



XIII Riunione Annuale
Network Cochrane Italiano



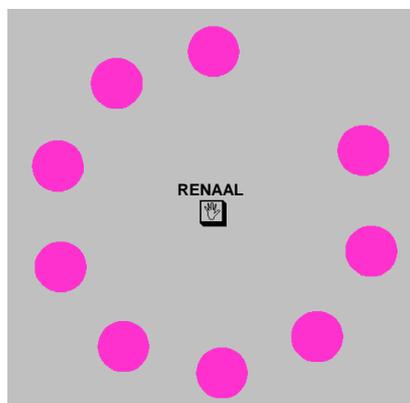
Le conoscenze e le innovazioni in medicina: il ruolo delle revisioni sistematiche

Opinioni a confronto:
I possibili utilizzi delle revisioni sistematiche
Punto di vista del ricercatore

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Punto di vista del ricercatore:

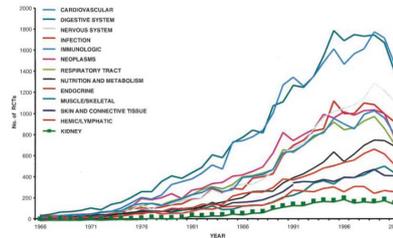
- look at the big picture
 - inform practice (see it from all/the right pov)
 - generate research hypotheses/about unmet need
- strippoli@negrisud.it



Possibili utilizzi: punto di vista del ricercatore

– Necessita' di sintesi

- Exp kidney diseases/
- Clinical trial.pt
- 1 and 2:
 - Un ricercatore nefrologo → 7465 trials
 - Questi numeri raddoppieranno in 20 anni



– Maggiore capacita' di rilevare gli effetti di interventi terapeutici

- Evitare ritardi nell'introduzione di interventi efficaci—prevenire il continuato utilizzo di interventi dannosi
 - Nei sogni del ricercatore—perche' spesso i tempi sono prolungati

- Generare idee di ricerca in aree di 'unmet need' vs 'la solita ricerca monotematica'
- Cleaning the scene (nella mia esperienza nefrologica)

Due esempi dell'esperienza di un ricercatore

1. ACEi o ARB o ACEi+ARB in pazienti con nefropatia diabetica?

Linee guida: le due classi sono equivalenti, meglio la combinata

2. Hb >11 g/dL o Hb 10-12 g/dL in soggetti con CKD?

Linee guida: >11, adesso 11-12 ma non >13, 10-12 (molta confusione)

Linee guida...

Table 6. Clinical Trial and Guideline Basis for Compelling Indications for Individual Drug Classes

High-Risk Conditions With Compelling Indication ^a	Recommended Drugs						Clinical Trial Basis ^b
	Diuretic	β-Blocker	ACE Inhibitor	ARB	CCB	Aldosterone Antagonist	
Heart failure	•	•	•	•	•	•	ACC/AHA Heart Failure Guideline, ⁴⁰ MERIT-HF, ⁴¹ COPERNICUS, ⁴² CIBIS, ⁴³ SOLVD, ⁴⁴ AIRE, ⁴⁵ TRACE, ⁴⁶ Val-HEFT, ⁴⁷ RALES ⁴⁸
Post-myocardial infarction		•	•			•	ACC/AHA Post-MI Guideline, ⁴⁹ BHAT, ⁵⁰ SAVE, ⁵¹ Capricorn, ⁵² EPHESUS ⁵³
High coronary disease risk	•	•	•		•		ALLHAT, ⁵⁴ HOPE, ⁵⁴ ANBP2, ⁵⁵ LIFE, ⁵² CONVINCE ⁵¹
Diabetes	•	•	•	•	•		NKF-ADA Guideline, ^{56,57} UKPDS, ⁵⁸ ALLHA
Chronic kidney disease			•	•			NKF Guideline, ⁵⁹ Captopril Trial, ⁶⁰ RENAAL, ⁶¹ IDNT, ⁶² REIN, ⁶³ AASK ⁶⁴
Recurrent stroke prevention	•		•				PROGRESS ⁶⁵

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; ACC/AHA, American College of Cardiology/American Heart Association; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; HOPE, Heart Protection Project; IDNT, Interventional Dialysis in Nephrotic Syndrome Trial; LIFE, Losartan Interventional Heart Failure Trial; MERIT-HF, Medical Research Trial in Heart Failure; RALES, Randomized Aldosterone Add-on Study; REIN, Randomized Evaluation of Nifedipine in the Treatment of Hypertension in African Americans; RENAAL, Randomized Evaluation of Nifedipine in the Treatment of Hypertension in African Americans; SAVE, Survival with ACE Inhibition in Heart Failure; TRACE, Treatment of Hypertension in the Prevention of Myocardial Infarction; UKPDS, United Kingdom Prospective Diabetes Study; Val-HEFT, Valerian Heart Failure Trial.

