# GP Research Review™

Making Education Easy

Issue 129 – 2018


## In this issue:



**Abbreviations used in this issue**
**AF** = atrial fibrillation
**CKD** = chronic kidney disease
**CVD** = cardiovascular disease
**HR** = hazard ratio
**IRR** = incidence rate ratio
**MMSE** = Mini-Mental State Examination
**OR** = odds ratio
**PCP** = primary care physician
**RR** = risk ratio
**RTI** = respiratory tract infection

Beat Bowel Cancer® AOTEAROA

NZMA New Zealand Medical Association

# Welcome to issue 129 of GP Research Review.

Fascinatingly, a large observational study from Norway involving more than 1.2 million people aged >50 years reports that warfarin appears to reduce the incidence of cancer among people on long-term warfarin therapy compared with warfarin nonusers. It will be interesting to see whether further prospective studies provide data backing these findings. In another paper, a systematic review and meta-analysis explores the sustainability of different diabetes prevention strategies on diabetes incidence in adults aged ≥18 years at risk for diabetes. It appears that while lifestyle modification and medications (weight loss and insulin-sensitising agents) successfully reduce diabetes incidence, medication has short-lived effects; lifestyle modification is more effective in the long term but declines with time. The study authors note that strategies are needed to maintain the effects of lifestyle modification.

Good evidence presented by a randomised controlled trial in the Natural Health section suggests that a traditional Chinese medicine, Niaoduqing particles, effectively and safely delayed the progression of chronic kidney disease in Chinese patients with moderate-to-severe renal dysfunction. Now, as the study authors acknowledge, further studies are needed to validate the clinical benefits of Niaoduqing particles in other populations. The second study in this section reports that physical activity is associated with reduced risk of mortality and CVD across 17 countries worldwide, representing different cultures, lifestyles and economic levels. The study authors conclude that incorporating physical activity into daily life is a simple, low-cost and globally applicable strategy that could reduce deaths and CVD in middle age.

I hope you enjoy this issue and I welcome your comments and feedback.

Kind regards,

Jim


**Assoc Professor Jim Reid**
jimreid@researchreview.co.nz


**Independent commentary by Associate Professor Jim Reid.**
Jim Reid has a private family medicine practice at the Caversham Medical Centre, Dunedin, New Zealand. **FOR FULL BIO CLICK HERE.**



**RACP MyCPD Program participants** can claim **one credit per hour** (maximum of 50 credits per year) **for reading and evaluating Research Reviews.**
***FOR MORE INFORMATION CLICK HERE***

## Association of broad- vs narrow-spectrum antibiotics with treatment failure, adverse events, and quality of life in children with acute respiratory tract infections

**Authors:** Gerber JS et al.

**Summary:** This US investigation compared the effectiveness of broad-spectrum and narrow-spectrum antibiotic treatment for acute respiratory tract infections (RTIs) in two cohorts of children aged 6 months to 12 years. In a retrospective study involving >30,000 children (19,179 with acute otitis media; 6,746 with group A streptococcal pharyngitis; and 4,234 with acute sinusitis), 14% received broad-spectrum antibiotics. Treatment failure rates were similar between these children and those prescribed narrow-spectrum antibiotics (3.4% vs 3.1%). Of 2,472 children enrolled in a prospective study (1,100 with acute otitis media; 705 with group A streptococcal pharyngitis; and 667 with acute sinusitis), 35% were prescribed broad-spectrum antibiotics. In this study, broad-spectrum antibiotics resulted in a slightly lower quality-of-life score (90.2 vs 91.5 for narrow-spectrum antibiotics). Broad-spectrum treatment was associated with a higher risk of adverse events as reported by the clinician (3.7% vs 2.7%) and the patient (35.6% vs 25.1%) compared with narrow-spectrum antibiotics.

**Comment:** There currently is intense publicity discouraging the over-use of antibiotics due to the increasing development of resistance. However, there is still a high rate of prescribing by doctors. Added to this is the demand from many patients who request them for self-limiting bacterial and viral infections in the belief that they are required and provide benefit. This study demonstrated that narrow-spectrum antibiotics had equal effect to broad-spectrum in the treatment of a variety of upper respiratory tract infections, and they had a lower rate of side effects. If an antibiotic is justified, narrow-spectrum is the way to go.

