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EVIDENCE FOR HEALTH

Aumentare il *value* delle risorse investite nella ricerca biomedica
La campagna Lancet-REWARD
Bologna, 9 novembre 2016

Raccomandazioni REWARD

Sessione I
Rilevanza delle priorità di ricerca

DISCUSSANT

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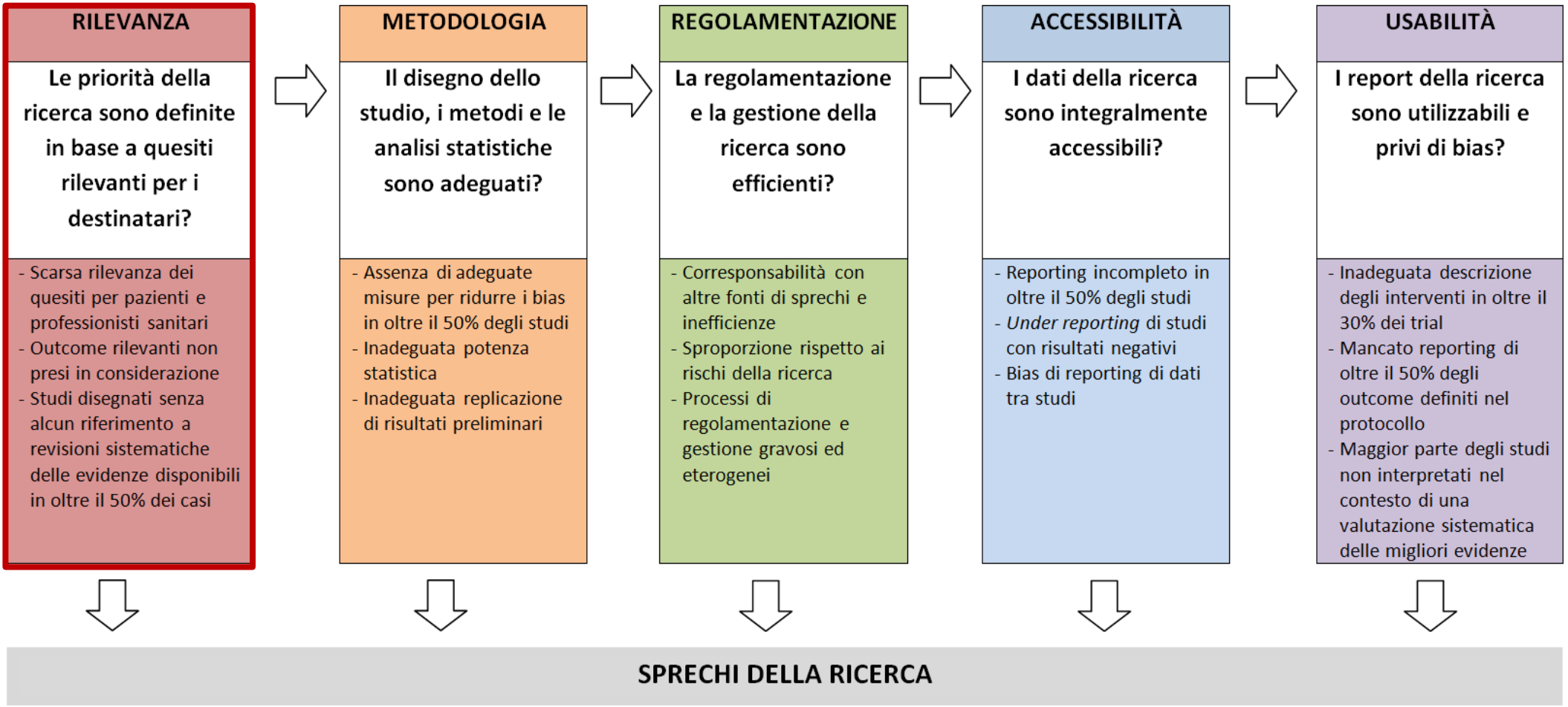

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How to increase value and reduce waste when research priorities are set

Iain Chalmers, Michael B Bracken, Ben Djulbegovic, Silvio Garattini, Jonathan Grant, A Metin Gülmezoglu, David W Howells, John P A Ioannidis, Sandy Oliver

Recommendations

1 More research on research should be done to identify factors associated with successful replication of basic research and translation to application in health care, and how to achieve the most productive ratio of basic to applied research
   - Monitoring—periodic surveys of the distribution of funding for research and analyses of yields from basic research

2 Research funders should make information available about how they decide what research to support, and fund investigations of the effects of initiatives to engage potential users of research in research prioritisation
   - Monitoring—periodic surveys of information on research funders' websites about their principles and methods used to decide what research to support

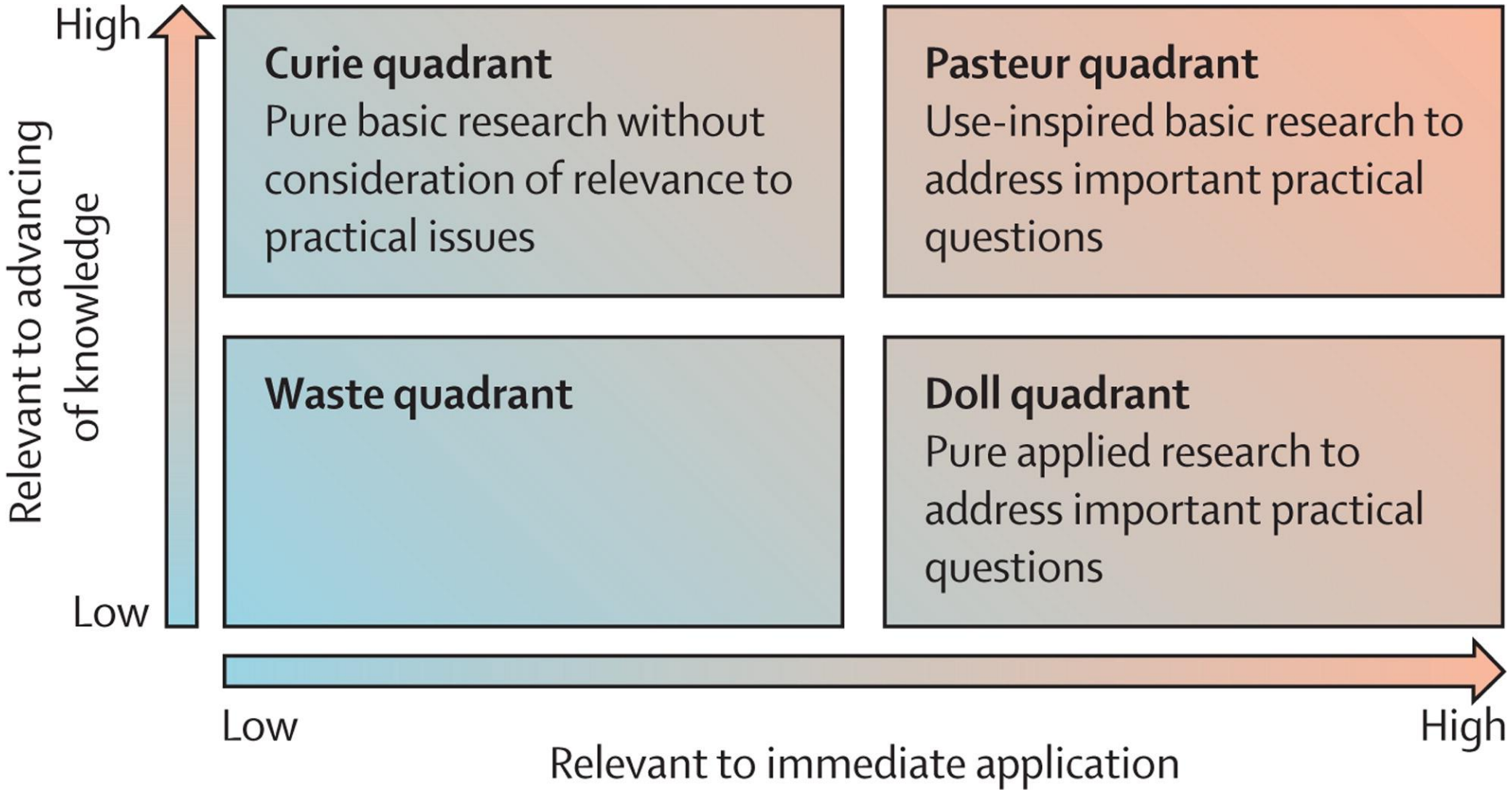
3 Research funders and regulators should demand that proposals for additional primary research are justified by systematic reviews showing what is already known, and increase funding for the required syntheses of existing evidence
   - Monitoring—audit proposals for and reports of new primary research

