



PROGETTO MATTONI INTERNAZIONALE

Portare la Sanità delle Regioni in Europa e nel Mondo
altresì l'Europa e il Mondo nei Sistemi Sanitari delle
Regioni italiane, nel quadro di una collaborazione
sinergica con il Sistema Paese.

DATABASE

E-MANUAL

BANDI EUROPEI

F.A.D.

BACHECA REGIONI



sotto Progetto DirMi - Direttiva
Assistenza Sanitaria
Transfrontaliera



sotto Progetto Presidenza
Italiana del Consiglio
dell'Unione Europea



sotto Progetto Politica di
coesione europea 2014-2020 -
Utilizzo dei Fondi Strutturali in
sanità



sotto Progetto per il supporto
dei Reference sites italiani
sull'ageing



EXCELLENCE IN HEALTH RESEARCH: THE BEST CLINICAL AND SOCIAL RESEARCH FOR A BETTER HEALTH

Assessorati Salute

GROUP LEADER: Regione Emilia-Romagna

REGIONI PARTECIPANTI: Campania, Lazio, Marche, Sicilia, Toscana,
Provincia Autonoma di Trento, Valle d'Aosta, Veneto

Al gruppo di lavoro ha preso parte il Ministero della Salute

Brussels, 6-7 November 2014

Best Research for best Health



Are we doing our best to make sure that Health research in Europe is the best (or good enough) for European health care?

Best Research for best Health

85% of public research investments gets lost *Chalmers I, Glasziou P Lancet 2009;374:86-89*

Comment

Biomedical research: increasing value, reducing waste

Of 1575 reports about cancer prognostic markers published in 2005, 1509 (96%) detailed at least one significant prognostic variable.¹ However, few identified biomarkers have been confirmed by subsequent research and few have entered routine clinical practice.² This pattern—initially promising findings not leading to improvements in health care—has been recorded across biomedical research. So why is research that might transform health care and reduce health problems not being successfully produced?

Global biomedical and public health research involves billions of dollars and millions of people. In 2010, expenditure on life sciences (mostly biomedical) research was US\$240 billion.³ The USA is the largest funder, with about \$70 billion in commercial and \$40 billion in governmental and non-profit funding annually,⁴ representing slightly more than 5% of US health-care expenditure. Although this vast enterprise has led to substantial health improvements, many more gains are possible if the waste and inefficiency in the ways that biomedical research is chosen, designed, done, analysed, regulated, managed, disseminated, and reported can be addressed.

In 2009, Chalmers and Glasziou⁵ identified some key sources of avoidable waste in biomedical research. They estimated that the cumulative effect was that about 85% of research investment—equating to \$200 billion of the investment in 2010—is wasted. This amount was calculated without consideration of the inefficiencies in the regulation and management of research. Although some real progress with the issues they identified has been made,^{6,7} at the present

others (table). Through consideration of these drivers, the economic, social, cultural, and political conditions that have shaped the research environment can be understood.⁸

Economic forces are important. Industry seeks to maximise profit by bringing new products to market and by protecting and expanding market share. In industry-funded clinical research, commercial motives can control the study design and comparators, and so-called seeding trials (in which the purpose is to promote familiarity with a new drug rather than generate knowledge) can be done for marketing purposes.⁹ The economic motivations of industry do much to characterise health as a commodity that can be bought, which informs and distorts the motivations of other actors. The profit motive is central to everything with which industry is involved, including its interactions with seemingly independent researchers and clinicians.¹⁰

Equally, advertising, publication charges, and charges for reprints make journal publication a highly profitable business, and attempts to maximise income are not always consistent with an ambition to publish only reports about research of the highest quality and relevance. Although peer review is supposed to uphold the quality of publications and grants awarded, the costs of the system are substantial,¹¹ raising questions about its cost-effectiveness.¹²

Governments and politicians have an important role. Funding is needed for research in areas important for the protection and restoration of human health even when the prospects for commercial profit are poor or non-existent. For example, the UK Health Technology

