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RESEARCH ARTICLE

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A whole of population retrospective observational study on the rates of polypharmacy in New Zealand 2014 to 2018 Polypharmacy in New Zealand: What is the current status?

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Abstract

Background and Aims: Polypharmacy (≥5 medicines) and hyperpolypharmacy (≥10 medicines) can significantly impact people's health. The literature surrounding polypharmacy focuses on the elderly, particularly rest home populations, with few studies looking into younger age bands. Moreover, there have been no recent studies looking into the rates of polypharmacy in New Zealand. This study aimed to determine whether polypharmacy rates have increased over time in the New Zealand population. Specifically investigating polypharmacy rates across age and ethnicity, and identifying which medicines are most commonly prescribed in people with polypharmacy.

Methods: A nationwide retrospective observational study was carried out between 2014 and 2018 on 4 697 274 New Zealanders (96% of the population) by linking dispensing data from the Pharmaceutical Collection to patient enrolment data using a National Health Identifier (NHI) to identify the rate of long-term medicine prescribing in New Zealand.

Results: Our study found the rate of polypharmacy to be 9.93% and hyperpolypharmacy to be 1.92% nationwide in 2018, a percentage increase of 4.1% and 7.11% from 2014, respectively. During the same period, we observed the greatest percentage increase (30.37%) in the rate of polypharmacy in the 20 to 29 age band while the rates decreased in older populations. Variation was also noted between ethnicities. Medicines contributing to polypharmacy differed by age group.

Conclusion: Current methods for minimizing polypharmacy and optimizing medicines use are narrowly focused on the elderly. Despite an increase in education and awareness raising campaigns, rates continue to rise in New Zealand's population.

KEYWORDS
Medicines use, New Zealand, Pharmacoepidemiology, Polypharmacy, Prevalence, Primary health care, quality use of medicines

1 | INTRODUCTION

Polypharmacy is the concurrent use of multiple medications. While these therapies are normally always indicated—treating several chronic conditions at the same time, they can cause side effects and worsen health.[1] Polypharmacy is associated with many issues, one of the major ones being increased drug-drug interactions.[2] People with polypharmacy are twice as likely to experience an adverse drug event,

and this risk increases exponentially as the number of medicines increases.[2-4] People with polypharmacy are also likely to be less compliant with their treatment regimen compared to those without, which is an issue in itself.[5]

1.1 | Prescription of polypharmacy medicines

Despite polypharmacy being a well-identified problem, it is largely unknown which medicines are most commonly prescribed to those experiencing polypharmacy. This is important as not all polypharmacy is inappropriate. Appropriate polypharmacy has been described as "prescribing for an individual for complex conditions or for multiple conditions in circumstances where medicines use has been optimized and where the medicines are prescribed according to best evidence."[4,6] Previous studies have found polypharmacy to be associated with suboptimal prescribing. The more drugs a patient is exposed to, the more likely they are to be prescribed inappropriately.[7]

1.2 | Current polypharmacy status

Being viewed primarily as a condition of the elderly, the vast majority of polypharmacy studies investigate elderly populations, commonly in aged care facilities.[3,8,9] Moreover, there are few studies on the prevalence of polypharmacy in young people, and these largely focus on specific youth populations, for example, those taking psychotropic medicines.[10,11] Variations in the definitions of polypharmacy make it difficult to compare studies.[4,12] It is not known what other age groups, besides the elderly, contribute to the rates of polypharmacy.

In 2014, the best practice advocacy center New Zealand (bpac^{nz}) reported a slightly increasing trend (9.8%-11.1% and 2.2%-2.6% in polypharmacy and hyper-polypharmacy, respectively) over the 5-year period from 2009/10 to 2013/14 in the proportion of New Zealand patients having polypharmacy.[13]

In 2017, the Health Quality and Safety Commission of New Zealand found that 33% of the elderly population used five or more long-term medicines. However, they did not report on rates of those under 65 years.

In a study of New Zealanders aged greater than 65 the rates of polypharmacy and hyperpolypharmacy were reported by ethnicity each year from 2005 to 2013.[14]

By better understanding who is affected by polypharmacy and which medicines are contributing, we can better ensure the quality use of medicine.

