# The story continues: the forgotten half of Cochrane's Random Reflections in Bentham's path

Gabriel M Leung

June 14, 2013

Inaugural Victorian Psycho-oncology Research Conference Melbourne, Australia





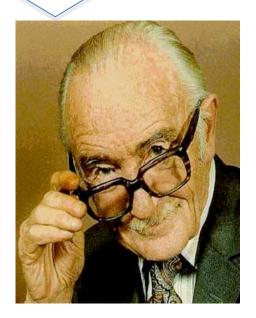
JOINT MEETING OF
IPOS 14<sup>th</sup> World Congress and
COSA's 39<sup>th</sup> Annual Scientific Meeting
Brisbane Convention and Exhibition Centre

13th - 15th November 2012

"It must be remembered that there is nothing more difficult to plan, more doubtful of success, nor more dangerous to manage than a new system. For the initiator has the enmity of all who would profit by the preservation of the old institution and merely lukewarm defenders in those who gain by the new ones."

"What I decided I could not continue doing was making decisions about intervening when I had not idea whether I was doing more harm than good." c1972

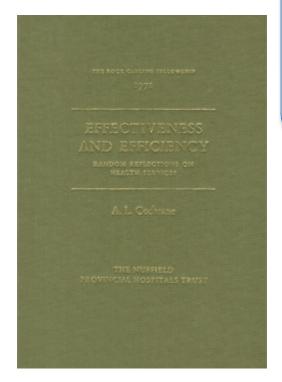






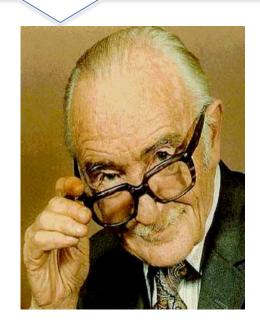
# The Cochrane Collaboration

Working together to provide the best evidence for health care



c1971

"It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials" c1979





# Screening mammography: Does it work?

#### Screening for breast cancer with mammography (Review)

#### Gøtzsche PC, Nielsen M



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 4

http://www.thecochranelibrary.com

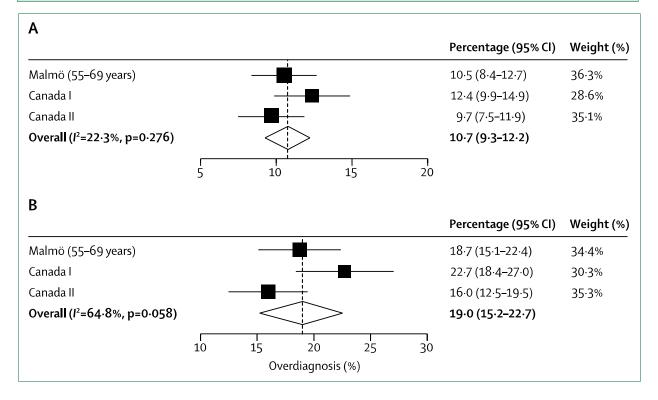


reening n/N	Study or subgroup	No screening n/N	Risk Ratio M-H Fixed,95% Cl	Weight	Risk Ratio M-H,Fixed,95% Cl
	1 Adequately randomised tria				<u> </u>
5/25214	Canada 1980a	108/25216	-	86 %	0.97 [ 0.74, 1.27 ]
7/19711	Canada 1980b	105/19694	+	83 %	1.02 [ 0.78, 1.33 ]
7/20695	Malm 1976	108/20783	-	85 %	0.81 [ 0.61, 1.07 ]
5/53884	UKage trial 1991	251/106956	-	133 %	0.83 [ 0.66, 1.04 ]
19504	Subtotal (95% CI)	172649	•	38.7 %	0.90 [ 0.79, 1.02 ]
o sareenir	Total events: 404 (Screening),	)			
= 0.54);	Heterogeneity: Chi <sup>2</sup> = 2.16, a	=0.0%			
0.10)	Test for overall effect: Z = 1.6				
	2 Suboptimally randomiæd tr				
8/21650	Gteborg 1982	162/29961	-	10.8 %	0.75 [ 0.58, 0.97 ]
6/38589	Kopparberg 1977	104/18582		11.1 %	0.58 [ 0.45, 0.76 ]
3/31000	New York 1963	262/31000	-	20.7 %	0.83 [ 0.70, 1.00 ]
6/40318	Stockholm 1981	45/19943		48 %	0.73 [ 0.50, 1.06 ]
5/38491	stergtland 1978	173/37403	-	139 %	0.76 [ 0.61, 0.95 ]
70048	Subtotal (95% CI)	136889	•	61.3 %	0.75 [ 0.67, 0.83 ]
o screenii	Total events 633 (Screening),	ı			
°= 029);	Heterogeneity: Chi <sup>2</sup> = 4.94, c	= 19%			
0.00001)	Test for overall effect: $Z = 5.3$				
89552	Total (95% CI)	309538	•	100.0 %	0.81 [ 0.74, 0.87 ]
No scree	Total events 1037 (Screening	ng)			
P= 0.16)	Heterogeneity: Chi <sup>2</sup> = 11.82,	! =32%			
0.00001)	Test for overall effect: $Z = 5.1$				
			02 05 1 2 5		

	A	В	С	D
Malmö I ages 55–69 years	11.7% (82/698)	10.5% (82/780)	18.7% (82/438)	29.1% (82/282)
Canada I	14·1% (82/581)	12.4% (82/663)	22.7% (82/361)	29.4% (82/279)
Canada <b>II</b>	10.7% (67/626)	9.7% (67/693)	16.0% (67/420)	19.8% (67/338)

Numbers of excess cancers are expressed as a percentage of different denominators. A=excess cancers as a proportion of cancers diagnosed over whole follow-up period in unscreened women. B=excess cancers as a proportion of cancers diagnosed over whole follow-up period in women invited for screening. C=excess cancers as a proportion of cancers diagnosed during screening period in women invited for screening. D=excess cancers as a proportion of cancers detected by screening in women invited for screening.

Table 4: Estimates of overdiagnosis in randomised trials without systematic end-of-trial screening of the control group, according to four calculation methods



- CRUK review (Marmot et al *Lancet* 2012) confirmed 20% RRR for screening in 50-79yos
- Affirms likely presence of overdiagnosis (see L panels)
- "the Panel estimates that for 10,000 UK women invited to screening from age 50 for 20 years, about 681 cancers will be found of which 129 will represent overdiagnosis, and 43 deaths from breast cancer will be prevented. In round terms, therefore, for each breast cancer death prevented about three overdiagnosed cases will be identified and treated."

# Routine health checks: Does it work?

#### General health checks in adults for reducing morbidity and mortality from disease (Review)

Krogsbøll LT, Jørgensen KJ, Grønhøj Larsen C, Gøtzsche PC



Thisis areprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library*. 2013, I saue 1 http://www.thecochranelibrary.com



Outcomes	(		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk with intervention				
<b>Total mortality</b> Deaths Follow-up: 4-22 years	75 per 1000	<b>74 per 1000</b> (71 to 77)	<b>RR 0.99</b> (0.95 to 1.03)	155,899 (9 studies)	nigh	
Cardiovascular mortal- ity Deaths from cardiovas- cular causes Follow-up: 4-22 years		Control	<b>RR 1.03</b> (0.91 to 1.17)	152,435 (8 studies)	□□□⊖ moderate	There was substantia heterogeneity which ma
	37 per 1000	<b>38 per 1000</b> (34 to 43)				reflect the different out- come definitions used in the trials
Cancer mortality Cancer deaths Follow-up: 4-22 years			RR 1.01	139,290	0000	
	21 per 1000	<b>21 per 1000</b> (19 to 24)	(0.92 to 1.12)	(8 studies)	high	



#### **NHS Health Check**

Helping you prevent heart disease, stroke, diabetes and kidney disease

#### Response to the Cochrane Review

#### Front Page

#### NHS Health Check - Response to the Cochrane Review

This eBulletin is produced by NHS Diabetes and Kidney Care in conjunction with the Department of Health to support the NHS Health Check Learning Network. This is a useful tool for anyone working in health or social care with an interest in the prevention of vascular disease and vascular risk assessment and management. To subscribe or unsubscribe, please contact Eleanor Kent-Dyson.

In response to demand from NHS Health Check commissioners, we have put together a further assessment of the Cochrane review published on 17<sup>th</sup> October 2012.

The Cochrane review is a systematic review of the published literature on randomised trials of general health checks. The principal end point reviewed was mortality, for which nine trials provided evidence. A metanalysis of these trials showed no difference in deaths overall, or from cardiovascular disease or cancer, between intervention and control groups.

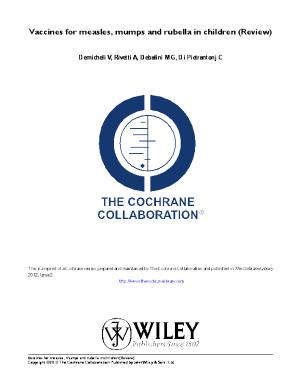
The review also comments on comparisons of morbidity between intervention and control groups, although this was not the primary intention of the review and no meta-analysis was possible. Some trials showed differences, but the review authors did not consider these useful, partly as a result of the poor quality of the evidence in many individual trials.

There are some major difficulties in interpreting the results of this review:

(a) There was no specification of what constitutes a 'general health check', its content or its objectives. It is clear that there was significant heterogeneity between different trials. Some interventions included relevant measures such as blood pressure and cholesterol, but not all. In keeping with the 'general health check' terminology, most were not well focused on specific enquiries and tests but included non-specific searches for any abnormal finding including those suggestive of cancer.

- NHS Health Check programme quickly posted an online rebuttal of the Cochrane review
- The Cochrane authors sought to post a counterpoint defending their original SR on the same NHS website, but was denied
- Currently the authors are attempting to publish the scientific and process content of the whole saga in a general medical journal for wider dissemination

## MMR and autism: is it real?



1.2 to 4.7). Exposure to the Minik vaccine was unlikely to be associated with autism, astrima, leukaemia, hay rever, type i diabetes pat disturbance. Crohn's disease, demyelinating diseases, bacterial or viral infections.

#### Authors condusions

In e design and reporting or sarety outcomes in IVIVIE vaccine studies, both pre-and post-marketing, are largely inadequate. The svidence of adverse events following immunisation with the MMR vaccine cannot be separated from its role in preventing the target diseases.

#### Early report

## Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

#### Summary

**Background** We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associate by the parents, with measles, mumps, and rub vaccination in eight of the 12 children, with measi infection in one child, and otitis media in ar All 1 children had intestinal abnormalities angin from lymphoid nodular hyperplasia to a noid ul ration. Histology showed patchy chronic inflam. perplasia in in 11 children and reactive ilea mpho seven, but no granulomas. Be floural disor s included autism (nine), disintegrative systems (one), an possible postviral or vaccinal encephalitis o). There were no focal neurological abamalities and and EEG tests were normal. Abnormal laboratory results are significantly raised urinary thylmal c acid compared with ageo=≤03), low haemoglobin in four matched control low s m IgA in ar children. children, a

Interpretation e identification de associated gastrointestinal discrete and evelopmental regression in a group of previously a marconical, which was generally associated in time to possible environmental triggers.

Lancet 1998 **251:** 637–41 See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield Frecs, A Anthony MB, J Linnell Pnol, A P Dhillion Merceath, S E Davies MacPath) and the University Departments of Paediatric Gastroenterology (S H Murch MB, D M Casson MBCP, M Malik MBCP, M A Thomson Frecy, J A Walker-Smith Frech), Child and Adolescent Psychiatry (M Berelowitz FRCPsych), Neurology (P Harvey FRCP), and Radiology (A Valentine Frech), Royal Free Hospital and School of Medicine, London NW3 2QG, UK

Correspondence to: Dr A J Wakefield

#### Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal amptoms, alluding abdominal pain, diarrhoea, and cating and, it some cases, food intolerance. We distribe as clinical futings, and gastrointestinal feature of these charges.

#### Patients and metings

12 children, constrained, a cred to to department of paediatric gastro derology to a highly of a pervasive developmental order with loss traces ed skills and intestinal symptoms of arriting abdominal rain, bloating and food intolerance), were investigated. All children were admitted to the ward for threek, accomplicated by their parents.

