A "systematic" scoping review of adherence to reporting standards in the clinical literature

Zena Samaan, Lawrence Mbuagbaw, Daisy Kosa, Victoria Borg Debono, Rejane Dillenburg, William Zhang, Vincent Fruci, Brittany Dennis, Monica Bawor, Lehana Thabane

August 7-8, 2012

Scientific Approaches to Strengthening Research Integrity in Nutrition and Energetics

(organized by the Obesity Nutrition Research Centre, The University of Alabama at Birmingham)

Centre for Evaluation of Medicines

St. Joseph's Healthcare Hamilton

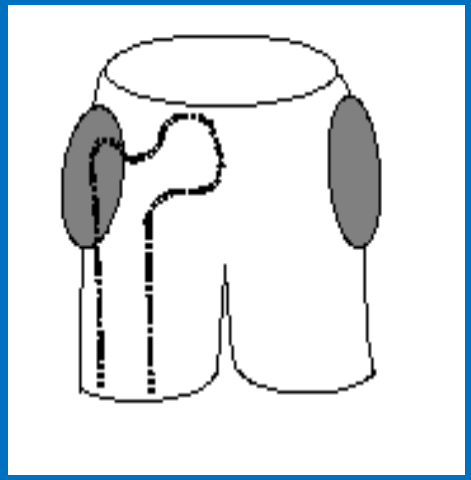
McMaster University

Inspiring Innovation and Discovery

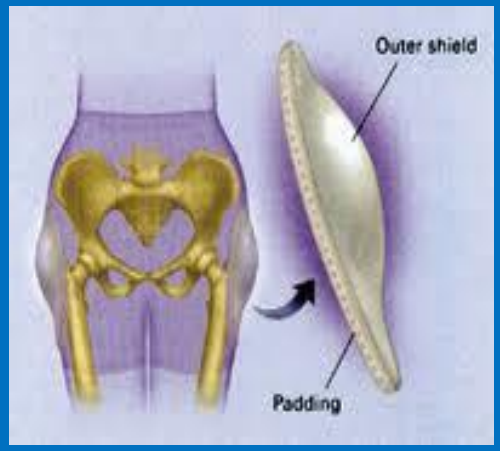
Disclosures

- ✓ Support from conference organizers
- ✓ Involved in a case I will be discussing today
- ✓ Academic credit
- ✓ Recipient of funding from pharmaceutical companies and government (with industry partnerships) grants

The story of hip protectors



- ✓ Designed to protect the hips from possible fractures in case of falls



- ✓ Former PhD student, Dr Anna Sawka, conducted a scoping review to assess effect of hip protectors in trials of institutional and community-dwelling elderly

OPEN ACCESS Freely available online

PLoS one

A Scoping Review of Strategies for the Prevention of Hip Fracture in Elderly Nursing Home Residents

Anna M. Sawka[1,2*], Nofisat Ismaila[1], Ann Cranney[3], Lehana Thabane[4], Monika Kastner[5,6], Amiram Gafni[4], Linda J. Woodhouse[7,8], Richard Crilly[9], Angela M. Cheung[1,2,10], Jonathan D. Adachi[11,12], Robert G. Josse[2,13], Alexandra Papaioannou[14,15]

- ✓ We excluded one RCT on the basis of design and methodological quality
  - Kiel DP et al. Efficacy of a Hip Protector to Prevent Hip Fracture in Nursing Home Residents: The HIP PRO Randomized Controlled Trial. *JAMA* 2007;298(4):413-422.

- ✓ **Reasons for exclusion: Methodological concerns**
  - ✓ Some trial **participants were not truly randomized**— brought in to replace dropouts/deaths and the allocation of those replacements was not random
  - ✓ The trial **used 1-sided hip protector** while other trials used a 2-sided

- ✓ Exclusion criteria based on earlier systematic reviews:
  - ✓ J Clin Epidemiol 2007;60: 336–344
  - ✓ Osteoporos Int 2005; 16(12): 1461–1474

Criticized by the author for …

- **Incorrect interpretation of Hip Protector clinical trial**
  - Posted by D Kiel on **21 Jun 2010** at **17:48 GMT**
  - "The authors misinterpreted the design of my clinical trial of hip protectors in JAMA 2007. ….
    All subjects were randomized and there was no attempt to substitute recruited subjects for dropouts or deaths as the authors stated in this paper."

