Integridade em Ciência

João Lobo Antunes
Professor Catedrático da Faculdade de Medicina de Lisboa
Presidente do Instituto de Medicina Molecular

Integridade em Ciência

- Integridade = (In) “tangere”
  intocado, completo, puro, sólido

- Ciência – “qua” Conhecimento
  Cientista individual
  Instituição

Integridade a nivel individual

- Honestidade intelectual na proposta, execução e relato da investigação
- Rigor na representação da colaboração
- Justiça na “peer-review”
- Colegialidade na colaboração, incluindo comunicação e partilha de recursos
- Transparência nos conflitos de interesse
- Protecção dos participantes nas investigações
- Protecção dos animais
- Partilha da responsabilidade entre a investigadores e restantes membros da equipa.

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“Science has been enourmously successful as a strategy to command the future because it admits no distinction between ends and means.

There are no higher ends in science than truthful knowledge, and there are no other means allowed in the way than truthful knowledge.”

J. Bronowski “Technology and Culture Evolution”

Daedalus Spring 1972

O “telos” intrinseco (da ciência) é a vontade da verdade

Fernando Gil, “A ciência tal qual se faz”

“Científico “ tornou-se para todos os efeitos uma forma de louvor espistémico que significa “forte, confiável, seguro”

e contudo...

como todas as actividades humanas a ciência é falível, imperfeita, por vezes corrupta e, evidentemente, incompleta.

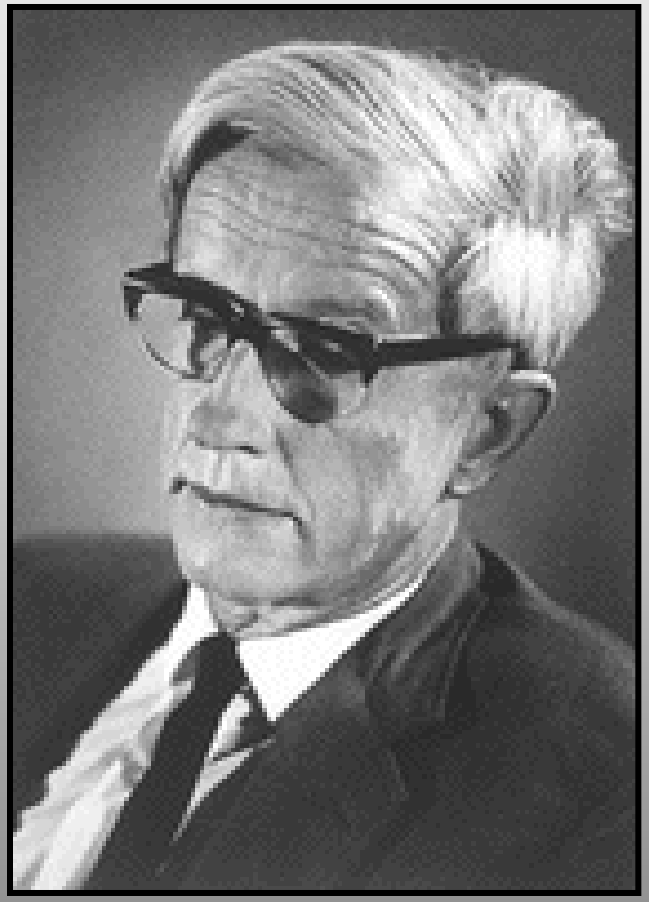
“Science does not exist until it is published”

Drummond Rennie Lancet 1998;352:SII18

Henry Oldenburg (1617-1677)
founder of Royal Society

- "Philosophical Transactions: giving some Accompt of the Present Undertakings, Studies and Labours of the Ingenious in Many Considerable Parts of the World" March 6, 1665

- *"... That a proper person might be found out to discover plagiarys and to assert inventions to their proper authors"*



Max Delbrück

(1906-1981)

Nobel speech, 1969

- “The artist’s communication is linked forever with its original form, that of the scientist is modified, amplified, fused with the ideas and results of others, and melts into the stream of knowledge.”

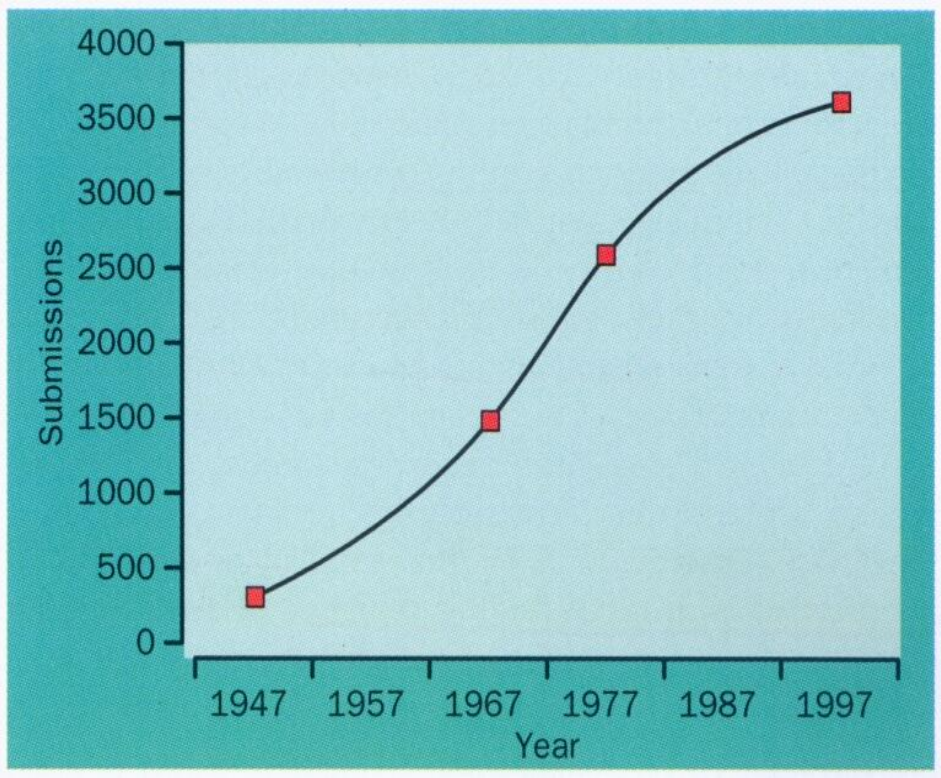
As **publicações** são unidades fundamentais, de troca de informação, prova de produtividade e creatividade, e base para futura investigação e desenvolvimento

