RESEARCH WASTE

Mona Nabulsi, MD, MS
Why Research Waste?
The scandal of poor medical research

We need less research, better research, and research done for the right reasons
What should we think about a doctor who uses the wrong treatment, either wilfully or through ignorance, or who uses the right treatment wrongly (such as by giving the wrong dose of a drug)? Most people would agree that such behaviour was unprofessional, arguably unethical, and certainly unacceptable.
What, then, should we think about researchers who use the wrong techniques (either wilfully or in ignorance), use the right techniques wrongly, misinterpret their results, report their results selectively, cite the literature selectively, and draw unjustified conclusions? We should be appalled. Yet numerous studies of the medical literature, in both general and specialist journals, have shown that all of the above phenomena are common.17 This is surely a scandal.
Why?

- Inappropriate design
- Unrepresentative samples
- Small samples
- Incorrect methods of analysis
- Faulty interpretation
Researchers compelled to publish for career reasons: *Publish or perish*

Researchers ill-equipped to conduct research

Good researcher = quantity of publications, NOT quality

Ethics reviews ➔ subject protection, not scientific issues ➔ poor research approved (unethical!!)

Bad papers easy to publish (few statisticians)
Problems in the Medical Profession

- Poor research quality widely acknowledged
- Leaders of medical profession not concerned, make no efforts for solution
- System encourages poor research “Publish or perish”
Increasing value and reducing waste in biomedical research: who’s listening?

David Moher, Paul Glasziou, Iain Chalmers, Mona Nasser, Patrick M M Bossuyt, Daniël A Korevaar, Ian D Graham, Philippe Ravaud, Isabelle Boutron

The biomedical research complex has been estimated to consume almost a quarter of a trillion US dollars every year. Unfortunately, evidence suggests that a high proportion of this sum is avoidably wasted. In 2014, The Lancet published a series of five reviews showing how dividends from the investment in research might be increased from the relevance and priorities of the questions being asked, to how the research is designed, conducted, and reported. 17 recommendations were addressed to five main stakeholders—funders, regulators, journals, academic institutions, and researchers. This Review provides some initial observations on the possible effects of the Series, which seems to have provoked several important discussions and is on the agendas of several key players. Some examples of individual initiatives show ways to reduce waste and increase value in biomedical research. This momentum will probably move strongly across stakeholder groups, if collaborative relationships evolve between key players; further important work is needed to increase research value. A forthcoming meeting in Edinburgh, UK, will provide an initial forum within which to foster the collaboration needed.

Introduction

More than 30 years ago, the adverse clinical consequences of biased under-reporting of research were clearly documented1 and non-publication of research remains five stages to identify common themes and examples of good practice across their programmes. For example, since 2013, NIHR has required applicants for support of new primary research to reference an existing systematic...
relevant on-going studies, eg, from trial registries”.22

In 2014 *The Lancet* published a Series (“Increasing value: reducing waste”)23–27 extending the 2009 analysis from 4 to 50 journal pages, with more than 40 authors focused on the five NIHR stages. As the Commissioning Editors noted: “Our belief is that research funders, scientific societies, school and university teachers, professional medical associations, and scientific publishers (and their editors) can use this Series as an opportunity to examine more forensically why they are doing what they do...and whether they are getting the most value for the time and money invested in science.”28

The Series, and an accompanying symposium,29 provided a voluminous body of evidence for the issues in biomedical research.
Figure: Stages of waste in the production and reporting of research evidence relevant to clinicians and patients.

- **Questions relevant to clinicians and patients?**
  - Low priority questions addressed
  - Important outcomes not assessed
  - Clinicians and patients not involved in setting research agendas

- **Appropriate design and methods?**
  - Over 50% of studies designed without reference to systematic reviews of existing evidence
  - Over 50% of studies fail to take adequate steps to reduce biases—e.g., uncontrolled treatment allocation

- **Accessible full publication?**
  - Over 50% of studies never published in full
  - Biased under-reporting of studies with disappointing results

- **Unbiased and usable report?**
  - Over 30% of trial interventions not sufficiently described
  - Over 50% of planned study outcomes not reported
  - Most new research not interpreted in the context of systematic assessment of other relevant evidence


- 50% of research
- 85% of research
Waste From Choosing Wrong Questions
Figure 1: Classification of different categories of research

