COCHRANE RENAL GROUP
A REVIEW GROUP OF THE COCHRANE COLLABORATION

Newsletter - April 2013



# Cochrane Renal Group — New reviews, protocols and titles

## New and updated reviews

In Issues 10-12, 2012 and 1-3, 2013 we published three new reviews and five updated reviews with new findings:

*New*

- Antioxidants for chronic kidney disease
- Antiplatelet agents for chronic kidney disease
- Thyroid hormones for acute kidney injury

*Updated with new findings*

- Antihypertensive agents for preventing diabetic kidney disease
- Antiviral medications for preventing cytomegalovirus disease in solid organ transplant recipients
- Cranberries for preventing urinary tract infections
- Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients
- Treatment for lupus nephritis

## New protocols

In Issues 10-12, 2012 and 1-3, 2013 we published 10 new protocols:

- Chinese herbal medicine for treating recurrent urinary tract infections in women
- Dialyser reuse for people with end-stage kidney disease requiring haemodialysis
- Dietary interventions for lowering cholesterol in dialysis patients
- Dietary interventions for mineral and bone disorder in people with chronic kidney disease
- Glucose targets for preventing diabetic kidney disease and its progression
- Interventions for preventing the progression of autosomal dominant polycystic kidney disease
- Loop diuretics for patients receiving blood transfusions
- Pharmacological interventions for treating acute hyperkalaemia in adults
- Reduction of dialysate temperature for intradialytic hypotension during haemodialysis
- Subcutaneous versus intravenous erythropoietin for long-term dialysis patients

## *Inside this issue:*

# New reviews, protocols and titles *(Cont'd)*

## New titles

- Antihypertensive agents for diabetic kidney disease: a network meta-analysis
- Antihypertensive agents for non-diabetic kidney disease: a network meta-analysis
- Altering dialysate sodium levels for haemodialysis
- Amphotericin B deoxycholate versus liposomal amphotericin B: effects on kidney function
- Calcium channel blockers for people with chronic kidney disease requiring dialysis
- Diet for preventing chronic kidney disease
- Diet for preventing death in patients with chronic kidney disease
- Early versus delayed erythropoietin for the anaemia of end-stage kidney disease
- Early versus late ureteric stent removal for kidney transplant recipients
- Fish oil for preventing haemodialysis graft thrombosis in patients with end-stage kidney disease
- HMG CoA reductase inhibitors (statins) for preventing acute kidney injury after surgical procedures requiring cardiac bypass
- Interventions for chronic euvolemic or hypervolemic hypotonic hyponatraemia
- Interventions for increasing organ donor registration
- Machine perfusion preservation versus static cold storage for cadaveric kidney transplantation
- Nutritional supplements for people with chronic kidney disease requiring dialysis
- Oral iron for people with chronic kidney disease
- Treatment for HCV-related cryoglobulinaemia

# Renal group news

## Visitors to the Cochrane Renal Group

### Visiting European Renal Best Practice (ERBP) Fellows

**Evi Nagler** returned to the CRG in October 2012 for a further six months.

She is a Specialist Registrar in Nephrology at Ghent University Hospital in Belgium and is an ERBP Fellow responsible for Development of the ERBP Guidelines on the management and evaluation of the kidney donor and recipient, and diagnosis and treatment of hyponatraemia. In this context, during her time with the Cochrane Renal Group she drafted a Cochrane protocol on the treatment of chronic hyponatraemia and completed a methodological paper outlining ERBP's guideline development methodology.

Following her return home Evi will now finish a master in statistical data analysis as well as a PhD focused on the clinical application of systematic review methods within the guideline development process.

**Maria Haller** also joined the Cochrane Renal Group in October 2012 for six months.

Maria has an ERBP Fellowship provided by the ERA-EDTA. She is a Resident for internal medicine at the Department of Nephrology, Rheumatology, Hypertension and Transplantation, Hospital Elisabethinen, Linz, Austria.

Whilst with the Cochrane Renal Group Maria contributed to updating the Cochrane Review on steroid withdrawal after kidney transplantation. Maria was also involved in a project comparing the methodological and organizational aspects of different renal guideline bodies around the world.

Maria has now returned to Austria where she is enrolled in a PhD program at the Medical University of Vienna. Her PhD will focus on decision analysis in the context of altruistic donor selection for living kidney transplantation.

# Renal group news *(Cont'd)*

## Cochrane Commentaries

Following a recent partnership with our colleagues at the journal *Nephrology*, our reviews can reach a wider audience.

Cochrane commentaries are short synopses of recent Cochrane reviews or review updates, each chosen because it is likely to be of interest to the *Nephrology* journal's readership and relevant to clinical practice.

Angela Webster has been working with our review authors to write each commentary and to date the following have been published:

**Induction and maintenance treatment of proliferativelupus nephritis**
DOI: 10.1111/nep.12011

**Parenteral versus oral iron therapy for adults and children with chronic kidney disease**
DOI: 10.1111/j.1440-1797.2012.01660.x

**Cardiac testing for coronary artery disease in potential kidney transplant recipients.**
DOI: 10.1111/j.1440-1797.2012.01624.x

## Cochrane Renal Group policy regarding acceptance of title registrations, and deadlines for protocol and review submissions

In our role of supporting review authors through the review process, we are constantly looking at ways to ensure the best use of our limited resources. To this end we have decided to place a strong focus on the registration of priority titles only. All potential titles will be compared to a priority list that has been put together with input from our editors and Advisory Board members. The list was created by asking "what are your top 5 review questions that need answering".

The questions must be topical; relevant to patients, health care providers and policy makers and have some evidence in the form of RCTs.

In addition we will be more strictly adhering to our prespecified timelines for the various stages of the review process. These include:

- From title registration to submission of draft protocol: **6 months.**
- From publication of a protocol to submission of draft review: **12 months**
- From publication of a review to submission of draft review update: **2 years**

Naturally reminders will be sent out to the contact/corresponding author to let them know that submission deadlines are approaching. Requests for extensions will be considered but cannot be guaranteed.

We also understand that the refereeing process can take some time—as with most journals some topic areas are harder to identify referees than others. Factoring in the complexity and size of Cochrane systematic reviews, there can at times be extensive delays. To help speed up the internal checks needed when a draft protocol or review is submitted, a pre-submission checklist will be required to be submitted by the author team. This lists the majority of checks we have to undertake before submitting for editorial approval for refereeing.

