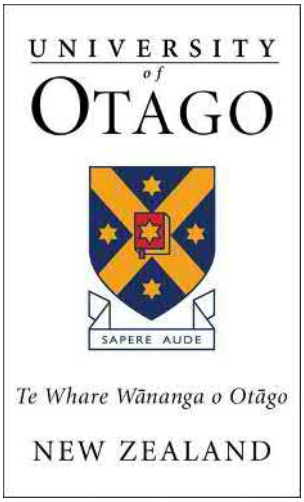

Equity of Access for Exceptional Circumstances (NPPA) Applications

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ABSTRACT

Systemic inequities in access and outcomes exist between socio-demographic groups in New Zealand. This study sought to describe inequities within the Named Patient Pharmaceutical Assessment, one of PHARMAC's exceptional circumstances schemes. The study population comprised 5903 eligible patient applications in NPPA database from March 2012 to November 2017.

Sociodemographic variables examined were ethnicity, deprivation level, age, gender and geographic region. These were analysed in terms of total and funded application rates, and the consequent success rate.

There were statistically significant differences between sociodemographic groups. Māori, Pacific peoples and Asian groups had lower total application rates but higher success rates than the NZEuropean/Other. In terms of deprivation, quintile 2 had a lower total application rate than quintile 1 (the least deprived) and 5 (the most deprived). Females had a higher total application rate but were less successful than males.

Given the higher health burden in general of Māori, and those in higher socioeconomic deprivation, to achieve equity we might expect consequently higher total application rates for these groups. This was not the case and so this signals possible inequity in access to the NPPA scheme. Within the NPPA scheme, the higher success rates of Māori and Pacific peoples signals they are treated equitably and this may be the result of them having higher unmet health need and creating more exceptional clinical circumstances. Any inequity in access to NPPA compromises PHARMAC's ambition to secure the best health outcomes for all New Zealanders.

INTRODUCTION

Inequities in access to care and health outcomes exist within the health system. These inequities align with socio-demographic characteristics. Māori in New Zealand frequently have poorer access and health outcomes than the New Zealand European population. Similar differences are seen for those with living in a high deprivation level and in rural as opposed to urban New Zealand (1).

The Pharmaceuticals Management Agency, PHARMAC, is the Government agency that evaluates and decides publicly funded medicines in New Zealand (2). The cost of medicines has soared over the last 40 years and PHARMAC was formed in 1993 in response to this. Its statutory objective is ensuring that New Zealanders secure the best health outcomes from the Government spending on medicines (3,4).

Alongside managing the pharmaceutical schedule for subsidised medicines, PHARMAC has a legislative obligation to operate an 'Exceptional Circumstances' scheme (5). One arm of this is the Named Patient Pharmaceutical Assessment, NPPA, process which is designed to assess medicines access for individual patients with exceptional clinical circumstances (5). A prescriber applies on behalf of the patient for a treatment that is not on the pharmaceutical schedule either at all or for the indication warranted. The principles of NPPA are 1. a pathway to consider those whose clinical circumstances cannot be met through the Pharmaceutical Schedule at a given point in time; 2. complementing (not undermining) the Pharmaceutical Schedule and the Schedule decision-making process; 3. individual assessment (not groups of patients) (6,7). Application must meet all three principles, and if does it is further evaluated using PHARMAC's Factors for Consideration (7). NPPA started in March 2012 and this study follows up an audit of the NPPA precursor (8).

This studentship project was born out of PHARMAC's development of three bold strategic goals - specifically the first goal: 'Eliminating inequities in access to medicines by 2025'. These goals were developed to guide PHARMAC's future work, and if achieved will substantially benefit New Zealand's health system. This project's focus is on the NPPA pathway, to determine and describe inequities in access by socio-demographic characteristics. The null hypothesis is that that there will be no inequities within the NPPA, unlike those seen throughout the health system. Inequities within the NPPA would compromise PHARMAC's objective of achieving the best health outcomes for New Zealanders.

MATERIALS AND METHODS

Study Design and Population.

This study was an audit of the Medical Authority Database, MAD, being the PHARMAC database where the NPPA applications and documentation is stored securely and confidentially. Applications made from 1 March 2012 to 15 November 2017 were eligible for inclusion in the audit. For the audit's exclusion criteria (ie those cases not included in the audit), see the Endnote 1.

Outcomes

The outcomes considered in this audit were the total application rate, the total funded rate and the success rate. In MAD, there were eight possible outcomes (Endnote 1), and for analytical purposes three new outcomes were generated by combining variables into 'Funded', 'Not Funded' and 'Pending' applications.