Promoção académica

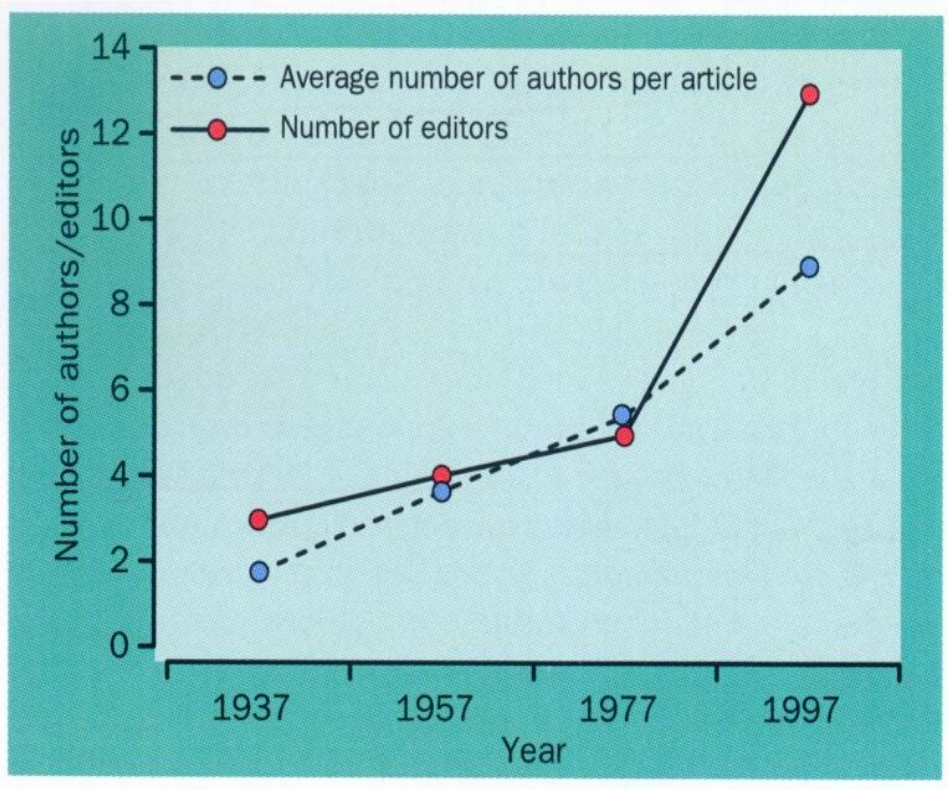
- Produtividade (quantidade)
- Independência (1.º autor/senior)
- Relevância (qualidade)

Há mais de 16000 jornais médicos

Manuscripts submitted to NEJM



Authors/article and Editors do NEJM



Drummond Rennie. Lancet 1998;352:SII18

The New England
Journal of Medicine

Volume 329 SEPTEMBER 2, 1993 Number 10

AN INTERNATIONAL RANDOMIZED TRIAL COMPARING FOUR THROMBOLYTIC STRATEGIES FOR ACUTE MYOCARDIAL INFARCTION

THE GUSTO INVESTIGATORS*

Abstract *Background.* The relative efficacy of streptokinase and tissue plasminogen activator and the roles of intravenous as compared with subcutaneous heparin as adjunctive therapy in acute myocardial infarction are unresolved questions. The current trial was designed to compare new, aggressive thrombolytic strategies with standard thrombolytic regimens in the treatment of acute myocardial infarction. Our hypothesis was that newer thrombolytic strategies that produce earlier and sustained reperfusion would improve survival.

Methods. In 15 countries and 1081 hospitals, 41,021 patients with evolving myocardial infarction were randomly assigned to four different thrombolytic strategies, consisting of the use of streptokinase and subcutaneous heparin, streptokinase and intravenous heparin, accelerated tissue plasminogen activator (t-PA) and intravenous heparin, or a combination of streptokinase plus t-PA with intravenous heparin. ("Accelerated" refers to the administration of t-PA over a period of 1½ hours — with two thirds of the dose given in the first 30 minutes — rather than the conventional period of 3 hours.) The primary end point was 30-day mortality.

Results. The mo

groups were as follows: streptokinase and subcutaneous heparin, 7.2 percent; streptokinase and intravenous heparin, 7.4 percent; accelerated t-PA and intravenous heparin, 6.3 percent; and the combination of both thrombolytic agents with intravenous heparin, 7.0 percent. This represented a 14 percent reduction (95 percent confidence interval, 5.9 to 21.3 percent) in mortality for accelerated t-PA as compared with the two streptokinase-only strategies ($P = 0.001$). The rates of hemorrhagic stroke were 0.49 percent, 0.54 percent, 0.72 percent, and 0.94 percent in the four groups, respectively, which represented a significant excess of hemorrhagic strokes for accelerated t-PA ($P = 0.03$) and for the combination strategy ($P<0.001$), as compared with streptokinase only. A combined end point of death or disabling stroke was significantly lower in the accelerated–t-PA group than in the streptokinase-only groups (6.9 percent vs. 7.8 percent, $P = 0.006$).

Conclusions. The findings of this large-scale trial indicate that accelerated t-PA given with intravenous heparin provides a survival benefit over previous stand- Engl J Med 1993;329:

972 autores

2 palavras por autor

SINCE the landm
nase by the Gr
Streptochinasi nell
1986,[1] there has b
thrombolytic regim
benefit in patients
except for the important addition of aspirin.[2] Collectively, the large trials of thrombolytic therapy demonstrated a 25 percent reduction in 30-to-35-day mortality in patients presenting to the hospital within six hours of the onset of symptoms.[3] Neither the GISSI-2/International trial nor the Third International Study of Infarct Survival (ISIS-3) trial[4-6] of

a difference in associ-
of streptokinase and
activator (t-PA)[4,5] or
and that of anistre-
ion of subcutaneous
t significantly reduce
mortality as compared with no use of heparin.[5,6] Although clear differences between thrombolytic agents are evident in the speed with which the agents achieve reperfusion, the similar survival rates in these previous trials suggested that factors other than rapid or sustained coronary reperfusion might be important in reducing mortality.

Recent data suggest that more rapid and effective infarct-artery patency can be achieved with accelerated t-PA,[7-9] that lower rates of reocclusion are observed with the use of combination thrombolytic therapy,[10-12] and that infarct-artery patency can be sustained longer with the use of intravenous heparin as an adjunct to thrombolytic therapy.[13-15] ("Accelerated" t-PA refers to the rapid intravenous administra-

Address reprint requests to Dr. Eric Topol at the Department of Cardiology, One Clinic Center, Cleveland Clinic Foundation, Cleveland, OH 44195.

Supported by a combined grant from Bayer, CIBA-Corning, Genentech, ICI Pharmaceuticals, and Sanofi Pharmaceuticals.

Dr. Topol, as chairman of the study, assumes full responsibility for the overall content and integrity of the manuscript.

*A list of the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) investigators appears in the Appendix.

