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ORIGINAL REPORT

Ethnic inequality in non-steroidal anti-inflammatory drug-associated harm in New Zealand: A national population-based cohort study

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Abstract

Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with many serious complications and they are widely used in New Zealand (NZ). However, differences in NSAID-associated risk for these complications between ethnic groups are largely unknown. We assessed ethnic disparities in risk of hospital admission for upper gastrointestinal bleeding (UGIB), heart failure, and acute kidney failure (AKF) in NZ's primary care population prescribed and dispensed NSAIDs.

Methods: Retrospective cohort study utilising national pharmaceutical dispensing and hospital admissions data 2007 to 2015. Patient follow-up included 90-day periods following the dispensing of NSAIDs. Risk for each adverse outcome in Maori, Pacific, European, and Asian patients was estimated using multivariable Poisson regression adjusting for age, sex, deprivation, comorbidity and concurrent drug use.

Results: 3 023 067 patients were dispensed NSAIDs between 2008 and 2015. Their total intended duration of NSAID treatment encompassed 2 353 140 patient-years. Maori, Pacific and Asian patients were younger than European patients (all $P < .001$). After adjusting for other risk factors, Maori (rate ratio: 2.54, 95% confidence interval: 2.23-2.90) and Pacific patients (3.17, 2.69-3.74) were more likely to be hospitalised for UGIB than Europeans (reference), and heart failure (Maori: 2.48, 2.24-2.74; Pacific: 1.97, 1.69-2.30). Risk of AKF was higher in Maori (1.46, 1.23-1.74). Higher risk for UGIB and HF in Maori and Pacific patients was most pronounced in males and patients aged <60 years.

Conclusions: Inequalities exist in the incidence of serious adverse outcomes experienced by different ethnic groups in NZ while using NSAIDs. Interventions to promote safer use of these medicines are required to reduce this inequity.

KEYWORDS

adverse drug event, ethnicity, pharmacoepidemiology, primary care, risk

1 | INTRODUCTION

The use of non-steroidal anti-inflammatory drugs (NSAIDs) is associated with a number of serious complications including upper

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gastrointestinal bleeding (UGIB),[1-4] kidney injury,[5-8] and adverse cardiovascular outcomes including heart failure,[9] myocardial infarction,[10]stroke,[11] and atrial fibrillation.[12,13] Given the widespread use of NSAIDs in New Zealand (NZ) the potential development of these complications represents a significant public health risk in terms of hospitalisations and other health care.

A range of patient risk factors including age, existing cardiovascular disease, type 2 diabetes and reduced renal function put patients at increased risk of NSAID-related complications.[14] Significant ethnic differences in the prevalence of many of these risk factors have been demonstrated in NZ. Māori and Pacific people have a higher prevalence of cardiovascular disease than other ethnic groups after adjusting for age and other risk factors,[15] and experience stroke at a significantly younger age than Europeans.[16] The prevalence of diabetes is also greater among Māori, Pacific and Indian people than Europeans,[17] with chronic kidney disease most prevalent among Māori and Pacific people.[18] Māori have also been shown to be at higher risk for preventable adverse events in hospital compared with non-Māori, a result of differences in the healthcare provided across the two groups.[19]

Preventable adverse events include medicines-related harm. Medicines such as NSAIDs, that are frequently prescribed and have known adverse drug effects (ADEs), are associated with high levels of harm, particularly in the community.[20] While some ethnic differences in risk awareness, communication and behaviour have been identified with NSAID use in the United States,[21] the differences in associated risk of NSAID-related ADEs between ethnic groups in NZ is largely unknown. More specifically, we have found no international research investigating ethnic-related differences in NSAID-associated harm.

In this study, we assessed ethnic differences in rates of hospital admission for UGIB, heart failure and acute kidney failure, associated with NSAIDs prescribed and dispensed to NZ primary care patients. This would provide us with a better understanding of the magnitude and characteristics of potential inequalities in the NZ health care system related to the use of these medicines. It would also help inform improvements in patient care aimed at reducing disparities in risk for serious outcomes in patients from different ethnic backgrounds.

