

Coordination with the Cochrane Renal Group: Making best use of the Renal Trial Registry

Angela Webster

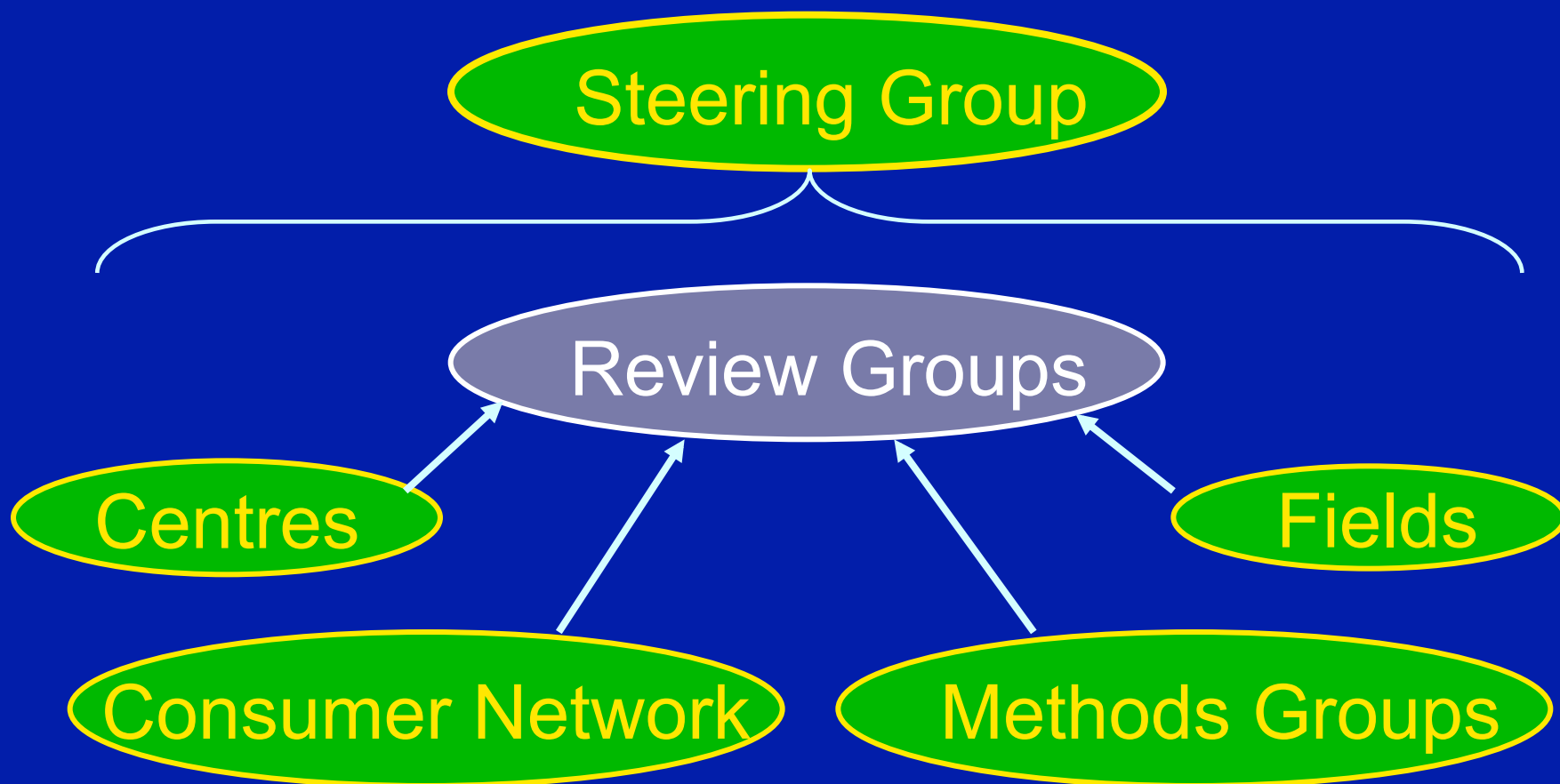
Editor, Cochrane Renal Group





The Cochrane
Renal Group

Cochrane Collaboration



<http://www.cochrane.org/index.htm>



cochrane renal group

A REVIEW GROUP OF THE COCHRANE COLLABORATION

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Endorsed by:

Asian Pacific Society of Nephrology
International Society of Nephrology
International Pediatric Nephrology Association
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CRG

- Based in Sydney (since 2000)
- Core work
 - Producing and updating systematic reviews
 - Renal trials registry - RCTs
 - Trial registration (prospective)
 - Diagnostic test accuracy studies and reviews
 - Training and support
 - Collaboration