- In Methods section of JAMA 2007:
  - "due to the expected high rate of resident withdrawal from the study (ie. from death, transfer, loss of mobility), residents who withdrew were replaced to maintain a reasonably constant census of active residents"

- **No objection to exclude on the basis of the use of 1- vs 2-sided hip-protectors**

And then…

Front Page Boston Globe July 1, 2011

http://www.boston.com/news/local/massachus
Thabane, Lehana - Outlook W...
Elders not told of risks in hi...
Osteoporosis International, Vol...
File Edit View Favorites Tools Help
SONY
bing

Local Search Site Search
GO

HOME TODAY'S GLOBE NEWS YOUR TOWN BUSINESS SPORTS LIFESTYLE A&E THINGS TO DO TRAVEL CARS JOBS REAL ESTATE
Local National World Politics Business Education Health Science Green Obituaries Special reports Traffic Weather Lottery

HOME / NEWS / LOCAL / MASS.

The Boston Globe

Elders not told of risks in hip study, US alleges

By Kay Lazar and Carolyn Y. Johnson
Globe Staff / July 1, 2011

E-mail | Print | Reprints | Comments (16) Text size

Federal health regulators have accused a research team led by a Harvard doctor of ethical violations after the scientists failed to inform elderly nursing home residents of serious health risks discovered during a study of hip fractures.

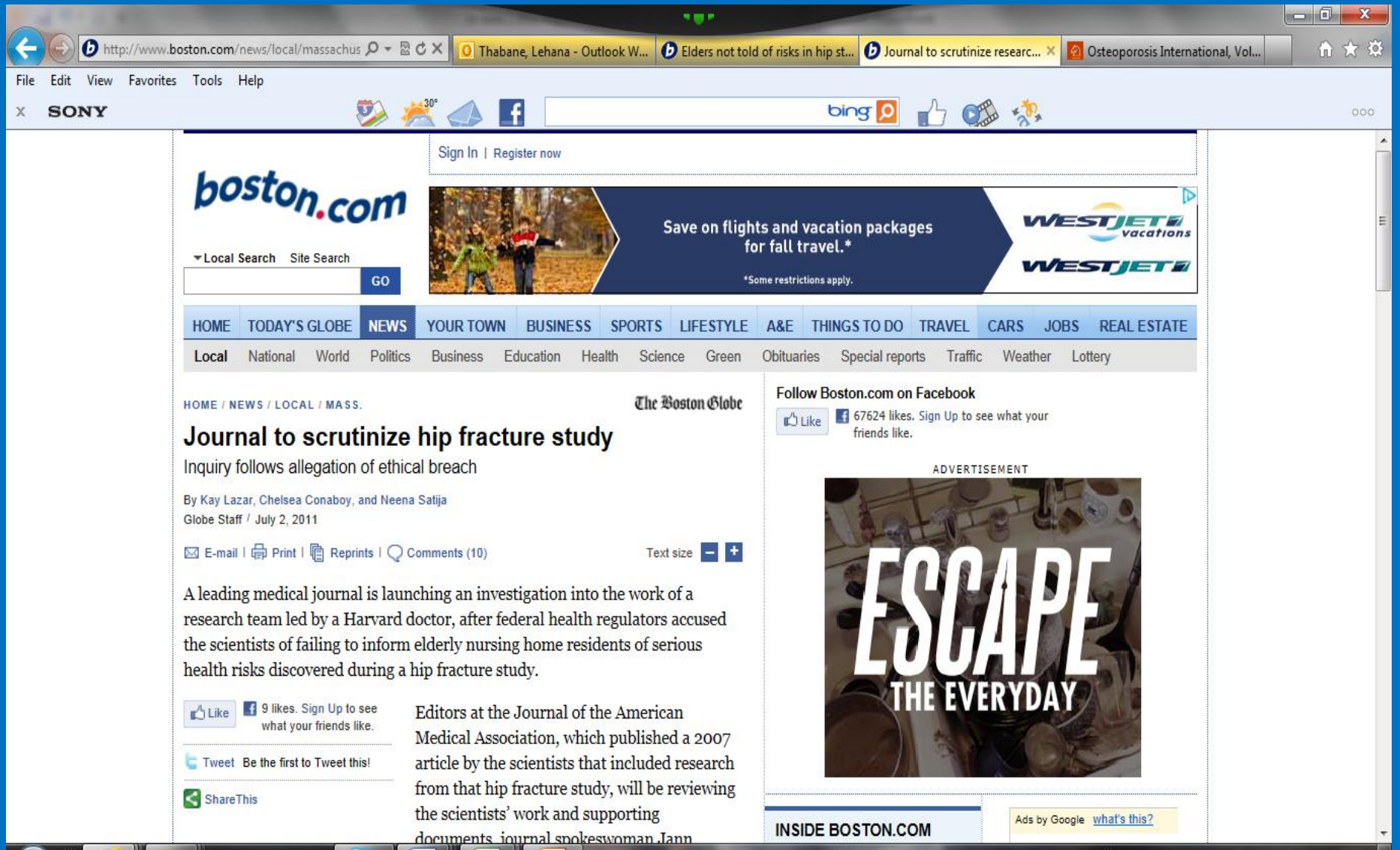
In a letter sent last week to a Harvard-affiliated institution and two other major research universities, the Department of Health and Human Services concluded that the scientists suppressed information about the dangers to elders participating in research on how to reduce often lethal hip injuries. The regulators said the scientists should have shared their findings about the use of protective padded underwear with patients and safety boards that routinely oversee medical studies.