KEY POINTS

- The risk of upper gastrointestinal bleeding (UGIB), heart failure, and acute kidney failure associated with NSAID treatment in New Zealand varies according to patient ethnicity.
- Maori and Pacific patients were more likely to be hospitalised for UGIB and heart failure and Maori more likely to be hospitalised for acute kidney failure during NSAID treatment than Europeans.
- The relative risk of UGIB and heart failure compared with Europeans was greatest in Maori and Pacific patients under 60 years of age.
- Recognition of ethnic inequality in NSAID associated harm in New Zealand is important for healthcare planning and risk management. Further research is necessary to explore the reasons for this disparity.
- Studies investigating variability in medicine-related harm by ethnicity are rare. Further studies utilising national healthcare data collections are required to investigate ethnic inequalities in health outcomes associated with the use of prescribed medicines.

2 | METHODS

We conducted three retrospective cohort studies examining risk for UGIB, heart failure and acute kidney failure in primary care patients dispensed NSAIDs. Data from three national healthcare databases managed by the Ministry of Health were analysed to identify the primary care patient population, quantify the dispensing of NSAIDs to these patients from 2007 to 2015 and identify their hospital admissions over the same period. The data sources included the Primary Health Organisation Enrolment Collection, which lists all patients registered with a general practice in New Zealand, the Pharmaceutical Collection, which records information on all nationally subsidised medicines dispensed from New Zealand community pharmacies, and the National Minimum Dataset for Hospital Events (NMDS), which provides records on all inpatient and day case discharges from New Zealand public hospitals and many private hospitals. Pharmaceuticals were classified under the Anatomical Therapeutic Chemical (ATC) system.[22] Patient records from the three databases were linked using each patient's unique encrypted National Health Index code.

2.1 | Primary care population

The primary care population included all patients registered with a general practice for between two and eight consecutive years between 2007 and 2015. Each patient was defined to be at risk in a particular year if they were registered at a practice in the first quarter of that year, or had a date of last consultation during the year at any practice, or had any medicine dispensed or any hospital admission during that year. These criteria provided evidence that patients were resident in New Zealand at some stage during the year and at risk for medicine exposure and hospitalisation. A patient's first day at risk was 1 January of their first year at risk or their date of birth if born during that year. Each patient's demographic information and NZDep2013 socioeconomic index of deprivation group[23,24] were taken from the most recent practice register on which they were listed. We excluded patients if their recorded age or sex was not consistently recorded in the three national datasets. Patient prioritised ethnicity was categorised as European, Māori, Pacific, Asian and other or unknown.[25]

Patient deprivation status was grouped into five quintiles (1 - least deprived; 5 - most deprived).

2.2 | Study cohort

The study cohort included all patients within the primary care population dispensed an NSAID between 1 January 2008 and 31 December 2015 (ATC code M01A). This excluded aspirin. Cox-2 inhibitors were also excluded as these were not subsidised for general use during the study period. Each patient's follow-up commenced at least 1 year after their first day at risk. This provided a baseline period of at least 1 year to determine patient co-morbidity prior to NSAID treatment and identify patients with no NSAID treatment during the baseline year (new users). Follow-up for each patient potentially included multiple episodes of NSAID treatment based on a 90-day period following the dispensing date for the NSAID.[26] Each period of NSAID treatment started on the date it was dispensed and finished 90 days later if no other prescription for an NSAID had been issued during this time. Total follow-up duration for each cohort patient equalled the number of days exposed to NSAIDs across the 8 years 2008 to 2015. Follow-up for each patient for each of the three study outcomes ceased on their first hospital admission date for the outcome or their last day of NSAID treatment.