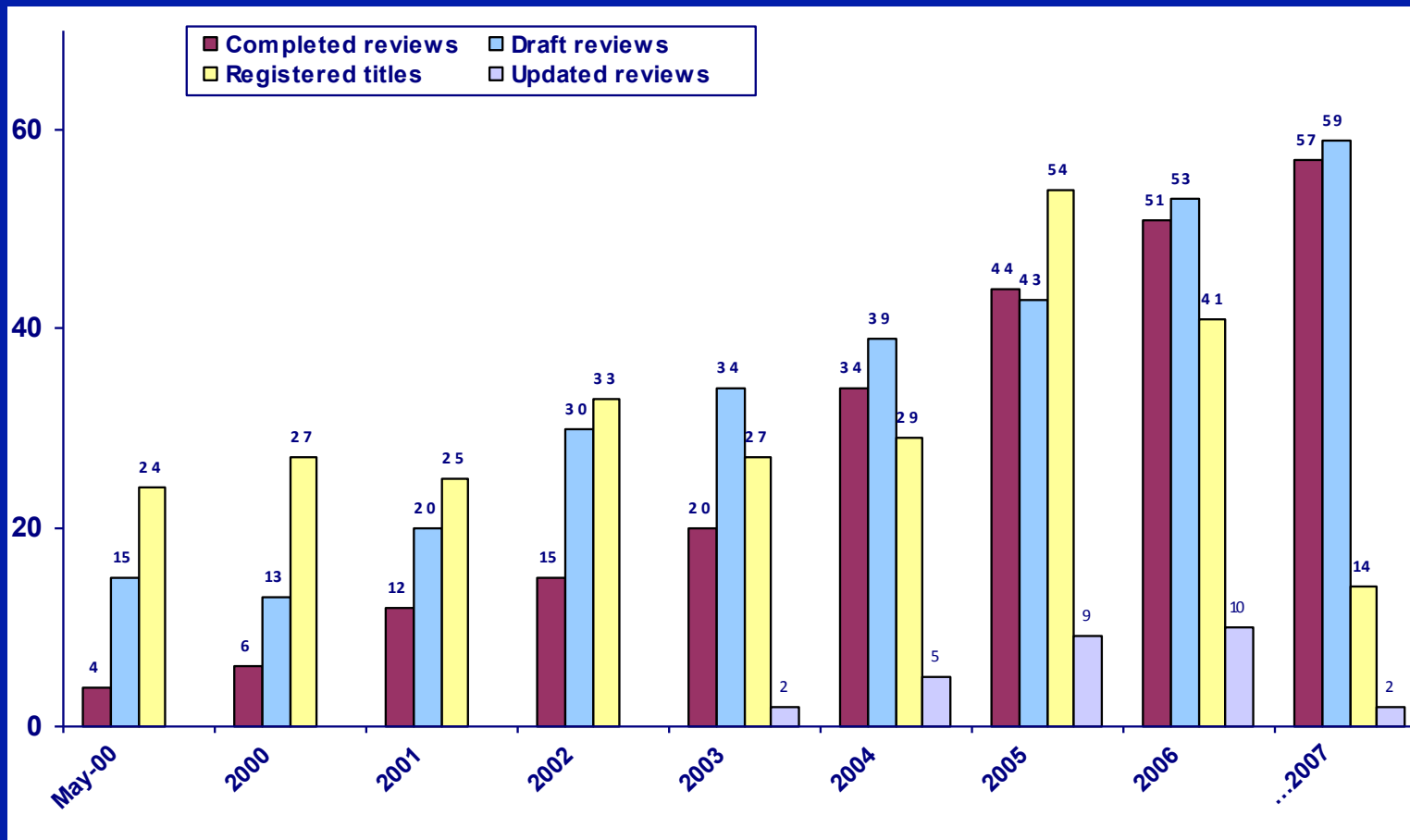


CRG

- Based in Sydney (since 2000)
- Core work
 - Producing and updating systematic reviews
 - All aspects of renal disease
 - Overlap with other review groups – endocrine, hypertension, PVD
 - Co-publication in medical journals
 - Renal trials registry
 - Trial registration (prospective)
 - Diagnostic test accuracy studies
 - Training and support

