

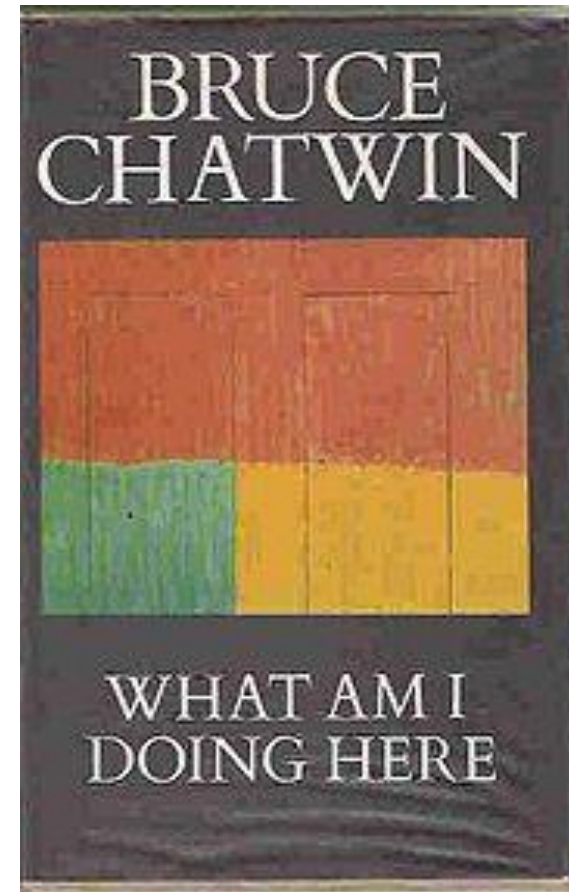
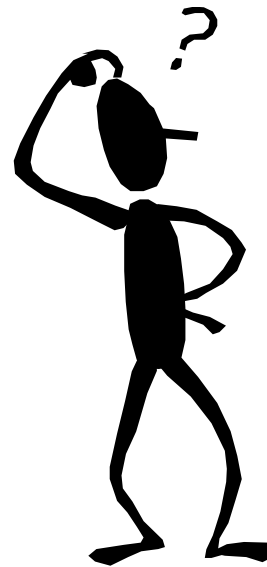


Introduzione delle nuove tecnologie basata su evidenze: revisioni Cochrane e registri

Gustavo Zanolì, Ferrara Italy
zanolig@me.com

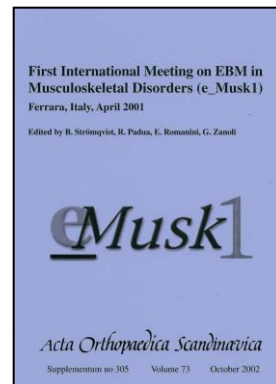
What am I doing here?

1. Represent Cochrane
2. Lessons learned from Italian Registry
3. Experience as a countryside Orthopaedic Surgeon



GLOBE 1998

Gruppo di Lavoro Ortopedia Basata su prove di Efficacia



2001 E-Musk1 *Hot Topic* “National Registres”

2000 SIOT – GLOBE *meeting* “The role for registries in EBM”

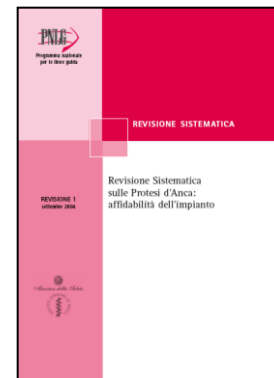
2001 EFORT Symposium “National Registers”