- Curie quadrant: Pure basic research without consideration of relevance to practical issues.
- Pasteur quadrant: Use-inspired basic research to address important practical questions.
- Waste quadrant.
- Doll quadrant: Pure applied research to address important practical questions.
Research Funding
Who Gets What?
2010: Worldwide, $124 billion spent on biomedical research

>2/3 → basic research

- Previous claim: Basic research → 62% of essential clinical advances
- Replication → 2-21% of clinical advances are due to basic research

Basic research innovations:
- Development of PCR
- Platinum effect on bacterial growth → Cis-platinum
- Fungi & Cholesterol → Statins
Yield from basic research is poor:

- 1979-1983: 25,000 basic research reports in 6 leading basic-science journals

- 101 claimed that new discoveries had clear clinical potential

- By 2003: 5 interventions were licensed for clinical use

- Only 1 led to development of a widely-used intervention
<10% is spent on treatment evaluation (applied clinical research)

Applied research: large health, social & economic effects (10-25 yrs max.)

How to set priorities for basic research?

- Burden of disease: Poor correlation between disease burden & public research funding (mental health, dementia, stroke vs. rare diseases)
- More funding of use-inspired basic research (e.g. SR on drugs in experimental autoimmune encephalitis in rodents → 3 off-patent drugs worth trying in MS)
- Need for replication of promising experiments (gene studies)
Treatments evaluated in research are of low priority for patients & clinicians (mismatch)

- Patients: Interventions focusing on functional, social or emotional well-being, AEs or long-term outcomes (more difficult than drug trials)

- Knee osteoarthritis:
  - Evaluation of physiotherapy & surgery
  - Assessment of educational & coping strategies
  - Drug interventions: 9% of patients vs. 80% of trials
Figure 2: Interventions mentioned in research priorities identified by James Lind Alliance patient-clinician Priority Setting Partnerships and in registered trials, 2003–12

Legend:
- Education and training, service delivery, psychological interventions, physical interventions, exercise, complementary interventions, diet, and other
- Radiotherapy, surgery and perioperative interventions, devices, and diagnostic interventions
- Drugs, vaccines, and biologicals
Mismatch between funders’ and patients’/clinicians’ priorities

Rheumatoid arthritis (outcomes):
- Patients: Fatigue as symptom of most concern
- Research: Focus on pain

Asthma (patients):
- AEs of long-term use of steroids or other drugs
Waste from Conducting Unnecessary Studies
Knowledge gap ➔ New research
- No evidence
- Existing evidence is unsatisfactory
- Replication for confirmation

New research designed in context of available total evidence (SRs: 2500/year)

Survey of trialists:
- 11/24 authors did not know of existing SR when they designed their own trials
<table>
<thead>
<tr>
<th>Claim</th>
<th>May, 2009 (n=29)</th>
<th>May, 2012 (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claims that clinical trial is the first to address the question</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Contains an updated systematic review that was used to inform trial design</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Previous systematic review* discussed that was not used in trial design</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Contains references to other randomised trials</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Does not contain references to other randomised trials or claim to be the first trial</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>


Table 2: Analysis of Introduction sections of reports of controlled trials published in five medical journals in May, 2009, and May, 2012.
Only 4/446 (1%) protocols submitted to British Ethics Committees used data from previous meta-analysis to plan sample sizes

Under-citation of non-supportive studies → bias
- Ex. Studies on B-amyloid accumulation in Alzheimer → non-supportive references ignored in publications & grants applications (even if from same lab)

Enough in 1992?
<table>
<thead>
<tr>
<th>Year of study</th>
<th>Number of patients</th>
<th>Blood transfusion RR (95% CI)</th>
<th>Myocardial infarction RR (95% CI)</th>
<th>Death RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>38</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>1991</td>
<td>81</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>1995</td>
<td>30</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>1996</td>
<td>145</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>1998</td>
<td>86</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2000</td>
<td>39</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2001</td>
<td>99</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2003</td>
<td>40</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2004</td>
<td>102</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2005</td>
<td>120</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2006</td>
<td>312</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2006</td>
<td>40</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2006</td>
<td>62</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2006</td>
<td>29</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2006</td>
<td>100</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2007</td>
<td>222</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2007</td>
<td>50</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2007</td>
<td>67</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2008</td>
<td>55</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2008</td>
<td>64</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2008</td>
<td>147</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2009</td>
<td>202</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2009</td>
<td>100</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2010</td>
<td>110</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2010</td>
<td>660</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2011</td>
<td>39</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2011</td>
<td>44</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2011</td>
<td>63</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
<tr>
<td>2011</td>
<td>200</td>
<td>NR</td>
<td>NR</td>
<td>NE</td>
</tr>
</tbody>
</table>