4 Research funders and research regulators should strengthen and develop sources of information about research that is in progress, ensure that they are used by researchers, insist on publication of protocols at study inception, and encourage collaboration to reduce waste
   - Monitoring—periodic surveys of progress in publishing protocols and analyses to expose redundant research

RILEVANZA

Le priorità della ricerca sono definite in base a quesiti rilevanti per i destinatari?

- Scarsa rilevanza dei quesiti per pazienti e professionisti sanitari
- Outcome rilevanti non presi in considerazione
- Studi disegnati senza alcun riferimento a revisioni sistematiche delle evidenze disponibili in oltre il 50% dei casi



Translation of Highly Promising Basic Science Research into Clinical Applications

Despina G. Contopoulos-Ioannidis, MD, Evangelia E. Ntzani, MD, John P. A. Ioannidis, MD

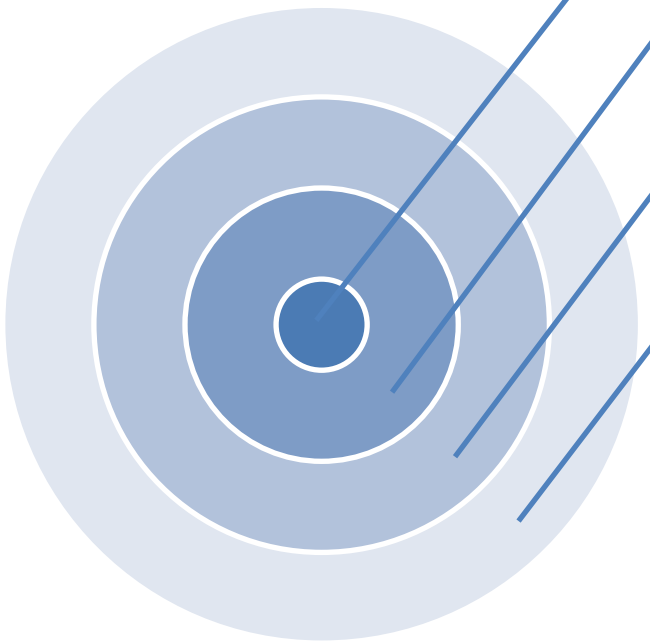
PURPOSE: To evaluate the predictors of and time taken for the translation of highly promising basic research into clinical experimentation and use.

METHODS: We identified 101 articles, published between 1979 and 1983 in six major basic science journals, which clearly stated that the technology studied had novel therapeutic or preventive promises. Each case was evaluated for whether the promising finding resulted in relevant randomized controlled trials and clinical use. Main outcomes included the time to published trials, time to published trials with favorable results ("positive" trials), and licensed clinical use.

RESULTS: By October 2002, 27 of the promising technologies had resulted in at least one published randomized trial, 19 of which had led to the publication of at least one positive randomized trial. Five basic science findings are currently licensed for clinical use, but only one has been used extensively for the licensed indications. Promising technologies that did not lead to a published human study within 10 to 12 years were unlikely to be tested in humans subsequently. Some form of industry involvement in the basic science publication was the strongest predictor of clinical experimentation, accelerating the process by about eightfold (95% confidence interval: 3 to 19) when an author had industry affiliations.

CONCLUSION: Even the most promising findings of basic research take a long time to translate into clinical experimentation, and adoption in clinical practice is rare. **Am J Med. 2003; 114:477–484.**

L'inefficienza della ricerca di base



1 intervention used widely

5 resulted in licensed clinical interventions by 2003

101 claimed that new discoveries had clear clinical potential

>25,000 reports in 6 basic science journals 1979-83

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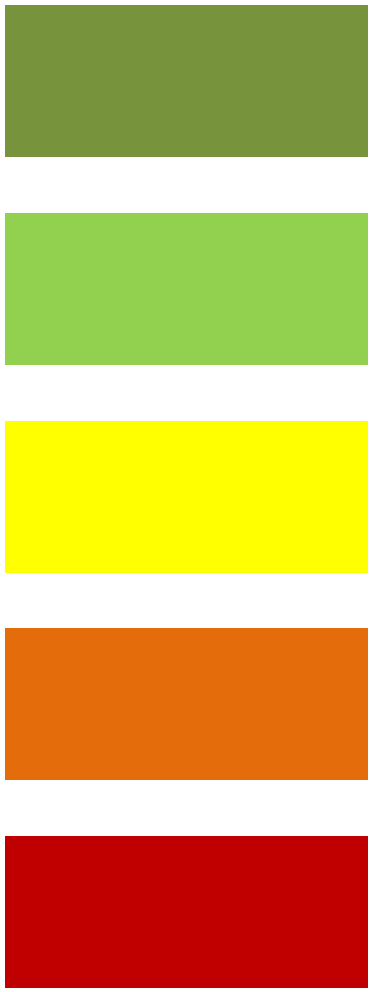
Priorità raccomandazioni REWARD



5= Indispensabile

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RILEVANZA

1. Sarebbe opportuno condurre un numero maggiore di studi per identificare:

- i fattori associati al successo della riproducibilità della ricerca di base e al trasferimento delle evidenze all'assistenza sanitaria
- le modalità per raggiungere l'equilibrio ottimale tra ricerca di base e ricerca applicata

