

# 4<sup>th</sup> Pharmacoepidemiology Research Network Symposium

# Wednesday 21 November 2018, 10:00am – 4:30pm Arana College University of Otago Dunedin

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# ABSTRACTS

# Prescribed medicines in pregnancy

#### **Irene Petersen**

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Many women of childbearing potential are treated with prescribed medicines. However, few medications have been licenced for use in pregnancy. This leaves women and their health care professional(s) in a treatment dilemma when women become pregnant as they need to balance the health of the woman with that of the unborn child.

In this presentation, I will demonstrate how data from electronic health records can be used to examine the use and potential effects of prescribed medicines in pregnancy. Using data from large primary care databases in the UK we have developed cohorts of more than 700,000 pregnancies and created a linked mother and child cohort. I will illustrate how pregnancy is a determinant for many drug treatments. For example, we have observed that only 1 in 5 women continue antidepressant treatment in pregnancy and the patterns of discontinuation is similar for other psychotropic medications. I will also demonstrate how we can use electronic health records to evaluate drug safety in pregnancy and discuss some of the challenges that we are faced with when working with observational data.

# The International Pregnancy Safety Study (InPreSS)

**Helga Zoega**<sup>1,2</sup>, Krista F. Huybrechts<sup>3</sup>, Brian T. Bateman<sup>3</sup>, Helle Kieler<sup>4</sup>, Carolyn Cesta<sup>4</sup>, Kari Furu<sup>5</sup>, Jacqueline Cohen<sup>5</sup>, Kristjana Einarsdottir<sup>2</sup>, Mette Norgaard<sup>6</sup>, Henrik Toft Sørensen<sup>6</sup>, Mika Gissler<sup>7</sup>, Leena Saastamoinen<sup>7</sup>, Alys Havard<sup>1</sup>, Andrea Schaffer<sup>1</sup>, Sonia Hernandez-Diaz<sup>8</sup>; on behalf of the InPreSS Consortium

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#### Background

The use of prescription medicines has increased significantly among pregnant women in recent years, yet evidence regarding medicine safety is largely lacking for this population. As pregnant women are typically excluded from clinical trials, linkage of routinely collected pharmaceutical dispensing and health data is the only practical way to assess the use and effects of medicines during pregnancy.

## Aim

The goal of the International Pregnancy Safety Study (InPreSS) collaboration is to provide the best available human data on the safety of prescription medicines during pregnancy by combining high quality data from several countries and applying state-of-the art research methods.

## Methods

The InPreSS consortium is a collaboration among research groups with access to linked health care data with proven ability to study the safety of medicines in pregnancy. To date InPreSS has included: nationwide US Medicaid data that cover close to 50% of pregnancies in the country, the national registries in the five Nordic

countries that cover virtually all pregnancies resulting in live births or stillbirths, and data from the MUMS study in New South Wales, Australia's most populous state. By pooling such large-scale data, containing information on prescription medicine use, maternal health, pregnancy, labour, and birth outcomes, it is possible to study rare *in-utero* medicine exposures and rare outcomes, which would not otherwise be possible to examine, e.g. in smaller datasets or in pre-marketing settings.

#### Results

I will give an overview of InPreSS and provide a few examples of recent study results produced within the consortium, including on the risks of congenital malformations with early pregnancy use of ADHD medicines and beta-blockers; and on utilisation patterns of antipsychotics, antiepileptics and antidiabetics across the pregnancy period.

#### Conclusions

InPreSS has already yielded high-impact work on medicine use and safety in pregnancy. It has extensive plans to study neurodevelopmental outcomes in children exposed to medicines *in-utero*, as well as the potential consequences of discontinued treatment in pregnancy on maternal health. We expect these international research efforts will help guide clinicians and women to optimal treatment solutions for women of childbearing age, especially during pregnancy.

# The safety and effectiveness of smoking cessation pharmacotherapies during pregnancy: findings from the Smoking MUMS (Maternal Use of Medications and Safety) Study

**Alys Havard<sup>1</sup>**, Duong T Tran<sup>1</sup>, Stephanie KY Choi<sup>1</sup>, Preen B David<sup>2</sup>, Anna Kemp-Casey<sup>2</sup>, Deborah Randall<sup>3</sup>, Kristjana Einarsdottir<sup>4</sup>, Michael Daube<sup>5</sup>, Louisa R Jorm<sup>1</sup>

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#### Background

Evidence regarding the safety and effectiveness of smoking cessation pharmacotherapies during pregnancy is limited, preventing informed decision making regarding use of these medicines during pregnancy.