2002 SIOT – GLOBE *meeting* “Evidence-based hip prosthesis”

2003 EFORT *Special Symposium* “Evidence-based Surgery”

2004 Sistematic Review on hip implants for Italian NIH

2005 Hip National registry (board)



Cochrane Musculo Skeletal Group

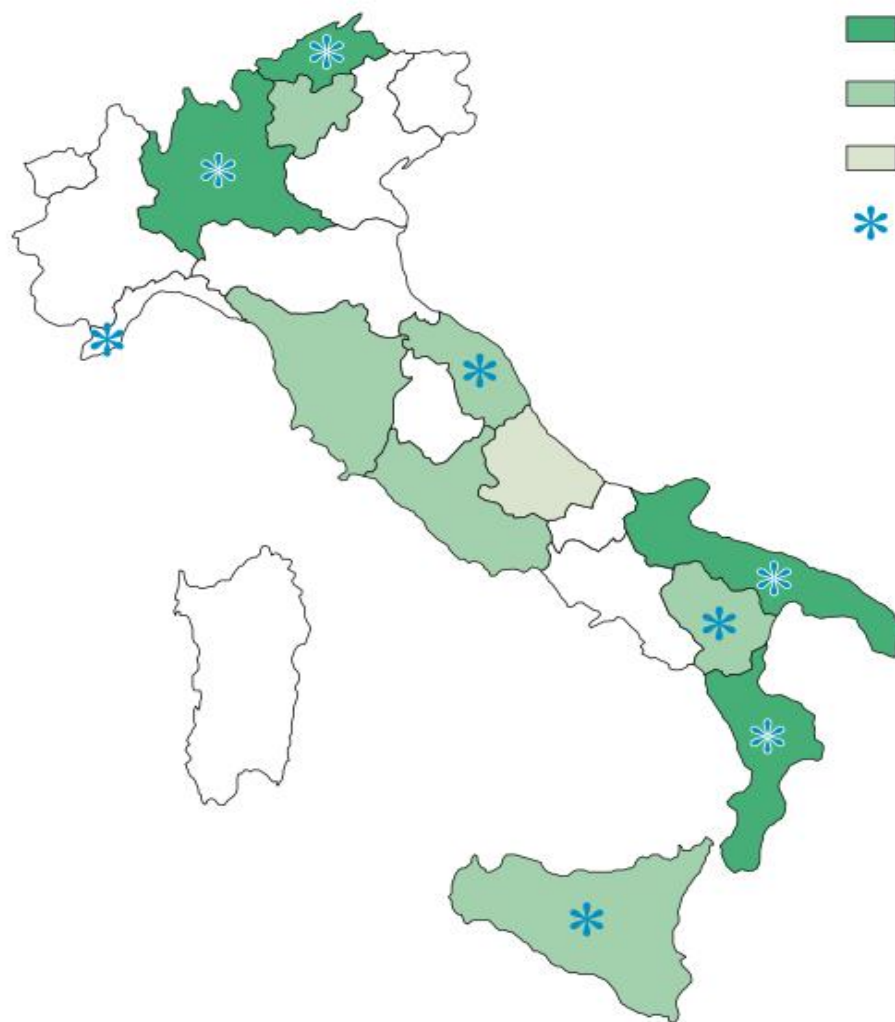


- **Since 2003: surgical editor**
- **(possibly the only available one)**
- **not the first one, though...and not alone anymore**



Registro Italiano Artroprotesi – RIAP

Regioni arruolate



- Partecipanti (Registro regionale/provinciale)
- Partecipanti
- Arruolamento nel 2014
- * Anca e Ginocchio

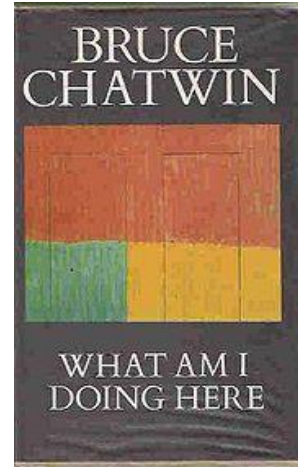


1st Report 2014

Disclosure

- **Private general orthopaedic surgeon**
 - Patients approx. 40%
 - NHS approx. 40%
 - Insurances approx. 20%
- **Teaching (0,5%)**
- **Voluntary research activity**
 - (Cochrane work is actually at my own costs...)
 - 5000€ from Janssen 2014
 - (occasional invitations, travel expenses)
 - Depuy, Stryker, Braun, Thornier etc. ...
 - **No travel funding for this trip**

What am I doing here?



- **Represent Cochrane**
 - What is Cochrane?
 - RCTs VS Registries
 - What can Cochrane do for Registries?
 - What can Registries do for Cochrane?
- Lessons learned from Italian Registry
- Experience as a countryside Orthopaedic Surgeon

Cochrane reviews & TJR

- More than 30 reviews
- Mostly non surgical
- Sparse
- Surgical ones very often inconclusive
 - No evidence: who's to blame?
 - Often not even quoting registries
 - Wrong questions no answers
- Overviews of Reviews?



RCTs in hip replacement 1988 vs 2010 vs 2016

Copyright 1988 by The Journal of Bone and Joint Surgery, Incorporated

A Critique of the Methodologies Used in Clinical Studies of Hip-Joint Arthroplasty Published in the English-Language Orthopaedic Literature*

BY MICHAEL GROSS, M.D., F.R.C.S., F.R.C.S.(C)†, HALIFAX, NOVA SCOTIA, CANADA

Gross JBJS Am 1988

it was concluded that adequate surgical trials should be completed before new procedures or new designs of prostheses, such as those used in hip-joint arthroplasty, are made available for general use.