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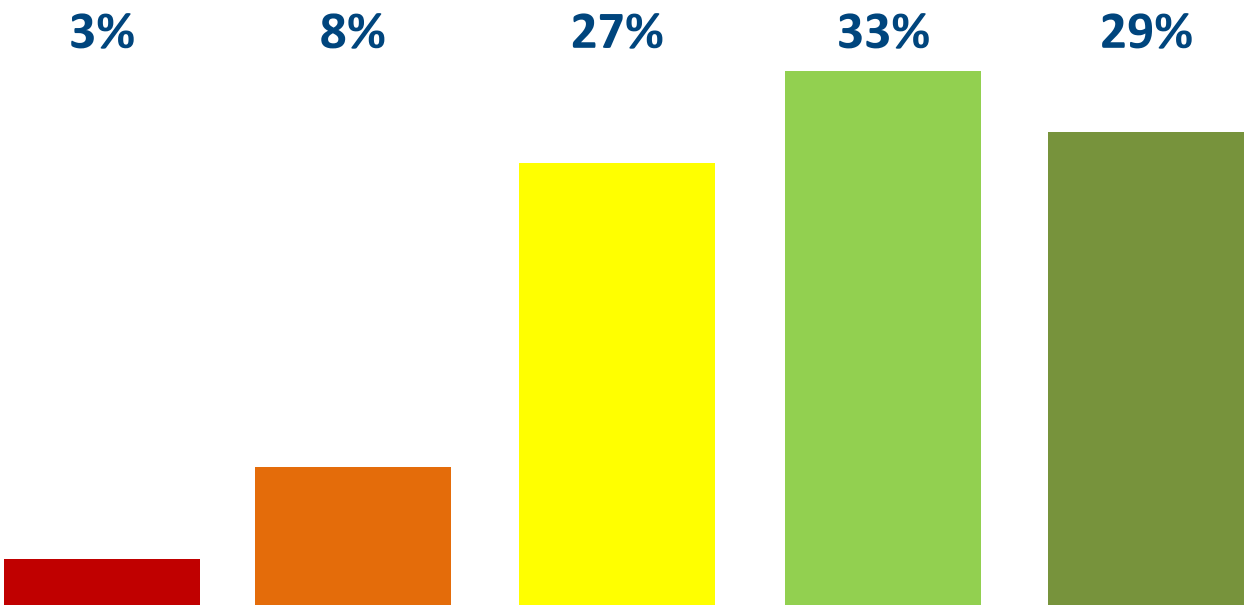
Raccomandazione 1

Media	DS
3.77	± 1.05



Domecq et al. BMC Health Services Research 2014, 14:89
http://www.biomedcentral.com/1472-6963/14/89

BMC
Health Services Research

RESEARCH ARTICLE Open Access

Patient engagement in research: a systematic review

Juan Pablo Domecq[1,2,5], Gabriela Prutsky[1,2,5], Tarig Elraiyah[1,5], Zhen Wang[1,5,6], Mohammed Nabhan[1,5], Nathan Shippee[1,5,6], Juan Pablo Brito[1,4,5], Kasey Boehmer[1,5], Rim Hasan[1,5,8], Belal Firwana[1,5,8], Patricia Erwin[1,7], David Eton[1,5,6], Jeff Sloan[1,5,6], Victor Montori[1,2,4,5,6], Noor Asi[1,5], Abd Moain Abu Dabrh[1,5] and Mohammad Hassan Murad[1,3,5,6*]

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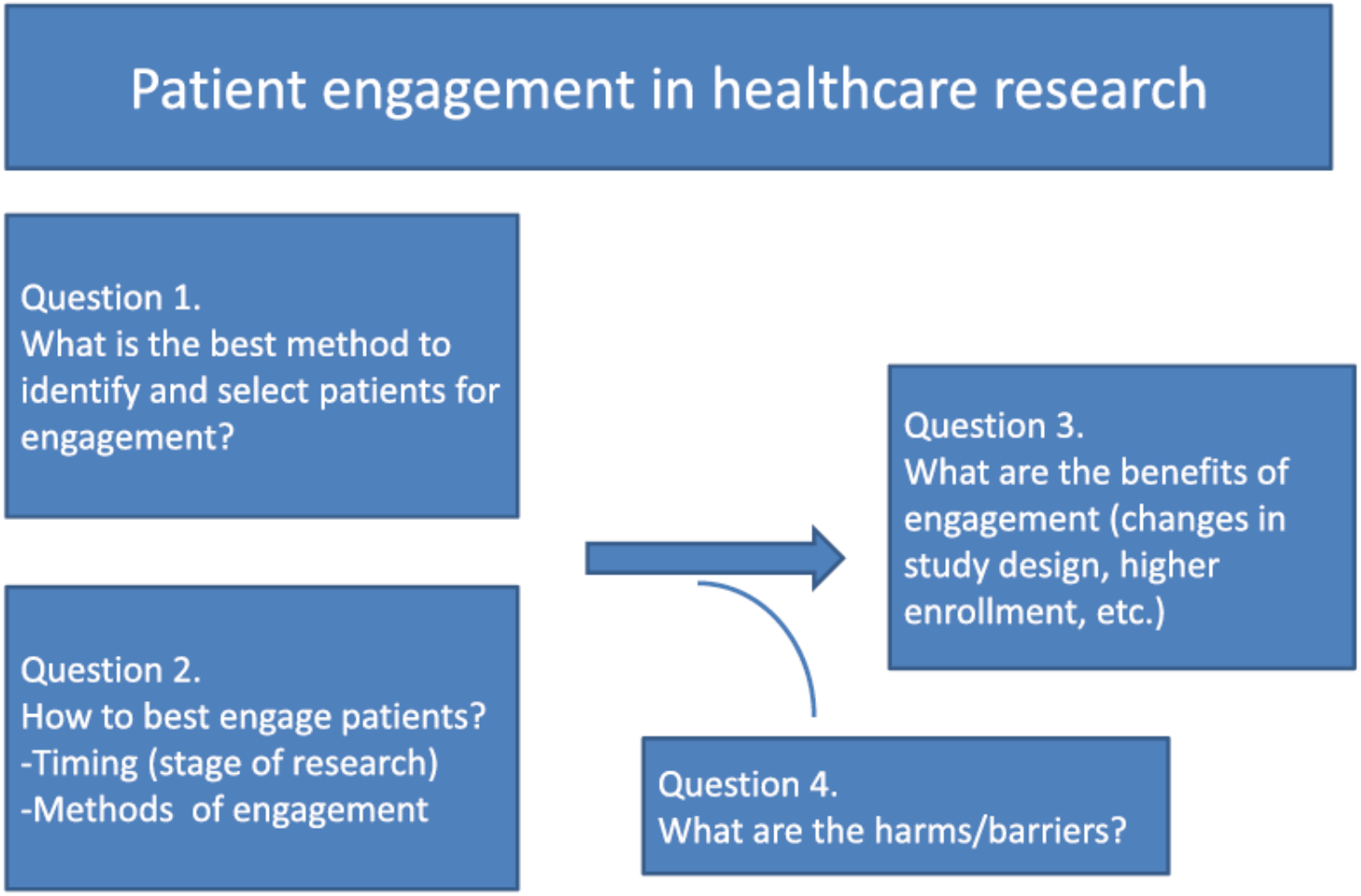
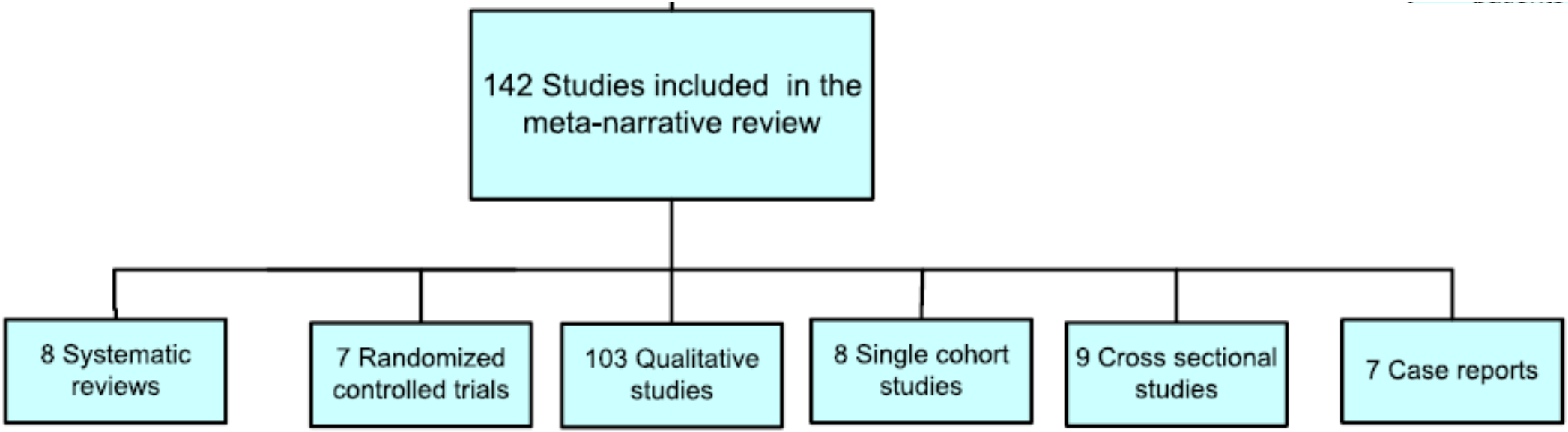


