Title: Antidepressant dispensing trends and prevalence in pregnant New Zealand mothers between 2007/08 and 2017/18

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Abstract

Worldwide, gestational antidepressant exposure has increased substantially across the past 30 years. It was of interest to determine whether such a trend was present in New Zealand's pregnant population. Therefore, this current study investigated antidepressant dispensing in all resident New Zealanders with at least one successful pregnancy, over the period 20007/08 to 2017/18. Pharmaceutical dispensing data was accessed through the national Integrated Data Infrastructure (IDI). We explored dispensing by medication type, trimester, ethnicity, age and area-level deprivation quintiles, with the purpose of determining whether variation within these categories existed. In 2017/18 total antidepressant dispensing had reached 4.4%, an increase of 66.3% from the start of the study period. All subgroups showed increased dispensing, though with considerable variation within categories. The SSRIs were the most frequently dispensed medication type and consistently accounted for approximately 80% of all antidepressant dispensing. Trimester specific dispensing identified highest dispensing for trimester 3 and lowest dispensing for trimester 1, across the entire study period of interest. Antidepressant dispensing by age, exhibited a pattern of increased dispensing with increasing age, where the age group ≥35 years had the highest dispensing prevalence over time. The most deprived quintile had a dispensing prevalence that was markedly lower than all other quintiles. Breakdown of dispensing by ethnicity revealed considerable differences. The Other and New Zealand European categories consistently had the highest dispensing prevalence, while the Asian and Pasifika groups had the lowest. Ultimately, our study demonstrated an increased antidepressant use among pregnant New Zealanders that parallels global trends. Further research is required to determine underlying causes of the existing differences in dispensing across trimesters, ethnic, socioeconomic and age groups.

Globally, around 4.4% of the population suffer from a form of depression (World Health Organization, 2017). Women show a higher prevalence compared to men, with estimates of 5.1% and 3.6% respectively (World Health Organization, 2017). A major life event that sees this gender difference increase significantly is pregnancy, during which 7 to 13% of women suffer from antenatal depression (Bennett, Einarson, Taddio, Koren & Einarson, 2004; Gavin, Gaynes, Lohr, Meltzer-Brody, Gartlehner & Swinson, 2005). When left untreated during pregnancy, the condition has been linked to a number of adverse health outcomes, such as increased risk of preeclampsia, preterm birth, low birth weight and post-natal depression (Alwan, Reefhuis, Rasmussen & Friedman, 2013; Andersson, Sundstrom-Poromaa, Wulff, Astrom & Bixo, 2004; Grote, Bridge, Gavin, Melville, Lyengar & Katon, 2010; Jarde, Morais, Kingston, Giallo, MacQueen, Giglia, Beyene, Wang & McDonald, 2016; Milgrom, Gemmill, Bilszta, Hayes, Barnett, Brooks, Ericksen, Ellwood & Buist, 2008; Qiu, Williams, Calderon-Maralit, Cripe & Sorensen, 2009).

Studies from numerous developed countries have indicated that antenatal depression treatment, like depression treatment in general, has become heavily reliant on antidepressant medication over the last 30 years (Andrade, Raebel, Brown, Labe, Livington, Boudreau, Rolnick, Roblin, Smith, Willy & Plat, 2008; Exeter, Robinson & Wheeler, 2009; Jimenez-Solem, Andersen, Peterson, Broedbaek, Andersen, Torp-Pedersen & Poulsen, 2013; Petersen, Gilbert, Evans, Man & Nazareth, 2010; Rosholm, Andersen & Gram, 2001). For instance, the UK witnessed a 4-fold increase in antidepressants prescribed during pregnancy between 1992 and 2006, from 0.8% to 3.2% (Petersen et al., 2010). Similarly, in the US, there was a near 4-fold increase in gestational antidepressant prescriptions between 1996 and 2005, from 2% to 7.6% (Andrade et al., 2008).

The selective serotonin reuptake inhibitors (SSRIs) are the group of antidepressants responsible for the majority of this increase (Alwan et al., 2004; Bakker, Kölling, Van Den

Berg, De Walle & De Jong Van den Berg, 2007; Cooper, Willy, Pont & Ray, 2007; Jimenez-Solem et al., 2013; Peterson et al., 2010; Ververs, Kaasenbrood, Visser, Schobben, de Jong-van den Berg, & Egberts, 2006; Zoega, Lewis, Nørgaard, Furu, Valdimirsdottir, Brandt & Haglund, 2015). A national database study conducted in the UK reported that 80% of women who were prescribed antidepressants during pregnancy received a type of SSRI. Fluoxetine was the most prescribed, followed by sertraline and citalopram (Petersen et al., 2010). Although the frequency of different SSRI forms varies slightly from country to country, a similar pattern has been found across Europe, Canada and the US (Alwan et al., 2004; Bakker et al., 2007; Cooper et al., 2007; Jimenez-Solem et al., 2013; Peterson et al., 2010; Ververs et al., 2006; Zoega, et al., 2015).