This study aimed to determine whether polypharmacy rates have increased over time in the New Zealand population. In addition, we aimed to:

- Investigate polypharmacy rates across age, and ethnicity; and
- determine which medicines are most commonly prescribed in people with polypharmacy.

2 | METHODS

2.1 | Study Design

This retrospective nationwide observational study used two of New Zealand's administrative databases: The Pharmaceutical Collection, which captures all community dispensed medicines except those given as a hospital inpatient, and the Primary Health Organization (PHO) database, which captures demographic details of patients who are enrolled in an NZ general practice (family physician).[15] Every New Zealander has a unique National Health Index (NHI) code, an alphanumeric identifier that is used in all interactions with the health system over their life. This code makes it possible to link an individual's health data across a range of databases. By combining the registration details at general practice and the medicines recorded in the Pharmaceutical Collection, we can identify the medicine utilization rates for all New Zealanders.

In this study, we define polypharmacy as occurring when a person concurrently takes five or more long-term medicines and hyperpolypharmacy when a person is taking 10 or more medicines. We followed the World Health Organization's definition of polypharmacy and bpac^{nz}'s definition of hyperpolypharmacy.[13,16]

2.2 | Defining medicines exposure

The study population was all New Zealanders who were enrolled in a New Zealand general practice between 2014 and 2018. This period was chosen as it follows on from the last reported data in New Zealand.[13] Enrolment data were linked (using each person's unique NHI number) to the Pharmaceutical Collection[17] . We defined a medicine as being utilized if the patient had been dispensed the medicine three or more times during the given calendar year from an original prescription (did not count multiple repeat dispensing; most people are given a 3-month supply of medicines with each prescription.[18] This limit was to ensure that only long-term medicines were captured to meet our definition of polypharmacy, although this will exclude short term therapies and medicines trials that contribute to a patient's medicine burden. We excluded any medicine belonging to the Therapeutic Group 1 "Infections - Agents for Systemic Use," which includes medicines from the following Therapeutic Groups 2: "Anthelmintics," "Antibacterials," "Antifungals," "Antimalarials," "Antiparasitics," "Antitrichomonal Agents," "Antituberculotics and Antileprotics," "Antivirals," "Antiretrovirals," "Immune Modulators," and "Urinary Tract Infections."[19] In children of less than 10 years of age, we also excluded any prescription for ibuprofen and paracetamol as these are given to children for regular fevers and pain relief but not used as a long-term medicine[19] and, therefore, we believed this could artificially increase our reported rates of polypharmacy.

2.3 | Covariates

We analyzed peoples age (by date of birth) and ethnicity (self-reported) as recorded in the Primary Health Organization (PHO) database. A

person's age was defined as the oldest age they were recorded as in that yearly quarter then placed in the appropriate age band accordingly. We grouped ethnicity according to Statistics New Zealand reporting standards; Asian, Maori, MELAA defined as Middle Eastern, Latin American, and African, NZ European/European, Other, and Pacific Islander.[20]

2.4 | Analysis

A count of individual medicines a person had utilized in the calendar year was generated from our search query of the database. This was used to create a table for each year displaying the number of people in each age band and ethnicity against the number of medicines they had utilized. Rates of polypharmacy (resp. hyperpolypharmacy) for each age band and ethnicity and trends over time were calculated as the number of people taking ≥5 (resp. ≥10) medicines over the total population in that age band or with that ethnicity. 95% confidence intervals for the rates and for the changes between the rates in 2014 and 2018 for individual age bands and ethnicities were obtained using *Z*-tests implemented by the R function prop. test. Dispensing with a missing NHI was excluded from the analysis.

2.5 | Ethnicity rates

Rates of polypharmacy and 95% confidence intervals were calculated for each ethnicity. In an attempt to reduce bias and adjust for the known medicines access equity issues we also calculated the rates for each ethnicity only including those who had received at least one medicine.[21]

2.6 | Medicines associated with polypharmacy

To investigate which medicines are most commonly dispensed in polypharmacy patients we generated a list ranking the 10 most frequently utilized medicines for people with polypharmacy.

The medicines most commonly dispensed to people with polypharmacy were analyzed and compared to the most commonly dispensed medicines (for all New Zealanders) in each age band to see if any trends or potential contributors could be identified.

2.7 | Ethical considerations

This study received ethical approval from the University of Otago ethics committee (#19027). Individual patient consent is not required to use this data. Anonymity is preserved through the use of encrypted NHI.