#### fical investigations

took histori including details of immunisations and en sure to infect as diseases, and assessed the children. In 11 case the history as obtained by the senior clinician (JW-S). Neure, to load psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria. Developmental is included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

#### Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously. Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample t test. Urinary creatinine was estimated by routine spectrophotometric

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done The INDEPENDENT





## MMR scare doctor breaks his silence: Measles outbreak in Wales proves I was right



Discredited doctor who triggered the MMR scare 15 years ago has pinned the blame for the outbreak of measles in Wales on the Government as cases in the Swansea area rises

Timeline: How the MMR scare story spread

Full statement by Dr Andrew Wakefield: "The Government has tried to cover up putting price before children's health"

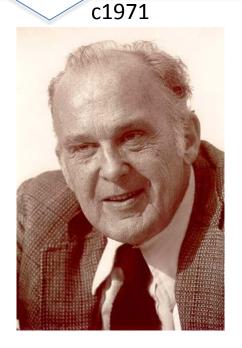
Andrew Wakefield's baleful legacy

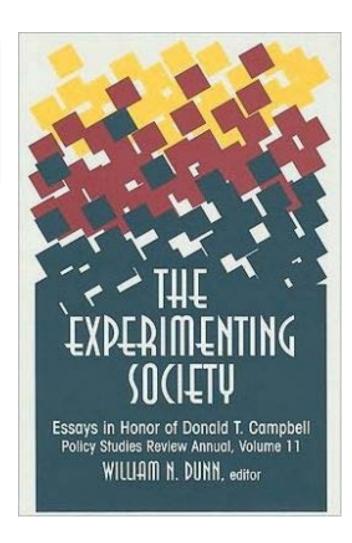


# THE CAMPBELL COLLABORATION

What helps? What harms? Based on what evidence?

"...the experimenting society is a process utopia...it seeks to implement that recommendation of Popper's, 'a social technology is needed whose results can be tested by piecemeal social engineering."





Exploratory meeting in 1999 @





# Going beyond "Does it work?" Buying in the bizarre health care bazaar...



"I believe that cure is rare while the need for care is widespread, and that the pursuit of cure at all costs may restrict the supply of care..."

Archie Cochrane, 1972



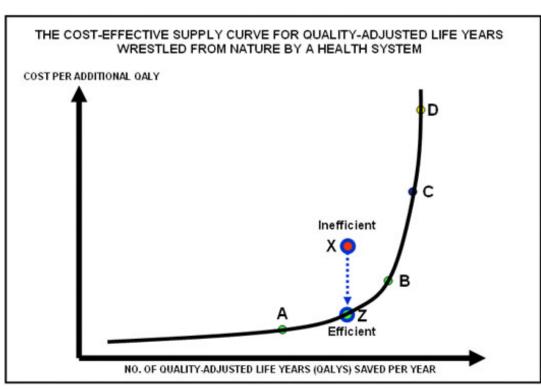
# The theory goes...

#### The Principle of Utility



- Recognizes the fundamental role of Pain and Pleasure in human life.
- 2. Approves or disapproves of an action on the basis of the amount of pain or pleasure brought about ("consequences").
- 3. Equates the good with the pleasurable and evil with pain.
- 4. Asserts that pleasure and pain are capable of "quantification"-- and hence of measure.

Source: www.williamette.edu



Source: Uwe Reinhardt @ NYTimes Economix blog

# Reality check...

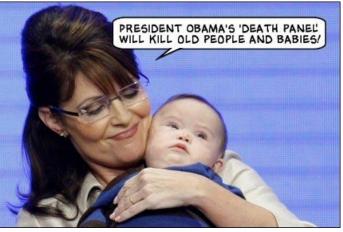












The New Hork Times

#### **Economix**

Explaining the Science of Everyday Life

MARCH 13, 2009, 6:45 AM

'Cost-Effectiveness Analysis' and U.S. Health Care

By UWE E. REINHARDT



THE WALL STREET JOURNAL.





#### Life or death rations

ADAM CRESSWELL, HEALTH EDITOR THE AUSTRALIAN SEPTEMBER 26, 2009 12:00AM

THE grape-sized lump Bronwyn Wells first felt in her left breast was so big, she thought it had to be a cyst because she "couldn't believe a cancer could get that big that quickly". Knowing her scans had been clear eight months earlier and feeling no great sense of urgency, Wells, then aged 41, waited three weeks before she saw her GP. The doctor agreed: probably a cyst. But she referred her to a breast clinic, where the news darkened.



January 16, 2012

# Ontario sets out to change the way doctors work

American exceptionalism?

Upcoming contract talks with the Ontario Medical Association will be about more than wage rerstraint

#### **RATIONING CARE**

Doctors have traditionally had a great deal of discretion in administering care. That's led to a belief among people in and around government that prescriptions or referrals are sometimes offered more to keep patients happy than out of medical necessity – and that setting tighter guidelines for when to write them could save large sums of money.



Rationing of treatment has increased in the NHS and GPs are now forced to apply for funding for IVF treatment, obesity surgery, and for drugs to stop people going blind, a report claims.

# Has rationality prevailed with professionals?

#### Basis of clinical practice

Basis for clinical decisions	Marker	Measuring device	Unit of measurement	
Evidence	Randomised controlled trial	Meta-analysis	Odds ratio	
Eminence	Radiance of white hair	Luminometer	Optical density	
Vehemence	Level of stridency	Audiometer	Decibels	
Eloquence (or elegance)	Smoothness of tongue or nap of suit	Teflometer	Adhesin score	
Providence	Level of religious fervour	Sextant to measure angle of genuflection	International units of piety	
Diffidence	Level of gloom	Nihilometer	Sighs	
Nervousness	Litigation phobia level	Every conceivable test	Bank balance	
Confidence*	Bravado	Sweat test	No sweat	

<sup>\*</sup>Applies only to surgeons.

Source: Isaacs & Fitzgerald BMJ 1999

# Societal values-driven behaviour → Egosyntonic resolution



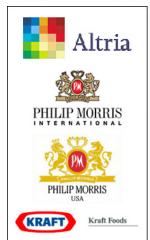
# Psycho-oncology writ large

- Primarily concerned with the psychological, behavioural, and ethical aspects of cancer
- Addresses the 2 major psychological dimensions of cancer:
  - psychological responses of patients to cancer at all stages of the disease and that of their families and caregivers
  - psychological, behavioural, and social factors that may influence the disease process
- That all cancer patients throughout the world receive optimal psychosocial care at all stages of disease and survivorship

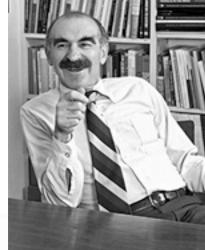
# **Marketing Myopia**

by Theodore Levitt

Sustained growth depends on how broadly you define your business—and how carefully you gauge your customers' needs.











# Implementing cancer risk assessment tools in primary care

Prof Jon Emery Professor of General Practice, University of Western Australia.

Herman Professor of Primary Care Cancer Research,

University of Melbourne
Director of PC4



Cutyour cancer risk
One third of cancers can be prevented

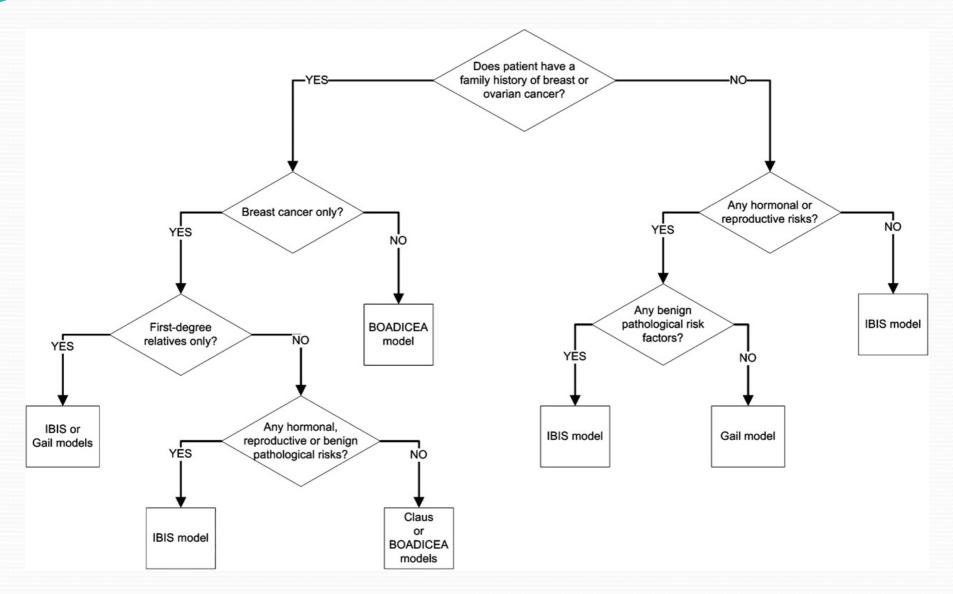


# Colorectal cancer risk models

Table 1. Summary of the previously developed CRC risk prediction models (26)

Study	Year	Family	Environmental	Screening	High-risk	Low-	Residual
		History	factors		mutations	risk SNPs	familial risk factors
Ma(68)	2010	No	Yes	No	No	No	No
Imperial(69)	2003	No	Yes	Sigmoidoscopy	No	No	No
Driver(70)	2007	No	Yes	No	No	No	No
Freedman(71)	2009	1st degree	Yes	Sigmoid/Colonoscopy	No	No	No
Wei(72)	2009	1 <sup>st</sup> degree	Yes	Sigmoid/Colonoscopy	No	No	No
Colditz(73)	2000	1st degree	Yes	FOBT, Sigmoidoscopy	No	No	No
Chen (74)	2006	1st & 2nd degree	No	No	MMR genes	No	No
Cleveland (75)	NA	1st & 2nd degree	Yes	Sigmoid/Colonoscopy	No	No	No

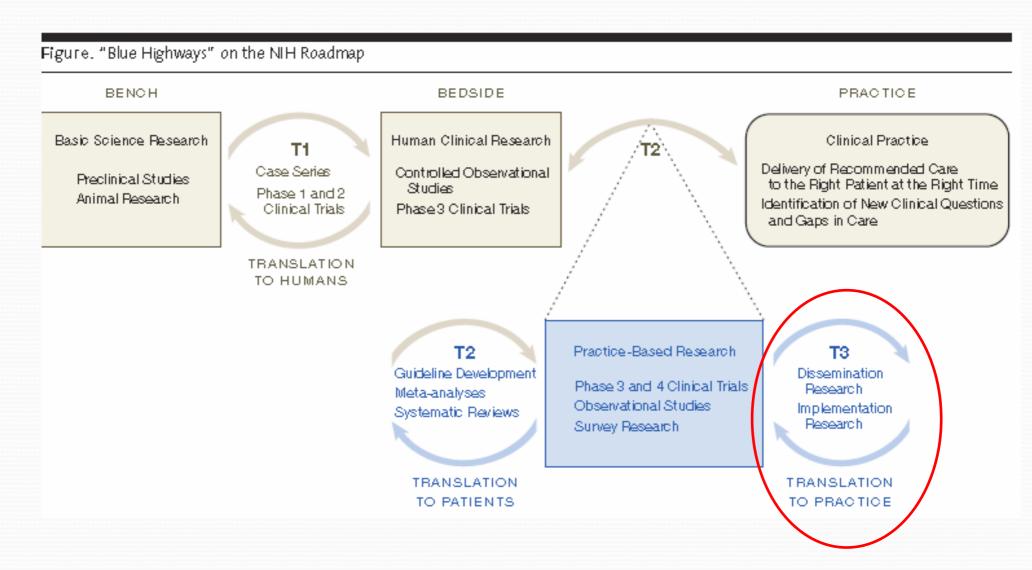
### **Breast cancer risk models**



Amir E et al. JNCI J Natl Cancer Inst 2010; jnci.djq088



# Lost in translation



How do we get cancer risks models used in clinical practice?

Will they alter clinician and patient behaviours?



#### A FRAMEWORK FOR DEVELOPMENT AND EVALUATION OF RCTs FOR COMPLEX INTERVENTIONS TO IMPROVE HEALTH

This document is a discussion document drafted by members of the MRC Health Services and Public Health Research Board. It is intended to provide a framework for individuals considering the evaluation of a complex intervention. It does not set out a set of required steps in carrying out trials in this area.