Despite the substantial increase in pregnancies exposed to antidepressants, and SSRIs in particular, antidepressant use in pregnant women is much lower than in the non-pregnant female population. In fact, several studies have reported that a large proportion of women who use antidepressants prior to conception discontinue use in pregnancy (Andrade et al., 2008; Ramos, Oraichi, Rey, Blais & Bérard, 2007; Jimenez-Solem et al., 2013; Petersen et al., 2010; Ververs et al., 2006; Zoega et al., 2015). For example, in Canada, 6.6% of women were prescribed antidepressants 6 months before pregnancy, compared to 3.7% during their first trimester. This number further declined during their second and third trimester, to 1.6% and 1.1% respectively (Ramos, et al., 2007).

The high rate of cessation is likely due to an unwillingness to prescribe antidepressants for expectant mothers that has followed studies linking SSRI use during early pregnancy to increased risk of persistent pulmonary hypertension of the new-born (Chambers, Hernandez-Diaz, Van Marter, Werler, Louik, Jones & Mitchell, 2006; Kieler, Artama, Engeland, Ericsson, Furu, Gissler, Nielsen, Nørgaard, Stephansson, Valdimarsdottir, Zoega & Haglund, 2012). Further, to third trimester antidepressant use being linked to increased risk of withdrawal

syndrome in the newborn (Galbally, Lewis, Lum & Buist, 2009; Nordeng, Lindemann, Perminov & Reikvam, 2001). In addition, cessation could be influenced by Paroxetine use in the first trimester of pregnancy having been linked to increased risk of congenital malformations, especially heart defects in the newborn (Bérard, Ramos, Rey, Blais, St-André & Oraichi, 2006; Källén & Olausson, 2007; Malm, Artama, Gissler & Ritvanen, 2011; Wurst, Poole, Ephross & Olshan, 2009). Though, this risk is debated as several studies have not found an association at a statistically significant level (Huybrechts, Palmsten, Avorn, Cohen, Holmes, Franklin, Mogun, Levin, Kowal, Setoguchi & Hernández-Díaz, 2014; Vasilakis-Scaramozza, Aschengrau, Cabral & Jick, 2013).

For those who continue antidepressant use during pregnancy, the most recurrent predictors are low income and older maternal age (>35 years) (Jimenez-Solem et al., 2013; Petersen et al., 2010; Ramos et al., 2007; Ververs et al., 2006). The positive correlation between low income and greater gestational antidepressant use can probably be seen in relation to a higher incidence of antenatal depression among those of low socioeconomic status (Leigh & Milgrom, 2008; Murphy, Olivier, Monson, Sobol, Federman & Leighton, 1991). The second predictor, older maternal age, is more unexpected as reports consistently show a higher prevalence of antenatal depression in pregnant women of a younger age (<25 years) (Fransson, Örtenstrand & Hjelmstedt, 2011; Kitamura, Yoshida, Okano, Kinoshita, Hayashi, Toyoda, Ito, Kudo, Tada, Kanazawa, Sakumoto, Satoh, Furukawa & Nakano, 2006; Rubertsson & Waldenström, 2003). This discrepancy could be associated with the ‘black box’ warning that all antidepressants carry which specify an increased risk of suicidality for adolescent and young adult (18-24 years) users (Fornaro, Anastasia, Valchera, Carano, Orsolini, Vellante, Rapini, Olivieri, Di Natale, Perna, Martinotti, Di Giannantonio & De Berardis, 2019). However, this is debated as a US study reported decreased usage during gestation for all age bands, following

the initial addition of a suicide warning on antidepressant packaging in 2003 (Huybrechts, Palmsten, Mogun, Kowal, Avorn, Setogutchi-Iwata & Hernández-Díaz, 2013).

To date, no studies have looked at gestational antidepressant use in New Zealand. Though, trends and prevalence of antidepressant use in the New Zealand population overall have been identified for the period between 2004 and 2015 (Bowden, Gibb, Thabrew, Audas, Camp, Taylor & Henrick, 2019; Exeter, et al., 2009; Wilkinson & Mulder, 2018). Like the rest of the developed countries, New Zealand has seen a sharp increase in antidepressant prescriptions but with substantial differences between gender, age and ethnicity (Bowden et al., 2019; Exeter et al., 2009; Middleton, Gunnell, Whitley, Dorling & Frankel, 2001; Wilkinson & Mulder, 2018). Between 2004 and 2007 women received two thirds of the country's antidepressant prescriptions (Exeter et al, 2009). Further, in 2015, 16% of female New Zealanders aged 15 or above were prescribed an antidepressant (Wilkinson & Mulder, 2018). With regards to antidepressant use by ethnicity, the New Zealand European population were prescribed a significantly higher proportion of antidepressants than the Māori, Pasifika and Asian population (Exeter et al., 2009).