As politicas de publicação

- O sítio onde se publica é mais importante que a mensagem
- A ânsia da publicidade

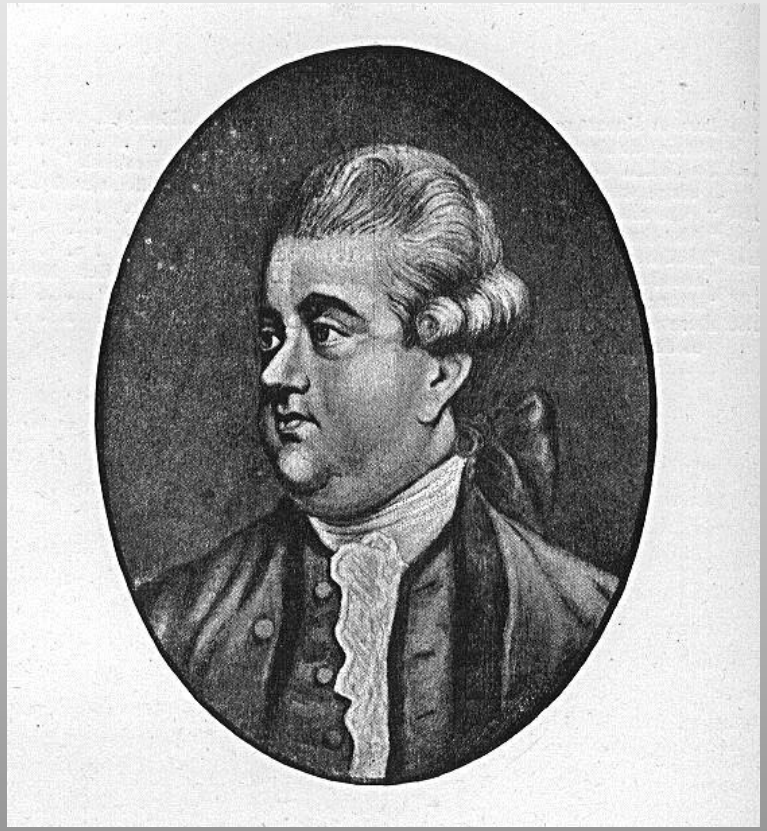
Uma “short letter” na Nature ou um “report” na Science vale mais que um “full article” num jornal mais especializado.

Publicação às fatias - “Salami publication”(MPU – minimal publishable unit)

Aumenta a probabilidade de aceitação:

- expressões “chave” – “paradigma”
- ligação, mesmo que ténue, a doença humana

(Peter Lawrence, Nature 422: 259, 2003)

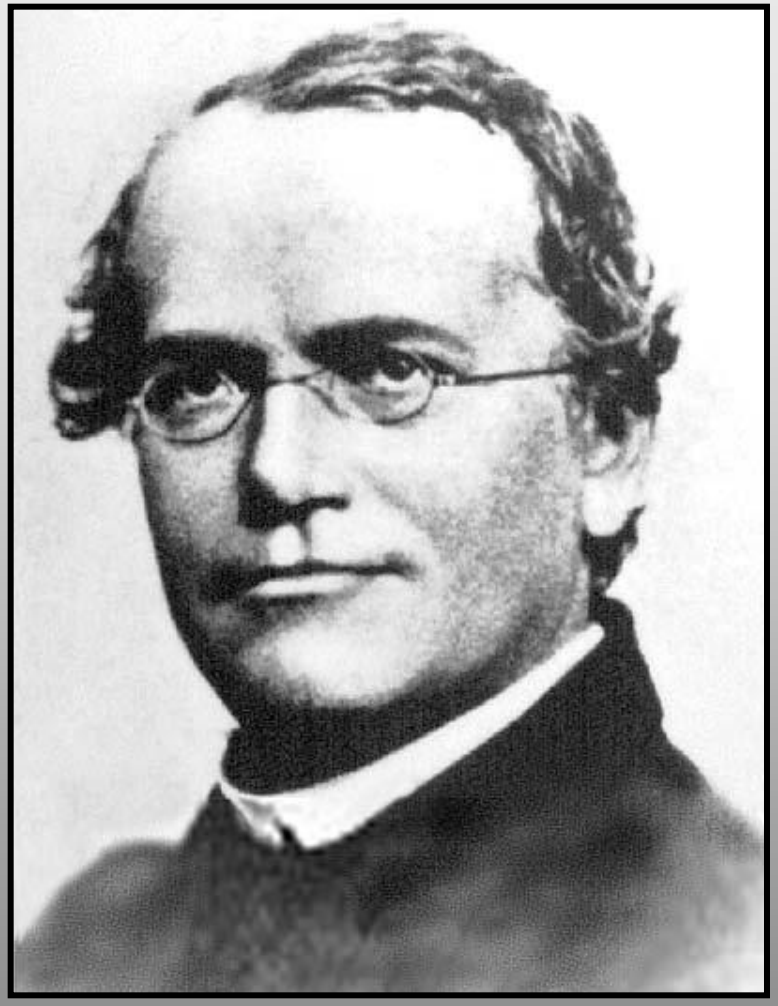


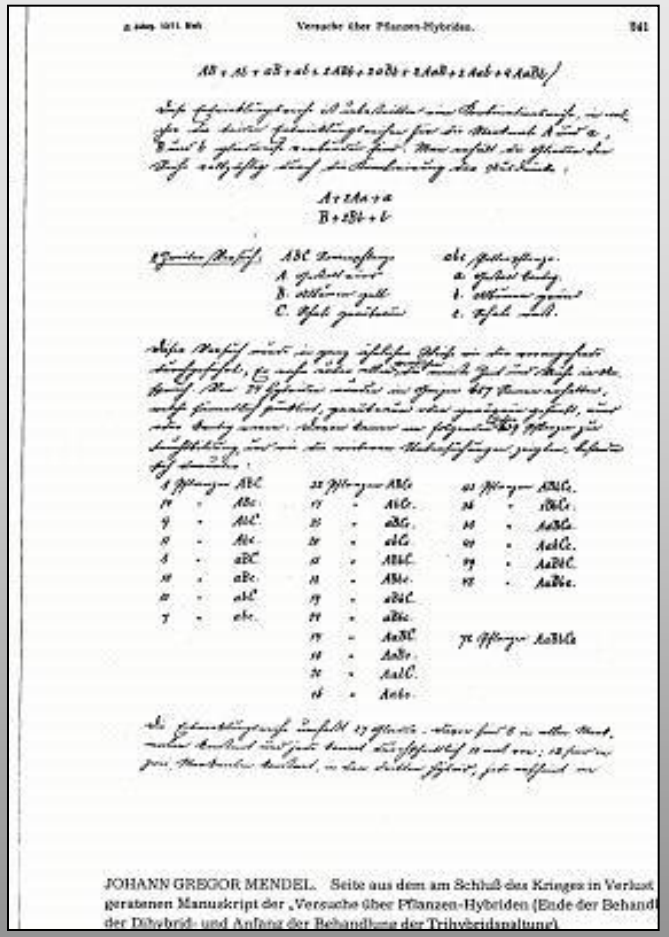
Edward Gibbon

(1737-1794)

"The History of the Decline and Fall of the Roman Empire"

"Consider me not as a contemptible thief but as an honest and industrious manufacturer"