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed

Arthroplasty, Replacement, Hip [Mesh]

[Display Settings:](#) ☒ Summary, 20 per page, Sorted by Recently Added

Limits Activated: Randomized Controlled Trial, published in the last 1 year

Results: 1 to 20 of 59
Romanini, estemporaneo 2010

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed

Arthroplasty, Replacement, Hip [Mesh]

[Display Settings:](#) ☒ Summary, 20 per page, Sorted by Recently Added

Limits Activated: Randomized Controlled Trial, published in the last 1 year

Results: 1 to 20 of 59
Zanoli, estemporaneo 2016

4 in 22 yrs (66-87)

59 in 12 months (09/10)

- Arthroplasty, Replacement, Hip [Mesh]
- last 1 year
- RCT, RS e metanalisi

79 in 12 months (07/16)

- Arthroplasty, Replacement, Hip [Mesh]
- last 1 year
- RCT, RS e metanalisi

79 RCTs in 1 year but...

Clinical questions:

- Anaesthesia, DVT, ecc.
- Rehab (types, timing)
- Surgical Access (MIS, navigation)
- Implant head to head comparison
- Surgical Indications

Raccomandazioni/prospettive

Non esistono attualmente indicazioni dall'analisi della letteratura che consentano di scegliere il miglior modello protesico per un determinato paziente e non è verosimile che tale informazione sarà disponibile in tempi brevi.

Esiste anche una domanda più radicale: gli RCT sono davvero il gold standard nella scelta degli impianti protesici? Saremmo disposti a utilizzare un determinato modello di protesi solo perché ha dato risultati migliori nei pazienti selezionati di un grande studio multicentrico, abbandonando il modello protesico che conosciamo da anni e che non ci ha mai traditi?



RCTs: problems in TJR



- long-distance outcomes (funding)
- Rare outcomes (like adverse events)
- Patient selection (inclusion/exclusion)
- Technical skills
 - difference between surgeons surgeon
 - different familiarity with techniques)
- Etical (sham o placebo-surgery)
- (too) Rapid innovation

Registers vs. (RCTs)

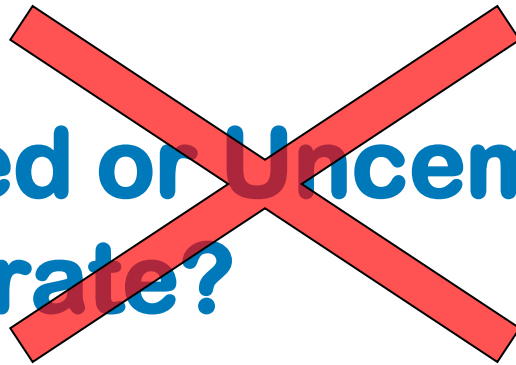
	% survival rate	% primary	% revisions
USA	98/100%	82,7%	17,3%
Sweden	94,8%	92,5%	7,5%

- **Sources:**
- **Robertson O. EFORT Meeting 2003 (mod)**
- **Wennberg JE. Dartmouth Atlas of Musculoskeletal Health Care. AHA Press; 2000**
- **Malchau H. Prognosis of total hip replacement AAOS Annual Meeting 2002**

RCTs and clinical questions in TJR

- Drain or not for blood loss?
- Tourniquet or not for blood loss?
- ...etc

- Cemented or Uncemented for revision rate?



What does the countryside Ortopaedic Surgeon need?

***“Politics rather than promising
paradise should avoid hell” (Mario Giro)***



**AFS – Intercultura centennial meeting
Trento e Rovereto May 1-3 2015**

What does the countryside Ortopaedic Surgeon need?