Due to the negative health outcomes associated with both gestational antidepressant use and untreated antenatal depression, there is a need for data that is specific to New Zealand's pregnant population. Therefore, this study will aim to identify the prevalence of gestational antidepressant use in New Zealand. It will explore trends per fiscal year over the past decade (2007/08 to 2017/18) and look for prevalence differences between the three trimesters of pregnancy. In addition, the study will seek out any prescription rate differences between separate age groups, ethnicities and area deprivation levels. We hypothesize that:

1. New Zealand has seen a substantial increase in gestational antidepressant use between 2007/08 and 2017/18, consistent with global trends (Cooper et al., 2007; Jimenez-Solem et al., 2013; Peterson et al., 2010; Ververs et al., 2006; Zoega, et al., 2015).
2. SSRIs are the most commonly prescribed antidepressant for expectant mothers, in line with global trends of increased reliance on SSRIs to treat both general- and antenatal depression (Cooper et al., 2007; Exeter et al., 2009; Jimenez-Solem et al, 2013; Peterson et al., 2010; Rosholm et al., 2001; Ververs et al., 2006; Zoega et al., 2015).
3. The majority of expectant mothers cease antidepressant use for the duration of their pregnancy, in line with the tendency observed in several other developed countries (Andrade et al., 2008; Petersen et al., 2010; Ramos et al., 2007; Zoega et al., 2015).
4. The age band ≥35 years shows the highest percentage of antidepressants prescribed during pregnancy, consistent with previous research findings where older maternal age has been associated with higher likelihood of continued antidepressant use during gestation (Jimenez-Solem et al., 2013; Ramos et al., 2007; Ververs et al., 2006).
5. High area level deprivation is associated with a higher proportion of gestational antidepressant usage compared to low- and medium area level deprivation, following previous findings that have specified low income and being on welfare as characteristics linked to greater gestational antidepressant use **(**Jimenez-Solem et al., 2013; Ramos et al., 2007).
6. Antidepressant use is higher for pregnant New Zealanders that identify as New Zealand European and/or Other than for pregnant Māori, Pasifika and Asian, consistent with the trend witnessed in the general New Zealand population (Bowden et al., 2019; Exeter et al., 2009; Wilkinson & Mulder, 2018).

Methods

Study population

All data used in this study was collected from Statistics New Zealand's Integrated Data Infrastructure (IDI), an extensive database of de-identified administrative and survey data about people and households, all linked at the individual level. A more comprehensive description of the IDI can be found in Milne et al.'s (2019) paper. The IDI enables us to identify a resident pregnant population, so that we can estimate population denominators, and link to sociodemographic information to explore differences in dispensing prevalence across our sociodemographic groups of interest.

The study population consisted of repeated cross-sections of women with at least one successful pregnancy, taken for each fiscal year between 1st July 2007 and 30th June 2018. The study population count for each fiscal year is presented in Table 1. The time period of interest was selected as it represents when reliable data are available for this study. Women with at least one successful pregnancy within a fiscal year were identified using the department of internal affairs (DIA) birth records. Further, we determined how many of these women were in the resident population through activity in the following key datasets: health, tax, education and injury claims (Gibb, Bycroft, & Matheson-Dunning, 2016; Zhao, Gibb, Jackson, Mehta, & Exeter, 2018) . Through applying this method to find the approximate resident population, the estimation falls within 2% of the official resident population estimate (Gibb et al., 2016). The DIA birth records were also used to obtain the gestational age of the child at birth, from which a back calculation to determine estimated date of conception was performed. The resulting approximations were used to calculate trimester start dates.

Antidepressant medication dispensing

Information on antidepressant medication dispensing was obtained by linking data from the Ministry of Health community pharmaceutical dispensing collection to the study

population. The pharmaceutical collection is recorded by the New Zealand Pharmaceutical Management Agency (PHARMAC) and contains information about subsidised prescription drugs dispensed by community pharmacists.

For each fiscal year, individuals were classified as obtaining a dispensing if they received at least one dispensing during their pregnancy for a medication classified as an antidepressant. The same method was used to determine dispensing within each trimester. There were 19 separate medications in total. Five selective serotonin re-uptake inhibitors (SSRIs) (Citalopram, Fluoxetine, Paroxetine, Escitalopram and Sertraline), three monoamine oxidase inhibitors (MAOIs)/ reversible inhibitors of monoamine oxidase A (RIMAs) (Tranylcypromine, Phenelzine and Moclobemide), one serotonin and noradrenaline re-uptake inhibitor (SNRI) (Venlafaxine), eight tricyclic antidepressants (TCAs) and related agents (Amitriptyline, Nortriptyline, Dosulepin, Doxepin, Clomipramine, Imipramine, Trimipramine and Maprotiline), one tetracyclic antidepressants (TeCA) (Miansein) and one noradrenergic and specific serotonergic antidepressant (NaSSA) (Mirtazapine).

Sociodemographic information

Age was calculated at the end of each fiscal year (i.e. 30th June) and then categorized into the following three bands: $\leq$ 24 years, 25–34 years, and $\geq$35 years. Many resident New Zealanders identify with multiple ethnic identities and ethnicity was therefore measured in a total response format (Statistics New Zealand, 2005). The current study focused on the following six ethnic groups, using Level 1 Statistics New Zealand categorisation: European; Māori; Pasifika; Asian; Middle Eastern, Latin American and African (MELAA); Other (Statistics New Zealand, 2005).