Published Online
January 8, 2014
[http://dx.doi.org/10.1016/S0140-6736\(13\)62329-6](http://dx.doi.org/10.1016/S0140-6736(13)62329-6)
See Series pages 156, 166, and 176
See Online Comment
[http://dx.doi.org/10.1016/S0140-6736\(13\)62678-1](http://dx.doi.org/10.1016/S0140-6736(13)62678-1)
See Online Series
[http://dx.doi.org/10.1016/S0140-6736\(13\)62296-5](http://dx.doi.org/10.1016/S0140-6736(13)62296-5), and
[http://dx.doi.org/10.1016/S0140-6736\(13\)62218-X](http://dx.doi.org/10.1016/S0140-6736(13)62218-X)

Biomedical research: increasing value reducing waste

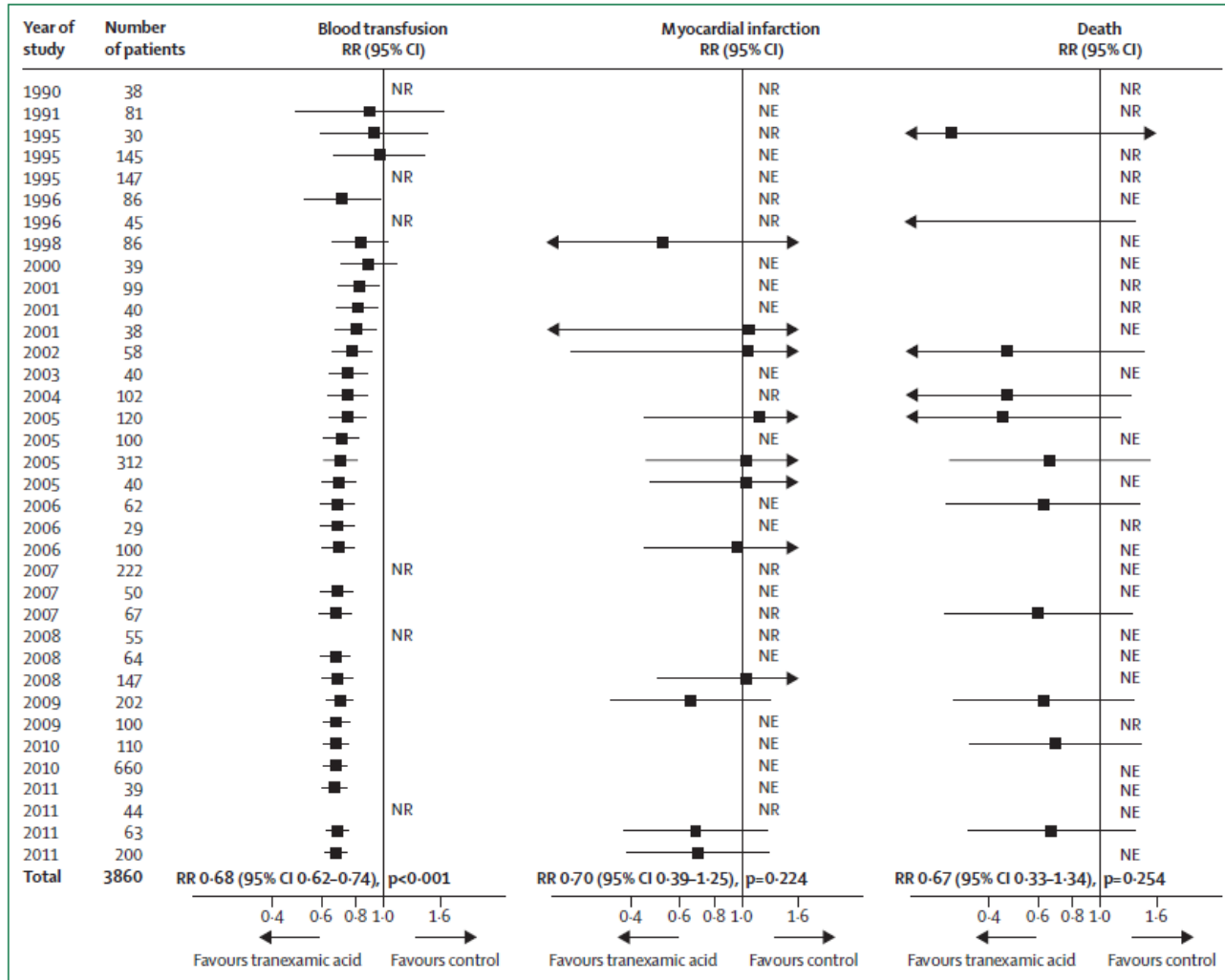


Figure 3: Cumulative meta-analyses of 36 trials of tranexamic acid during surgery

Data taken from Ker et al.⁶⁰ The effects of tranexamic acid on risk of bleeding and subsequent blood transfusion were clearly established a decade ago, but the effects of the drug on risk of myocardial infarction and death were still unknown in 2011. RR=risk ratio. NR=not reported. NE=no events.

Biomedical research: increasing value reducing waste

Correspondence

Winfred Wang and colleagues' report that hydroxycarbamide therapy can now be considered for all very young children with sickle-cell anaemia, whether or not they have clinical symptoms. However, secondary cancer is a substantial concern in patients who receive long-term hydroxycarbamide.¹ Complications and clinical efficacies must be balanced. In Wang and colleagues' trial, some patients were asymptomatic, and the severity of the underlying disease varied widely between patients. Whether early initiation of hydroxycarbamide is beneficial in asymptomatic patients as well as those with severe sickle-cell anaemia remains unknown.

We declare that we have no conflicts of interest.

*Yukie Takahashi, Jinichi Mori, Masaharu Tsubokura, Tomoko Matsumura, Masahiro Kami bearyukie@hotmail.co.jp

Tokyo Metropolitan Cancer and Infectious Disease Center, Komagome Hospital, 113-8677 Tokyo, Japan (YT, JM); and Division of Exploratory Research, Institute of Medical Science, University of Tokyo, Tokyo, Japan (MT, TM, MK)

- 1 Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle cell anaemia: a multicentre, randomised, controlled trial (BABY HUG). *Lancet* 2011; **377**: 1663-72.
- 2 Schultz WH, Ware RE. Malignancy in patients with sickle cell disease. *Am J Hematol* 2003; **74**: 249-53.