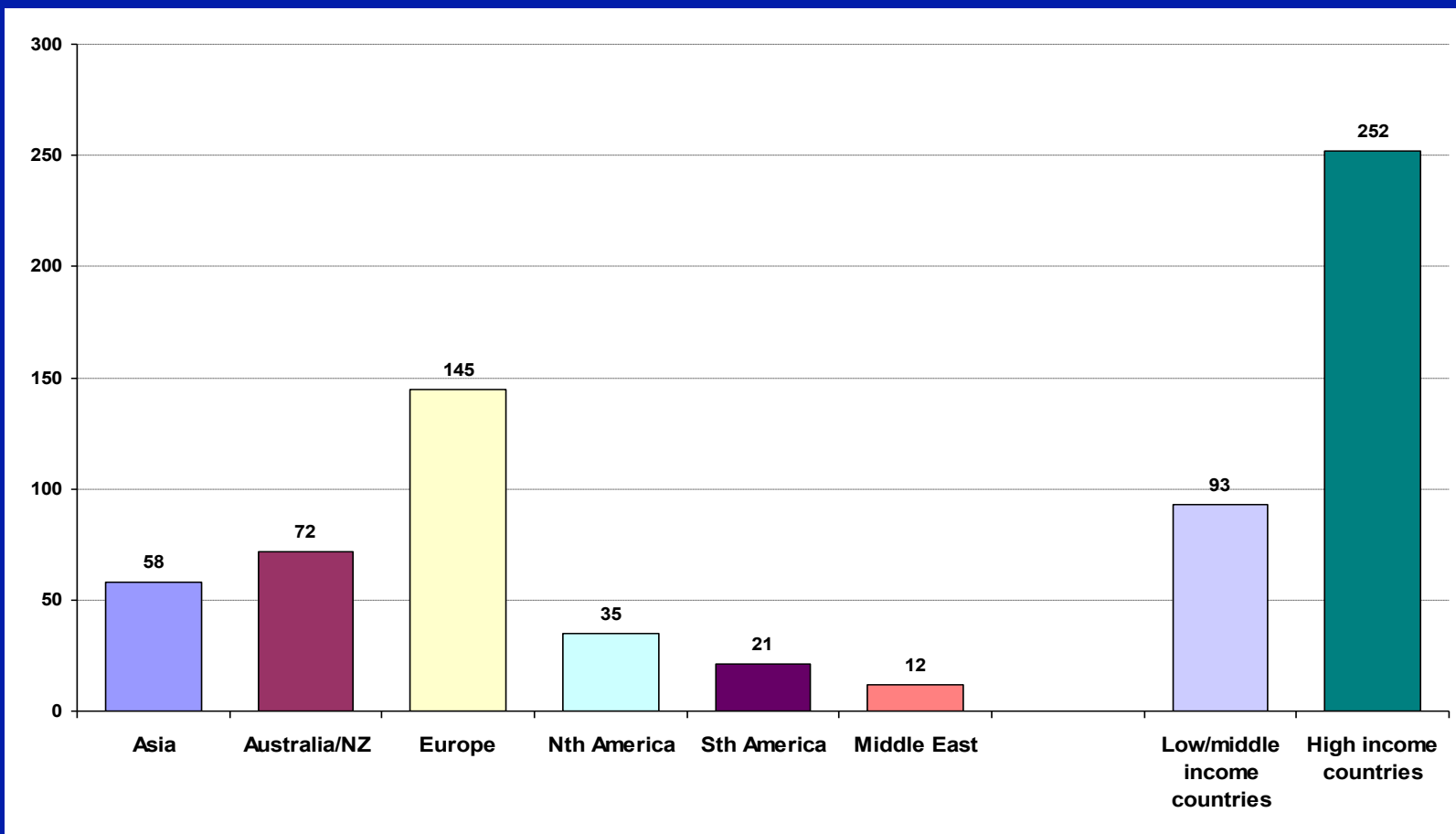


Producing and updating reviews





Review authors



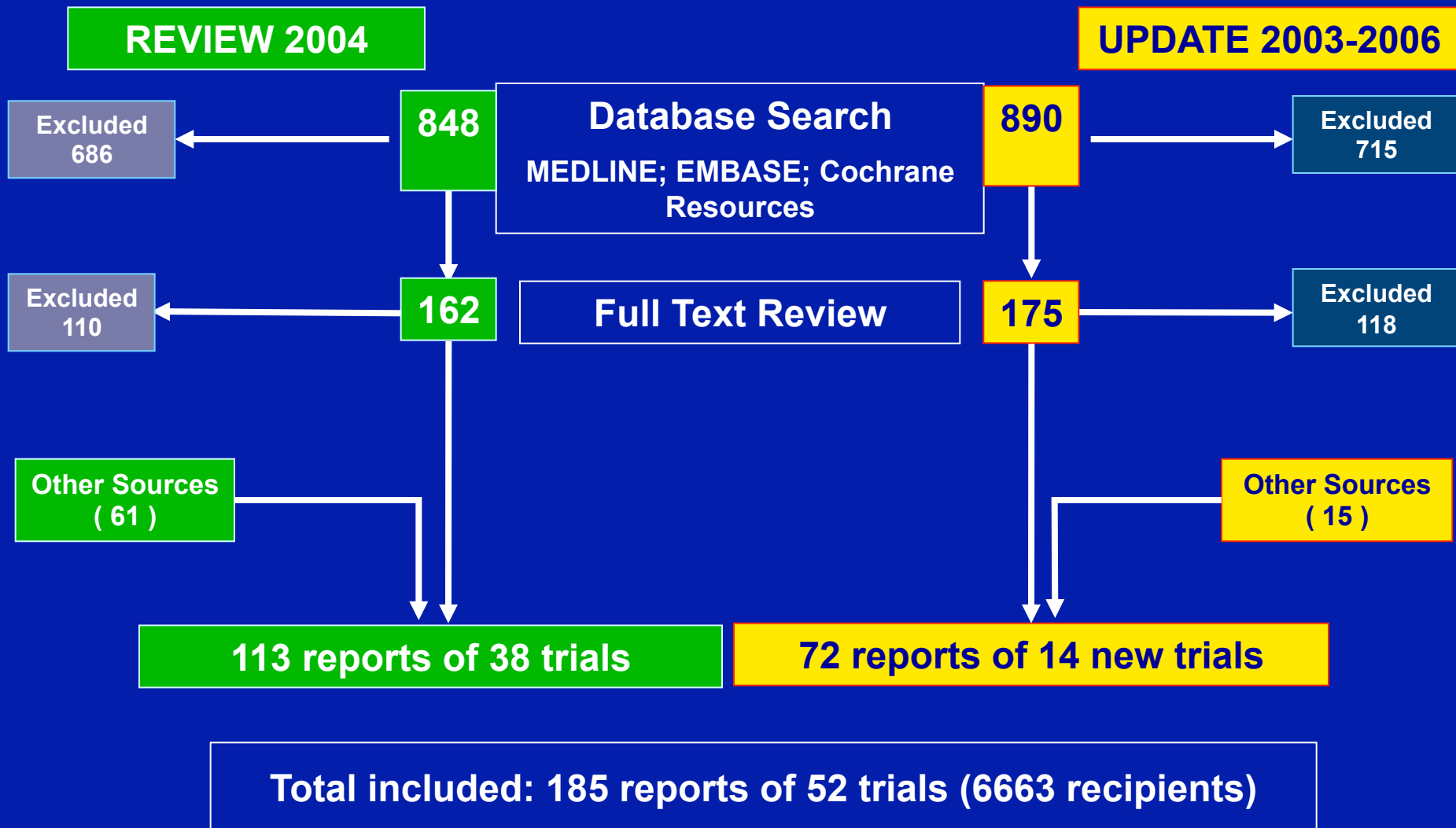


Updating reviews

- Reviews are often out of date after 2-3 years
- Updating is a unique feature of Cochrane reviews
- We ‘encourage’ our authors to update every 2 years
 - Regular re-runs of search strategy
 - Forwarding copies of new trial reports

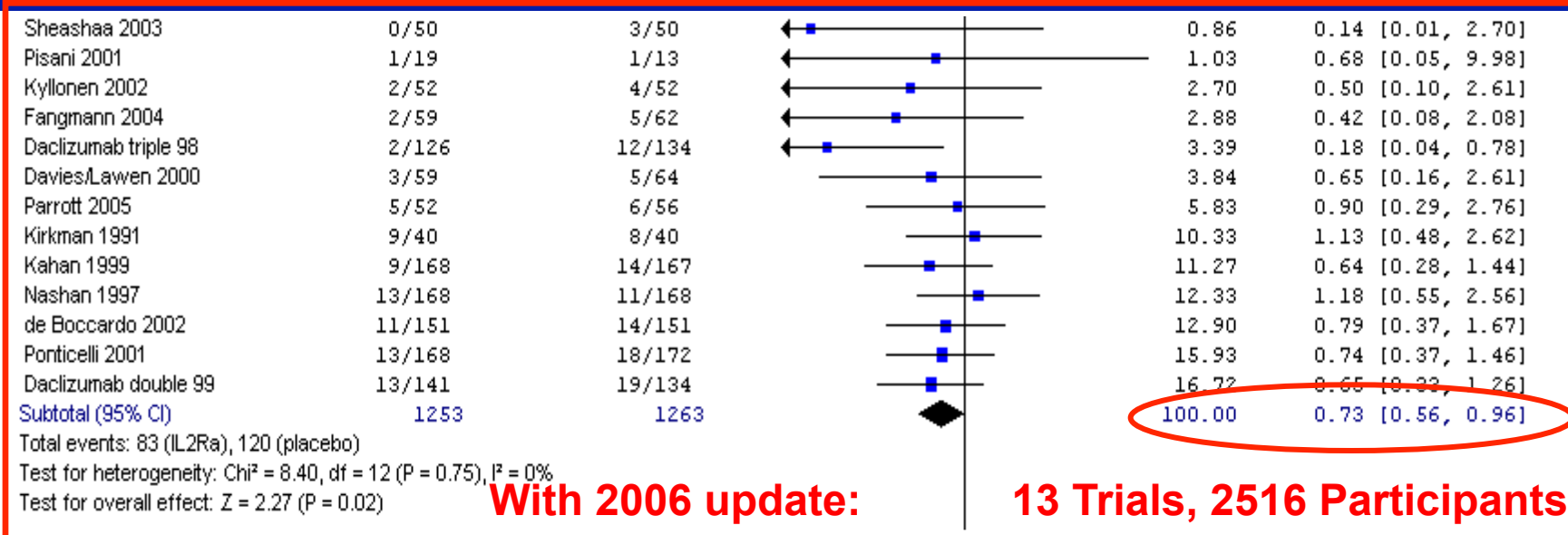
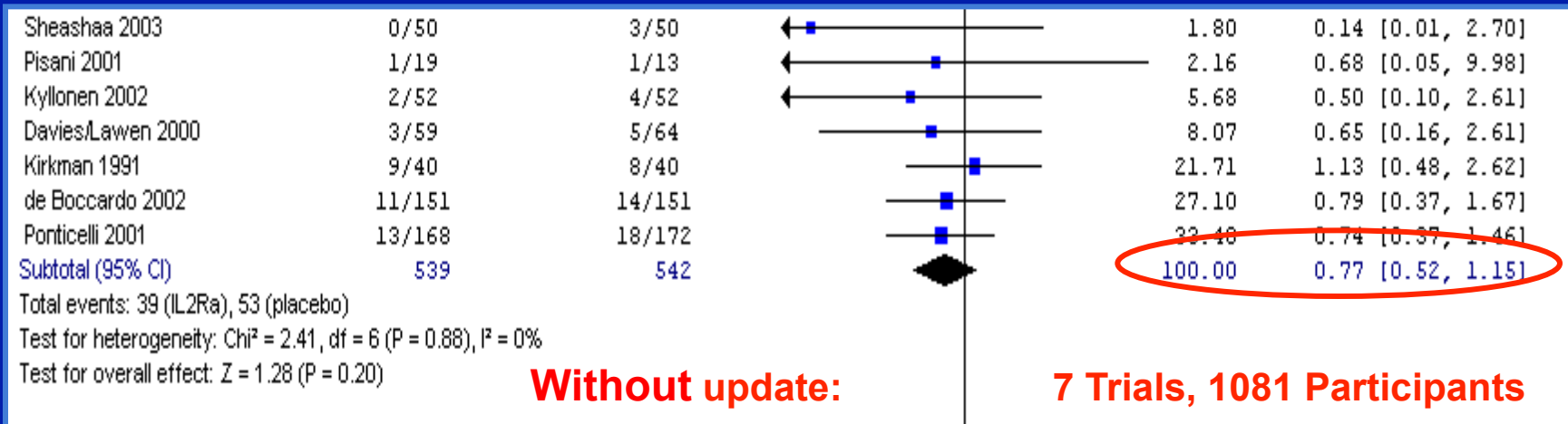


IL2Ra for kidney transplant recipients





Updating makes a difference...

