UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Feedback da palestra

Conflict of interests: from research to clinical

Dr. Marco Bobbio
16ª Atualização em Bioética
Instituto de Bioética da PUCRS
10/09/2015

Apresentação: Bióol. Andréia Rocha

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

SOBRE O AUTOR

Marco Bobbio

-Professor, cardiologista e diretor chefe do Ospedale S.Croce e Carle di Cuneo (Itália);

- Integra o movimento médico *Slow Medicine;*

- Autor do livro: O Doente Imaginado.

http://medicinahospitalar.blogspot.com.br/2015/08/fazer-mais-nao-significa-fazer-melhor.html

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

SLOW MEDICINE

- Movimento médico nascido na Itália na última década;

> *"O lema é praticar uma medicina o menos invasiva possível, que respeite a vontade do paciente."*
> Marco Bobbio

- Visa uma medicina:

Sóbria – capacidade de agir com moderação, de forma gradual e essencial;
Respeitosa – encoraja uma comunicação honesta, cuidadosa e completa com os pacientes;
Justa – cuidados adequados e de boa qualidade para todos.

http://www.slowmedicine.it/Manifesto_PORT.pdf

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

CONFLITO DE INTERESSE X CORRUPÇÃO

CONFLITO DE INTERESSE:

- Ocorre comumente;

-É normal!

CORRUPÇÃO:

- Sob hipótese alguma deveria ocorrer;

- É "anormal";

-Passível de sanções criminosas (?);

"No sistema de saúde, é a mãe da morte e da vida"....

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Acerca do Conflito de Interesse...

- **Como a informação é produzida?**
- **Como a informação é difundida?**
- **Como a informação é validada?**

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Como a informação é produzida?

- Resultados positivos " enviesados";

Ex.: Caso GSK

Paxil: In the criminal information, the government alleges that, from April 1998 to August 2003, GSK unlawfully promoted Paxil for treating depression in patients under age 18, even though the FDA has never approved it for pediatric use. The United States alleges that, among other things, GSK participated in preparing, publishing and distributing a misleading medical journal article that misreported that a clinical trial of Paxil demonstrated efficacy in the treatment of depression in patients under age 18, when the study failed to demonstrate efficacy. At the same time, the United States alleges, GSK did not make available data from two other studies in which Paxil also failed to demonstrate efficacy in treating depression in patients under 18. The United States further alleges that GSK sponsored dinner programs, lunch programs, spa programs and similar activities to promote the use of Paxil in children and adolescents. GSK paid a speaker to talk to an audience of doctors and paid for the meal or spa treatment for the doctors who attended. Since 2004, Paxil, like other antidepressants, included on its label a "black box warning" stating that antidepressants may increase the risk of suicidal thinking and behavior in short-term studies in patients under age 18. GSK agreed to plead guilty to misbranding Paxil in that its labeling was false and misleading regarding the use of Paxil for patients under 18.

http://www.justice.gov/opa/pr/glaxosmithkline-plead-guilty-and-pay-3-billion-resolve-fraud-allegations-and-failure-report

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

- Manipulações no Protocolo (pacientes, endpoints, comparadores, follow-up...);

Productivity of authors in the field of diabetes: bibliographic analysis of trial publications

BMJ 2015 ;351 doi: http://dx.doi.org/10.1136/bmj.h2638 (Published 01 July 2015)

Frits Holleman, internist [1], Mick Uijldert, student [1], Lennart F Donswijk, house officer in internal medicine [2], Edwin A M Gale, professor [3]

Results 3782 articles from 13 592 authors were identified. The top 110 authors were named in 1227 (32.4%) of all articles, and the top 11 authors in 397 (10.5%) of all articles. The top 110 authors published 991 RCTs for a median of 20 (range 4-77) RCTs per author; the top 11 published 354 RCTs for a median of 42 (36-77) RCTs per author. Of the 110 top authors, 48 were employed by a pharmaceutical company. Of the 991 RCTs, 906 were commercially sponsored. Of 704 articles that could be assessed for conflicts of interest, only 42 (6%) were considered fully independent. Medical writing assistance was acknowledged in 439 (44.3%) of 991 RCTs.

Conclusion The past two decades have seen an explosive increase in the number of published clinical trials regarding glucose lowering treatment. Some authors have made a disproportionate contribution to the therapeutic evidence base; one third of the RCT evidence base on glucose lowering drug treatment for diabetes was generated by <1% of authors. Of these, 44% were company employees and 56% were academics who work closely with the pharmaceutical companies.

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Managing Conflicts of Interest in the Conduct of Clinical Trials

Karine Morin, LLM; Herbert Rakatansky, MD; Frank A. Riddick, Jr, MD; Leonard J. Morse, MD; John M. O'Bannon III, MD; Michael S. Goldrich, MD; Priscilla Ray, MD; Matthew Weiss, MD; Robert M. Sade, MD; Monique A. Spillman, MD, PhD

JAMA. 2002;287(1):78-84. doi:10.1001/jama.287.1.78.

- Conflito de funções: médico como investigador;
- Conflito financeiro, entre outros.

PLoS Med. 2005 Aug; 2(8): e124.
Published online 2005 Aug 30. doi: 10.1371/journal.pmed.0020124

Why Most Published Research Findings Are False

John P. A. Ioannidis

Modeling the Framework for False Positive Findings Go to:

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a *p*-value less than 0.05. Research is not most appropriately represented and summarized by *p*-values, but, unfortunately, there is

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Como a informação é difundida?

The effects of pharmaceutical firm enticements on physician prescribing patterns. There's no such thing as a free lunch.

