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GP Research Review™

Making Education Easy

Issue 25 - 2009

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NEW ZEALAND MEDICAL ASSOCIATION

Welcome to the twenty-fifth issue of GP Research Review.

Amongst the papers that we cover this month, two deserve special mention. Should complementary and alternative medicines use in New Zealand be regulated? The authors of our first paper believe so; their research raises serious concerns as to the quality of health care advice provided by health food store staff.

In our second noteworthy article, the findings indicate that the therapeutic indications of glitazones and their clinical usefulness may be overcome by combination treatment with rosiglitazone and coenzyme Q10; patients, GPs and diabetologists will surely be intrigued by this paper.

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

Kind Regards,

Jim

Assoc Professor Jim Reid

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High blood pressure advice given by natural health food stores

Authors: Siebers R et al

Summary: Using a hypothetical scenario of an individual with newly diagnosed hypertension, a disorder where complementary and alternative medicines are widely used but are not registered medicines, 26 health food stores and 26 pharmacies were visited by a 52-year-old male for advice. Twenty-five of the 26 pharmacists recommended an immediate visit to a general practitioner; one pharmacist recommended antioxidants and multivitamins and suggested that these together with stress reduction, regular exercise, and a fish meal once a week would reduce blood pressure within 2 weeks. In contrast, staff in 25 out of 26 health food stores did not refer the researcher to a medical practitioner; instead they recommended and sold a wide variety of compounds of unproven efficacy.

Comment: The paper makes for sobering reading and presents a problem which may be all too common. By the very nature of the title and the use of the word "natural" and "health" there is the implication that all things natural are harmless and healthy. Such of course is not the case. However, what is even more concerning is the anti-scientific medicine ideology behind much of this [complementary and alternative medicine] industry, and when the factor of profit is included a dangerous mix can occur.

Seven years ago these authors published a similar paper using an asthma model. It is disappointing that 7 years after the publication of the asthma paper, an even worse result is obtained. Is no one listening?

Reference: *N Z Med J. 2009;122(1293):11-5.*

<http://www.nzma.org.nz/journal/abstract.php?id=3566>

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This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

Mortality results from a randomized prostate-cancer screening trial

Authors: Andriole GL et al

Summary: This report presents interim results from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial on prostate-cancer mortality. From 1993 through 2001, 76,693 men were randomised to either 6 rounds of annual screening with prostate-specific antigen (PSA) plus 4 annual digital rectal exams (DREs; n=38,343) or to usual care as the control (n=38,350). Usual care sometimes included screening, as some organisations have recommended. In the screening group, rates of compliance were 85% for PSA testing and 86% for digital rectal examination. Rates of screening in the control group increased from 40% in the first year to 52% in the sixth year for PSA testing and ranged from 41 to 46% for digital rectal examination. At 7 years' follow-up, screening was associated with a relative increase of 22% in the rate of prostate cancer diagnosis, compared with the control group. However, over an 11-year median follow-up, combined screening with PSA testing and a DRE did not reduce mortality; the rate of death from prostate cancer was very low and did not differ significantly between the two study groups.

Comment: There is much emotion tied up in this issue, and the question of individual screening on symptomatic men is still not answered by this paper. From a population perspective, however, this paper indicates that screening for prostate cancer is not effective.

Reference: *New Engl J Med.* 2009;360(13):1310-19.

<http://content.nejm.org/cgi/content/full/NEJMoa0810696>

Screening and prostate-cancer mortality in a randomized European study

Authors: Schröder FH et al

Summary: Data are reported from the European Randomized Study of Screening for Prostate Cancer (ERSPC), initiated in the early 1990s to evaluate the effect of screening with prostate-specific-antigen (PSA) testing on death rates from prostate cancer. 182,000 men aged 50–74 years were randomly assigned to a group that was offered PSA screening at an average of once every 4 years or to a control group that did not receive such screening. During a median follow-up of 9 years, the cumulative incidence of prostate cancer was 8.2% in the screening group and 4.8% in the control group. PSA screening was associated with a 20% reduction in the rate of death from prostate cancer. The study showed an absolute reduction of approximately 7 prostate-cancer-related deaths per 10,000 men screened.