Need to realign patient-oriented and commercial and academic research

Clinical research is motivated by several factors. Some are more defensible than others, but most clinical researchers would state that their research is intended to improve health-care effectiveness and safety. There are examples where patients have succeeded in influencing what gets studied,^{1,2} but these are exceptions.

I have had the opportunity to consider from more than one perspective the mismatch between

what clinical researchers do and what patients need. I am a researcher; I have responsibility for allocating funding for research, and I have had multiple myeloma for the past decade. A few years ago I stated publicly that several uncertainties I faced at the beginning of my disease were avoidable.³ Almost 10 years later—after a relapse of my disease—I looked at the “epidemiology” of myeloma studies on ClinicalTrials.gov. On July 31, 2011, a search using the term “multiple myeloma” identified 1384 studies. Of these, 107 were phase 2/3 comparative studies. However, in only 58 of these studies was overall survival an endpoint, and in only ten of these was it the primary endpoint. No trial was a head-to-head comparison of different drugs or strategies. Meanwhile, experts feel that cytogenetic studies and gene-expression profiling will lead to personalised treatment in myeloma,⁴ and pharmaceutical companies avoid research that might show that new and expensive drugs are no better than another comparator already on the market.

If we want more relevant information to become available, a new research governance strategy is needed. Left to themselves, researchers cannot be expected to address the current mismatch. Researchers are trapped by their own internal competing interests—professional and academic—which lead them to compete for pharmaceutical industry funding for early-phase trials instead of becoming champions of strategic, head-to-head, phase 3 studies.

Nor are patients' groups alone likely to change the prevailing pattern of research: given the lack of explicit mechanisms for research prioritisation, they are often dominated by experts with vested interests. Neither would funding alone solve the problem.⁵ Policies developed in the preapproval phase of drug development are needed, and this process needs strict collaboration with pharmaceutical

companies and with input from regulatory bodies.

