Drugs & Aging

An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019

--Manuscript Draft--

Manuscript Number:	DRAA-D-22-00056R1
Full Title:	An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019
Article Type:	Original Research Article
Funding Information:	
Abstract:	Background Psychotropic medicines utilisation in older adults continues to be of interest because of overuse and concerns surrounding their safety and efficacy. Objective This study aimed to characterise the utilisation of psychotropic medicines in older people in New Zealand. Methods We conducted a repeated cross-sectional analysis of national dispensing data from 1 January 2005 to 31 December 2019. We defined utilisation using the Anatomical Therapeutic Chemical classification /defined daily dose system. Utilisation was measured in terms of the defined daily dose (DDD) per 1,000 older people per day (TOPD). Results Overall, the utilisation of psychotropic medicines increased marginally by 0.42% between 2005 and 2019. The utilisation increased for antidepressants (72.42 to 75.21 DDD/TOPD) and antipsychotics (6.06 to 19.04 DDD/TOPD). In contrast, utilisation of hypnotics and sedatives (53.74 to 38.90 DDD/TOPD) and anxiolytics decreased (10.20 to 9.87 DDD/TOPD). The utilisation of atypical antipsychotics increased (4.06 to 18.72 DDD/TOPD), with the highest percentage change in DDD/TOPD contributed by olanzapine (520.6 %). In comparison, utilisation of typical antipsychotics was relatively stable (2.00 to 2.06 DDD/TOPD). The utilisation of venlafaxine increased remarkably by 5.7 times between 2005 and 2019. The utilisation of zopiclone was far greater than that of other hypnotics in 2019. Conclusion: There was only a marginal increase in psychotropic medicines utilisation from 2005 to 2019 in older adults in NZ. There was a 5-fold increase in the utilisation of antipsychotic medicines. Continued monitoring of psychotropic medicine utilisation will be of interest to understand the utilisation of antidepressants and antipsychotic medicines during the COVID-19 pandemic year.
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Author Comments:	We would like to oppose the following reviewer: Mohammed.Salahudeen@utas.edu.au
Response to Reviewers:	An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019 Nishtala et.al

Response to reviewers

Dear Editor,

Thank you for the opportunity to revise our manuscript and clarify the comments raised by the reviewers. We are grateful for the reviewers' useful comments to improve the manuscript, and the reviewers share our judgment that the findings of this study are interesting and important. Please see below, in blue, our detailed response to comments. All page and line numbers refer to the manuscript file in the track changed copy. Please note that only the text and title page have been track changed, and we have uploaded the updated Figures and Tables without track changes.

Reviewer #1: This is a retrospective national study on medicine utilization in New Zeeland for 022.The study has been methodologically correctly performed and nicely drafted.
Given the unusual dispensing patterns in 2020 I would suggest limiting the analysis and the report to the period 205-2019 and leave the aspect of COVID-19 out of the scope of the paper.
I would be useful to provide in the text a summary of the information from Table 1 with regard to the most prevalent agents per drug class in the last year/current situation.
Adding a brief recommendation for daily practice based on the main findings would be an added value.

Response: We have taken the reviewer's suggestions on board to limit the analyses from 2005 to 2019 and excluded the unusual dispensing patterns of 2020. Accordingly, the Tables and Figures have been updated.
We have considered the reviewer's suggestion to highlight the most prevalent psychotropic agents within their drug classes and appended a brief recommendation, wherever applicable, for daily practice in the text.

Reviewer #2: The authors conducted a study using repeated cross-sectional analysis of national dispensing in New Zealand from 2005-2020 of psychotropic use in older adults. While they found that there was a marginal increase in psychotropic utilization overall, there was a 5 fold increase in antipsychotics and a significant increase in antidepressants.

Comments:
1) This is an important analysis as it spans the epidemic period.
2) While psychotropic use overall has remained stable, the findings confirm an increase for atypical antipsychotics and antidepressants as well as decreases in use of typical antipsychotics and benzodiazepine hypnotics.

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Reviewer #3: With this work, the authors intend to describe the trends in the consumption of psychotropic drugs since 2005, in New Zealand. An analysis of consumption of these drugs is important at the level of all countries. Despite the relevance of the study, there is some information that is a little confusing. Here my comments.
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Response: We agree with the reviewer's comments, and consistent with our response to reviewer#1, we have limited our analyses from 2005 to 2019 and excluded the unusual dispensing patterns of 2020. Accordingly, the Tables, Figures and the title of the manuscript have been updated.

	We deleted the objective section and updated the title and aim of the manuscript. The first topic of the results section is not a result of this work … it seems more a justification for not use data from 2020 … Please revise the text and use the correct nomenclature for the ATC code N05C and N05B Lines 20-22 - "Important to note that PHARMAC funded melatonin in 2017, and its utilization in 2020 was remarkably high (10.98) compared to other hypnotics and sedatives." Data from 2020 or 2019??? However, consumption values in 2020 are also presented in the tables that are included in the results, but are not described in the descriptive analysis of the results. In my opinion, the article would be more interesting if the authors did an analysis of prescriptions including 2020, through adequate statistics, for example, interrupted time series, analyzing the impact of COVID on the consumption trends of these medicines. And discuss the results with publications that assess this impact in different countries. Response: In the main text, we have amended the nomenclature for ATC codes N05C and NO5B. In addition, all consumption values are compared to 2019. We share the judgment of the reviewer that an interrupted time series to understand the impact of COVID 19 on psychotropic drug consumption will be interesting. We have recently acquired data for 2021 and plan to pursue this in our next paper as we feel the 2020 data is incomplete due to the impact of COVID 19. And we also agree with reviewer#1 that the impact of COVID on psychotropic drug consumption is beyond the scope of the current study. However, we are very thankful for the reviewer's suggestion and will address the impact of COVID-19 using interrupted time series analyses in our next paper. We have deleted our discussion on melatonin as we have insufficient information on its consumption before 2020. Table 1 has a lot of information and about many drugs. Why did the authors include drugs that were withdrawn from the market? If the study aims is to analyze trends of consumption It doesn't seem necessary to include drugs that were withdrawn from the market before 2019 ... Response: We request the reviewer to allow us to keep the information for withdrawn drugs on the table as we feel it is important information for the readers to understand how psychotropic drug subsidy changed during the study period 2005 to 2019. For example, alprazolam was withdrawn in 2016 by PHARMAC due to concerns of abuse, and this information would be very useful for our readership to understand how policy or reimbursement changes could have impacted psychotropic drug consumption. Discussion section needs to be improved. Instead of analyzing by topics as presented in the result, it is necessary for the authors to analyze and compare the results in an integrated way and discuss them with possible health policies, guidelines, etc... Response: We initially considered presenting our analyses and discussing our findings in an integrated way but felt this severely impacted the flow of information. In the current format, the results and discussion are separated by topics which the readers can easily follow. A similar format was followed in our previous publication on psychotropic drug consumption, accepted in Drugs & Aging [1]. #Editorial comments: General comments: Please, provide units when discussing data Please define all abbreviations at first mention, i.e. ECG and CTc in the last sentence of section 5.2. Please check the full manuscript for undefined abbreviations. Response: Thank you. We have defined all abbreviations on the first mention and

	provided units for all data presented. References 1. Ndukwe HC, Tordoff JM, Wang T, Nishtala PS. Psychotropic medicine utilization in older people in New Zealand from 2005 to 2013. Drugs Aging. 2014;31(10):755-68. doi:10.1007/s40266-014-0205-1.
Suggested Reviewers:	Rajender Aparasu rraparasu@uh.edu Expert in pharmacoepidemiology
	Mina Tadrous mina.tadrous@utoronto.ca expert in drug safety

Cover Letter

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20 March 2022

Editor-in-chief,
Drugs & Aging

Ref: An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2020

I am pleased to submit the above manuscript to be considered for publication in Drugs & Aging.

This national study aimed to describe and characterise the utilisation of psychotropic medicines in older people in New Zealand between 2005 and 2020. This study sequels our national study on psychotropic medicine utilisation in older people in New Zealand from 2005 to 2013.

Following our study published in Drugs & Aging in 2013, antipsychotics (paliperidone) and hypnotics and sedatives (melatonin) have been introduced or psychotropics discontinued (mianserin, fluphenazine decanoate, trifluoperazine, alprazolam, and lormetazepam). An update of psychotropic utilisation in this vulnerable cohort will be of interest to researchers and clinicians in older people's health.

This work is not under active consideration for publication, has not been accepted for publication, nor has it been published, in full or in part. However, I confirm that the Human and Ethics Committee has approved the study at the University of Bath.

I attest that all authors listed on the title page have read the manuscript, agree to the validity and legitimacy of the data and its interpretation, and agree to its submission.

Author Contributions: P.N and T.C designed the study, analysed data and drafted the manuscript. All authors assisted with data interpretation and revision of the manuscript. In addition, all authors contributed to data interpretation, critically commented on the manuscript for intellectual content, and approved the final manuscript.

Yours sincerely,

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An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019

Nishtala et.al

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#Editorial comments:

General comments:
Please, provide units when discussing data
Please define all abbreviations at first mention, i.e. ECG and CTc in the last sentence of section 5.2. Please check the full manuscript for undefined abbreviations.

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References

1. Ndukwe HC, Tordoff JM, Wang T, Nishtala PS. Psychotropic medicine utilization in older people in New Zealand from 2005 to 2013. Drugs Aging. 2014;31(10):755-68. doi:10.1007/s40266-014-0205-1.

An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019

Running title: Psychotropic medicine utilisation in older New Zealanders

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Keywords: Drug utilisation; antidepressants; antipsychotics; population-level; benzodiazepines

Wordcount: 2241

Declarations: The authors have no conflict of interest.

Data Sharing

The data is owned by the Analytical Services, Ministry of Health New Zealand, and hence we cannot share raw data for this study.