The NZDep2013 Index was used as a measure of area-level deprivation. Areas for the NZDep2013 Index are referred to as mesh blocks, with each mesh block receiving a deprivation decile value from 1 (least deprived) to 10 (most deprived), based on socioeconomic indicators from the 2013 NZ census (Atkinson, Salmond, & Crampton, 2014). Mesh blocks are evenly distributed across each deprivation level. For the current study, deprivation scores were converted into quintiles by joining adjacent deciles.

Table 1 presents the count of individuals in the study population within a fiscal year, broken down by age bands. Table 2 presents the count of individuals in the study population within a fiscal year, stratified by total response ethnicity and area-level deprivation.

Data analysis

Dispensing prevalence rates for each fiscal year were calculated for every pregnancy and each individual trimester. This was carried out separately for each fiscal year by dividing the number of pregnant women who received a dispensing within our period of interest (i.e. entire pregnancy, first trimester only), by the total number pregnant women in our study population in that year (note that these counts were random rounded to a base of 3 to reduce the likelihood of disclosure risk, as per the confidentiality rules of Statistics New Zealand). This method was used to calculate the dispensing prevalence across pregnancy for the total population and by age band, ethnicity and deprivation quintiles. Dispensing rates for each antidepressant medication type were also calculated. Though, dispensing rates for MOAIs and TeCAs were excluded, due to very low counts (<6 per fiscal year). All data management and analyses were conducted using SAS version 7.1. In the current study, dispensing prevalence rates are presented as ‘per 1000 population’.

Results

The total number of pregnancies exposed to antidepressants increased by 66.3% between 2007/08 and 2017/18, from 2.6% to 4.4% (see Table 4). Across the entire study period SSRIs were the most commonly prescribed antidepressant type. In the fiscal year 2007/08, 83.4% of all gestational antidepressants dispensed were SSRIs. This percentage steadily decreased over the study period, reaching 79.7% in 2017/18. This was a result of higher dispensing rate increases for SNRIs (328.5%) especially, and TCAs (18.9%), than for SSRIs (13%).

A trend of greater antidepressant use for trimesters 2 and 3, compared to trimester 1, was observed for the entire study period (Figure 1). All trimesters saw an increase in dispensing rates between 2007/08 and 2017/18, though increases for trimester 2 and 3 (83.9% and 74.5%) were higher than for trimester 1(50.3%), producing further disparity in dispensing rates between trimesters. In 2007/08 dispensing rates were 1.1% for trimester 1, 1.3% for trimester 2 and 1.8% for trimester 3. Whereas in 2017/18 these rates had increased to 1.7% for trimester 1, 2.4% for trimester 2, and 3.2% for trimester 3.

Classified by age bands, the group ≥35 years showed the highest dispensing rates over the entire study period, followed by 25 to 34 year olds, and lastly the group ≤24 years (Figure 2). Rates increased over time for all age groups, with the largest increase seen for those ≤24 years old (94.6%) and lowest for the group ≥35 years (46.7%).

Dispensing prevalence by NZDep quintiles is shown in Figure 3. Across the entire study period quintiles 1 to 4 had very similar dispensing rates, while Quintile 5 showed dispensing rates that were markedly lower. All quintiles saw increases in dispensing rates between 2007/08 to 2017/18. Quintile 5 had the highest rate increase (80.1%), followed by

Quintile 3 (74.5%), Quintile 1 (58.6%), Quintile 4 (61.5%) and finally Quintile 2, with the lowest rate increase of 49%.

Figure 4 presents dispensing prevalence by ethnicity. The Other and European categories consistently show the highest dispensing rates across all fiscal years included in the study, and the Pasifika and Asian category show the lowest. Dispensing rates increased for all ethnicities over the documented period. The Pasifika category had the largest increase (161%), followed by the Other category (152%), Māori (106%), European (80%), Asian 31%) and MELAA (27%).

Table 1. Population counts per fiscal year, stratified by age band.

Fiscal year	**Total Population**	**≤24 yrs**	**25 to 34 yrs**	**≥35 yrs**
2007/08	60,843	13,392	30,876	16,575
2008/09	60,390	13,569	30,528	16,293
2009/10	61,323	13,518	31,389	16,419
2010/11	60,105	13,107	31,002	15,999
2011/12	58,674	12,576	30,621	15,480
2012/13	57,642	11,769	30,726	15,147
2013/14	55,947	10,812	30,489	14,649
2014/15	55,848	10,032	31,443	14,373
2015/16	55,713	9,483	31,410	14,820
2016/17	56,142	8,922	32,508	14,712
2017/18	55,194	8,475	32,154	14,565

Table 2. Counts per fiscal year, stratified by total response ethnicity.