2.3 | Patient outcomes

Data for each hospital discharge included the admission and discharge dates and up to 20 discharge diagnoses coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). We identified all patients in the study cohort with a first-time primary hospital discharge diagnosis for each of the three adverse outcomes where these

TABLE 1 Patients using NSAIDs and hospital admission rates for adverse events by ethnic group 2007 to 2015

	European	Māori	Pacific	Asian	All patients[a]
Patients using NSAIDs	2 010 125	438 757	225 198	264 911	3 023 067
Males (%)	953 784 (47.4)	207 914 (47.4)	112 378 (49.9)	121 198 (45.8)	1 435 544 (47.5)
Age at study start (years)					
Mean (SD)	37.4 (23.2)	26.0 (20.1)	26.2 (19.7)	29.6 (20.0)	34.0 (22.7)
<40 (%)	1 041 555 (51.8)	320 566 (73.1)	166 271 (73.8)	182 186 (68.8)	1 771 161 (58.6)
40-59 (%)	593 536 (29.5)	92 302 (21.0)	46 325 (20.6)	64 069 (24.2)	814 061 (26.9)
≥60 (%)	375 034 (18.7)	25 889 (5.9)	12 602 (5.6)	18 656 (7.0)	437 845 (14.5)
Deprivation quintile					
1 – least deprived	479 352 (23.8)	30 196 (6.9)	8728 (3.9)	40 315 (15.2)	573 673 (19.0)
2	437 592 (21.8)	42 796 (9.8)	14 296 (6.3)	46 338 (17.5)	556 514 (18.4)
3	388 934 (19.3)	62 276 (14.2)	22 486 (10.0)	48 436 (18.3)	537 204 (17.8)
4	331 598 (16.5)	94 789 (21.6)	45 179 (20.1)	57 359 (21.7)	544 479 (18.0)
5 - most deprived	210 181 (10.5)	175 836 (40.1)	120 816 (53.6)	46 527 (17.6)	568 386 (18.8)
Unknown	162 468 (8.1)	32 864 (7.5)	13 693 (6.1)	25 936 (9.8)	242 811 (8.0)
Intended duration of NSAID use per patient					
Median (mean) (days)	180 (297.4)	180 (264.5)	180 (278.1)	174 (233.0)	180 (284.3)
Upper gastrointestinal bleeding					
Total patient-years using NSAIDs	1 636 362	317 599	171 335	168 946	2 352 348
Hospital admissions (/10 000 pyar)	1289 (7.9)	323 (10.2)	194 (11.3)	83 (4.9)	1912 (8.1)
Mean age at admission (years)	70.8	60.4	59.4	60.8	67.4
Heart failure					
Total patient-years using NSAIDs	1 634 269	316 872	171 153	168 309	2 349 473
Hospital admissions (/10 000 pyar)	2294 (14.0)	562 (17.7)	208 (12.2)	67 (4.0)	3179 (13.5)
Mean age at admission (years)	77.3	63.8	61.0	70.5	73.7
Acute kidney failure					
Total patient-years using NSAIDs	1 636 317	317 671	171 443	168 970	2 352 698
Hospital admissions (/10 000 pyar)	914 (5.6)	187 (5.9)	53 (3.1)	32 (1.9)	1210 (5.1)
Mean age at admission (years)	68.1	57.8	47.3	48.3	64.9

[a]84 076 patients were of other or unspecified ethnicity. Pyar: patient years of NSAID use.

occurred during patient follow-up(UGB K250-2,K254-6,K260-2,K264-6,K270-2,K274-6,K280-2,K284-6; heart failure I50; and acute kidney failure N17).

2.4 | Patient co-morbidity and concurrent medicine use

We identified patient co-morbidity recorded in the year prior to each NSAID episode from hospital diagnoses and/or medicines dispensed. This included long-term conditions identified by NHS Scotland as significant for health service planning[27]: coronary heart disease, atrial fibrillation, hypertension, cerebrovascular disease, peripheral vascular disease, diabetes, thyroid disorders, anaemia, chronic lower respiratory disease, rheumatoid arthritis and other inflammatory arthropathies, liver disease, kidney disease, dyspepsia, inflammatory bowel disease, pain, depression, schizophrenia/bipolar disorder, anxiety/neurotic disorders, dementia, Parkinson's disease, multiple sclerosis, epilepsy, mental disorders due to psychoactive substance abuse, and cancer. For each patient, we also identified any prescribed and dispensed treatment with other medicines known to be associated with an increased risk of each outcome,[7,9,28,29] where these were dispensed within the 90 days prior to the NSAID episode or during the NSAID episode, and any dispensed antiulcerants.