As a result, the federal agency is now ordering the researchers to develop a plan to contact nursing home residents in Boston, St. Louis, and Baltimore who

INSIDE BOSTON.COM
SPOTTED IN BOSTON

EN 3:08 PM 25/07/2012

Front page of Metro section Boston Globe July 2, 2011:



Office for Human Research Protections

Determination letter

June 23, 2011

(http://www.hhs.gov/ohrp/detrm_letrs/YR11/june11a.pdf)

In light of the evidence detailed above, we also determine that investigators failed to report unanticipated problems, i.e., increased falling to the pocketed side and the associated risk of possible fractures, to their respective IRBs, institutional officials, the funding agency and OHRP, in contravention of the requirements of HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5).

We will come back to the conclusion of the story…

What I plan to share

- ✓ A scoping review of the adherence of reporting standards in clinical research
- ✓ Determine key factors associated with adherence to reporting standards; and
- ✓ Provide recommendations to enhance adherence for future studies to minimize biased reporting

Collaborative Effort by

MARS

McMaster Adherence to Reporting Standards

Since the introduction of reporting guidelines,

- ✓ what is the level of adherence to reporting standards in the clinical literature?
- ✓ what are the factors associated with adherence to the reporting standards?
- ✓ What guidance can we provide based on the current state of knowledge on adherence to reporting standards?

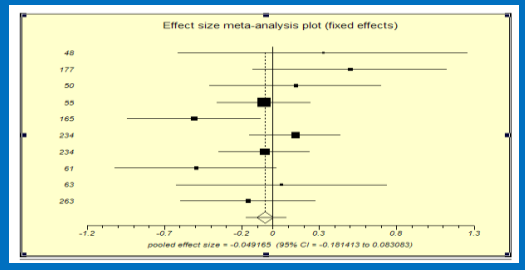
Which guidelines?

- ✓CONSORT
- ✓TREND
- ✓STROBE
- ✓PRISMA (formerly called QUOROM)
- ✓MOOSE

Why are transparency and completeness of reporting important?