Fiscal year	European	Māori	Pasifika	Asian	MELAA	Other
2007/08	41,229	14,757	7,179	6,096	978	621
2008/09	40,716	14,742	7,227	6,189	1,008	591
2009/10	41,049	14,778	7,179	6,630	1,023	558
2010/11	39,816	14,346	7,335	7,035	1,044	546
2011/12	38,328	13,941	7,080	7,410	993	510
2012/13	37,020	13,323	6,678	8,262	981	483
2013/14	35,889	12,795	6,417	8,205	1,080	471
2014/15	35,205	12,651	6,228	9,084	1,155	486
2015/16	34,932	12,780	6,270	9,273	1,197	498
2016/17	34,509	12,701	6,102	10,263	1,341	444
2017/18	33,996	12,408	6,282	9,957	1,317	492

Table 3. Annual dispensing by NZDEP2013 Quintiles.

Fiscal year	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
2007/08	9,354	10,293	11,187	12,075	16,590
2008/09	9,075	10,473	11,097	12,243	16,386
2009/10	9,192	10,395	11,574	12,570	16,575
2010/11	9,219	10,395	11,253	12,030	16,368
2011/12	8,904	9,957	11,016	12,084	16,077
2012/13	8,862	10,125	10,986	11,817	15,294
2013/14	8,757	9,762	10,791	11,562	14,466
2014/15	8,985	9,807	10,656	11,454	14,367
2015/16	8,838	9,714	10,740	11,466	14,454
2016/17	8,925	10,068	10,875	11,307	14,511
2017/18	8,589	9,885	10,605	11,409	14,232

Table 4. Annual dispensing prevalence (per 1000 population) overall and by trimester.

Fiscal year	Overall	Trimester 1	Trimester 2	Trimester 3
2007/08	26	11	13	18
2008/09	29	12	15	20
2009/10	31	13	16	21
2010/11	33	14	17	23
2011/12	33	13	18	24
2012/13	33	13	17	24
2013/14	35	13	18	25
2014/15	35	14	18	25
2015/16	38	15	20	28
2016/17	41	17	22	31
2017/18	44	17	23	32

Figure 1. Dispensing trends by trimester.

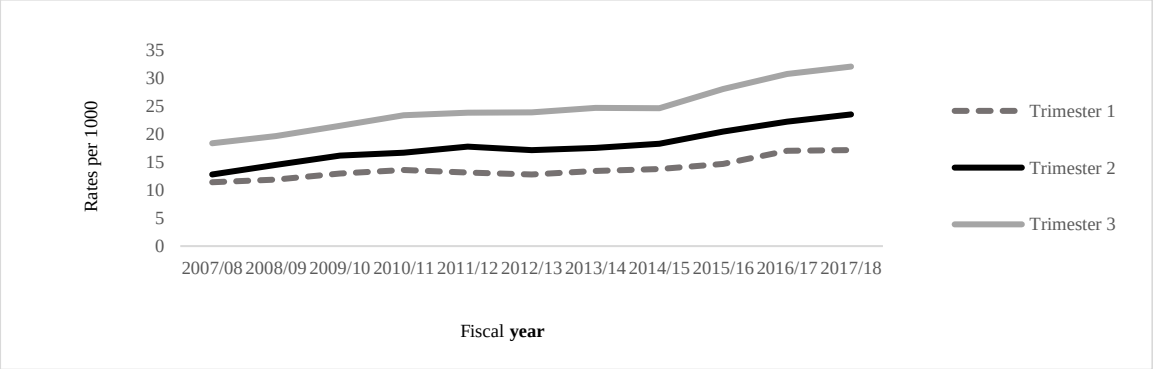


Figure 2. Dispensing trends by age categories.

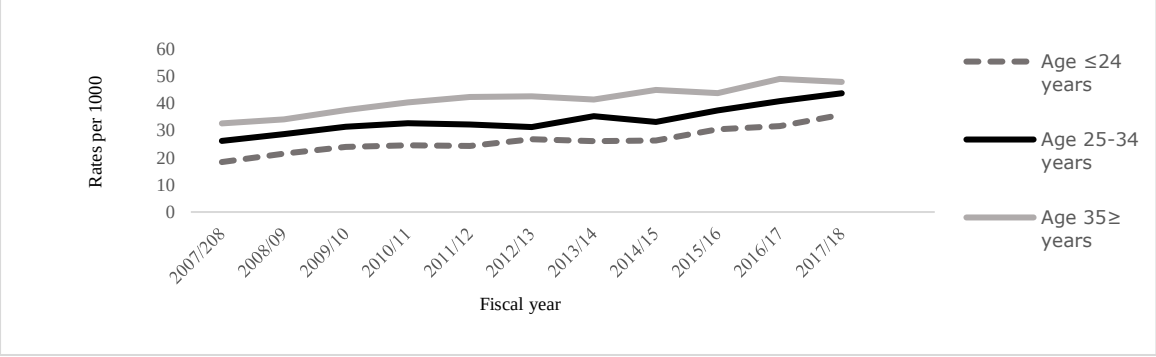


Figure 3. Dispensing trends by area deprivation level quintiles.