2.5 | Statistical analysis

We calculated the total patient-years of NSAID treatment by ethnic group, age at start of follow-up and sex. Unadjusted incidence rates for each outcome over the eight-year period 2008 to 2015 were calculated based on age at the start of each NSAID episode. Adjusted incidence rates were then estimated for each ethnic group using multivariable Poisson regression adjusting for age, sex, deprivation quintile, concurrent use of other drugs and patient co-morbidity. Co-morbidity and drug treatment covariates were excluded based on backwards stepwise elimination of variables where $P > .10$ specified removal from the model.[30] Adjusted incidence rates were also calculated for new users of NSAIDs, females and males, and by age group, within each ethnic group. Age differences between ethnic groups were tested using the Wilcoxon rank-sum test. Statistical analyses were conducted using STATA version 11.0 (StataCorp, College Station, Texas).

3 | RESULTS

A total of 4 772 213 primary care patients of all ages were identified as at risk for NSAID exposure and hospitalisation in two or more consecutive years 2007-2015. Of these, 3 023 067 patients (63.3%) were dispensed at least one course of NSAIDs between 2008 and 2015. A total of 12 176 253 NSAID courses were dispensed during this time with 2 353 140 patient-years of intended NSAID treatment (median course duration: 90 days; interquartile range: 49-90 days). The mean number of days of intended NSAID treatment per patient was 297.4 for European, 264.5 for Maori, 278.1 for Pacific, and

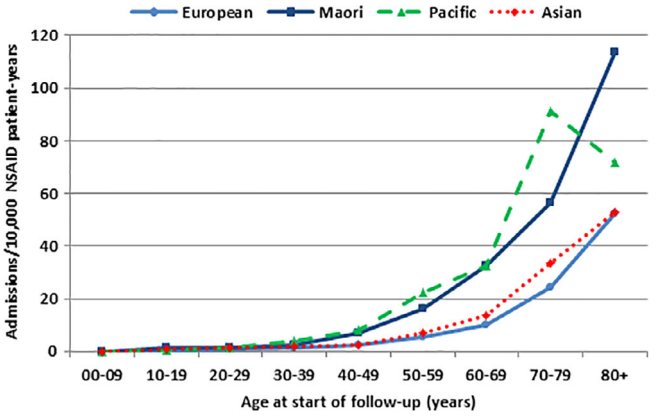

FIGURE 1 Hospital admission rates for upper gastrointestinal bleeding by ethnicity and age group