#### Aims

To examine the risk of adverse birth outcomes and congenital malformations associated with the use of bupropion, varenicline and nicotine replacement therapy (NRT) patches during pregnancy, and to compare varenicline and NRT with respect to adverse birth outcomes and smoking cessation.

#### Methods

Perinatal data for all births (2003 - 2012) in New South Wales and Western Australia were linked to pharmaceutical dispensing, hospital separations and

mortality data. When examining the safety of varenicline, bupropion and NRT, exposed pregnancies were propensity score matched with pregnancies among untreated smokers (1:10). In Cox-proportional hazard models, exposure was treated as time-dependent, and follow-up varied according to the outcome (e.g. 13 weeks for congenital malformations, 37 weeks for preterm birth). When comparing varenicline and NRT with respect to birth outcomes, exposed pregnancies were matched (1:1) on year of conception and week of exposure and analysed using multivariable Cox models. Pregnancies exposed to varenicline and NRT during the first 20 weeks were compared in terms of smoking cessation, defined as no smoking after the 20th week. These treatment groups were balanced using inverse probability of treatment weighting with propensity scores.

#### Results

There was no elevated risk of adverse birth outcomes with any pharmacotherapy during pregnancy, compared with no treatment. Varenicline use was associated with a lower risk of preterm birth (hazard ratio, HR 0.72 [95% CI 0.57 – 0.91]), small for gestational age (HR 0.73 [95% CI 0.61 – 0.88]) and a composite measure of birth outcomes (HR 0.81 [95% CI 0.73 – 0.91]). No increased risk of major congenital malformations (HR 0.95 [95% CI 0.59 – 1.53]) existed. Congenital malformations were not examined for bupropion and NRT due to insufficient statistical power. When compared to NRT, varenicline was associated with a lower risk of any adverse birth outcome (HR 0.57 [95% CI 0.38 – 0.83]), and a higher rate of smoking cessation (rate difference 15.7% [95% CI 5.5 – 25.8]).

#### Conclusions

These findings suggest a need for further evidence to inform clinical guidelines which currently advise against the use of varenicline and bupropion during pregnancy, and recommend use of NRT when the expected benefits outweigh the risks.

# Trajectories of antipsychotic use before and during pregnancy and related maternal and birth characteristics: an Australian population-based study (2005 – 2012)

**Andrea L Schaffer**<sup>1</sup>, Helga Zoega<sup>1,2</sup>, Duong T Tran<sup>1</sup>, Nicholas A Buckley<sup>3</sup>, Sallie Pearson<sup>1,4</sup>, Alys Havard<sup>1</sup>

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#### Background

There is no clear guidance for the use of antipsychotics during pregnancy due to limited safety evidence. However, antipsychotic use in pregnancy is increasing, and there is a lack of detailed information about variations in patterns of treatment.

#### Aim

To identify trajectories of antipsychotic use prior to and during pregnancy, and to describe the maternal sociodemographic and mental health characteristics and pregnancy and birth outcomes associated with different trajectories of antipsychotic use.

## Methods

We used administrative claims data to conduct a retrospective cross-sectional study of women who were concessional beneficiaries and gave birth in New South Wales, Australia (2005 - 2012). We estimated the antipsychotic daily dose and duration of use in the 450 days prior to conception and during pregnancy using dispensing claims. We used group-based trajectory modelling to identify differential patterns of antipsychotic use over time. We characterised women with different trajectories according to maternal sociodemographic characteristics, mental health diagnoses and hospitalisations, use of psychotropic medicines, and birth outcomes.

### Results

Of 135,252 women who gave birth, 2741 (2.0%) were exposed to an antipsychotic prior to or during pregnancy. We identified six distinct trajectories: in two trajectories, women used low daily doses of antipsychotics in the short-term prior to pregnancy only (51.7%), while women in three trajectories had long-term use of low (20.7%), moderate (11.0%), and high (2.0%) daily doses with continuing use in pregnancy. Women in one trajectory (15.0%) had increasing use during pregnancy. Women with long-term use were more likely to have a schizophrenia or bipolar disorder diagnosis, to have used mood stabilisers, and to have a mental health hospitalisation during pregnancy. Compared to women with no antipsychotic exposure, women using antipsychotics had a higher rate of preterm birth, a baby admitted to NICU or diagnosed with neonatal abstinence syndrome. Women with the greatest exposure to antipsychotics had the highest rates of gestational diabetes and gestational hypertension.