An essential component of any new governance strategy would be to bring together all the stakeholders, starting from an analysis of existing and ongoing research, produced independently of vested interests. Patient advocacy groups in myeloma spend millions to support research, hoping to promote better care. With public support they should be in a strong position to call for a redefinition of the research agenda, in the interests of patients. I hope this approach can be further debated in *The Lancet* for many other areas of clinical research in oncology and beyond.

I thank Mariangela Tarisco, Ian Chalmers, Gianni Ciccone, Michele Caro, Nicola Maggini, and Roberto Santoli for useful comments in preparation of this letter. I declare that I have no conflicts of interest.

Alessandro Liberati

alessandro.liberati@unimore.it

Università di Modena and Reggio Emilia, Modena, Italy; and Agenzia Sanitaria e Sociale Regionale, Bologna, Italy

- 1 Buckley RS, Grant A, Glazer CMA. Care study and prioritized evidence gaps and stimulated research involvement. *J Clin Epidemiol* 2011; published online Aug 3. DOI:10.1016/j.jclinep.2011.03.016.
- 2 Stewart RJ, Caldwell J, Oliver K, Oliver S. Patients' and clinicians' research priorities. *Health Aff (Millwood)* 2010; published online Dec 22. DOI:10.1186/1745-6215-2010-00548-x.
- 3 Liberati A. An unfinished trip through the uncertainties. *BMJ* 2004; **328**: 531-32.
- 4 Russel SJ, Raghunath SV. Multiple myeloma and the road for personalised medicine. *Lancet Oncol* 2011; **12**: 617-19.
- 5 Liberati A, Maga PL, Tiotto J, Traversa G. Feasibility and challenge of independent research on drugs: the Italian Medicines Agency (AIFA) experience. *Eur J Clin Invest* 2010; **40**: 69-86.