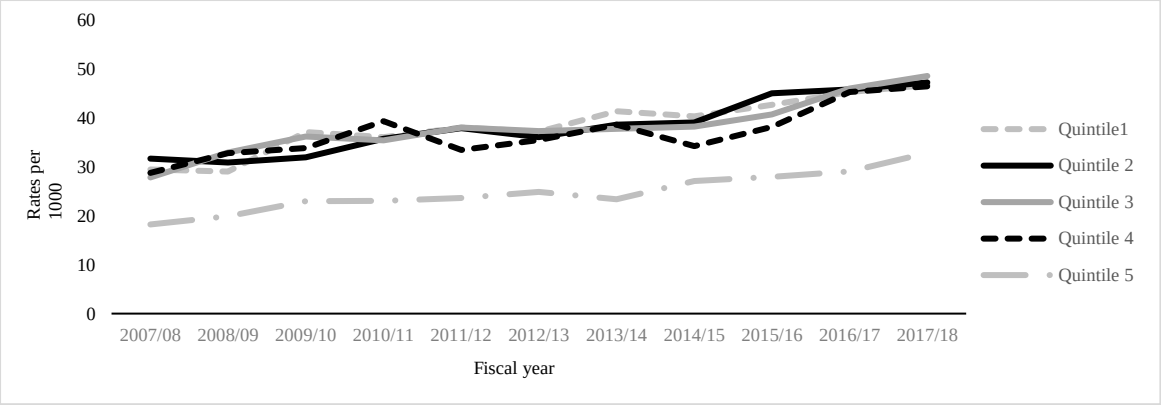
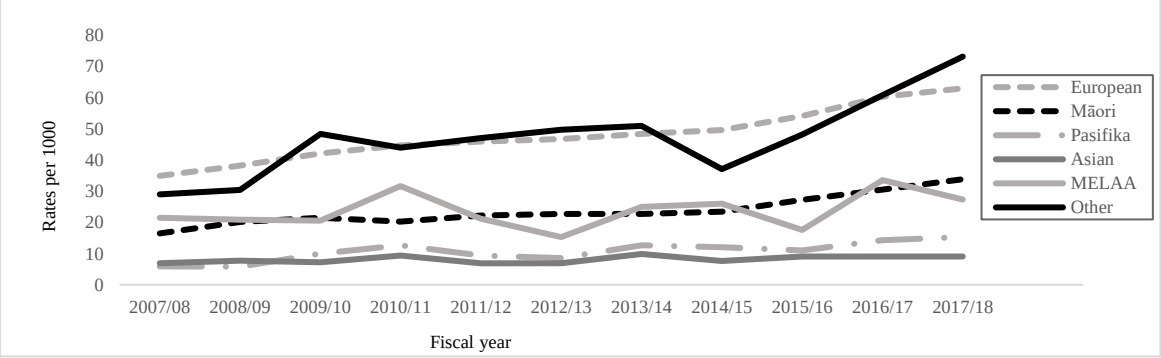


Figure 4. Dispensing trends by ethnicities.



Discussion

We explored gestational antidepressant dispensing trends and prevalence in New Zealand through the analysis of administrative community pharmaceutical dispensing data. Between 2007/08 and 2017/18 antidepressant dispensing for pregnant women increased by 66.3%, from 2.6% to 4.4%. This finding is consistent with our hypothesis and follows global trends of increased reliance on antidepressants as a treatment for more severe antenatal depression (Cooper et al., 2007; Jimenez-Solem et al., 2013; Peterson et al., 2010; Ververs et al., 2006; Zoega, et al., 2015). The increased dispensing may be a product of better access to antidepressants, combined with increased use of SSRIs and SNRIs in treating psychiatric disorders beyond depression (Bowden et al., 2019; Jimenez-Solem et al., 2013; Shatzberg, 2000).

There was evidence of increased dispensing across all age groups, trimesters, ethnicities and area level deprivation quintiles, though with considerable variation within each set of classifications. Dispensing rates were lower for all categories (1.7–6.3%) than the estimated global prevalence of antenatal depression (7–13%) (Bennet et al, 2004; Gavin et al., 2005). This suggests that a considerable amount of women, particularly within certain ethnicities and deprivation area levels, live with untreated antenatal depression and face increased risks of poor health outcomes for both themselves and their child (Alwan et al., 2013; Andersson et al., 2004; Jarde et al., 2016; Wang & McDonald, 2016; Qiu et al., 2009**)**. It is likely that some women sought non-medical treatment for the condition. However, prior research has established that many women receive no formal treatment for antenatal depression at all (Marcus, Flynn, Blow and Barry, 2004). As such, non-medical treatment is unlikely to explain the entire difference between prevalence and dispensing. Further research that includes prevalence of non-pharmacological treatment is necessary in order to determine the magnitude of undertreatment.

As predicted by our hypothesis, SSRIs were the most frequently dispensed medication type. In 2017/18, they accounted for 79.7% of all antidepressants dispensed during gestation, a slight decrease from the start of the study period. Internationally, the SSRIs consistently make up 80–90% of all antidepressants dispensed during pregnancy, placing our finding within the lower end of global trends (Alwan et al., 2013; Andrade et al., 2008; Petersen et al., 2010). Widespread SSRI preference reflects the overall tolerability and broad therapeutic range of this class of antidepressants (Marken & Munro, 2000). The reduction in SSRI market dominance observed for this current study, was the result of higher relative dispensing rate increases for SNRIs and TCAs compared to SSRIs. In particular, the increased SNRI dispensing (328%), was responsible for this shift. Venlafaxine (SNRI), the sole SNRI that is funded through Pharmac, is recommended for use during pregnancy where treatment resistant depression exists (Waitemata District Health Board, 2019). For that reason, it is hypothesized that the substantial increased SNRI dispensing is owed to a growing awareness of Venlafaxine as a second-line pharmacological treatment option during gestation.