## Conclusion

Pregnant women using antipsychotics were heterogeneous in terms of their mental health characteristics and birth outcomes. This variability should be considered not only in clinical practice, but in research evaluating the safety of antipsychotic use during pregnancy.

# Prescription medicine use during pregnancy in New Zealand, 2005 – 2015

**Sarah Donald<sup>1,2</sup>**, Dave Barson<sup>1,2</sup>, Katrina Sharples<sup>1,3,4</sup>, Simon Horsburgh<sup>1,2</sup>, Lianne Parkin<sup>1,2</sup>

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Internationally, prescription medicine use during pregnancy is increasing with respect to both the proportion of women taking at least one medicine, and the number of different medicines to which pregnant women are exposed. Patterns of prescription medicine use in pregnancy in New Zealand have not been described. We undertook a study to describe dispensing patterns in pregnancy in New Zealand over the time period 2005 - 2015.

Pregnancies in the New Zealand Pregnancy Cohort with a last menstrual period date from 1 May 2005 to 15 March 2015 (n=912,964) were linked with their dispensing history in the Pharmaceutical Collection, from 120 days prior to conception through to the end of the pregnancy. Exposure was defined as at least one dispensing of a prescription medicine in the period of interest. Vitamins, minerals, and folic acid were excluded from the present analyses, as were vaccines and non-medicinal products. We investigated the overall proportion of pregnancies during which at least one prescription medicine was dispensed, and changes in this proportion over the study timeframe. We also looked at the number of different medicines dispensed to pregnant women who were dispensed at least one medicine. Dispensing patterns were analysed by sociodemographic factors including maternal age, ethnicity, NZDep quintile, smoking status, body mass index and parity. We explored which therapeutic groups were dispensed to the highest proportions of pregnant women overall and compared patterns of use pre-

pregnancy and during pregnancy. Changes over time in the proportions of women with at least one dispensing from these therapeutic groups during pregnancy were also investigated.

In this talk I will present provisional results from the study.

# PHARMAC elimination of inequities in access to medicines by 2025

#### Sandy Bhawan<sup>1</sup>, Jason Arnold<sup>1</sup>

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Not all New Zealanders are achieving 'best health outcomes' from medicines funded by PHARMAC. Research suggests that there is inequitable access to medicines. PHARMAC's updated research report on Māori uptake of medicines shows Māori are continuing to receive funded medicines in the community at a lower rate than non-Māori, despite their health need being higher. This was seen particularly in chronic conditions like diabetes, heart disease, asthma and chronic obstructive pulmonary disease. The Health Quality & Safety Commission's Atlas of Healthcare Variation and Equity Explorer also provides examples of inequities in relation to health outcomes and medicines access.

The causes of inequities are complex, and solutions do not lie solely with the funding of medicines, or within the health system.

PHARMAC presenters will explore the drivers of inequity and show how analysis can be used to understand the drivers. In particular, we will examine how we can sequence an individual's usage for a class of medication in a 6-month period in terms of starting, stopping, one off or short-term usage. This sequencing can then be used to determine if people's medication choices change over time or if changes in policy impact on people's choices. As an example, we will look at how people's medication choices changed following the introduction of free treatment and medication for under 13s.

# Using the M<sup>2</sup> scheme to investigate safety signals

**Maria Storey<sup>1</sup>**, Ruth Savage<sup>2</sup>, Johanna Stenlund<sup>3</sup>, Michael Tatley<sup>2</sup>, Susan Kenyon<sup>1</sup>

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# Background

The Centre for Adverse Reactions Monitoring (CARM) is contracted by Medsafe to collect voluntary reports of adverse reactions to medicines affecting New Zealanders. Safety signals are identified from these reports by CARM and Medsafe. One option for investigating these safety signals further is to use the Medicines Monitoring scheme (M<sup>2</sup>). More information about this scheme can be found on Medsafe's website (www.medsafe.govt.nz/safety/EWS/EWS.asp).

 $M^2$  is part of an early warning system for advising of safety concerns with medicines and medical devices. The intention of the scheme is to highlight the concern, encourage further reporting and help investigate the signal.

# Objective

To use an example of dabigatran and a potential association with gout to show how the  $M^2$  scheme operates as a method to investigate safety concerns.

# Discussion

The speaker will outline how a safety signal is identified and regarded suitable for  $M^2$ , describe the steps in the process and discuss the outcome of placing the signal on  $M^2$ .