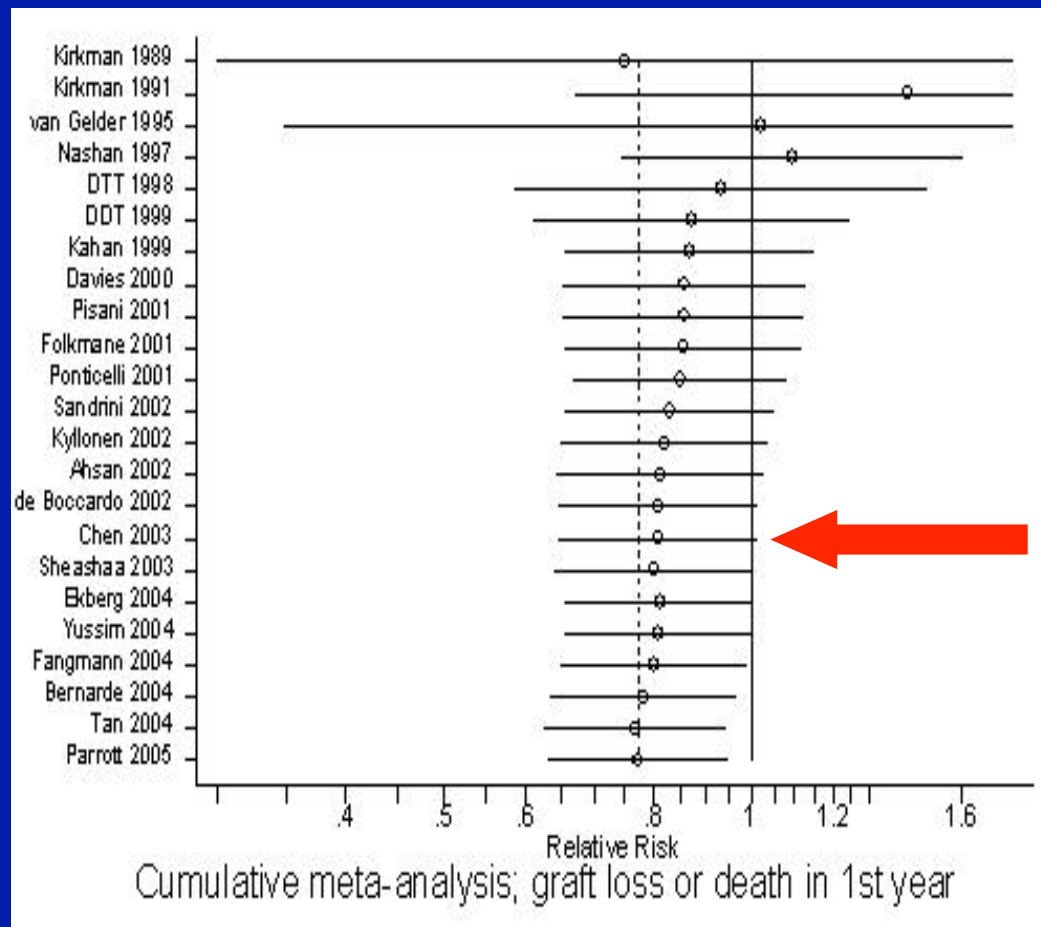


0.1 0.2 0.5 1 2 5 10
 Favours IL2Ra Favours placebo



Cumulative meta-analysis

- Evidence of reduction in graft loss since 2003
- 1047 persons have since been randomised