3 | RESULTS

3.1 | Overall rates

In 2018, 4 697 274 New Zealanders (96% of the population) were enrolled in a general practice clinic. Our definition of polypharmacy (≥5 medicines) was met by 9.93% of the population (n = 466 379), while 1.92% (n = 90 261) had hyper-polypharmacy (≥10 medicines). Between 2014 and 2018, there was a 4.10% increase (net rate = 0.39%, 95% confidence interval [CI] 0.35%-0.43%) increase in the rate of polypharmacy, this equated to an additional 41 968 patients across the five-year span. A percentage increase of 7.11% (net rate = 0.13%, 95% CI 0.11%-0.15%) was seen in hyper-polypharmacy over the same period.

There was an increasing trend in both the rates of polypharmacy and hyper-polypharmacy as age increased (Tables 1 and 2).

Older patients made up the vast majority of those with polypharmacy. In 2018, despite only making up 22% of the total population, 75% of those with polypharmacy were 60 years or older. For hyper-polypharmacy, the same age group was responsible for 82% of the total cases.

TABLE 1 Yearly polypharmacy rates in age bands from 2014 to 2018

Age	Rate 2014	Rate 2015	Rate 2016	Rate 2017	Rate 2018	Net rate change 2014 to 2018	95% confidence interval	*P* value	Percentage change from 2014 to 2018
0 to 9	0.40%	0.39%	0.39%	0.40%	0.37%	−0.03%	−0.05 to −0.01% **	.0088	−7.26%
10 to 19	0.29%	0.31%	0.32%	0.34%	0.36%	0.07%	0.05 to 0.09% ***	1.06E-11	24.49%
20 to 29	0.66%	0.70%	0.77%	0.79%	0.87%	0.20%	0.17 to 0.23% ***	1.70E-36	30.37%
30 to 39	1.58%	1.62%	1.67%	1.72%	1.77%	0.19%	0.15 to 0.24% ***	1.10E-15	12.19%
40 to 49	4.18%	4.28%	4.38%	4.46%	4.56%	0.39%	0.31 to 0.46% ***	2.53E-25	9.21%
50 to 59	10.41%	10.47%	10.60%	10.59%	10.78%	0.37%	0.26 to 0.48% ***	3.57E-11	3.56%
60 to 69	22.91%	22.73%	22.39%	22.12%	22.05%	−0.86%	−1.02 to −0.69% ***	8.45E-24	−3.74%
70 to 79	41.68%	41.38%	40.89%	40.25%	39.88%	−1.80%	−2.05 to −1.55% ***	5.61E-46	−4.32%
80 to 89	58.02%	57.81%	57.51%	56.99%	56.87%	−1.16%	−1.52 to −0.80% ***	2.82E-10	−2.00%
90 plus	62.71%	62.54%	62.37%	61.24%	60.92%	−1.79%	−2.54 to −1.05% ***	2.24E-06	−2.86%
Total	9.54%	9.67%	9.77%	9.82%	9.93%	0.39%	0.35 to 0.430% ***	2.73E-88	4.10%

TABLE 2 Yearly hyperpolypharmacy rates in age bands from 2014 to 2018

Age	Rate 2014	Rate 2015	Rate 2016	Rate 2017	Rate 2018	Net rate change 2014 to 2018	95% confidence intervals	*P* value	Percentage change from 2014 to 2018
0 to 9	0.02%	0.02%	0.02%	0.02%	0.02%	0.00%	−0.003 to 0.01%	.3608	12.73%
10 to 19	0.02%	0.02%	0.02%	0.02%	0.02%	0.01%	0.001 to 0.01%*	0.02866	36.15%
20 to 29	0.05%	0.06%	0.07%	0.07%	0.08%	0.03%	0.02 to 0.04%***	4.25E-10	58.43%
30 to 39	0.16%	0.18%	0.19%	0.20%	0.20%	0.04%	0.02 to 0.05%***	1.00E-05	21.56%
40 to 49	0.52%	0.54%	0.56%	0.58%	0.60%	0.08%	0.06 to 0.11% ***	5.54E-10	16.21%
50 to 59	1.51%	1.55%	1.58%	1.63%	1.69%	0.18%	0.13 to 0.22% ***	9.72E-15	11.71%
60 to 69	3.83%	3.87%	3.84%	3.88%	3.98%	0.15%	0.07 to 0.23%***	0.0002	3.85%
70 to 79	8.44%	8.39%	8.36%	8.28%	8.31%	−0.14%	−0.28 to 0.01%	0.0598	−1.59%
80 to 89	14.53%	14.38%	14.06%	13.98%	13.88%	−0.65%	−0.90 to −0.39% ***	6.01E-07	−4.45%
90 plus	16.61%	16.55%	15.73%	15.29%	15.61%	−1.00%	−1.57 to −0.44%***	0.00049	−6.03%