**Total**: 3860

**Blood transfusion**
- RR 0.68 (95% CI 0.62-0.74), \( p < 0.001 \)

**Myocardial infarction**
- RR 0.70 (95% CI 0.39-1.25), \( p = 0.224 \)

**Death**
- RR 0.67 (95% CI 0.33-1.34), \( p = 0.254 \)

Figure 2: Cumulative meta-analyses of 36 trials of tranexamic acid during surgery

Data taken from Ker et al.\(^6\). 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.
SIDS research→ 1-decade delay in assessing existing evidence about risk factors!!
  - How many deaths could have been avoided?

Early studies overestimate effects (bias)
  - Need to replicate
  - Need to balance: unnecessary duplication vs. need to confirm results to avoid wasteful research
Wasteful Research Due to Inappropriate Design or Conduct
- Misuse of statistical methods
  - 71 articles/6 journals misused Fisher’s exact test

- Inadequate training in methods (license to practice)
  - 2001: 38% of Nature and 25% of BMJ papers reported P values that did not correspond to the given statistical tests

- Poor research not reproducible
  - 43/67 oncological or CV findings of academic publications could not be replicated by Bayer
  - Amgen ➔ 47/53 potential oncological drug targets
- Effect-bias ratio:
  - Small effects are difficult to distinguish from bias
  - Design features can affect the magnitude of effects
    - In 234 trials, allocation concealment (selection bias → exaggerate effect) was:
      - Inadequate (18%)
      - Unclear (26%)
    - In 487 diagnostic accuracy studies:
      - 20% used different reference standards for positive & negative tests → Overestimation of test performance
      - Only 17% used double-blind reading of tests
Poor protocols & designs: No reporting of protocol changes (post-hoc)

Small studies-uninformative → unnecessary duplications

Outcomes chosen are of minimal clinical relevance

Are these problems avoidable?
Waste Due to Research Regulation & Management
- Regulatory approval required by international & national laws

- Increasing complexity of regulation

- Ethics committees:
  - Failure to stop unnecessary research (based on SR)
  - Failure to require clinical trial registration & full reporting

- From protection of HSR ➔ Harm of HSR
ECs requirement of the 3 Rs:
- Reduction: No. of animals used
- Replacement: non-animal experiments
- Refinement

Underpowered studies:
- Sample size calculated in 2% of studies

Failure to replicate & confirm findings
IC requirements by EC: not commensurate with risk (survey vs. trial; drug vs. device)

Inefficiency & delays in approvals (multi-center)
  ▪ Wasted resources (autism study)
  ▪ Slow recruitment & poor retention
    ▫ Inefficient recruitment strategies (Teaching EBM)
    ▫ Complex protocols due to regulatory requirement (research in non-IRB sites)

Paucity of research on how to improve efficiency
Panel 1: An example from Sweden of the bureaucracy involved in applications for central research ethics committee approval

In 2010, a group of researchers in Sweden wanted to pool data from several cohort studies to identify risk factors for subarachnoid haemorrhage. They identified about 20 studies, and spent about 300 h contacting all investigators and getting signed data-sharing agreements and data security processes agreed. Sweden has a central research ethics committee to approve projects. The team recorded the time taken for each step of the approval process. About 200 h of office time was spent on the ethics approval and resubmission process alone. The research ethics committee wanted to see all information that the participants of all cohorts had been given about the purpose of the study. These documents had to be provided as 18 copies and submitted manually. It took the team 6 months to collect all the information sheets from the 20 different cohorts, several of which began recruitment in the 1960s and for which little knowledge about what information was given by whom to whom in the recruitment phase was poor. The research ethics committee eventually had the team advertise in national newspapers about the pooling project, listing all original cohorts so that all individuals who did not want the team to use their data for this project could withdraw their consent for the study. Not one participant withdrew. It took more than 3 years to reach the stage of pooling data from the cohorts, ready for analysis.
Figure 3: Number of participants recruited into National Institute Health Research Clinical Research Network portfolio studies in England by primary study design
*Category includes studies that have not specified their primary study design.
Waste From Failure to Publish Full Report Inaccessible Research
In 2010, Alessandro Liberati explained the difficulties he encountered when he had to make decisions about his treatment for multiple myeloma: “When I had to decide whether to have a second bone-marrow transplant, I found there were four trials that might have answered my questions, but I was forced to make my decision without knowing the results because, although the trials had been completed some time before, they had not been properly published....I believe that research results must be seen as a public good that belongs to the community—especially patients.”¹ The
Full reporting (methods & results):
- Critical appraisal
- Interpretation of findings
- Appropriate replication
- Improves clinical practice & policy
- Prevent unnecessary duplication
- Informs future research