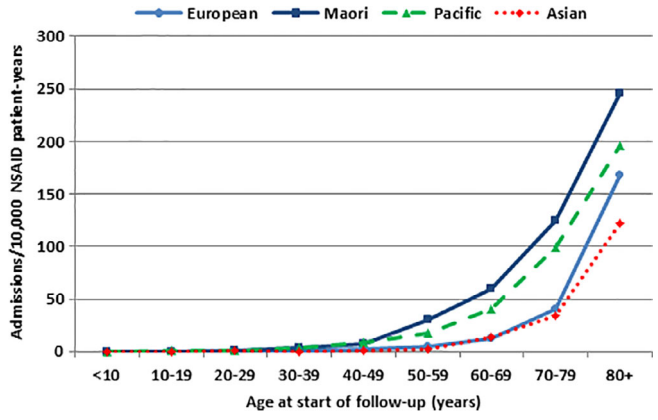

FIGURE 2 Hospital admission rates for heart failure by ethnicity and age group

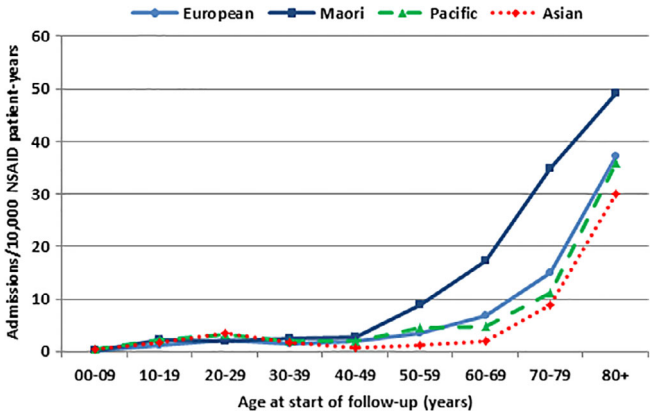

FIGURE 3 Hospital admission rates for acute kidney failure by ethnicity and age group

233.0 for Asian patients. There were 2 293 896 new users of publically-funded dispensed NSAIDs (75.9%) with no obvious treatment with NSAIDs in the year prior to their start of follow-up.

The NSAID cohort included 2 010 125 patients of European ethnicity (66.5%), 438 757 Māori (14.5%), 264 911 Asian (8.8%), and 225 198 Pacific (7.4%) with 84 076 patients (2.8%) of other or unspecified ethnicity (Table 1). Māori ($P < .001$), Pacific ($P < .001$) and Asian NSAID patients ($P < .001$) were significantly younger than European patients. Over 40% of Māori and Pacific patients resided in the most deprived areas of the country. Incidence rates of admission to hospital with UGIB were highest in Māori and Pacific patients despite their younger age profiles than Europeans, with admission rates for heart failure and acute kidney failure highest in Māori patients. Figures 1 to 3 depict the actual incidence rates for these three outcomes by age and ethnic group.

Concurrent treatment with antiulcerants and antidepressants was lowest in Māori and Pacific patients, with antiplatelet therapy more common than in Europeans and Asians (Table 2). Of the groups of medicines associated with an increased risk of heart failure, treatment with metformin, pioglitazone and calcium channel blockers was most prevalent in Māori and Pacific patients. Māori patients in all age groups and Pacific patients over the age of 60 years were also more likely to be prescribed and dispensed inhaled beta-adrenoceptor agonists. Of the medicines potentially associated with acute kidney failure, the use of antihypertensives, and allopurinol for the treatment of gout, was far more prevalent among Māori and Pacific patients.

After adjusting for age, sex, deprivation status, concurrent medicine therapy and significant patient co-morbidity, Māori and Pacific patients were more than twice as likely to be admitted to hospital for UGIB than Europeans (Table 3). Admission rates for heart failure were

