with Māori in north of the country being 4.78 times, 3.01 times and 5.45 more likely to develop AP, CP and DP, respectively, than those in the south of the country. Pacific people mirror the pattern, with those residing in north being 13.67 times and 7.3 times more likely to develop AP, CP and DP, respectively, than those residing in the south of New Zealand. The New Zealand deprivation index illustrates the difference between the north and the south of the country: while most of the North Island has a deprivation index of five to ten, with ten being most deprived, the South Island has a deprivation index of one to five, with one being least deprived. Deprivation indices are based on household income, access to healthcare, unemployment, housing and other factors. Facilities that may compromise health, such as alcohol outlets and advertising of unhealthy products, are preferentially located in most deprived areas often due to more affordable price barriers and utility costs.

Findings from our study bring to the forefront the ethnic disparities across New Zealand in terms of the diseases of the pancreas. That Māori and Pacific people often reside in the most deprived areas, while New Zealand Europeans populate the least deprived areas, may help explain the stark inequality in the incidence rates of pancreatitis and DP between Māori and Pacific people and New Zealand Europeans. This marked geographical variance necessitates further research into socioeconomic factors such as availability of resources and access to healthcare, and potentially the need to develop area-based prevention strategies.

This population-based study has several limitations. First, only public hospital records nationwide were used to determine the incidence rates of pancreatitis and DP. It is possible that cases diagnosed in the community and private hospitals were not transferred to public hospitals and were thus not entered into the used database, resulting in underestimation of incidence rates. In future, population-based studies should strive to combine data from both public and private records to provide more accurate estimates of incidence rates. Second, definitions of AP, CP and DP were determined solely from the ICD-10 codes rather than from clinical, laboratory or pathological evidence. Third, the “other” ethnic group was heterogeneous. No further information was available to tease out each individual ethnicity constituting the “other” group and explore the high incidence rates of diseases of the pancreas observed in this group. Further, the study focused a priori on the ethnicities that are highly prevalent in New Zealand. Last, the healthcare costs associated with AP, CP and DP could not be investigated, as this data were not readily available and are government funded. In future studies, information on costs associated with pancreatitis and DP should be ascertained to get a better insight into the socioeconomic burden these disease states pose on New Zealand’s healthcare system.

In conclusion, this nationwide population-based study shows that New Zealanders in general have one of the highest incidence rates of AP in the world, with Māori having the highest reported incidence of AP worldwide. It has also estimated the incidence of DP, which is a growing problem nationally and internationally, and showed that DP affects Māori and Pacific people disproportionately. Further, geographical location appears to be an important factor of inequity in incidence of pancreatitis and DP throughout the country. High quality research is needed in New Zealand to better understand the drivers of AP, CP and DP, and relationships between these three diseases to develop preventive and treatment strategies that are needed for everyone, but particularly for Māori who are worst affected by these diseases.
Competing interests:
Nil.

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