Yet, half of health-related studies are unreported ➞ waste of $240 billion/yr
Positive studies:
- Twice as published as negative ones
- Appear 1 year earlier in journals
- True for clinical & preclinical studies

Incomplete & biased subset of findings

Selective reporting:
- Compromises patient care & decision-making
- Poor resource allocation
- Inadequate prioritization of research questions
- Redundant misguided & potentially harmful research
Figure 2: Reporting of completed trials, by study characteristic
Data taken from Ross and colleagues’ analysis of a random sample of 677 completed trials registered with ClinicalTrials.gov between 2000 and 2007.
- Inaccessibility due to language barriers:
  - Most of literature is non-English
  - E.g.: Only 6% of 2500 Chinese medical journals are indexed in Medline
  - Often excluded from SRs ➔ substantial waste of research data

- Inaccessibility of full study reports (lengthy, not published in full in journals)

- Poor access to (lack of sharing) participant-level data
Figure 4: Key sources of information about study methods and results, with associated information loss and potential for selective reporting.
Oseltamivir Story

TYPE OF BIASED DISSEMINATION

- Trials with 60% of patient data not reported
- Full study reports inaccessible for 29% of trials
- Missing modules for 16/17 available full study reports
- Discrepancies between published articles & full study reports

EFFECTS

- 2009: $3.3 billion spent worldwide to stockpile a drug that did not reduce hospitalizations or pulmonary complications in pandemic influenza, and that had unclear harms
- Under-publication or over-publication = unscientific & unethical misconduct

- Suppressed reporting of serious AEs (Cardiovascular risks of Vioxx)

- Failure to publish negative studies (Studies of antidepressants in adolescents)

- Public distrust in research integrity
Waste Due to Incomplete or Unusable Reports of Research
Research reports should answer 4 questions:
- What questions were addressed & why
- What was done (methods)
- What was shown (direction, size & uncertainty of effects)
- What the findings mean (in context of other research)

Answers should be readable & complete
Problems in Reporting

- Missing or incomplete information
  - Missing treatment details
  - Outcomes in methods not shown in results
  - Selective presentation of data

- Incorrect or misleading information
  - Misleading figures
  - Incorrect statistical analysis
  - Change of primary outcome
  - Spin in conclusions
Problems in Reporting

- Inconsistent information
  - Differences between report summaries in trial registers & papers in peer-reviewed journals

- Poorly written text & poor use of tables/figures

- Information presented in obscure format
## Question & Methods

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Number &amp; selection of studies</th>
<th>Items absent in reports &amp; % studies that included items</th>
</tr>
</thead>
</table>
| **Animal studies (ARRIVE)** | - Jan 99 to Mar 05  
- 271 original research reports  
- Live rats, mice & non-human primates | - 59% reported hypothesis, objective, no. & characteristics of animals.  
- 0% explained sample size.  
- 46% reported exact no. of animals in methods & results. |
| **Observational studies**   | - Jan 04 to Apr 07  
- 174 observational studies of interventions  
- 5 general medical & 5 epidemiological journals | - 10% details of selection.  
- 51% inclusion of confounders. |
| **Diagnostic studies**      | - 2004 to 2006  
- 90 diagnostic accuracy studies of commercial tests for Tb, malaria & HIV | - 0% methods for calculation & estimates of reproducibility.  
- 10% estimates of diagnostic accuracy in subgroups.  
- 11% distribution of severity or other conditions. |
### Abstract
Trials: missing effect size and confidence interval (38%); no mention of adverse effects (49%)\(^7\)