Author Contributions

Study concept and design: Prasad S Nishtala, Statistical analysis: Prasad S Nishtala, Te-yuan Chyou; Interpretation of data: All authors; Drafting of the manuscript: Prasad S Nishtala, Critical revision of the manuscript for important intellectual content: All authors; Study supervision: Prasad S Nishtala.

Abstract

Background Psychotropic medicines utilisation in older adults continues to be of interest because of overuse and concerns surrounding their safety and efficacy.

Objective This study aimed to characterise the utilisation of psychotropic medicines in older people in New Zealand.

Methods We conducted a repeated cross-sectional analysis of national dispensing data from 1 January 2005 to 31 December 2019. We defined utilisation using the Anatomical Therapeutic Chemical classification /defined daily dose system. Utilisation was measured in terms of the defined daily dose (DDD) per 1,000 older people per day (TOPD).

Results Overall, the utilisation of psychotropic medicines increased marginally by 0.42% between 2005 and 2019. The utilisation increased for antidepressants (72.42 to 75.21 DDD/TOPD) and antipsychotics (6.06 to 19.04 DDD/TOPD). In contrast, utilisation of hypnotics and sedatives (53.74 to 38.90 DDD/TOPD) and anxiolytics decreased (10.20 to 9.87 DDD/TOPD). The utilisation of atypical antipsychotics increased (4.06 to 18.72 DDD/TOPD), with the highest percentage change in DDD/TOPD contributed by olanzapine (520.6 %). In comparison, utilisation of typical antipsychotics was relatively stable (2.00 to 2.06 DDD/TOPD). The utilisation of venlafaxine increased remarkably by 5.7 times between 2005 and 2019. The utilisation of zopiclone was far greater than that of other hypnotics in 2019.

Conclusion: There was only a marginal increase in psychotropic medicines utilisation from 2005 to 2019 in older adults in NZ. There was a 5-fold increase in the utilisation of antipsychotic medicines. Continued monitoring of psychotropic medicine utilisation will be of interest to understand the utilisation of antidepressants and antipsychotic medicines during the COVID-19 pandemic year.

1 Introduction

The utilisation of psychotropic medicines in older adults (65 years or older) continues to be of interest because of overuse [1] and concerns surrounding their safety and efficacy [2, 3]. Psychotropic medicines are associated with adverse clinical outcomes in older adults, including impairments in physical and cognitive functioning [4], greater hospitalisations [5], and higher mortality risk [6]. Broadly, as a class, they can cause several adverse effects, including weight gain [7], oversedation [8], anticholinergic side effects [9], extrapyramidal symptoms [10, 11], and dependence [12, 13].

Several factors drive psychotropic utilisation, including reimbursement policies [14, 15], subsidy arrangements [16], co-payments, clinical guidelines [8], and pharmaceutical policies [17]. For example, in New Zealand (NZ), the Pharmaceutical Management Agency (PHARMAC) subsidises prescription and therapeutics, and the Royal Australian and New Zealand College of Psychiatrist's Faculty of Psychiatry of Old Age have recommended guidelines to rationalise psychotropic medicines [18, 19]. Collectively, examining psychotropic utilisation can inform research and clinical practice, help understand prescribing patterns, rates of off-label use [20], funding restrictions [21] and study the impact of regulatory warnings on prescribing [22].

This study sequels our national study on psychotropic medicine utilisation in older people in New Zealand (NZ) from 2005 to 2013 [23]. Several small-scale studies have been conducted on psychotropic utilisation in NZ. For example, in the residential care setting, Tucker and Hosford found that 54.7% of older people in the Hawke's Bay region in NZ were prescribed one or more psychotropic medicines [24]. In addition, Roberts and Norris reported an increase in antidepressant utilisation between 1993 and 1997 in all regions of NZ [25]. Similarly, Ndukwe et al. found a variation in psychotropic prescribing ranging from 7% to 74% across district health boards in NZ from 2000 to 2013 [26]. However, there is limited data on understanding the trends in psychotropic utilisation over a long period. Since the most recent study published in NZ in 2015 [23], antipsychotics (paliperidone) and hypnotics and sedatives (melatonin) have been introduced or psychotropics discontinued (mianserin, fluphenazine decanoate, trifluoperazine, alprazolam, and lormetazepam).

The aim of this study, therefore, was to provide an updated analysis to describe and characterise the national trend in the utilisation of psychotropic medicines in older people by age, sex, and type based on the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) drug classification system of psychotropic medicines used in New Zealand from 2005 to 2019.

2 Methods

This study was approved by the Human Ethics Committee of the University of Bath, United Kingdom (form number 7423).

2.1 Study design

A retrospective, national study of medicine utilisation was undertaken for those 65 years and above.

2.2 Data source

We obtained de-identified dispensing claims data for individuals aged 65 years or older for 2005–2019 from the New Zealand (NZ) Ministry of Health (MoH). The Pharms database is a national dispensing claims database maintained by the MoH, which captures subsidised prescriptions dispensed by community pharmacies in NZ. Pharms contain medicines funded by the Pharmaceutical Management Agency (PHARMAC). PHARMAC is the New Zealand government agency that decides which pharmaceuticals to fund in NZ publicly and provides funded access to pharmaceuticals for all New Zealanders [18].

2.3 Defined Daily Dose (DDD) per 1000 older people per day

A defined daily dose (DDD) is the average maintenance dose for the medicine for its main indication in adults. The WHO collaborating centre for drug statistics methodology updates DDDs every three years. It is a recommended metric for drug utilisation studies as it allows comparison across countries and regions and evaluates trends over time [27]. The DDD per 1,000 older people per day (TOPD) measures the proportion of people treated with a defined daily dose of medicine per 1,000 older people per day [8].

2.4 Psychotropic drug utilisation

Psychotropic medicines were categorised based on the Anatomical Therapeutic Chemical classification system (ATC) of the WHO collaborating centre for drug statistics methodology [28]. For this analysis, we considered antidepressants (NO6A), antipsychotics (NO5A), anxiolytics (N05B) and hypnotics and sedatives (N05C). We completed the analyses at the therapeutic and chemical levels. The total quantity dispensed for each chemical was extracted from Pharms data and converted to DDD equivalents. DDD/TOPD was derived by summing the total DDD for one year, dividing by the census population, and multiplying by 1000. For example, the value of 14 DDD for citalopram in 2005 suggests that 14 out of the 1000 older people in NZ were dispensed a standard dose of 20mg of citalopram per day. A customised census population data was extracted from NZ statistics [28].

3 Results

3.1 Overall psychotropic medicine utilisation

Psychotropic medicine utilisation was relatively unchanged from 2005 to 2019 (142.42 to 143.02 DDD/TOPD, corresponding to a 0.42 per cent increase in psychotropic utilisation (**Table 1**). In addition, utilisation increased for antipsychotics (6.06 to 19.04 DDD/TOPD) and antidepressants (72.42 to 75.21 DDD/TOPD). On the other hand, utilisation decreased for anxiolytics (10.20 to 9.87 DDD/TOPD) and hypnotics and sedatives (53.74 to 38.90 DDD/TOPD) (**Table 1, Figure 1**).

3.2 The utilisation of psychotropic medicines by age and sex

The utilisation of psychotropic medicines by age (five-year bands) and sex (DDD/TOPD) and type from 2005 to 2019 increased and peaked in the 95 years and over age group (**Figure 2**). The utilisation of antidepressants was highest among all age groups and across both sexes except for the 90-94 and 95+ age groups, where hypnotics and sedatives were higher than the utilisation of antidepressants. The utilisation of typical antipsychotics decreased across age groups in both sexes. In contrast, the utilisation of atypical antipsychotics increased remarkably across all age groups and in both sexes.

3.3 Antidepressants

The utilisation of antidepressants increased by 3.08 % from 2005 to 2019 (72.42 to 75.21 DDD/TOPD). Specifically, the utilisation of selective serotonin reuptake inhibitors (SSRIs) declined slightly (47.67 to 45.36 DDD/TOPD). In contrast, tetracyclic antidepressants (TeCA) and SNRIs increased considerably. Interestingly, the utilisation of tricyclic antidepressants (TCA) declined substantially (20.37 to 5.44 DDD/TOPD) (**Table 1, Figure 3**).

3.4 Antipsychotics

Atypical antipsychotic (AAPA) medicine utilisation increased (4.06 to 18.72 DDD/TOPD) markedly, mainly driven by olanzapine (1.31 to 8.13 DDD/TOPD) and quetiapine (0.78 to 3.99 DDD/TOPD) (**Table 1, Figure 4**). It is noteworthy that in 2014 PHARMAC funded paliperidone, and its utilisation in 2019 was 0.18 DDD/TOPD. On the other hand, the utilisation of typical antipsychotics (TAPA) is relatively low and remains almost unchanged (2.00 to 2.06 DDD/TOPD) over the study period (**Table 1, Figure 5**).

3.5 Anxiolytics

Benzodiazepines (BDZ) utilisation (9.05 to 9.68 DDD/TOPD) remained unchanged except for a rise in the use of lorazepam (5.10 to 7.00 DDD/TOPD). On the other hand, for buspirone, a non-BDZ anxiolytic medicine, the utilisation was relatively steady (0.15 to 0.19 DDD/TOPD) (**Table 1, Figure 6**).

3.6 Hypnotics and sedatives

In 2019, the utilisation of zopiclone was also relatively high (25.67 DDD/TOPD) compared to other hypnotics (13.23 DDD/TOPD). Interestingly, among the BDZ-hypnotic class, the utilisation for nitrazepam, temazepam, and triazolam decreased considerably by 85.9%, 57.0%, and 79.4 %, respectively (**Table 1, Figure 7**).

4 Discussion

4.1 Overall psychotropic utilisation

The utilisation of psychotropic medicines measured in DDD/TOPD was relatively stable in people 65 years and older in New Zealand from 2005 to 2019.