# Do Australians need fewer warnings about harm from medicine use? A 10-year overview of post-market regulatory safety advisories in Australia, Canada, the United Kingdom (UK) and the United States (US)

Lucy Perry<sup>1</sup>, Alice Bhasale<sup>1</sup>, Joel Lexchin<sup>2</sup>, Lorri Puil<sup>3</sup>, Maisah Joarder<sup>1</sup>, **Barbara Mintzes<sup>1</sup>** 

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#### Background

National regulatory agencies use safety advisories to communicate emerging risks of medicines to clinicians and the public. There has been little international comparative analysis of differences between regulators in the decision to warn or how Australia's Therapeutic Goods Administration (TGA) compares with other regulators.

#### Aim

The aim of this study is to compare the frequency, timing and content of postmarket safety advisories in Australia, Canada, the UK and the US from 2007 to 2016.

#### Methods

This is a retrospective analysis of safety advisories, based on information from regulators' websites, with duplicate independent coding of content on drugs, safety concerns and regulatory advice. We used Anatomical Therapeutic Coding (ATC) and MedDRA coding to group these advisories into drug-specific safety concerns for comparison. We assessed warning rates per country only for drugs approved when the first advisory was issued in each country. Warnings on product quality, drug shortages, medication errors and over-the-counter drugs were excluded.

#### Results

Over this decade, we identified 1441 advisories, 469 from the UK, 382 from the US, 370 from Canada and 220 from Australia. Most focused on a single drug (n=1034) and in total, there were 680 drug or class-specific safety concerns. The TGA was the least likely to issue an advisory, with none issued for 436 safety concerns (70.4% of advisories on drugs approved in Australia), and the UK the most likely. Included countries issued the same warnings in only 70 cases, representing 10% of identified safety concerns. The most frequently featured drugs were rosiglitazone, varenicline, natalizumab, mycophenolate and pioglitazone. Cardiac and nervous system disorders were the most frequent safety concerns.

#### Conclusions

This is the first comprehensive overview of post-market safety advisories in four countries. We found extensive differences, raising concerns about the information prescribers and the public obtain about the safety of medicines, with implications for public health. We also plan follow-up pharmacoepidemiological analyses using discrepancies between countries as a set of 'natural experiments' to examine the effects of safety advisories on medicine use and health outcomes.

# Evidence-practice gaps in post-discharge cardiac care: demonstrating the benefits of programmatic, crossjurisdictional data linkage in Australia

Andrea Schaffer<sup>1</sup>, Michael Falster<sup>1</sup>, Louisa Jorm<sup>1</sup>, Andrew Wilson<sup>2</sup>, David Brieger<sup>3</sup>, Arthur Nasis<sup>2</sup>, Melanie Hay<sup>4</sup>, **Sallie Pearson<sup>1</sup>** 

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#### Background

Australia spends more on cardiovascular disease than on any other disease group. Making best use of the data generated through day-to-day interactions with the health care system has the potential to improve cardiac health outcomes and drive evidence-informed policy. In December 2016, the Australian Health Ministers' Advisory Council approved the National Data Linkage Demonstration Project (NDLDP) to determine the value of linking data from Commonwealth and State health care agencies to inform health policy. The Victorian Agency for Health Innovation is leading a program using this data collection to identify evidence-practice gaps in cardiac care.

## Aim

To examine the post-discharge pharmacological management of patients admitted to hospital with acute myocardial infarction (AMI) or atrial fibrillation (AF) in NSW and Victoria.

## Methods

We used hospital data, dispensing claims and mortality data from the NDLDP (July 2011 – December 2013) to examine dispensing of recommended pharmacological therapy within 30 days of discharge, between-hospital variation in post-discharge dispensing at 30-days, and persistence at 1-year.

## Results

We identified 24,583 patients with a primary diagnosis of AMI; 57.1% were dispensed a P2Y12 receptor antagonist within 30 days of discharge and 74.7% of those with a dispensing within 30 days were persistent at 1 year. We observed significant variation by hospital in predicted rates of 30-day dispensing, ranging from 32% to 71% of patients. We identified 82,996 patients hospitalised with an AF diagnosis. 33.0% were dispensed an oral anticoagulant within 30 days of discharge, most commonly warfarin (91.2%). Dispensing was highest in high-risk patients (33.8%) and 60.4% of those with a dispensing within 30 days were persistent at 1 year. Variation in predicted rates of 30-day dispensing ranged from 22% to 53%.