Note: *Statistically significant with *P*-value <.05; **statistically significant with *P*-value <.01; ***statistically significant with *P*-value <.001.

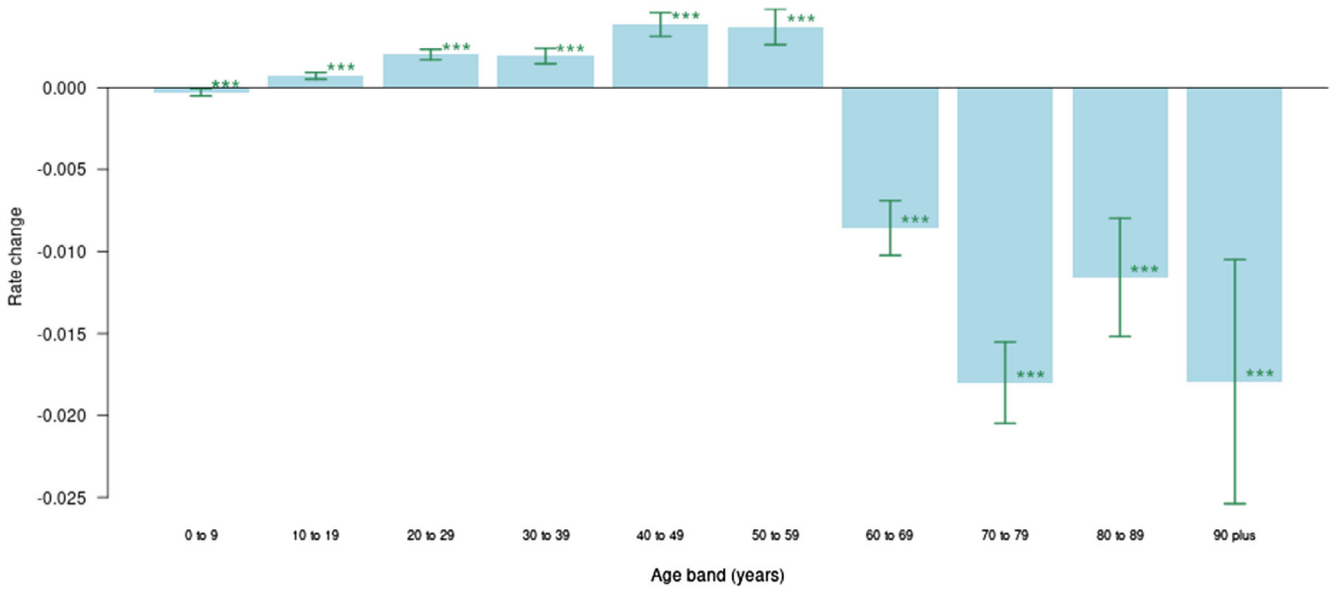

FIGURE 1 Net change of polypharmacy rates across age bands from 2014 to 2018

3.2 | Growth in polypharmacy rates

Table 1 shows the proportion of each age group experiencing polypharmacy in each year. To investigate the difference across the 5-year period the change in the rate between 2014 and 2018 was calculated. Between 2014 and 2018, higher rates of growth were observed in those aged 20 to 60 (percentage changes of 24.49%, 30.37%, 12.19% 9.21%, and 3.56% respective to each age band from 20s to 50s) compared to those 60+ years (percentage changes of −3.74%, −4.32%, −2.00%, and −2.86% respective to each age band from 60 to 90+), whose rates decreased during this period (Table 1 and Figure 1).

3.3 | Medicines contributing to polypharmacy

There were more differences between the 10 most commonly dispensed medicines in polypharmacy patients and all patients younger than 40 years compared to older age bands (Table 3).