4.2 Antidepressants

The slight increase in the utilisation of SSRI antidepressants and a corresponding decrease in utilisation of anxiolytics and TCAs in our study may be driven by multiple factors, including expanding indications for SSRIs beyond the treatment of depression, including obsessive-compulsive disorders [29], panic disorders [30], chronic pain [31], and its preferential use over anxiolytics for anxiety disorders [32]. Citalopram continued to be the favoured SSRI with the highest utilisation both in 2005 and 2019. An expert consensus guideline on pharmacotherapy of depressive disorders for older adults rated citalopram the highest for efficacy and tolerability among the SSRIs [33]. The utilisation of tricyclic antidepressants decreased substantially. The increased utilisation of SNRIs and TeCAs is largely driven by venlafaxine and mirtazapine, respectively. Venlafaxine and mirtazapine are recommended second-line treatments for depression after an initial trial of an SSRI, and a systematic review found that they are more effective than paroxetine and fluoxetine [34].

Interestingly, randomised clinical trials that compared venlafaxine to other SSRIs found its safety in older adults is comparable to SSRIs, and the risk for venlafaxine-induced electrocardiogram **(**ECG) changes and corrected QT (QT_c) prolongation is low [35, 36]. In clinical practice, the selection of antidepressants in older adults must be guided by patient-specific factors such as comorbidity and susceptibility to anticholinergic effects. Citalopram and sertraline have few drug interactions, are less anticholinergic than TCAs, and are recommended for treating depression in older adults [33].

4.3 Antipsychotics

Despite the increased risk for cardiovascular and metabolic adverse effects [37, 38], the utilisation of atypical antipsychotic medicines increased (4.06 to 18.72 DDD/TOPD) in older people. However, a corresponding decline in typical antipsychotic medicines (2.0 to 2.6 DDD/TOPD) utilisation occurred because of the increased risk of extrapyramidal symptoms and the perceived benefit of better efficacy

for atypical antipsychotics [39]. Nevertheless, the preferential use of atypical antipsychotics over typical antipsychotics is a consistent finding in NZ [40] and internationally [41] despite no evidence for their superiority in terms of efficacy or safety [42]. In 2019, among the typical antipsychotic medicines, haloperidol utilisation was the highest, and among the typical antipsychotic medicines, olanzapine was the highest. Additionally, in a study comparing 16 countries, quetiapine was the antipsychotic used in most countries, followed by risperidone and olanzapine [43].

Furthermore, the increased use of atypical antipsychotics may be attributed to them often being prescribed for other mental disorders, including mood and anxiety disorders, insomnia, and agitation [44]. The utilisation of clozapine increased from 0.18 to 0.81 DDD//TOPD. An international study involving 17 countries found that clozapine is still underutilised across several countries despite increased use in recent years. The study found that Finland, followed by New Zealand, has the highest clozapine utilisation rates [45].

In older adults, the risk of anticholinergic effects, extrapyramidal symptoms, and the adverse cardiovascular effects of typical antipsychotic medicines and the risk of metabolic adverse effects posed by atypical antipsychotic medicines must be considered. Therefore, the recommendation to treat psychosis in older adults is to use low dose atypical antipsychotic medicines for the shortest possible duration and wherever feasible on a case-to-case basis to switch to non-pharmacological options [46].

4.4 Anxiolytics

Benzodiazepine (BDZ) utilisation decreased slightly. In 2019, lorazepam was the widely used benzodiazepine. In our published study in 2015, we highlighted concerns regarding using alprazolam and concerns about abuse, dependence, and tolerance [47]. Interestingly, in 2016, PHARMAC stopped funding for alprazolam for new patients [48].

4.5 Hypnotics and sedatives

Overall, the utilisation of hypnotics and sedatives has declined in NZ older adults (53.74 to 38.90 DDD/TOPD). However, zopiclone continued to be the most utilised hypnotic in 2019. The higher utilisation of zopiclone relative to other BDZs is alarming. Similar concerns of high prescribing of zopiclone in older adults relative to other BDZs were reported in Europe and England [49]. Although, in 2015, we highlighted the risk posed by zopiclone which accounted for more than 50% of utilisation of hypnotics, as it has been associated with cognitive impairment [50], confusion, and falls or fractures in older people [51], the reduction in the utilisation of zopiclone in 2019 (30.36 DDD/TOPD) compared to 2005 (26.23 DDD/TOPD) is a welcome change. However, the rising trend in the utilisation of melatonin funded by PHARMAC in 2017 should be monitored closely [52]. Although, a recent review found insufficient scientific evidence for the potential side effects of melatonin at optimal doses, particularly in older adults, where long-term use may be unavoidable [53, 54].

The high utilisation of zopiclone is of concern and could be attributed to the increased prevalence of insomnia in older adults [55, 56]. Hence, the use of zopiclone should be restricted to short-term use to mitigate harm in older adults, and non-pharmacological interventions for the management of insomnia must be given precedence as interventions based on cognitive behavioural therapy are superior to zopiclone in older adults [57].

4.6 Strengths and limitations

One limitation of the study was that the WHO uses doses for main indications to compute DDDs, but several psychotropic medicines have expanded indications. Therefore, we could not examine the appropriateness of treatment due to the lack of information on the indication for using psychotropic medicine. We also assumed that all adhered to their prescribed psychotropic regimen; hence actual utilisation may be overestimated. However, it is pertinent to highlight that the Pharmaceutical collections maintained by the MoH are comprehensive. In addition, the reimbursement system captures greater than 95% of the prescription coverage of the census population of older adults, strengthening the validity of our study findings.

5 Conclusions

In conclusion, psychotropic medicines utilisation was relatively stable from 2005 to 2019 in older adults in NZ. Though antidepressant utilisation remained relatively stable, there was a 5-fold increase in antipsychotic medicines mainly driven by the increased utilisation of atypical antipsychotics. Our findings suggest that a high proportion of older adults have been prescribed olanzapine and zopiclone, and the reasons for their use and risk-benefit ratio warrant further investigation. In addition, the rising trend in the utilisation of melatonin recently funded by PHARMAC should be monitored closely. Continued monitoring of psychotropic medicine utilisation will be of great interest to understand if the unusually high utilisation of psychotropic medicines, particularly antidepressants and antipsychotic medicines, during the COVID-19 pandemic year is temporary or will change relative to previous years and how the changes will impact the health of older adults in the long-term.

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An updated analysis of Psychotropic Medicines Utilisation in Older People in New Zealand from 2005 to 2019~~20~~

Running title: Psychotropic medicine utilisation in older New Zealanders

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Data Sharing

The data is owned by the Analytical Services, Ministry of Health New Zealand, and hence we cannot share raw data for this study.

Author Contributions

Study concept and design: Prasad S Nishtala, Statistical analysis: Prasad S Nishtala, Te-yuan Chyou; Interpretation of data: All authors; Drafting of the manuscript: Prasad S Nishtala, Critical revision of the manuscript for important intellectual content: All authors; Study supervision: Prasad S Nishtala.

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Abstract

Background Psychotropic medicines utilisation in older adults continues to be of interest because of overuse and concerns surrounding their safety and efficacy.

Objective This study aimed to characterise the utilisation of psychotropic medicines in older people in New Zealand.

Methods We conducted a repeated cross-sectional analysis of national dispensing data from 1 January 2005 to 31 December 202190. We defined utilisation using the Anatomical Therapeutic Chemical classification /defined daily dose system. Utilisation was measured in terms of the defined daily dose (DDD) per 1,000 older people per day (TOPD).

Results Overall, the utilisation of psychotropic medicines increased marginally by 0.42% between 2005 and 2019. The uUtilisation increased for antidepressants (72.42 to 75.21 DDD/TOPD), and antipsychotics (6.06 to 19.04 DDD/TOPD)., In contrast, utilisation of hypnotics and sedatives (53.74 to 38.90 DDD/TOPD) and anxiolytics decreased (10.20 to 9.87 DDD/TOPD). The utilisation of atypical antipsychotics increased (4.06 to 18.72), with the highest percentage change in DDD/TOPD contributed by olanzapine (520.6 %). In comparison, utilisation of typical antipsychotics was relatively stable (2.00 to 2.06 DDD/TOPD). The utilisation of venlafaxine increased remarkably by 5.7 times between 2005 and 2019. The utilisation of zopiclone was far greater than that of other hypnotics in 2019.

Conclusion: There was only a marginal increase in psychotropic medicines utilisation from 2005 to 2019 in older adults in NZ. There was a 5-fold increase in the utilisation of antipsychotic medicines. Continued monitoring of psychotropic medicine utilisation will be of interest to understand the unusually high utilisation of antidepressants and antipsychotic medicines, during the COVID-19 pandemic year.

1 Introduction

The utilisation of psychotropic medicines in older adults (65 years or older) continues to be of interest because of overuse [1] and concerns surrounding their safety and efficacy [2, 3]. Psychotropic medicines are associated with adverse clinical outcomes in older adults, including impairments in physical and cognitive functioning [4], greater hospitalisations [5], and higher mortality risk [6]. Broadly, as a class, they can cause several adverse effects, including weight gain [7], oversedation [8], anticholinergic side effects [9], extrapyramidal symptoms [10, 11], and dependence [12, 13].

Several factors drive psychotropic utilisation, including reimbursement policies [14, 15], subsidy arrangements [16], co-payments, clinical guidelines [8], and pharmaceutical policies [17]. For example, in New Zealand (NZ), the Pharmaceutical Management Agency (PHARMAC) subsidises prescription and therapeutics, and the Royal Australian and New Zealand College of Psychiatrist's Faculty of Psychiatry of Old Age have recommended guidelines to rationalise psychotropic medicines [18, 19]. Collectively, examining psychotropic utilisation can inform research and clinical practice, help understand prescribing patterns, rates of off-label use [20], funding restrictions [21] and study the impact of regulatory warnings on prescribing [22].