#### Conclusions

This large data resource of linked Commonwealth and State data has facilitated the investigation of best-practice guideline adherence in cardiac care and demonstrated the value in examining patient care pathways across hospital and community-based services. The NDLDP is a high-value national resource with the potential to inform clinical and policy practice in cardiovascular and other non-communicable diseases.

# Improving metformin adherence and persistence in people with type 2 diabetes: an update

**Simon Horsburgh**<sup>1,2</sup>, Lianne Parkin<sup>1,2</sup>, Dave Barson<sup>1,2</sup>, Katrina Sharples<sup>1,3,4</sup>, Jimmy Zeng<sup>1,2</sup>, Lisa Te Morenga<sup>5</sup>, Faumuina Fa'afetai Sopoaga<sup>6</sup>

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The 2016/2017 New Zealand Health Survey estimates that around 197,000 New Zealanders aged 25 or over (6.2% of that population) have been diagnosed with type 2 diabetes mellitus (T2DM), with markedly higher prevalences observed in Māori, Pacific Peoples and people in higher deprivation areas. Metformin is an effective antidiabetic medication, and is recommended as the first-line pharmaceutical treatment for T2DM. Overseas research has found that many patients have suboptimal metformin adherence and persistence, reducing the effectiveness of metformin for achieving good levels of glycaemic control and increasing the risk of T2DM complications. In this project, we sought to examine adherence in new metformin users in the New Zealand context and identify potential factors which might influence adherence.

A national cohort of people with T2DM who initiated metformin monotherapy between 1 January 2006 and 30 September 2014 was identified from the Virtual Diabetes Register. Data from the Ministry of Health data collections (NHI, Pharms, NMDS, GMS, PHO, LAB, Mortality, NZCR) were obtained for this cohort, and a follow-up history of medication use and health events from metformin initiation until dispensing of another antidiabetic, death, or end of follow-up (31 December 2015) was created. After applying exclusion criteria, we arrived at a cohort of 85,093 individuals.

Adherence was measured using the Medication Possession Ratio (MPR), calculated annually, and time of discontinuation (defined as a possession gap of more than 90 days). We used a linear mixed spline model with a knot at the end of one year to examine changes in MPR by demographic and clinical factors. Competing risk models were used to examine factors associated with metformin discontinuation.

I will present some selected preliminary findings from the study.

# Proton pump inhibitor use and pneumonia in infants: is there a relationship?

Mei-Ling Blank<sup>1,2</sup>, Lianne Parkin<sup>1,2</sup>, Jimmy Zeng<sup>1,2</sup>, Dave Barson<sup>1,2</sup>

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#### Background

Several observational studies have found an association between proton pump inhibitor (PPI) use and community-acquired pneumonia in adults, although these findings might reflect various biases and confounding by indication rather than a true effect of PPIs. While concerningly high levels of off-label PPI use have been reported in infants, very few studies have explored the possible link between PPIs and community-acquired pneumonia in this age group.

#### Aims

We undertook a nationwide nested case-control study to examine the relationship in infants between current use of PPIs and (i) community-acquired pneumonia, and (ii) all community-acquired lower respiratory tract infections (LRTIs).

#### Methods

Data from the Ministry of Health's National Collections were used to identify a cohort of infants who were born between 1 January 2005 and 31 December 2012, were dispensed a PPI at least once in the first year of life, and did not have a history of pneumonia or LRTI before cohort entry (first PPI dispensing). Potential cases of community-acquired pneumonia and LRTI during follow-up were identified using routinely collected hospital discharge and mortality data. To validate diagnoses, hospital discharge letters, chest radiography reports, and post-mortem findings were requested from hospitals. For each case, risk set sampling was used to randomly select up to 10 controls, matched on date of birth and sex. Potential cases and controls with a major illness or congenital abnormality which might have increased the risk of lung infection were not eligible for inclusion in the analyses. Conditional logistic regression was used to estimate odds ratios and 95% confidence intervals (95% CIs).

## Results

The underlying cohort included 21,991 infants from which 65 and 566 cases of incident community-acquired pneumonia and LRTI, respectively, were identified during follow-up. For community-acquired pneumonia, the adjusted odds ratio for current versus past use of a PPI was 0.88 (95% CI 0.36 – 2.16); the corresponding odds ratio for community-acquired LRTI was 1.13 (95% 0.87 - 1.48).