- A (short) list of implants that are:
 - widely used
 - with average good results
 - by average surgeons
- to choose from according to personal experience

“Surgeons rather than promising (or being promised) paradise should avoid hell” (GZ)

Evidence-based introduction of new technologies

- Citizens and health authorities should be interested in “avoiding hell”:
 - Inferior implants
 - Underperforming centers



Unhappy is the land that needs a hero

Il caso ASR/XL

- 2005: introduzione sul mercato (FDA)
- 2008: prime segnalazioni di fallimenti
- agosto 2010: richiamo volontario dell'azienda
- Ministero
- gennaio 2012: *striscia la notizia*



Il “caso”: recall mondiale di ASR e ASR XL (DePuy)

93.000 protesi impiantate nel mondo a partire dal 2003

(4.500 in Italia dal marzo 2004)

- 2005 eccessive revisioni segnalate da singoli chirurghi
- 2007 Registro australiano: RR a 2 anni 5.2% vs 2%
- 2009 ritiro dal mercato australiano
- 4/2010 Registro inglese: notifica a MHRA RR a 7 anni 12% vs 3%
- (MDA 2010/033 All MoM: alert)
- 5/2010 MDA 2010/044 ASR: Azioni per il f-up
- 8/2010 ASR ritiro volontario dal mercato mondiale. Avviso di sicurezza Ministero della Salute. Richiamo dei pazienti
- 9/2010 MDA 2010/069 ASR recall: divieto di impianto, richiamo dispositivi, informazione ai pazienti e attivazione f-up
- 2/2012 MDA 2012/008 All MoM: f-up pazienti
- 4/2012 MDA 2012/016 MITCH/Accolade stem: divieto di impianto
- 6/2012 MDA 2012/035 R3S&N metal liner: recall
- 6/2012 MDA 2012/036 All MoM updated f-up

CORRIERE DELLA SERA
Reumatologia

RITIRATE DAL COMMERCIO NEL 2010

Anca: un tipo di protesi «richiamata»
Ma non tutti gli interessati in Italia lo sanno

*Il caso DePuy ASR. Non tutti sono stati avvisati.
Il registro sugli interventi del ministero non è ancora partito*



MILANO - Non doveva creare allarmismi, ma evidentemente qualcosa non ha funzionato. Il ritiro dal mercato delle protesi d'anca DePuy modello ASR, cominciato un anno e mezzo fa sta ancora suscitando allarme tra i pazienti. Un servizio di Striscia



Medical Device Alert

Action

Ref: MDA/2010/044 Issued: 25 May 2010 at 14:30

Device

DePuy ASRTM acetabular cups used in hip resurfacing arthroplasty and total hip replacement.