Antidepressant dispensing in the overall study population (2.6-4.4%) stayed well below the prevalence that Wilkinson and Mulder (2018) uncovered for New Zealand's female population aged 15 and over (16%), across the entire study period. Consequently, it is highly likely that a large number of women terminated antidepressant use for the entire duration of pregnancy. Consistent with our hypothesis, this finding follows the international tendency towards large-scale antidepressant cessation during pregnancy (Andrade et al., 2008; Ramos et al., 2007; Jimenez-Solem et al., 2013; Petersen et al., 2010; Ververs et al., 2006; Wilkinson & Mulder, 2018; Zoega et al., 2015). The small increases in risks to the baby that are associated with antidepressant exposure through gestation are believed to be the cause of this widespread discontinuance (Bérard et al., 2006; Chambers et al., 2006; Huybrechts, et al., 2014; Källén & Olausson, 2007; Kieler et al., 2012).

Trimester specific analysis revealed a pattern of increased dispensing following the first trimester. Relative dispensing rate increases were greater for trimesters 2 and 3 compared to trimester 1, which caused the difference in trimester dispensing to increase across the study period. In 2017/18, antidepressant dispensing was 37% higher for trimester 2, and 87% higher for trimester 3, than for trimester 1. Our results are unique and contrasts those of prior studies, where significant decreases in dispensing with progressing pregnancy is consistently reported (Andrade et al., 2008; Petersen et al., 2010; Ramos et al., 2007; Zoega et al., 2015). Policies on antenatal depression treatment in New Zealand follow international guidelines that recommend antidepressant for severe depression, as well as moderate depression that has been unresponsive to non-pharmacological treatment (Community HealthPathways Canterbury; Molenaar, Kamperman, Boyce & Bergink, 2018). Without any clear separation between New Zealand and global recommendations regarding treatment of antenatal depression, there is an indication that something beyond clinical guidelines is influencing the trimester dispensing observed for this study.

Considering the association between first trimester antidepressant exposure, and heightened risk of foetal malformations and persistent pulmonary hypertension, our results may reflect a greater unwillingness to prescribe antidepressants during the earliest stage of gestation, compared to mid-to-late pregnancy (Bérard et al., 2006; Källén & Olausson, 2007; Malm et al., 2011, Medsafe, 2013; RNZCA, 2015; Wurst et al., 2009). However, as dispensing was greatest for trimester 3, a stage of pregnancy where antidepressant exposure is linked to increased risk of withdrawal syndrome, risk assessment is unlikely to justify the entire disparity in trimester dispensing (Galbally et al., 2009; Nordeng, et al., 2001). An additional factor that could have shaped the observed trimester dispensing was identified by Bennet et al. (2004). In their study on antenatal depression Bennet et al. (2004) found prevalence rates of 7.4% for trimester 1, 12.8% for trimester 2 and 12% for trimester 3. Greater prevalence of depression

during trimesters 2 and 3 could account for the increased dispensing observed during mid-to-late pregnancy for this current study. Though, as pointed out by Bennet et al. (2004), their findings have potential confounds and should be used with caution. For instance, antenatal depression sufferers may be less likely to seek early prenatal care (Bennet et al., 2004).

Consistent with our hypothesis, the oldest maternal age group (≥35 years) displayed the highest dispensing rate. Despite young maternal age (<25 years) being linked to a higher incidence of antenatal depression, numerous previous studies report findings similar to ours (Fransson et al. 2011; Kitamura et al. 2006; Jimenez-Solem et al., 2013; Petersen et al., 2001; Ramos et al., 2007; Rubertsson & Waldensrtöm; Ververs et al., 2006). Antidepressant use in the general New Zealand population also increases with age **(**Exeter et al., 2009; Wilkinson & Mulder, 2018**).** Statistically, women of older maternal age are therefore more likely to have had prior experience with antidepressants than younger expectant mothers. As a result, our findings may reflect that older mothers are more prepared to use antidepressants during pregnancy, as a result of prior use that has proven helpful. In support of this suggestion, Ververs et al. (2006) found that antidepressant use was higher in mothers of older maternal age preconceptionally. Further, Petersen et al. (2001) results showed that beyond young maternal age, discontinuation of antidepressants during gestation, was also associated with having none or just 1 antidepressant prescription in the 6-months prior to pregnancy. In order to fully determine whether increased exposure to antidepressants with increasing age is causing the discrepancy, additional investigation is required.