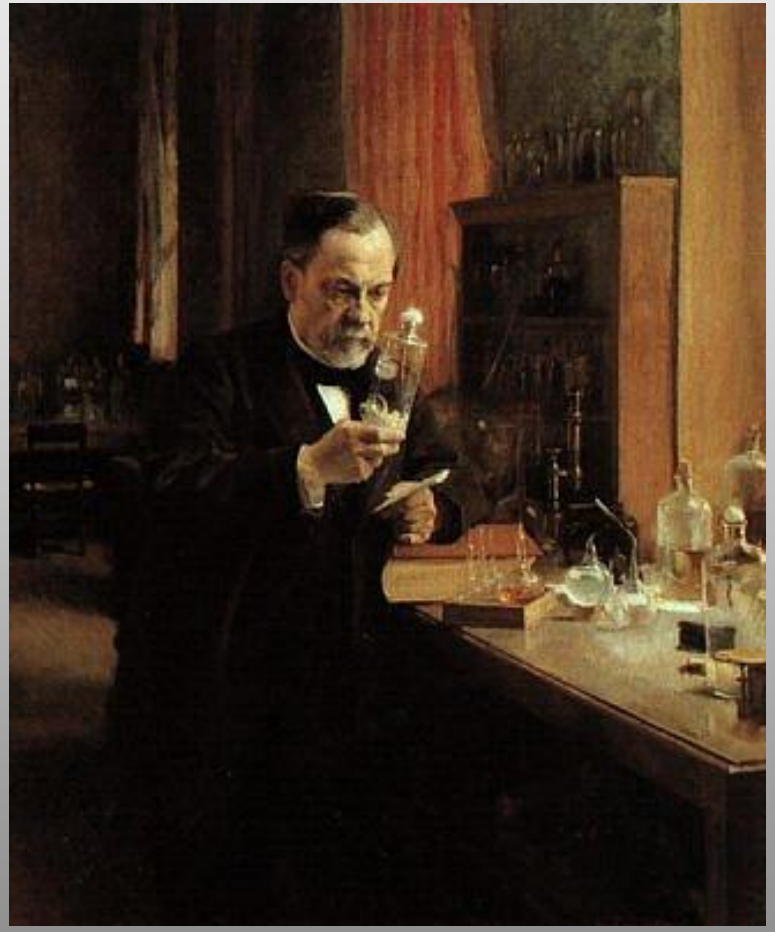




JOHANN GREGOR MENDEL. Seite aus dem am Schluß des Krieges in Verlust geratenen Manuskript der „Versuche über Pflanzen-Hybriden (Ende der Behandl der Dihybrid- und Anfang der Behandlung der Trihybridanalyse)

Gregor Johan Mendel

(1822-1884)



Louis Pasteur

(1822-1895)

COMPTES RENDUS

DES SÉANCES

DE L'ACADÉMIE DES SCIENCES.

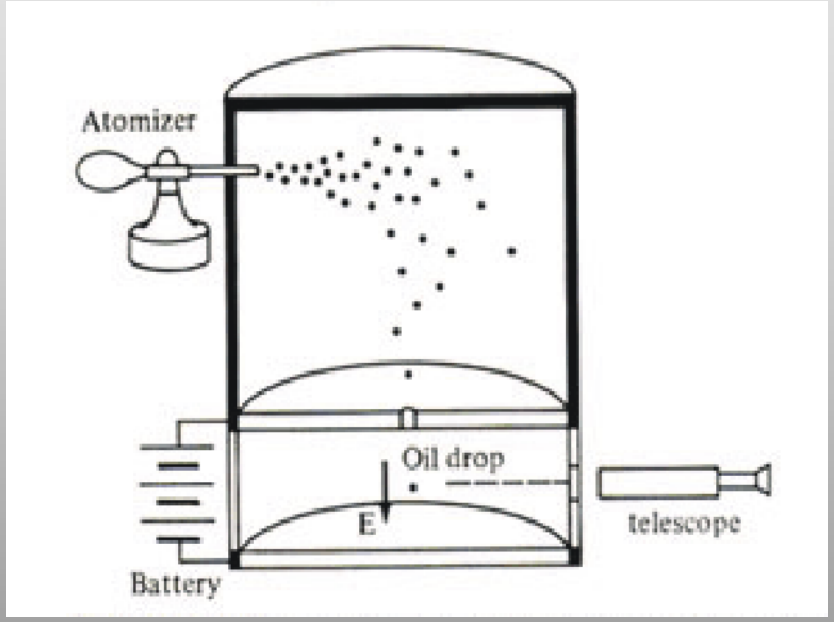
SÉANCE DU LUNDI 13 JUIN 1881.

PRÉSIDENCE DE M. WURTZ.

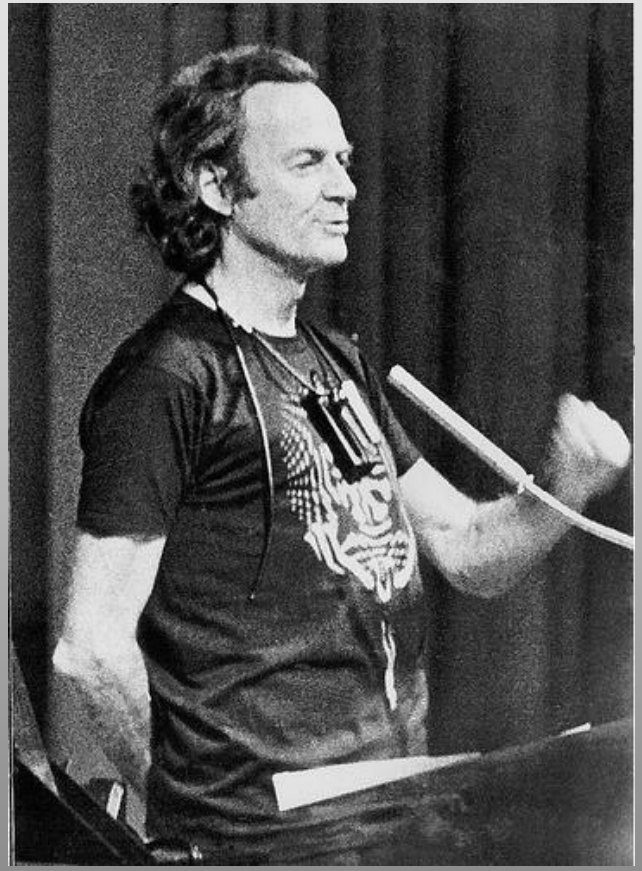
» Afin de rendre les expériences plus comparatives, on inocula alternativement un animal vacciné et un animal non vacciné. L'opération faite, rendez-vous fut pris, par toutes les personnes présentes, pour le jeudi 2 juin, par conséquent après quarante-huit heures seulement depuis le moment de l'inoculation virulente générale.

Robert A. Millikan

(1868-1953)



The Wisdom of Richard Feynman



Richard Feynman
(1918-1988)

... If you are doing an experiment, you should report everything that you think might make it invalid – not only what you think is right about it.

... The first principle is that you must not fool yourself – and you are the easiest person to fool.

...You should not fool the layman when you're talking as scientist.