If your have a draft submission that is currently overdue, please email us (contact details) to discuss any assistance we may be able to offer.

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## We are now on Twitter!

We have a Twitter account and hope to keep you up-to-date with news and events relating to our group, The Cochrane Collaboration and kidney disease.

Follow us now **@CochraneRenal**

# Recent abstracts (*new*)

## Antioxidants for chronic kidney disease

Min Jun, Vinod Venkataraman, Mona Razavian, Bruce Cooper, Sophia Zoungas, Toshiharu Ninomiya, Angela C Webster, Vlado Perkovic

**Background**
Chronic kidney disease (CKD) is a significant risk factor for premature cardiovascular disease and death. Increased oxidative stress in people with CKD has been implicated as a potential causative factor for some cardiovascular diseases. Antioxidant therapy may reduce cardiovascular mortality and morbidity in people with CKD.

**Objectives**
To examine the benefits and harms of antioxidant therapy on mortality and cardiovascular events in people with CKD stages 3 to 5; dialysis, and kidney transplantation patients.

**Search methods**
We searched the Cochrane Renal Group's specialised register (July 2011), CENTRAL (Issue 6, 2011), MEDLINE (from 1966) and EMBASE (from 1980).

**Selection criteria**
We included all randomised controlled trials (RCTs) investigating the use of antioxidants for people with CKD, or subsets of RCTs reporting outcomes for participants with CKD.

**Data collection and analysis**
Titles and abstracts were screened independently by two authors who also performed data extraction using standardised forms. Results were pooled using the random effects model and expressed as either risk ratios (RR) or mean difference (MD) with 95% confidence intervals (CI).

**Main results**
We identified 10 studies (1979 participants) that assessed antioxidant therapy in haemodialysis patients (two studies); kidney transplant recipients (four studies); dialysis and non-dialysis CKDpatients (one study); and patients requiring surgery (one study). Two additional studies reported the effect of an oral antioxidant inflammation modulator in patients with CKD (estimated glomerular filtration rate (eGFR) 20 to 45 mL/min/1.73 $m^2$), and post-hoc findings from a subgroup of people with mild-to-moderate renal insufficiency (serum creatinine ≥125 µmol/L) respectively. Interventions included different doses of vitamin E (two studies); multiple antioxidant therapy (three studies); co-enzyme Q(one study); acetylcysteine (one study); bardoxolone methyl (one study); and human recombinant superoxide dismutase (two studies).

Compared with placebo, antioxidant therapy showed no clear overall effect on cardiovascular mortality (RR 0.95, 95% CI 0.70 to 1.27; P = 0.71); all-cause mortality (RR 0.93, 95% CI 0.76 to 1.14; P = 0.48); cardiovascular disease (RR 0.78, 95% CI 0.52 to 1.18; P = 0.24); coronary heart disease (RR 0.71, 95% CI 0.42 to 1.23; P = 0.22); cerebrovascular disease (RR 0.91, 95% CI 0.63 to 1.32; P = 0.63); or peripheral vascular disease (RR 0.54, 95% CI 0.26 to 1.12; P = 0.10). Subgroup analyses found no evidence of significant heterogeneity based on proportions ofmales (P = 0.99) or diabetes (P = 0.87) for cardiovascular disease. There was significant heterogeneity for cardiovascular disease when studies were analysed by CKD stage (P = 0.003). Significant benefit was conferred by antioxidant therapy for cardiovascular disease prevention in dialysis patients (RR 0.57, 95% CI 0.41 to 0.80; P = 0.001), although no effect was observed in CKD patients (RR 1.06, 95% CI 0.84 to 1.32; P = 0.63).

Antioxidant therapy was found to significantly reduce development of end-stage of kidney disease (ESKD) (RR 0.50, 95% CI 0.25 to 1.00; P = 0.05); lowered serum creatinine levels (MD 1.10 mg/dL, 95%CI 0.39 to 1.81; P = 0.003); and improved creatinine clearance (MD 14.53 mL/min, 95% CI 1.20 to 27.86; P = 0.03). Serious adverse events were not significantly increased by antioxidants (RR 2.26, 95% CI 0.74 to 6.95; P = 0.15).

Risk of bias was assessed for all studies. Studies that were classified as unclear for random sequence generation or allocation concealment reported significant benefits from antioxidant therapy (RR 0.57, 95% CI 0.41 to 0.80; P = 0.001) compared with studies at low risk of bias (RR 1.06, 95% CI 0.84 to 1.32; P = 0.63).

**Authors' conclusions**
Although antioxidant therapy does not reduce the risk of cardiovascular and all-cause death or major cardiovascular events in people with CKD, it is possible that some benefit may be present, particularly in those on dialysis. However, the small size and generally suboptimal quality of the included studies highlighted the need for sufficiently powered studies to confirm this possibility. Current evidence suggests that antioxidant therapy in predialysis CKD patients may prevent progression to ESKD; this finding was however based on a very small number of events. Further studies with longer follow-up are needed for confirmation. Appropriately powered studies are needed to reliably assess the effects of antioxidant therapy in people with CKD.

## Antiplatelet agents for chronic kidney disease

Suetonia C Palmer , Lucia Di Micco , Mona Razavian , Jonathan C Craig , Vlado Perkovic , Fabio Pellegrini , Meg J Jardine , Angela C Webster , Sophia Zoungas and Giovanni FM Strippoli

**Background**
Antiplatelet agents are widely used to prevent

# Recent abstracts (*new*)

*...Cont'd*

cardiovascular events. The risks and benefits of antiplatelet treatment may be different in people with chronic kidney disease (CKD) for whom occlusive atherosclerotic events are less prevalent, and bleeding hazards might be increased.

### Objectives
To summarise the effects of antiplatelet treatment (antiplatelet agent versus control or other antiplatelet agent) for the prevention of cardiovascular and adverse kidney outcomes in individuals with CKD.

### Search methods
In January 2011 we searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and the Cochrane Renal Group's Specialised Register without language restriction.