Numerator Data

The variables present in the MAD were examined (Endnote 2); of these variables the following were considered the useful for this audit: DHB of Patient, NZ Deprivation Index, Gender and Patient Age.

Table 1: Ethnicity Grouping and Prioritisation

Modified Ethncity Prioritisation		
Level 2	Modified Level 1	Priority Level
NZ Māori	Māori	1
Tokelauan	Pacific Peoples	2
Fijian	Pacific Peoples	2
Niuean	Pacific Peoples	2
Tongan	Pacific Peoples	2
Cook Island Māori	Pacific Peoples	2
Samoan	Pacific Peoples	2
Other Pacific Peoples	Pacific Peoples	2
South East Asian	Asian	3
Indian	Asian	3
Chinese	Asian	3
Other Asian	Asian	3
Middle Eastern	NZEuropean/Other	4
Latin American	NZEuropean/Other	4
African	NZEuropean/Other	4
Other	NZEuropean/Other	4
Other European	NZEuropean/Other	4
NZ European/Pākehā	NZEuropean/Other	4
Not Stated	NZEuropean/Other	4

Ethnicity is not part of the data collected for NPPA and is not stored. Ethnicity was considered an important variable to investigate. The patient national health index (NHI) number is included within MAD, and in the Ministry of Health NMDS database up to three ethnicities are attached to an NHI. Using the NHI Look Up Service, the three stored ethnicities were extracted. The NHI ethnicity data was coded at a level-2 ethnicity (Endnote 6) and this was re-coded to level-1 ethnicity. In order to match to relevant NZ national census or PHO enrolment denominator data, the NZ European, MELAA and Other ethnicities were incorporated into a new variable called NZEuropean/Other. The ethnicity variable was prioritised. The four ethnicities finally used in this analysis were: Māori, Pacific Peoples, Asian, and NZ European/Other.

Table 2: DHB Network

DHB Network	
DHB	DHB Network
Northland	Northern
Waitemata	Northern
Auckland Counties	Northern
Manukau	Northern
Waikato	Midland
Bay of Plenty	Midland
Lakes	Midland
Tairawhiti	Midland
Taranaki	Central
Whanganui	Central
Hawke's Bay	Central
MidCentral	Central
Wairarapa	Central
Hutt Valley	Central
Capital & Coast	Central
Nelson	Southern
West Coast	Southern
Canterbury	Southern
South Canterbury	Southern
Southern	Southern

Patient DHB was selected as each patient's geographic region. In this audit, this was the DHB in which the patient was recorded as permanently residing. A new DHB Network variable was developed by grouping the DHB's into regional groups using the regional cancer network's of Northern, Midland, Central and Southern. The DHB network was the geographic variable analysed (9).

The New Zealand Deprivation (NZDEP) Index 2013 was used as a measure of the patient's deprivation level (10). NZDEP2013 measures the deprivation score of a small geographic location based on a variety of socio demographic/economic factors. Each individual patient was assigned the NZDEP2013 score of their resident area. This audit used NZDEP score quintiles (NZDEP2013 1-2,3-4,5-6,7-8,9-10) rather than centiles (NZDEP2013 1,2,3,4,5,6,7,8,9,10), to simplify the analysis. Quintile 1 is the score assigned to the least socioeconomically deprived areas and quintile 5 is assigned to the most deprived (10).

Gender was recorded in the database as either female, male or indeterminant. In some instances, this information was missing from MAD. If unable to be found, then the patient's name was evaluated between the student and a NPPA funding co-ordinator to assign gender probabilistically.

Age, in years, of the patient at the time of the application was grouped into age groups (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+) according to the 2001 Māori age structure and the denominator age structure to allow age standardisation of the other variables to the 2001 Māori age structure (11,12).

Denominator Data

The denominator data was population level and was based on the 2013 and prior censuses and It included data for the denominator variables from 2001-2016 that were used. It was obtained by PHARMAC from the Ministry of Health.

Age standardisation

The data was age standardised to the 2001 Māori population (11,12,13).

Analysis

Bivariate statistical analysis was performed in Microsoft Excel 2016. Initially age specific rates were calculated for each variable: Ethnicity, DHB network, NZDEP2013 quintile, Gender and Age-group (13,14,16). These were then age standardised to the 2001 Māori population by applying the 2001 Māori age group specific proportion to each age group and summing the total to derive the age standardised rate. These age standardised rates were then used to calculate the rate ratios for each variable by 95% confidence intervals for rate ratios for age standardised rates for funded and total rates and success rate of ethnicity, DHB network and NZDEP quintile; these were calculated using NZEuropean/Other, Central

network, and Quintile 1 as the reference comparators (13,14,16). We did not undertake poisson regression multivariate analysis of total application rates or logistic regression multivariate analysis of success rates.