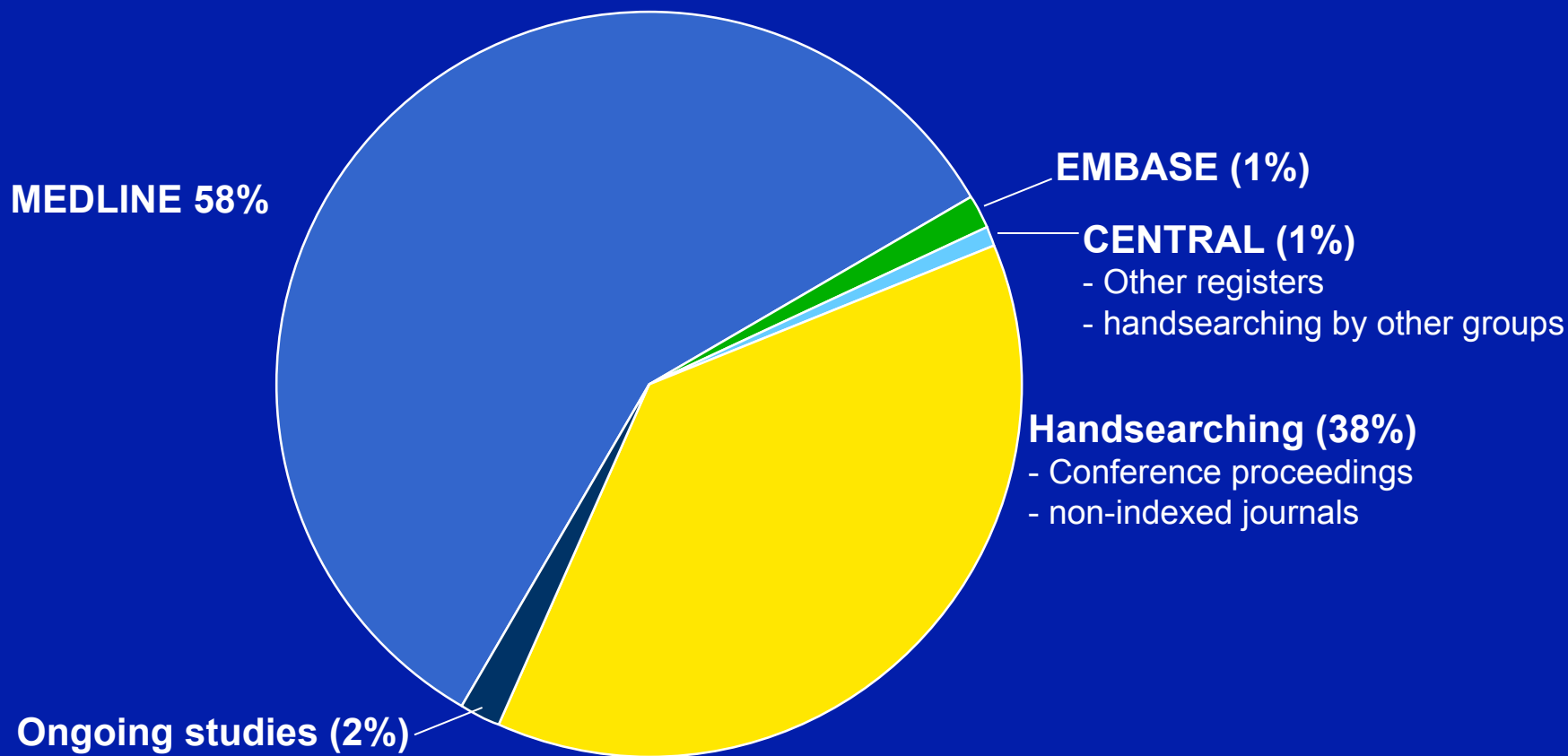


CRG

- Based in Sydney (since 2000)
- Core work
 - Producing and updating systematic reviews
 - Renal trials registry
 - Databases 1970
 - Hand-searching all major conferences 1980
 - Trial registration (prospective)
 - Diagnostic test accuracy studies
 - Training and support

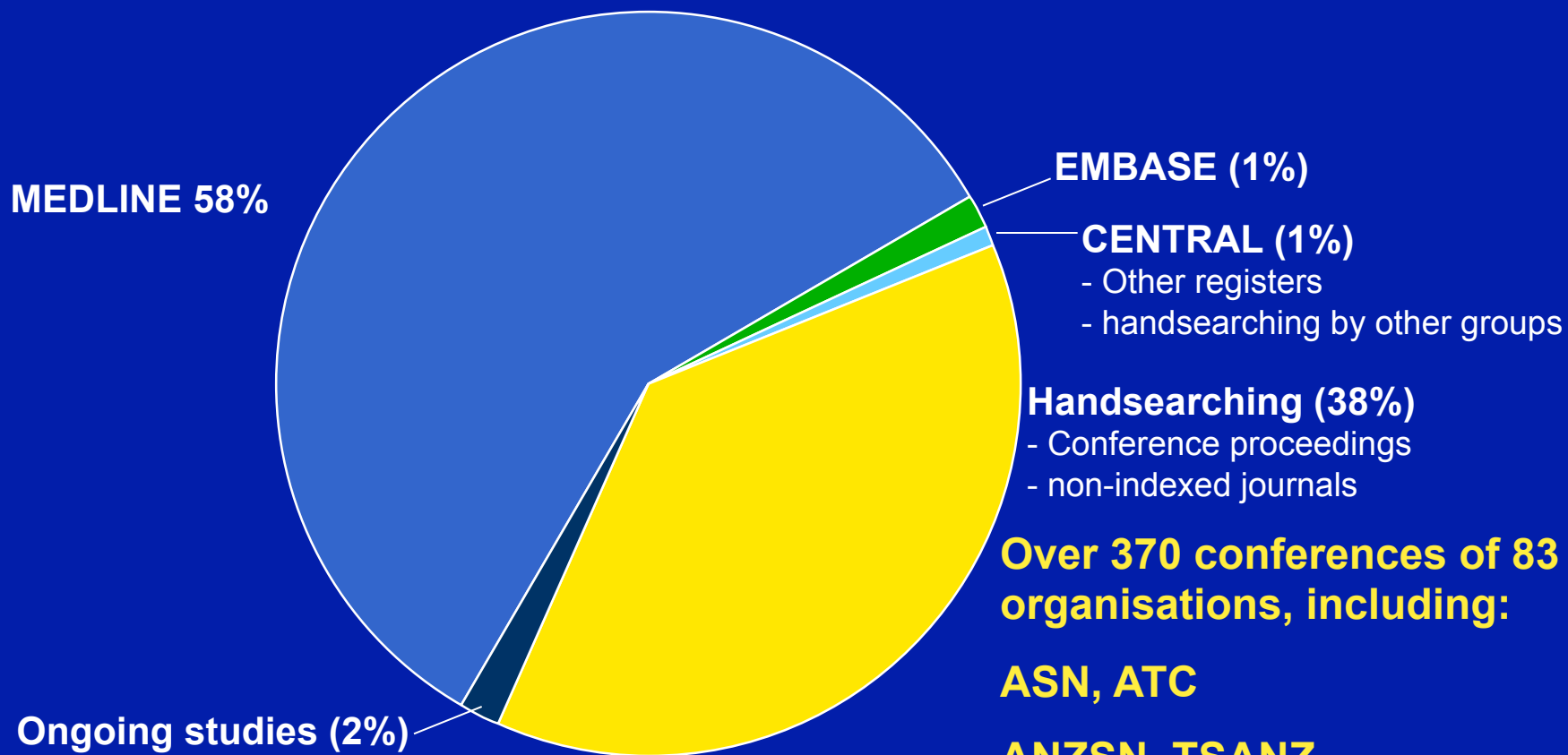


CRG Renal trials register





CRG Renal trials register



Over 370 conferences of 83 organisations, including:

ASN, ATC

ANZSN, TSANZ

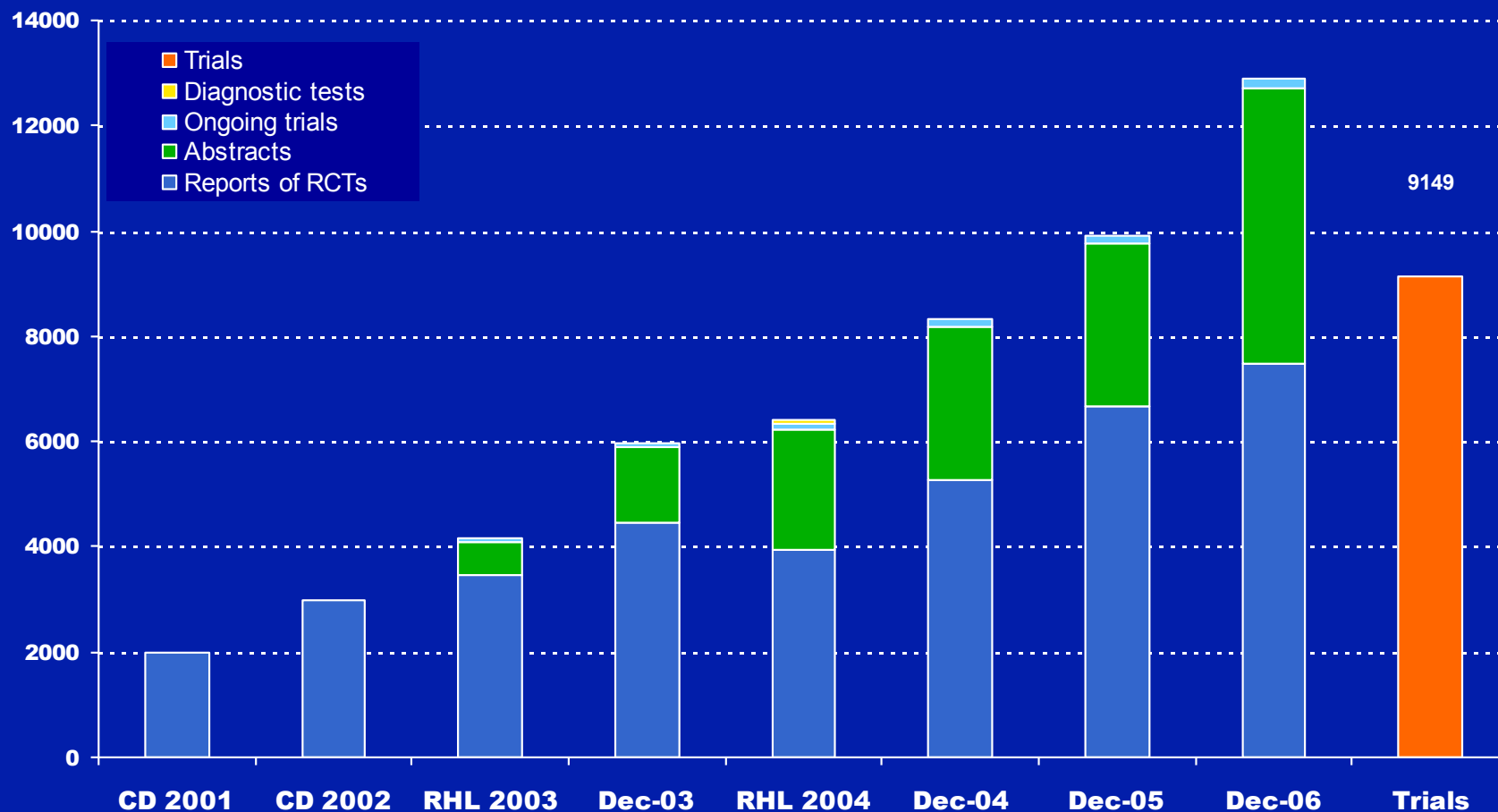
EDTA, ERA

ISN, WTC

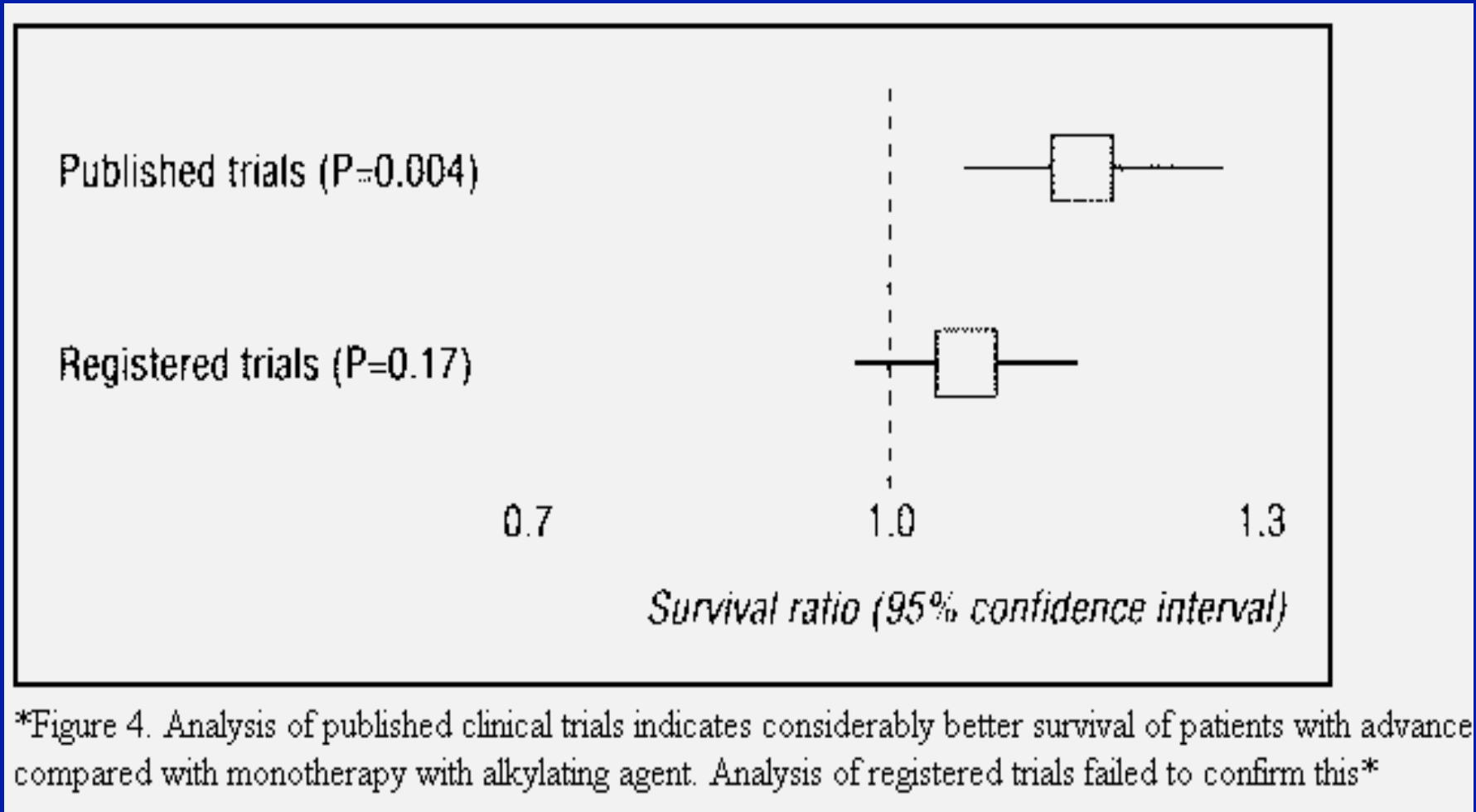
One off meetings - journals



Trials versus reports: a trial based register



Handsearching and publication bias





Impact of duplicate publication

Outcome	Relative risk (95% CI)	
	Trial based analysis	report based analysis
Acute rejection 6 months	0.66 (0.59,0.74)	0.65 (0.61, 0.70)
Graft loss 1 year	0.84 (0.66, 1.05)	0.69 (0.58, 0.83)

- **IL2 versus placebo/no treatment**
 - Falsely increased precision of estimate (acute rejection)
 - Falsely significant estimate of effect (graft loss)



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Prospective register of RCTs

- Established in July 2005
- data set requested complies with the fields described in WHO International Clinical Trials Registry Platform (ICTRP)
- unique registration number assigned after data completeness checked
- Currently 120 trials from 19 countries
 - topic areas include: peritoneal dialysis, diabetic nephropathy, glomerulonephritis and transplantation
 - Regular yearly contact with trialists