April 2000



# Developing and evaluating complex interventions:

new guidance

Prepared on behalf of the Medical Research Council by:

Reter Craig, MRC Population Health Science: Research Networt

Reul Diappe, Nuffield Department of Orthopsedic Surgery University of Codord

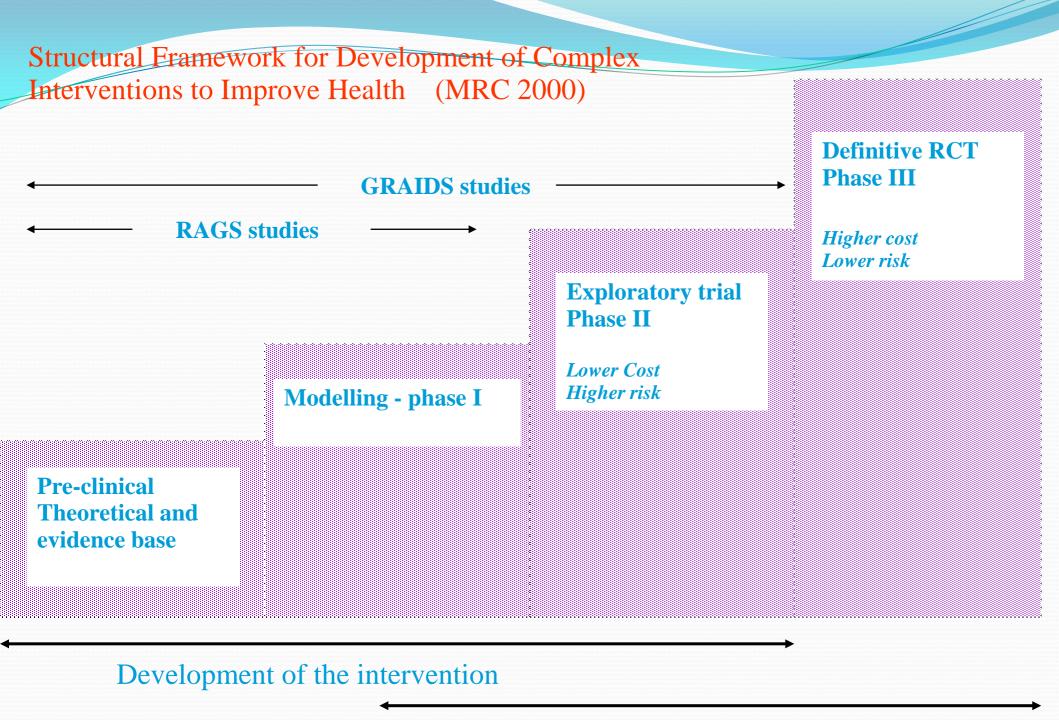
Sally Medicityre, MRC Social and Public Health Sciences Unit

Suan Midnie, Centre for Outcomes Research and Effectiveness, University College London

Invin Nazzerth, MRC General Predice Research Permeworti

Mari Retiservy, Department of Ruthir Health and Policy, London School of Hygiene and Tropical Medicine

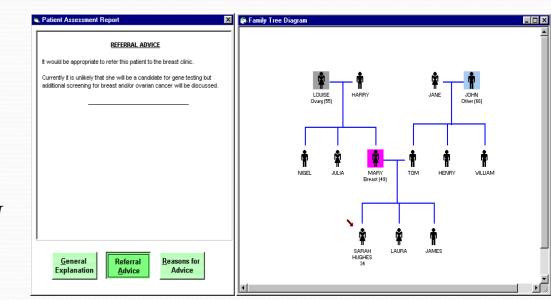
www.mrc.ac.ulc/complexinterventionsguidance



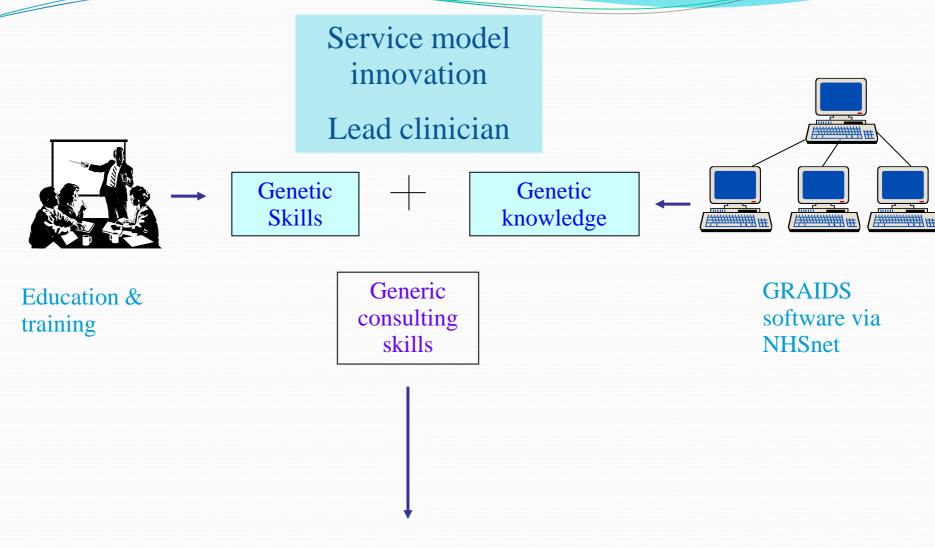
Evaluation of the intervention

# The RAGs Studies

- Risk Assessment in GeneticS
- Computerised pedigree drawing and decision support for breast and ovarian cancer
- Theoretical and Phase 1 studies
  - systematic review of primary care genetics *Fam Pract* 1999; 16: 426-445
  - qualitative study of RAGs *BMJ* 1999; 319: 32-36
  - experimental comparative study of RAGs BMJ 2000; 321: 28-32



# The GRAIDS Trial



High quality cancer genetic advice in primary care

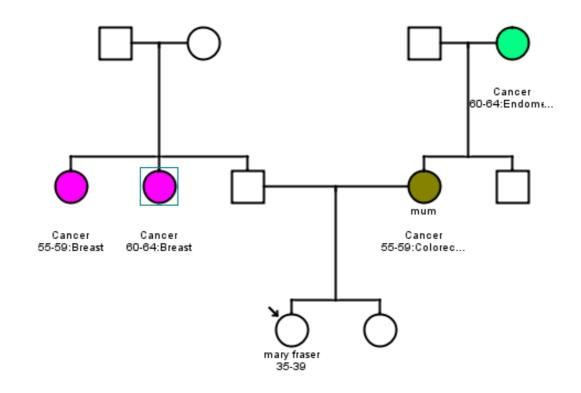
Emery et al Brit J Cancer 2007; 97:486-493.

# GRAIDS trial design

- Cluster randomisation
  - Stratified by practice size and distance from genetics clinic
- 23 intervention practices: train lead clinician + password access to GRAIDS software
- 22 comparison practices: educational meeting and mailed paper guidelines



# General Practice and Primary Care Research Unit, University of Cambridge The GRAIDS Research Programme





Design to Well-

Assess R<u>i</u>sk



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#### Risk Report for "mary fraser"

#### **Breast Cancer Management Summary**

Help

2

Tools

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View

ack

Favorites

Although this patient's risk may be slightly higher than that of the general population, it is not raised sufficiently to warrant additional screening or referral to the genetics clinic. This advice is derived from the Eastern Regional Referral Guidelines for Familial Breast Cancer. .

Your patient may wish to hear about symptoms that may be signs of breast cancer, e.g. changes in the shape, appearance and feel of the breasts; a lump in one breast or armpit which is different from the other side or new; any puckering or dimpling of the skin, discomfort or pain in one breast that is different from normal; nipple discharge, rash or a change in nipple position.

#### Return to Family Tree

Institute of Public Health General Practice and Primary Care Research Unit Enquiries: The GRAIDS Trial team

Link



#### Lifetime Breast Cancer Risk

Help

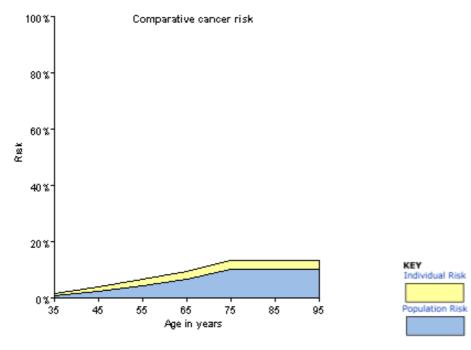
Favorites

View

Tools

The likelihood of the patient developing breast cancer during the patient lifetime, based on the patient family history, is 14%.

In other words, if we chose at random a group of 7 women with this level of risk, by the time that group reached the age of 85, 1 of the women would develop breast cancer; 6 women would remain free of breast cancer.



<u>Figure: Breast Cancer Risk Curve</u>. Graph showing the risk for "mary fraser" of developing breast cancer compared to an average woman in the UK.

#### **Return to Family Tree**

Institute of Public Health
General Practice and Primary Care Research Unit
Enquiries: The GRAIDS Trial team

# Software use and referrals

- Software used 220 times during trial in 23 practices (mean followup 17 months)
- Mean 7.7 uses per year per 10,000 registered patients

- Referrals:
  - Intervention: 168
  - Control: 84
- Intervention: 6.4 referrals per practice per year per 10,000 registered patients
- Control: 3.2
- Mean difference 3.1 (95% CI
   1.4-4.9. p=0.001)

# Referrals II

		Intervention	Control	Odds Ratio (95% C.I.)
Proportion	Breast	93% (99/107)	75% (44/59)	4.2 (1.5 to 12.2)
meeting referral	Bowel	99% (75/76)	92% (23/25)	6.5 (0.5 to 83.7)
guidelines	Combined	95% (174/183)	80% (67/84)	4.9 (1.6 to 14.8), p=0.007
Proportion at	Breast	77% (60/78)	70% (23/33)	1.4 (0.6 to 3.5)
increased risk	Bowel	56% (30/54)	85% (17/20)	0.2 (0.1 to 0.8)
determined by RGC	Combined	68% (90/132)	75% (40/53)	0.7 (0.3 to 1.5), p=0.35

# Patient outcomes

	Intervention arm			Comparison arm	
	Not referred	Referred	Mean diff		Mean difference between referred populations (95% CI)
Knowledge Breast cancer	NA	5.77 n=65	NA	5.66 n=38	0.11 (-1.05 to1.27)
Colorectal cancer	NA	5.70 n=44	NA	4.86 n=14	0.64 (-1.01 to 2.29)
Cancer worry	4.95 n=57	5.74 n=110	0.79 (-0.19 to 1.76)	7.18 n=51	1.44 (-2.64 to -0.23) p=0.02
Risk perception	4.25 n=51	4.99 n=104	0.74 (0.38 to 1.09)** P<0.0001	5.04 n=47	0.09 (-0.34 to 0.51)



#### Summary

- Translating cancer risk models requires complex interventions with staged development and evaluation.
- Importance of choice of risk model to translate and potential for unintended consequences
- Practitioner-administered software needs to integrate with local practices and systems to increase likelihood of use.
- Potential to improve assessment and management of people at increased risk of cancer in primary care

The GRAIDS Trial: a cluster randomised controlled trial of computer decision support for the management of familial cancer risk in primary care

#### J Emery<sup>M,1</sup>, H Morris<sup>2</sup>, R Goodchild<sup>2</sup>, T Fanshawe<sup>2</sup>, AT Prevost<sup>3</sup>, M Bobrow<sup>4</sup> and AL Kinmonth<sup>2</sup>

"General Produc, School of Phromy, Borgnol and Rural Health Care, Unvestor, of Western Australa, 328 Studing Highway, Garennan, Western Australa 60 (0, Rustrala, "General Produce & Pirmary, Care Research Unit, University of Cambridge, Institute of Public Health, Robinson Woy, Cambridge, Institute of Rubbi Health, Robinson Woy, Cambridge CB2 25R, UK, "Department of Medical General, University of Cambridge, Addenbrookes NHS Hospital Trust Cambridge, UK.