### Methods
**Trials:** 40–89% inadequate treatment descriptions\(^{11, 13}\)
**fMRI studies:** 33% missing number of trials and durations\(^3\)
**Survey questions:** 65% missing survey or core questions\(^{25}\)
**Figures:** 31% graphs ambiguous\(^4\)

### Results
**Clinical trials:** outcomes missing: 50% efficacy and 65% harm outcomes per trial incompletely reported\(^6\)
**Animal studies:** number of animals and raw data missing\(^{17}\) (54%, 92%); age and weight missing (24%)
**Diagnostic studies:** missing age and sex (40%)\(^{15}\)

### Discussion
Trials: no systematic attempt to set new results in context of previous trials (50%)\(^{69}\)

### Data
Trials: most data never made available; author-held data lost at about 7% per year

*Figure 3:* Estimates of the prevalence of some reporting problems (see publication column, figure 1)
fMRI = functional MRI.
Full & Clear Reporting of Results

- Study results ➔ answers to study questions

- Outcomes & analysis = in protocol = what is stated in methods

- Adequate data & detail to allow incorporation in future analysis:
  - Characteristics of sample (age, sex, etc..)
  - Was study completed as planned? (CONSORT flow diagram: 60% do not report how many patients actually received Rx)
Selective reporting of outcomes & analyses

- In 128 papers, 41 primary outcomes of new drug applications to FDA were omitted more favorable results.

- 127/682 (19%) of studies included a variable not known at baseline in survival analysis

- Only 16/49 (33%) antiretroviral trials reported all AEs (selective AE reporting)

- 31% of all JAMA graphs (1999-2000) could not be interpreted
2006: 72 trials had distorted presentations of results:
- Non-significant primary outcomes → positive subgroup or secondary outcome analysis
- COI effect
- Abstract most prone to spin in results
Initiatives for Improvement in Reporting
Responsible reporting of research should be an essential part of research training.
Presubmission Stage

- Reporting guidelines:
  - CONSORT
  - STARD
  - PRISMA
  - ARRIVE
  - Etc…

- Mandatory by high impact journals

- EQUATOR Network:
  www.equator-network.org
Protocol registration in an international register:
- WHO & WMA mandate to register trial protocols in international registries (transparency, tracking of reporting) and frequent updating till publication

International Committee of Medical Journals’ Editors (ICJME) publication tied to prior registration in trial registers
Lactose-free Milk in Infants With Acute Diarrhea in a Developing Country

This study is currently recruiting participants. (see Contacts and Locations)

Verified July 2016 by American University of Beirut Medical Center

Sponsor:
American University of Beirut Medical Center

Information provided by (Responsible Party):
Mona Nabulsi, American University of Beirut Medical Center

ClinicalTrials.gov Identifier:
NCT02248010

First received: September 18, 2014
Last updated: July 15, 2016
Last verified: July 2016

Purpose

The purpose of this study is to determine whether lactose-free milk will shorten the diarrhea duration and decrease its severity in formula-fed infants presenting to the Emergency Department (ED) or pediatric clinics with acute diarrhea.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Gastroenteritis</td>
<td>Dietary Supplement: Lactose-free milk</td>
</tr>
</tbody>
</table>
A complex breastfeeding promotion and support intervention in a developing country: study protocol for a randomized clinical trial

Mona Nabulsi¹*, Haya Hamadeh¹, Hani Tamim², Tamar Kabakian³, Lama Charafeddine¹, Nadine Yehya⁴, Durriyah Sinno¹ and Saadieh Sidani³

Abstract

Background: Breastfeeding has countless benefits to mothers, children and community at large, especially in developing countries. Studies from Lebanon report disappointingly low breastfeeding exclusivity and continuation rates. Evidence reveals that antenatal breastfeeding education, professional lactation support, and peer lay support are individually effective at increasing breastfeeding duration and exclusivity, particularly in low-income settings. Given the complex nature of the breastfeeding ecosystem and its barriers in Lebanon, we hypothesize that a complex breastfeeding support intervention, which is centered on the three components mentioned above, would significantly increase breastfeeding rates.

