

# Antiepileptic medicine utilization in older people over a 9-year study period



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## ABSTRACT

**Background:** The aim of this population-level study was to describe and characterize the utilization of AEDs in older people in New Zealand from 2005 to 2013.

**Methods:** De-identified individual level dispensing data for people aged 65 years and over for the period 2005–2013 were obtained from New Zealand Ministry of Health. AEDs were categorized using the ATC classification system of the WHOCC and Norwegian institute of public health. Utilization rates by year, age, sex, ethnicity and district health boards were measured as DDD per TOPD.

**Results:** The prevalence of AEDs utilization (DDD/TOPD) increased from 14.23 in 2005 to 14.39 in 2013. The newer AEDs increased from 0.64 in 2005 to 1.82 in 2013, but the prevalence for older AEDs decreased over the same study period from 13.59 to 12.57. AEDs utilization in males over the 9-year period was 17.18 (33.22% higher than females). Highest utilization was observed in those aged between 65 and 69 years, with average of 15.44 (28.88% higher than 85 plus age group). Sodium valproate followed by phenytoin and carbamazepine were the most common AEDs. Among the newer AEDs, gabapentin followed by lamotrigine was most frequently utilized.

**Conclusion:** Utilization of AEDs increased over the 9-year study period in older New Zealanders. The newer AEDs may have contributed to this increase. Further research is required to examine the utilization of AEDs by therapeutic indications.

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## 1. Introduction

Antiepileptic drugs (AEDs) are mainly indicated for treatment of epilepsy, but have extended indications in bipolar affective disorders, neuropathic pain, migraine prophylaxis and management of behavioral and psychological symptoms of dementia (Brodie, 2010; Cavanna, Ali, Rickards, and McCorry, 2010; Moore, Wiffen, and Kalso, 2014; Mulleners, McCrory, and Linde, 2015). Newer AEDs have been introduced late in New Zealand compared to other developed countries (Knoester, Deckers, van der Vaart, Leufkens, and Hekster, 2005). Hence, it is important to examine trends in utilization of newer AEDs compared to older AEDs.

The main objective of this study was to describe and characterize the trend in national utilization of antiepileptic medicines in New Zealand's older population from 2005 to 2013, stratified by year, age, sex, ethnicity and District Health Boards (DHBs) based on World Health Organization Collaborating Centre for Drug Statistics Methodology's (WHOCC) Anatomical Therapeutic Chemical (ATC) classification system (World Health Organisation Collaborating Centre for Drug Statistics Methodology, WHOCC, 2013).

## 2. Methods

This study was approved by the Human Ethics Committee of the University of Otago, New Zealand (HD15/006). A repeated cross-sectional analysis of population level dispensing data was aggregated yearly from 1st January 2005 to 31st December 2013 for individuals aged 65 years and above. Data on AEDs (WHOCC/ATC code N03 antiepileptic) was extracted, aggregated, and analyzed for patterns based on year, age, sex, ethnicity and District health boards (DHBs).

De-identified individual level dispensing data for people aged 65 years and over for the period 2005–2013 were obtained from New Zealand Ministry of Health. AEDs were categorized using the ATC classification system of the WHOCC and Norwegian institute of public health (World Health Organisation Collaborating Centre for Drug Statistics Methodology, WHOCC, 2013). The ATC classification system has been sub-grouped in to five levels with anatomical, therapeutic, pharmacological, chemical and chemical substance subgroup, in descending order. The ATC therapeutic classes analyzed at board levels were barbiturates and derivatives (N03AA), hydantion derivatives (N0AB), oxazolindine derivatives (N03AC), succinimide derivatives (N03AD), benzodiazepine derivatives (N03AE), carboxamide derivatives (N03AF), fatty acid derivatives (N03AG), other antiepileptics (N03AX).

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The WHO Defined daily dose (DDD) method was used to describe the number of older people on a defined standard daily dose per thousand older people ( $\geq 65$  years) per day (TOPD). The standard DDD dose for each antiepileptic medicine was obtained from the WHO ATC/DDD index. Utilization rates by year, age, sex, ethnicity and DHBs were measured as DDD per TOPD. DDDs were computed for each antiepileptic medicine consumed by an individual, yearly, per annual population size of New Zealand.

### 3. Results

Data showed that 20, 370 individuals were prescribed antiepileptic medicines in 2005, which increased to 25,932 in year 2013 (Fig. 1). Each year around 55–57% users were females. The analysis showed that the national utilization of AEDs (DDD/TOPD) increased from 14.23 in 2005 to 14.39 in 2013 (Fig. 2). AEDs utilization increased by 10.75% from 2005 to 2008 and decreased 9.26% from 2008 to 2010. After 2010, AEDs utilization remained constant. Average AEDs utilization was 14.81 DDD/TOPD over the 9-year period.

AEDs utilization by sex, age (five year bands) and ethnicity showed similar trend to overall AEDs utilization over the 9-year study period. As shown in Fig. 1, AEDs utilization in males was higher compared to females. On average, AEDs utilization in males over the 9-year period was 17.18 DDD/TOPD (33.22% higher than females). Highest DDD/TOPD was observed in those aged between 65 years and 69 years as shown in Fig. 2, with average of 15.44 DDD/TOPD (28.88% higher than 85+ age group). As shown in Fig. 2 those aged 85 years and above had the lowest DDD/TOPD (average 11.98 DDD/TOPD).