### Selection criteria
We selected randomised controlled trials of any antiplatelet treatment versus placebo or no treatment, or direct head-to-head antiplatelet agent studies in people with CKD. Studies were included if they enrolled participants with CKD, or included people in broader at-risk populations in which data for subgroups with CKD could be disaggregated.

### Data collection and analysis
Two authors independently extracted data from primary study reports and any available supplementary information for study population, interventions, outcomes, and risks of bias. Risk ratios (RR) and 95% confidence intervals (CI) were calculated from numbers of events and numbers of participants at risk which were extracted from each included study. The reported RRs were extracted where crude event rates were not provided. Data was pooled using the random-effects model.

### Main results
We included 50 studies, enrolling 27,139 participants; 44 studies (21,460 participants) compared an antiplatelet agent with placebo or no treatment, and six studies (5679 participants) directly compared one antiplatelet agent with another. Compared to placebo or no treatment, antiplatelet agents reduced the risk of myocardial infarction (17 studies; RR 0.87, 95% CI 0.76 to 0.99), but not all-cause mortality (30 studies; RR 0.93, 95% CI 0.81 to 1.06), cardiovascular mortality (19 studies; RR 0.89, 95% CI 0.70 to 1.12) or stroke (11 studies; RR 1.00, 95% CI 0.58 to 1.72). Antiplatelet agents increased the risk of major (27 studies; RR 1.33, 95% CI 1.10 to 1.65) and minor bleeding (18 studies; RR 1.49, 95% CI 1.12 to 1.97). In terms of dialysis access outcomes, antiplatelet agents reduced access thrombosis or patency failure but had no effect on suitability for dialysis. Meta-regression analysis indicated no differences in the relative benefit or harms of treatment (risk of all-cause mortality, myocardial infarction, or major bleeding) by type of antiplatelet agent or stage of CKD. Limited data were available for direct head-to-head comparisons of antiplatelet drugs, treatment in kidney transplant recipients, primary prevention, or risk of ESKD.

### Authors' conclusions
Antiplatelet agents reduce myocardial infarction but increase major bleeding. Risks may outweigh harms among people with low annual risks of cardiovascular events, including those with early stages of CKD who do not have clinically-evident occlusive cardiovascular disease.

## Thyroid hormones for acute kidney injury

Sagar U Nigwekar , Giovanni FM Strippoli and Sankar D Navaneethan

### Background
Acute kidney injury (AKI), which is common in hospitalised patients, is associated with significant morbidity and mortality. Despite recent advances in treatment, AKI outcomes have not changed substantially during the past four decades, and incidence is increasing. There is an urgent need to explore novel therapeutic agents and revisit some older drugs to review their roles in the management of AKI. Although thyroid hormone therapy has shown promise in experimental animal studies, clinical efficacy and safety have not been systematically assessed for the management of people with AKI.

# Recent abstracts (*new*) *...Cont'd*

### Objectives
To evaluate the benefits and harms of thyroid hormones for the treatment of hospitalised adults with AKI of any aetiology.

### Search methods
We searched the Cochrane Renal Group's Specialised Register, CENTRAL, MEDLINE, and EMBASE. We also checked the reference lists of retrieved studies and articles.
Date of search: November 2012

### Selection criteria
Randomised controlled trials (RCTs) and quasi-RCTs (in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) that compared any dose or form of thyroid hormone therapy alone or in combination with other agents compared with placebo or supplemental treatment (such as furosemide, dopamine, or atrial natriuretic peptide) in adult AKI patients.

### Data collection and analysis
Two authors independently assessed study quality and extracted data. The quality of included studies was assessed using the Cochrane Collaboration's risk of bias assessment tool. For dichotomous outcomes (death, need for renal replacement therapy (RRT), progression to end-stage kidney disease (ESKD)), we planned to express results as risk ratios (RR) with 95% confidence intervals (CI). Where continuous scales of measurement were used to assess the effects of treatment (length of hospital stay, durations of AKI and RRT), we planned to use the mean difference (MD).

### Main results
Two studies, enrolling 97 participants, met our inclusion criteria. The studies differed significantly in terms of study populations, natural history of AKI (multifactorial AKI in patients with native kidneys versus delayed graft function associated with acute tubular necrosis in transplant recipients), and study interventions; hence, data were not meta-analysed. One study reported a significant increase in the risk of all-cause mortality associated with thyroid hormone interventions compared with placebo (59 participants, RR 3.32, 95% CI 1.21 to 9.12); no deaths were reported in the other study. Both studies reported no significant difference in the need for RRT associated with thyroid hormone therapy when compared to placebo. Neither study reported incidence of progression to ESKD. There was a significantly longer duration of AKI (MD 2.00 days, 95% CI 0.18 to 3.82) and RRT (5.00 days, 95% CI 2.05 to 7.95) associated with thyroid hormone therapy compared with placebo in one study; no differences in durations of AKI (MD 2.00 days, 95% CI -3.53 to 7.53) and RRT (MD 2.00 days, 95% CI -2.36 to 6.36) were noted in the other study. One study reported similar lengths of stay in the intensive care unit and hospital in both intervention and control arms (MD -0.20 days, 95% CI -8.17 to 7.77); the other did not report this outcome. No adverse events were noted to be associated with thyroid hormone therapy in either study. Adequate data were not available to assess changes in kidney function or numbers of RRT sessions. Both included studies were small and methodological quality was suboptimal.

### Authors' conclusions
We found a paucity of large, high quality studies to inform analysis of thyroid hormone interventions for the treatment of people with AKI. Current evidence suggested that thyroid hormone therapy may be associated with worse outcomes for patients with established AKI; therefore, its use for these patients should be avoided. The role of thyroid hormone therapy in preventing AKI has not been adequately investigated and may be considered in future clinical studies.

# Recent abstracts (*updated with new findings*)

## Antihypertensive agents for preventing diabetic kidney disease

Jicheng Lv , Vlado Perkovic , Celine V Foote , Maria E Craig , Jonathan C Craig and Giovanni FM Strippoli

### Background
Various blood pressure-lowering agents, and particularly inhibitors of the renin-angiotensin system (RAS), are widely used for people with diabetes to prevent the onset of diabetic kidney disease (DKD) and adverse cardiovascular outcomes. This is an update of a Cochrane review first published in 2003 and updated in 2005.