Table 1. Published guidelines on Hb targets in patients with CKD^a

Guidelines	Country	Year	Target Hb Level (g/L)
National Kidney Foundation-Dialysis Outcome Quality Initiative (NKF-DOQI)	United States	2000	110–120
British Renal Association (BRA)	United Kingdom	2002	≥100
Canadian Society of Nephrology (CSN)	Canada	1999	110–120
European Best Practice Guidelines (EBPG)	Europe	2004	>110 ^b
Health Care and Financing Administration (HCFA)	United States	2000	103–120
Caring for Australians with Renal Impairment (CARI)	Australia	2003	≤120 ^c 120–140 ^d

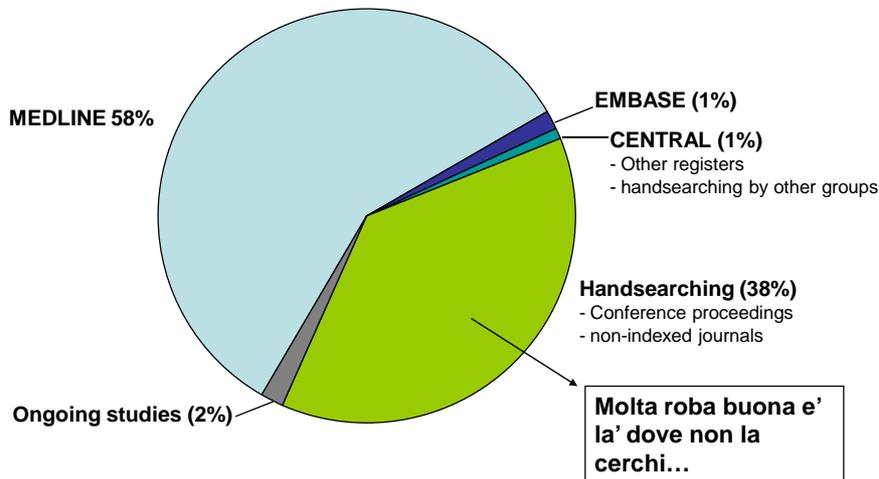
^a Hb, hemoglobin; CKD, chronic kidney disease.
^b Hb concentrations >120 g/L are not recommended for patients with severe cardiovascular disease unless continuing severe symptoms dictate otherwise.
^c In patients with proven or likely significant cardiovascular disease (level I evidence).
^d In patients without cardiovascular disease (suggestion for clinical care).

In merito a questi due quesiti, cosa leggono e conoscono quasi tutti...

- AHA in DN
 - Grandi trials (mixed causation HTN, inclusi diabetici)
 - Specific trials
 - RENAAL
 - IDNT
 - HOPE
 - COOPERATE
- Hb
 - Collins, registro US
 - Besarab, NHS
 - Choir (pre-dialisi)
 - Create (predialisy)
 - ...
 - E le linee guida

- Letture di pronta consegna

CRG trials register: tutto quel che ci sarebbe da leggere...



Perche' non lo leggiamo?

- Quel che citano tutti vs nessuno
- A volte evidenza in conflitto totale



NDT Advance Access published April 9, 2007

Nephrol Dial Transplant (2007) 22, 1111-1112
doi:10.1093/ndt/gfm055

Editorial Comment

Anaemia of CKD—the CHOIR study revisited¹

Ajay K Singh¹, Lynda Szecsei², Kathleen L Tang³, Huijuan Barakatt⁴, Shelly Supp⁵,
Martha Wolfson⁶ and Donald Rossini^{6*}

NDT
Nephrology Dialysis Transplantation

THE NEW ENGLAND JOURNAL OF MEDICINE

EDITORIALS



Haemoglobin targets: we were wrong, time to move on

See also page 20. Anaemia occurs in nearly all patients with moderate- to-severe chronic kidney disease. The most widely used treatment option are erythropoiesis-stimulating agents (eg, Epoetin, Pooetin, and Aranesp), with an economic burden of US\$10 billion in sales worldwide in 2006, and 12 billion Medicare expenditure for dialysis patients in 2006 in the USA alone. Administration of erythropoietin rapidly increases haemoglobin