Comment: The treatment of prostate cancer is not a benign process and there is a relatively high incidence of incontinence, and erectile dysfunction following prostatectomy as well as bowel problems following radiation. This study is twice the size of that reported above and while it did report a reduction in death over a nine-year period, this was at the cost of overdiagnosis and consequent unnecessary treatment. This was at a payoff of 0.71 deaths / 1000 men. The percentage reduction is not important, put in this perspective. The jury is still out!

Reference: *New Engl J Med.* 2009;360(13):1320-8.

<http://content.nejm.org/cgi/content/full/NEJMoa0810084>

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Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Management of erectile dysfunction in general practice

Authors: De Berardis G et al

Summary: These researchers used a written questionnaire to investigate general practitioners' (GPs) sociodemographic characteristics and their beliefs and attitudes toward the management of erectile dysfunction (ED). Each GP was asked to recruit consecutive men aged ≥18 years and sexually active, with already known erectile problems or with newly diagnosed ED. Questionnaires were completed by 127 GPs and 124 enrolled patients for the study. Only 9.5% of the GPs reported routinely inquiring about ED of patients >40 years of age, whereas 45.7% did it only when the patient raised the problem. GPs' gender and age were associated with their beliefs about ED treatment and referral to specialist care. Overall, 932 patients were enrolled, of whom 38% had newly diagnosed ED. The problem was initiated by patients in 80% of cases, and 84.8% of men were prescribed a treatment. Patients who on their own initiative raised their condition were almost three times more likely to be treated than those whose GP began the discussion about ED (OR 2.6). Patients followed by female physicians were significantly more likely to be referred to a specialist than those followed by male physicians (OR 3.3).

Comment: One of the major benefits of direct to consumer advertising has been the empowerment of both patients and their partners to raise this issue with GPs. Enquiry is often made by practices that conduct "well men's checks" but frequently the subject is swept under the carpet. Often if enquiry is not made no mention is made. This is a GP and not a specialist problem. It is important to rule out physical and psychological reasons for erectile dysfunction, and having done so (with the cards on the table) to offer appropriate treatment. The only problem for most, is the cost.

Reference: *J Sex Med.* 2009;6(4):1127-34.

<http://tinyurl.com/o2lxs>



Independent commentary by Associate Professor Jim Reid.

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Primary health care providers surveyed commonly misinterpret 'first void urine' for chlamydia screening

Authors: Lusk MJ et al

Summary: An open question survey of general practitioners (GP) and hospital emergency department (ED) doctors revealed that the term 'FVU' (first void urine) used for urine chlamydia testing, is ambiguous, potentially leading to incorrect urine sample collection and barriers to effective screening. The data indicate that only 4.3% of GP and 6.9% of ED doctors respectively, correctly interpreted the meaning of FVU. The majority of clinicians surveyed misunderstood 'FVU' to require the first urine void of the day (i.e. 68.1% of GPs and 37.9% of ED doctors).

Comment: Chlamydia is a significant health problem in NZ and it is so easy to screen for. First void means the first part of the stream, and not the first void in the morning.

Reference: *Sex Health*. 2009;6(1):91-3.

<http://www.publish.csiro.au/nid/164/paper/SH08087.htm>

Weekend admission and treatment of patients with renal colic: a case of avoidable variation?

Authors: Strobe SA et al

Summary: Data from the Florida State Inpatient Database for 2005 were used to identify admissions (n=8589) for symptomatic urolithiasis, to determine whether the thresholds to intervene and the nature of the intervention might be susceptible to practice style differences that vary by day of presentation. Weekend admission was associated with a lower likelihood of surgery (OR 0.88). Patients with complicating factors, such as fever, were more likely to undergo surgery than those without such characteristics (adjusted OR 1.28). However, when surgery was performed, the use of definitive surgery was similar between the patients admitted on the weekend and those admitted on weekdays (adjusted OR 1.02).