The objective was to evaluate the effect of an assessment strategy using the computer decision support system (the GRAIDS software), on the management of familial cancer risk in British general practice in comparison with best current gractice. The design included duster randomised controlled trial, and involved forty-live general practice teams in East Anglia, UK. Randomised to GRAIDS (Genetic Risk Assessment on the Internet with Decision Support) support (intervention n = 23) or comparison (n = 22). Training in the new assessment strategy and access to the GRAIDS software (GRAIDS arm) was conducted, compared with an educational session and guidelines about managing familial breast and colorectal cancer risk (comparison) were mailed. Outcomes were measured at practice, practitioner and patient levels. The primary outcome measure, at practice level, was the proportion of referrals made to the Regional Genetics Clinic for familial breast or colorectal cancer that were consistent with referral guidelines. Other measures included practitioner confidence in managing familial cancer (GRAIDS arm only) and, in patients: cancer worry, risk perception and Innowledge about familial cancer. There were more referrals to the Regional Genetics Clinic from GRAIDS than comparison practices (mean 6.2 and 3.2 referrals per 10,000 registered patients per year, mean difference 3.0 referrals; 95% confidence interval (Cf) 1.2-4.8; P = 0.001); referrals from GRAIDS gractices were more likely to be consistent with referral guidelines (odds ratio (OR) =5.2; 95% CI 1.7-15.8, P = 0.006). Patients referred from GRAIDS practices had lower cancer worry scores at the point of referral (mean difference -1.44 95% CI -2.64 to -0.23, P=0.02). There were no differences in patient Ignowledge about familial cancer. The intervention increased GPs confidence in managing familial cancer. Compared with education and mailed guidelines, assessment including computer decision support increased the number and quality of referrals to the Regional Genetics Clinic for familial cancer risk, improved practitioner confidence and had no adverse psychological effects in patients. Trials are registered under NOI BIT44343 in the UK National Research Register. British Journal of Concer (2007) 4, 000 000. doi:10.1038/sj.bjc.6603897 www.bjcancer.com

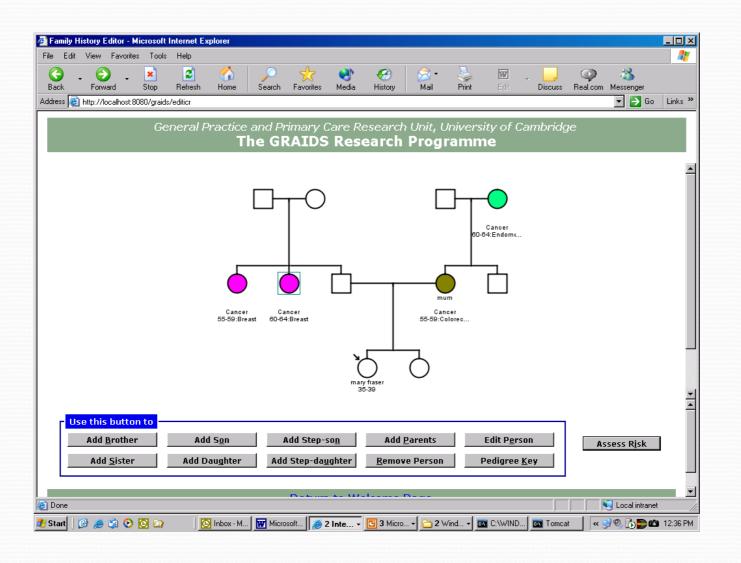
© 2007 Cancer Research UK

## Implementation research

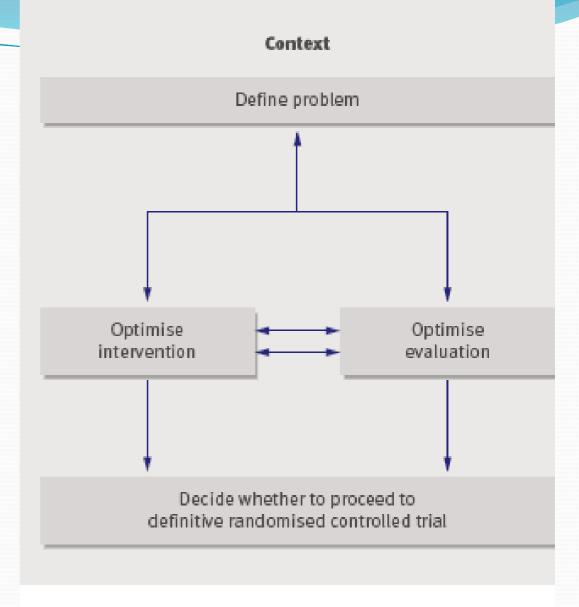


### Integration into routine practice

# Why is GRAIDS not in routine practice?



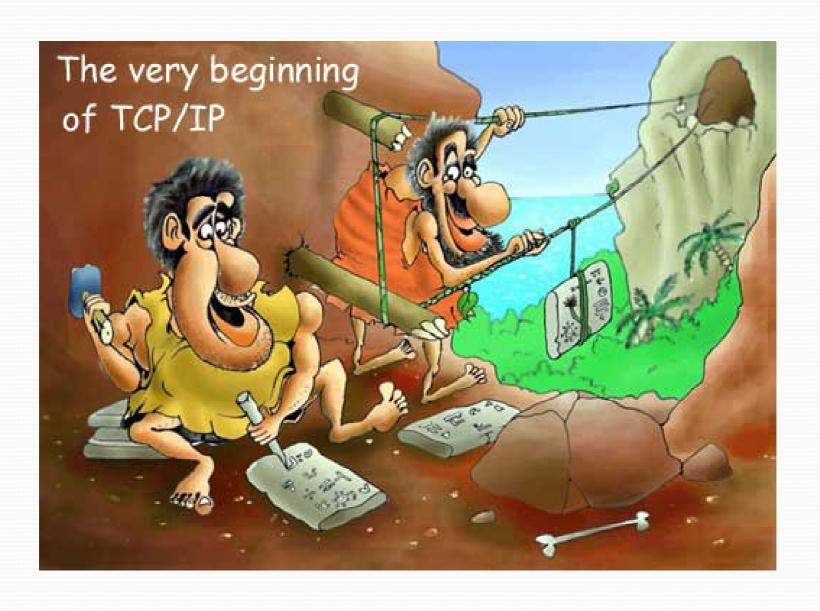
#### **Context matters**



Relation between context, problem definition, intervention, and evaluation for complex interventions

BMJ 2007;334: 445-459 Campbell, Murray, Darbyshire, Emery et al

#### Limited bandwidth in NHSnet





Search

What is NPT?

NPT Toolkit

How do you use NPT?

Theory behind NPT

Bibliography

Implementing and evaluating complex interventions, new technologies, and business processes in healthcare is complex and demanding. This website offers a set of conceptual tools and explanatory models (Normalization Process Theory, or NPT) intended to support the work of implementation and evaluation. If you are a researcher, clinician, manager, or someone else who has to practically implement and integrate some form of innovation, this website could help you think through the processes involved. It offers three resources:

- \* A toolkit to help you think through your implementation/evaluation problems, and a quick introductory guide to the toolkit that you can download
- \* An outline of NPT's basic concepts, and an introductory powerpoint that you can download.
- \* An introduction to ways to use NPT in research, along with links to key journal articles and book chapters, and as we collect them examples of studies and evaluations that you can download.

#### Thinking about implementation using normalization process theory



'a sociological toolkit that we can use to understand the dynamics of implementing, embedding, and integrating some new technology or complex intervention in healthcare.'

#### Normalisation Process Theory

- Coherence (sense-making)
  - Do GPs have a shared sense of purpose of the intervention and do they value the potential benefits?
- Cognitive participation (engagement)
  - Do GPs see the point of the intervention and will they be prepared to invest time and energy to work on it?

#### Normalisation Process Theory

- Collective action (work done to make intervention happen)
  - How compatible is the intervention with existing work practices and does it fit with the overall activities of the practice?
- Reflexive monitoring (appraisal of benefits and costs)
  - Will GPs perceive benefits of the intervention once in use for a while?
  - Can the intervention be improved on basis of GP experience?



#### Centre for Research Excellence:

Optimising Screening for

Colorectal Cancer





# KEEP CALM AND LEARN FROM THE PAST



#### Innovations in knowledge organisation: the evidence base in neurotrauma

Russell L. Gruen MBBS PhD FRACS

Professor of Surgery & Public Health, The Alfred & Monash University Director, The National Trauma Research Institute NHMRC Practitioner Fellow



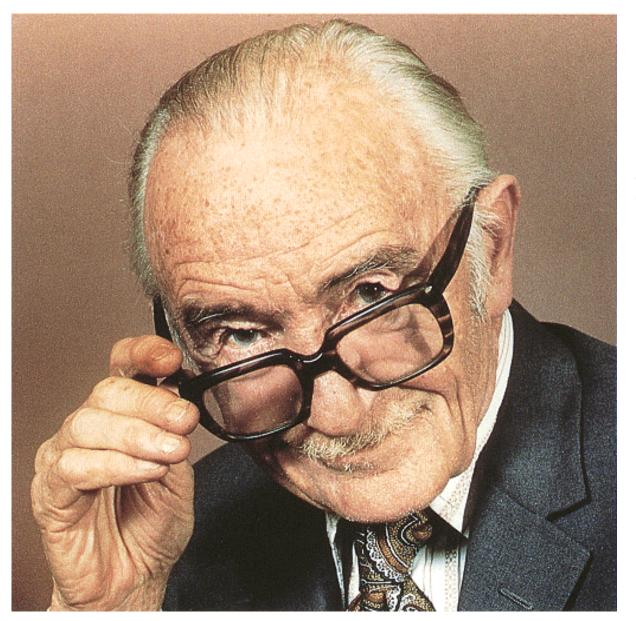








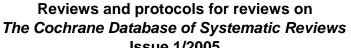




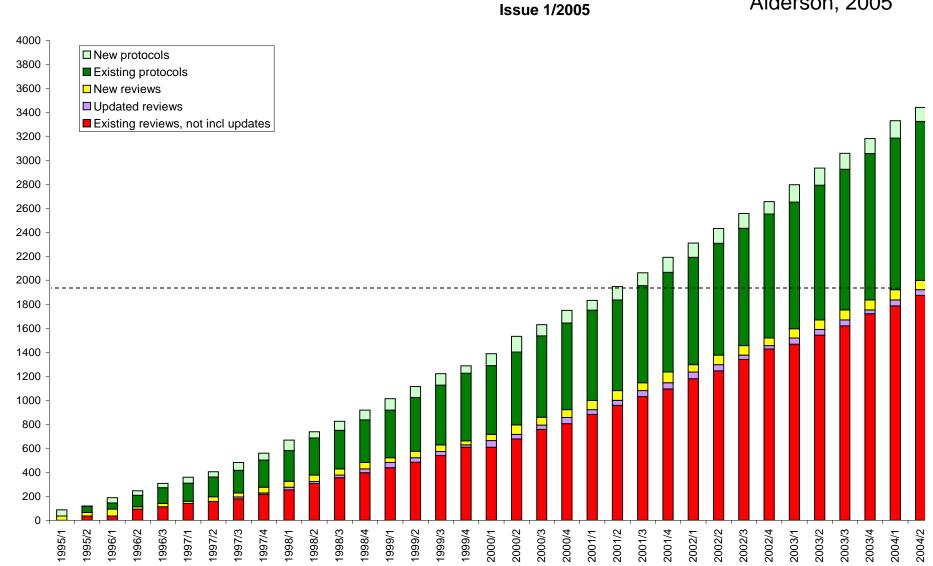
"It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, of all relevant randomised controlled trials"