CARGO CULT SCIENCE

Caltech's 1974 Commencement Address

RETRACTION

Post date 12 January 2006

The final report from the Investigation Committee of Seoul National University (SNU) (*1*) has concluded that the authors of two papers published in *Science* (*2*, *3*) have engaged in research misconduct and that the papers contain fabricated data. With regard to Hwang *et al.*, 2004 (*2*), the Investigation Committee reported that the data showing that DNA from human embryonic stem cell line NT-1 is identical to that of the donor are invalid because they are the result of fabrication, as is the evidence that NT-1 is a bona fide stem cell line. Further, the committee found that the claim in Hwang *et al.*, 2005 (*3*) that 11 patient-specific embryonic stem cells line were derived from cloned blastocysts is based on fabricated data. According to the report of the Investigation Committee, the laboratory "does not possess patient-specific stem cell lines or any scientific basis for claiming to have created one." Because the final report of the SNU investigation indicated that a significant amount of the data presented in both papers is fabricated, the editors of *Science* feel that an immediate and unconditional retraction of both papers is needed. We therefore retract these two papers and advise the scientific community that the results reported in them are deemed to be invalid.

As we post this retraction, seven of the 15 authors of Hwang *et al.*, 2004 (*2*) have agreed to retract their paper. All of the authors of Hwang *et al.*, 2005 (*3*) have agreed to retract their paper.

Science regrets the time that the peer reviewers and others spent evaluating these papers as well as the time and resources that the scientific community may have spent trying to replicate these results.

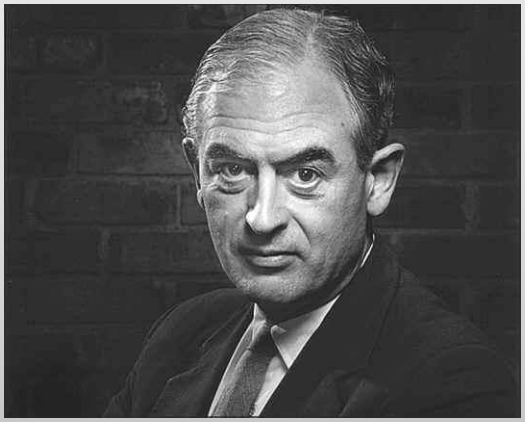
Donald Kennedy
Editor-in-Chief

References

1. Investigation Committee Report, Seoul National University, 10 Jan. 2006. (Members: Chairman Myung-Hee Chung, SNU, Uhtaek Oh, SNU, Hong-Hee Kim, SNU, Un Jong Pak, SNU, Yong Sung Lee, Hanyang University, In Won Lee, SNU, In Kwon Chung, Yonsei University, Jin Ho Chung, SNU).
2. W.-S. Hwang *et al.*, Evidence of A Pluripotent Human Embryonic Stem Cell Line Derived From a Cloned Blastocyst, *Science* **303**, 1669 (2004).
3. W.-S. Hwang *et al.*, Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts, *Science* **308**, 1777 (2005).

Published online 12 January 2006; in print 20 January 2006
10.1126/science.1124926

Porque é que o fazem?



Peter Medawar
1915-1987

- Hunger for scientific reputation and the esteem of colleagues
- The passionate belief in the truth and significance of a theory or hypothesis which is disregarded or not believed

"Scientific Fraud", In: "The Threat and the Glory"

Sidney Brenner
1927-

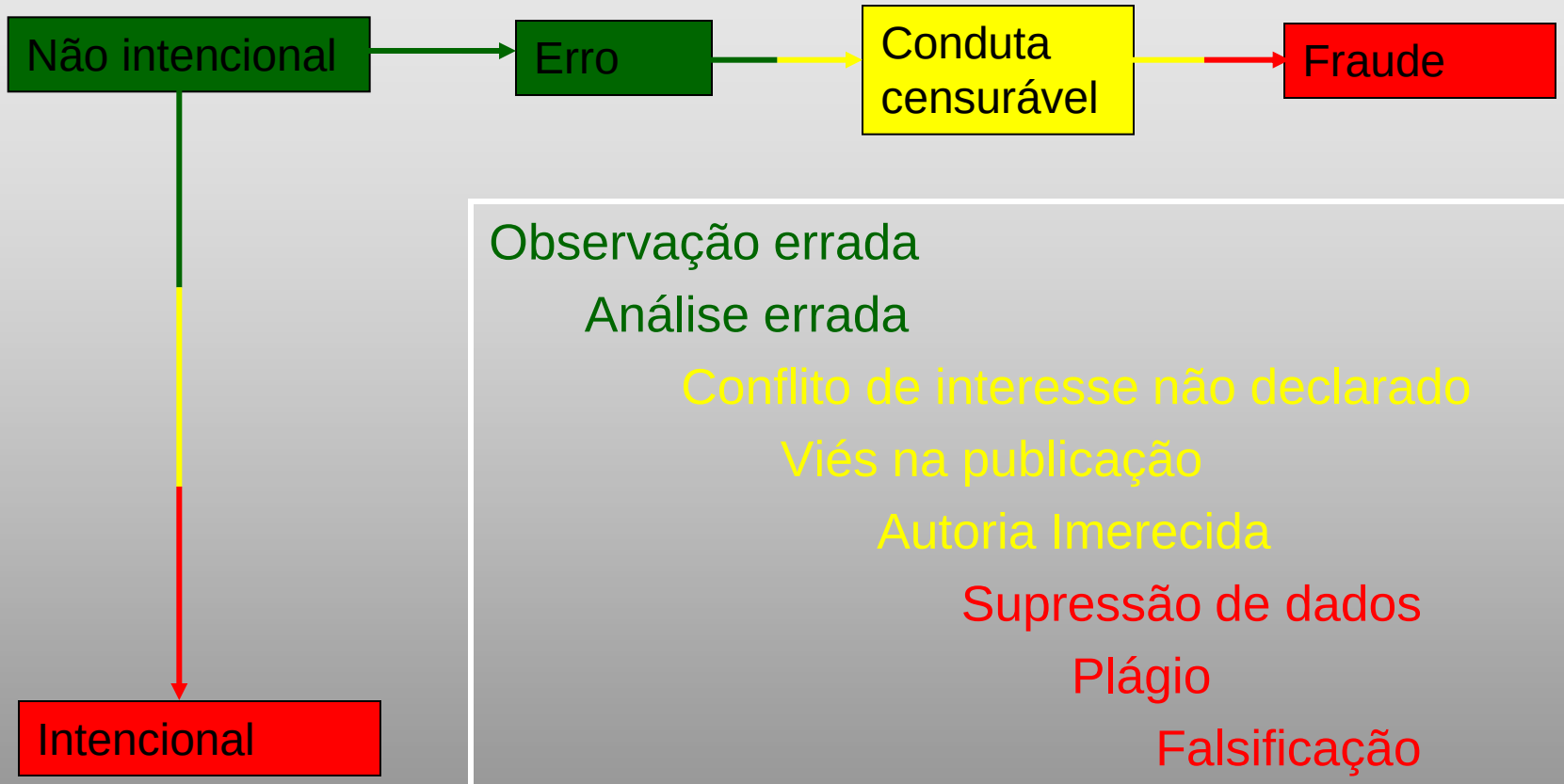
- Is the product of the work structure, because we now have a managerial structure
- There is the problem of the scientist who gets hold of an idea that he then falls in love with and can't let go