- ✓ Incomplete reporting is associated with bias and distortions of effect estimates

- ✓ To facilitate meta-analyses in systematic reviews for guideline development



- ✓ Used as a surrogate marker of study quality

It is an important element of scientific integrity

Methods

- ✓ **Systematic scoping review**

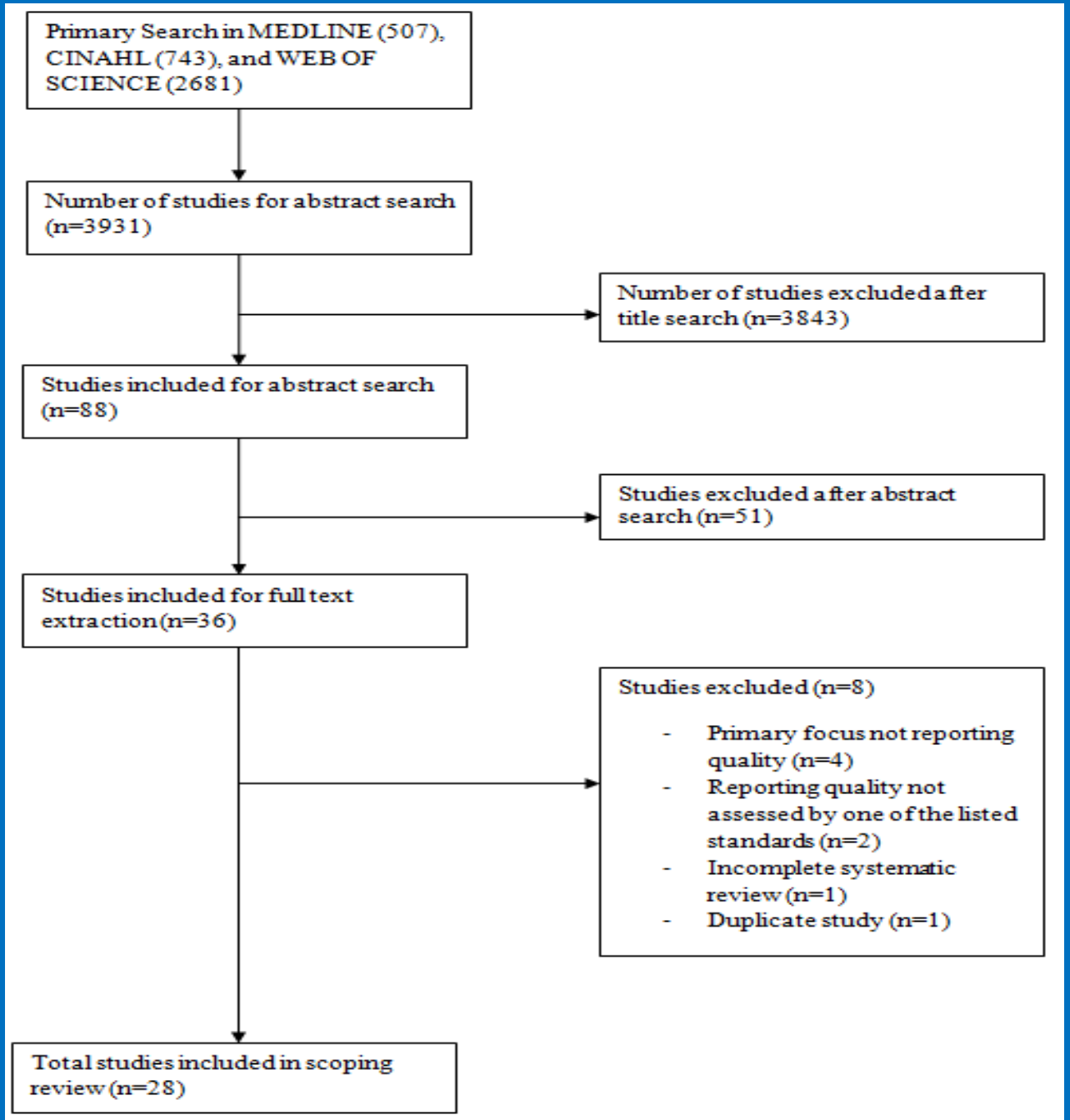
- ✓ **Searched electronic databases**

  CINAHL, Web of Science, and Medline (from 1996 [date of CONSORT] to June 1st 2012)

- ✓ **Search terms:**
  - (Systematic reviews OR reviews OR quality of reporting or completeness of reporting) AND (CONSORT OR STROBE OR QUOROM OR PRISMA OR TREND OR MOOSE) OR adherence.