Common Indications and Medicines

Lists of the top 20 indications and medicines were generated from the database. The data required cleaning due to spelling errors, abbreviations, and multiple names for same condition.

RESULTS

Number of Applications and Percentage Funded by Year

Overall there were 7762 total applications in the NPPA pathway from 1 March 2012 to 15 November 2017. There were 455 (6%) automatic applications and 7307 (94%) manual applications. Within the manual applications, there were 5903 (80.8%) initial applications (32 pending) and 1404 (20.2%) renewal applications. The success rate of the renewal applications was 94.5% and were excluded from further analysis due to this very high rate. Twenty five percent of funded manual initial applications go onto be renewed at least once.

The year with the lowest total applications (942, see Table 1) was 2012, this was the year the NPPA pathway began. The total applications were highest in 2013 at 1220 and from then on, the total steadily reduced to 832 in 2017. For funded applications, the year 2013 had the highest number at 738 and since then had dropped consistently to 323 in 2017. Conversely, the number of not funded applications had increased since 2012 and reached its highest value in 2017 at 509. Of these total applications, 1183 (24%) were not processed further as they did not meet the principles of NPPA. Overall, the average success rate for NPPA has been 56%

Table 3: Annual NPPA Applications and Outcome

Year	Funded Initial		Not Funded Initial		Total Applications
2012	574	75%	188	25%	762
2013	738	60%	482	40%	1220
2014	681	58%	487	42%	1168
2015	552	57%	411	43%	963
2016	429	46%	497	54%	926
2017	323	39%	509	61%	832
Overall	**3297**	**56%**	**2574**	**44%**	**5871**

Table 4: NPPA Applications by Outcomes

Outcome	Individual Outcome							
	Approved	Declined	Internal Assessment	No further Info Received	Prerequisites Not Met	Principles Not Met	Withdrawn	Total NPPA
Funded NPPA	3297(56%)							3297(56%)
Not Funded NPPA		129(2%)		280(5%)	527(9%)	856(15%)	782(13%)	2574(44%)
Pending			32(1%)					32(1%)
Total NPPA	3297	129	32	280	527	856	782	5903

Demographics of NPPA Applications

Seventy three percent of applicants were in the NZEuropean/Other ethnicity group, and Pacific peoples were the smallest group at 6%. This distribution was very similar to the New Zealand 2013 census ethnicity structure, where ethnicity was reported by 75% of the population as NZEuropean/Other 75%, Māori at 15%, Asian 12% and Pacific peoples 7% (15). The greatest number of NPPA applications were for patients between 50-59 years at 16% of the total and the 80+ year group had the lowest percentage of

applications at 4%. The majority, 55%, of applications were for patients aged between 40-79 years. The median age of New Zealand is 38.0 years, younger than the 44.0 year median NPPA application age. Applications from females comprised 52% of total applicants, similar to the female gender prevalence in the general population (females 51.7%). In terms of NZDEP2013 measures of socioeconomic deprivation of domicile, each quintile contributed similarly with quintile 1 (20%) the highest and quintile 2 the lowest at 17%. Most patients resided in the Northern DHB network (38%) and the least applications came from Central at 18%.

Table 5: NPPA Application Demographics and Outcomes

NPPA Demographics	NPPA Outcome				
Variable	**Funded**	**Not Funded**	**Pending**	**Total**	**Total %**
Ethnicity					
Māori	506	297	3	806	14%
Pacific Peoples	223	110	1	334	6%
Asian	262	142	5	409	7%
NZEuropean/Other	2303	2012	23	4338	73%
Missing	3	13	0	16	0%
NZDEP Quintile					
1	677	499	5	1181	20%
2	550	472	7	1029	17%
3	594	476	12	1082	18%
4	632	506	5	1143	19%
5	677	453	3	1133	19%
Missing	167	168	0	335	6%
DHB Network					
Central	610	455	3	1068	18%
Midland	670	553	3	1226	21%
Northern	1277	942	17	2236	38%
Southern	740	624	9	1373	23%
Gender					
Male	1660	1179	13	2852	48%
Female	1637	1394	19	3050	52%
Indeterminate	0	1	0	1	0%
Age Range					
0-9	683	178	0	861	15%
10-19	335	190	0	525	9%
20-29	283	205	0	488	8%
30-39	283	216	0	499	8%
40-49	344	362	0	706	12%
50-59	496	460	0	956	16%
60-69	455	444	0	899	15%
70-79	308	374	0	682	12%
80+	109	145	0	254	4%
Missing	1	0	32	33	1%