"My life in Science"

A fraude cientifica é uma representação deliberadamente falsa da verdade

É diferente de

- “Má ciência”
- Interpretações erradas de dados
- Erro na prova
- Comportamento eticamente censurável
- Negligência



M. Nylenna, S. Simonsen
Lancet 367:1882, 2006

- Pub Med 2000-2002

- 400,000 78 artigos retirados (0.02%)

Integridade científica em Ensaios clínicos

4.7% dos inquiridos – envolvidos em projectos em que ocorreu comportamento fraudulento nos últimos 10 anos

40% tinham conhecimento pessoal de fraude durante 30 anos de carreira

Gardner et al, Contemp Clin Trials 26:244-255, 2005

Table 1 | Percentage of scientists who say that they engaged in the behaviour listed within the previous three years ($n = 3,247$)

Top ten behaviours	All	Mid-career	Early-career
1. Falsifying or 'cooking' research data	0.3	0.2	0.5
2. Ignoring major aspects of human-subject requirements	0.3	0.3	0.4
3. Not properly disclosing involvement in firms whose products are based on one's own research	0.3	0.4	0.3
4. Relationships with students, research subjects or clients that may be interpreted as questionable	1.4	1.3	1.4
5. Using another's ideas without obtaining permission or giving due credit	1.4	1.7	1.0
6. Unauthorized use of confidential information in connection with one's own research	1.7	2.4	0.8 ***
7. Failing to present data that contradict one's own previous research	6.0	6.5	5.3
8. Circumventing certain minor aspects of human-subject requirements	7.6	9.0	6.0 **
9. Overlooking others' use of flawed data or questionable interpretation of data	12.5	12.2	12.8
10. Changing the design, methodology or results of a study in response to pressure from a funding source	15.5	20.6	9.5 ***
Other behaviours			
11. Publishing the same data or results in two or more publications	4.7	5.9	3.4 **
12. Inappropriately assigning authorship credit	10.0	12.3	7.4 ***
13. Withholding details of methodology or results in papers or proposals	10.8	12.4	8.9 **
14. Using inadequate or inappropriate research designs	13.5	14.6	12.2
15. Dropping observations or data points from analyses based on a gut feeling that they were inaccurate	15.3	14.3	16.5
16. Inadequate record keeping related to research projects	27.5	27.7	27.3

Note: significance of χ^2 tests of differences between mid- and early-career scientists are noted by ** ($P < 0.01$) and *** ($P < 0.001$).

33% admitiram um ou mais dos "top" 10

Percentagem de resposta
"Mid career" 52%
"Early career" 43%

B. C. Martinson et al: Scientists behaving badly
Nature 435:737, 2005

Fraude em publicação

Mais comum

- Instituição “major” e jornais de grande impacto
- Ciências biológicas
- Investigação clínica

Committee on Publication Ethics (COPE) (UK)

TAXONOMY OF MISCONDUCT

- Falsification
- Fabrication
- Plagiarism
- Failure to get ethical approval
- Not admitting that some data are missing
- Ignoring outliers without declaring it
- Not including data on side effects on a clinical trial
- Conducting research without informed consent
- Publication of post-hoc analysis without declaring it
- Gift /honorary authorship
- Not attributing other authors
- Redundant publication
- Not disclosing conflicts interest
- Not attempting to publish completed research
- Failure to do an adequate search of existing research before beginning new research
- “Shotgunning” - simultaneous submission of a manuscript to more than one journal.

Os três “major”

Fabrication – making up data or results and recording or reporting them

Falsification – manipulating research materials, equipment or processes, or changing or omitting data or results such that the research is not accurately represented in the research record

Plagiarism – appropriation of another person’s ideas, processes, results or words without giving appropriate credit

(National Science Foundation, USA)

Como a “NET” os apanha

The Intracellular Enzymatic Response of Neutrophils and Lymphocytes in Patients with Precancerous States and Cancer of the Larynx [1979]

Tatiana Gierek, Jerzy Lisiewicz, Jan Pilch

Summary: In patients with precancerous states and cancer of the larynx prior to and after radiotherapy exhibit the decreased activity of neutrophil beta-glucuronidase. Moreover patients treated by radiotherapy before the age of 6 to 9 years demonstrate deficiency of N-acetyl-beta-glucosaminidase in the above cells. The main finding in lymphocytes of the patients studied was in the appearance by diffusion of the above enzymes and of acid phosphatase in the cytoplasm, reflecting their release from lysosomes and immunological mobilization of these cells. The authors discuss the possible role of neutrophil enzymatic deficiency in lowering the antitumour cytotoxic effect of these cells.

Material and Methods

Our studies comprised 24 men with precancerous states of the larynx, i.e. leucoplakia, pachydermia, and papilloma, aged 32 to 58 years, 20 men with untreated cancer of the larynx prior to radiotherapy, aged 35 to 65 years, 30 men with cancer of the larynx after radiotherapy before 6 to 9 years, and a control group of 20 healthy men, 20 to 40 years of age.

The intracellular enzymatic response of neutrophils and lymphocytes in patients with precancerous states and cancer of the uterine cervix [1991]

A. Jendryczko and M. Dróżdż

Abstracts: In patients with precancerous states and cancer of the uterine cervix prior to and after radiotherapy exhibit the decreased activity of neutrophil beta-glucuronidase. Moreover, patients treated by radiotherapy before the age 6 to 9 years demonstrate deficiency of N-acetyl-beta-glucuronidase in the above cells. The main finding in lymphocytes of the patients studied was in the appearance by diffusion of the above enzymes and of acid phosphatase in the cytoplasm, reflecting their release from lysosomes and immunological mobilization of these cells. The authors discuss the possible role of neutrophil enzymatic deficiency in lowering the antitumor cytotoxic effect of these cells.

Materials and methods

Our studies comprised 24 women with precancerous states of the uterine cervix, i.e. leukoplakia, pachydermia and papilloma, aged 34 to 58 years, 20 women with untreated cancer of the uterine cervix prior to radiotherapy, aged 33 to 61 years, 30 women with cancer of the uterine cervix after radiotherapy before 6 to 9 years, and a control group of 20 women, 27 to 55 years of age.

Programas de detecção de Plágios

Ithenticate Crosscheck “Déjàvu”

- Até 20/02/2009 9120 entries with high levels of citation similarity and no overlapping authors
- 212 pairs of articles with signals of potential authors plagiarism
  - Average similarity 86,2%
  - Average number of shared references 73,1%
  - Only 22,2% cited the original paper
  - Impact factor of the original article av. 3.87

copy av. 1.6

original cited av. 28

copy av. 2

(T.C. Longo et al.: Responding to possible Plagiarism Science 323:1293, 2009)

“Os vigilantes”
The Peer-review system

% de aceitação

JAMA 9%

Academic Medicine 15%

Nature 5%

Remoto

Misterioso

Grosseiro

Pouco estudado

mas indispensável

86% dos estudos não publicados tinham resultados negativos

45% dos estudos publicados tinham resultados negativos

As falhas – Viés confirmatório

Viés contra resultado negativo

Crédito desproporcionado aos já famosos

Preconceito teórico

Politicamente correcto

Conflitos de interesse [competidores / antagonistas]

Concordância entre “referees” 10-15%

Processo cego não é solução.Podiam advinhar-se os autores em 46% dos manuscritos

(JAMA 272: 143, 1994)

“Partida” (“Hoax”)

“Fraud practiced with the intention to be discovered to the ridicule of those who have credited it”.