***Reference: JAMA. 2017;318(23):2325-36***
Abstract

## Association of warfarin use with lower overall cancer incidence among patients older than 50 years

**Authors:** Haaland GS et al.

**Summary:** Using national, prescription, and cancer registries, this population-based cohort study involved 1,256,725 Norwegians born between 1 January 1924 and 31 December 1954 residing in Norway between 1 January 2006 and 31 December 2012. The cohort was divided into 2 groups: warfarin users (7.4%) and nonusers (92.6%). Warfarin use was defined as taking ≥6 months of a prescription and ≥2 years from first prescription to cancer diagnosis of any type during the 7-year observation period. A total of 10.6% of the cohort had cancer. Compared with nonusers, warfarin users had a significantly lower age- and sex-adjusted incidence rate ratio (IRR) in all cancer sites (0.84; 95% CI, 0.82 to 0.86) and in prevalent organ-specific sites (IRR lung, 0.80 [95% CI, 0.75 to 0.86]; IRR prostate, 0.69 [95% CI, 0.65 to 0.72]; and breast, 0.90 [95% CI, 0.82 to 1.00) but not colon cancer (IRR, 0.99; 95% CI, 0.93 to 1.06). In a subgroup analysis of patients with atrial fibrillation (AF) or atrial flutter, the IRR was lower in all cancer sites (IRR, 0.62; 95% CI, 0.59 to 0.65) and in prevalent sites (lung, 0.39 [95% CI, 0.33 to 0.46]; prostate, 0.60 [95% CI, 0.55 to 0.66]; breast, 0.72 [95% CI, 0.59 to 0.87]; and colon, 0.71 [95% CI, 0.63 to 0.81]).

**Comment:** This is a large, well-designed Norwegian study that looked at cancer occurrence between those who took warfarin and non-takers. The group on warfarin for AF were treated as a subgroup. Warfarin users had reduced cancer prevalence in all sites except the bowel, whereas those with AF demonstrated a lower rate of cancer in all sites including the bowel. This calls for a prospective, controlled study with variable warfarin dosage to objectively confirm the finding.

***Reference: JAMA Intern Med. 2017;177(12):1774-80***
Abstract

## Comparison of hospital resource use and outcomes among hospitalists, primary care physicians, and other generalists

**Authors:** Stevens JP et al.

**Summary:** These US researchers retrospectively examined differences in the use of health care resources and outcomes among hospitalised patients cared for by hospitalists, their own primary care physicians (PCPs, i.e. the physicians who provided a plurality of ambulatory visits in the year preceding admission), or other generalists (not the patients' PCPs). The analysis involved 560,651 admissions for the 20 most common medical diagnoses among elderly fee-for-service Medicare patients (mean age 80 years) throughout 2013. Specialty consultations were used more often by PCPs (RR 1.03; 95% CI, 1.02 to 1.05) and other generalists (RR 1.06; 95% CI, 1.05 to 1.07) compared with hospitalists. Lengths of stay were longer among patients cared for by PCPs (adjusted IRR [aIRR] 1.12; 95% CI, 1.11 to 1.13) and in those cared for by other generalists (aIRR 1.06; 95% CI, 1.05 to 1.07) compared with those cared for by hospitalists. PCPs were more likely to discharge patients home (adjusted OR [aOR] 1.14; 95% CI, 1.11 to 1.17) than other generalists (aOR 0.94; 95% CI, 0.92 to 0.96). Relative to hospitalists, patients cared for by PCPs had similar readmission rates at 7 days (aOR 0.98; 95% CI, 0.96 to 1.01) and 30 days (aOR 1.02; 95% CI, 0.99 to 1.04), whereas other generalists' readmission rates were greater than hospitalists' rates at 7 (aOR 1.05; 95% CI, 1.02 to 1.07) and 30 (aOR 1.04; 95% CI, 1.03 to 1.06) days. Adjusted 30-day mortality was lower among patients cared for by PCPs (aOR 0.94; 95% CI, 0.91 to 0.97) and higher among patients of other generalists (aOR 1.09; 95% CI, 1.07 to 1.12) compared to patients cared for by hospitalists.

**Comment:** Although this was a US study, primary care physicians (PCPs; read GPs or family physicians) came off well with respect to others. While length of hospital stay for PCP patients was longer, they were more likely to be discharged home (probably with continuing personal medical care) and had reduced mortality within 30 days of discharge. This is a different model of care to New Zealand, but one wonders about outcome if the patient's GP had the opportunity to at least contribute to hospital care.

***Reference: JAMA Intern Med. 2017;177(12):1781-7***
Abstract

**New Zealand Research Review subscribers can claim CPD/CME points** for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our **CPD page**.