Top 20 Medicines and Indications in NPPA

The greatest number of NPPA applications were made for rituximab (n=284). This is a chimeric monoclonal antibody against the cell surface protein CD20 which is primarily found on the surface of B-cells. Binding of rituximab to CD20 triggers cell death and this is an important medicine in the treatment of diverse haematological, oncological and autoimmune conditions (15). Overall, the top 20 medicines comprised 33% of the total applications and they had an average funding approval success rate of 71%. The highest success rates (97%) were for alpha tocopheryl acetate (vitamin-E supplement) and teniposide (a chemotherapy agent).

Multiple myeloma had the greatest number (105) of NPPA applications. This is a cancer of the immunoglobulin producing B-cells. Overall, the top 20 clinical indications comprised 11% of the total conditions applied for. The top 20 indications had an average funding success rate of 63%. The highest success rates (100%) were for multidrug resistant tuberculosis.

Table 6: Top 20 Medicine NPPA Applications

Top 20 Medicines	**Outcome**				
Medicine	**Funded**	**Not Funded**	**Pending**	**Total**	**Success Rate**
Rituximab	179	103	2	284	63%
Alpha tocopheryl acetate	207	4	3	214	97%
Cinacalcet	90	39		129	70%
Enoxaparin	71	42		113	63%
Temozolomide	88	16		104	85%
Moxifloxacin	71	25	1	97	73%
Cyclosporin	71	16		87	82%
Rifaximin	70	15		85	82%
Ribavirin	71	6		77	92%
Pregabalin	6	71		77	8%
Pemetrexed	68	9		77	88%
Voriconazole	58	16		74	78%
Plerixafor	58	16		74	78%
Levonorgestrel	21	49		70	30%
Tacrolimus	51	17	1	69	74%
Adalimumab	28	37	3	68	41%
Teniposide	63	2		65	97%
Eltrombopag	41	16		57	72%
Aflibercept	7	47		54	13%
Progesterone	45	8		53	85%
Top 20	**1364**	**554**	**10**	**1928**	**71%**
Top 20/Total	**33%**				

Table 7: Top 20 Indications NPPA Applications

Top 20 Indications	Outcome				
Indications	Funded	Not Funded	Pending	Grand Total	Success Rate
Multiple Myeloma	68	36	1	105	65%
Neuroendocrine Tumour	72	21		93	77%
Cystic Fibrosis	77	14		91	85%
Mesothelioma	69	3		72	96%
Hepatic Encephalopathy	60	3		63	95%
Hypertension	3	49		52	6%
Menorrhagia	17	31		48	35%
Multiple Sclerosis	8	35		43	19%
Hepatitis C	25	18		43	58%
Liver Disease	38		2	40	95%
Diabetes Type 1	17	23		40	43%
Neuropathic Pain	5	27		32	16%
Short Gut Syndrome	28	1		29	97%
Oral Mucositis	23	5		28	82%
Aplastic Anaemia	25	3		28	89%
Rheumatoid Arthritis	4	23		27	15%
Recurrent Respiratory Papillomatosis	23	2	1	26	88%
Age Related Macular Degeneration	1	25		26	4%
Melanoma	3	22		25	12%
Multi-drug Resistant Tuberculosis	25			25	100%
Top 20	**591**	**341**	**4**	**936**	**63%**
Top 20/Total	**16%**				

Variables

Total Application Rates.

NZEuropean/Others ethnicity group had statistically significantly the highest age standardised rate of total NPPA applications at 21.2 per 100,000, whereas the Asian ethnicity group had the lowest rate at 13.0. Pacific peoples and Māori were similar at 18.7 and 18.8 respectively. In terms of NZDEP, quintile 1 was the comparator group and had 16.0 total applications, and only quintile 2 with the lowest rate of 14.0 was significantly different; the highest NZDEP rate was quintile 4 with 17.1 per 100,000 age standardised total applications. With regard to geographic (DHB network), there was no significant differences in total applications between DHB Networks (where Central Network had the highest age standardised rate at 20.9 and Southern Network had the lowest at 18.0 per 100,000). The total application rate was compared to the DHB population size and there was minimal correlation (R^2 0.1077). Female gender had a statistically higher total application rate at 9.9 compared to male at 9.4. There were no statistical differences in the total application rates between age groups; the 70-79 age-group had the highest age specific rate of 41.9 compared to ages 20-29 which had 13.5 per 100,000.