As for ethnicity, AEDs utilization in Māori group was the highest (average 17.68 DDD/TOPD) followed by NZ Europeans (average 16.27 DDD/TOPD). AEDs utilization was lowest among the Asian ethnic group (average 6.08 DDD/TOPD) (Fig. 2). As shown in Fig. 3, AEDs utilization was highest in West Coast DHB (average 18.01 DDD/TOPD) followed by Tairāwhiti DHB, Sothern DHB and Hutt Valley. West Coast and Tairāwhiti DHBs showed steeper increase after year 2011 compared to rest of the DHBs (Table 1).

The most frequently prescribed AED over the 9-year period was sodium valproate (N03AG01), with an average DDD/TOPD of 4.84. Utilization of sodium valproate increased over the 9-year period (Fig. 4). Hydantion derivative phenytoin (N03AB02) was ranked second followed by carbamazepine a carboxamide derivative, the utilization in DDD/TOPD were 4.17 and 2.63 respectively. However, utilization of the both AEDs decreased over the 9-year period (Fig. 4). The utilization of sodium valproate, lamotrigine, levetiracetam, topiramate increased over the 9-year period and the utilization of phenytoin, carbamazepine, gabapentin, phenobarbitone

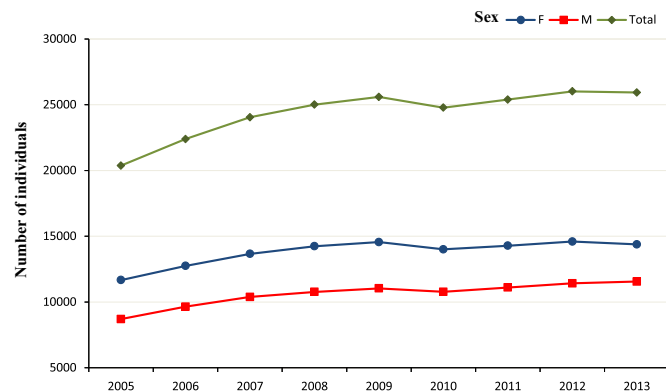


Fig. 1. Antiepileptic drug population stratified by sex and year.

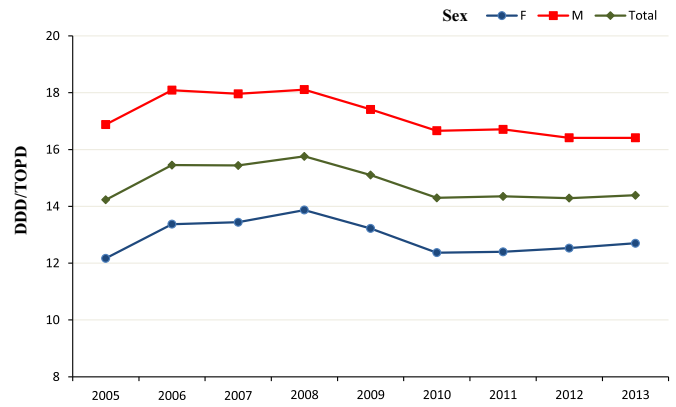


Fig. 2. Overall antiepileptic drug utilization (DDD/TOPD) stratified by sex from 2005 to 2013.

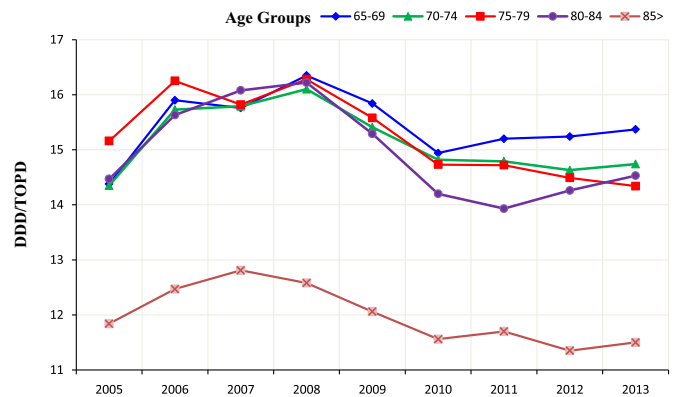


Fig. 3. Antiepileptic drug utilization (DDD/TOPD) stratified by age groups from 2005 to 2013.

decreased over the 9-year period. The utilization of primidone and clonazepam remained constant from 2005 to 2009. As shown in Table 2, utilization of older AEDs (DDD/TOPD) decreased by 7.47% from 13.59 in 2005 to 12.57 in 2013. In contrast, the utilization of newer AEDs increased by 184.77% from 0.64 in 2005 to 1.82 in 2013. Utilization of newer AEDs increased over the 9-year period (Fig. 3).

### 4. Discussion

The total utilization of AEDs increased modestly from 2005 to 2013. While utilization of older AEDs decreased, a shift towards utilization of newer AEDs was observed. Interestingly, AEDs utilization increased from 2005 to 2008 and decreased from 2008 to 2010. A similar trend was observed in a population based study of AEDs utilization in Italy, in which the average AEDs utilization (DDD/TOPD) was 7.33 (Alacqua et al., 2009). However, a nationwide study in Australia for all ages observed an increase in AEDs utilization over the study period with an average AEDs utilization (DDD/TOPD) of 9.78 (Hollingworth and Eadie, 2010). Similarly a nationwide study in Taiwan observed an increase in AEDs utilization from 12.6 in 2003 to 13.8 2007 (Hsieh and Huang, 2011). In this study, age was inversely associated with utilization of AEDs. Age 65–69 individuals had highest utilization with average DDD/TOPD of 15.44 compare to 11.98 that of age 85 over individuals. These results were consistent with other population level studies conducted in Australia and Sweden (Hollingworth and Eadie, 2010; Johnell and Fastbom, 2011). However, a study conducted in Taiwan reported no obvious change in AED utilization across all age groups (Hsieh and Huang, 2011). Our finding of increased

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