TABLE 2 Concurrent drug use of NSAID users

	<40 years				40-59 years				≥60 years			
	Euro.	Māori	Pacific	Asian	Euro.	Māori	Pacific	Asian	Euro.	Māori	Pacific	Asian
Number of NSAID episodes (thousand)	2722	803	438	423	2919	582	309	282	2941	244	107	112
Upper gastrointestinal bleeding												
Antiulcerant[a]	8.0	5.6	5.6	8.4	27.1	21.6	17.7	28.5	46.4	35.5	31.6	45.8
Antiplatelet	0.5	0.6	0.9	0.5	8.1	12.7	14.8	11.2	33.3	37.3	40.9	34.0
Oral anticoagulant	0.1	0.1	0.1	0.0	0.5	1.0	0.5	0.2	2.3	4.1	1.8	0.9
Antidepressant[b]	12.0	7.2	2.7	3.9	24.6	16.2	6.1	11.5	23.5	15.4	7.8	13.4
Heart failure												
Calcium channel blocker	0.3	0.4	0.5	0.3	4.6	7.6	7.0	5.6	16.3	21.1	19.9	18.0
Alpha-adrenoceptor blocker	0.3	0.2	0.2	0.3	1.9	1.9	1.6	1.7	8.4	7.4	7.2	7.5
Antiarrhythmic (sotalol or flecainide)	0.1	0.1	0.1	0.0	0.4	0.6	0.3	0.2	2.1	2.8	1.3	0.6
Diabetes (metformin or pioglitazone)	0.5	0.8	1.5	1.0	3.0	7.5	12.0	8.8	5.6	15.1	22.8	15.8
Inhaled beta-adrenoceptor agonist	10.6	12.8	9.4	8.7	9.4	14.5	8.8	6.6	8.3	16.2	15.0	8.8
Acute kidney failure												
ACE inhibitor/angiotensin II antagonist	1.0	1.7	2.6	1.4	15.5	24.0	27.0	18.7	37.5	50.1	52.8	38.7
Diuretic	0.5	0.5	0.5	0.3	6.3	7.8	4.9	4.0	21.9	22.9	16.1	13.8
Statin	0.6	1.0	1.9	1.7	14.7	19.4	24.2	23.6	38.0	45.6	51.3	48.1
Systemic antibacterial	51.7	55.9	55.6	55.8	34.1	39.1	41.1	38.6	33.4	37.5	42.1	37.0
Paracetamol	55.9	58.5	63.1	61.5	42.1	46.3	58.5	50.9	48.2	49.5	69.0	57.5
Antigout (allopurinol)	0.2	1.0	2.8	0.3	1.9	6.7	10.2	2.2	5.4	14.8	15.9	4.9
Drug for bone metabolism	0.1	0.0	0.0	0.0	0.9	0.3	0.2	0.8	6.7	2.1	1.4	6.1
Chemotherapeutic agent	0.6	0.4	0.4	0.4	2.5	2.0	1.7	1.9	3.0	2.8	2.5	2.4

Note: Data are % of NSAID use episodes except where noted otherwise. Other concurrent drug use for heart failure: antipsychotics (clozapine, lithium), topical cholinergic agents, topical beta blockers, antifungals (itraconazole, amphotericin B), antimalarial (hydroxychloraquine), immunosuppressant (adalimumab), antiepileptic (carbamazapine). Acute kidney failure: antiviral (acyclovir).

[a]Also concurrent drug use for acute kidney failure.

[b]Also concurrent drug use for heart failure.

TABLE 3 Adjusted incidence rate ratios for upper gastrointestinal bleeding, heart failure and acute kidney failure by ethnic group[a]

	Ethnic group	Upper gastrointestinal bleeding	Heart failure	Acute kidney failure
All patients	Māori	2.54 (2.23–2.90) <0.001	2.48 (2.24–2.74) <0.001	1.46 (1.23–1.74) <0.001
	Pacific	3.17 (2.69–3.74) <0.001	1.97 (1.69–2.30) <0.001	0.76 (0.57-1.01) 0.063
	Asian	1.08 (0.86-1.35) 0.528	0.74 (0.58-0.95) 0.018	0.61 (0.43-0.87) 0.007
Age: <40 years	Māori	2.43 (1.43-4.12) 0.001	2.85 (1.56-5.21) 0.001	1.22 (0.78-1.92) 0.376
	Pacific	2.66 (1.42-4.99) 0.002	3.12 (1.50-6.47) 0.002	1.24 (0.72-2.14) 0.446
	Asian	1.35 (0.67-2.73) 0.404	0.31 (0.04-2.34) 0.258	1.19 (0.68-2.09) 0.542
Age: 40–59 years	Māori	2.56 (2.02-3.24) <0.001	3.03 (2.42-3.80) <0.001	1.47 (1.06-2.04) 0.020
	Pacific	3.22 (2.45-4.25) <0.001	2.30 (1.71-3.09) <0.001	0.77 (0.46-1.29) 0.321
	Asian	0.93 (0.62-1.39) 0.716	0.52 (0.28-0.96) 0.037	0.28 (0.11-0.69) 0.005
Age: ≥60 years	Māori	1.99 (1.68-2.36) <0.001	1.46 (1.29-1.64) <0.001	1.26 (1.00-1.58) 0.048
	Pacific	2.33 (1.86-2.91) <0.001	1.09 (0.90-1.33) 0.365	0.40 (0.24-0.67) 0.001
	Asian	0.91 (0.68-1.23) 0.538	0.61 (0.46-0.80) <0.001	0.45 (0.25-0.79) 0.006
Females	Māori	2.23 (1.82-2.74) <0.001	2.15 (1.82-2.54) <0.001	1.57 (1.20-2.04) 0.001
	Pacific	2.14 (1.59-2.87) <0.001	1.87 (1.45-2.41) <0.001	0.69 (0.42-1.15) 0.153
	Asian	0.60 (0.39-0.92) 0.020	0.48 (0.30-0.76) 0.002	0.54 (0.30-1.00) 0.049
Males	Māori	2.81 (2.37-3.35) <0.001	2.69 (2.36-3.07) <0.001	1.37 (1.10-1.72) 0.006
	Pacific	3.89 (3.17-4.76) <0.001	2.00 (1.65-2.42) <0.001	0.79 (0.55-1.13) 0.197
	Asian	1.51 (1.15-1.97) 0.003	0.94 (0.70-1.25) 0.655	0.66 (0.42-1.02) 0.063
New users	Māori	2.70 (2.24-3.25) <0.001	2.43 (2.10-2.81) <0.001	1.49 (1.18-1.87) 0.001
	Pacific	3.16 (2.49-3.99) <0.001	2.06 (1.66-2.56) <0.001	0.89 (0.61-1.29) 0.529
	Asian	1.23 (0.93-1.63) 0.148	0.73 (0.53-1.01) 0.054	0.75 (0.50-1.14) 0.177