1348

58

Biomedical research: increasing value reducing waste

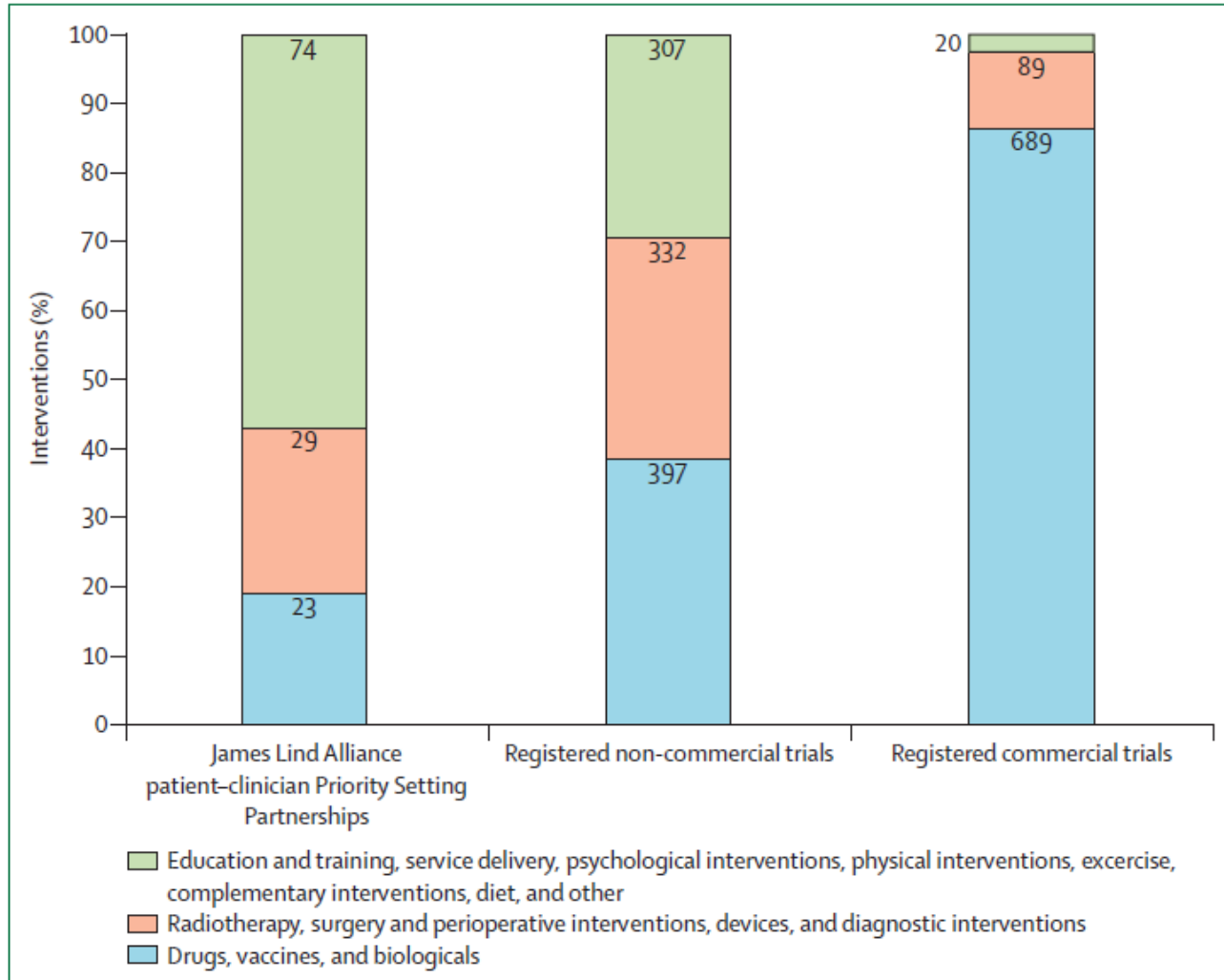


Figure 2: Interventions mentioned in research priorities identified by James Lind Alliance patient-clinician Priority Setting Partnerships⁹⁰ and in registered trials, 2003-12

Survey on research activities supported by the Italian Regions

Which kind of:

- ✓ Governance
- ✓ Priority setting
- ✓ Pay back analysis
- ✓ Disseminating activities of the results