This study sequels our national study on psychotropic medicine utilisation in older people in New Zealand (NZ) from 2005 to 2013 [23]. Several small-scale studies have been conducted on psychotropic utilisation in NZ. For example, in the residential care setting, Tucker and Hosford found that 54.7% of older people in the Hawke's Bay region in NZ were prescribed one or more psychotropic medicines [24]. In addition, Roberts and Norris reported an increase in antidepressant utilisation between 1993 and 1997 in all regions of NZ [25]. Similarly, Ndukwe et al. found a variation in psychotropic prescribing ranging from 7% to 74% across district health boards in NZ from 2000 to 2013 [26]. However, there is limited data on understanding the trends in psychotropic utilisation over a long period. Since the most recent study published in NZ in 2015 [23], antipsychotics (paliperidone) and hypnotics and sedatives (melatonin) have been introduced or psychotropics discontinued (mianserin, fluphenazine decanoate, trifluoperazine, alprazolam, and lormetazepam).

The aim of this study, therefore, was to provide an updated analysis to describe and characterise the national trend in the utilisation of psychotropic medicines in older people by age, sex, and type based on the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) drug classification system of psychotropic medicines used in New Zealand from 2005 to 20192020.

~~2 Objectives~~

~~The main objective of this study was to describe and characterise the national trend in the utilisation of psychotropic medicines in older people by age, sex, and type from 2005 to 2020.~~

~~3~~2 Methods

This study was approved by the Human Ethics Committee of the University of Bath, United Kingdom (form number 7423).

~~3.1~~2.1 Study design

A retrospective, national study of medicine utilisation was undertaken for those 65 years and above.

~~3.2~~2.2 Data source

We obtained de-identified dispensing claims data for individuals aged 65 years or older for 2005–2019~~20~~ from the New Zealand (NZ) Ministry of Health (MoH). The Pharms database is a national dispensing claims database maintained by the MoH, which captures subsidised prescriptions dispensed by community pharmacies in NZ. Pharms contain~~s~~ medicines funded by the Pharmaceutical Management Agency (PHARMAC). PHARMAC is the New Zealand government agency that decides which pharmaceuticals to fund in NZ publicly and provides funded access to pharmaceuticals for all New Zealanders [18].

~~3.3~~2.3 Defined Daily Dose (DDD) per 1000 older people per day

~~Defined~~ A defined d~~D~~aily d~~D~~ose (DDD) is the average maintenance dose for the medicine for its main indication in adults. The WHO collaborating centre for drug statistics methodology updates DDDs every three years. It is a recommended metric for drug utilisation studies as it allows comparison across countries~~,~~ and regions~~,~~ and evaluat~~ion of~~es trends over time [27]. The DDD per 1,000 older people per day (TOPD) measures the proportion of people treated with a defined daily dose of medicine per 1,000 older people per day [8].

2~~3~~.4 Psychotropic drug utilisation

Psychotropic medicines were categorised based on the Anatomical Therapeutic Chemical classification system (ATC) of the WHO collaborating centre for drug statistics methodology [28]. For this analysis, we considered antidepressants (NO6A), antipsychotics (NO5A), anxiolytics ~~and hypnotics~~ (N05B) and hypnotics and sedatives (N05C). We completed the analyses at the therapeutic and chemical levels. The total quantity dispensed for each chemical was extracted from Pharms data and converted to DDD equivalents. DDD/TOPD was derived by summing the total DDD for one year, dividing by the census population, and multiplying by 1000. For example, the value of 14 DDD for citalopram in 2005 suggests that 14 out of the 1000 older people in NZ were dispensed a standard dose of 20mg of citalopram per day. A customised census population data was extracted from NZ statistics [28].

~~4~~3 Results

~~4.1 Impact of Covid-19 pandemic~~

~~Before discussing the main findings, we would like to update the impact of COVID-19 on psychotropic utilisation. In March 2020, PHARMAC introduced a Pharmaceutical Schedule change that required pharmacies to move to monthly dispensing, rather than all-at-once dispensing, to mitigate the effects of global supply issues affecting NZ's stock of some medicines. This change meant that a patient would have to go into a pharmacy three times for a normal 90-day prescription. NZ returned to normal dispensing for most medicines on 1 August 2020.~~ ~~As a result, there will be unusual utilisation patterns of psychotropics in 2020, with a significant increase in the total number of dispensing. These changes should be considered within the context of the COVID-19 pandemic.~~

~~In light of the unusual dispensing patterns in 2020, all utilisation changes will be discussed from 2005 to 2019.~~

3.1~~4.2~~ Overall psychotropic medicine utilisation

Psychotropic medicine utilisation was relatively unchanged from 2005 to 2019 (DDD per TOPD from 142.42 to 143.02 DDD/TOPD, corresponding to a 0.42 per cent increase in psychotropic utilisation (**Table 1**). In addition, utilisation increased for antipsychotics (6.06 to 19.04 DDD/TOPD) and antidepressants (72.42 to 75.21 DDD/TOPD). On the other hand, utilisation decreased for anxiolytics (10.20 to 9.87 DDD/TOPD) and hypnotics and sedatives (53.74 to 38.90 DDD/TOPD) (**Table 1, Figure 1**).

3.2~~4.3~~ The utilisation of psychotropic medicines by age and sex

The utilisation of psychotropic medicines by age (five-year bands) and sex (DDD/1000 older people/day) and type from 2005 to 2019 increased and peaked in the 95 years and over age group (**Figure 2**). The utilisation of antidepressants was highest among all age groups and across both sexes except for the 90-94 and 95+ age groups, where ~~the utilisation of hypnotics and sedatives was~~hypnotics and sedatives were higher than the utilisation of antidepressants. The utilisation of typical antipsychotics decreased across age groups in both sexes. In contrast, the utilisation of atypical antipsychotics increased remarkably across all age groups and in both sexes.

3.3~~4.4~~ Antidepressants

The utilisation of antidepressants increased by 3.08 % from 2005 to 2019 (72.42 to 75.21 DDD/TOPD). Specifically, the utilisation of selective serotonin reuptake inhibitors (SSRI) declined slightly (47.67 to 45.36 DDD/TOPD). In contrast, tetracyclic antidepressants (TeCA) and SNRIs increased considerably.

Interestingly, the utilisation of tricyclic antidepressants (TCA) declined substantially (20.37 to 5.44 DDD/TOPD) (**Table 1, Figure 3**).

3.4~~4.5~~ Antipsychotics

Atypical antipsychotic (AAPA) medicine utilisation increased (4.06 to 18.72 DDD/TOPD) markedly, mainly driven by olanzapine (1.31 to 8.13) and quetiapine (0.78 to 3.99) (**Table 1, Figure 4**). It is noteworthy that in 2014 PHARMAC funded paliperidone, and its utilisation in 2019~~20~~ was 0.18 ~~1.87~~ DDD/TOPD. On the other hand, the utilisation of typical antipsychotics (TAPA) is relatively low and remains almost unchanged (2.00 to 2.06 DDD/TOPD) over the study period (**Table 1, Figure 5**).

3.5~~4.6~~ Anxiolytics

Benzodiazepines (BDZ) utilisation (9.05 to 9.68 DDD/TOPD) remained unchanged except for a rise in the use of lorazepam (5.10 to 7.00 DDD/TOPD). On the other hand, for buspirone, a non-BDZ anxiolytic medicine, the utilisation was relatively steady (0.15 to 0.19 DDD/TOPD) (**Table 1, Figure 6**).

3.6~~4.7~~ Hypnotics and sedatives

~~Important to note that PHARMAC funded melatonin in 2017, and its utilisation in 2020 was remarkably high (10.98) compared to other hypnotics and sedatives.~~ In 2019, the utilisation of zopiclone was also relatively high (25.67 DDD/TOPD) compared to other hypnotics (13.23 DDD/TOPD). Interestingly, among the BDZ-hypnotic class, the utilisation for nitrazepam, temazepam, and triazolam decreased considerably by 85.9%, 57.0%, and 79.4 %, respectively (**Table 1, Figure 7**).

~~5~~4 Discussion

~~4~~5.1 Overall psychotropic utilisation

The utilisation of psychotropic medicines measured in DDD/TOPD was relatively stable in people 65 years and older in New Zealand from 2005 to 2019.

~~4~~5.2 Antidepressants

The slight increase in the utilisation of SSRI antidepressants and a corresponding decrease in utilisation of anxiolytics and TCAs in our study may be driven by multiple factors, including expanding indications for SSRIs beyond the treatment of depression, including obsessive-compulsive disorders [29], panic disorders [30], chronic pain [31], and its preferential use over anxiolytics for anxiety disorders [32]. Citalopram continued to be the favoured SSRI with the highest utilisation both in 2005 and 2019. An expert consensus guideline on pharmacotherapy of depressive disorders for older adults

rated citalopram the highest for efficacy and tolerability among the SSRIs [33]. The utilisation of tricyclic antidepressants decreased substantially. The increased utilisation of SNRIs and TeCAs is largely driven by venlafaxine and mirtazapine, respectively. Venlafaxine and mirtazapine are recommended second-line treatments for depression after an initial trial of an SSRI, and a systematic review found that they are more effective than paroxetine and fluoxetine [34].

Interestingly, randomised clinical trials that compared venlafaxine to other SSRIs found its safety in older adults is comparable to SSRIs, and the risk for venlafaxine-induced electrocardiogram (ECG) changes and corrected QT (QT_c) ~~ECG changes and QT_c~~ prolongation is low [35, 36]. In clinical practice, the selection of antidepressants in older adults must be guided by patient-specific factors such as comorbidity and susceptibility to anticholinergic effects. Citalopram and sertraline have few drug interactions, are less anticholinergic than TCAs, and are recommended for treating depression in older adults [33].