Comment: But what this paper did not address was outcome. Did the weekend patients who were associated with a less likelihood of surgery have an eventual worse outcome. This is not answered by this paper. One of the most difficult things doctors have to learn is to keep their mouths shut, and their hands in their pockets! **Reference:** *Urology*. 2009;73(4):720-4.

[http://www.goldjournal.net/article/S0090-4295\(08\)01800-1/abstract](http://www.goldjournal.net/article/S0090-4295(08)01800-1/abstract)

A population-based study of the drug interaction between proton pump inhibitors and clopidogrel

Authors: Juurlink DN et al

Summary: Evidence suggests that various proton pump inhibitors (PPIs) inhibit P450 2C19, which would alter the effectiveness of clopidogrel and potentially lead to an increased risk of adverse cardiovascular outcomes. To assess the potential effects of the drug interaction, these researchers identified 13,636 patients prescribed clopidogrel following an acute myocardial infarction (MI). Of these, 734 patients were readmitted with MI and 2057 served as event-free controls matched based on age, percutaneous coronary intervention (PCI), and risk score. Among patients currently prescribed a PPI plus clopidogrel, the risk of reinfarction within 90 days was 27% greater than among those taking clopidogrel only. The risk was limited to those currently taking a PPI and was not associated with pantoprazole, a drug that does not interfere with the conversion of clopidogrel to its active form.

Comment: The prescribing of PPIs is common in this country, and with the increasing use of clopidogrel following myocardial infarction and/or stent installation this paper identifies an important drug interaction. The take home message is that if patients are on clopidogrel and require a PPI, pantoprazole is the only way to go.

Reference: *CMAJ*. 2009;180(7):713-8.

<http://tinyurl.com/r3sztn>

Moderate alcohol consumption is associated with reduced long-term cardiovascular risk in patients following a complicated acute myocardial infarction

Authors: Brügger-Andersen T et al

Summary: Alcohol use in relation to all-cause mortality, cardiovascular (CV)-related mortality and hospitalisation was examined in a total of 5477 patients participating in the OPTIMAAL trial; all had heart failure and/or evidence of left ventricular dysfunction following myocardial infarction (MI). Patients were asked to assess their average alcohol consumption prior to the index infarction. Patients were stratified by the frequency of the use of alcohol into either non-users (n=2160), moderate users (1-7 drinks/week, n=2753) and heavy users (>7 drinks/week, n=545) and related to prespecified clinical outcomes in the groups. During a 2.7-year follow-up, 946 deaths were reported. Analyses adjusted for age and smoking status revealed that moderate alcohol use was associated with a 24% lower risk of all-cause death (p<0.001), 26% lower risk of CV-related death (p<0.000) and 8% lower risk for hospitalisation (p=0.030) than non-use. There was no significant difference between non-drinkers and heavy drinkers with regard to survival following adjustment for age and smoking status.

Comment: So a drink a day keeps the doctor away (and helps to keep the undertaker away as well). This is a well-designed study that demonstrated that after correction for age and smoking, on a population basis, moderate use of alcohol (1 to 7 drinks a week), on a population basis reduced the risk of cardiovascular death over two and a half years by 26%. But bad news for abstainers and heavy drinkers – they both had poorer prognosis.

Reference: *Int J Cardiol*. 2009;133(2):229-32.