Point to considers

Governance

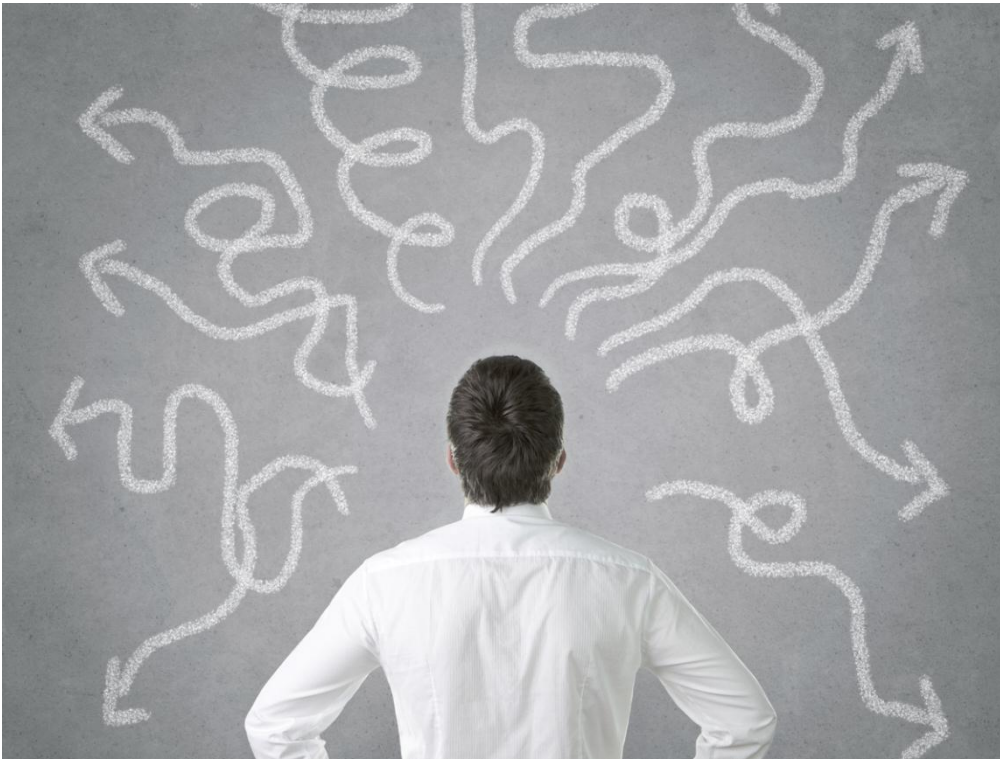
Not only
administration
of funds



- Infrastructure supporting research activities
- Supporting research quality
- Peer review process
- Involvements of all local stakeholders
- Governance of innovations



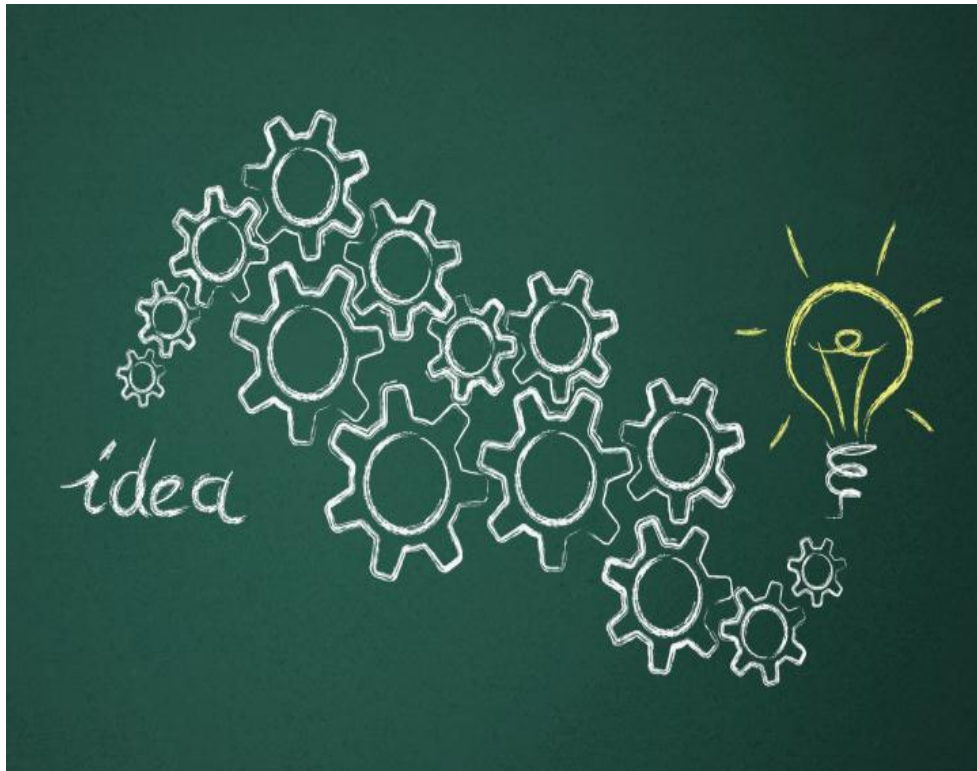
Priority setting



*Clinical questions or thematic identified through a **priority setting** mechanism for Healthcare involving:*

- Regional health Authorities
- Regional health care guidelines
- Local clinical specialist and opinion leaders
- Consultation with panel of experts
- Literature analysis

Pay back analysis



Assessing research impact on Regional Health service

- Bibliometric indicators
- Clinical and operational Guidelines
- Health Technology assessment activities
- Economical activities
- Interaction with Policy makers