### Objectives
This systematic review aimed to assess the benefits and harms of blood pressure lowering agents in people with diabetes mellitus and a normal amount of albumin in the urine (normoalbuminuria).

### Search methods
In January 2011 we searched the Cochrane Renal Group's Specialised Register through contact with the Trials Search Co-ordinator.

### Selection criteria
Randomised controlled trials (RCTs) comparing any antihypertensive agent with placebo or another agent in hypertensive or normotensive patients with diabetes and no

# Recent abstracts (*updated with new findings*) *...Cont'd*

kidney disease (albumin excretion rate < 30 mg/d) were included.

**Data collection and analysis**
Two investigators independently extracted data on kidney and other patient-relevant outcomes (all-cause mortality and serious cardiovascular events), and assessed study quality. Analysis was by a random effects model was applied to analyse results which were expressed as risk ratio (RR) and 95% confidence intervals (CI).

**Main results**
We identified 26 studies that enrolling 61,264 participants. Angiotensin-converting enzyme inhibitors (ACEi) reduced the risk of new onset of microalbuminuria, macroalbuminuria or both when compared to placebo (8 studies, 11,906 patients: RR 0.71, 95% CI 0.56 to 0.89), with similar benefits in people with and without hypertension (P = 0.74), and when compared to calcium channel blockers (5 studies, 1253 participants: RR 0.60, 95% CI 0.42 to 0.85). ACEi reduced the risk of death when compared to placebo (6 studies, 11,350 participants: RR 0.84, 95% CI 0.73 to 0.97). No effect was observed for angiotensin receptor blockers (ARB) when compared to placebo for new microalbuminuria, macroalbuminuria or both (5 studies, 7653 participants: RR 0.90, 95% CI 0.68 to 1.19) or death (5 studies, 7653 participants: RR 1.12, 95% CI 0.88 to 1.41); however, meta-regression suggested possible benefits from ARB for preventing kidney disease in high risk patients. There was a trend towards benefit from use of combined ACEi and ARB for prevention of DKD compared with ACEi alone (2 studies, 4171 participants: RR 0.88, 95% CI 0.78 to 1.00).The risk of cough was significantly increased with ACEi when compared to placebo (6 studies, 11,791 patients: RR 1.84, 95% CI 1.24 to 2.72), however there was no significant difference in the risk of headache or hyperkalaemia. There was no significant difference in the risk of cough, headache or hyperkalaemia when ARB was to placebo. On average risk of bias was judged to be either low (27% to 69%) or unclear (i.e. no information available) (8% to 73%). Blinding of participants, incomplete outcome data and selective reporting were judged to be high in 23%, 31% and 31% of studies, respectively.

**Authors' conclusions**
ACEi were found to prevent new onset DKD and death in normoalbuminuric people with diabetes, and could therefore be used in this population. More data are needed to clarify the role of ARB and other drug classes in preventing DKD.

## Antiviral medications for preventing cytomegalovirus disease in solid organ transplant recipients

Elisabeth M Hodson , Maleeka Ladhani , Angela C Webster, Giovanni FM Strippoli and Jonathan C Craig

**Background**
The risk of cytomegalovirus (CMV) infection in solid organ transplant recipients has resulted in the frequent use of prophylaxis with the aim of preventing the clinical syndrome associated with CMV infection. This is an update of a review first published in 2005 and updated in 2008.

**Objectives**
To determine the benefits and harms of antiviral medications to prevent CMV disease and all-cause mortality in solid organ transplant recipients.

**Search methods**
We searched MEDLINE, EMBASE and the Cochrane Central Registry of Controlled Trials (CENTRAL) in The Cochrane Library to February 2004 for the first version of this review. The Cochrane Renal Group's specialised register was searched to February 2007 and to July 2011 for the first and current updates of the review without language restriction.

**Selection criteria**
We included randomised controlled trials (RCTs) and quasi -RCTs comparing antiviral medications with placebo or no treatment, comparing different antiviral medications and comparing different regimens of the same antiviral medications in recipients of any solid organ transplant. Studies examining pre-emptive therapy were excluded.
Data collection and analysis

Two authors independently assessed study eligibility, risk of bias and extracted data. Results were reported as risk ratios (RR) or risk differences (RD) with 95% confidence intervals (CI) for dichotomous outcomes and by mean difference (MD) with 95% CI for continuous outcomes. Statistical analyses were performed using the random-effects model. Subgroup analysis and univariate meta-regression were performed using restricted maximum-likelihood to estimate the between study variance. Multivariate meta-regression was performed to investigate whether the results were altered after allowing for differences in drugs used, organ transplanted, and recipient CMV serostatus at the time of transplantation.

# Recent abstracts (*updated with new findings*) ...Cont'd

**Main results**
We identified 37 studies (4342 participants). Risk of bias attributes were poorly performed or reported with low risk of bias reported for sequence generation, allocation concealment, blinding and selective outcome reporting in 25% or fewer studies.

Prophylaxis with aciclovir, ganciclovir or valaciclovir compared with placebo or no treatment significantly reduced the risk for CMV disease (19 studies; RR 0.42, 95% CI 0.34 to 0.52), CMV infection (17 studies; RR 0.61, 95% CI 0.48 to 0.77), and all-cause mortality (17 studies; RR 0.63, 95% CI 0.43 to 0.92) primarily due to reduced mortality from CMV disease (7 studies; RR 0.26, 95% CI 0.08 to 0.78). Prophylaxis reduced the risk of herpes simplex and herpes zoster disease, bacterial and protozoal infections but not fungal infection, acute rejection or graft loss.

Meta-regression showed no significant difference in the relative benefit of treatment (risk of CMV disease or all-cause mortality) by organ transplanted or CMV serostatus; no conclusions were possible for CMV negative recipients of negative organs.

Neurological dysfunction was more common with ganciclovir and valaciclovir compared with placebo/no treatment. In direct comparison studies, ganciclovir was more effective than aciclovir in preventing CMV disease (7 studies; RR 0.37, 95% CI 0.23 to 0.60) and leucopenia was more common with aciclovir. Valganciclovir and IV ganciclovir were as effective as oral ganciclovir. The efficacy and adverse effects of valganciclovir/ganciclovir did not differ from valaciclovir in three small studies. Extended duration prophylaxis significantly reduced the risk of CMV disease compared with three months therapy (2 studies; RR 0.20, 95% CI 0.12 to 0.35). Leucopenia was more common with extended duration prophylaxis but severe treatment associated adverse effects did not differ between extended and three month durations of treatment.