<http://linkinghub.elsevier.com/retrieve/pii/S0167527308000934>

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Adherence with urate-lowering therapies for the treatment of gout

Authors: Harrold L et al

Summary: These researchers examined the level and determinants of non-adherence with urate-lowering drugs (ULDs) prescribed for gout, in a cohort of 4166 gout patients aged ≥ 18 years who initiated use of allopurinol, probenecid or sulfinpyrazone from 1 January 2000 to 30 June 2006. Non-adherence was measured using the medication possession ratio (MPR) over the first year of therapy and defined as an MPR < 0.8 . Median MPR for any ULD use was 0.68. Over half of the patients (56%) were non-adherent (MPR < 0.8). In adjusted analyses, predictors of poor adherence included younger age (OR 2.43 for ages < 45 and OR 1.44 for ages 45 to 49), fewer comorbid conditions (OR 1.46), no provider visits for gout prior to urate-lowering drug initiation (OR 1.28), and use of NSAIDs in the year prior to urate-lowering drug initiation (OR 1.15).

Comment: I suspect that gout is similar to many other conditions for which we expect our patients to accept prophylactic medication – hypertension, asthma and type 2 diabetes to name three. If there are no symptoms, then it is difficult for patients to accept the need to take medication. Unfortunately, attacks of gout are often widely separated and are seen by patients as only being related to joint pain. My common sense tells me that adherence to a regime is related to education, but studies do not support this. How the patient relates to his/her doctor is much more important.

Reference: *Arthritis Res Ther.* 2009;11(2):R46.
<http://tinyurl.com/orcgyg>

Dr Christopher Tofield

Dr Tofield completed his medical training at St Bartholomew's and the Royal London Hospital in London and is now a fulltime General Practitioner in Tauranga.

Chris has extensive experience in medical writing and editing and while at medical school published a medical textbook on pharmacology. He is responsible for sourcing studies for all Research Review journals.

Evidence based natural health by Dr Chris Tofield

Coadministration of coenzyme Q prevents rosiglitazone-induced adipogenesis in *ob/ob* mice

Authors: Carmona MC et al

Summary: *Ob/ob* mice already receiving thiazolidinedione (TZD) were given additional treatment with either coenzyme Q10 (CoQ10) or rosiglitazone, or in combination, for 13 days. Combination therapy with CoQ10 and rosiglitazone improved metabolic parameters and also prevented the thiazolidinedione-induced increase in body weight and adiposity, as determined by real-time PCR. Changes in mRNA expression of genes of energy dissipation and storage were detected by an increasing lipid oxidation in adipose tissue, a reduction in lipid synthesis and balancing of adipokine gene expression.

Comment: Coenzyme Q10 has many reported beneficial effects, particularly in patients with myopathies and cardiovascular complications. This French study on mice produced some significant results. The CoQ10 group showed improved metabolic parameters and, importantly, an absence of weight gain usually associated with the gliptazones. GPs and diabetologists alike would find this study of interest.

Reference: *Int J Obes (Lond).* 2009;33(2):204-11.
<http://www.nature.com/ijo/journal/v33/n2/full/ijo2008265a.html>

Effects of Transcendental Meditation on mental health: a before-after study

Authors: Yunesian M et al

Summary: These researchers sought to determine the potential benefits of a 12-week Transcendental Meditation course in enhancing mental health among 80 individuals aged 20–55 years. At 12 weeks, mean scores on the 28-item General Health Questionnaire (GHQ) were improved in the areas of somatisation and anxiety but there was no significant change on depression and social dysfunction scores. The overall score of the GHQ-28 was also improved significantly from 25.1 before the course to 21.3 after the course ($p < 0.001$).

Comment: This study employed a type of meditation that uses a 'mantra' (a sound, word or phrase repeated silently) to prevent thoughts from entering and distracting the mind. The results are positive, as shown by the statistically significant increase in the General Health Questionnaire scores. I can't see our mental health teams embracing this method, but it certainly represents a no-risk treatment option that GPs can give their anxious/worried well patients.

Reference: *Clin Pract Epidemiol Ment Health.* 2008;4:25
<http://www.cpementalhealth.com/content/4/1/25>

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