CLICK HERE to read previous issues of GP Research Review

## Long-term sustainability of diabetes prevention approaches: a systematic review and meta-analysis of randomized clinical trials

**Authors:** Haw JS et al.

**Summary:** This systematic review and meta-analysis pooled data from 43 randomised controlled trials (49,029 participants; mean age, 57.3 years) that evaluated lifestyle modification (LSM) and medication interventions (weight loss and insulin-sensitising agents; >6 months) for diabetes prevention in adults (age ≥18 years) at risk for diabetes. All trials were published between 1 January 1990 and 1 January 2015. Nineteen trials tested medications, 19 evaluated LSM, and 5 tested combined medications and LSM. Active interventions lasted for 0.5 to 6.3 years. At the end of the active intervention, LSM was associated with a relative risk (RR) reduction of 39% (RR 0.61; 95% CI, 0.54 to 0.68) and medications with a RR reduction of 36% (RR 0.64; 95% CI, 0.54 to 0.76). When the study researchers used the reported incidence rates to compute pooled risk differences (RDs), they observed a RD for LSM and medication studies of 4.0 cases per 100 person-years or a number-needed-to-treat of 25. At the end of the washout or follow-up periods, LSM studies (mean follow-up, 7.2 years) achieved a RR reduction of 28% (RR 0.72; 95% CI, 0.60 to 0.86), while medication studies (mean follow-up, 17 weeks) showed no sustained RR reduction (RR 0.95; 95% CI, 0.79 to 1.14).

**Comment:** New Zealand is on the brink of a diabetes epidemic, and there are some who would say we are over the brink and that we have an epidemic now. There are over 200,000 diagnosed NZ diabetics, at least another 100,000 not diagnosed, and goodness know how many prediabetics. This study looked at diabetes prevention and suggests that medication effect for prediabetics is short-lived. Lifestyle modification is effective in reducing relative risk by nearly 40%, but this falls off with time. The concept that these modifications must be lifelong to be effective must be accepted by the population at large. Until there is acceptance the problem will continue to rise.

***Reference: JAMA Intern Med. 2017;177(12):1808-17***
Abstract

## Validation and diagnostic accuracy of predictive curves for age-associated longitudinal cognitive decline in older adults

**Authors:** Bernier PJ et al.

**Summary:** These Canadian researchers explain how they developed cognitive charts based on the Mini-Mental State Examination (MMSE) score for use in clinical practice to facilitate early detection and clinical follow-up of age-associated cognitive decline. They obtained data from the Canadian Study of Health and Aging, in which 7,569 participants aged ≥65 years completed a MMSE at baseline and again after 5 and 10 years. This linear regression model was validated by a separate data set of 6,501 participants from the National Alzheimer's Coordinating Center's Uniform Data Set. Baseline measurements showed high sensitivity (80%), high specificity (89%), and a very high negative predictive value (99%) for distinguishing healthy controls from participants with dementia. Similar sensitivities and specificities were observed for a decline over time greater than 1 percentile zone from the first measurement. Results in the validation sample were comparable, albeit with lower sensitivities.

**Comment:** This is an interesting concept. Like many measurements in medicine, a single reading is often meaningless. With this concept, the authors used the MMSE in a serial fashion to determine whether changes were successful in determining whether decline was "physiological ageing" or progressing dementia. The charts are available in the original article.

***Reference: CMAJ. 2017;189(48):E1472-80***
Abstract



## 'Validation of ultrasound examinations performed by general practitioners'

**Authors:** Lindgaard K et al.

**Summary:** This Danish study explored the inter-rater agreement between GPs and radiologists/gynaecologists in point-of-care ultrasound examinations for certain abdominal and gynaecological conditions of low-to-moderate complexity. The study recruited 114 patients presenting with abdominal pain or discomfort, possible pregnancy or known risk factors toward abdominal aortic aneurism. They underwent initial scans in general practice and subsequent validation examinations in a hospital setting. Inter-rater agreement (Kappa statistic and percentage agreement) was defined for the following conditions: gallstones, ascites, abdominal aorta >5 cm, intrauterine pregnancy and gestational age. The overall Kappa value was 0.93 (95% CI, 0.87 to 0.98). The Kappa values for ascites, abdominal aortic diameter >5 cm and intrauterine pregnancy were 1.

**Comment:** I am old enough to remember when it was generally thought that GPs were incapable of doing and interpreting ECGs. I now frequently hear the same with respect to spirometry. However, with something as complex as ultrasound, GPs did very well with common conditions of low-to-moderate complexity. Maybe as GPs we are capable of more than we are given credit for!