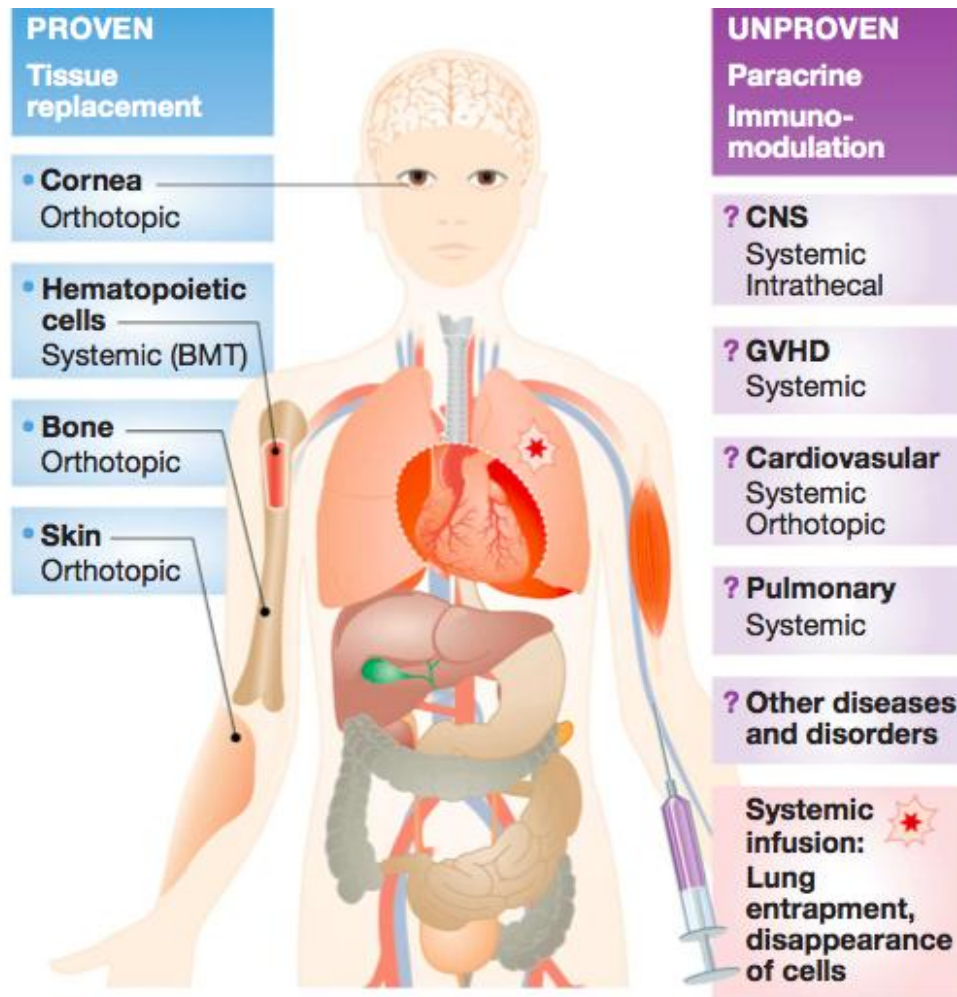
Disseminating and communicating results



Measuring the access to the knowledge produced

- Open access
- Clinical Trial Databases
- Research promotion
- Research communications
- Disclosure and acknowledgments

Proven and Unproven stem cell therapies



THE
EMBO
JOURNAL

The EMBO Journal (2013) 32, 1489–1495
www.embojournal.org

Figure 1 To date, there are very few examples of proven stem cell therapies. These therapies include BMT with populations that

[▶▶ Nature's news team scoop two prizes at journalism awards](#)
[▶▶ Find out more](#)

NATURE | NEWS

Italian stem-cell trial based on flawed data

Scientists raise serious concerns about a patent that forms the basis of a controversial stem-cell therapy.

[Alison Abbott](#)

02 July 2013


[Journal home](#)
[Current issue](#)
[For authors](#)
[Subscribe](#)
[E-alert sign up](#)
[RSS feed](#)

[E-alert](#)
[RSS](#)
[Facebook](#)
[Twitter](#)

Submit today!