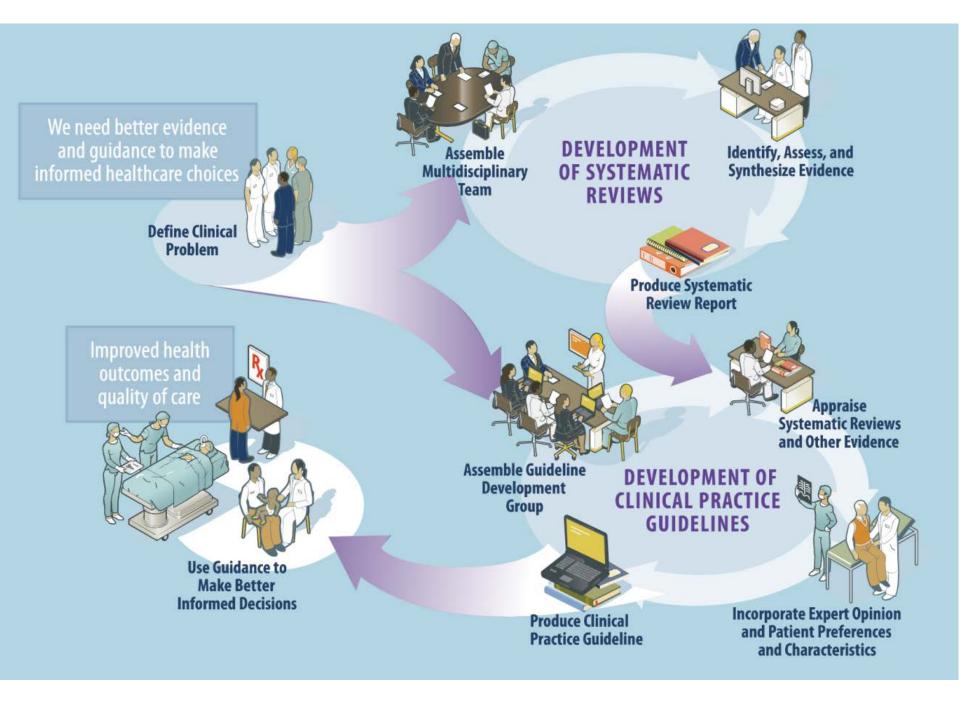
-Archie Cochrane



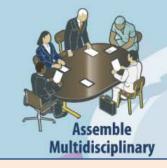


Alderson, 2005

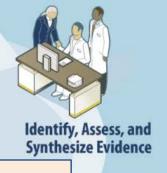




We need better evidence and guidance to make informed healthcare choices



DEVELOPMENT OF SYSTEMATIC

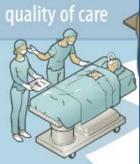


Define Clinica Problem

#### Four key challenges:

Deluge of biomedical research

Improved health outcomes and quality of care



Inefficient business processes

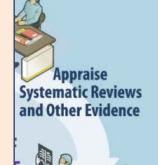
Duplication of effort

Poor engagement of end users

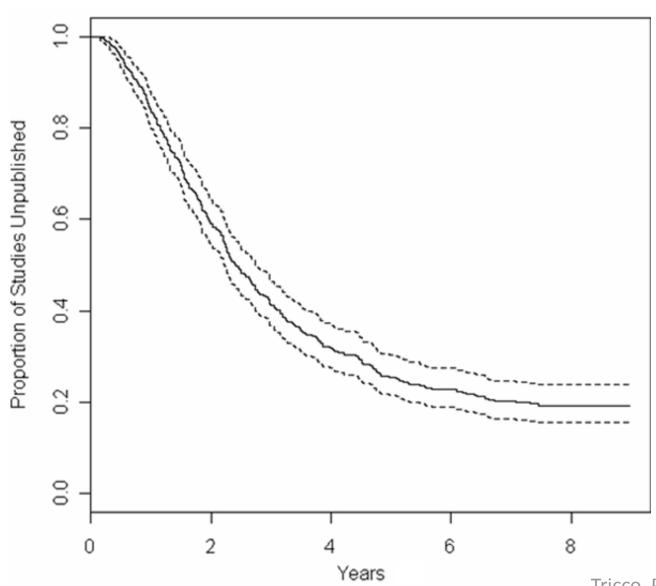
Make Better
Informed Decisions



Incorporate Expert Opinion and Patient Preferences and Characteristics

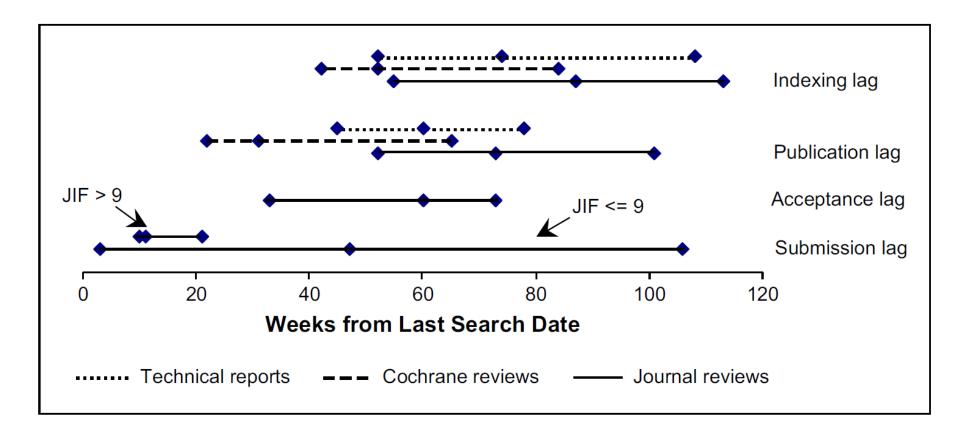


#### Time to publication of Cochrane reviews

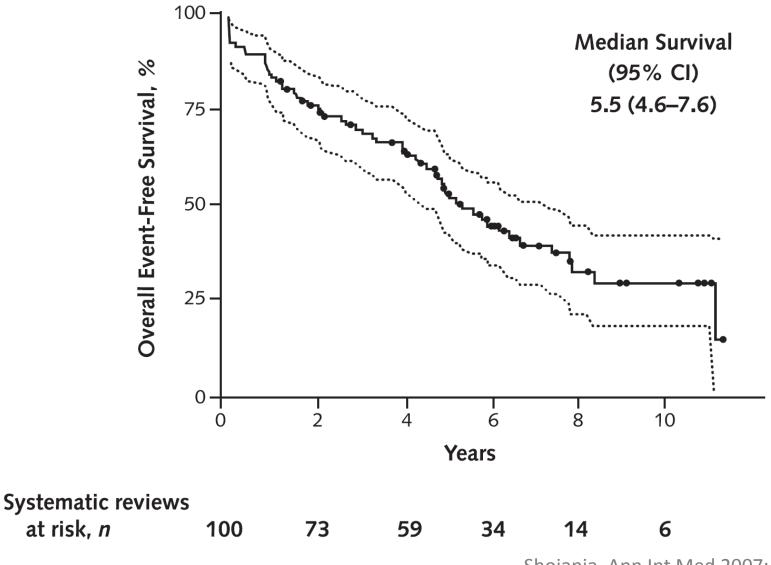


Tricco, PLoS ONE 2008; 3:e3684

#### Time from search to publication



#### Systematic review 'survival'







STANDARDS FOR SYSTEMATIC REVIEWS



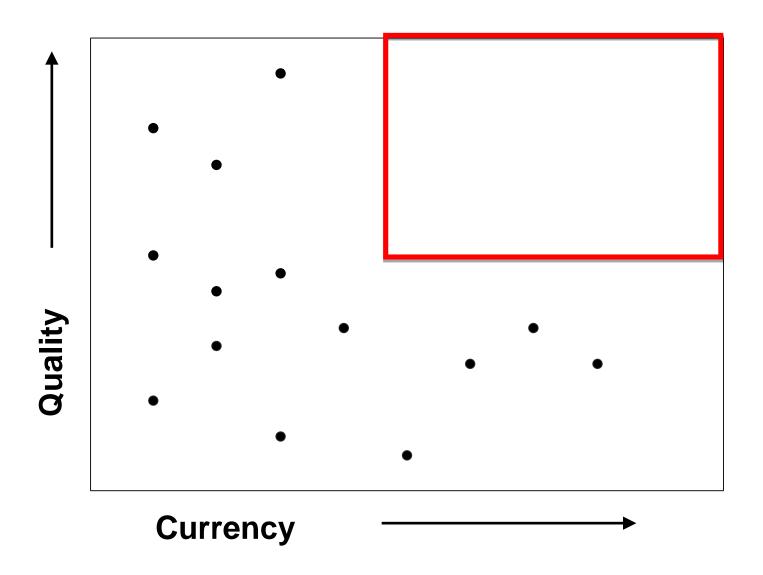
Systematic review standards

"set a high bar
that will be difficult to achieve
for many reviews,
yet the evidence and experience
are not reassuring that it is safe
to cut corners if resources are
limited"





#### Trade-off between quality and currency



#### The vision

"The updating of trial overviews as new information becomes available may be a task for which electronic publishing has something to offer...

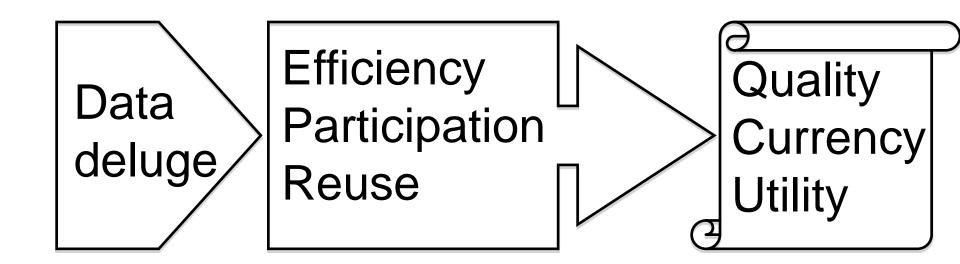
Besides registers of published and unpublished trials and trials in progress or planned, the [Oxford Database of Perinatal Trials] will include a library of trial overviews which will be updated when new data become available."

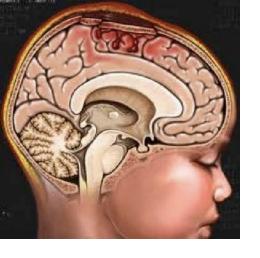
#### Living systematic reviews

"comprehensive and authoritative compilations of systematic reviews...

accessible as living web-based resources."

#### The journey



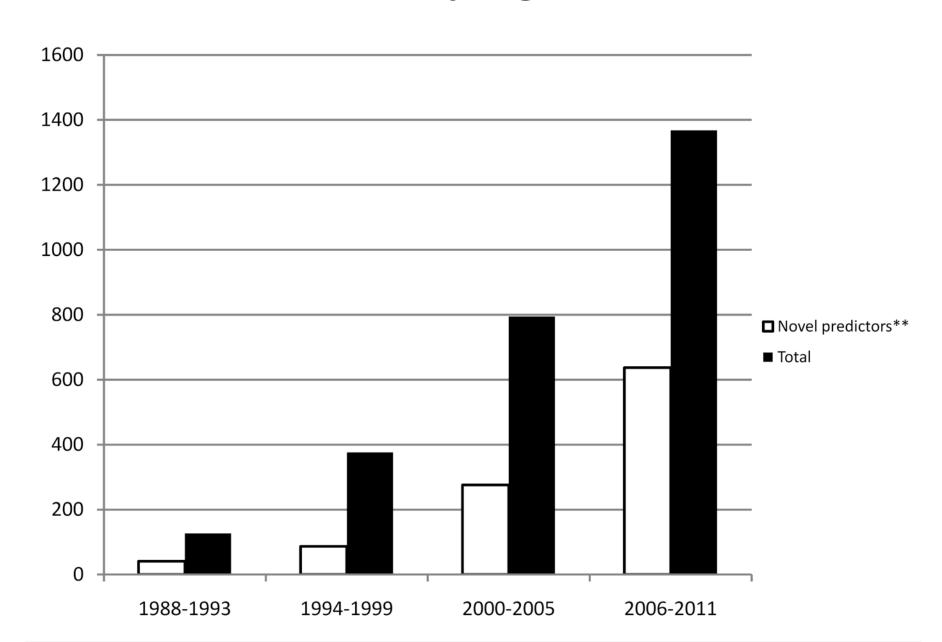


# Moderate to Severe Traumatic Brain Injury in Victoria

- Over 600 new cases per year
- Major cause of mortality, long-term disability, individual, family and social loss
- Estimated cost \$2.2 billion/year \*
  - Half is attributable to lost productivity
  - Two-thirds borne by individuals

	Year of study	N	Setting	GCS on admission	Mortality	% unfav.	Author	
Older observational studies	(prior to 1999)	•						
	1968-1975	700	UK/NL/US	Coma ≥ 6hrs	51%	62%	Jennett et al 1977 <sup>1</sup>	
Traumatic Coma Data Bank (TCDB)	1984-1987	746	US	≤ 8	39%	58%	Foulkes et al 1991 <sup>2</sup>	
UK4 Centre	1986-1988	988	UK	≤ 8	39%	57%	Murray et al 1999 <sup>3</sup>	
European Brain Injury Consortium (EBIC) core data	1995	796 481*	Europe Europe	≤ 12 ≤ 8	31% 40%	49% 60%	Murray et al 1999 <sup>4</sup>	
Weighted average				•	42%	59%		
Observational studies (1999	D-2005)							
Austria	1999-2004	492	Austria	≤ 8	38%	51%**	Rusnak et al 2007 <sup>5</sup>	
Australasian Traumatic Brain Injury Study (ATBIS)			Australia- New Zealand	≤ 8	32%	55%	Myburgh et al 2008 <sup>6</sup>	
	1999-2004	672	Singapore	≤ 8	36%	51%	Ng et al 2006 <sup>7</sup>	
Weighted average			36%	52%				
More recent studies (2005-2	2010)							
	2005-2007	518	Paris	≤ 8	51%	66%	Darnoux et al 2011 <sup>8</sup>	
Prospective Observational COhort Neurotrauma (POCON) study	2008-2009	339	The Netherlands	≤8	46%	60%	Andriessen et al 2011 <sup>9</sup>	
Ontario Prehospital Advance Life Support (OPALS) Major Trauma Study	?	538	Ontario (Canada)	≤8	33%***	63%***	Dowling et al 2010 <sup>10</sup>	
	2008-2010	748	Latin America	≤ 8	31%	54%	Chesnut et al 2011 <sup>11</sup>	
Weighted average	•	39%	60%					

#### Publications on TBI prognosis 1988-2011



#### Barriers to compliance with evidence-based care in trauma

Nadine Rayan, MHA, Sunni Barnes, PhD, Neil Fleming, PhD, Rustam Kudyakov, MD, MPH, David Ballard, MD, PhD, MSPH, Larry M. Gentilello, MD, and Shahid Shafi, MD, MPH, Dallas, Texas

J Trauma Acute Care Surg 2012; 72: 585–93.