What did we find?

Flow Diagram of Selection of Studies



- Agreement between raters:
  - 0.69 (95% CI 0.54, 0.85) for abstract screening
  - 0.92 (95% CI 0.77, 1.00) for full text screening

- Key Characteristics of included reviews
  - CONSORT (24/28),
  - PRISMA (2/28)
  - STROBE (1/28)
  - Both CONSORT and STROBE (1/28)
  - No studies on MOOSE, TREND or QUOROM guidelines
  - Number of studies in reviews: 8 to 369

Adherence to reporting

Type of Guideline	Total Number of Studies	Number of Studies Concluding that "some improvements are needed, reporting inadequate, poor, medium, suboptimal, etc"
CONSORT	24	23
PRISMA	2	2
STROBE	1	1
CONSORT and STROBE	1	1

Factors associated with adherence to reporting

First Author	Sample Size	Factors Associated with Adherence ↑↓
Areia	120	1. Poor design (↓) * 2. Journal requiring use of CONSORT (↑) 3. Journal being RCT vs other types of studies, eg. observational (↑)*
Capili	10	1. Journal requiring the use of CONSORT (↑)
Cook	130	1. Time (↑)* 2. Journal being RCT vs other types of studies, eg. observational (↑)*
de Vries	107	1. Presence of industrial sponsoring (↑)
Farrokhyar	50	1. Sample size (↑)* 2. Published in recent years (↑)* 3. Location (↑)* 4. Source of Funding (↓) 5. Type of primary outcome in the study-categorical (↓)
Kiehna	27	1. Article published in a journal endorsing the CONSORT statement (↑)*
Ladd	127	1. RCT article published after 1996 (↑)*
Moberg-Mogren	14	1. Year of publication (↑)*
Montane	92	1. Year of publication (↑)* 2. Impact factor (↑)* 3. Studies with placebo control group (↑)

* - significant increase/decrease, $p \leq 0.05$

Factors associated with adherence to reporting

First Author	Sample Size	Factors Associated with Adherence ↑↓
Montgomery	76	1. Year of publication (↑)*
Plint	8	1. Reporting of method of sequence generation (↑)* 2. Reporting of allocation concealment (↑)* 3. Reporting of overall consort items (↑)
Rios	89	1. Industrial funding (↑)* 2. Journal of publication (↑)* 3. Sample size (↑)*
Stretch	105	1. Reporting of secondary outcomes (↑)* 2. Reporting of adverse events (↑)* 3. Interpretations of results with regard to totality of data (↑)*
Thabane	63	1. Larger sample sizes (↑)* 2. Publication after publication of the CONSORT statement (↑)* 3. Type of Intervention (pharmacologic intervention versus non pharmacologic intervention) (↑)*
Zhong	153	1. Non Chinese reports (compared to those published in mainland China) (↑)* 2. CONSORT-adopters (↑)*
Zigas	261	1. Publication date post- CONSORT publication (↑)* 2. High Impact Factor (↑)*

*** - significant increase/decrease, $p \leq 0.05$**

Take home messages

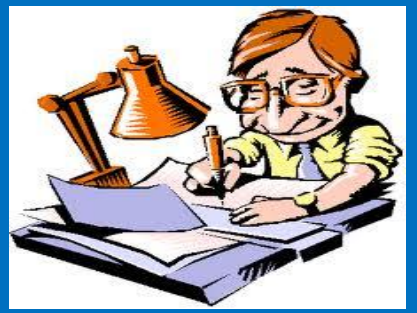
- ✓ Overall adherence to reporting standards is suboptimal
- ✓ Factors associated with better quality or completeness of reporting include:
  - **Study design**: larger sample size
  - **Timing of publication**: Recently published studies
  - **Study Sponsor**: Industry sponsored studies
  - **Journal**: Studies published in journals with a high impact factor; endorsing relevant Statement; requiring Statement checklist