Methods/Design: A multi-center randomized controlled trial. Study population: 443 healthy pregnant women in their first trimester will be randomized to control or intervention group. Intervention: A “prenatal/postnatal” professional and peer breastfeeding support package continuing till 6 months postpartum, guided by the Social Network and Social Support Theory. Control group will receive standard prenatal and postnatal care. Mothers will be followed up from early pregnancy till five years after delivery. Outcome measures: Total and exclusive
Reviewing Stage

- Editorial & peer-reviews → improve quality

- Check whether reporting standards are met
  - Journals enforcing reporting guidelines had improved quality of reports
  - Need for a dedicated peer-reviewer to check whether reporting items were missed (RCT)
Pre-publication Stage

- Technical editing by journals
  - Improve readability
  - Improve quality of abstracts, tables, figures
  - Reduce errors in references

- Provision of better linkage to additional materials
  - Full report
  - Participant level data sharing
  - Full protocol
  - Full description of interventions
Post-publication Stage

- Reviews: letters, rapid responses, retractions

- Underused, poorly managed & poorly linked: retracted papers continue to be cited for a long time

- Need revisions of journal policies regarding timing for letters & other post-publication feedback (Lancet-sublingual anticonvulsants)
136 trials of pain prevention methods from propofol injections published after 2002:
- 27% did not cite a SR published in 2000
- 75% of trials considered inappropriate (did not use SR to inform study design)

A study of 227 MA, later trials cited:
- A median of 21% of citable literature
Poor citation of relevant research is selective:

- 530 RCTs of hepatobiliary diseases
- 11 journals, 1985-1996
- Positive studies 2X cited than negative → publication bias

Positive observational studies cited long after shown to be incorrect in large RCTS:

- Vitamin E reducing ischemic heart disease
- B-carotene reducing cancer
Figure 2: Percentage (and number) of trials that set their results in the context of a systematic review by 4 year intervals
Data from references 69 and 70.
Funders

- French Institute of Health & Medical research (INSERM)
- EQUATOR
- Wellcome Trust
- National Health & Medical Research Council-UK
- Heads of International Research Organizations’ meeting, Ottawa
- The National Center for the Replacement, Refinement & Reduction of Animals in Research
Funders

- Conferences: “Improving reporting to decrease the waste of research” 2014.
- Discussions of Lancet series for strategic planning.
- Requirements for SRs before initiation of primary studies
- Requirements for trial registration
- Requirements for reporting guidelines
- Requirements for FULL publication
- Enforcement of requirements
Regulators

- No ethics approval for scientifically poor protocols (unethical)

- Health Research Authority (HRA)-UK: “Any project should build on a review of current knowledge. Replication to check the validity of previous research is justified, but unnecessary duplication is unethical”.

- Reduce waste from inefficiencies: hyper-regulation

- Reduce biased under-reporting of results: UK-Ethics approval tied to public trial registration
Guidance to authors & reviewers on need to set trials in context of the totality of evidence

The Lancet→ Research in Context Panel

ICJME→ mandate to use the Reporting Guidelines

IOM→ Data sharing

Requirement of detailed information of Methods-interventions
Academic Institutions

- Very little attention to the Lancet Series
- Iran, 2015: 2 workshops; 55 medical universities
- Most institutions do not enforce FDA mandate to register trials, publish results
- Data sharing: encouraged (Cambridge & Bristol) not enforced
Around half of clinical trials have never been reported. This is the story of the campaign to find them—and to fix medicine.

Read the AllTrials story
Clinical Trials Day, WHO and Health Canada consultation

AllTrials Campaign <alltrials@senseaboutscience.org>
Fri 5/19, 7:18 PM
Mona Nabulsi

Dear AllTrials friends and supporters

It’s Clinical Trials Day and we have huge news from the WHO. Major global funders and international NGOs have agreed to adopt the WHO’s strong standards on clinical trial transparency. This means all clinical trials they fund or support will be registered and the results reported. This is a big step forward.

Dr Ben Goldacre said:

This is truly fantastic news. We cannot make informed choices about which treatments work best when the results of completed clinical trials are routinely withheld from doctors, researchers and patients. The scandal of unreported clinical trials has arisen because of a longstanding failure to take responsibility, throughout the whole ecosystem of medicine.
- GRADE method
- Data sharing (data repositories)
- Collaboration & standardization of efforts
- Training in critical appraisal, research methods, CE activities
- Minimize COI: design, conduct, analysis involvement

- Involve stakeholders (patients)

- Reward systems:
  - Replication vs new discovery
  - Quality vs quantity
  - Full reporting
We need less research, better research, and research done for the right reasons.