In the 10 to 19 age band, three of the top 10 medicines were associated with asthma; salbutamol, fluticasone, and prednisone, from which we inferred that asthmatics make up a large proportion of polypharmacy patients in that age band.

In the 20 to 39 age band, medicines typically used in mental health: quetiapine, zopiclone, venlafaxine, and lorazepam (20-29 years) and quetiapine and zopiclone (30-39 years), were in the

TABLE 3 Commonly dispensed medicines by age band comparing all people and those with polypharmacy

Ageband	Rank	All people	People with polypharmacy
0-9	1	Paracetamol	Paracetamol
	2	Amoxicillin	Unknown
	3	Ibuprofen	Hydrocortisone
	4	Salbutamol	Salbutamol
	5	Loratadine	Cetomacrogol with glycerol
	6	Prednisolone	Loratadine
	7	Cetomacrogol with glycerol	Prednisolone
	8	Hydrocortisone	Ibuprofen
	9	Cefalexin	Water
	10	Chloramphenicol	Hydrocortisone butyrate
10-19	1	Paracetamol	Salbutamol
	2	Ibuprofen	Insulin aspart
	3	Amoxicillin	Methylphenidate hydrochloride extended-release
	4	Salbutamol	Omeprazole
	5	Flucloxacillin	Methylphenidate hydrochloride
	6	Loratadine	loratadine
	7	Methylphenidate hydrochloride extended-release	Cetirizine hydrochloride
	8	Ethinyloestradiol with levonorgestrel	Ethinyloestradiol with levonorgestrel
	9	Cetirizine hydrochloride	Fluticasone propionate
	10	Amoxicillin with clavulanic acid	Prednisone
20-29	1	Paracetamol	Paracetamol
	2	Ibuprofen	Quetiapine
	3	Amoxicillin	Zopiclone
	4	Ethinyloestradiol with levonorgestrel	Omeprazole
	5	Salbutamol	Tramadol hydrochloride
	6	Amoxicillin with clavulanic acid	Codeine phosphate
	7	Codeine phosphate	Ibuprofen
	8	Tramadol hydrochloride	Salbutamol
	9	Flucloxacillin	Venlafaxine
	10	Cetirizine hydrochloride	Lorazepam
30-39	1	Paracetamol	Paracetamol
	2	Ibuprofen	Omeprazole
	3	Amoxicillin	Quetiapine
	4	Salbutamol	Zopiclone
	5	Omeprazole	Codeine phosphate
	6	Amoxicillin with clavulanic acid	Tramadol hydrochloride
	7	Codeine phosphate	Salbutamol
	8	Tramadol hydrochloride	Ibuprofen
	9	Diclofenac sodium	Metformin hydrochloride
	10	Prednisone	Prednisone
40-49	1	Paracetamol	Paracetamol
	2	Ibuprofen	Omeprazole

(Continues)

TABLE 3 (Continued)

Ageband	Rank	All people	People with polypharmacy
	3	Omeprazole	Atorvastatin
	4	Salbutamol	Metformin hydrochloride
	5	Amoxicillin	Cilazapril
	6	Atorvastatin	Zopiclone
	7	Zopiclone	Salbutamol
	8	Prednisone	Aspirin
	9	Tramadol hydrochloride	Tramadol hydrochloride
	10	Diclofenac sodium	Codeine phosphate
50-59	1	Paracetamol	Atorvastatin
	2	Atorvastatin	Paracetamol
	3	Omeprazole	Omeprazole
	4	Cilazapril	Aspirin
	5	Aspirin	Metformin hydrochloride
	6	Metformin hydrochloride	Metoprolol succinate
	7	Ibuprofen	Cilazapril
	8	Metoprolol succinate	Salbutamol
	9	Salbutamol	Prednisone
	10	Prednisone	Ibuprofen
60-69	1	Atorvastatin	Atorvastatin
	2	Aspirin	Aspirin
	3	Omeprazole	Omeprazole
	4	Paracetamol	Paracetamol
	5	Metoprolol succinate	Metoprolol succinate
	6	Cilazapril	Metformin hydrochloride
	7	Metformin hydrochloride	Cilazapril
	8	Colecalciferol	Colecalciferol
	9	Levothyroxine	Simvastatin
	10	Felodipine	Felodipine
70-79	1	Atorvastatin	Aspirin
	2	Aspirin	Atorvastatin
	3	Omeprazole	Omeprazole
	4	Paracetamol	Paracetamol
	5	Metoprolol succinate	Metoprolol succinate
	6	Cilazapril	Colecalciferol
	7	Colecalciferol	Cilazapril
	8	Simvastatin	Metformin hydrochloride
	9	Metformin hydrochloride	Simvastatin
	10	Felodipine	Furosemide [Frusemide]
80-89	1	Paracetamol	Paracetamol
	2	Aspirin	Aspirin
	3	Metoprolol succinate	Metoprolol succinate
	4	Omeprazole	Omeprazole