~~4~~5.3 Antipsychotics

Despite the increased risk for cardiovascular and metabolic adverse effects [37, 38], the utilisation of atypical antipsychotic medicines increased (4.06 to 18.72 DDD/TOPD) in older people. However, a corresponding decline in typical antipsychotic medicines (2.0-2.6 DDD/1000 older people/day) utilisation occurred because of the increased risk of extrapyramidal symptoms and the perceived benefit of better efficacy for atypical antipsychotics [39]. Nevertheless, the preferential use of atypical antipsychotics over typical antipsychotics is a consistent finding in NZ [40] and internationally [41] despite no evidence for their superiority in terms of efficacy or safety [42]. In 2019, among the typical antipsychotic medicines, haloperidol utilisation was the highest, and among the typical antipsychotic medicines, olanzapine was the highest. Additionally, in a study comparing 16 countries, quetiapine was the antipsychotic used in most countries, followed by risperidone and olanzapine [43].

Furthermore, the increased use of atypical antipsychotics may be attributed to them often being prescribed for other mental disorders, including mood and anxiety disorders, insomnia, and agitation [44]. The utilisation of clozapine increased from 0.18 to 0.81 DDD//TOPD. An international study involving 17 countries found that clozapine is still underutilised across several countries despite increased use in recent years. The study found that Finland, followed by New Zealand, has the highest clozapine utilisation rates [45].

In older adults, the risk of anticholinergic effects, extrapyramidal symptoms, the adverse cardiovascular effects of typical antipsychotic medicines and the risk of adverse metabolic effects posed by atypical antipsychotic medicines must be considered. Therefore, the recommendation to treat psychosis in older adults is to use low dose atypical antipsychotic medicines for the shortest possible duration and wherever feasible on a case-to-case basis to switch to non-pharmacological options [46].

45.4 Anxiolytics

Benzodiazepine (BDZ) utilisation decreased slightly. In 2019, lorazepam was the most widely used benzodiazepine. In our published study in 2015, we highlighted concerns regarding using alprazolam and concerns about abuse, dependence, and tolerance [47]. Interestingly, in 2016, PHARMAC stopped funding for alprazolam for new patients [48].

45.5 Hypnotics and sedatives

Overall, the utilisation of hypnotics and sedatives has declined in NZ older adults (53.74 to 38.90, but the higher utilisation of zopiclone relative to other BDZs is alarming. Similar concerns of high prescribing of zopiclone in older adults relative to other BDZs were reported in Europe and England [49]. Although, in 2015, we highlighted the risk posed by zopiclone which accounted for more than 50% of utilisation of hypnotics, as it has been associated with cognitive impairment [50], confusion, and falls or fractures in older people [51], the reduction in the utilisation of zopiclone in 2019 (30.36) compared to 2005 (26.23) is a welcome change. ~~However, the rising trend in the utilisation of melatonin funded by PHARMAC in 2017 should be monitored closely [52]. Although, a recent review found insufficient scientific evidence for the potential side effects of melatonin at optimal doses, particularly in older adults, where long-term use may be unavoidable [53, 54].~~

The high utilisation of zopiclone is of concern and could be attributed to the increased prevalence of insomnia in older adults [52, 53]. Hence, the use of zopiclone should be restricted to short-term use to mitigate harm in older adults, and non-pharmacological interventions for the management of insomnia must be given precedence as interventions based on cognitive behavioural therapy are superior to zopiclone in older adults [54].

45.6 Strengths and limitations

One limitation of the study was that the WHO uses doses for main indications to compute DDDs, but several psychotropic medicines have expanded indications. Therefore, we could not examine the appropriateness of treatment due to the lack of information on the indication for using psychotropic medicine. We also assumed that all adhered to their prescribed psychotropic regimen; hence actual utilisation may be overestimated. However, it is pertinent to highlight that the Pharmaceutical collections maintained by the MoH are comprehensive. In addition, the reimbursement system captures greater than 95% of the prescription coverage of the census population of older adults, strengthening the validity of our study findings.

~~6~~5 Conclusions

In conclusion, psychotropic medicines utilisation was relatively stable from 2005 to 2019 in older adults in NZ. Though antidepressant utilisation remained relatively stable, there was a 5-fold increase in antipsychotic medicines mainly driven by the increased utilisation of atypical antipsychotics. Our findings suggest that a high proportion of older adults have been prescribed olanzapine and zopiclone, and the reasons for their use and risk-benefit ratio warrant further investigation. In addition, the rising trend in the utilisation of melatonin recently funded by PHARMAC should be monitored closely. Continued monitoring of psychotropic medicine utilisation will be of great interest to understand if the ~~unusually high~~ utilisation of psychotropic medicines, particularly antidepressants and antipsychotic medicines, during the COVID-19 pandemic year ~~is temporary or~~ will change relative to previous years and how the changes will impact the health of older adults in the long-term.

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Table 1: Psychotropic medicine utilisation in defined daily dose (DDD) per 1000 older people per day (TOPD) from 2005 to 2019

Therapeutic subgroup	Pharmacological /chemical group	Medicine name	ATC	DDD	Subsidised	Weight	Formulation	2005 DDD/TOPD	2019 DDD/TOPD	Change (%)
Antidepressants	SSRI	Citalopram	N06AB04	20	Yes	20	Tab	13.79	24.08	74.6
		Fluoxetine	N06AB03	20	Yes	20	cap, tab	16.54	7.65	-53.7
		Paroxetine	N06AB05	20	Yes	20	tab	17.34	5.44	-68.6
		Sertraline*	N06AB06	100	Started'2010	50, 100	tab	-	8.19	NA
		Sub-total						**47.67**	**45.36**	**-4.8**
	TCA	Amitriptyline	N06AA09	75	Yes	10, 25, 50	tab	9.23	2.41	-73.9
		Clomipramine	N06AA04	100	Yes	10, 25	tab	0.50	0.21	-58.0
		Desipramine	N06AA01	100	Stopped'2008	25	tab	0.06	-	NA
		Dosulepin[β]	N06AA16	150	Yes	25, 75	tab	2.55	0.25	-90.2
		Doxepin	N06AA12	100	Yes	10, 25, 50	cap	3.41	0.40	-88.3
		Imipramine	N06AA02	100	Yes	10, 25	tab	0.72	0.09	-87.5
		Nortriptyline	N06AA10	75	Yes	10, 25	tab	3.09	2.08	-32.7
		Trimipramine	N06AA06	150	Stopped'2010	25	tab	0.81	-	NA
		Sub-total						**20.37**	**5.44**	**-74.0**
	TeCA	Maprotiline	N06AA21	100	Yes	25, 75	tab	0.10	0.03	-70.0
		Mianserin	N06AX03	60	Stopped'2017	30	tab	0.08	-	NA
		Mirtazapine*	N06AX11	30	Started'2009	30, 45	tab	-	12.46	NA
		Sub-total						**0.18**	**12.49**	**6838.9**
	MAOI	Tranylcypromine	N06AF04	10	Yes	10	tab	0.36	0.20	-44.4
		Phenelzine*	N06AF03	60	Started'2006	15	tab	-	0.01	NA
		Sub-total						**0.36**	**0.21**	**-41.7**
	SNRI	Venlafaxine	N06AX16	100	Yes	75, 150, 225	cap, tab	1.95	10.80	284.0
	RIMA	Moclobemide	N06AG02	300	Yes	150, 300	tab	1.89	0.91	-51.9
	Antidepressants	**Total**						**72.42**	**75.21**	**3.08**
Antipsychotics	TAPA	Chlorpromazine	N05AA01	300	Yes	10, 25, 50, 100	tab, ml	0.17	0.11	-35.3
		Flupenthixol decanoate	N05AF01	6	Yes	20, 40, 100	inj	0.06	0.13	116.7
		Fluphenazine decanoate	N05AB02	10	Stopped'2019	12.5 ,25 ,50, 100	inj	0.02	-	NA
		Haloperidol	N05AD01	8	Yes	0.5, 1.5 ,2 ,2.5	tab, ml	0.53	1.29	143.4
		Haloperidol decanoate	N05AD01	8	Yes	50, 100	inj	0.04	0.08	100.0
		Levomepromazine[δ]	N05AA02	300	Yes	1	tab	0.06	0.15	150.0
		Pericyazine	N05AC01	50	Yes	2.5, 5	tab, inj	0.04	0.03	-25.0
		Pimozide	N05AG02	4	Stopped'2007	2	tab	0.09	-	NA
		Prochlorperazine	N05AB04	100	Yes	3[k], 5, 12.5, 25	tab, inj, sup	0.58	0.12	-79.3
		Thioridazine	N05AC02	300	Stopped'2008	10,25,50,100, 200	tab	0.16	-	NA