17% compliance with BTF guidelines for craniotomy, intracranial pressure monitoring, and reversal of coagulopathy

TABLE 3.	Independent Predictors of Compliance With
T-POC: Mu	ıltivariate Analysis

Predictor	OR (95% Confidence Interval)
Blunt traumatic injury	1.49 (1.12–1.20)
AIS injury of the head	0.86 (0.81-0.92)
Glasgow Coma Scale	1.04 (1.02-1.06)
Intensive care unit stay	1.49 (1.22–1.82)
Length of stay (d)	1.02 (1.02–1.03)

#### Using a Cost-Benefit Analysis to Estimate Outcomes of a Clinical Treatment Guideline: Testing the Brain Trauma Foundation Guidelines for the Treatment of Severe Traumatic Brain Injury

Mark Faul, PhD, Marlena M. Wald, MLS, MPH, Wesley Rutland-Brown, MPH, Ernest E. Sullivent, MD, and Richard W. Sattin. MD

*J Trauma* 2007, **6**: 1271 – 1278

- Proportion with "good" outcomes would rise from 35% to 66%
- Proportion with "poor" outcomes would fall from 34% to 19%

Table 2 Overall Cost Savings and Lives Saved Resulting From Adoption of BTF Guidelines—Total Costs									
	Deaths	Direct Medical Costs	Rehabilitation Costs	Societal Costs	Implementation Costs	Total Costs			
BTF adoption	3,466	\$ 1,154,116,956	\$ 64,008,683	\$ 3,859,102,789	\$ 60,906,282	\$ 5,138,134,710			
Current state	7,073	\$ 1,416,538,024	\$ 107,428,632	\$ 7,696,680,328	\$ 0	\$ 9,220,646,983			
Difference	3,607	\$ 262,421,068	\$ 43,419,949	\$ 3,837,577,538	\$ 60,906,282	\$ 4,082,512,273			

Calculated medical costs probabilities are subject to rounding errors.



#### Aims:

- To improve outcomes for people with TBI
- To create a network of neurotrauma clinicians and researchers with expertise in KT and evidencebased practice
- To contribute knowledge to the field of KT research

#### **NET Program**

Theme	Program activity
Theme 1: Evidence Resources	Systematic reviews; Agreement on standards; Locally relevant guidelines
Theme 2: Understanding Practice	Data, Practice surveys & Interviews
Theme 3: Planning & Instituting Change	Theory-informed interventions; Intervention studies, including cluster RCTs
Theme 4: Capacity Building	Training; Clinician fellowships; Networks and collaboration



#### The Global Evidence Mapping Initiative

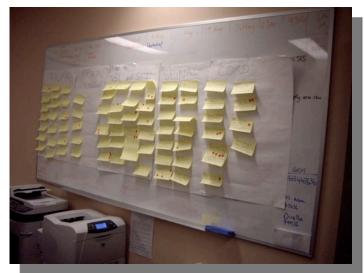
- Funded in 2007 by the Victoria Neurotrauma Initiative to develop 'evidence maps' to describe the available research in priority topics in Traumatic Brain Injury and Spinal Cord Injury
- Pre-hospital, acute, rehabilitation and long-term care





#### Generating & Prioritising Questions

- Multiple phases
  - A. Expert consultation
  - B. Preliminary literature search
  - C. Mapping workshop
  - D. Online survey
  - E. Question development
- Wide stakeholder engagement (policy-makers, managers, clinicians, consumers, carers, researchers)





#### What is the effect of early versus delayed surgery for unstable spinal injuries on clinical outcomes and length of stay in SCI patients?

Comparisons	n	Systematic Review	RCT	Cross Over Studies	Cohort Studies	Case- Control	Interrupted Time Series	Case Series	Cross- sectional	Case Reports	Other	Ongoing Studies
Various timing of stabilisation	1	1										
Various timing of spinal fixation	2	2										
Various timing of decompressive	4	4			io.							
surgery	25 <b>4</b> 50											
Time of surgery from injury:												
<8h vs. >8h	1							1				
<8h vs. 8-24h vs. no surgery	1		1									
<24h vs. >24h	5	Į.			4 (retro.)							1†
<24h vs. >24h vs. Conservative Tx	1							1				
<24h vs. 24-48h vs. >48h	1							1				
<24h vs. 24-72h	2				1 (prosp.)							1
<24h vs. 24-72h vs. >72h	1							1				
<24h vs. 24h-1wk vs. >1wk	1							1				
<48h vs. >48h	1				1 (retro.)							
<48h vs. >48h vs. No Surgery	1							1				
<72h vs. >72h	4				4 (retro.)							
<72h vs. >5d	1		1									
<72h vs. <10-14d	1		1 (pseudo)		6							
<100h vs. >100h vs. no surgery	1				1 (prosp.)							
≤5d vs. > 5d	1		1 (pseudo)									
<5d vs. >6wk	1											1
<1wk vs. <1-4wk vs. >4wk	1							1				
<4wk vs. >4wk	1							1				
<1wk vs. <2wk vs. <3wk vs. <4wk vs. >4wk vs. No Surgery	1							1				

SCI SURGERY TIMING Page 1 of 13





<72h vs. >72h (n=4)

#### Cohort (retrospective)

Chipman JG, Deuser WE, Beilman GJ. Early surgery for thoracolumbar spine injuries decreases complications. J Trauma 2004;56(1):52-7.

Croce MA, Bee TK, Pritchard E, Miller PR, Fabian TC. Does optimal timing for spine fracture fixation exist? Ann Surg 2001;233(6):851-8.

Mirza SK, Krengel WF 3rd, Chapman JR, Anderson PA, Bailey JC, Grady MS, et al. Early versus delayed surgery for acute cervical spinal cord injury. Clinical Orthopaedics & Related Research 1999(359):104-14.

Schlegel J, Bayley J, Yuan HS, Fredricksen B. Timing of surgical decompression and fixation of acute spinal fractures. Journal of Orthopaedic Trauma 1996;10(5):323-330.

<72h vs. >5d (n=1)

RCT

Vaccaro AR, Daugherty RJ, Sheehan TP, Dante SJ, Cotler JM, Balderston RA, et al. Neurologic outcome of early versus late surgery for cervical spinal cord injury. Spine 1997;22(22):2609-13.

<72h vs. <10-14d (n=1)

RCT (pseudo)

Xiao YQ, Wang YS, Yao M, Qi H, Gao L. Effect of surgical intervention time on nervous function recovery after cervical spinal cord injury. Chinese Journal of Clinical Rehabilitation 2006;10(36):167-9.

<100h vs. >100h vs. no surgery (n=1)

Cohort (prospective)

Duh MS, Shepard MJ, Wilberger JE, Bracken MB. The effectiveness of surgery on the treatment of acute spinal-cord Injury and Its relation to pharmacological treatment. Neurosurgery 1994;35(2):240-248.



ACUTE REPORT





ACUTE REPORT



## What is the effect of early versus delayed surgery for unstable spinal injuries on clinical outcomes and length of stay in SCI patients?

#### BACKGROUND

The main role of surgery in spinal cord injury (SCI) is to prevent secondary injury to the cord and stabilise the spinal column. Surgery can also help to reduce the magnitude and impact of secondary injury mechanisms (e.g. ischaemia and inflammation) (Ball 2006; Fehlings 2006; La Rosa 2004). Early stabilisation can also help to reduce the morbidity and mortality associated with other injuries, particularly lung and intracranial injuries, and facilitates sitting and mobilising, which minimises the development of pressure areas and decubitus ulcers.

The optimal timing for SCI surgery is unclear (Fehlings 2006). The benefits of early correction of cord compression have been primarily based on animal studies (Carlson 1997; Carlson 2003; Delamarter 1995; Dimar 1999).

This evidence map identified studies investigating the timing of SCI stabilisation surgery.

### CRITERIA FOR CONSIDERING STUDIES

The following inclusion criteria were used to identify relevant studies:

Study type, Participants, Phase of Care

See inclusion criteria (Appendix)

Intervention

Timing of surgery in patients undergoing decompression, reduction or fixation surgery

#### SEARCH STRATEGY

We searched seven English (Medline, CINAHL, EMBASE, PsycINFO, PubMed, ISI Web of Science, and The Cochrane Library); four non-English (LILACS, Panteleimon, IndiaMed, KoreaMed) and two clinical trials databases (WHO – International Clinical Trials Registry, The UK National Research Register) up to October 2008. Search strategies for SCI were combined with pertinent terms for spinal surgery (search strategies available on request). Reference lists of relevant articles were also searched.

An updated search was conducted in February 2010.

### VIELD

The number of citations identified from our search strategy, full text reviewed, final included articles and non-English studies are shown in the table below.

Three ongoing studies examining the timing of surgery were identified.

Data Carrol	Citations	Full Text Articles		Included		
Date Search conducted		Search Strategy	Ref. list search	Search Strategy	Ref. list search	Non- English
October 2008	1368	118	20	45	15	7
February 2010*	1683	2	0	0	0	0
Total	3051	14	140 60		7	

\* yield from search addressing multiple questions

Ref.: reference

#### STUDY INTERVENTIONS, DESIGN AND CHARACTERISTICS

Of the 60 eligible studies, there were seven systematic reviews, two randomised controlled trials (RCTs), three pseudo-RCTs, 16 cohort studies, 31 case series and one case report on this topic. Study settings for the primary studies were the USA (46), France (2), Italy (2), with one study each from Austria, China, Germany, India, Iran, Israel, Norway, Turkey, the UK and the United Arab Emirates. The majority of studies (36) investigated adult populations; four studies were mixed population, two paediatric and eighteen did not describe patient

SCI SURGERY TIMING Page 1 of 14 SCI SURGERY TIMING

Copyright © 2010 What is the effect of early vs. delayed surgery for unstable spinal injuries on clinical outcomes and length of stay in SCI patients?