TABLE 3 (Continued)

Ageband	Rank	All people	People with polypharmacy
	5	Colecalciferol	Colecalciferol
	6	Atorvastatin	Atorvastatin
	7	Furosemide [Frusemide]	Furosemide [Frusemide]
	8	Docusate sodium with sennosides	Docusate sodium with sennosides
	9	Cilazapril	Cilazapril
	10	Simvastatin	Simvastatin
90 plus	1	Paracetamol	Paracetamol
	2	Amoxicillin	Colecalciferol
	3	Colecalciferol	Furosemide [Frusemide]
	4	Furosemide [Frusemide]	Aspirin
	5	Aspirin	Docusate sodium with sennosides
	6	Omeprazole	Omeprazole
	7	Docusate sodium with sennosides	Metoprolol succinate
	8	Metoprolol succinate	Levothyroxine
	9	Amoxicillin with clavulanic acid	Cilazapril
	10	Salbutamol	Zopiclone

Note: Yellow highlights show the differences in medicines use between those with polypharmacy and those without.

TABLE 4 Rates of medicine use separated by ethnic groups

Ethnicity	Rate 2014	Rate 2018	Net rate change 2014 to 2018	95% confidence interval	*P* value	Percentage rate change
Maori	0.06	0.06	0.00	0.003-0.005 ***	2.10E-24	0.07
Pacific Islander	0.07	0.08	0.01	0.010-0.013 ***	1.07E-74	0.17
Asian	0.06	0.06	0.00	0.001-0.002 ***	8.05E-04	0.03
MELAA	0.05	0.05	0.00	–0.002-0.003	8.61E-01	0.00
NZ European/Other	0.11	0.12	0.01	0.011 to 0.012 ***	0.00E+00	0.11

Note: *Statistically significant with *P*-value <.05; **statistically significant with *P*-value <.01; ***statistically significant with *P*-value <.001.

TABLE 5 Rates of medicine use separated by ethnic groups if at least one medicine has been dispensed

Ethnicity	Rate 2014	Rate 2018	Net rate change	95% Confidence interval	*P* value	Percentage rate change
Maori	0.26	0.26	0.01	0.002 to 0.008 ***	.001	0.02
Pacific Islander	0.30	0.31	0.01	0.005 to 0.014 ***	.000	0.03
Asian	0.24	0.24	0.00	–0.001 to 0.006	.100	0.01
MELAA	0.20	0.20	0.00	–0.006 to 0.012	.538	0.01
NZ European/Other	0.27	0.28	0.01	0.006 to 0.008 ***	.000	0.03

Note: *Statistically significant with *P*-value <.05; **statistically significant with *P*-value <.01; ***statistically significant with *P*-value <.001.
[a]Middle Eastern, Latin American, African.

polypharmacy group's top 10 medicines but not in the general populations.

Metformin hydrochloride featured in the polypharmacy's top 10 medicines for both the 30 to 39 and 40 to 49 age bands but not in the general population.

3.4 | Ethnic differences in polypharmacy

Differences in the rates of polypharmacy were observed when people were separated by ethnic groups (Table 4). New Zealand European's had the greatest rate at 11.82% (95% CI 11.78%-11.85%) and while

MELAA had the lowest at 4.72% (95% CI 4.57%-4.87%). However, by only including people who had been prescribed at least one medication, to attempt to account for access to treatment, the rates became far more similar (Table 5). All ethnicities saw a slight increase in the rate of polypharmacy from 2014 to 2018, these were statistically significant for all ethnicities except MEELA .