**Authors' conclusions**
Prophylaxis with antiviral medications reduces CMV disease and CMV-associated mortality in solid organ transplant recipients. These data suggest that antiviral prophylaxis should be used routinely in CMV positive recipients and in CMV negative recipients of CMV positive organ transplants.

***The following review update was #2 on the list of top stories in The Cochrane Library's media coverage for 2012***

## Cranberries for preventing urinary tract infections

Ruth G Jepson, Gabrielle Williams and Jonathan C Craig

**Background**
Cranberries have been used widely for several decades for the prevention and treatment of urinary tract infections (UTIs). This is the third update of our review first published in 1998 and updated in 2004 and 2008.

**Objectives**
To assess the effectiveness of cranberry products in preventing UTIs in susceptible populations.

**Search methods**
We searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL in The Cochrane Library) and the Internet. We contacted companies involved with the promotion and distribution of cranberry preparations and checked reference lists of review articles and relevant studies.
Date of search: July 2012

**Selection criteria**
All randomised controlled trials (RCTs) or quasi-RCTs of cranberry products for the prevention of UTIs.

**Data collection and analysis**
Two authors independently assessed and extracted data. Information was collected on methods, participants, interventions and outcomes (incidence of symptomatic UTIs, positive culture results, side effects, adherence to therapy). Risk ratios (RR) were calculated where appropriate, otherwise a narrative synthesis was undertaken. Quality was assessed using the Cochrane risk of bias assessment tool.

**Main results**
This updated review includes a total of 24 studies (six cross-over studies, 11 parallel group studies with two arms; five with three arms, and two studies with a factorial design) with a total of 4473 participants. Ten studies were included in the 2008 update, and 14 studies have been added to this update. Thirteen studies (2380 participants) evaluated only cranberry juice/concentrate; nine studies (1032 participants) evaluated only cranberry tablets/capsules; one study compared cranberry juice and tablets;

## Recent abstracts (*updated with new findings*) *...Cont'd*

and one study compared cranberry capsules and tablets. The comparison/control arms were placebo, no treatment, water, methenamine hippurate, antibiotics, or lactobacillus. Eleven studies were not included in the meta-analyses because either the design was a cross-over study and data were not reported separately for the first phase, or there was a lack of relevant data. Data included in the meta-analyses showed that, compared with placebo, water or not treatment, cranberry products did not significantly reduce the occurrence of symptomatic UTI overall (RR 0.86, 95% CI 0.71 to 1.04) or for any the subgroups: women with recurrent UTIs (RR 0.74, 95% CI 0.42 to 1.31); older people (RR 0.75, 95% CI 0.39 to 1.44); pregnant women (RR 1.04, 95% CI 0.97 to 1.17); children with recurrent UTI (RR 0.48, 95% CI 0.19 to 1.22); cancer patients (RR 1.15 95% CI 0.75 to 1.77); or people with neuropathic bladder or spinal injury (RR 0.95, 95% CI: 0.75 to 1.20). Overall heterogeneity was moderate ($I^2$ = 55%). The effectiveness of cranberry was not significantly different to antibiotics for women (RR 1.31, 95% CI 0.85, 2.02) and children (RR 0.69 95% CI 0.32 to 1.51). There was no significant difference between gastrointestinal adverse effects from cranberry product compared to those of placebo/no treatment (RR 0.83, 95% CI 0.31 to 2.27). Many studies reported low compliance and high withdrawal/dropout problems which they attributed to palatability/acceptability of the products, primarily the cranberry juice. Most studies of other cranberry products (tablets and capsules) did not report how much of the 'active' ingredient the product contained, and therefore the products may not have had enough potency to be effective.

**Authors' conclusions**

Prior to the current update it appeared there was some evidence that cranberry juice may decrease the number of symptomatic UTIs over a 12 month period, particularly for women with recurrent UTIs. The addition of 14 further studies suggests that cranberry juice is less effective than previously indicated. Although some of small studies demonstrated a small benefit for women with recurrent UTIs, there were no statistically significant differences when the results of a much larger study were included. Cranberry products were not significantly different to antibiotics for preventing UTIs in three small studies. Given the large number of dropouts/withdrawals from studies (mainly attributed to the acceptability of consuming cranberry products particularly juice, over long periods), and the evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs. Other preparations (such as powders) need to be quantified using standardised methods to ensure the potency, and contain enough of the 'active' ingredient, before being evaluated in clinical studies or recommended for use.

## Conferences

May 18 – 21, 2013
**ERA-EDTA 50th Congress,** Istanbul, Turkey
www.era-edta2013.org/

May 18 – 22, 2013
**American Transplant Congress 2013,** Seattle, WA, USA
http://2012.atcmeeting.org/future-atc-meeting-dates

May 31 – June 4, 2013
**ISN World Congress of Nephrology 2013,** Hong Kong
www.wcn2013.org/

August 31 – September 4, 2013
**The Sixteenth Congress of the IPNA,** Shanghai, China
www.ipna2013.org/ipna/

September 8-10, 2013
**The Seventh International Congress on Peer Review and Biomedical Publication,** Chicago, IL, USA
www.ama-assn.org/public/peer/peerhome.htm

September 8-11, 2013
**ESOT 2013: 16th Congress of the European Society for Organ Transplantation,** Vienna, Austria
http://vienna.esot.org/

September 18-23, 2013
**21st Cochrane Colloquium,** Quebec City, Canada
http://colloquium.cochrane.org/colloquium-2013

November 5 – 10, 2013
**ASN Kidney Week 2013,** Atlanta, GA, USA
www.asn-online.org/education_and_meetings/

# Recent abstracts (*updated with new findings*) *...Cont'd*

## Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients

Daniel S Owers , Angela C Webster , Giovanni FM Strippoli , Kathy Kable and Elisabeth M Hodson

**Background**
Cytomegalovirus (CMV) is a significant cause of morbidity and mortality in solid organ transplant recipients. Pre-emptive treatment of patients with CMV viraemia using antiviral agents has been suggested as an alternative to routine prophylaxis to prevent CMV disease. This is an update of a Cochrane review first published in 2005.