Some Caveats or limitations

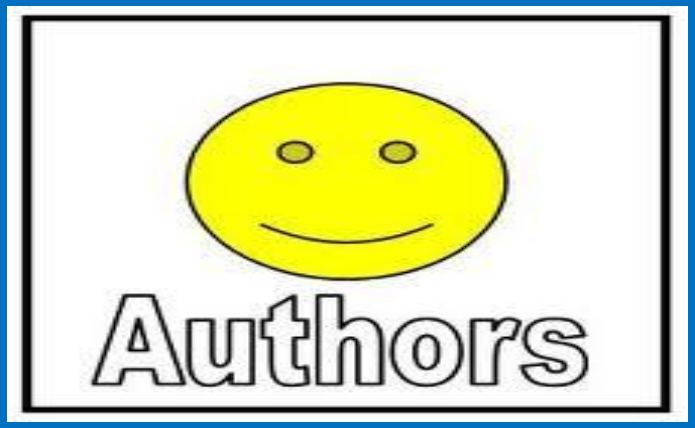
- No reviews addressing adherence to MOOSE, TREND, QUOROM/PRISMA
- **Substantial heterogeneity between reviews**
  - Definitions of outcomes
  - Design/Methods: Sample size determination; Choice of predictor variables
  - Reporting of results
- **No established framework or standards** for the conduct and reporting of reviews assessing the adherence to reporting standards

What guidance can we provide to enhance adherence?

For Editors



- ✓ Endorsement of the standards by journals
  - Include adherence to standards as part of editorial policy
- ✓ Make assessment of adherence to standards as part of peer-review process
  - provide guidelines to peer-reviewers
- ✓ Inclusion of checklist should be a MUST
- ✓ Encourage publication of protocols



- ✓ Include checklists for the respective standards as part of manuscripts
  - this has been shown to enhance completeness of reporting
- ✓ Design large studies
- ✓ Publish the protocol—to get feedback

For IRBs

- ✓ Require protocols to state clearly what "standards" will be used (depending on the design)
  - Ensures investigator awareness of the standards
- ✓ Require inclusion of part of checklist as part of IRB application (ie. background, objectives, methods)

For Educators

- ✓ Incorporate reporting guidelines in research ethics training
- ✓ Provide ongoing training through workshops at professional meetings
- ✓ Emphasize factors shown to improve quality of reporting

Concluding Remarks

- ✓ Transparent reporting of studies is essential to maintain research integrity
- ✓ It is our collective responsibility

What happened to the hip protectors story?

THE CONCLUSION

"Harvard study placed elderly subjects at risk"

Boston Globe: July 20, 2012|Kay Lazar

More than 1,300 nursing home residents who participated in a Harvard-led study on preventing hip fractures, including 268 in Massachusetts, **will soon be receiving letters detailing serious risks that federal regulators say they were exposed to by the researchers**….

……

"**Investigators failed to provide subjects with significant new findings about these risks developed during the course of the research which may have related to the subject's willingness to continue participation,"** the Office for Human Research Protections stated in July 5 notices that were made public Wednesday….

Lessons from the HIP PRO Trial

① Inadequate reporting (based on CONSORT)

- Randomization process (Items 8a-10)
- Harms: "All important harms or unintended effects in each group" (Item 19)

We judged the trial design as poor based on poor reporting—this was a RED FLAG!

② Poor and unethical trial design
(OHRP determination Letter: June 23, 2011)

- "The use of this one-sided protection was a departure from the way that hip protection underwear is actually used clinically, where hip protection, if offered, is provided on both hips. …"

- "The purpose behind this aspect of the study design was that each subject could serve as their own control: they would each have a "protected" and an "unprotected" hip. "

Scientists have the obligation to use ethical designs in pursuit of new knowledge:

Another RED FLAG!

③ Failure to disclose relevant info on adverse events to…

- IRBs
- DSMB
- Study participants
- Funding agency
- OHRP
- JAMA Editors

… Even after JAMA reviewers specifically asked about adverse event distribution between 1-vs 2-sided hip-protector vs no hip-protection

It is important to acknowledge the challenges of conducting trials in nursing home populations

- ✓ Many residents are cognitively impaired
- ✓ High competing risks of death
- ✓ Comorbidities
- ✓ Ethical challenges with a vulnerable population

Thanks to

- MARS group
- Dr Anna Sawka
- David's team of conference organizers
- You—the attendees!