4 | DISCUSSION

Although there are a number of large-scale polypharmacy studies, this is one of the few to report polypharmacy rates for a country's entire population, allowing us to see for the first-time the full extent of polypharmacy[22.9] The overall rate of polypharmacy in New Zealand continues to increase through contributions from young adults, however, this rate has slowed compared to previous publications[13.5]

Our findings are comparable to those reported by bpac[nz] in 2014, who reported polypharmacy rates of 11.2% for 2013/2014. We attempted to use the same definitions and inclusion criteria to be able to directly compare the rates, however, we included paracetamol and ibuprofen in those older than 9 years, unlike the bpac[nz] report.[13] These medicines were included because they are commonly taken long-term[23] and have the potential for harm[24.25]

The prevalence of polypharmacy in this study (46.6%) is comparable to that of other studies, although slightly higher. For example, 36.1% of Australians (over 70 years), 27% of Canadian seniors, and 28.6% of Scottish seniors have been reported to experience polypharmacy,[21,2627] . As discussed earlier, differing definitions of polypharmacy make direct comparisons difficult and that these studies only sampled from older populations, but it does show countries with similar population demographics and health policies, are facing comparably high rates of polypharmacy.

There is little information available on the prevalence of polypharmacy or its effects in the general pediatric population.[28] Most of the literature on the prevalence of polypharmacy in children focuses on specific conditions such as psychiatry[2911.30] Similar to adult studies, a widely accepted definition is lacking[12] and the true impacts of polypharmacy in children are rarely studied since they are rarely included in the drug development process.[31] International programes such as "Choosing Wisely" have called for more studies, like ours, to address this gap.[28]

4.1 | Polypharmacy by age

The increase in the rate of polypharmacy across age bands was expected. As people age, they develop more conditions and take more medicine, hence the rate of polypharmacy increases.[32] Our findings agree with the literature regarding polypharmacy rates as people age; given that life expectancy is increasing, the problem of polypharmacy is likely to worsen[3322.4]

The reduction in the rate of polypharmacy growth in those older than 60 years potentially shows that our current methods of minimizing polypharmacy, such as avoiding systematic prescribing, considering nonpharmacological treatments first line, questioning adherence before increasing doses, and carrying out medicine reviews, are working in the groups most commonly associated with polypharmacy.[34] In New Zealand, there has been a strong national push to create awareness around the impact of polypharmacy in elderly populations,[13,.35] However, the growth in younger age bands, causing the overall rates to increase, shows that we need to consider polypharmacy in all age groups to control its increase.

While the elderly appear to be at greater risk of adverse drug events, age has not been established as an independent risk factor,[36,37.38] However, the increasing number of young people with polypharmacy is reason enough to intervene to prevent it from becoming a large-scale issue.[28] Growth rates and development in children influence pharmacokinetics and the high-level use of off-label drugs on this population potentially increases the likelihood of adverse effects[39.40] A recent scoping review describing the outcome measures assessed in pediatric polypharmacy identified 363 studies. Most studies (73%) reported on harms (adverse event, adverse drug reaction, and side effect) however, no conclusion was made regarding the outcomes of these adverse effects. This leaves clinicians with the task of determining up the benefit vs harms ratio. With what appears to be an increasing trend in pediatric polypharmacy, the creation of thorough guidelines and pediatric-focused initiatives would be useful.[41]

The lack of information regarding polypharmacy in young people means that we do not know if typical interventions would be effective or if novel methods need to be developed and trialed. One possibility is raising awareness of medicines at high risk of causing adverse effects; analgesics, antiepileptics, antibacterials, systemic antimycotics, corticosteroids, and immunosuppressants. Although not all of these are possible to reduce, awareness could help clinicians to put closer monitoring in place or provide comprehensive patient information around adverse effect detection.[28,42] This is an interesting area with the potential for further research.

4.2 | Ethnicity and polypharmacy

New Zealand, like many OECD countries, has a major issue with medicines inequities[43]; the differences observed between ethnic groups may be due to access to treatment.[44] The rates of polypharmacy among people who had received at least one medicine were much more similar as shown in Table 4, leading to the potential explanation that well-documented differences in access to medicines between ethnicities are contributing to the differing rates of polypharmacy rather than the effect of interventions.[45]

4.3 | Strengths and limitations

The polypharmacy rates presented here are conservative estimates, as only medicines which had been prescribed and dispensed three or

more times throughout the year were included. Given 3 months is the standard period of supply for a prescription[18] we are only capturing long-term treatments that patients have taken for the majority of the year, and intentionally missing a lot of short-term treatments or trials of drugs which also contribute to a patients medicine burden.