## Conclusion

In otherwise healthy infants, current use of a PPI does not appear to increase the risk of community acquired pneumonia or LRTI.

# Under-use of beta-blockers by New Zealand patients with chronic obstructive pulmonary disease and co-morbid acute coronary syndrome

**Joshua Quon**<sup>1</sup>, Lianne Parkin<sup>2,3</sup>, Katrina Sharples<sup>2,4,5</sup>, Dave Barson<sup>1,2</sup>, Jack Dummer<sup>1,4</sup>

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#### Background

Clinical guidelines recommend the use of beta-blockers and other cardiovascular prevention drugs for patients with acute coronary syndrome (ACS). International chronic obstructive pulmonary disease (COPD) management guidelines advise that patients with ischaemic heart disease and COPD should receive the same treatment as patients without COPD, and this includes the provision of beta-blockers. Despite this, studies in several countries have found that beta-blockers are under-used in patients with COPD and co-morbid heart disease – though none have examined use across a whole country.

#### Aims

We undertook a nationwide cohort study in New Zealand (i) to describe the use of beta-blockers at the time patients with COPD initiated long-acting bronchodilator therapy, and (ii) for those who had an ACS event during follow-up, to describe the use of beta-blockers and other cardiovascular prevention drugs before and after that event.

## Methods

Health and pharmaceutical dispensing data from the Ministry of Health's National Collections were used to derive the study cohort (all patients aged  $\geq$  45 years who initiated therapy for COPD with a long-acting muscarinic antagonist and/or long-acting beta-agonist between 1 February 2006 and 31 December 2013), to identify cohort members who were admitted to hospital with ACS and/or heart failure before cohort entry and during follow-up, and to ascertain use of cardiovascular prevention drugs.

# Results

The study cohort included 83,435 patients, with 290,400 person-years of followup. Of 2,367 patients with  $\geq 1$  ACS admission during follow-up, only 56.6% received a beta-blocker (mostly cardio-selective) in the 6 months following the first admission. The proportions receiving aspirin and a statin were much higher (87.7% and 81% respectively). Patients with a history of previous ACS and/or heart failure were slightly more likely to receive a beta-blocker than those without a history (61.9% versus 53.5%), but concomitant heart failure had no impact.

# Conclusions

The use of beta-blockers following an ACS admission was much lower in this cohort of patients with COPD than would be expected based on the findings of a general audit of ACS management in New Zealand. Conversely, the proportions using aspirin and a statin were similar to those found in the audit. This suggests a particular reluctance to prescribe beta-blockers to patients with COPD.

# Adherence among new statin users in New Zealand: is there a difference between primary and secondary prevention?

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Maintaining adherence to statins, lipid lowering medications, reduces the risk of an initial cardiovascular disease (CVD) event in high-risk individuals (primary prevention) and additional CVD events following the first event (secondary prevention). The effectiveness of statin therapy is limited by the level of adherence maintained by the patient, with poor statin adherence being associated with poor CVD outcomes. This project's aim was to investigate if statin adherence differed between primary and secondary prevention.

Dispensing data from New Zealand community pharmacies were used to identify patients who received their first statin dispensing between 2006 and 2011. The supply period of each dispensing was calculated and patients were coded as discontinuing therapy if there was a period of 91 days or more of no statin supply starting within 365 days of their first dispensing. The Medication Possession Ratio (MPR) was calculated by dividing the total days of statin supply in the first year by 365. Patients with a MPR  $\geq 0.8$  were considered to be adherent. Logistic regression was used to calculate the odds ratios and 95% confidence intervals for both discontinuation and adherence while adjusting for age, sex, ethnicity, deprivation, comorbidities, first statin characteristics, year of first dispensing and vocation of first dispensing doctor.

Some preliminary findings from this study will be presented.

# IDI trends in antidepressant dispensing to New Zealand children and young people between 2007/08 and 2015/16

**Nicholas Bowden**<sup>1,2</sup>, Sheree Gibb<sup>1,3</sup>, Hiran Thabrew<sup>1,4</sup>, Rick Audas<sup>1,2</sup>, Justine Camp<sup>1,2</sup>, Barry Taylor<sup>5</sup>, and Sarah Hetrick<sup>1,4</sup>

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#### Aims

To examine trends in antidepressant dispensing to young people in New Zealand aged 1 - 24 years between 2007/08 and 2015/16 using the national Integrated Data Infrastructure (IDI), and to determine whether these trends vary by age, sex, ethnicity and socioeconomic deprivation.