Figure 1 Analytical framework.



Conclusions: Patient engagement in healthcare research is likely feasible in many settings. However, this engagement comes at a cost and can become tokenistic. Research dedicated to identifying the best methods to achieve engagement is lacking and clearly needed.

Il **coinvolgimento nella ricerca**. Stiamo ancora inventando la ruota?

L'apporto che i cittadini possono dare al disegno e allo svolgimento degli studi clinici è fondamentale. Ma ancora non è chiaro come tradurre in pratica questa necessità.

Cristina Da Rold

Quello che manca è la sintesi, e in questo senso la revisione suggerisce una possibile strada per affrontare questo problema. Uno studio che valuti in parallelo tre approcci: quello che non comprende il coinvolgimento del paziente, quello che comprende il coinvolgimento di pazienti selezionati fra chi soffre della stessa patologia che è materia dello studio, e un terzo approccio, quello che vede cioè il coinvolgimento di pazienti indipendentemente dalla patologia su cui si focalizza lo studio.

James Lind Alliance

Priority Setting Partnerships

The James Lind Alliance

The James Lind Alliance (JLA) is a non-profit making initiative established in 2004. It brings patients, carers and clinicians together in Priority Setting Partnerships (PSPs) to identify and prioritise the Top 10 uncertainties, or unanswered questions, about the effects of treatments.

The aim of this is to make sure that health research funders are aware of the issues that matter most to patients and clinicians.

The PSPs

Top 10s

The JLA Guidebook

James Lind Alliance
Priority Setting Partnerships

The James Lind Alliance Guidebook

Version 6

February 2016

James Lind Alliance

Priority Setting Partnerships

Top 10s of priorities for research

The final workshop of a Priority Setting Partnership (PSP) enables patients, carers and clinicians to agree on the order of priority of a shortlist of unanswered questions. The main focus of the workshop is to agree the list of the Top 10 priorities for future research.

Acne (2014)	Kidney Transplant (2016)
Anaesthesia and Perioperative Care (2015)	Lyme Disease (2012)
Asthma (2007)	Mesothelioma (2014)
Autism (2016)	Mild to Moderate Hearing Loss (2015)
Bipolar (2016)	Multiple Sclerosis (2013)
Cavernoma (2015)	Neuro-oncology (2015)
Childhood Disability (2014)	Palliative and end of life care (2015)
Cleft Lip and Palate (2012)	Parkinson's (2014)
Dementia (2013)	Pressure Ulcers (2013)
Depression (2016)	Preterm Birth (2014)
Diabetes (Type 1) (2011)	Prostate Cancer (2010)
Ear, Nose and Throat (Aspects of Balance) (2011)	Schizophrenia (2011)
Early Hip and Knee Osteoarthritis (2016)	Sight Loss and Vision (2013)
Eating Disorders (Netherlands) (2016)	Spinal Cord Injury (2014)
Eczema (2012)	Stillbirth (2015)
Hair Loss (2015)	Surgery for Common Shoulder Problems (2015)
Hidradenitis Suppurativa (2013)	Stroke in Scotland (2011)
Hip & Knee Replacement for Osteoarthritis (2014)	Tinnitus (2012)
Inflammatory Bowel Disease (2015)	Urinary Incontinence (2008)
Intensive Care (2014)	Vitiligo (2010)
Kidney Cancer (Canada) (2015)	Womb Cancer (2016)

James Lind Alliance

Priority Setting Partnerships

Autism Top 10

1. Which interventions improve mental health or reduce mental health problems in autistic people? How should mental health interventions be adapted for the needs of autistic people?
2. Which interventions are effective in the development of communication/language skills in autism?
3. What are the most effective ways to support/provide social care for autistic adults?
4. Which interventions reduce anxiety in autistic people?
5. Which environments/supports are most appropriate in terms of achieving the best education/ life/ social skills outcomes in autistic people?
6. How can parents and family members be supported/educated to care for and better understand an autistic relative?
7. How can autism diagnostic criteria be made more relevant for the adult population? And how do we ensure that autistic adults are appropriately diagnosed?
8. How can we encourage employers to apply person-centred interventions & support to help autistic people maximise their potential and performance in the workplace?
9. How can sensory processing in autism be better understood?
10. How should service delivery for autistic people be improved and adapted in order to meet their needs?