[a]Reference group = European (1.00). Data are adjusted incidence rate ratios (95% confidence interval), *P*.

also significantly higher in Māori and Pacific patients with rates of admission for acute kidney failure almost 50% higher for Māori than Europeans. Higher incidence rates for UGIB and heart failure in Māori and Pacific patients were most pronounced among patients under 60 years of age and in males more than females.

4 | DISCUSSION

The aim of this study was to investigate differences in NSAID-related harms between ethnic groups in NZ. NSAIDs are commonly used with 63.3% of the total primary care population prescribed and dispensed NSAIDs at some point over our study time frame. Although they are known to lead to potentially serious adverse events, differences in harm associated with their use between ethnic groups had not been evaluated. Previous research has demonstrated inequity across ethnic groups associated with the prevalence of certain diseases and appropriate medical treatment, but there are significant knowledge gaps specific to the use of medicines and medicines-related harm. The potential consequences of NSAID-related harm are not insignificant as 2002 (23.7%) out of the NZ total of 8457 hospital admissions for UGIB 2008-2015 occurred during treatment with NSAIDs, as did 4264/69400 (6.1%) of all admissions for HF and 1294/10174 (12.7%) of all admissions for AKF.

Our findings indicate that Māori and Pacific people dispensed NSAIDs experience greater rates of hospital admission for serious health conditions during NSAID treatment after adjusting for other significant risk factors for these conditions. It is of concern that Māori and Pacific people are prescribed NSAIDs at a younger age and have a higher incidence of hospitalisation for NSAID-related harms. Rates of hospitalisation for UGIB were more than twice as high for Māori and Pacific patients than European patients, yet their likelihood of being prescribed gastro-protective antiulcerants was lower. Although most current guidelines advocate the use of an antiulcerant, usually a proton pump inhibitor (PPI), for all patients over 65 years of age taking an NSAID, particularly if they have other risk factors, concurrent treatment with PPIs was lower in Māori and Pacific people compared with Europeans in this age group. Furthermore NSAID-associated UGIB occurred more frequently in Māori and Pacific in all age groups, including less than 65 years. These observations suggest that PPIs are under-prescribed in Māori and Pacific patients over 60 years receiving NSAIDs and that they should also be considered as treatment for younger Māori and Pacific patients due to their increased NSAID-associated risk for UGIB.