As a result, it is possible that people who started long-term medications later in the year would not have been included as there was not enough time for them to collect three prescriptions. We expect this exclusion will balance out with people who stop a medication after already collecting three scripts in the year. Therefore, only people on the boundary of five or 10 medicines would have affected our reported figures.

This is a nationwide study of approximately 96% of New Zealand's population, and thus, reducing sampling bias that is seen in many large polypharmacy prevalence studies[22.9]

We excluded hospital inpatient medicine, over-the-counter medicine, and herbal or dietary products. Some of these can have serious impacts on a patient's health and could increase the polypharmacy rates. We have also assumed that patients who were dispensed these medicines actually take them and, therefore, have not factored in non-adherence.

4.4 | Practice implications

An elderly patient with several conditions could easily be indicated for five medicines[146] However, it would be much less likely for hyper-polypharmacy to be the optimal treatment.[7] The real concern is less so with polypharmacy and more so to do with the inappropriate prescribing associated with it[47.48] The only way to determine if polypharmacy is appropriate or not is to extensively review a patient's medical history. The result of this process would likely differ in many cases between different health professionals, depending on their personal opinion. Therefore, it is impractical to calculate the proportion of those with inappropriate polypharmacy at a population level, and we are assuming that they made up a constant proportion of total polypharmacy and increasing comparatively across years.

It is difficult to determine when the harms outweigh the benefits of a patient's treatment regime. There are many factors to consider when reviewing a patient's medicine.

1. Prescriptions are very poor at stating what indication the medicine is being taken for.[49]
2. It is common for patients to have multiple prescribers. Without a universal shared care record in New Zealand, it is often unknown when or why a patient is taking a particular medicine.[2] Patients on 5 to 9 medicines had an average of 3.2 prescribers while those with 10 or more medicines had an average of 4.3 prescribers, per a 2014 BPAC report.[13]
3. It is often hard for a clinician to determine if a patient's medicine is harmful or beneficial due to the lack of communication between the healthcare team, and not wanting to override someone else's decisions makes them unlikely to remove the medicine.[47]

Practically, it is unrealistic to expect clinicians to be able to review all 466 379 people with polypharmacy when you consider that is nearly a tenth of patients in New Zealand. It would be more useful if we were able to automatically triage patients into review services, taking into account factors such as: "inappropriate prescribing," hyper-polypharmacy, and adverse event occurrence. As artificial intelligence and clinical decision support tools continue to become more sophisticated and become able to effectively and efficiently undertake such reviews, we need to determine how best to integrate this into current workflows and funding models to ensure improved patient outcomes[50.51]

5 | CONCLUSION

Our study found that polypharmacy is a major issue in New Zealand. Significant rates of polypharmacy are found in all age groups and not just the elderly, although rates do increase significantly with age. While the rates are lower than in the 2014 bpac^{nz} report, the continued increase is concerning, particularly in younger age groups. Reductions are being seen in elderly, which may indicate that the focus of clinicians and literature on those populations is effective. This highlights the need to expand our focus and understanding that polypharmacy can affect any age groups. While younger patients tend to be more durable and less affected by taking multiple medicines, it would not be best practice to unnecessarily expose them to this risk. Our current practices need to be supported and improved to keep up with the large numbers of patients and to prevent the rate of polypharmacy increasing any further.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: James Nind, Alesha Smith
Data curation: Alesha Smith
Formal analysis: James Nind, Benoit Auvray
Investigation: James Nind
Methodology: Alesha Smith
Visualization: Benoit Auvray
Writing—original draft preparation: James Nind
Writing-review and editing: Alesha Smith, Manjula Devananda, Benoit Auvray

All authors have read and approved the final version of the manuscript.

James Nind had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

James Nind affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the New Zealand Ministry of Health. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors www.airmed.co.nz with the permission of The Ministry of Health, New Zealand. Instructions on how to obtain data can be obtained from https://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections. On request, data from national collections can be made available to researchers and the public.

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