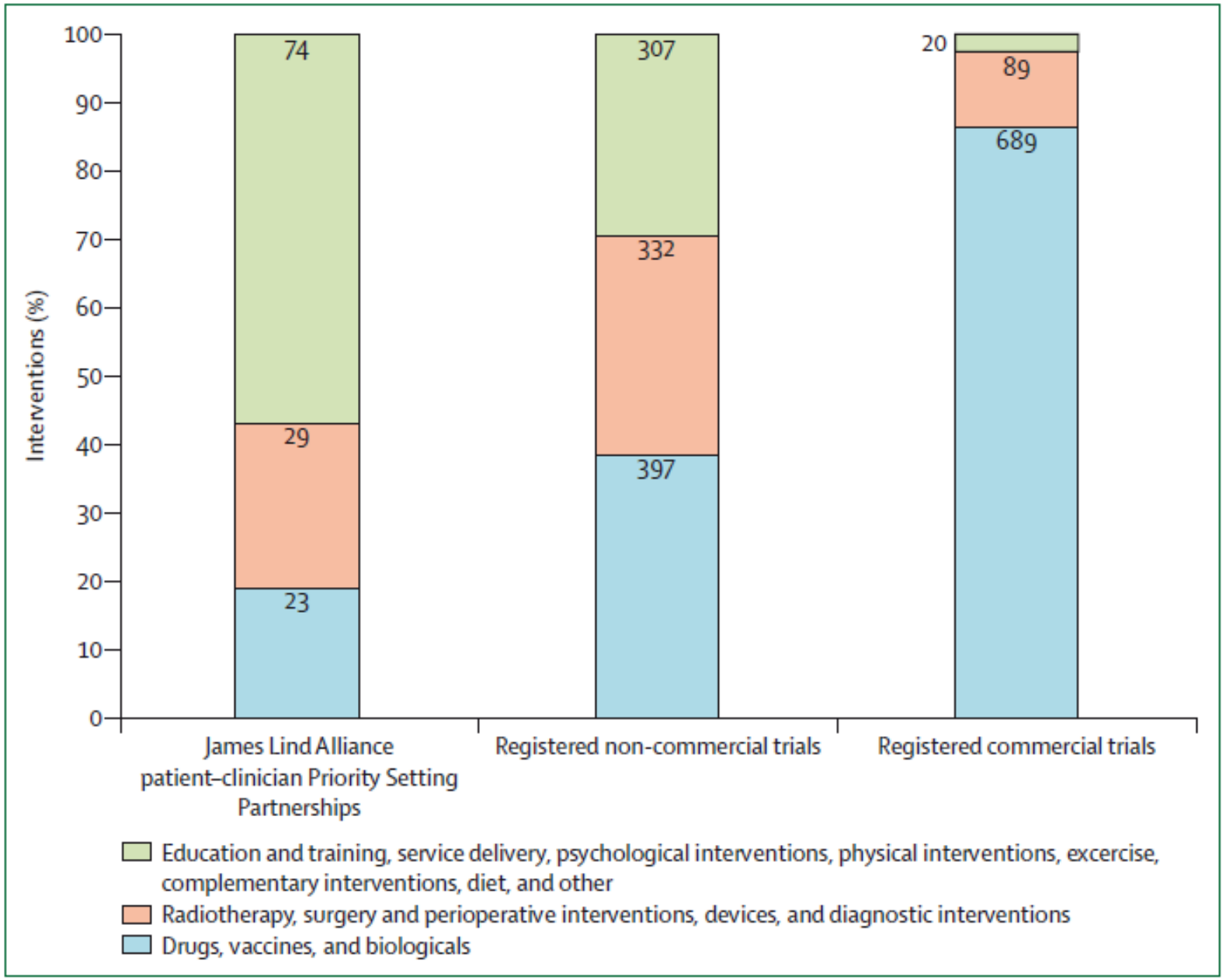
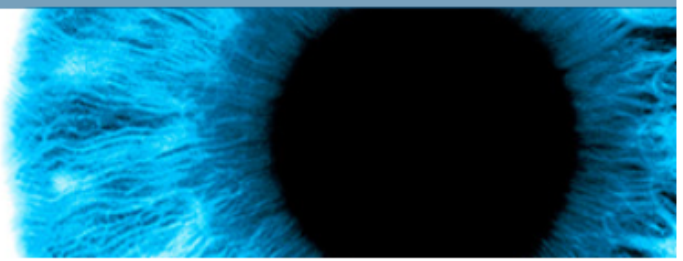


Figure 2: **Interventions mentioned in research priorities identified by James Lind Alliance patient–clinician Priority Setting Partnerships[90] and in registered trials, 2003–12**

NICE

From 1 January 2016 NICE is no longer maintaining the UK DUETs website. To search for up-to-date research uncertainties please go to NICE Evidence search

DUETs



UK DUETs

UK DUETs: where uncertainties about the effects of treatment are collected and published

From 1 January 2016 NICE is no longer maintaining the UK DUETs website. To search for up-to-date research uncertainties please go to NICE Evidence search.

What is UK DUETs?

The UK Database of Uncertainties about the Effects of Treatments (UK DUETs) publishes treatment uncertainties from patients, carers, clinicians, and from research recommendations, covering a wide variety of health problems.

James Lind Alliance Priority Setting Partnerships (PSPs) have prioritised the uncertainties for the conditions listed below. To see these uncertainties click on the topics or go to the JLA Website to see the Top 10 in ranked order.

Anaesthesia
Asthma
Balance
Brain and spinal cavernomas
Childhood disability

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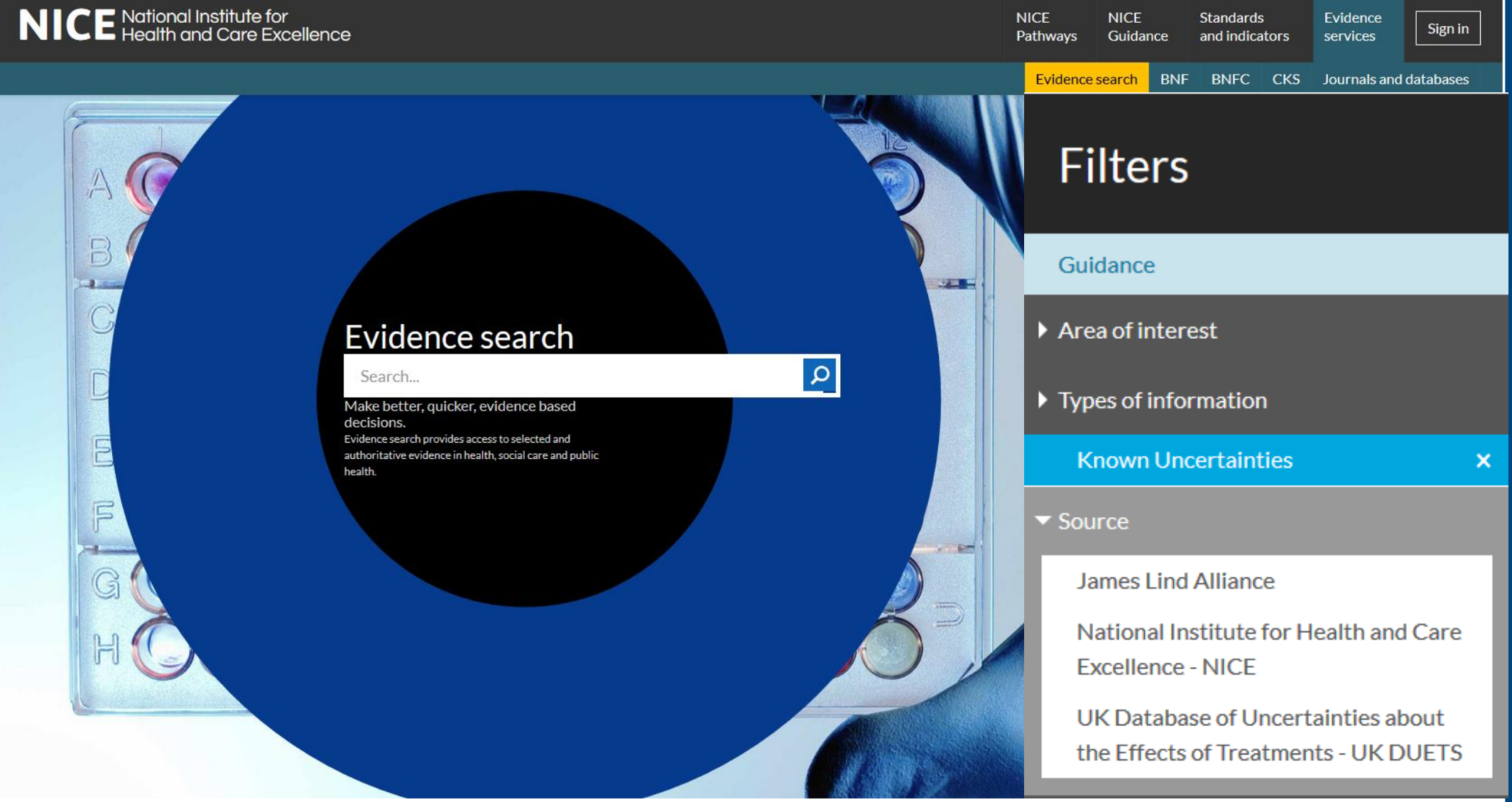