		Trifluoperazine	N05AB06	20	Stopped'2018	1, 2, 5, 15	tab, cap	0.24	-	NA
		Zuclopenthixol decanoate	N05AF05	30	Yes	200	inj	0.01	0.08	700.0
		Zuclopenthixol dihydrochloride*	N05AF05	30	Started'2009	10	tab	-	0.07	NA
		Sub-total						**2.00**	**2.06**	**3.0**
		Amisulpride*	N05AL05	400	Started'2008	100, 200, 400	tab	-	0.32	NA
		Aripiprazole*	N05AX12	15	Started'2008	10, 15, 20	tab	-	0.84	NA
		Clozapine	N05AH02	300	Yes	25, 50, 100, 200	tab	0.18	0.81	350.0
	AAPA	Olanzapine	N05AH03	10	Yes	2.5, 5, 10	tab, inj, waf	1.31	8.13	520.6
		Paliperidone	N05AX13	6	Started'2014	25	inj	-	0.18	NA
		Quetiapine	N05AH04	400	Yes	25,100,200, 300	tab	0.78	3.99	507.6
		Risperidone	N05AX08	5	Yes	0.5, 1, 2, 3, 4	tab, ml, inj	1.79	4.38	144.7
		Ziprasidone*	N05AE04	80	Started'2007	20, 40, 60, 80	tap	-	0.07	NA
		Sub-total						**4.06**	**18.72**	**361.1**
	Antipsychotics	**Total**						**6.06**	**19.04**	**214.2**
		Alprazolam	N05BA12	1	Stopped'2018	0.25, 0.5, 1	tab	0.46	-	NA
		Clobazam	N05BA09	20	Yes	10	tab	0.16	0.35	118.8
	BDZ	Diazepam	N05BA01	10	Yes	2, 5, 10	tab,ml,inj,ene	3.11	1.91	-38.6
Anxiolytics		Lorazepam	N05BA06	2.5	Yes	1, 2.5	tab	5.10	7.00	37.3
		Oxazepam	N05BA04	50	Yes	10, 15	tab	1.22	0.42	-65.6
		Sub-total						**9.05**	**9.68**	**7.0**
	Non-BDZ anxiolytic	Buspirone	N05BE01	30	Yes	5, 10	tab	**0.15**	**0.19**	**26.7**
		Total						**10.20**	**9.87**	**7.3**
		Lormetazepam	N05CD06	1	Stopped'2019	1	tab	0.22	-	NA
	BDZ-hypnotic derivatives	Clonazepam	N03AE01	8	Yes	0.5, 1, 2, 2.5	tab,ml.inj	0.76	1.00	31.6
Hypnotics and Sedatives		Midazolam	N05CD08	15	Yes	5, 15	inj	1.92	6.61	70.9
		Nitrazepam	N05CD02	5	Yes	5	tab	3.06	0.43	-85.9
		Temazepam	N05CD07	20	Yes	10	tab	6.74	2.90	-57.0
		Triazolam	N05CD05	250	Yes	0.125[k], 0.250[k]	tab	11.14	2.29	-79.4
	Melatonin receptor agonists	Melatonin	N05CH01	2	Started'2017	2	tab	-	-	NA
		Sub-total		Total				**23.84**	**13.23**	**3.4**
	Z-hypnotic	**Zopiclone**	**N05CF01**	**7.5**	**Yes**	**7.5**	**tab**	**29.90**	**25.67**	**-14.1**
		Total		Total				**53.74**	**38.90**	**-24.3**
Grand Total								**142.42**	**143.02**	**0.42**

SSRI= Selective serotonin reuptake inhibitors, TCA= Tricyclic antidepressants, TeCA= Tetracyclic antidepressants, MAOI = Monoamine oxidase inhibitor, SNRI = Serotonin noradrenaline reuptake inhibitor, RIMA = Reversible inhibitor of monoamine oxidase-A, TAPA = Typical antipsychotic agents, APA = Atypical antipsychotic agents, BDZ = Benzodiazepine, Z-hypnotic = Non-BDZ hypnotic, Dosulepin[β]=Dothiepin, Levomepromazine[ð] = Methotrimeprazine, *Subsidised after 2005, [k] partial subsidy by Government. NA= Not Applicable; not included during computation for percentage change. ATC = Anatomical therapeutic and chemical classification. Weight[l] = Medication weight available in

milligrams in New Zealand. DDD/TOPD= Defined daily doses per 1000 older people per day. Formulation = Formulations ; tab=tablets, cap=capsules, ml=liquid, inj=injection, waf=wafer, ene-enema, Change (% from 2005 and 2019) = (Post - Pre)*100/Pre