**Objectives**
This review was conducted to evaluate the efficacy of pre-emptive treatment with antiviral medications in preventing symptomatic CMV disease.

**Search methods**
For this update, we searched the Cochrane Renal Group's Specialised Register (to 16 January 2013) through contact with the Trials' Search Co-ordinator using search terms relevant to this review.

**Selection criteria**
We included randomised controlled trials (RCTs) of pre-emptive treatment compared with placebo, no specific treatment or with antiviral prophylaxis in solid organ transplant recipients.

**Data collection and analysis**
Four authors assessed the quality and extracted all data. Analyses used a random-effects model and results were expressed as risk ratio (RR) and 95% confidence intervals (CI).

**Main results**
We identified 15 eligible studies (1098 participants). Of these, six investigated pre-emptive treatment versus placebo or treatment of CMV when disease occurred (standard care), eight looked at pre-emptive treatment versus antiviral prophylaxis, and one reported on oral versus intravenous pre-emptive treatment.

Assessment of risk of bias identified that the processes reported for sequence generation and allocation concealment were at low risk of bias in only five and three studies, respectively. All studies were considered to be at low risk of attrition bias, and seven studies were considered to be at low risk of bias for selective reporting. Only one study reported adequate blinding of participants and personnel; no study reported blinding of outcome assessment. Compared with placebo or standard care, pre-emptive treatment significantly reduced the risk of CMV disease (6 studies, 288 participants: RR 0.29, 95% CI 0.11 to 0.80) but not acute rejection (3 studies, 185 participants: RR 1.21, 95% CI 0.69 to 2.12) or all-cause mortality (3 studies, 176 participants: RR 1.23, 95% CI 0.35 to 4.30). Comparative studies of pre-emptive therapy versus prophylaxis showed no significant differences in preventing CMV disease between pre-emptive and prophylactic therapy (7 studies, 753 participants: RR 1.00, 95% CI 0.36 to 2.74) but there was significant heterogeneity ($I^2$ = 63%). Leucopenia was significantly less common with pre-emptive therapy compared with prophylaxis (6 studies, 729 participants: RR 0.42, 95% CI 0.20 to 0.90). Other adverse effects did not differ significantly or were not reported. There were no significant differences in the risks of all-cause mortality, graft loss, acute rejection and infections other than CMV.

**Authors' conclusions**
Few RCTs have evaluated the effects of pre-emptive therapy to prevent CMV disease. Pre-emptive therapy is effective compared with placebo or standard care. Despite the inclusion of five additional studies in this update, the efficacy of pre-emptive therapy compared with prophylaxis to prevent CMV disease remains unclear due to significant heterogeneity between studies. Additional head-to-head studies are required to determine the relative benefits and harms of pre-emptive therapy and prophylaxis to prevent CMV disease in solid organ transplant recipients.

## Treatment for lupus nephritis

Lorna Henderson , Philip Masson , Jonathan C Craig , Robert S Flanc , Matthew A Roberts , Giovanni FM Strippoli and Angela C Webster

**Background**
Cyclophosphamide, in combination with corticosteroids has been used to induce remission in proliferative lupus nephritis, the most common kidney manifestation of the multisystem disease, systemic lupus erythematosus. Cyclophosphamide therapy has reduced mortality from over 70% in the 1950s and 1960s to less than 10% in recent years. Cyclophosphamide combined with corticosteroids preserves kidney function but is only partially effective and may cause ovarian failure, infection and bladder toxicity. Several new agents, including mycophenolate mofetil (MMF), suggest reduced toxicity with equivalent rates of remission. This is an update of a Cochrane review first published in 2004.

**Objectives**
To assess the benefits and harms of different immunosup-

# Recent abstracts (*updated with new findings*) *...Cont'd*

pressive treatments in biopsy-proven proliferative lupus nephritis.

### Search methods
For this update, we searched the Cochrane Renal Group's Specialised Register (up to 15 April 2012) through contact with the Trials' Search Coordinator using search terms relevant to this review.

### Selection criteria
Randomised controlled trials (RCTs) and quasi-RCTs comparing any treatments for biopsy-proven lupus nephritis in both adult and paediatric patients with class III, IV, V +III and V +IV lupus nephritis were included. All immunosuppressive treatments were considered.

### Data collection and analysis
Data were abstracted and quality assessed independently by two authors, with differences resolved by discussion. Dichotomous outcomes were reported as risk ratio (RR) and measurements on continuous scales reported as mean differences (MD) with 95% confidence intervals (CI).

### Main results
We identified 50 RCTs involving 2846 participants. Of these, 45 studies (2559 participants) investigated induction therapy, and six studies (514 participants), considered maintenance therapy.

Compared with intravenous (IV) cyclophosphamide, MMF was as effective in achieving stable kidney function (5 studies, 523 participants: RR 1.05, 95% CI 0.94 to 1.18) and complete remission of proteinuria (6 studies, 686 participants: RR 1.16, 95% CI 0.85 to 1.58). No differences in mortality (7 studies, 710 participants: RR 1.02, 95% CI 0.52 to 1.98) or major infection (6 studies, 683 participants: RR 1.11, 95% CI 0.74 to 1.68) were observed. A significant reduction in ovarian failure (2 studies, 498 participants: RR 0.15, 95% CI 0.03 to 0.80) and alopecia (2 studies, 522 participants: RR 0.22, 95% CI 0.06 to 0.86) was observed with MMF. In maintenance therapy, the risk of renal relapse (3 studies, 371 participants: RR 1.83, 95% CI 1.24 to 2.71) was significantly higher with azathioprine compared with MMF. Multiple other interventions were compared but outcome data were relatively sparse. Overall study quality was variable. The internal validity of the design, conduct and analysis of the included RCTs was difficult to assess in some studies because of the omission of important methodological details. No study adequately reported all domains of the risk of bias assessment so that elements of internal bias may be present.