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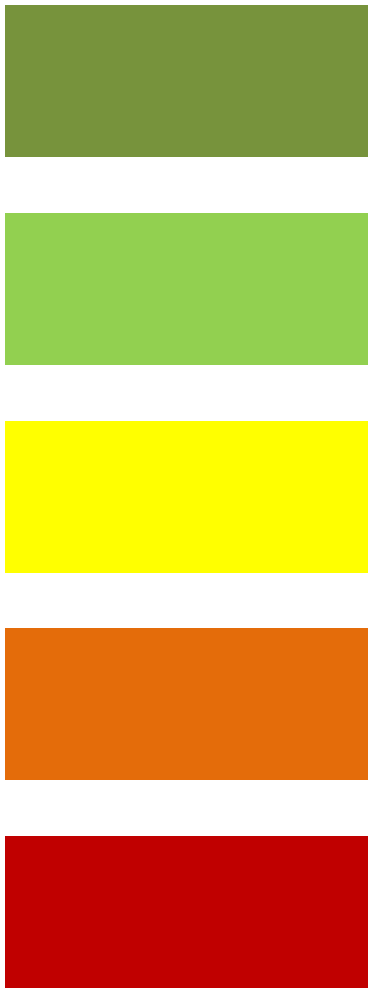
Priorità raccomandazioni REWARD



5= Indispensabile

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2. I finanziatori dovrebbero:

- rendere esplicite le modalità con cui selezionano gli studi da finanziare
- finanziare studi per valutare l'efficacia del coinvolgimento dei potenziali utilizzatori della ricerca nella definizione delle priorità

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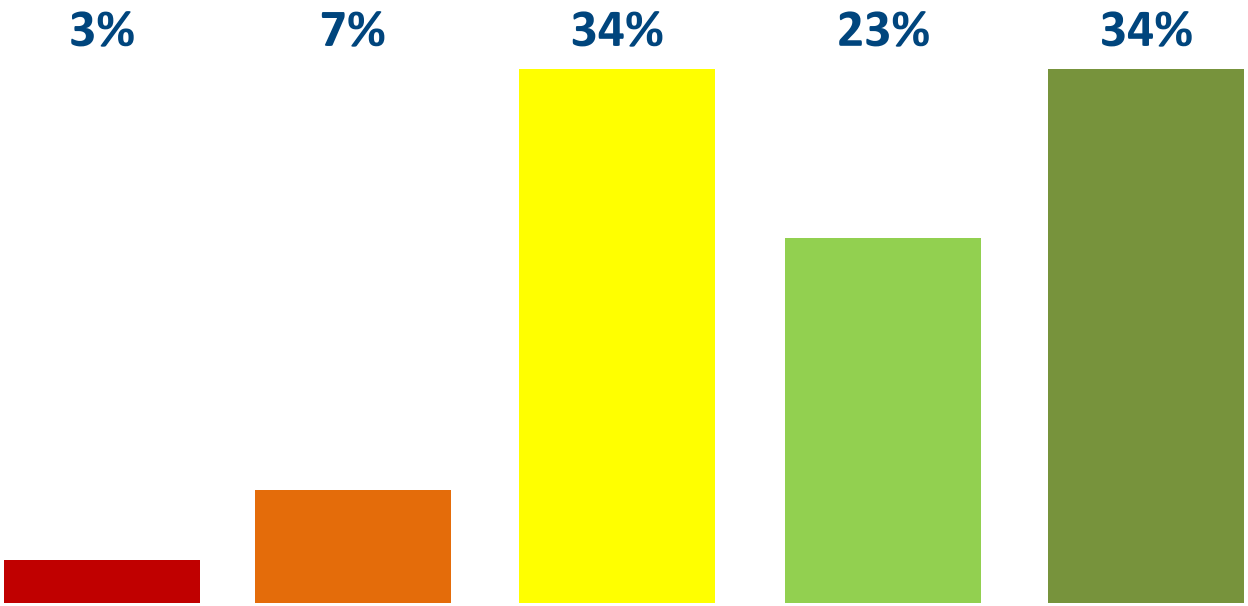
Raccomandazione 2

Media	DS
3.78	± 1.07



Limitato riferimento a revisioni sistematiche

	May, 2009 (n=29)	May, 2012 (n=35)
Claims that clinical trial is the first to address the question	5	5
Contains an updated systematic review that was used to inform trial design	1	1
Previous systematic review* discussed that was not used in trial design	10	13
Contains references to other randomised trials	4	10
Does not contain references to other randomised trials or claim to be the first trial	9	6

Analysis of reports published in *The Lancet*, *New England Journal of Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, and *Annals of Internal Medicine*.[64] *Systematic review in the topic area of the trial cited.

Table 2: **Analysis of Introduction sections of reports of controlled trials published in five medical journals in May, 2009, and May, 2012**

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A new network to promote evidence-based research

*Iain Chalmers, Magne Nylenna
James Lind Initiative, Oxford OX2 7LG, UK (IC); and The Norwegian Knowledge Centre for the Health Services, Oslo, Norway (MN)

www.thelancet.com Vol 384 November 29, 2014

The Evidence-Based Research Network

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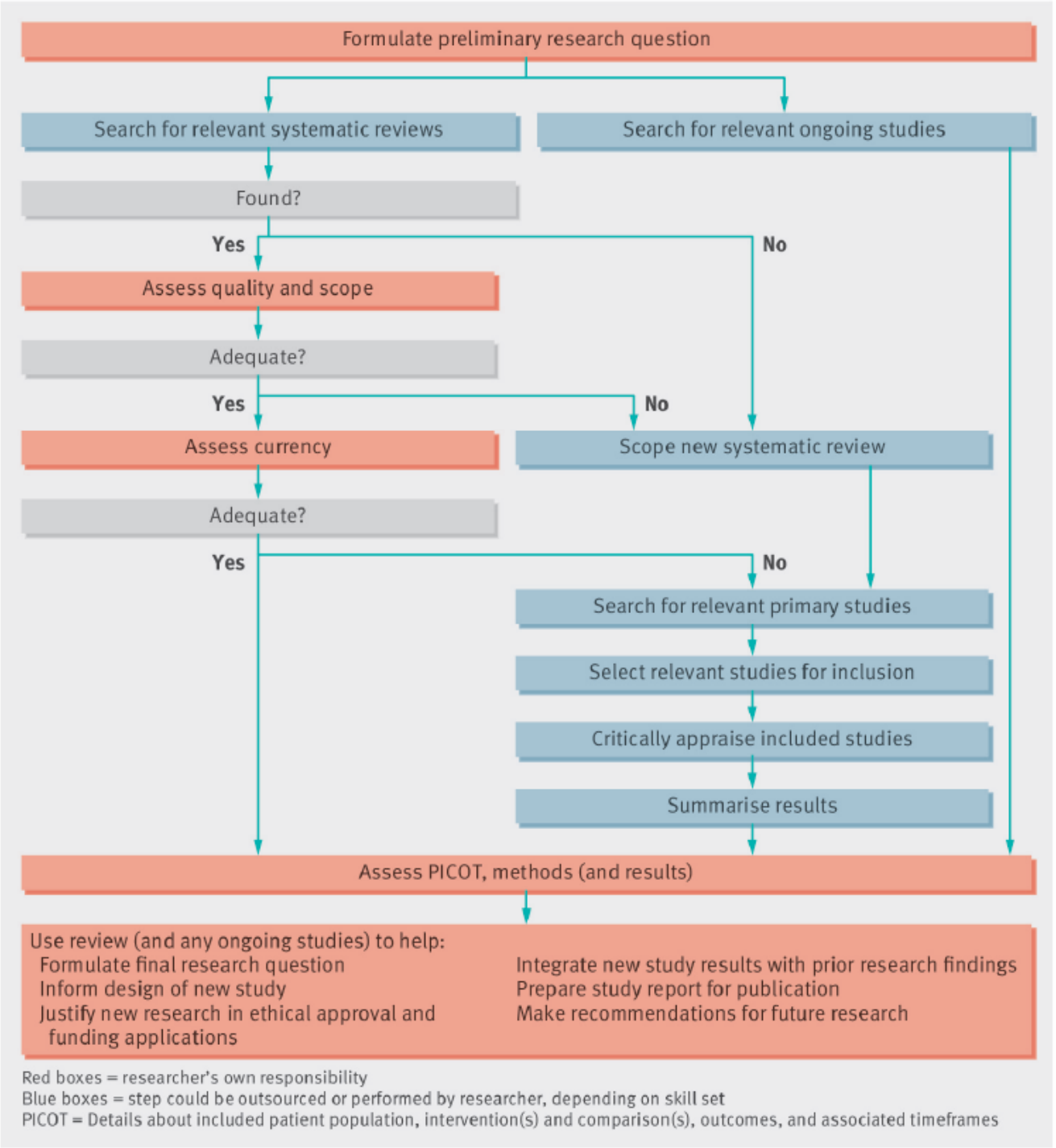
ANALYSIS