Figure 1

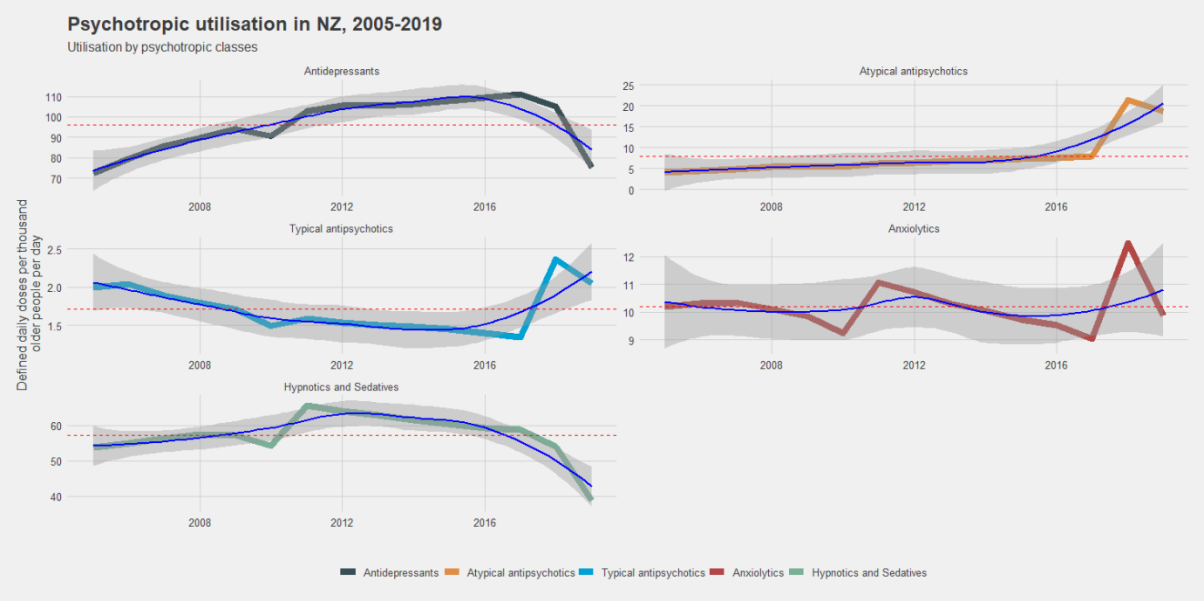


Figure 2

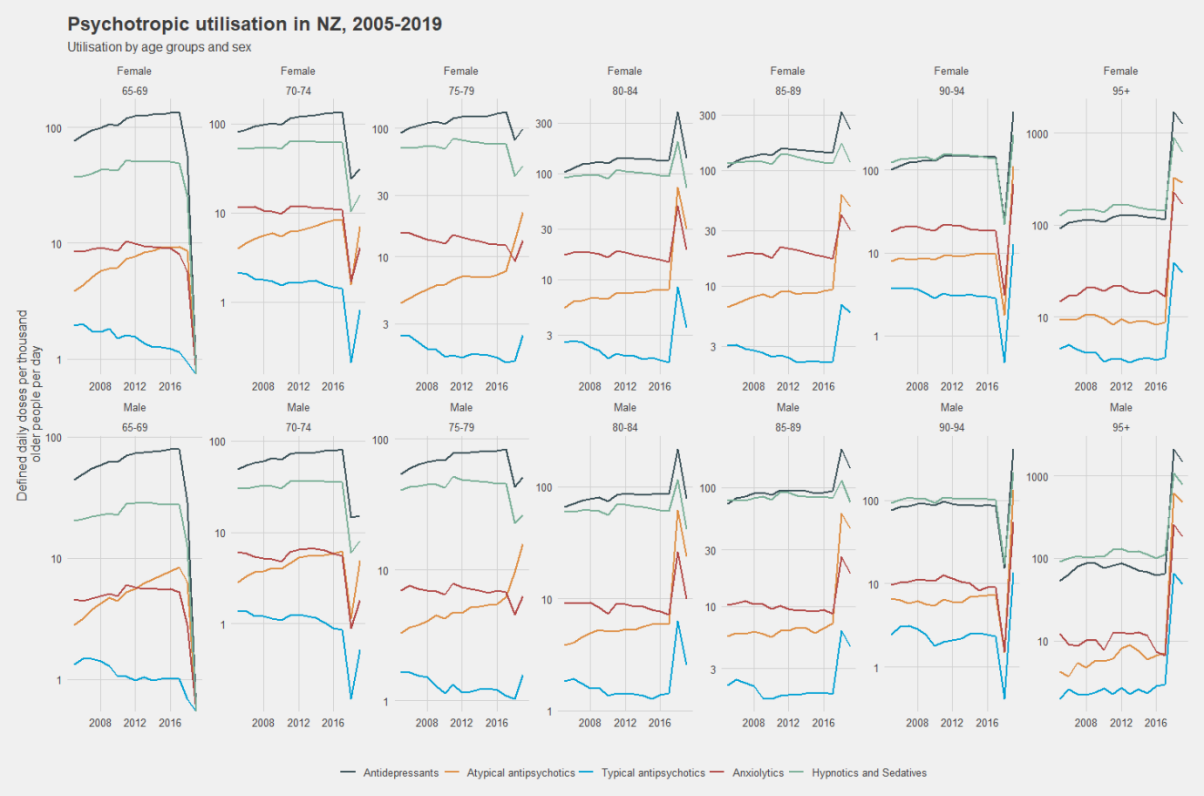


Figure 3

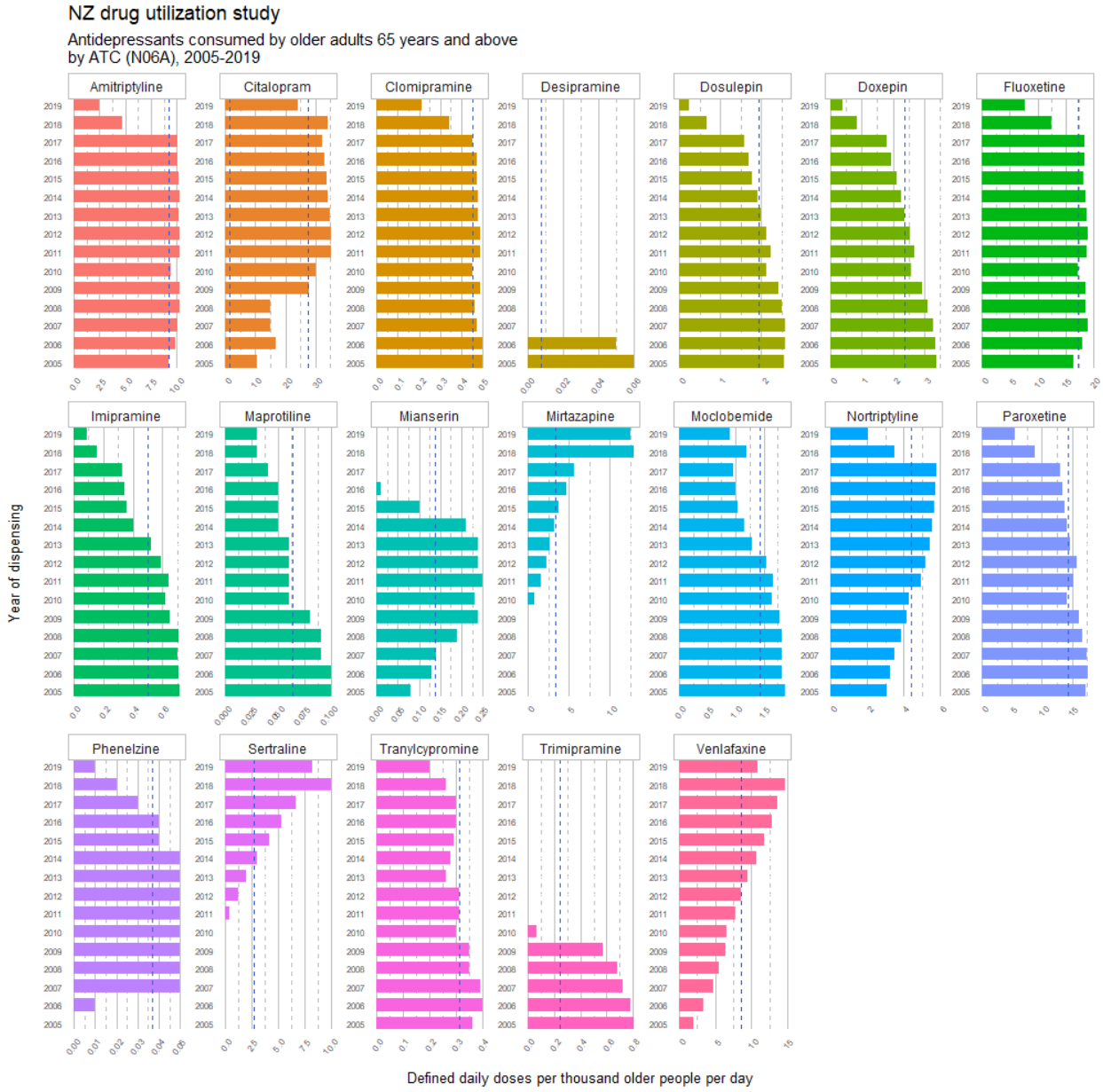

NZ drug utilization study
Antidepressants consumed by older adults 65 years and above
by ATC (N06A), 2005-2019
Amitriptyline
Citalopram
Clomipramine
Desipramine
Dosulepin
Doxepin
Fluoxetine
Imipramine
Maprotiline
Mianserin
Mirtazapine
Moclobemide
Nortriptyline
Paroxetine
Phenelzine
Sertraline
Tranylcypromine
Trimipramine
Venlafaxine
Year of dispensing
Defined daily doses per thousand older people per day

Figure 4

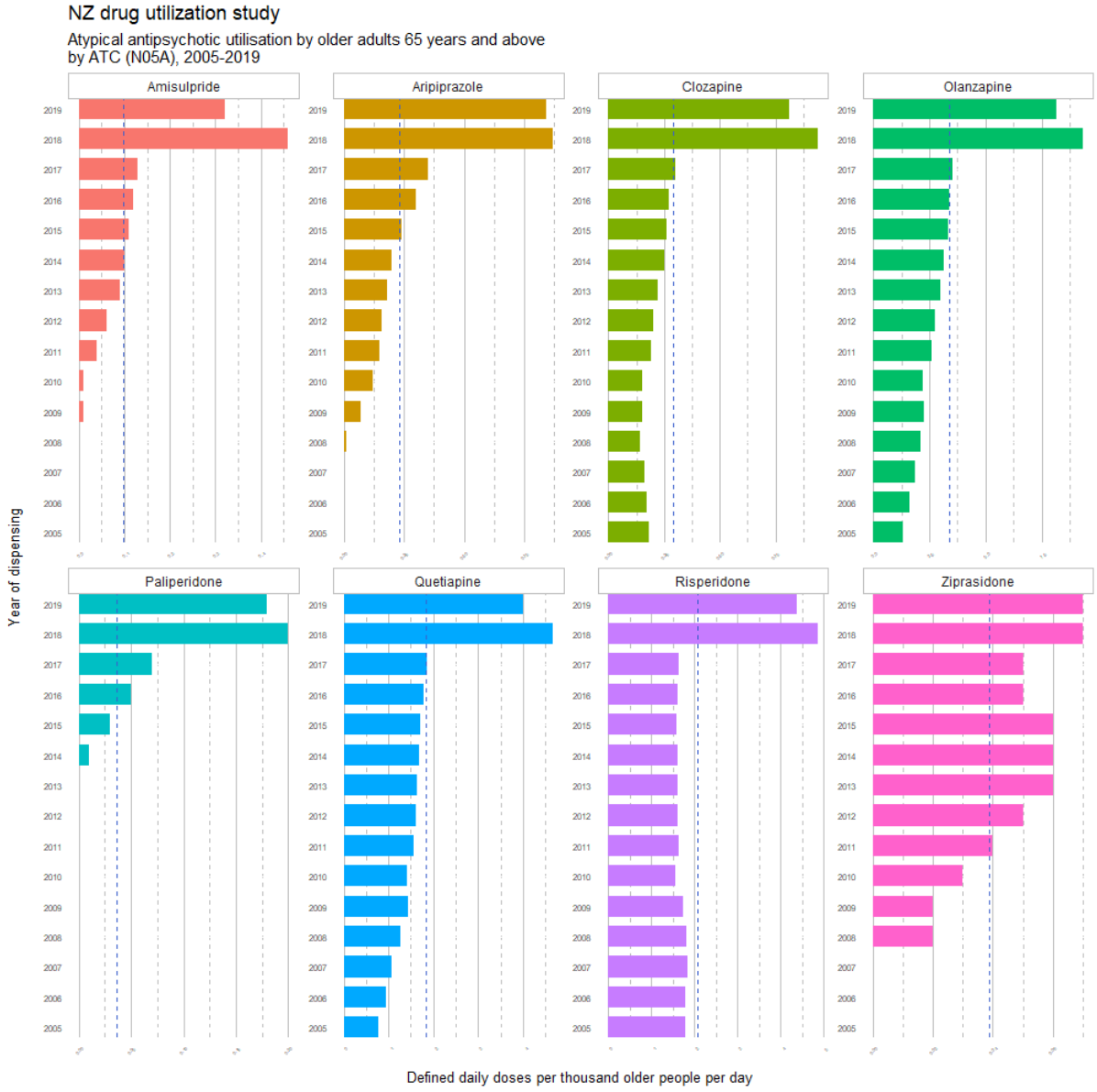

NZ drug utilization study
Atypical antipsychotic utilisation by older adults 65 years and above
by ATC (N05A), 2005-2019
Amisulpride
Aripiprazole
Clozapine
Olanzapine
Paliperidone
Quetiapine
Risperidone
Ziprasidone
Year of dispensing
Defined daily doses per thousand older people per day

Figure 5

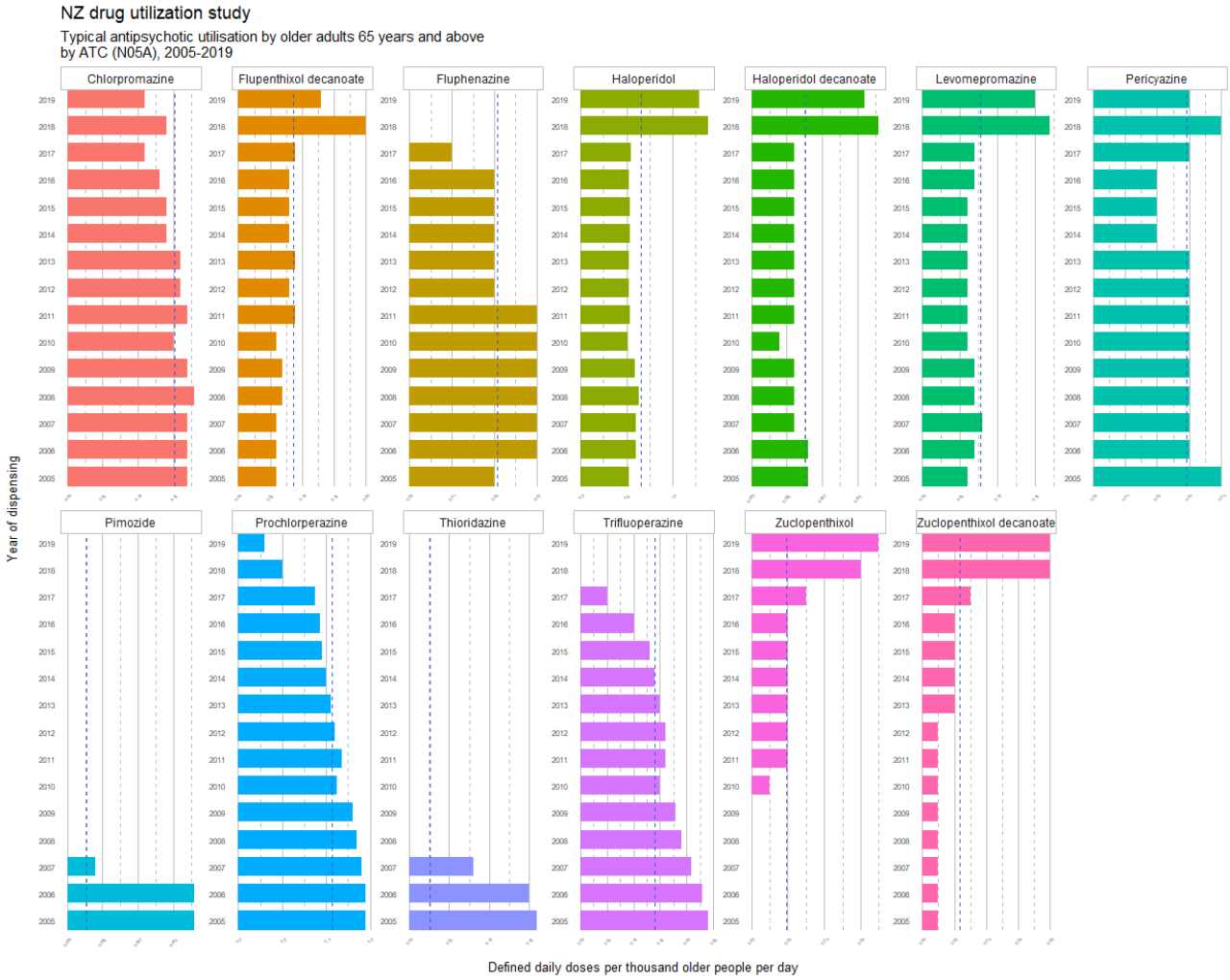

NZ drug utilization study
Typical antipsychotic utilisation by older adults 65 years and above
by ATC (N05A), 2005-2019
Chlorpromazine
Flupenthixol decanoate
Fluphenazine
Haloperidol
Haloperidol decanoate
Levomepromazine
Pericyazine
Pimozide
Prochlorperazine
Thioridazine
Trifluoperazine
Zuclopenthixol
Zuclopenthixol decanoate
Year of dispensing
Defined daily doses per thousand older people per day