Recent

Read

Commented

Emailed

1. [Bioengineers look beyond patents](#)
Nature | 03 July 2013
2. [China gears up to tackle tainted water](#)
Nature | 03 July 2013
3. [Stem-cell transplants may purge HIV](#)
Nature | 03 July 2013
4. [Italian stem-cell trial based on flawed data](#)
Nature | 02 July 2013
5. [European deal cuts red tape](#)
Nature | 02 July 2013

Biomedical research: increasing value reducing waste

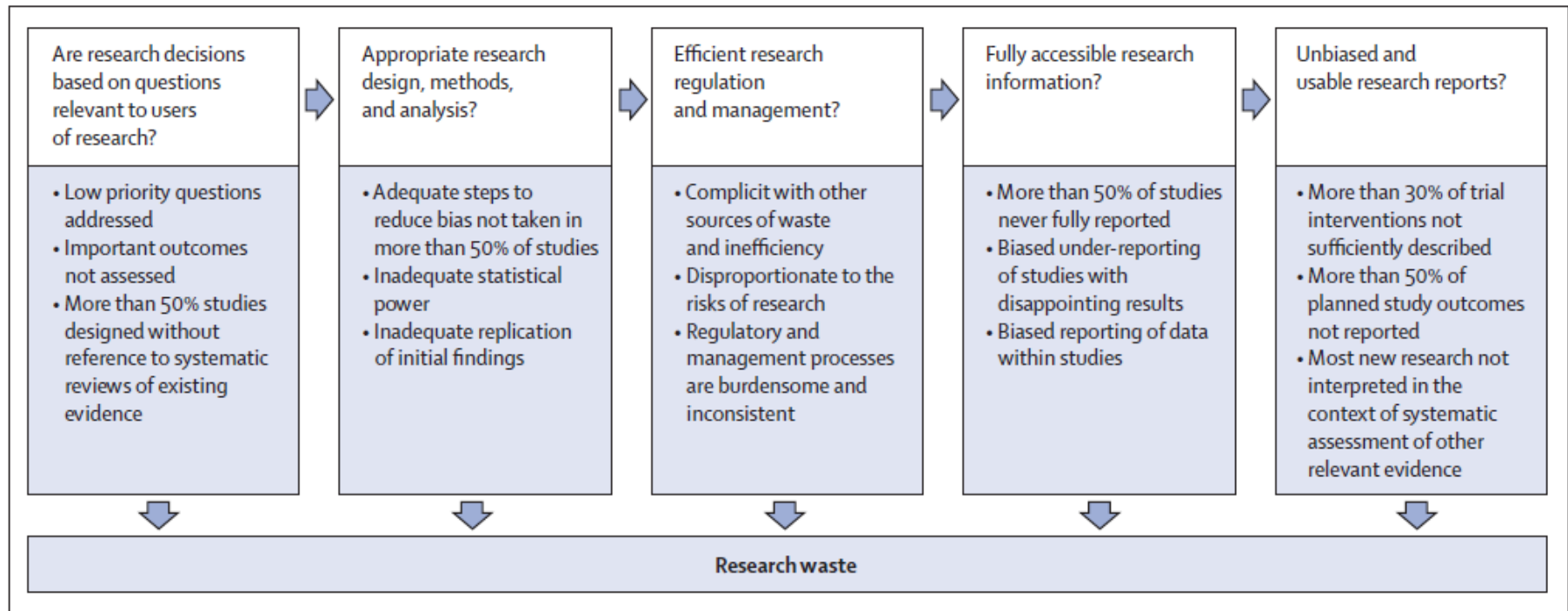


Figure: Avoidable waste or inefficiency in biomedical research

Conclusions



“I have had the opportunity to consider from more than one perspective the mismatch between what clinical researchers do and what patients need. I am a researchers and I have had multiple myeloma for the past decade”

“If we want more relevant information to become available, a new research governance strategy is needed.”

Alessandro Liberati The Lancet 19.11.2011

Thanks

Antonio Addis

Research Governance Area

Agenzia Santaria e Sociale Regionale

Emilia Romagna

aaddis@regione.emilia-romagna.it

<http://www.laniusletter.it/>