Towards evidence based research

To avoid waste of research, no new studies should be done without a systematic review of existing evidence, argue **Hans Lund and colleagues**

Hans Lund *professor*[1 2], Klara Brunnhuber *product manager*[3], Carsten Juhl *associate professor*[1 4], Karen Robinson *associate professor*[5], Marlies Leenaars *associate professor*[6], Bertil F Dorch *director*[7], Gro Jamtvedt *dean*[2 8], Monica W Nortvedt *dean*[2], Robin Christensen *professor*[9], Iain Chalmers *coordinator*[10]



Red boxes = researcher's own responsibility
Blue boxes = step could be outsourced or performed by researcher, depending on skill set
PICOT = Details about included patient population, intervention(s) and comparison(s), outcomes, and associated timeframes

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Key message

- Embarking on research without reviewing systematically what is already known, particularly when the research involves people or animals, is unethical, unscientific, and wasteful
- A systematic review of relevant evidence can establish whether the proposed research is truly needed
- Some research funders now require applicants to refer to a systematic review of existing research
- Research waste can also be reduced by efficient production, updating, and dissemination of systematic reviews

THE
MILBANK QUARTERLY
A MULTIDISCIPLINARY JOURNAL OF POPULATION HEALTH AND HEALTH POLICY

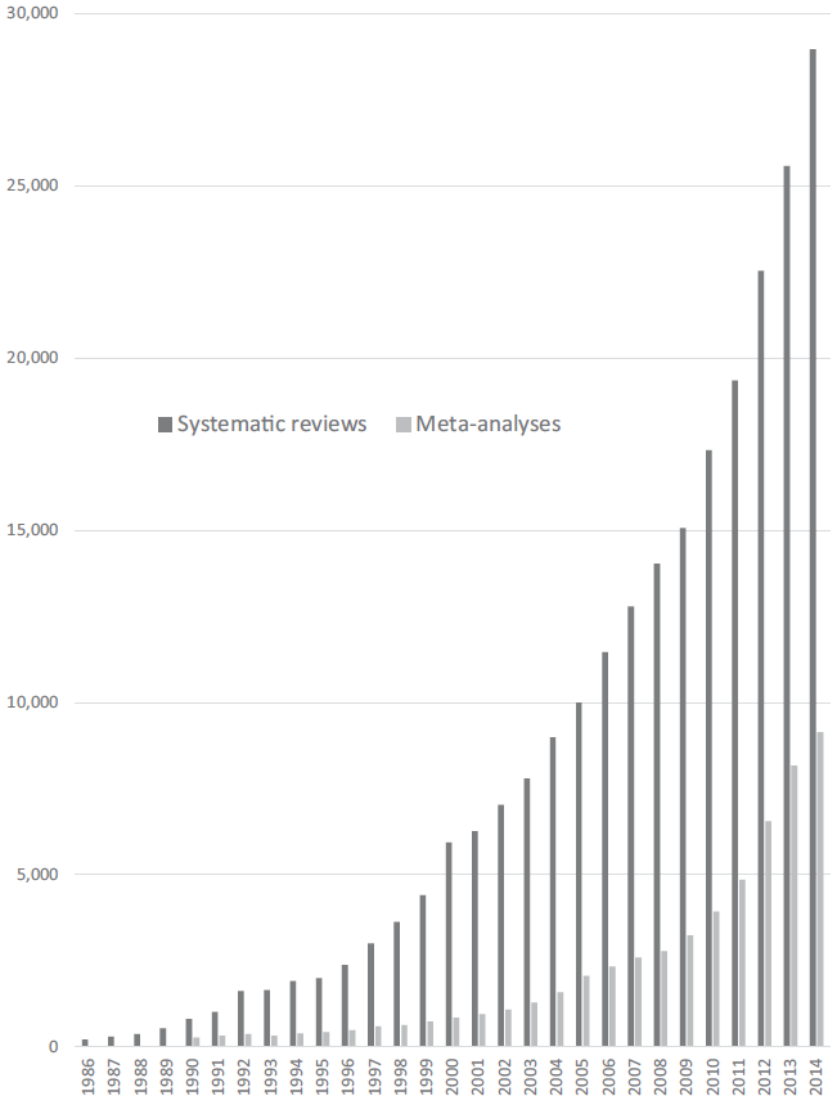
Original Investigation

The Mass Production of Redundant, Misleading, and Conflicted Systematic Reviews and Meta-analyses