Medical Device Alert

Immediate action / update

Ref: MDA/2010/069 Issued: 07 September 2010 at 13:00

Device

Medical Device Alert

Ref: MDA/2012/008 Issued: 28 February 2012 at 11:00

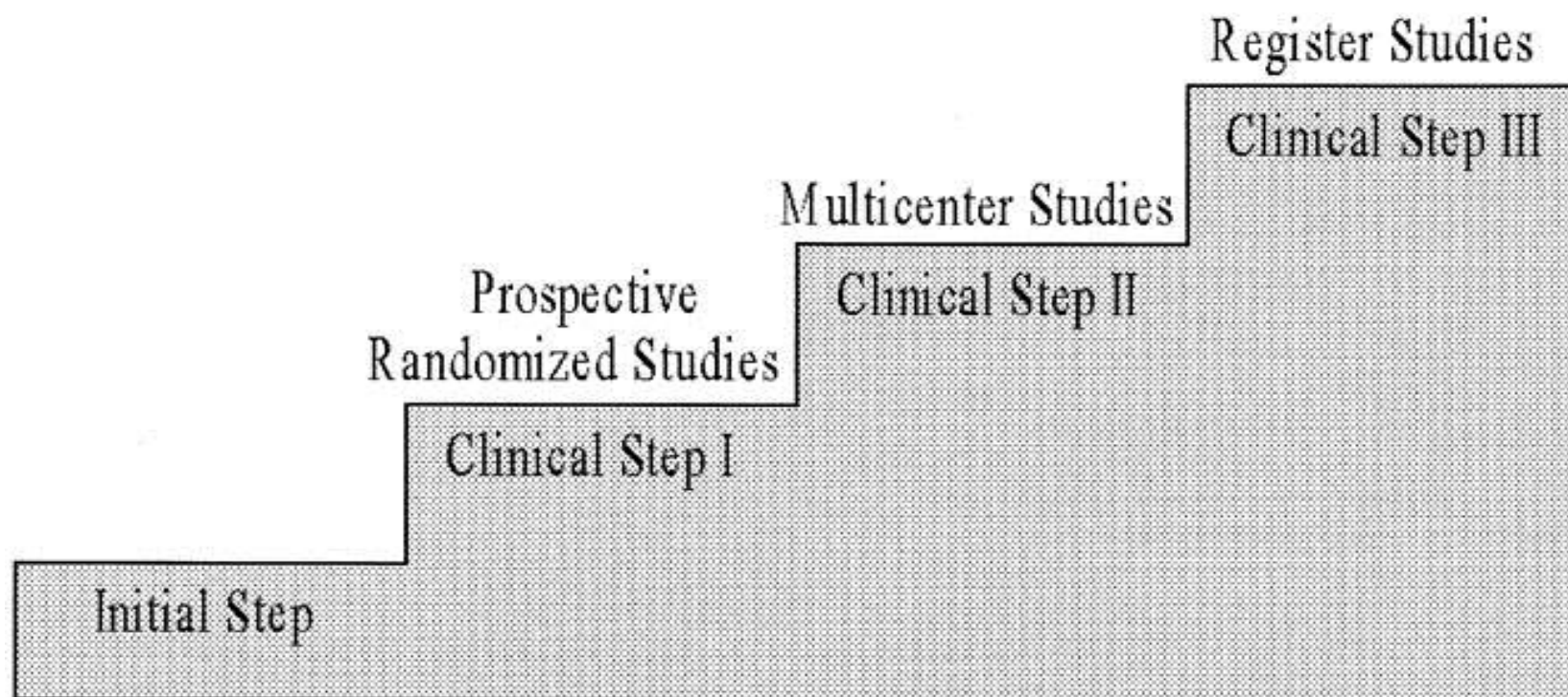
Device

All metal-on-metal (MoM) hip replacements

- The Changi TMH (total metal hip) does not exist. It is a large diameter metal-on-metal hip prosthesis invented by the *BMJ* and the *Daily Telegraph* to test Europe's systems for regulating high risk medical devices. It was modelled on an implant that has been described as one of the biggest disasters in orthopaedic History (*the just mentioned ASR total hip implant*)
- And it got clearance – CE marking

Stepwise introduction of new technologies

(Malchau, PhD Thesis 1995)



eMusk 2001

FRIDAY April 6th, 2001

14.00-15.00

Hot Topic: National Registries
(we have it/we would like to)

in collaboration with

stryker®

Howmedica

R. Pitto (Erlangen, D) - Joint Replacement Registry, Germany

A. Toni (Bologna, D) - Emilia-Romagna Joint Registry, Italy

H. Malchau (Göteborg, S) - Swedish Hip Registry

L. Ryd (Lund, S) - Swedish Knee Registry

B. Strömqvist (Lund, S) - Swedish Spine Registry

F. Anderson (Worcester, USA) - Hip and knee registry, U



SATURDAY April 7th, 2001

9.00-10.00

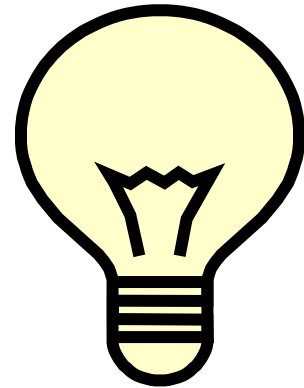
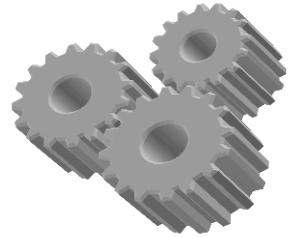
**Role of the Cochrane Collaboration
in Musculo-Skeletal Diseases**

Cochrane Groups:

- Back
- Musculo-skeletal
- Musculo-skeletal injuries
- Pain Pallative and Supportive Care