Success Rates.

Māori, Pacific peoples and Asian groups had a statistically greater age standardised success rate than the comparator group of NZEuropean/Other; Pacific peoples had the highest at 0.71 compared to NZEuropean/Other which had a rate of 0.56. There were no statistical differences in success rates amongst the NZDEP quintiles (where quintiles 3 and 4 had the lowest rate at 63% and quintile 5 had a rate of 67%). Similarly, there were no differences in the DHB regional networks success rates (the

Northern region having the highest success rate at 69% and Midland the lowest with 62%) nor by gender. Female gender had a statistically significant lower success rate than male gender at 63% compared to 66% (rate ratio 0.94 (95% CI 0.89-0.98). The 70-79 and 80+ age groups had significantly lower success rates at 45-51% than the 0-9 comparator age group (79%).

Funded Applications

Compared to NZEuropean/Other (13.4) only the Asian ethnic group had a statistically significant difference in the age standardised funded application rate of 9.3 per 100,000. The Pacific peoples had the highest rate of 13.8 per 100,000. In terms of NZDEP quintile, there was no difference the funded application rate. Quintile 5 had the highest rate at 11.4 and quintile 2 had the lowest at 9.2 per 100,000. There were no statistical differences between the networks compared to Northern network. The Central network had had the highest rate of funded applications (14.2) and Southern had the lowest at 11.6. There was no significant difference between male and female funded application rates. The 20-29 age group had a significantly lower age specific funded application rate (8.3) compared to the 0-9 age group (18.8); it was also the lowest rate. The 70-79 age group had the highest rate of 21.2 per 100,000.

Table 8: NPPA Outcome Analysis by Variable

	Age-standarised outcomes per 100,000				Rate Ratio 95% CI		
Characteristic	**Funded**	**Not Funded**	**Total**	**Success Rate**	**Funded**	**Total**	**Success Rate**
Ethnicity							
NZEuropean/Other	13.4	7.8	21.2	56%	-	-	-
Māori	12.4	6.3	18.8	65%	0.93 (0.83-1.03)	0.88 (0.81-0.96)	1.15 (1.08-1.22)
Pacific peoples	13.8	4.9	18.7	71%	1.03 (0.88-1.20)	0.88 (0.78-0.99)	1.27 (1.17-1.37)
Asian	9.3	3.8	13.0	66%	0.69 (0.60-0.80)	0.61 (0.55-0.68)	1.18 (1.09-1.28)
NZDEP Quintile							
1	10.6	5.4	16.0	66%	-	-	-
2	9.2	4.8	14.0	66%	0.86 (0.75-1.00)	0.87 (0.78-0.98)	0.98 (0.91-1.06)
3	9.4	5.6	15.0	63%	0.88 (0.77-1.02)	0.94 (0.84-1.05)	0.97 (0.90-1.05)
4	10.8	6.3	17.1	63%	1.02 (0.89-1.17)	1.06 (0.96-1.18)	0.99 (0.92-1.06)
5	11.4	5.6	16.9	67%	1.07 (0.94-1.22)	1.06 (0.95-1.17)	1.06 (0.98-1.13)
DHB Network							
Central	14.2	6.7	20.9	68%	-	-	-
Northern	12.8	6.8	19.6	65%	0.90 (0.80-1.01)	0.94 (0.73-1.20)	1.00 (0.94-1.07)
Midland	11.9	7.3	19.2	62%	0.84 (0.73-0.96)	0.92 (0.71-1.20)	0.95 (0.88-1.02)
Southern	11.6	6.4	18.0	64%	0.82 (0.71-0.94)	0.86 (0.67-1.12)	0.96 (0.89-1.03)
Gender							
Male	6.3	3.2	9.4	66%	-	-	-
Female	6.3	3.6	9.9	63%	1.00 (0.95-1.07)	1.05 (1.04-1.06)	0.94 (0.89-0.98)
Age							
0-9	18.8	4.9	23.7	79%	-	-	-
10-19	9.3	4.9	14.2	66%	0.49 (0.23-1.08)	0.60 (0.31-1.15)	0.83 (0.54-1.27)
20-29	8.2	5.3	13.5	61%	0.44 (0.19-0.99)	0.57 (0.29-1.11)	0.77 (0.48-1.24)
30-39	9.2	6.2	15.4	60%	0.49 (0.22-1.08)	0.65 (0.34-1.23)	0.75 (0.48-1.19)
40-49	10.1	9.4	19.6	52%	0.54 (0.25-1.15)	0.82 (0.45-1.50)	0.65 (0.41-1.05)
50-59	15.6	12.6	28.2	55%	0.83 (0.42-1.62)	1.19 (0.69-2.05)	0.70 (0.47-1.03)
60-69	18.5	15.3	33.8	55%	0.98 (0.52-1.87)	1.42 (0.84-2.40)	0.69 (0.48-1.00)
70-79	21.2	20.7	41.9	51%	1.13 (0.61-2.10)	1.76 (1.07-2.92)	0.64 (0.44-0.92)
80+	12.2	15.0	27.2	45%	0.65 (0.31-1.33)	1.14 (0.66-1.99)	0.56 (0.35-0.90)