JOHN P.A. IOANNIDIS

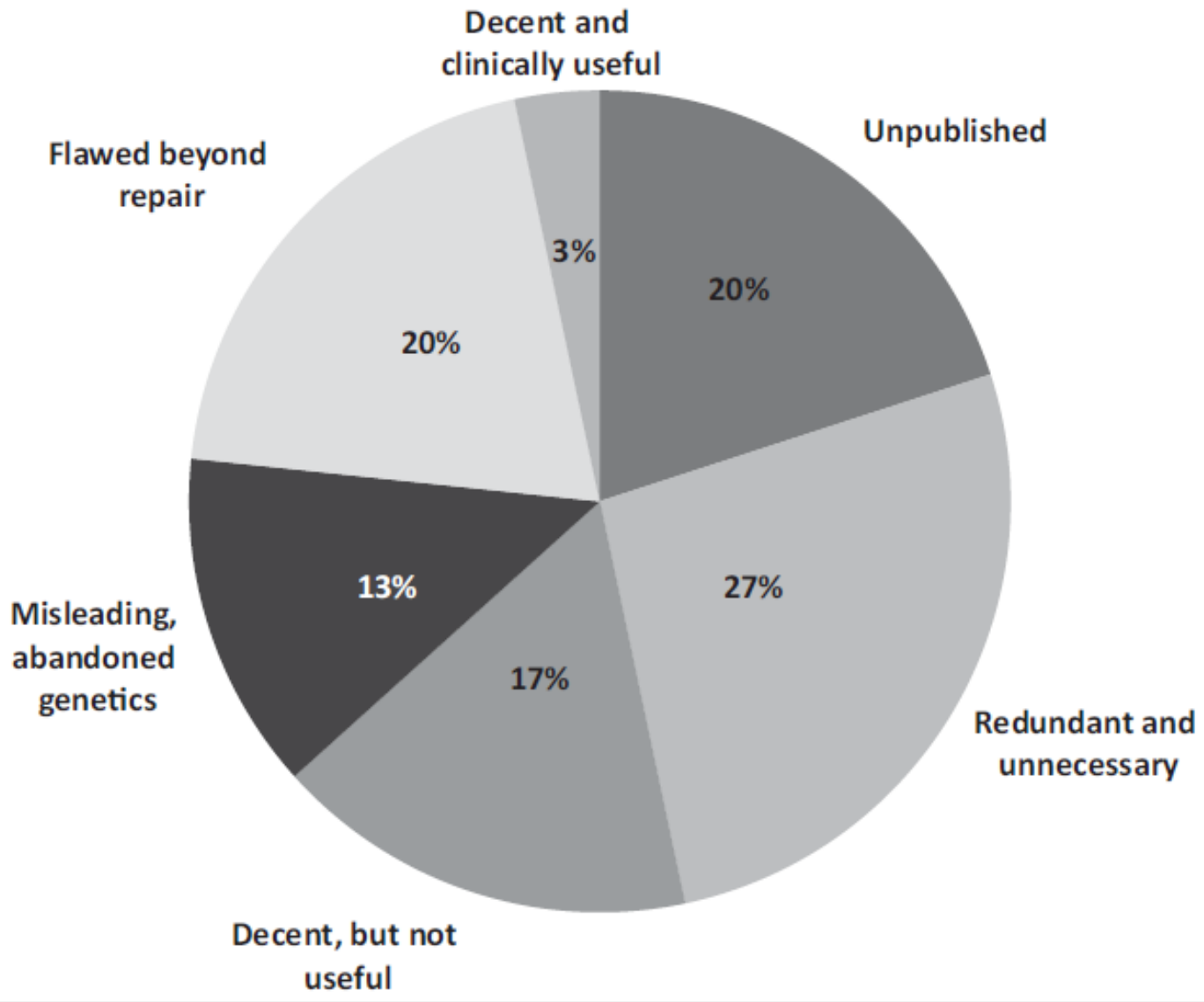
The Milbank Quarterly, Vol. 94, No. 3, 2016 (pp. 485-514)

Figure 1. Number of PubMed-Indexed Articles Published Each Year Between 1986 and 2014 That Carry the Tag "Systematic Review" or "Meta-analysis" for Type of Publication

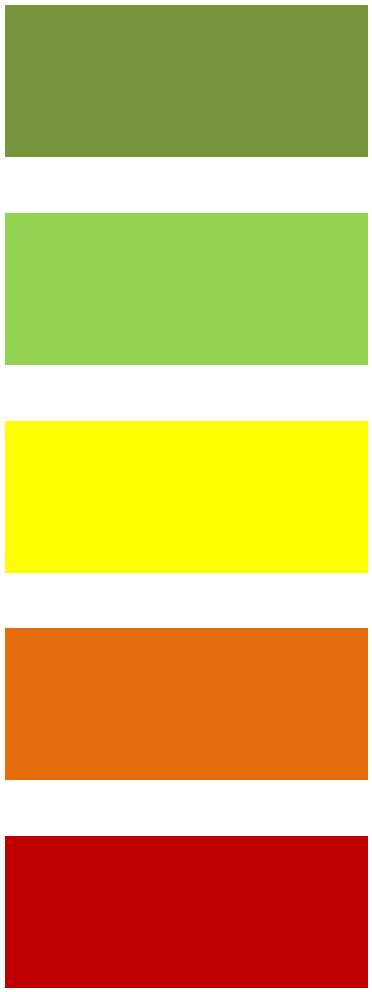


- The production of systematic reviews has reached epidemic proportions
- Possibly, the large majority of produced systematic reviews are unnecessary, misleading, and/or conflicted
- Good and truly informative systematic reviews are a small minority

Figure 4. A Summary Overview of Currently Produced Meta-analyses



Priorità raccomandazioni REWARD



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3. Finanziatori ed enti regolatori dovrebbero:

- richiedere che le proposte di nuovi studi primari siano giustificate da revisioni sistematiche delle evidenze disponibili
- aumentare i finanziamenti per realizzare sintesi delle evidenze disponibili

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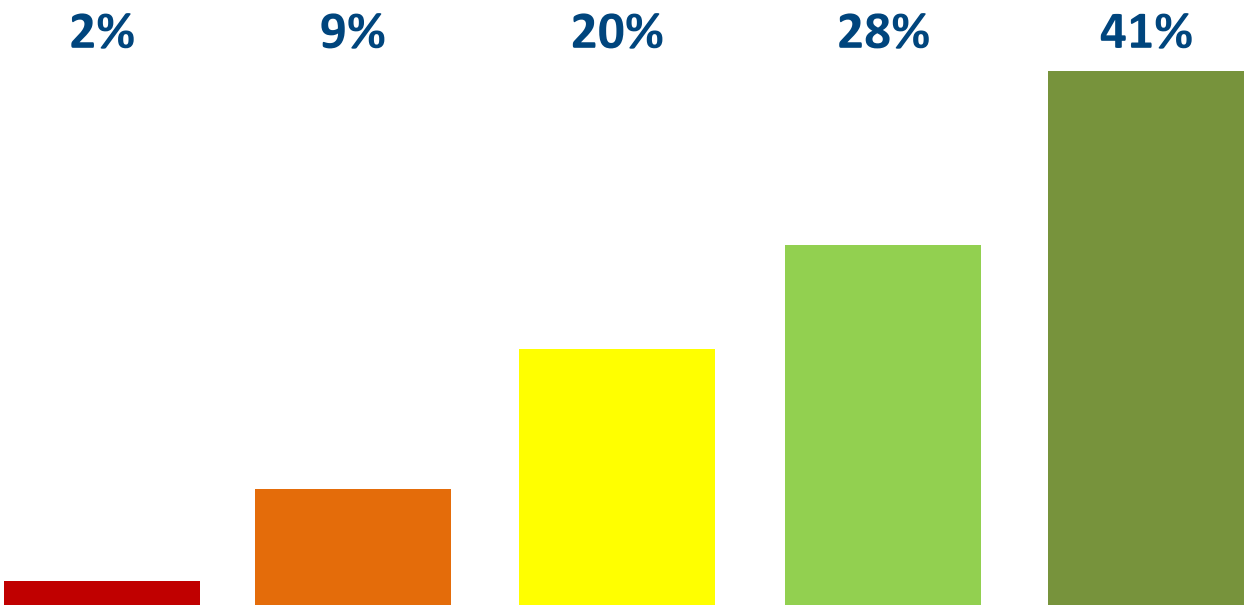
Raccomandazione 3

Media	DS
3.98	± 1.07



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4. Finanziatori ed enti regolatori dovrebbero:

- rafforzare e sviluppare fonti informative sugli studi in corso, assicurandosi che vengano utilizzate dai ricercatori
- richiedere la pubblicazione dei protocolli all'avvio dello studio
- incoraggiare la collaborazione per ridurre gli sprechi

Raccomandazione 4

Media	DS
4.31	± 0.94