Fully searchable

Search

Field(s)

Query Examples	
blood and heart	finds records that contains ANY of these words (blood, and, heart)
"blood" and "heart"	finds records that contains BOTH these words (blood, heart)
"blood and heart" and "disease" not "plasma"	finds records that contains BOTH phrases ("blood and heart","disease") but not "plasma"

crg_id	titleoftrial	leadsurname	leadgivennames	
CRG050600001	A RANDOMIZED, CONTROLLED TRIAL OF STRAIGHT VERSUS COILED TENCKHOFF CATHETERS IN PERITONEAL DIALYSIS PATIENTS	Johnson	David Wayne	View >>
CRG050600002	A RANDOMIZED, CONTROLLED TRIAL OF FLUDROCORTISONE FOR THE TREATMENT OF HYPERKALAEMIA IN HAEMODIALYSIS PATIENTS	Johnson	David Wayne	View >>
CRG050600003	A randomised study comparing universal valacyclovir prophylaxis with quantitative PCR based preemptive therapy for cytomegalovirus (CMV) disease in renal transplant recipients.	Reischig	Tomas	View >>
CRG060500004	A randomised double blind, placebo controlled, cross-over study of the effect of amiloride over 6 weeks, on renal water handling in individuals with a bipolar or unipolar disorder, requiring lithium therapy?.	Walker	Robert	View >>

CRG040600073	Clinical benefits of icodextrin-based solutions in high-transporter, prevalent, diabetic patients in peritoneal dialysis: A randomized clinical trial	Paniagua	Ramon	View >>
ID PENDING	Influence on hemodynamics of conversion from Calcineurin Inhibitor to Sirolimus in Renal and Liver Transplant patients	Eisenberger	Ute	View >>



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Register of diagnostic test accuracy studies (DTAS)

- CRG a pilot group for DTAS reviews and for developing a DTAS trials register
- Trial identification not straight forward
 - development of database search strategies and (re-)handsearching
- 1% of published articles in KI, JASN and AJKD are DTAS (pilot study 2004)



Reviews of Diagnostic Test Accuracy Studies

Information about this initiative can be found on the Cochrane Collaboration's website at <http://www.cochrane.org/docs/diagnostictestreviews.htm>

New Register of Diagnostic Test Accuracy Studies

We have successfully submitted a proposal to the Cochrane Collaboration Steering Group for two-year funding to develop a Cochrane-wide study-based register of reports of diagnostic test accuracy.

This exciting initiative will ultimately lead to better support for authors and review groups doing Cochrane systematic reviews of diagnostic test accuracy, by providing a clean and comprehensive register of potential studies for their reviews.

Searching for diagnostic test accuracy studies is more difficult and time consuming than for reports of randomised controlled trials. This is due both to poor reporting by the authors of these studies, and inconsistent indexing in Medline and other databases, making it difficult to develop search strategies that are both sensitive and specific i.e. that will retrieve all relevant studies without too many irrelevant records.^{1,2,3} This adds an extra burden of time for systematic review authors, who often have to screen thousands of records to find a few relevant to their reviews.

Our objectives for the next two years include:

- setting up a database to house the register
- developing and implementing search strategies and protocols for retrieving relevant studies from Medline
- developing coding to enable accurate retrieval of studies from the register
- developing and implementing a training package for trials search coordinators in how to search for these studies on Medline and screen search results.
- providing support in search strategy development for the authors and trials search coordinators of pilot reviews



[\[Details\]](#)



Register your nephrology trial in accordance with the criteria recommended by the International Committee of Medical Editors and the WHO International Clinical Trials Registry Platform (ICTRP) Initiative

[\[Details\]](#)



New Reviews Cochrane Library Issue 3 July 2007

NEW Intermittent versus continuous renal replacement therapy for acute renal failure in adults
[\[Full text\]](#) [\[Subscription may be required\]](#)

15th Cochrane Colloquium Sao Paulo, Brasil 23-27 Oct 2007



Systematic Review Workshops

26-27 July 2007 OR 6-7 Dec 2007
Centre for Kidney Research
The Children's Hospital at Westmead
[\[Details\]](#)

Are you interested in writing a review?

Check our potential review titles or just contact us!

[Help us with our Renal Trials](#)



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Education and training

- 2-day systematic review workshops
 - How to write a review protocol
 - Plan and structure, search strategy design, rationale for inclusion and exclusion criteria, quality assessment
 - Introduction to analysis and meta-analysis
 - Data extraction, analysis and interpretation
- Finding the evidence
 - One day workshop on how to search the electronic databases
- Work shops with renal conferences
 - WTC 2008 critical appraisal of evidence
- Direct support for reviewers
 - Copies of trial reports
 - desk space
 - Occasional bursaries, undergraduate summer scholarships



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 - Diagnostic test accuracy studies and reviews
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 - Collaboration
 - Guidelines!
 - new RCTs in clinically relevant areas
 - improved explicitly reported RCTs



Guideline collaborations

- CARI guidelines
- EBPG guidelines
- KDIGO transplant
- Others in discussion.....

- ▼ About CARI
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- ▼ For Peer Reviewers
- ▼ For Consumers
- ▼ Annual Report
- ▼ Newsletters
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- ▼ SEARCH

CARI Guidelines

The CARI guidelines are now divided into three disease stages - Dialysis; Chronic Kidney Disease; and Transplantation. Each guideline comprises various subtopics and their recommendations.

The status of the different guidelines are outlined below:

Chronic Kidney Disease Guidelines	Status
Prevention of Progression of Kidney Disease	Published April 2006
Nutrition and Growth in Kidney Disease	Published Dec 2005
Cardiovascular Risk Factors	Published Dec 2005
Vitamin D, Calcimimetics and Phosphate Binders	Published April 2006
Urine Protein as Diagnostic Test	Published Oct 2004
Evaluation of Renal Function	Published Oct 2005
Kidney Stones	Published Feb 2007
Renal Vasculitis	Under development and for comment until 1 Oct 2007
Previous Guidelines	Archived

Dialysis Guidelines	Status
Acceptance onto Dialysis	Published Oct 2005
Biochemical and Haematological Targets	Published April 2006
Dialysis Adequacy	Published Oct 2005
Evidence for Peritonitis Treatment and Prophylaxis	Published Oct 2004
Vascular Access	Under development & for comment til 1 Oct 2007
Previous Guidelines	Archived

Transplantation Guidelines	Status
Deceased Kidney Donor Suitability	Published Oct 2005
CMV Disease and Kidney Transplantation	Published Oct 2004
Calcineurin Inhibitors in Renal Transplantation	Published Feb 2007
Living Kidney Donors	Under development and for comment til 1 Oct 2007
Previous Guidelines	Archived