DISCUSSION

NPPA is the NZ legislated mechanism for considering the medication needs of patients with exceptional circumstances (2). This study demonstrates that in application and success rates for NPPA vary across socio-demographic groups and is congruent with a commonly occurring result in health research: that in New Zealand at the system and population level there are inequities in access amongst socio-demographic groups. Therefore, there may be inequities in access exist within the NPPA pathway.

It is well documented that Māori and Pacific peoples have an overall greater health need and disease burden than other ethnic groups in New Zealand (1,19,20,21). If access was equitable in NPPA, and if higher disease burden overall extends to the rare disorders considered through NPPA, then Māori and Pacific people would be expected to have higher per capita NPPA application rates than other ethnic groups. Similarly, Māori and Pacific peoples are known to have greater barriers to accessing healthcare and this could be the most likely driver of the differences in the rates of NPPA applications between the NZEuropean/Other, Māori and Pacific groups found in this audit.

Health need (e.g years lost from premature death, quality of life loss from suffering and disability) was not assessed in this audit, and it may be that the incidence of conditions that have the highest number of NPPA applications is higher in NZEuropean/Other compared to other groups. Cystic fibrosis predominantly affects Europeans (18); this had the 3rd most NPPA applications (1.5%). However, overall disease burden is higher in Māori and Pacific peoples for most disease groups.

While the overall application rates were lower for Māori and Pacific peoples, the success rates of the Māori and Pacific peoples were greater and therefore within the NPPA they were not disadvantaged. This likely due to the consequences of high unmet health needs being reflected in the applications (19). Clinicians submit more NZEuropean/Other applications which then have lower success rates; this may indicate that clinicians are more likely submit a NPPA application when the clinical circumstances of a NZEuropean/Other patient do not met the principles of NPPA or positive consideration of Factors. Overall, only the Asian group had a lower funded application rate. This could be due to unforeseen lower health need or ethnicity related barriers to accessing NPPA.

In this study, the only the second quintile had a lower total application rate. The success rate and funded rates were the same for all quintiles. Health need, outcomes and barriers to access are significant within the most deprived groups of society. It was pleasing to see that quintiles 4 and 5 did not have lower application or success rates. However they may well have higher health need in the rare diseases considered by NPPA too and may be underserved by not having higher rates. The equivalency in rates could be due to the least deprived groups utilising both the private and public health systems. Additionally, they may have higher levels of health literacy and forthrightness in seeking out non-schedule treatments through NPPA. The patients from quintile 2 may have lower capacity to use private services and lower disease burdens resulting in lower rates of total applications.

This study did not find statistically significant differences geographically in any outcome. In terms of gender, females had higher total applications than males yet a lower success rate, for reasons unknown. There were sporadic differences in the age groups. This characteristic had large confidence intervals in each outcome so results may not be meaningful, especially across the range of diseases/conditions

applied to under NPPA. Overall the outcome rates were relatively consistent between age groups and hence there is no apparent inequity in the access.

A previous study (8) investigating data (2001-2008) from the Community Exceptional Circumstances scheme, the precursor to NPPA, reported that there were no significant differences in terms of funding rates for ethnicity, deprivation level and gender. However, rates were higher for younger applicants and those made by applicant clinicians from Auckland DHB. This finding related to the referring applicant's DHB, not the DHB of patient residence (a very different feature, given a much higher proportion of applications could be expected from applicants working at large tertiary and quaternary DHBs like Auckland DHB who see patients from smaller DHBs). This present study has produced some similar results but does differ (when comparing the odds ratio to relative risk). In this study, Asians had a lower funding rate, only 20-29 year olds had lower funding rates and there were no DHB differences in applications (8).