Page 2 of 14

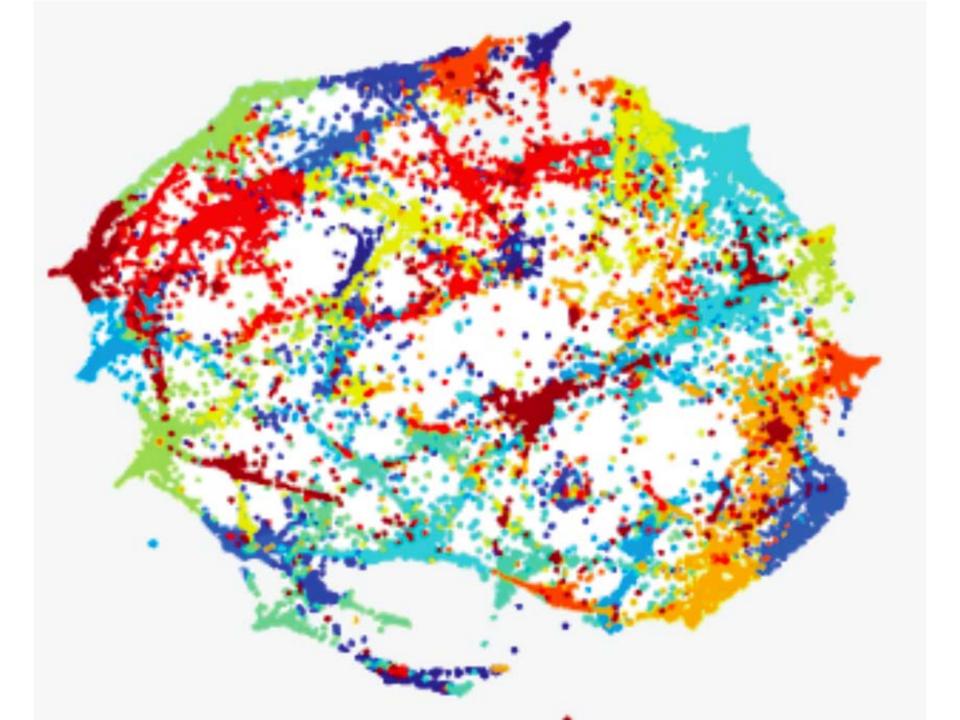
# An Overview of Published Research about the Acute Care and Rehabilitation of Traumatic Brain Injured and Spinal Cord Injured Patients

Peter Bragge, Marisa Chau, Veronica Jean Pitt, Mark Theodore Bayley, Janice Jennifer Eng, Robert William Teasell, Dalton Louis Wolfe, and Russell Lindsay Gruen

Table 1. Traumatic Brain Injury Acute Neurotrauma Evidence from the Global Evidence Mapping (GEM) Initiative and the Acquired Brain Injury Evidence-Based Review (ERABI): Intervention Topics

	Topic	SR	RCT	Other
1.	Pharmacological management for raised intracranial pressure	11	40	78
2.	Pre-hospital intubation	3	0	22
3.	Effectiveness/cost-effectiveness of repeat computed tomography scans	1	0	30
4.	Pharmacological and oxygen neuroprotective/intracranial pressure therapies	0	17	3
5.	Seizure prophylaxis and management	0	13	9
6.	Therapeutic hypothermia for management of raised intracranial pressure	0	8	9
7.	Interventions to promote emergence from coma	0	6	15
8.	Pre-hospital fluid therapy resuscitation	0	6	2
9.	Opioids for analgesia	0	4	5
10.	Surgical management of raised intracranial pressure	0	3	20
11.	Prevention of deep vein thrombosis and pulmonary embolism	0	3	6
12.	Dexamethasone for neurological recovery	0	3	0
13.	Pharmacological therapies for neurological recovery	0	2	6
14.	Hyperventilation	0	1	10
15.	Delayed versus immediate pre-hospital fluid resuscitation	0	1	0
16.	Pre-hospital use of mannitol	0	1	0
17.	In-hospital fluid therapy resuscitation	0	1	0
18.	Therapeutic hypothermia	0	1	0
19.	Models of care including time factors, transport, specialization of acute hospital, staffing profiles	0	0	22
20.	Postural management of raised intracranial pressure	0	0	10
21.	Neurotrauma health care organization and delivery: Inpatient	0	0	3

SR, systematic review; RCT, randomized controlled trial.



## Early management of severe traumatic brain injury

Jeffrey V Rosenfeld, Andrew I Maas, Peter Bragge, M Cristina Morganti-Kossmann, Geoffrey T Manley, Russell L Gruen Lancet 2012; 380: 1088–98

Intervention	RCTs: Pre-2006	RCTs: 2006-	RCTs: Ongoing	Interpretation of trial findings
Recombinant Activated Factor VII		Kluger 2007 <sup>44</sup>		One trial has shown recombinant Activated Factor VII to be no different to placebo on mortality or frequency of thromboembolic or adverse events.
Rosuvastatin		Tapia-Perez 2008 <sup>45</sup>		One trial has shown Rosuvastatin to be superior to placebo on reduction in amnesia time, but no different on clinical outcomes.
Hyperventilation	Muizelaar 1991 <sup>46</sup>			One trial has shown hyperventilation to be inferior to normal ventilation on clinical outcomes and that the detrimental effects of hyperventilation are lessened by Tromethamine (THAM).
Cerebral blood flow- directed management	Robertson 1999 <sup>47</sup>			One trial has shown cerebral blood flow-targeted management to be no different to intracranial pressure-targeted management on clinical outcomes, to be superior on frequency of jugular desaturation, but to potentially increase incidence of adult respiratory distress syndrome.
Intracranial pressure- targeted management			Carney 2012 <sup>48</sup>	
Brain tissue oxygen monitoring-directed therapy			Diaz-Arrastia 2012 <sup>49</sup>	
Therapeutic hypothermia - systemic	Clifton 2001 <sup>50</sup> Jiang 2000 <sup>51</sup> Marion 1993 <sup>52</sup> Marion 1997 <sup>53</sup> Resnick 1994 <sup>54</sup> Shiozaki 1993 <sup>55</sup>	Bayir 2009 <sup>56</sup> Clifton 2011 <sup>57</sup> Hutchison 2008 <sup>58</sup> Hutchison 2011 <sup>59</sup> Jiang 2006 <sup>60</sup> Lee 2010 <sup>61</sup> Li 2009 <sup>62</sup> Qiu 2007 <sup>63</sup> Su 2010 <sup>64</sup> Yan 2010 <sup>65</sup> Zhao 2011 <sup>66</sup>	Andrews 2010 <sup>67</sup> Cooper 2011 <sup>68</sup>	Two trials have shown systemic therapeutic hypothermia to be superior to normothermia on mortality; six trials have shown no difference.  Eight trials have shown systemic therapeutic hypothermia to be superior to normothermia on intracranial pressure control; one trial has shown systemic therapeutic hypothermia to be inferior to normothermia on intracranial pressure control; one trial has shown no difference.  Five trials have shown systemic therapeutic hypothermia to be superior to normothermia on clinical outcomes; four trials have shown no difference.  One trial has shown long-term hypothermia (4 – 6 days) to be superior to short-term hypothermia (1 – 3 days) on intracranial pressure control and clinical outcomes.
Therapeutic hypothermia - local		Harris 2009 <sup>69</sup> Liu 2006 <sup>70</sup> Qiu 2006 <sup>71</sup>		Two trials have shown local therapeutic hypothermia to be no different to normothermia on mortality.  Two trials have shown local therapeutic hypothermia to be superior to normothermia on intracranial pressure control.  One trial has shown local therapeutic hypothermia to be superior to normothermia on clinical outcomes; two trials have shown no difference.
Hyperoxia	Ren 2001 <sup>72</sup> Rockswold 1992 <sup>73</sup>	Rockswold 2010 <sup>74</sup> Xie 2007 <sup>75</sup>	Ruokonen 2011 <sup>76</sup>	One trial has shown hyperbaric hyperoxia to be superior to standard care on mortality.  One trial has shown hyperbaric hyperoxia to be superior to standard care on intracranial pressure control.

continued...

Intervention	Trials	Mortality	Clinical	ICP
Pre-hospital Intubation	1			
Pre-hospital Hypertonic Saline	9			
Early volume resuscitation	1			
In Hospital Hypertonic Saline	8	Isotonic fluids	Mannitol	Isotonic Fluids  Mannitol
Mannitol	5			
Albumin	1			
Fresh frozen plasma	1			
Blood transfusion thresholds	1			
Tranexamic acid	3			
Erythropoietin	2			
Factor VIIa	1			
Rosuvastatin	1			
Hyperventilation	1		•	
CBF-directed management	1			
ICP-directed management	1			
PtO2-directed management	1			
Systemic hypothermia	19			
Cranial hypothermia	3			
Hyperoxia	5			
Steriods	16			

Barbiturates	5			
Opioids	4			
Propofol	1			
Midazolam	1			
Progesterone	5			
Magnesium	2	- High dose	- Low dose - High dose	_
Nimodipine	3			
Cistracurium	1			
Anticonvulsants	7			
Bradykinin Antagonists	4			
Competitive N-methyl-D-aspartate antagonist (Selfotel)	1			
Non-competitive N-methyl-D-aspartate antagonist (Traxoprodil)	1			
Ciclosporine	2			
Tromethamine (THAM)	1			
Free radical scavenger (Pegorgotein or PEG SOD)	1			_
Oxidative stress/Lipid peroxidation inhibitor (Tirilazad)	1			
NNZ 2566	1			
CDP-choline	1			
Cannabinoids (Dexanabinol)	2			
CSF drainage	1			
Nutrition – modes of delivery	5			
Nutrition – Rate/Timing of feeding	4			
Nutrition – Nutritional Agents	4			

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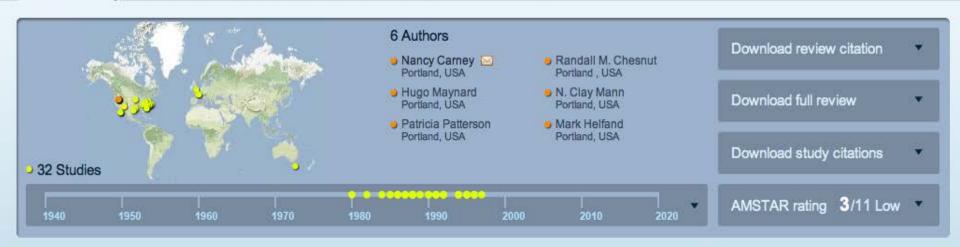




Effect of cognitive rehabilitation on outcomes for persons with traumatic brain injury: A systematic review.

Published: June 1999, Search last updated: January 1997

Overview Full Review Context & Interpretation Discussion



### Abstract

We evaluated evidence for the effectiveness of cognitive rehabilitation methods to improve outcomes for persons with traumatic brain injury (TBI). A search of MEDLINE, HealthSTAR, CINAHL, PsycINFO, and the Cochrane Library produced 600 potential references. Thirty-two studies met predetermined inclusion criteria and were abstracted; data from 24 were placed into evidence tables. Two randomized controlled trials and one observational study provided evidence that specific forms of cognitive rehabilitation reduce memory failures and anxiety, and improve self-concept and interpersonal relationships for persons with TBI. The durability and clinical relevance of these findings is not established. Future research utilizing control groups and multivariate analysis must incorporate subject variability and must include standard definitions of the intervention and relevant outcome measures that reflect health and function.

### Related Reviews

### Systematic Reviews



Rees Laura, Marshall Shawn, Hartridge Cheryl, Mackie David, Weiser Margaret, . Cognitive interventions post acquired brain injury. Brain Injury. 2007;21(2):161-200.

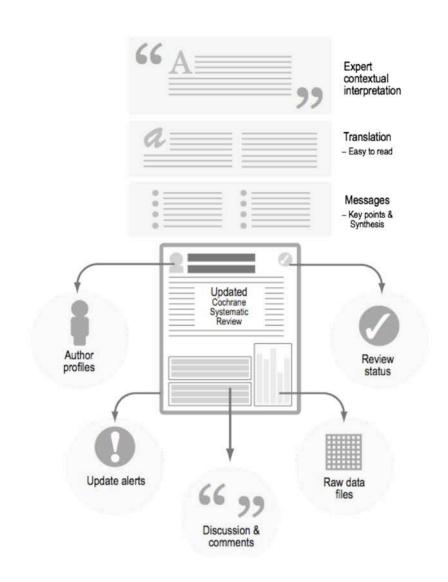


### Adding value to a review

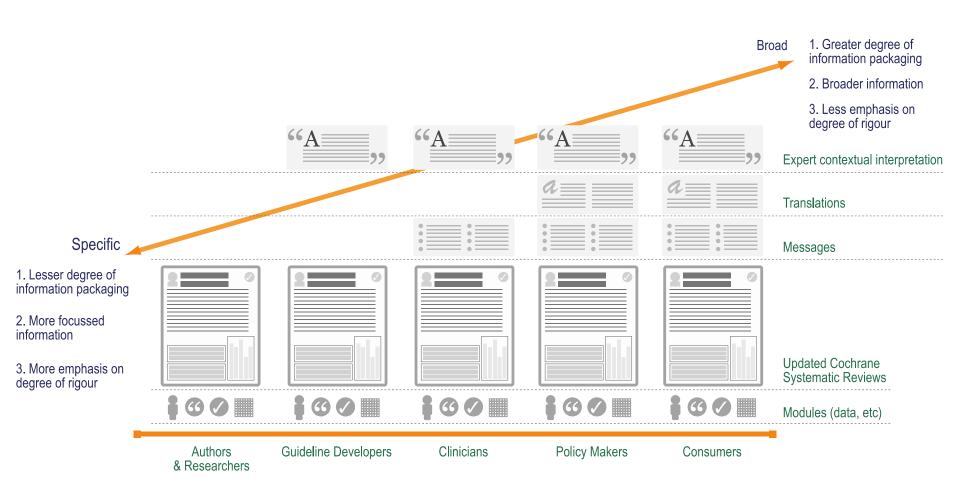
A knowledge resource could have a number of modules that are additional to the updated systematic review