### Authors' conclusions
MMF is as effective as cyclophosphamide in inducing remission in lupus nephritis, but is safer with a lower risk of ovarian failure. MMF is more effective than azathioprine in maintenance therapy for preventing relapse with no increase in clinically important side effects. Adequately powered trials with long term follow-up are required to more accurately define the risks and eventual harms of specific treatment regimens.

## Upcoming workshops 2013
### Australasian Cochrane Centre/ Cochrane Renal Group*

| | |
|---|---|
| **13-17 May** | Review completion workshop<br>Melbourne |
| **19-21 Jun** | Introduction to writing a Cochrane review<br>Gold Coast |
| **3-5 July** | Introduction to writing a Cochrane review<br>Sydney* |
| **30 Jul** | Cochrane Live! Webinar Summary of Findings tables with GRADE profiler<br>Melbourne 12PM AEST |
| **6-8 Aug** | Introduction to writing a Cochrane review<br>Adelaide |
| **26-27 Aug** | Introduction to systematic reviews of interventions (Note: this workshop is part of the Monash University Short Course program, and is open to non-Cochrane authors. Fees apply to all participants.)<br>Melbourne |
| **23 Oct** | Cochrane Live! Webinar Managing references for your review using EndNote<br>Melbourne 12PM AEDT |
| **11-15 Nov** | Review completion workshop<br>Melbourne |
| **15 Nov** | Cochrane Live! Webinar Assessing Risk of Bias<br>Melbourne 12PM AEDT |
| **4-6 December** | Introduction to writing a Cochrane review<br>Sydney* |

For further information on Australasian workshops please go to: http://acc.cochrane.org/2013-timetable-registration

For Review workshops offered by other Cochrane Centres please go to: www.cochrane.org/training

# Cochrane Collaboration news

## 'Cochrane20 Video' series

The Collaboration is celebrating twenty years of its existence throughout 2013. In a series of events to mark this anniversary, 24 videos (<10 minutes each) are being released, a new one every two weeks, focussing on the ideas, achievements and people that have contributed to its growth since 1993, drawing on about hundred interviews with past and present Cochrane contributors from all over the world.

The sixth in the Cochrane20 Video series, a profile of Iain Chalmers (with Muir Gray), has been released, at http://youtu.be/D1TsADPyMhI.

There are various ways in which you can access and track the Cochrane20 Video Series:

The latest edition of the Video Series is available on the homepage of the Anniversary website, at anniversary.cochrane.org (your Archie password is not required) and on The Cochrane Collaboration's YouTube channel at http://youtube.com/user/cochranecollab.

Please note that all videos are captioned in 60 languages, thanks to caption files provided by director Richard Davis and the services of Google Translate. To use the Captions feature, click the "Turn on Captions" button in the player once your selected video begins; then choose "Translate Captions - Beta" and your preferred language. Please note that quality of translations varies depending on language chosen.

There are also several other ways to keep up to date with these releases throughout the year:

Subscribe to YouTube: Navigate to the YouTube address listed above, then click on the 'Subscribe' button which appears under the video (you'll need a YouTube/Google account). Notifications for the release of the rest of the series will be sent to the email address that you provide when subscribing.

Subscribe to the 20th Anniversary RSS feed on Cochrane.org: Navigate to http://www.cochrane.org/tags/tags/20th-anniversary and look for the RSS icon under the news display column. Click on the icon, then select from the available options your preferred delivery method for receiving 20th Anniversary updates. (For more information on how RSS feeds work, please visit http://www.cochrane.org/rss-feeds#rss-explained.)

Check the Anniversary Videos page: Navigate to the 'Videos' page on the 20th Anniversary website (at http://anniversary.cochrane.org/media-archive-videos-audio-files-slide-presentations-etc) to find a permanent link to the Cochrane20 Video Series playlist on YouTube, showing all of the videos that have been released to date. This link will automatically update to include each new video as it is released.

## New Cochrane Heart Group satellite launched

What: New Cochrane Heart Group satellite launched
Where: Northwestern University Feinberg School of Medicine, Department of Preventive Medicine, Chicago, USA
Why: To increase Cochrane Heart Group systematic review capacity

We are pleased to announce that Northwestern University's Department of Preventive Medicine will serve as a new Cochrane Heart Group satellite. Their application has been accepted by the Cochrane Collaborative Monitoring and Registration Committee and editor-in-chief, Dr. David Tovey with the full support of the Cochrane Heart Group editorial unit at the London School of Hygiene and Tropical Medicine and US and UK Cochrane Centers. The satellite will serve as the editorial hub for US-based Cochrane Heart Group activities to write, review, edit, and publish Cochrane protocols, updates, and systematic reviews as well as support systematic review training.

Mark Huffman (MHuffman@nmff.org)
Cochrane Heart Group

# Cochrane Collaboration news

*...Cont'd*

## Cochrane Public Health Group and Public Health Evidence South Asia approved

It is with great please that the Cochrane Public Health Group announces the formation of a South Asia satellite based in India.

CPHG South Asia will sit within a new enterprise within the Manipal University, India, and will align with the Melbourne editorial team and organisational context under the broad title of Public Health Evidence South Asia (PHESA). A major task of PHESA will be to build capacity to address LMIC priorities in the domain of public health. The satellite plan includes mentoring reviewers for Public Health reviews from the South Asian region, production of reviews relevant to the region and translation of this knowledge into policy through a network of government and local level institutions.

The satellite will have a three pronged structure mainly:
a. Evidence synthesis (systematic reviews)
b. Primary research (Including methodological development)
c. Knowledge translation (i.e. linking evidence to policy).

Based at Manipal University led by Prof. Sreekumaran Nair, supported by his newly endowed Chair: the Dr. TMA Pai Endowment Chair in Systematic Reviews and Evidence Based Public Health, together with Dr Ruhi Saith from Oxford Policy Management in New Delhi , PHESA will facilitate the synthesis, production and dissemination of high quality evidence on the effects of public health interventions relevant to low and middle income countries. The satellite also has the unique advantage of deriving strength and support from the South Asian Cochrane Network and Centre at CMC Vellore headed by Prof. Prathap Tharyan.

The 2014 Cochrane Colloquium which will be held in Hyderabad, will have the theme of public health. This represents a great opportunity for the satellite, working with the SACN, to make a significant contribution to the colloquium.