Hospitalisations for heart failure and kidney failure were significantly higher for Māori than European and Asian patients. Māori and Pacific people have a higher incidence of cardiovascular disease and diabetes at a younger age than Europeans which may predispose

these groups to a higher risk of NSAID associated heart failure and acute kidney injury. Our research contributes to the findings of other NZ centres that have identified admissions for heart failure occurring at a younger age for Māori compared with Europeans,[31] regardless of NSAID use, and higher rates of admission for gastrointestinal bleeding in Māori.[32]

Avoidable differences in healthcare provision at both individual and population levels adversely impact health outcomes.[33] Māori have less access to medicines than other ethnic groups despite their health need being higher and there is an increasing sense of urgency for this to change.[34] Māori currently have a life-expectancy approximately 7 years less than that of non-Māori,[35] and Māori and Pacific people are two to three times more likely to die of conditions that could have been avoided if effective and timely healthcare had been available.[36] Māori also have a higher risk for preventable iatrogenic injuries compared with non-Māori, a result of differences in healthcare provided across the two groups.[19]

We acknowledge several limitations in our study. Members of the public that were more transitory or only required medical services on a casual basis were not included in our NSAID cohort since they were not enrolled with a general practice, but these patients may be over-represented by Maori and the impoverished. Our national ethnicity data was based on patient prioritised ethnicity, a NZ coding system in which patients belonging to more than one ethnic group are assigned to one ethnic group with Maori having priority coding, followed by Pacific, then Asian, then other ethnic groups, with people of only European ethnicities last.[37] This may have affected the relative risks for health outcomes in our study, however a small proportion of patients from all ethnic groups would have been priority coded as Maori. We may also have overestimated the years at risk for patients who had died during the study period in the absence of linked national data on death registrations. However our study included general practice patients identified from annual patient registers and NZ practices are obligated to remove deceased patients from their registers upon notification of their death since government capitation funding for practices is based on their number of registered patients.

The low-dose NSAIDs available "over the counter" (OTC) without a prescription were also not included in our analysis. Ibuprofen and diclofenac sodium were both available for purchase as low strength tablets (eg, 200 mg ibuprofen) without prescription in NZ but we were unable to capture the extent of this OTC usage during the study period. Although OTC NSAIDs are likely to be used at relatively low doses for a short period and are therefore unlikely to contribute significantly to patient harm compared with prescribed NSAIDs, this use could potentially have influenced our findings. A further limitation is that we were not able to account for potential variation in the efficacy and safety of NSAIDs between ethnic groups due to genetic factors.[38] Although clinical edits validate NZ hospital diagnoses and procedure codes in terms of ICD-10-AMcompatibility,[39] there may be a degree of uncertainty around misclassification of diagnoses and variability in recording levels of diagnoses between hospitals.

A better understanding of the magnitude and characteristics of inequities in health can help inform improvements in care,[40] and knowledge of inequities associated with medicines-related harm can help inform strategies to minimise this harm. These could include processes to address gaps in the clinical care of certain patient groups, and the identification of patients who might require a different level of care. They could potentially include controlling the prescribing of NSAIDs, or considering the provision of PPIs for Māori and Pacific patients at a younger age than current guidelines suggest. It is important that health care providers understand the risks involved when prescribing NSAIDs and that this risk is communicated effectively to people receiving or considering using these medicines. Our study provides further insight into the extent of serious adverse events that are associated with the use of NSAIDs and inequalities in the incidence of these events across different ethnic groups prescribed these medicines. We should now consider how to manage this health inequity, by implementing interventions to promote safer treatment with these frequently used medicines.

ETHICS STATEMENT

In New Zealand, ethics committee review is not required for secondary use of data for the purpose of quality assurance or outcome analysis where the researchers are bound by a professional or an employment obligation to preserve confidentiality and the patient information is not identifiable. Ethical guidelines for observational studies: National Ethics Advisory Committee. http://www.neac.health.govt.nz/

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception or design of the work and the interpretation of data, and all critically revised the manuscript. Andrew Tomlin, David Woods, Angela Lambie, Lisa Eskildsen and Jerome Ng contributed to the analysis and drafted the manuscript. Murray Tilyard contributed to the acquisition of data for the work. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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