***Reference: Scand J Prim Health Care. 2017;35(3):256-61***
Abstract

## Reliability of pulse palpation in the detection of atrial fibrillation in an elderly population

**Authors:** Jaakkola J et al.

**Summary:** This study explored the ability of elderly subjects to detect AF by pulse palpation. A cohort of 173 subjects aged ≥75 years received brief information on AF. All participated in a training session given by a nurse and were asked to palpate their own pulse regularly for a month. At the 1-month follow-up visit, their ability to distinguish sinus rhythm (SR), SR with premature ventricular contractions (PVC) and AF by pulse palpation was assessed using an anatomic human arm model programmable with various rhythms. A control group of 57 healthcare personnel received the same information on pulse palpation but not the training. There were no differences between the elderly and healthcare groups in detecting SR (97.3% vs 96.5%) or SR with PVCs (74.3% vs 71.4%), but the elderly subjects identified slow (81.8% vs 56.1%) and fast AF (91.9% vs 80.7%) significantly better than the healthcare group. In the elderly group, the ability to recognise SR with PVCs was independently predicted by previous experience of pulse palpation, secondary or higher level of education and a 1-point increase in MMSE score; the ability to correctly identify the other rhythms had no predictors.

**Comment:** This is important in the diagnosis of paroxysmal AF, which can be enormously tricky unless one is lucky enough to encounter it on examination, or on a Holter monitor. I had not thought to teach the patient him/herself to take their pulse (though it is blatantly obvious) but it is something I will do in the future.

***Reference: Scand J Prim Health Care. 2017;35(3):293-8***
Abstract

Time spent reading this publication has been approved for CME for Royal New Zealand College of General Practitioners (RNZCGP) General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes, provided that a Learning Reflection Form is completed. Please **CLICK HERE** to download your CPD MOPS Learning Reflection Form. One form per review read would be required.

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please **CLICK HERE**.

## The risk of major NSAID toxicity with celecoxib, ibuprofen, or naproxen: a secondary analysis of the PRECISION trial

**Authors:** Solomon DH et al.

**Summary:** These researchers performed a post hoc analysis of the PRECISION trial, in which 24,081 patients with osteoarthritis or rheumatoid arthritis at moderate or high cardiovascular risk received either twice-daily celecoxib 100–200 mg, ibuprofen 600 to 800 mg 3 x daily, or twice-daily naproxen 375–500 mg. The analysis examined the comparative risk of major NSAID toxicity across the study treatment arms. Over 1 to 2 years of follow-up, 4.1% of patients sustained any major toxicity in the celecoxib arm, 4.8% in the naproxen arm and 5.3% in the ibuprofen arm. In analyses adjusted for aspirin use and geographic region, patients in the naproxen arm had a 20% higher risk of major toxicity than celecoxib users and a 38% higher risk. These risks translate into numbers needed to harm for the primary major NSAID toxicity of 135 for naproxen compared with celecoxib and 82 for ibuprofen compared with celecoxib.

**Comment:** Non-steroidal anti-inflammatory (NSAI) medications are not without side effects, with emphasis on possible gastrointestinal, renal and cardiovascular negative outcomes. These patients had moderate-to-high risk cardiovascular risks, and 5% of the whole group experienced major toxicity over a two-year period. Out of naproxen, ibuprofen and celecoxib, the latter was the least toxic.

***Reference: Am J Med. 2017;130(12):1415-22***
Abstract

## Goodfellow Gems

### Cold cabbage leaves may be as good as cold gel packs for breast engorgement and better than nothing at all

A randomised trial of cold cabbage leaves versus cold gel packs versus control[1] reported that cabbage leaves were as good as the gel packs at reduction in pain at three time points after application compared with a no treatment control group.

Additionally, cabbage leaves were superior to gel packs at all three time points following application for hardness of breasts. Both intervention groups were better than the control group for hardness of breasts.

The study had some methodological flaws in the design. For example, the cabbage leaves were applied to both breasts in the leaf group and it is unclear if the application was to one or both breasts for the gel pack.

There was high satisfaction with the cabbage leaves. The leaf intervention used 3 large leaves over each breast. The leaves were rinsed in cold water and chilled in a zip-lock bag in the freezer for 15 minutes, or the fridge for one hour. The cold gel packs were chilled like the leaves.