If you would like to learn more about PHESA please contact Sree Nair: sree.nair@manipal.edu and Ruhi Saith at ruhi.saith@gmail.com.

We hope that it will provide a great opportunity to join up interest across the Collaboration for review groups, fields, methods groups and others across the Collaboration to build capacity for low and middle income countries and collaborators.

## Registration for the Campbell Collaboration Annual Colloquium 21-23 May 2013

Date: 21-23 May 2013
Location: Loyola University, Chicago

Details:
Our program includes three distinct ways to participate:
1. Plenary speakers will provide an overarching context for rigorous reviews and how we can improve and promote systematic review. We are excited to include: Howard White, Matt Stagner, Mark Lipsey, Larry Hedges, Tom Cook, Jens Ludwig, Eileen Gambrill, and Dan Fox.
2. Methodological training sessions will be held over 2 days offering 10 distinct sessions. Both new and experienced reviewers will learn from the leading meta-analysis methodologists.
3. Finally, on the third day, reviewers across the six coordinating groups will share completed reviews. These sessions offer participants a chance to interact with reviewers conducting ongoing Campbell reviews.

Website: www.luc.edu/education/campbellcollaborationcolloquium/

## Two day systematic review workshop; Qualitative approaches to Evidence Synthesis

Location: Leuven, Belgium
Date: 10-11 June 2013

The KU Leuven Methodology of Educational Sciences Research Group organizes a multi-disciplinary workshop designed to provide faculty, PhD, doctoral students, editors, reviewers and other researchers in the area of Educational, Behavioral, Social Welfare and Healthcare sciences with the fundamental background and skills required to conduct a qualitative evidence synthesis evaluating the feasibility, appropriateness, meaningfulness of particular interventions or programs, inventorying the experiences of people involved in treatments, interventions or therapies or exploring the lived experience of people having a particular disability, disease or life in challenging circumstances. The Group collaborates with the Cochrane Qualitative Research and Implementation Methods Group, the Belgian Campbell Group and the Belgian branch of the Cochrane Centre.

For information on the program and the subscription modalities, visit our website: http://ppw.kuleuven.be/english/mesrg/SR2013.

# Cochrane Collaboration news ...Cont'd

## The Nottingham Systematic Review Course 2013

Date: 2nd July - 5th July 2013
Location: The University of Nottingham, UK

Details: This course will appeal to all those interested in completing a Cochrane-style review. Experienced tutors and facilitators will be available to give you practical and individual advice. Study methods: Small group teaching, workshops, library-based interactive tutorials with hands on practical work at computer stations and group work. Read the opinions of a former delegate on the Nottingham Systematic Review Course recently published in BMJ Careers. http://careers.bmj.com/careers/advice/view-article.html?id=20000296
Contact: Please contact Lindsey Air +44 (0)115 823 1287, or visit
Email: lindsey.air@nottingham.ac.uk
Website: http://szg.cochrane.org/en/events.html to download an application form.

## Workshop Summer School Systematic Reviews

held by the Austrian Cochrane Branch (ACB)
Date: 8. - 12.7.2013
Location: Austrian Cochrane Branch (ACB), Danube University Krems, Dr.-Karl-Dorrek-Straße 30, A - 3500 Krems an der Donau, lecture room SE 1.7.

Details: The aim of this workshop is to give you a sound theoretical and practical insight into the process of systematic reviews. The workshop is a combination of lectures and instructor-led and independent practical work on a systematic review. International experts will provide you with the theoretical foundations. This workshop will be held in German and English.
Contact: Simon Ledinek
E-mail: simon.ledinek@donau-uni.ac.at
Website: www.cochrane.at/de/workshops-2013#3

## Developing a Cochrane Systematic Review workshop

Date: 17-19 July 2013
Location: Baltimore, Maryland (USA)
Details: This workshop guides participants through the steps of developing a systematic review and includes presentations about Cochrane Collaboration methodology, hands-on practice using the Cochrane Collaboration's Review Manager (RevMan) software, and a statistics review session. It is limited to Cochrane review authors who have a registered title, have published a protocol in The Cochrane Library or who have a protocol approved for publication by a Cochrane Review Group.
Website: http://eyes.cochrane.org/workshop-developing-cochrane-systematic-review

## 21st Cochrane Colloquium

Date: 19 -23 September 2013
Location: Québec City, Québec, Canada
Call for Abstracts and Workshops closes 4 April 2013

STIPENDS! Stipends! STIPENDS!
Consumer and Developing Country stipend applications open 4 April and close 16 May 2013
Do you need financial support to get to the Colloquium? A limited number of stipends to help cover registration, travel, accommodation and other expenses associated with attending the 21st Cochrane Colloquium are available for Cochrane consumers and contributors from developing countries. Find more information at http://colloquium.cochrane.org/colloquium-stipends.
The EARLY BIRD gets the Worm!
Take advantage of our Early registration fee to receive a 20 per cent discount.

- Early registration: ends 15 July 2013 - $1015
- Regular registration: 16 July to 6 September - $1265
- Low- & middle-income country registration: ends 6 September - $615
- Student registration: ends 6 September - $615
- Consumer registration: ends 6 September - $615

Visit http://colloquium.cochrane.org/registration-information for more information and registration policies.

2013 Colloquium WEBINAR SERIES
Welcome to the Cochrane Colloquium! Tips and Tricks for newcomers.
Wednesday, 14 August 2013, 12 - 1 p.m. EDT (Toronto, Canada time); conducted in French.
Thursday, 15 August 2013, 12 - 1 p.m. EDT (Toronto, Canada time); conducted in English.
This webinar will provide a short introduction to The Cochrane Collaboration and some tips and tricks for making the most of your Colloquium experience. A Cochrane Colloquium is a unique international event from which you can benefit in many ways if you plan carefully: don't miss any of the exciting opportunities to learn and collaborate! Hear from past participants about how to maximize your experience as a Colloquium newcomer. More information coming soon.

Cochrane Canada proudly hosts this Colloquium in collaboration with Université Laval. Visit http://colloquium.cochrane.org/ regularly for more information and updates.

THE COCHRANE COLLABORATION®

## *The Cochrane Collaboration*

***preparing, maintaining and promoting the accessibility of systematic reviews of the effects of health care interventions***

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