J P Orlowski and L Wateska

Chest 1992;102:270-273
DOI 10.1378/chest.102.1.270

We examined the impact on physician prescribing patterns of pharmaceutical firms offering all-expenses-paid trips to popular sunbelt vacation sites to attend symposia sponsored by a pharmaceutical company. The impact was assessed by tracking the pharmacy inventory usage reports for two drugs before and after the symposia. Both drugs were available only as intravenous preparations and could be used only on hospitalized patients. The usage patterns were tracked for 22 months preceding each symposium and for 17 months after each symposium. Ten physicians invited to each symposium were interviewed about the likelihood that such an enticement would affect their prescribing patterns. A significant increase in the prescribing pattern of both drugs occurred following the symposia. The usage of drug A increased from a mean of 81±44 units before the symposium to a mean of 272±117 after the symposium ($p<0.001$). The usage of drug B changed from 34±30 units before the symposium to 87±24 units ($p<0.001$) after the symposium. These changed prescribing patterns were also significantly different from the national usage patterns of the two drugs by hospitals with more than 500 beds and major medical centers over the same period of time. These alterations in prescribing patterns occurred even though the majority of physicians who attended the symposia believed that such enticements would not alter their prescribing patterns. *(Chest 1992; 102:270-73)*

- Outra artifício utilizado: retardo de publicações cujos resultados foram desfavoráveis.

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Como a informação é validada?

Relationships Between Authors of Clinical Practice Guidelines and the Pharmaceutical Industry FREE

Niteesh K. Choudhry, MD, FRCPC; Henry Thomas Stelfox, MD, FRCPC; Allan S. Detsky, MD, PhD, FRCPC

JAMA. 2002;287(5):612-617. doi:10.1001/jama.287.5.612.

Objective To quantify the extent and nature of interactions between authors of CPGs and the pharmaceutical industry.

Design, Setting, and Participants Cross-sectional survey of 192 authors of 44 CPGs endorsed by North American and European societies on common adult diseases published between 1991 and July 1999. One hundred authors (52%) provided usable responses representing 37 of 44 different CPGs that we identified.

Results Eighty-seven percent of authors had some form of interaction with the pharmaceutical industry. Fifty-eight percent had received financial support to perform research and 38% had served as employees or consultants for a pharmaceutical company. On average, CPG authors interacted with 10.5 different companies. Overall, an average of 81% (95% confidence interval, 70%-92%) of authors per CPG had interactions. Similarly, all of the CPGs for 7 of the 10 diseases included in our study had at least 1 author who had some interaction. Fifty-nine percent had relationships with companies whose drugs were considered in the guideline they authored, and of these authors, 96% had relationships that predated the guideline creation process. Fifty-five percent of respondents indicated that the guideline process with which they were involved had no formal process for declaring these relationships. In published versions of the CPGs, specific declarations regarding the personal financial interactions of individual authors with the pharmaceutical industry were made in only 2 cases. Seven percent thought that their own relationships with the pharmaceutical industry influenced the recommendations and 19% thought that their coauthors' recommendations were influenced by their relationships.

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Dronedarone for Atrial Fibrillation
The Limited Reliability of Clinical Practice Guidelines

Primiano Iannone, MD[1]; Enrico Haupt, MD[1]; Gaddo Flego, MD[2]; Paola Truglio, MD[1]; Monica Minardi, MD[3]; Simon Clarke, MD[3]; Nicola Magrini, MD[4]

JAMA Intern Med. 2014;174(4):625-629. doi:10.1001/jamainternmed.2013.14485.

Concerns have been expressed about the reliability of clinical practice guidelines. We analyzed 3 guidelines from medical specialty societies about dronedarone hydrochloride, an antiarrhythmic drug related to amiodarone hydrochloride, for treatment of patients with atrial fibrillation. We compared the recommendations in these guidelines with the conclusions about dronedarone that we reached by applying the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Method to the same evidence base. In our analysis, as a rate control drug, dronedarone was better than placebo only for a surrogate outcome (heart rate). As a rhythm control drug, dronedarone was associated with 13 (95% CI, −15 to 61) excess deaths per 1000 patients treated as compared with placebo. Compared with amiodarone, dronedarone was less effective (214 [95% CI, 130 to 294] more recurrences of atrial fibrillation per 1000 patients treated) and similarly tolerated (−28 [95% CI, −69 to 33] more serious adverse events requiring drug suspension per 1000 patients treated). Despite the limits of the evidence, all 3 guidelines recommended dronedarone for prevention of recurrences of atrial fibrillation; 2 of the guidelines recommended it as a rate control agent. Our findings raise questions about the reliability of these clinical practice guidelines, as well as the financial associations between many of the panel members and the manufacturer of dronedarone.

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

CONSIDERAÇÕES

- Problema de saúde pública (?)ç
- Segurança do paciente;
- Declaração de conflito de interesse:
  - CAÓTICA
  - INCONSISTENTE
  - INCOMPLETA

- Physician Payment Sunshine Act

Dollars for Doctors

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

A grande alternativa a este cenário

é o acesso aberto aos dados das pesquisas...

Concordam ???
Quais as implicações disto ???

www.isaia.com.br
Porto Alegre/RS

UNIDADE DE PESQUISA CLÍNICA
Centro de Medicina Reprodutiva Dr Carlos Isaia Filho Ltda.

Referências adicionais

https://www.tudofarma.com.br/noticias/noticiasInterna.asp?Textos_ID=50961

http://www.slowmedicine.it

http://www.slowmedicine.it/Manifesto_PORT.pdf

http://www.justice.gov/opa/pr/glaxosmithkline-plead-guilty-and-pay-3-billion-resolve-fraud-allegations-and-failure-report

www.isaia.com.br
Porto Alegre/RS