The overall similarity in dispensing rates between quintiles 1 to 4 does not support our prediction that gestational antidepressant use should increase with greater area level deprivation. Also inconsistent with our hypothesis, Quintile 5 showed a markedly lower dispensing rate than all other quintiles. This remained true across the entire study period, despite Quintile 5 seeing the highest relative dispensing rate increase. These results diverge

from the expectation created by Jimenez-Solem et al. (2013)'s and Ramos et al. (2007)'s reports of low income as a predictor of greater gestational antidepressant use. Further, from the link between low socioeconomic status and higher incidence of antenatal depression (Leigh & Milgrom, 2008; Murphy et al., 1991). Rather than imply that deprivation and antenatal depression is not associated in New Zealand, low dispensing for the most deprived quintile in all probability reflects financial barriers in accessing prescription medication (Bowden et al., 2019; Jatrana, Crampton & Norris, 2010; Leigh & Milgrom, 2008; Murphy, et al., 1991).

Categorized by ethnicity, a dispensing trend similar to that identified in New Zealand's youth and general population was established (Bowden et al., 2019; Wilkinson & Mulder, 2018). Dispensing rates were highest for the Other and the New Zealand European categories, followed by Māori, MELAA, Pasifika and Asian. In 2017/18 dispensing rates for New Zealand Europeans were 1.9 times higher than for Maori, 2.3 times higher than for MELAA, 4.1 times higher than for Pasifika and 7 times higher than for Asians. Women of Pasifika, Asian and Other (including MELAA) ethnicities in New Zealand are approximately twice as likely to suffer from antenatal depression as New Zealand Europeans (Waldie et al., 2015). Furthermore, Māori females aged 15 and over are about 1.3 times more likely to suffer from an anxiety or depressive disorder than Non-Māori (Ministry of Health, n.d.). As such, the observed difference cannot be explained by a higher prevalence of antenatal depression among New Zealand Europeans compared to other ethnicities. Factors such as stigma, scepticism towards mental health services and a general reluctance to accept the presence of mental health problems could inform why the women that identify as Asian displayed the lowest dispensing rate, as well as the lowest relative dispensing increase, across the entire study period (Lauber and Rossler, 2006). Indeed, Lauber and Rossler (2006) report a low use of mental health services across developing countries in Asia.

Results from the New Zealand Health Survey 2017/18 and Maori Health Statistics (2013) suggest that socioeconomic status is influencing the observed dispensing rates for Māori and Pasifika (Ministry of Health, 2019). In 2013, 23.5% of Māori lived in areas of the highest deprivation level, compared to 6.8% of Non-Māori (Kahukura, 2015). Moreover, in 2017/18, adults and children of Māori and Pasifika ethnicities, were over 2 times more likely to not fill prescriptions due to cost than New Zealand Europeans (Ministry of Health, 2019). Cultural views of mental health could also inform dispensing for Māori and Pasifika. These ethnicities have an understanding of health that is holistic and differs from the western biomedical approach **(**Agnew et al., 2004; Cram, Smith, & Jonstone, 2003; Mark & Lyons, 2010; Norris et al., 2011). Women of these ethnicities might therefore be choosing treatment models that are better suited to their cultural views than standard pharmacological based treatment.

We are aware that our study may have some limitations. Dispensing rates for the study population prior to pregnancy were not obtained. Therefore, we had to rely on antidepressant prevalence from another study, to determine whether cessation occurred. However, two factors make us confident that our results are sufficiently reliable. Firstly, there was a substantial difference between antidepressant prevalence during gestation and prevalence in the general population. Furthermore, all prior research have reported lower dispensing than prevalence (Cooper et al., 2007; Jimenez-Solem et al., 2013; Peterson et al., 2010; Ververs et al., 2006; Zoega, et al., 2015).

Another limitation of our study is that it is based on dispensing records without any access to diagnosis information. Thus, some dispensing could have been for conditions other than antenatal depression, in particular various anxiety disorders (Shatzberg, 2000). Further, with dispensing records we are unable to tell whether dispensed medication is actually used. Relating to this, our study was restricted to filled prescriptions, making it unlikely to reflect all prescriptions made for antidepressants. This is especially significant, considering findings

which indicate that some experience inability to fill prescriptions due to cost (Jatrana et al., 2010; Leigh & Milgrom, 2008; Murphy, et al., 1991).

Parallel with global trends, our results demonstrate that antidepressant use during gestation is increasing. We found evidence of increased dispensing for all age groups, ethnicities and across all trimesters. Despite the overall increase, dispensing rates were much lower than antenatal depression prevalence estimates. Supported by prior research, this suggests that undertreatment is prevalent (Marcus et al., 2004). Though, we are not able to determine the extent of undertreatment as the IDI does not provide information about non-pharmacological treatment prevalence.

Despite some data limitations, a great strength of this current study was the access that the IDI provided to dispensing information for all resident pregnant New Zealanders.
An additional advantage was the ability to link study findings at the socioeconomic, ethnicity and trimester specific level. Opposite global trends, we uncovered a pattern of increased dispensing following trimester 1. There is evidence of substantial variation in dispensing rates between different ethnicities and deprivation levels. We therefore stress the need to establish underlying causes in order to reduce health inequities. Future examination into prevalence of undertreatment and its causes are also essential to ensure better health outcomes for antenatal depression sufferers and their children.

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