**CRG
involved in
16 CARI
guidelines
between
2002 and
2006**





EBPG

- 2005 and presently in talks again
- 4 haemodialysis guidelines
 - Dialysis access
 - Nutrition
 - Dialysis strategies
 - Stability
- CRG registry searches
 - 1 guideline comprises up to 20 questions
 - Hard copy
- Diagnostic test search
- Cohort and observational searches



KDIGO transplantation

- All tx related systematic reviews
- all tx-related trial reports from CRG trial register
 - Hard/ electronic copy as required
- searches for diagnostic test accuracy
- PICO tables
 - Iterations
 - 49 questions for transplant
 - 7 questions for DTAS

PICO

2. Maintenance:

<u>Design etc</u>	<u>Population</u>	<u>Intervention/comparator</u>	<u>Outcomes of Interest</u>
Systematic Reviews (RCTs N ≥ 100)	KTX	Tac vs CSA (CsA or microemulsion) (with AZA, mmf, sirolimus, everolimus) CNI vs non-CNI regimens MMF vs AZA MMF formulation vs other MMF formulation CNI-sparing (withdrawal), CNI-free, Steroid withdrawal, Steroid avoidance	<ul style="list-style-type: none"> • Same as 1, except: • Fracture • HTN • Hyperuricemia • Quality of life • AE: Sirolimus: lipids

CVD RISK FACTOR

25, 26, 28, 30, 31 b. CVD Risk Factors Interventions

<u>Design etc</u>	<u>Population</u>	<u>Intervention/comparator</u>	<u>Outcomes of Interest</u>
RCT N ≥ 20 ≥ 6 mo	KTX, with CVD risk factor	Smoking cessation DM: Intensive vs standard HTN: ABPM vs Home BP Obesity: Weight loss Hcy: Vitamins	<ul style="list-style-type: none"> • Reduction in risk factor • Death • Graft survival • CVD

28Bc. Renal Artery Stenosis diagnosis

<u>Design etc</u>	<u>Population</u>	<u>Intervention/Comparator</u>	<u>Outcomes of Interest</u>
Cohort N ≥ 100(?)	KTX	Diagnostic test for RAS	Sn / Sp etc.

CRG delivered output

- Separate file of references by question
- excluding
 - pre-1985 trial reports
 - all conference proceedings abstracts
 - all Transplantation Proceedings reports
 - Trials <100 participants
- Not involved in searching for non RCT evidence



Developing guidelines...

Beware the Puddle of Doom!





Contribution of CRG to the guideline process

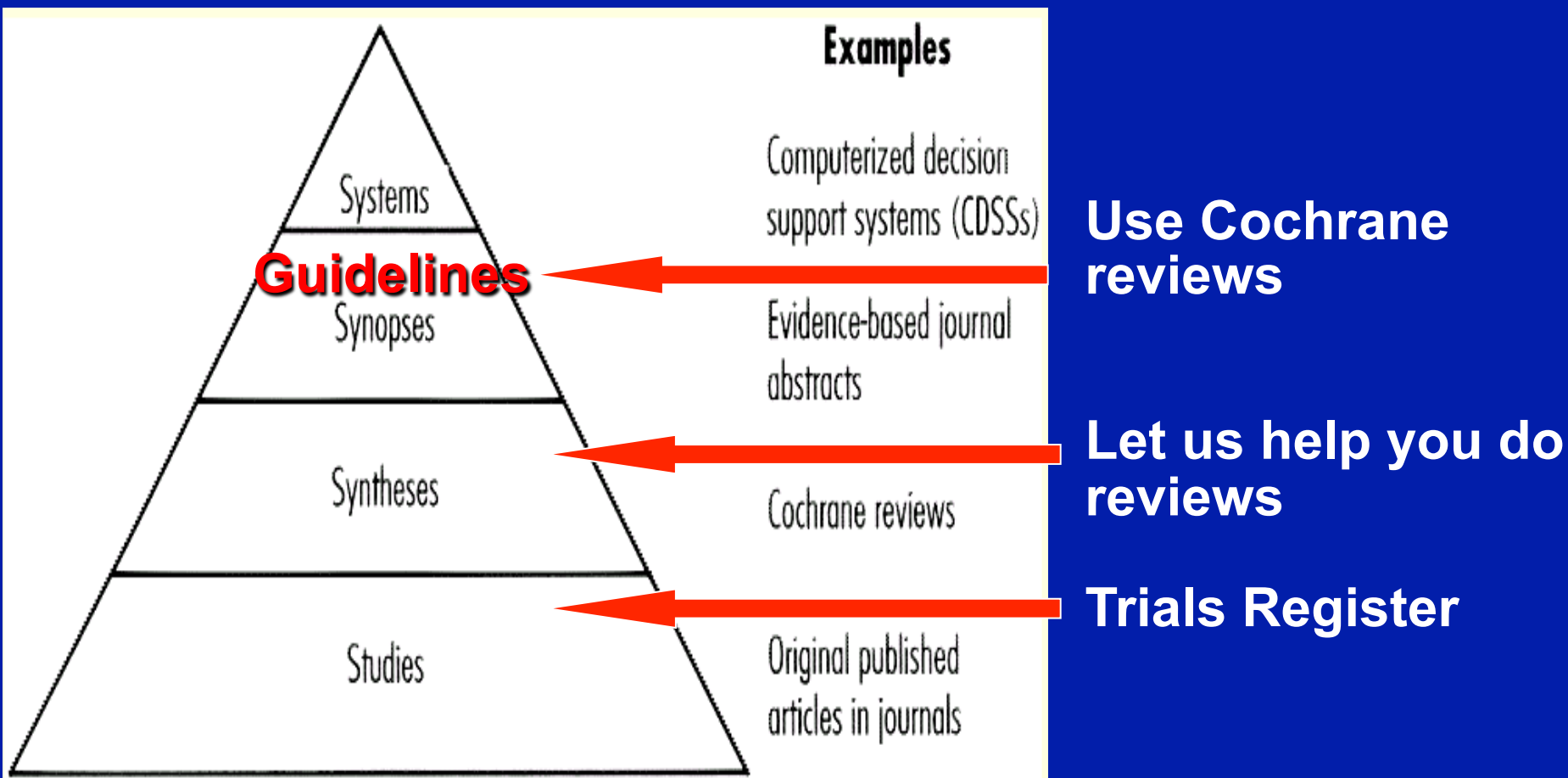


Figure. "4S" levels of organization of evidence from research.

From: Haynes: ACP J Club, Volume 134(2).March/April 2001.A-11-A-13

Future involvement?

- Minimise duplication of effort
 - CRG core work
- Maximise efficiency now and future guideline updates
 - Perform the systematic reviews that need doing in parallel to guideline development
 - Harness CRG training and support
- Add-ons
 - Searching for non-randomised studies
 - Potential for spin-off: methodology projects



Editorial team

- **Co-ordinating editor**
 - Jonathan Craig
- **Review group co-ordinator**
 - Narelle Willis
- **Trials search co-ordinators**
 - Gail Higgins
 - Ruth Mitchell
- **Administrative assistant**
 - Leslee Edwards
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 - Denis Fouque (Fra)
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