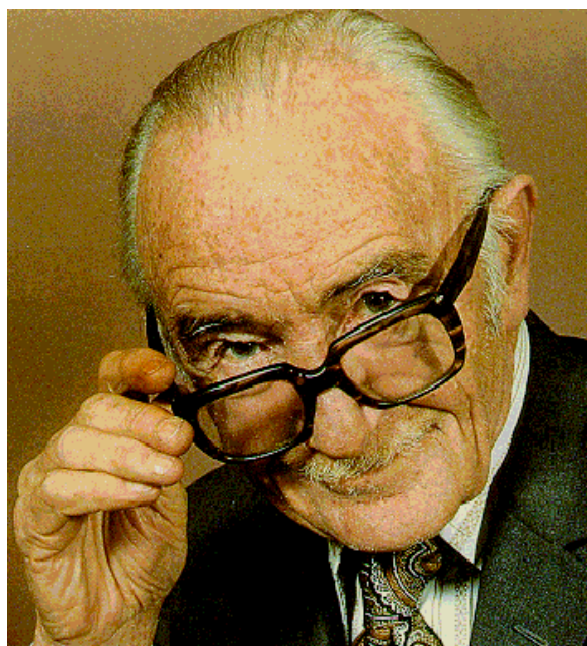
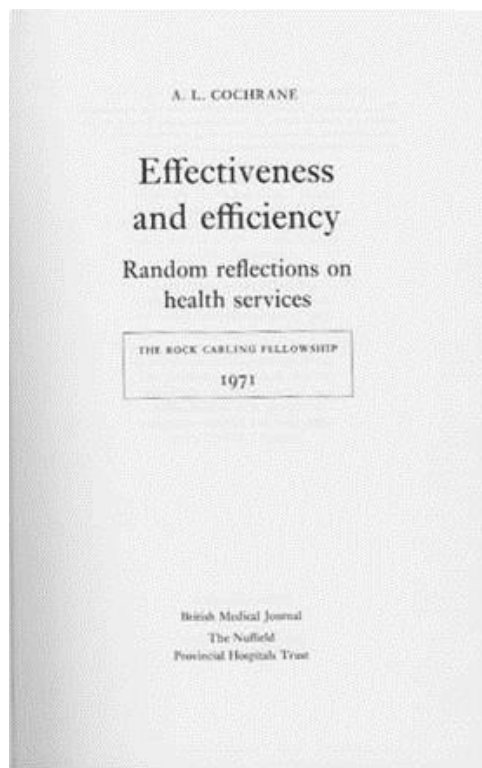
Towards an Ecology of Clinical Research

- RCTs = industrial revolution
positivistic, any answer is possible
- EBM: highest achievement and crisis
awareness of environmental effects
- Future of Clinical Research (EBM
driven): incorporate other types of
evidence



Zanoli Phd Thesis 2005

“... 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”



Archibald
Cochrane
Effectiveness & efficiency
1972

“... 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 **registry studies...**”