## They provide value for different user groups

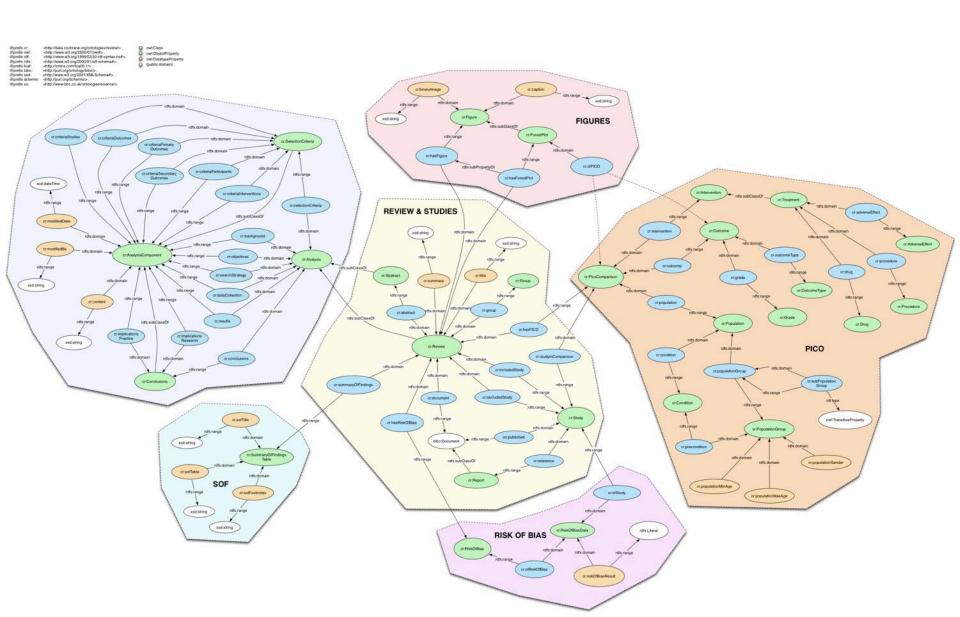
"It's all useful... it's really just that you might use different parts at different times, depending on what you do"



### **Community Roadmap**



## Cochrane Linked Data Project



## **Living Systematic Reviews**

Methods of collaboration & frequent updating

Technology to help the process

 A community of participants engaged as curators of knowledge in their areas of expertise

### Search



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Home > Research > Research Themes > Making Sense of Data > Biomedical Text Processing

### BIOMEDICAL TEXT PROCESSING

BioTALA is developing techniques to provide easier and faster access to valuable information buried in biomedical texts, saving time and cost for biomedical researchers and clinicians, and potentially enabling new insights and discoveries.

Processing and management of clinical records and research literature is a critical component of biomedical research and clinical practice. Our biomedical research partners, based in hospitals and institutes in the Melbourne biomedical precinct, have identified this cost as a significant bottleneck in their work, and see a strong need for methods for making sense of large volumes of text. Existing technology addresses neither of these specific needs, nor broader problems of searching and summarising massive specialised collections.

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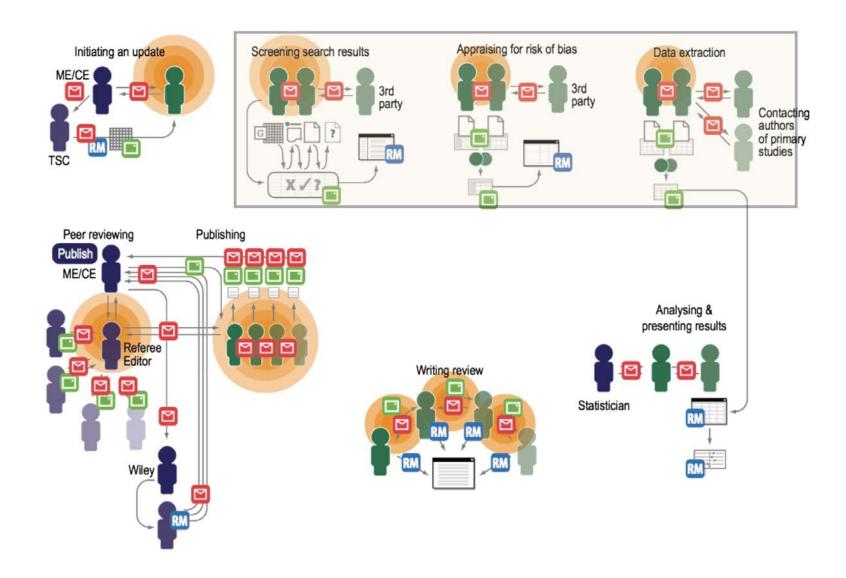
BioTALA --- BioMedical Text and Language Applications --- is developing "text mining" technologies to (semi-)automatically discover and visualise information from genetic and other biomedical research and clinical documents. Drawing on the team's leading strengths in information retrieval and natural language processing, we aim to develop and apply text mining techniques to a variety of practical problems faced by biomedical researchers.

We are developing fundamental algorithms and tools in the context of specific applications, basing our activities on issues identified as significant by our biomedical research collaborators. These biomedical researchers are investigating cutting-edge biomedical and clinical research topics in world-leading research institutes, and have found that issues with text are a critical bottleneck. We are developing innovative technologies that address specific problems identified by our partners where the technologies are deemed to be likely to be of broad value.

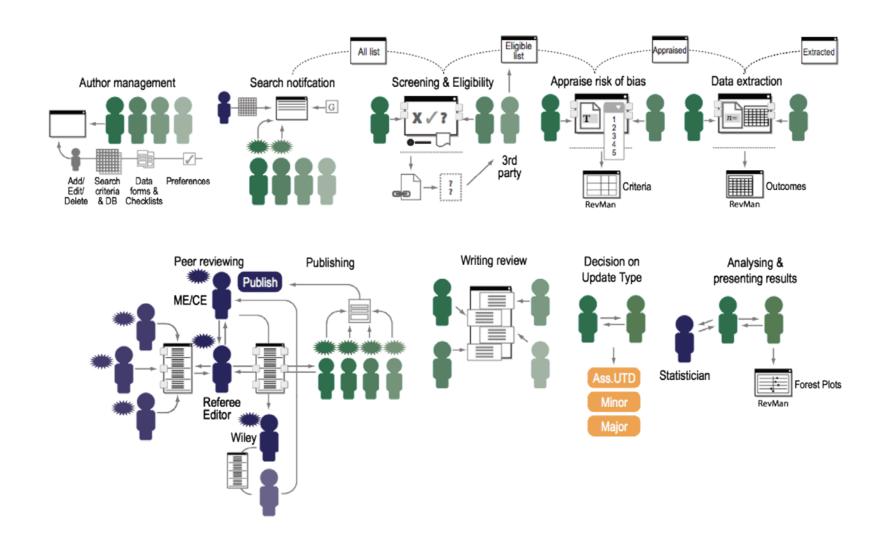
### Our Research

Language Technology and Information Retrieval have long histories in the medical domain dating back to the 1960s. Since the completion of the human genome project in 2001, researchers in both areas have become increasingly involved in the information management challenges that have arisen from the rate at which new publications are being added to the bibliome. However, despite the recent flurry of activity by the information retrieval, machine learning, and language technology communities in the biomedical arena, there has not been an enthusiastic uptake of these technologies by biomedical researchers. In an invited talk at the ACL-BioNLP workshop in 2007, Alfonso Valencia (Centro Nacional de Biotecnologia, Spain) stated that there is a growing gulf between what computer science researchers perceived to be of interest to biomedical personnel and what pain points these people are actually experiencing on a day-to-day basis. He implored researchers to focus their efforts on tasks that really mattered to the biomedical community.

### Excel, Word, Paper, Email...



## Living update process



### TBI Intubation

Overview Sci

Screen (468)

Select (36)

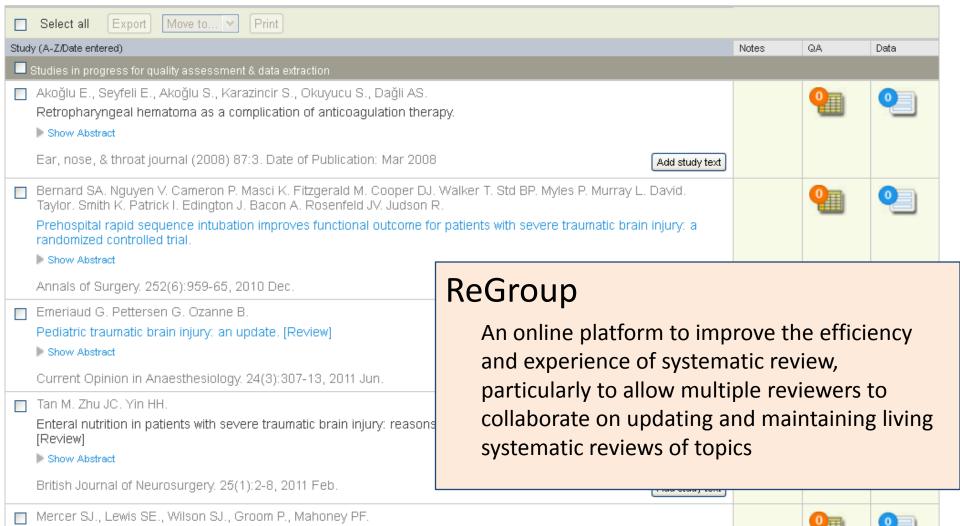
Included (20) Excluded (5)

(5)

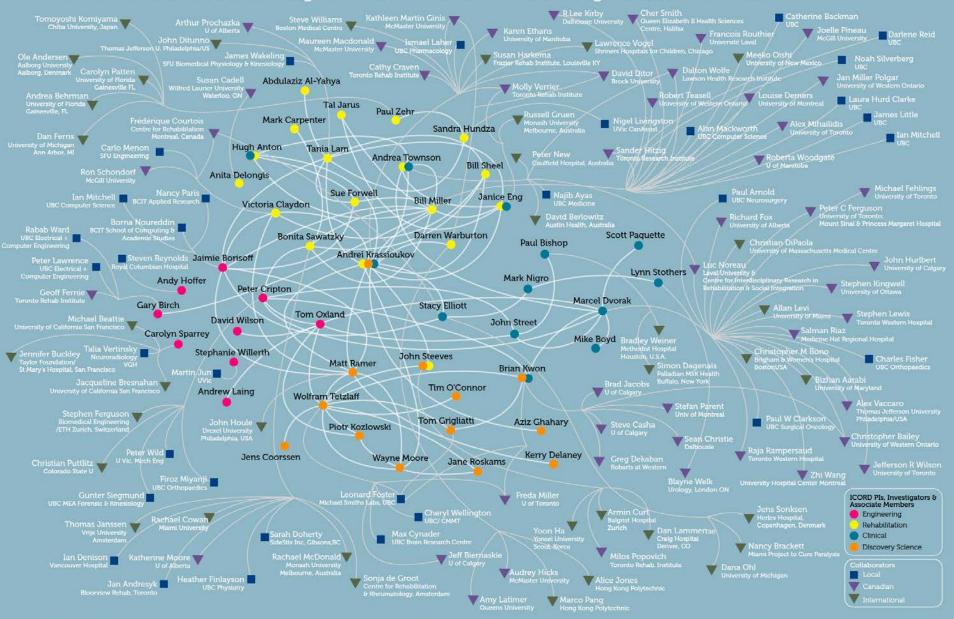
Irrelevant (9

Settings

### Included



### ICORD researchers: connecting with each other & connecting around the world



## Living Systematic Review Project

"...comprehensive and authoritative systematic reviews designed, populated, and updated by international networks with content and methodological expertise... structured to incorporate important contextual characteristics, designed to help users interpret evidence and be accessible as living web-based resources."

## Neurotrauma Knowledge Centres