Limitations of the audit - see Endnote 4
Strengths of the audit - see Endnote 5

The inequities in application and success rates identified by this study may hold strong clinical relevance, and such inequity is congruent with many other studies (1). The root causes of any systematic differences need to be addressed at a structural and politico-economic level and are likely to have the most impact compared to clinical improvements (22). Action at a clinical level is not futile and it is important to highlight these and similar inequities to clinicians so that they become aware of how their own inherent biases affect their management of the patient and so access to important exceptional circumstances schemes such as NPPA is widened. NPPA is a means of funding treatment for patients with exceptional circumstances for whom the pharmaceutical schedule is unable to meet their needs. It is important that patients who have the greatest health need, poorest health outcomes and who are unable to personally funding these treatments are not deprived of access to NPPA as these are the patients who need the scheme the most. Additionally, this audit may increase the knowledge of the NPPA scheme amongst clinicians and widen the access of their patients with exceptional circumstances to medicines they previously were unable to use. It also may widen clinicians' knowledge about how the NPPA scheme functions so that applications are more appropriate to the purpose of NPPA. This would reduce the number of low quality applications, reduce clinician workload and reduce the number of disappointed patients who were inappropriate for the scheme.

CONCLUSION

This study was an audit of PHARMAC's NPPA pathway, available to patients whose clinical circumstances fall beyond the Pharmaceutical Schedule. The results signal possible significant inequities between different socio-demographic characteristics. Māori and Pacific peoples had lower age standardised rates of applications than NZEuropean/other, but once successful were more likely to be successful than NZEuropean/other. For Asians, their application rates were much lower than any other group, raising suspicion of large access inequities. For them an application was more likely to be successful than for NZEuropean. Those who are most socio-economically deprived, quintile 5, were as likely as the least deprived, quintile 1, to have an application submitted, and both groups had the same likelihood of the application being successful. There was no geographical variation in rates of applications or success rates.

Similar research could be conducted into the rest of PHARMAC's exceptional circumstances scheme, being Special Authority and Hospital Medicine Restriction Waivers.

Thanks to my sponsor, PHARMAC, I thoroughly enjoyed my time at PHARMAC and gained an immense insight into the workings of organisation that produces enormous benefit to New Zealanders.

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Conflicts of Interest,

Nil

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ENDNOTES

1) Exclusion Criteria: NPPA Rapid Hospital Assessments for urgent cases are considered within individual District Health Boards (DHBs), and DHBs' protocol-based reporting to PHARMAC on cases funded were excluded due to incomplete reporting. DHBs are required to submit a document to PHARMAC indicating this process has occurred; it is unknown how comprehensively this is done. NPPA's are automatically approved in specific circumstances such as Pharmaceutical cancer treatments for paediatric oncological and haematological conditions.. Also in exceptional market circumstances;. prednisolone sodium phosphate oral liquid and alpha tocopheryl acetate applications are automatically approved due to supplier withdrawal. Automatic applications (455) have been excluded from the audit as they are not subject to the decision-making process. Renewal NPPA applications (1404) were excluded from the audit because they do not undergo the same decision-making process that an initial application does. Renewals are granted after an initial application and so long as the patient requires the therapy, the treatment remains efficacious, there are no new funded alternatives, and any other prospective renewal criteria specific to that case are met.
2) MAD Outcomes: Approved, Declined, Internal Assessment, No Further Info Received, Prerequisites Not Met, Principles Not Met, Withdrawn
3) MAD Variables: Application Type, Process Type, Decision, Decision On, Pharmac Days, Pathway, Location, Age at Decision, Gender, NZ Deprivation Index, Therapeutic Group, Disease, Chemical, Term, Indications, DHB of Patient, Paying DHB
4) Limitations:This audit has many limitations. These relate particularly that the risk that summarising variables may conceal heterogeneity of clinical importance. The ethnicity variable was prioritised and recoded for analytical purposes and there a variety of issues with this process (23). Similarly creating DHB networks and age groups conceal data heterogeneity and characteristics (24). For the ethnicity variable in this study, ethnicity prioritisation was used. This is because it was easier mathematically easier to do this and the population denominator data which was used was already prioritised (so to avoid numerator-denominator mismatch). Since 2004 Statistics New Zealand has moved away from prioritised ethnicity in favour of a total response or sole/combination ethnicity but it has persisted in health research. There are multiple issues with using prioritised ethnicities especially in a multicultural society such as New Zealand. It creates significant information losses in representation of Pacific, Asian and European populations and in the representation of young people. There is no logic to the prioritisation except for privileging indigenous people e.g. Māori, it places one ethnicity over another, an individual's preferences are altered and violates self-identification and it biases population measures by altering all ethnicity groups except for Māori. It is difficult to tell the effect prioritising ethnicity has had on the results of this audit. When the ethnicity was acquired it was coded at prioritisation level 2 and to enable easier statistical analysis it was recoded to level 1 and European, MELAA and Other were merged into NZEuropean/Other to avoid numerator-denominator mismatch. There may have been heterogeneity within the level 2 data which has been concealed and lost by these processes and the effect of this is hard to tell. [Level 1 ethnicity recoded from] Level 2 ethnicity: [NZEuropean]: European not further defined, New Zealand European, Other European; [Māori]: Māori; [Pacific Peoples]: Pacific Peoples not further defined, Samoan, Cook Island Māori, Tongan, Niuean, Tokelauan, Fijian, Other Pacific Peoples; [Asian]: Asian not further defined, Southeast Asian, Chinese, Indian, Other Asian; [Other]: Middle Eastern,