Gustavo
Zanolini
ISAR
2012

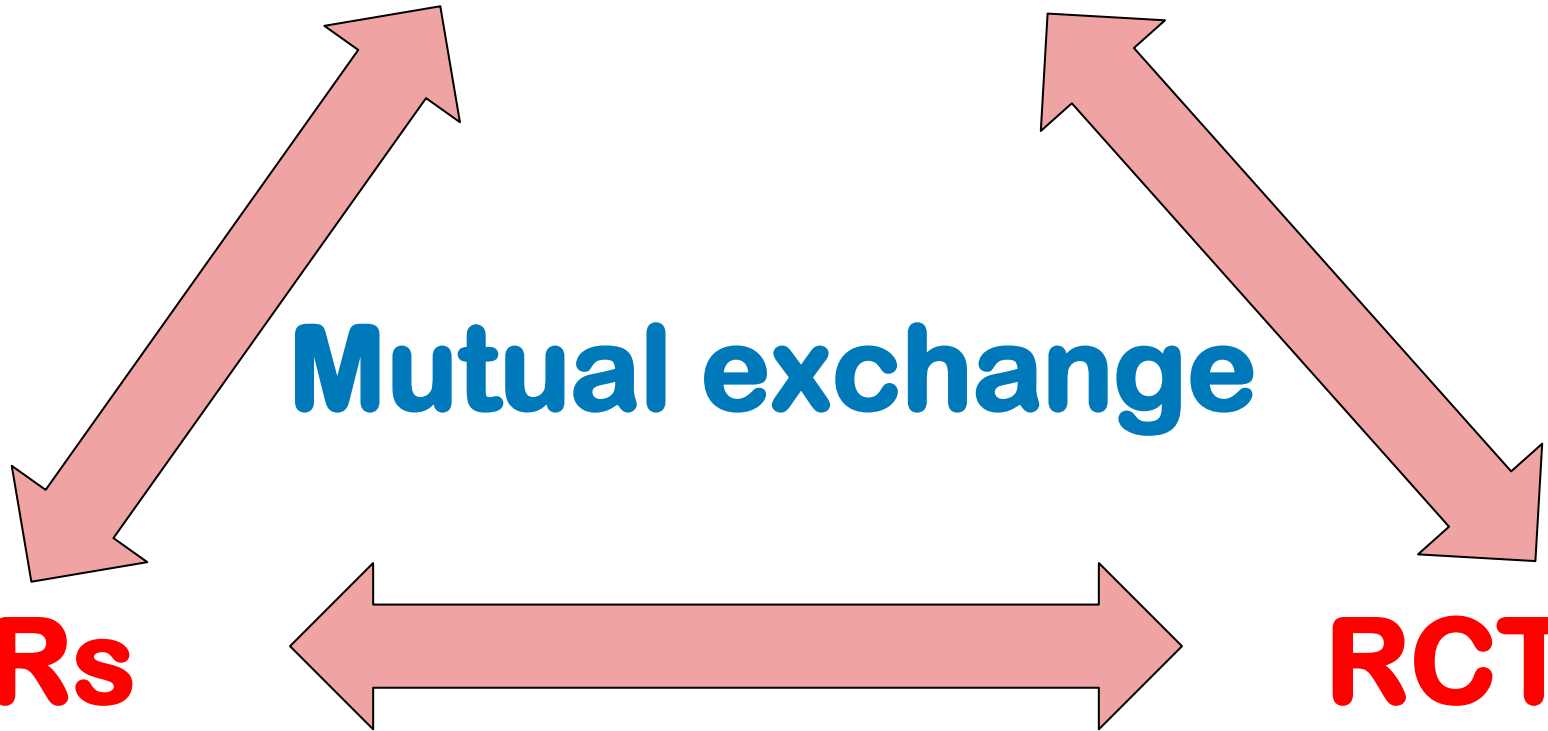
Links

Registries

Mutual exchange

SRs

RCTs



What's so good about Cochrane reviews?

- **Pros**

- Independent
- Transparent
- Overcome low sample sizes
- Visible, accessible, updated
- Methodologically sound

- **Cons**

- Far from real life situations?
 - Rare events & performance bias
- Slow
- Self-referring
- Not everywhere public access

What's so good about Arthroplasty Registries?

- **Pros**

- Independent
- Transparent
- Overcome low sample sizes
- **Close(r) to Real Life**
- **As fast as possible**

- **Cons**

- Visible, accessible, updated?
- Methodologically comparable?
- Self-referral

 **Difficult to establish (Regional first?)**

Registers achievement

- **Quality control**
 - **feedback**
- **Price control**
 - **transparency**
- **Innovation control**
 - **Good or bad?**
- **Rapid identification of failures**
 - **Metal on Metal (only the most recent)**



The Cochrane Collaboration on arthroplasty reviews and the role of evidence coming from registries.

A difficult but necessary way forward.

Gustavo Zanolì, Ferrara Italy

ISAR BERGEN 2012

What can we do together ?



What can Cochrane do for Registries?

- **Methodology**

- Focalize Research questions
- Harmonisation Of Registries
- Patients' involvement
- Meta-analysis

- **Dissemination**

- Well-known across Professionals, Administrators, Politicians & Media
- Publicly available (not everywhere for free, but authors can influence that)
- **Impact Factor!**

What can Registries do for Cochrane?

- **Methodology**

- **Focalize Research questions**
- **Choice of Outcomes**
- **Clinical interpretation (coauthors & advisory boards)**

- **Dissemination**

- **Well-known among Orthopaedic surgeons,**
- **Reliable real world data (even rare events)**

Registers & Cochrane (not exhaustive)

1. Advantages:

- Visibility, reference source, impact factor
- Accessibility, diffusion

2. Possibilities for collaboration

- Perform new SRs
- Advisory board, making sense out of reviews
- Outcome and format reporting standards
- Selection of clinical questions for RCTs or SR
- Simple citation in Cochrane SR vs. Link-out vs. ...?
- Incorporating Registry findings in “HARMS”
- Actually perform meta-analyses (ICOR?)

3. (Random) reflections or possible questions

- How do we solve disagreement in register studies?
- How do we meta-analyse register studies? (C Meth Gr)

4. More difficult questions

- Who owns the data? Authorships
- Funding

**Can someone else do it? Yes, of course.
But why not trying to use Cochrane?**

ICOR (lost occasion)



- **International Consortium of Orthopedic Registries**
 - **leverage data from existing registries**
 - **Advance methods to study device performance and patient outcomes**
 - **Help enhance and harmonize the registry data worldwide**
 - **Improve research collaboration**
- **FDA Public Workshop 2011**
- **35 registries present**
 - **All major stakeholders**

ICOR (someone did it)

ICOR

International Consortium of
Orthopaedic Registries

HOME

ABOUT US

PUBLICATIONS

RELATED LINKS

MEMBER LOGIN

► Publications

ICOR is a collaborative effort that brings together leaders in implant device regulatory research from around the world. Below you will find articles, presentations and op-ed pieces published as a result of this collaboration.