Charles Babage: “Reflections on the Decline of Science in England” (1830)

“Partida” ou Fraude?

“Transgressing the Boundaries: Towards a Transformative Hermeneutics of Quantum Gravity”

Alan D. Sokal Department of Physics, New York University

Social Text 46/47 (1996) 217-252

“It took me a lot of writing and rewriting and rewriting before the article reached the desired level of unclarity”

O que acontece depois

- Retirado – ignorar
- Expressão de preocupação – estamos a analizar
- Correcção – informação substituída

mas

os artigos continuam a ser citados depois de retirados

Exemplos:Jan Hendrik Schön, Nature publicado 2000
retirado 2003
citado 17X depois de retirado!

Conflito de interesse

Surge quando um indivíduo ou uma instituição têm

- compromisso primário

Bem estar do doente

Validade de investigação

- compromisso secundário

Ganho financeiro

Ganho académico

É um acontecimento

- não é um comportamento

Pode ser só aparência

Terça-feira
23 de Setembro de 1997

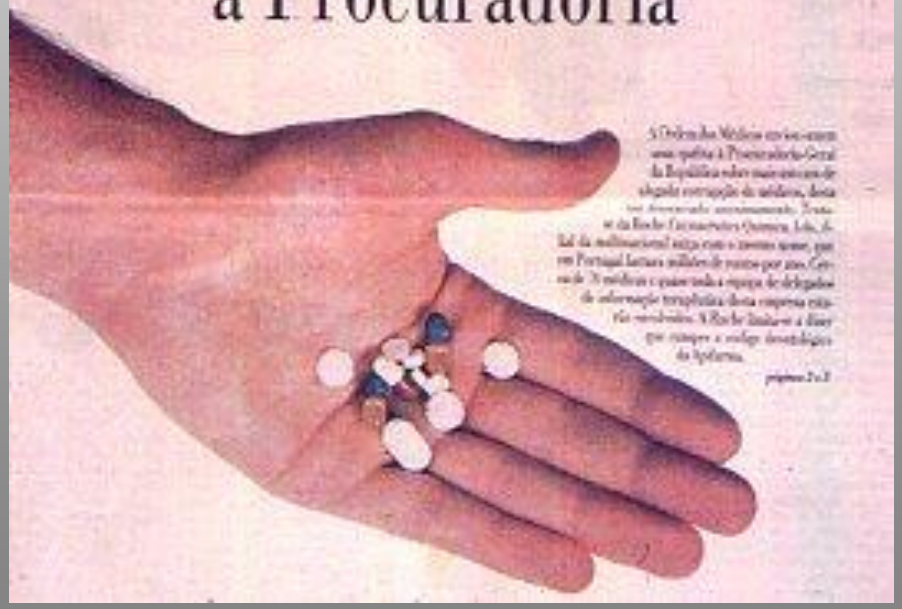
PÚBLICO

edição LISBOA

Documentos da Roche revelam práticas alegadamente ilícitas

Médicos em xeque

Ordem apresenta queixa à Procuradoria



Qual o objectivo da dádiva?

- Gravar a identidade do **dador** na mente de quem a recebe e criar, aberta ou subliminarmente a obrigação de **retribuir**.

As dádivas

- Criam expectativa de reciprocidade
- Afectam objectividade
- Aumentam os custos
- Criam a aparência de conflitos de interesse

Conflitos de interesse intelectual

- Quando uma paixão intelectual se torna um conflito de interesse
- Posição fanática àcerca de determinadas questões – álcool, droga, tabaco
- Compromisso político
  - Medicina nazi
  - Posição anticapitalista e o financiamento pela indústria
  - Compromisso com um enquadramento teórico

A Difference in Hypothalamic Structure Between Heterosexual and Homosexual Men

SIMON LEVAY

The anterior hypothalamus of the brain participates in the regulation of male-typical sexual behavior. The volumes of four cell groups in this region [interstitial nuclei of the anterior hypothalamus (INAH) 1, 2, 3, and 4] were measured in postmortem tissue from three subject groups: women, men who were presumed to be heterosexual, and homosexual men. No differences were found between the groups in the volumes of INAH 1, 2, or 4. As has been reported previously, INAH 3 was more than twice as large in the heterosexual men as in the women. It was also, however, more than twice as large in the heterosexual men as in the homosexual men. This finding indicates that INAH is dimorphic with sexual orientation, at least in men, and suggests that sexual orientation has a biological substrate.

SEXUAL ORIENTATION—SPECIFICALLY, the direction of sexual feelings or behavior toward members of one's own or the opposite sex—has traditionally been studied at the level of psychology, anthropology, or ethics (*1*). Although efforts have been made to establish the biological basis of sexual orientation, for example, by the application of cytogenetic, endocrinological, or neuroanatomical methods, these efforts have largely failed to establish any consistent differences between homosexual and heterosexual individuals (*2, 3*).

A likely biological substrate for sexual orientation is the brain region involved in the regulation of sexual behavior. In nonhuman primates, the medial zone of the anterior hypothalamus has been implicated in the generation of male-typical sexual behavior (*4*). Lesions in this region in male monkeys impair heterosexual behavior without eliminating sexual drive (*5*). In a morphometric study of the comparable region of the

Salk Institute for Biological Studies, San Diego, CA 92186.

Retenção de dados

Protecção de prioridade [“corridas”]
Restrições pelo contrato de financiamento

Custos materiais e financiamento de cedência de biomateriais

Cientistas em treino são aconselhados a não mostrar os dados

42% genética
38% outras ciências da vida

Blumenthal et al, Academ Med 81: 137, 2006

O que mudou na Ciência Biomédica

1. Não é tão nítida a distinção entre investigação clínica e investigação básica. Da Medicina à Biomedicina.
2. Internacionalização da investigação
    1. Diferença nos “padrões éticos”
    2. Colonização bioética e colonização científica
3. Investigação conduzida pela indústria e conflitos de interesse
4. O cientista como investidor
5. Preocupação pelos “desprotegidos” – embrião, feto, criança
6. A supremacia das comissões de ética.
7. A questão do placebo – será aceitável cirurgia-placebo?
8. Maior vigilância da fraude científica.