A Cochrane review had reported cabbage leaves as a promising intervention but more research needed. There was no difference in duration of breast feeding at 3 and 6 months.[2]

This gem has been checked by Dr Karen Hoare Associate-Professor Massey University.

**References:**

1. Application of cabbage leaves compared to gel packs for mothers with breast engorgement: Randomised controlled trial. Int J Nurse studies 2017. Click here
2. Treatments for breast engorgement during lactation. Cochrane Database of Systematic Reviews 2016. Click here

Gems are chosen by the Goodfellow director Dr. Bruce Arroll to be either practice changing or practice maintaining. The information is educational and not clinical advice.

**www.goodfellowunit.org/gems**

## EVIDENCE-BASED NATURAL HEALTH
*by Dr Chris Tofield*

### Efficacy and safety of Niaoduqing particles for delaying moderate-to-severe renal dysfunction: a randomized, double-blind, placebo-controlled, multicenter clinical study

**Authors:** Zheng Y et al.

**Summary:** This multicentre Chinese study enrolled 300 patients aged 18–70 years with stage 3b–4 chronic kidney disease (CKD) and an estimated glomerular filtration rate (eGFR) of 20–45 mL/min 1.73 $m^2$ and randomised them to receive either the traditional Chinese medicine, Niaoduqing particles, at a dose of 5 g 3 times daily and 10 g before bedtime for 24 weeks (test group), or to a placebo on the same dosing schedule (control group). In an intention-to-treat analysis at 24 weeks that involved 292 patients, the median change from baseline in serum creatinine was 1.1 and 11.7 µmol/L for the test and control groups, respectively ($Z$ = 2.642; p=0.008); corresponding median changes from baseline in eGFR were –0.2 and –2.2 mL/min per 1.73 $m^2$, respectively ($Z$ = –2.408; p=0.016). The adverse event profiles did not differ significantly between the groups.

**Comment:** I am not familiar with Chinese medicine, so am taking a bit of a plunge with this one. However, looking at the good study design, decent number of participants and impressive results, this Niaoduqing particle stuff deserves a mention. When given to people with moderate-to-severe renal dysfunction, there was a ten-fold slower deterioration in eGFR compared to placebo. Not bad.

***Reference: Chin Med J (Engl). 2017;130(20):2402-9***
Abstract

### The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study

**Authors:** Lear SA et al.

**Summary:** This study was conducted between 1 January 2003 and 31 December 2010 in 17 countries of various income levels and enrolled 168,916 individuals aged 18–70 years; 141,945 completed the International Physical Activity Questionnaire (IPQA). The study aimed to determine whether different amounts and types of physical activity are associated with lower mortality and cardiovascular disease (CVD) across different regions of the world. It recorded mortality and CVD over a mean 6.9 years of follow-up. Analyses were limited to the 130,843 participants without pre-existing CVD. During follow-up, compared with low physical activity (<600 metabolic equivalents [MET] × min/week or <150 min/week of moderate intensity physical activity), moderate (600–3000 MET × min/week or 150–750 min/week) and high physical activity (>3000 MET × min/week or >750 min/week) were associated with graded reductions in mortality (HR 0.80; 95% CI, 0.74 to 0.87 and HR 0.65; 0.60 to 0.71; p<0.0001 for trend) and major CVD (CVD mortality, incident myocardial infarction, stroke, or heart failure; HR 0.86; 95% CI, 0.78 to 0.93; p<0.001 for trend). Higher physical activity was associated with lower risks of CVD and mortality across all economic levels. The adjusted population attributable fraction for not meeting the physical activity guidelines was 8.0% for mortality and 4.6% for major CVD, and for not meeting high physical activity was 13.0% for mortality and 9.5% for major CVD. Both recreational and non-recreational physical activity were associated with benefits.

**Comment:** This is interesting. To date, we have thought that continuous physical activity (lasting at least 20–30 minutes) was required to reduce cardiovascular risk. But now this multinational study, using the IPAQ questionnaire that captures activity lasting a mere 10 minutes or more, found that even work-related physical activity has benefits. I suppose that's good news for a lot of people, though as sedentary GPs we would still need to squeeze in a quick run at lunchtime or a short gym session after work to benefit.

***Reference: Lancet. 2017;390(10113):2643-54***
Abstract

**Dr Christopher Tofield**
Dr Tofield completed his medical training at St Bartholomew's and the Royal London Hospital in London. He now works part time in general practice in Tauranga, is involved with clinical research, has published several medical papers and a textbook on pharmacology, and is clinical advisor to Bay of Plenty District Health Board. **For full bio CLICK HERE.**