Figure 6

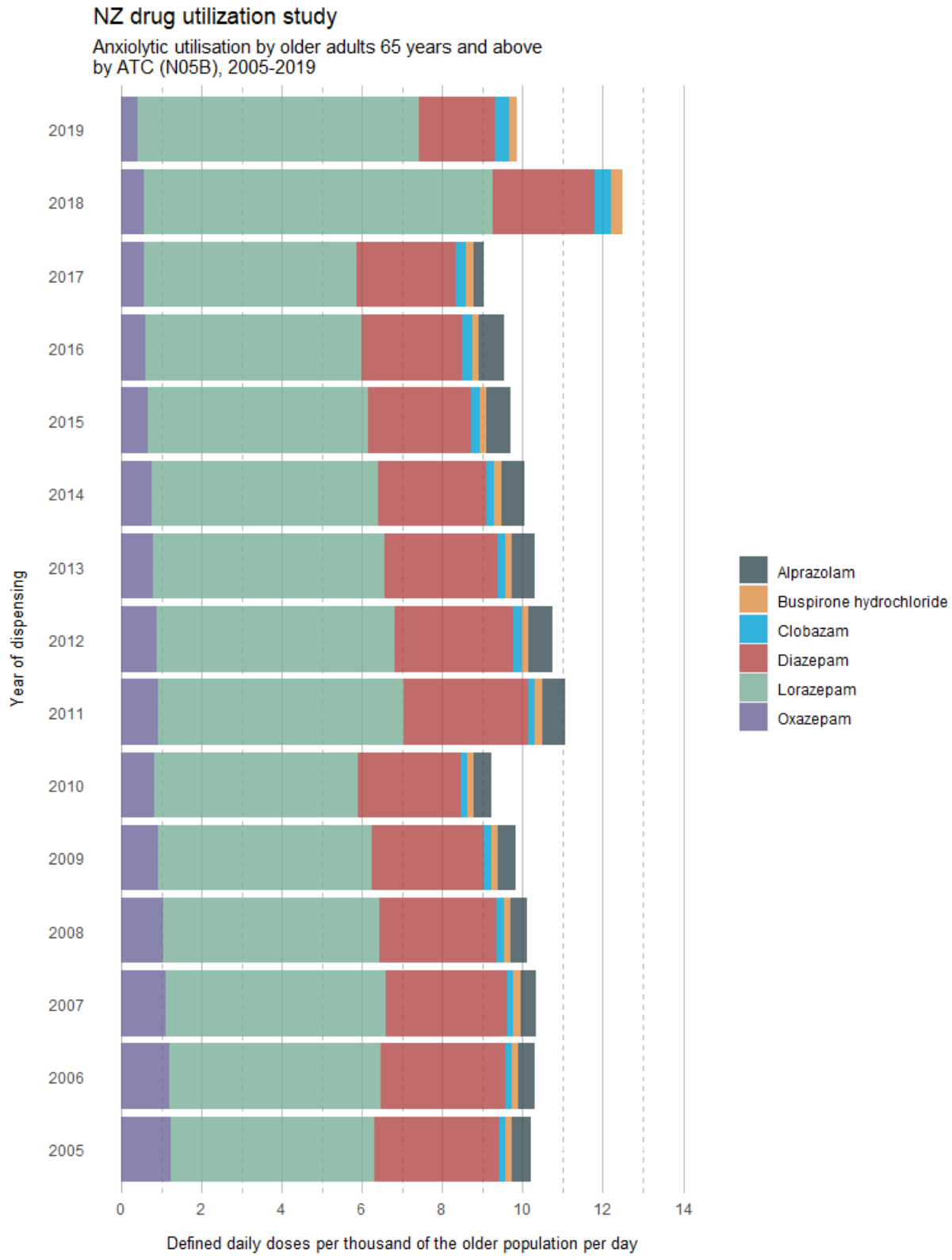
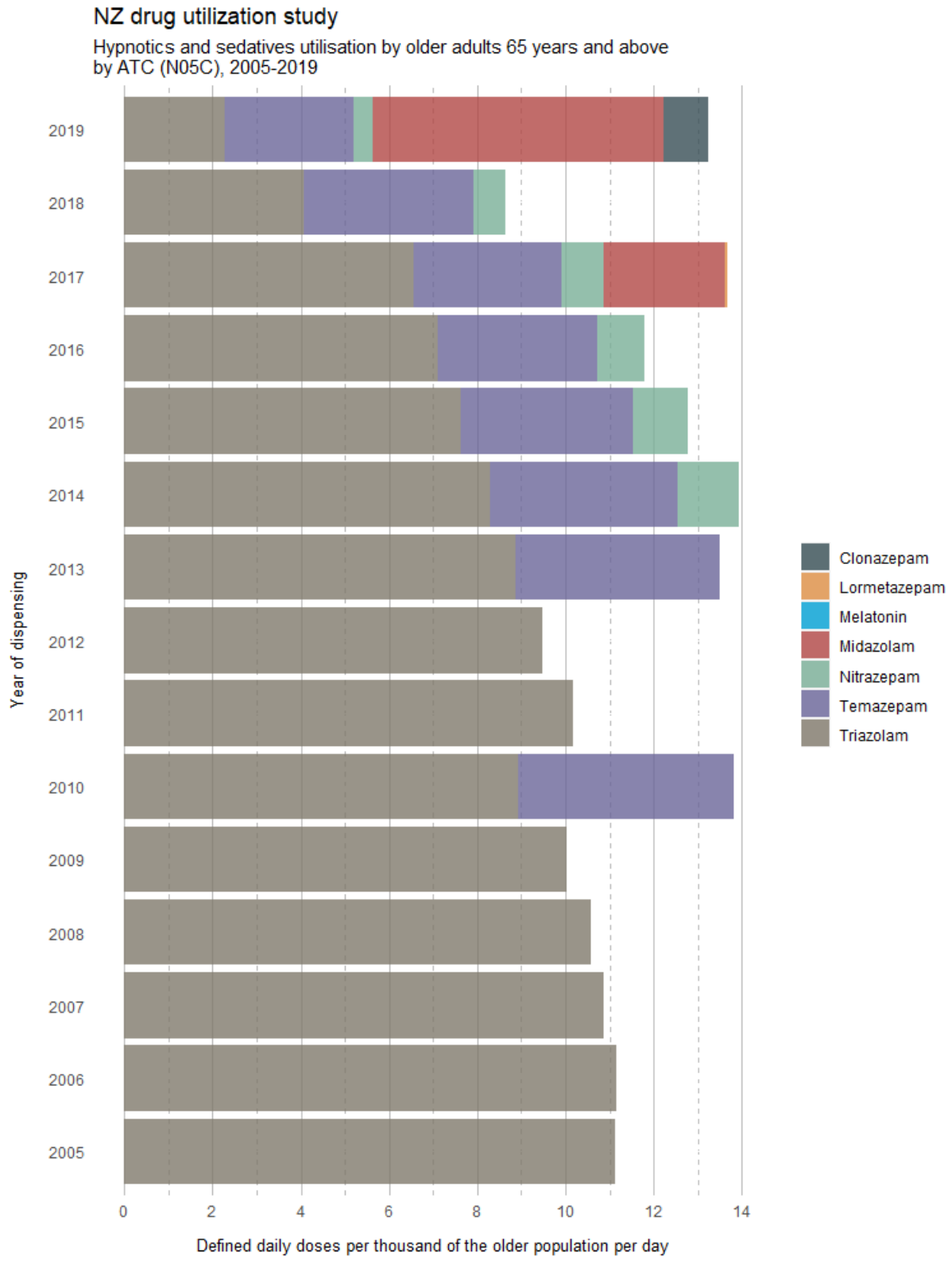

NZ drug utilization study
Anxiolytic utilisation by older adults 65 years and above
by ATC (N05B), 2005-2019
Year of dispensing
2019
2018
2017
2016
2015
2014
2013
2012
2011
2010
2009
2008
2007
2006
2005
0
2
4
6
8
10
12
14
Defined daily doses per thousand of the older population per day
Alprazolam
Buspirone hydrochloride
Clobazam
Diazepam
Lorazepam
Oxazepam

Figure 7


NZ drug utilization study
Hypnotics and sedatives utilisation by older adults 65 years and above by ATC (N05C), 2005-2019
Year of dispensing
2019
2018
2017
2016
2015
2014
2013
2012
2011
2010
2009
2008
2007
2006
2005
0
2
4
6
8
10
12
14
Defined daily doses per thousand of the older population per day
Clonazepam
Lormetazepam
Melatonin
Midazolam
Nitrazepam
Temazepam
Triazolam

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