- So far more than 25 publications based on aggregated data from several registries, especially the Nordic countries, UK, Australia and a regional US based registry
- All with documented data quality
- All after an attempt to harmonize data and statistical methods

Guest Editorial

The next critical role of orthopedic registries

Henrik Malchau

*Harris Orthopaedic Laboratory, Orthopedics Department,
Massachusetts General Hospital, Boston, MA, USA;
Department of Orthopedics, Sahlgrenska University
Hospital, Mölndal, Sweden
E-mail: hmalchau@mgh.harvard.edu*

Stephen E Graves

*Australian Orthopaedic Association National Joint
Replacement Registry, Adelaide;
Department of Surgery, Flinders University, Adelaide,
Australia*

Martyn Porter

Wrightington Hospital, Wigan, Lancashire, UK

William H Harris

*Harris Orthopaedic Laboratory, Orthopedics Department,
Massachusetts General Hospital, Boston, MA, USA*

Anders Troelsen

*Department of Orthopaedic Surgery, Clinical Orthopaedic
Research Hvidovre – CORH, Copenhagen University
Hospital Hvidovre, Copenhagen, Denmark*

Guest Editorial

The next critical role of orthopedic registries

- **The registries should not undertake the role of a regulatory authority, but in compliance with the industry and the orthopedic community they should ensure that a more cautious approach is used when new technology is introduced.**
- **This could lead to a better balance between the inborn conservatism that a registry represents and the continuous need for innovation.**

Guest Editorial

The next critical role of orthopedic registries

- 1. a pure observational study using reoperation data from multiple registries, as shown in several papers by the Nordic Arthroplasty Register Association (NARA)**
- 2. patient-reported outcome measures, either from national implant registries or from other registries for specific studies**
- 3. radiographic data plus other parameters such as blood levels of metal ions, based on specific needs for a new technology;**
- 4. options for randomized studies with use of, for example, RSA in the evaluation.**

And Cochrane?

- Still a great amount of methodological work to do
- Why not “nested studies” within protocols of future SRs?

Cochrane MSK Group & Registries' evidence

- Already including evidence from Registries for Harms endpoints
- Just starting a new transverse special interest group on Registries “COUGAR” :
 - COchrane Unified Group on Arthroplasty Registries
- Different types of Reviews Cochrane?



Ferrara Earthquake May 2012



- Many things we cannot control (like in Registries)
- Predictions (like RCTs) are there to be disconfirmed (e.g. never hot in Rome)
- This doesn't mean we should not try to prepare ourselves
- (Be RESILIENT!)

Degrowth

1. End of the low-cost fossil fuel ERA
2. Climate Changes
3. Economic (& moral) Crises

BMJ 2002;324:859-860 (13 April)

Editorials

Too much medicine?

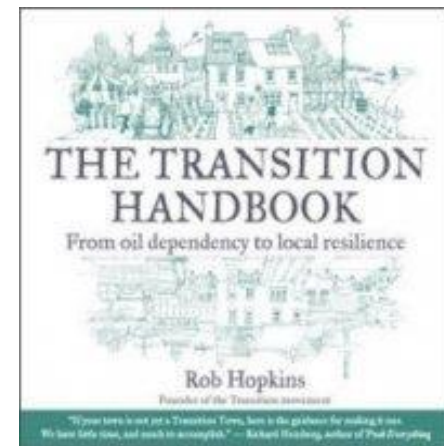
Almost certainly

• www.transitiontowns.org

→ **Resilient Medicine:**

- New Age alchemies or evidence-based choices?
- [back or forward?]
- System re-thinking,

lateral thinking



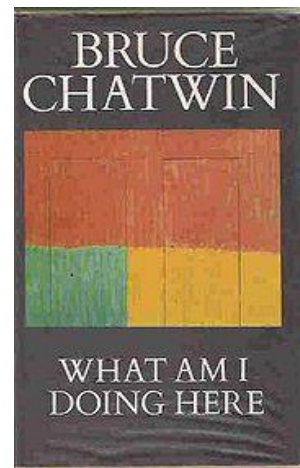
Car vs. Bike (Ivan Illich)



• ...time for some pedalling!

Take home points

- Surgeons (and patients, and health authorities) need evidence in TJA
- SRs of RCTs are not enough
- Registries' information is not easily accessible
- Cochrane & ISAR (and ICOR, and ISS, and...) can play a major role in driving evidence-based practice.
- Cochrane is prepared but needs “encouragement”...



Investment needed

- Easily repayable in few years with less complications, less failures etc
- High benefit/cost ratio
- (depends on who's paying the costs)



00:00



GRAZIE

EBASIE

Introduzione delle nuove tecnologie basata su evidenze: revisioni Cochrane e registri

Gustavo Zanolì

zanolig@me.com