#### Methods

In a novel endeavour, data on antidepressant dispensing, age, sex, ethnicity and socioeconomic status were sourced from the IDI, a linked individual-level database containing New Zealand government and survey microdata.

#### Results

The total rate of dispensing of antidepressants to young people increased by 49% over the nine-year period of this study. Increases were larger for the 13 - 17 age group (82%) than the 1 - 12 (16%) or 18 - 24 year (37%) age groups. New Zealand European/Other ethnicities had the highest dispensing rates (3,755 out of every 100,000 people received an antidepressant in 2015/16), followed by Māori (2,003/100,000), Asian (919/100,000), and Pasifika (818/100,000) had the lowest. Dispensing rates increased with increasing deprivation, except in the most deprived quintile, where rates were lower than all other quintiles.

#### Conclusion

This study demonstrates the value of utilising IDI data for health research, while providing directions for future use, including further linkage of IDI datasets. Overall there was a trend for an increase in the use of antidepressants across all age, sex and ethnic groups, but notable variation in dispensing between different ethnic and socioeconomic groups. Despite our inability to determine the clinical rationale for increased dispensing of antidepressants, the available data highlights some potentially significant improvements as well as disparities in healthcare.

# Paediatric epilepsy in New Zealand: a study of AED prescribing

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# Background

Epilepsy is the most common serious neurological disorder globally. International data have estimated the period prevalence of active epilepsy in children and young people 18 years and under is 4.8 per 1000 (95% confidence interval [CI] 4.2 - 5.5). The prevalence of paediatric epilepsy in New Zealand is unknown. Children who continue to have seizures or are on antiepileptic medication are defined as having active epilepsy.

## Aims

To identify the indications for paediatric prescriptions of AEDs and the period prevalence of active epilepsy in a New Zealand paediatric population.

## Methods

A search of the New Zealand Pharmaceutical Collection database for children and young people under the age of 18 years residing in the Wellington region and dispensed an AED between 1 January 2015 and 31 December 2015 was performed. The indication for AED use was determined from review of the hospital records.

# Results

During the study period 552 children (285 male) were dispensed an AED. Indications could be determined in the vast majority of cases (91%). AEDs were prescribed for seizures (71%), pain (7%), mental illness (6%), headache (4%), and sleep (1%).

The period prevalence of active epilepsy in individuals under 18 years of age was 3.4 per 1000 (CI 3.1 – 3.8, n=379). Forty-seven percent of individuals with epilepsy were female. The prevalence was higher in Māori (15 per 1000 [CI 12 – 18], n=85), than in Pacific Islanders (5 per 1000 [CI 3 – 7], n = 32), Europeans (4 per 1000 [CI 3 – 4], n=224) or Asians (3 per 1000 [CI 2 – 4], n=25). Socioeconomic status, as defined by the deprivation index, did not impact the prevalence of active epilepsy in this age group.

# Conclusions

AEDs were indicated for seizures in 71% of children and young people. Pain, mental health and headaches were much less frequent indications. In Wellington, the period prevalence of active epilepsy in the paediatric population is lower than what was internationally reported. But in Māori, active epilepsy was three times higher than international estimates. Māori were almost four times more likely than the European population to have active epilepsy.

# Predictors of inappropriate prescribing among older adults with complex care needs who have undergone the interRAI assessment

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#### Aim

To identify factors associated with prescription of potentially inappropriate medications (PIMs) in older adults ( $\geq 65$  years) with complex care needs who have undertaken a comprehensive geriatric risk assessment.

## Methods

A nationwide cross-sectional (retrospective, observational) study was performed. The national interRAI Home Care assessments conducted in New Zealand in 2015 for older adults were linked to the national pharmaceutical prescribing data (PHARMS). The 2015 Beers criteria were applied to the cross-matched data to identify the prevalence of PIMs. The factors influencing PIMs were analysed using a multinomial logistic regression model.

## Results

16,568 older adults were included in this study. Individuals diagnosed with cancer, dementia, insomnia, depression, anxiety, and who were hospitalized in the last 90 days, were more likely to be prescribed PIMs than those who were not diagnosed with the above disorders, and who were not hospitalized in the last 90 days. Individuals over 75 years of age, the Māori ethnic group among other ethnicities, individuals who were diagnosed with certain clinical conditions (diabetes, chronic obstructive pulmonary disease, stroke, or congestive cardiac failure), individuals requiring assistance with activities of daily living and better

self-reported health, were associated with a lesser likelihood of being prescribed PIMs.