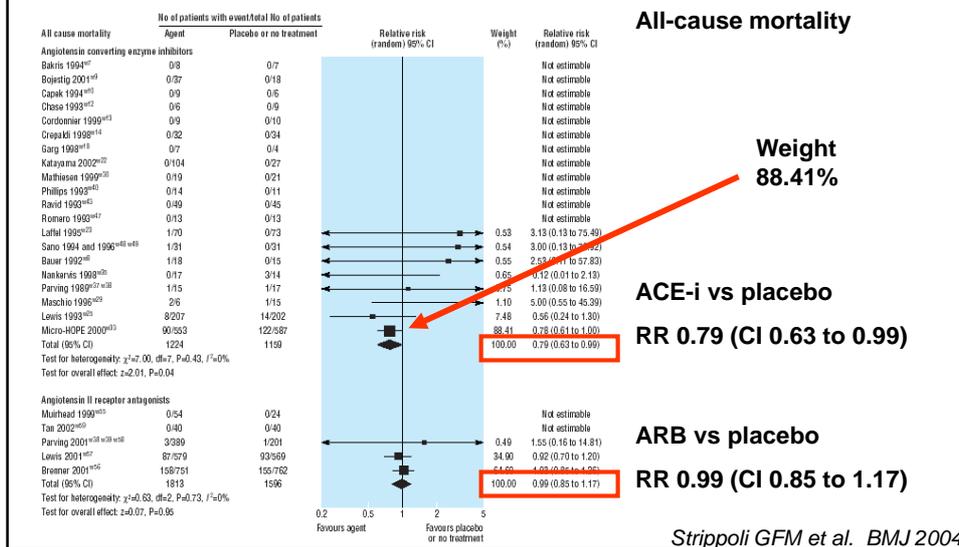
Correction of Anemia — Payoffs and Problems

Giuseppe Remuzzi, M.D., and Julie R. Ingelfinger, M.D.

- Per il ricercatore, un modo adeguato per leggere—capire il problema
- Un supporto per ricerca indipendente in presenza di un 'occultamento'

ACE o ARB: equivalenti in DN?

-trial comparativo inesistente-



Strippoli GFM et al. BMJ 2004

Hb target >11 o 10-12?

- (N=5000), oltre 12 il rischio CV aumenta del 20%--problema di DOSE?

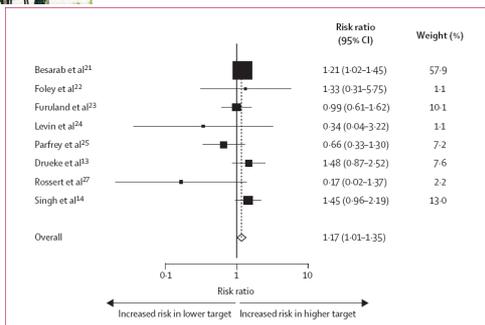


Figure 2: Risk of all-cause mortality in the higher haemoglobin target group compared with the lower haemoglobin target group (fixed effects analysis)
The Roger et al¹⁶ is not reported because there were no deaths in either group.

Phrommintikul A, Lancet 2007



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Nephrol Dial Transplant (2007) 22, 309-312

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Editorial Comment

Anaemia of CKD—the CHOIR study revisited¹

Ajay K Singh¹, Lynda Secrest², Kerhen I Tang³, Huiyan Rinkhart⁴, Shelly Supp², Marsha Wolfson¹ and Donald Reddan^{1,2}

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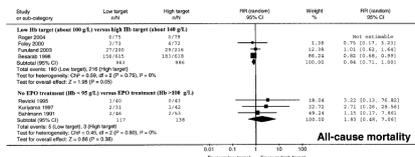
Editorial Comment

Understanding recent haemoglobin trials in CKD: methods and lesson learned from CREATE and CHOIR

Adheera Levin

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Strippoli GFM, JASN 2004



In 'essence'

1. without EBM we are helpless in the face of

- misguided experts
- overenthusiastic experts
 - Improper designs
- drug company hype

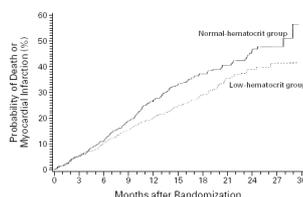
Kidney International, Vol. 63 (2002), pp. 207-204

HMG-CoA reductase inhibitors are associated with reduced mortality in ESRD patients

STEPHEN L. SELIGER, NOEL S. WEISS, DANIEL L. GILLEN, BRYAN KESSEBAUM, ADRIANNE BALL, DONALD J. SHERRARD, and CATHERINE O. STEINMAN-BREEN

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Besarab A, NEJM 1989



Con la revisione sistematica il ricercatore fa il punto dei quesiti attivi e di quelli risolti, ed individua aree tematiche di ricerca.

La revisione sistematica supporta la necessita' di finanziamenti per ricerca indipendente in area di unmet need.



Mortality and target haemoglobin concentrations in anaemic patients with chronic kidney disease treated with erythropoietin: a meta-analysis

Haemoglobin targets: we were wrong, time to move on

Article

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