Latin American/Hispanic, African (or cultural group of African origin), Other ethnicity, Don't know, Refused to answer, Response unidentifiable, Not stated. Similarly, amalgamating DHB's into networks simplified the analysis but may have concealed heterogeneity within the DHB's. It is difficult to know the effects of this. Additionally, there are 20 DHBs and so if 95% confidence intervals of age-standardised rate ratios are used to analysis the DHBs there is a high likelihood that a statistically significant result occurs due to chance not because of a true difference. In this study, the analysis has used age standardised rates and rate ratios, and any summary statistics such as these conceal information. If there is large heterogeneity amongst age groups, the usefulness of the summary statistics remains questionable. Similarly, when performing age standardisation careful consideration needs to be given to which standard population is used. Initially, the WHO Standard Population and the Segi World Population were used but it was later advised that the 2001 Māori population was a more appropriate standard population. As this study was examining differences in access to NPPA in NZ according to socio-demographic characteristics, it was important to consider the effects on Māori when standardising. Using the 2001 Māori population as standard more closely represents the true rates for the indigenous population. Rates standardised to the WHO and Segi reflect the rates for the non-Māori population. Using the other standards privileges the non-Māori NPPA experience altering the appearance of the potential disparities the Māori and other ethnic groups. Poisson regression and logistic regression for multivariate analyses of total application rates and success rates respectively would better control for confounding, beyond multiple bivariate analyses using age (via direct age standardisation) and single other variables.Another limitation is that New Zealand Deprivation (NZDEP) Index is a measure of socio-economic deprivation of a geographical area called a mesh block. In this study, the applicant was assigned the NZDEP2013 score of the (small) census area unit in which they lived, which is not the intention of NZDEP (10). However, it is a reasonable assumption that on average a person will have the NZDEP score of the small area they live in.

5) Strengths: The strengths of this study include that the data used were of high quality. Once the data were cleaned, NZDEP quintile had the highest number of missing data points at merely 335 or 6% of the total. DHB network and gender had no missing data points.Complete datasets minimise potential biases and provides a strong platform from which conduct analyses. The data used is also of high quality because case capture is likely to be very high to complete; most NPPA applications are made using an online form that is reliably translated into the MAD database, where applications are emailed to staff who then enter the data into MAD (and with subsequent correction by PHARMAC staff of data-entry errors when assessing applications). Any supporting documentation is associated with the application and stored therefore was accessible to find missing data points during this audit. The NPPA process has not changed throughout the time analysed by the audit and thus has high internal consistency. Other data obtained by PHARMAC from the Ministry of Health was from the 2013 and previous censuses and is high quality clean data. Another strength of the database and the study was there were no logical inconsistencies. In terms of data quality derivable from variables recorded within the MAD database, the NZDEP quintile derived variable had the highest number of missing data points at 335 or 6%, whereas DHB Network and Gender had no missing data points. All renewal applications had previously had an initial application approved. There were some medicines that were in recorded in the MAD database in multiple therapeutic groups, despite medications only being able to belong to one.

Table 9: Number of missing data points in database after data cleaning.

Missing Data	Total	%
Ethnicity	16	0%
NZDEP Quintile	335	6%
DHB Network	0	0%
Gender	0	0%
Age	33	1%
Total = 5903		