### Conclusion

The study emphasizes the identification of the predictors of PIMs during the first completed comprehensive geriatric assessment. Targeted strategies to reduce modifiable predictors of PIMs in subsequent assessments has the potential to improve medication management in older adults.

# Do commonly used drugs reduce the risk of Parkinson's?

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Abstract not available

# Effectiveness of pneumococcal conjugate vaccine by dose and Aboriginality in a large birth cohort estimated using linked data

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#### Background

Most studies use indirect cohort or case-control methods to estimate vaccine effectiveness (VE) of 7 and 13-valent pneumococcal conjugate vaccines (PCV7 and PCV13) against invasive pneumococcal disease (IPD). Neither method can measure the benefit vaccination programs afford the unvaccinated and many studies were unable to estimate dose-specific VE. We linked immunisation register and health data from Western Australia and New South Wales (~ 42% of Australian population) to calculate IPD incidence by vaccination status and VE for a 3+0 PCV schedule (doses at 2, 4, 6 months, no booster) among a cohort of 1.4 million births.

#### Methods

Births records for 2001 - 2012 were probabilistically linked to IPD notifications, hospitalisations, deaths, and vaccination history (available until December 2013). IPD rates in vaccinated and unvaccinated children < 2 years old were estimated using Cox proportional hazards models (adjusting for potential confounders), with VE= (1 – adjusted hazard ratio) x 100 for all-cause, PCV7, PCV13 and PCV13-non-PCV7 serotype-specific IPD, and for Aboriginal and non-Aboriginal children.

## Results

Following universal PCV7 in 2005, PCV7 serotype and all-cause IPD in unvaccinated children declined 89.5% and 61.4%, becoming similar to incidence in vaccinated children. Among non-Aboriginal children, VEs for 3 doses were 94.2% (95% CI 81.9 – 98.1) for PCV7 IPD, 85.6% (95% CI 60.5 – 94.8) for PCV13-non-PCV7 IPD and 80.1% (95% CI 59.4 – 90.3) for all-cause IPD. We found no statistically significant differences between VE of 3, 2 or 1 dose against PCV13 and PCV13-non-PCV7 IPD, or between Aboriginal and non-Aboriginal children.

# Conclusion

This study demonstrates that rapid attainment of high coverage (> 90%) of PCV generated individual and herd protection within 12 months. High VE for even one dose supports moves to reduced-dose schedules (1+1 and 2+1) internationally.

# Long-term impact of pneumococcal conjugate vaccines in children with risk factors for invasive pneumococcal disease: a cohort study using linked administrative data

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#### Background

Little is known about the long-term incidence of invasive pneumococcal disease (IPD) by risk factor (RF) status in populations with high coverage pneumococcal conjugate vaccine (PCV) programs. We measured IPD in children with specific RFs and estimated changes in IPD incidence by RF status and time post PCV introduction.

#### Methods

Retrospective birth cohort in New South Wales (NSW), Australia, born alive from 1 January 2001 to 31 December 2012. RFs for IPD identified from birth records and International Classification of Diseases (ICD) codes in linked hospitalisations.

#### Results

1251 IPD cases were identified in ~ 1.1 million children born over a 13-year period. 75,404 children (6.8% of cohort) with at least one identified RF accounted for 255 (20.3%) IPD cases (61 per 100,000 person-years) versus 996 in others (14 per 100,000 person-years). Hospitalisation for asthma was the most common RF (n=41,074; 3.6%) but highest IPD incidence was in 2452 children (0.2% of cohort) with ICD codes for immunosuppression, splenic dysfunction or breach in CSF barrier (aHR ~ 20; PAF 0.7-1.8%) versus asthma (aHR 5.3; PAF 14.8%). Compared to the birth cohort 2001 – 2004 (eligible for targeted PCV only), IPD incidence in the most recent PCV-eligible cohort (born 2009 – 2012) declined by 78% (95% CI -72 to -82%) in children with no RFs. In children with RFs, IPD declined by only 13% (95% CI -70 to +138%) in those with highest IPD incidence but by 67% (95% CI -43 to -82%) in others.

#### **Conclusions and relevance**

By 8 years post introduction of universal PCV, total IPD reduced significantly except in the small proportion (0.2%) of the birth cohort at highest risk. For these severely immunocompromised children, antibiotic prophylaxis and additional vaccine doses are recommended, but compliance and effectiveness is uncertain.