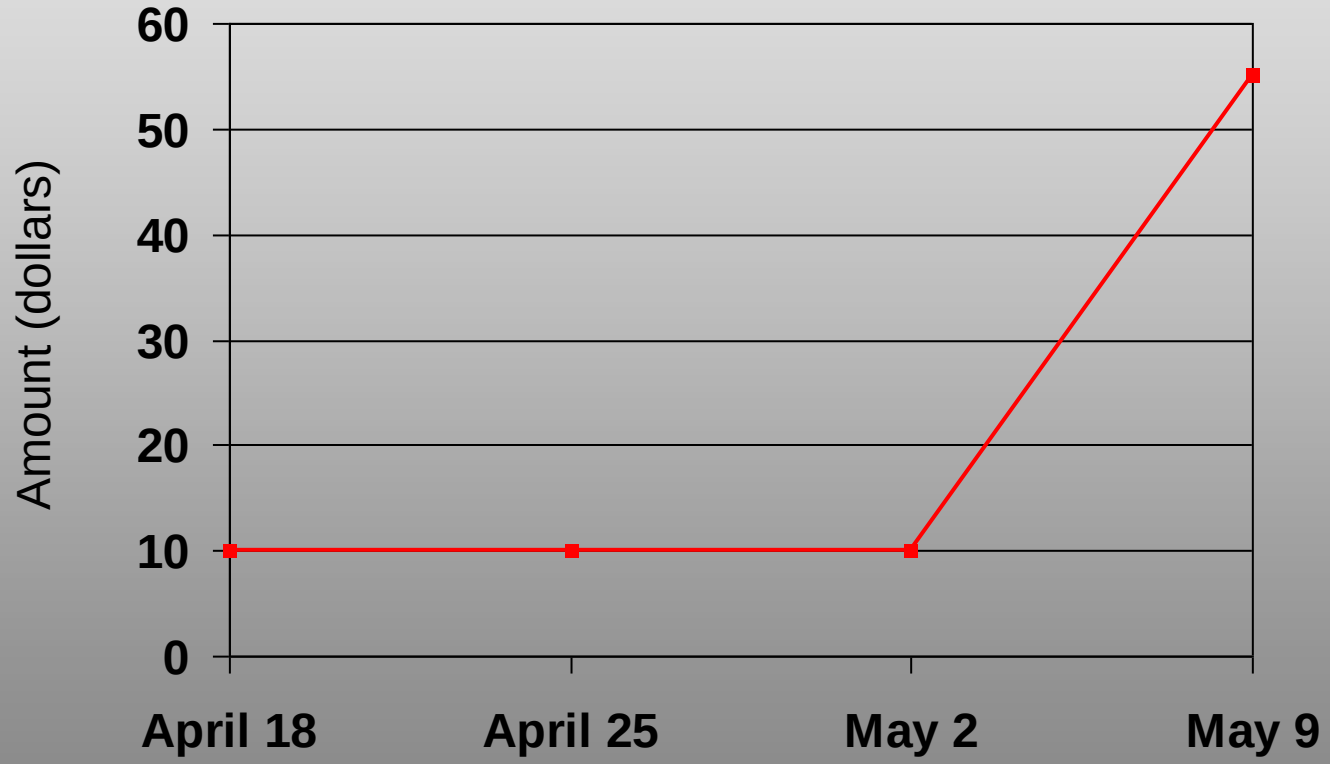
"We want you to do some pure disinterested fundamental research into something immensely profitable."

O alarme e as preocupações

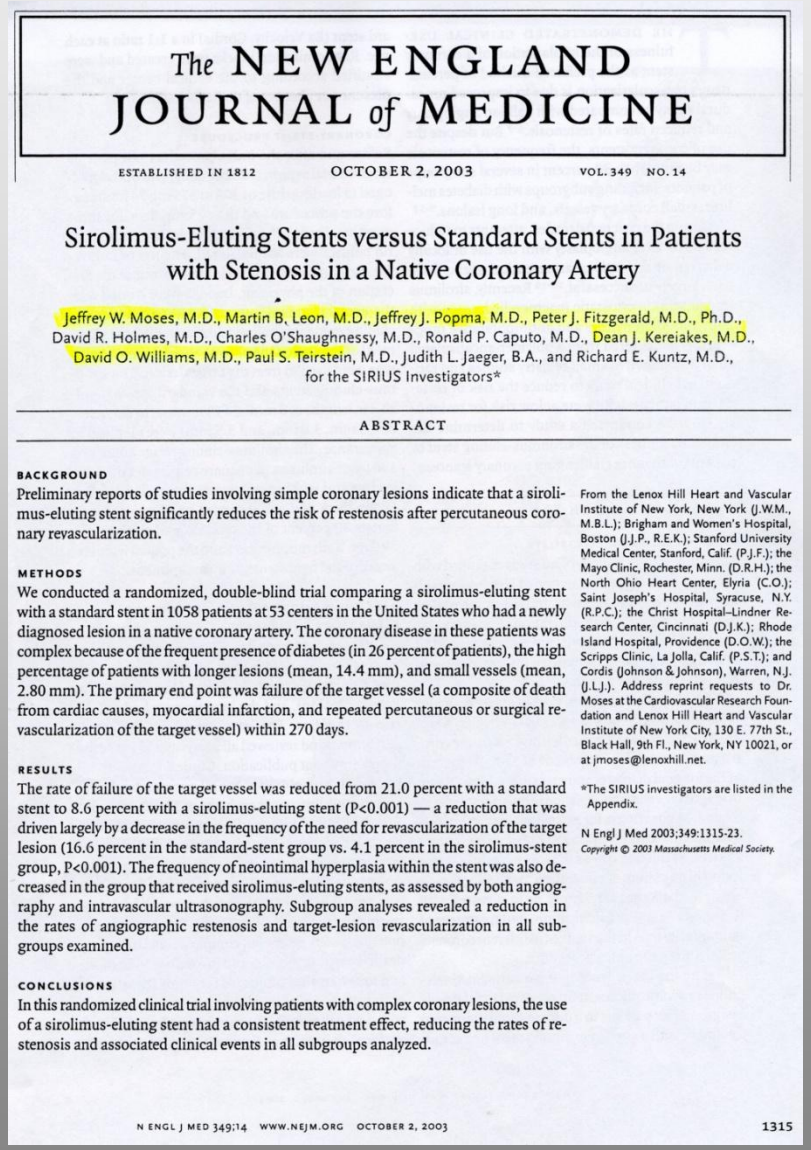
- Morte de um voluntário num ensaio de fase 1 de terapia genética
  - O médico e a instituição tinham interesses financeiros
- Enviezamento na publicação
  - Autores que publicam favoravelmente sobre antagonismo dos canais de cálcio tinham ligação à indústria (1)
  - Estudos que relatam resultados favoráveis com novo tratamento são mais frequentes quando os estudos são patrocinados pela indústria. (2)
  - 5% dos estudos de farmacoeconomia de drogas anti-cancer apoiados pela indústria têm resultados desfavoráveis.

    38% se não são patrocinados pela indústria. (3)

(1) Stelfox et al. N Engl J Med 338: 101, 1998
(2) Davidson. J Gen Int Med 1: 155, 1986
(3) Friedberg et al. JAMA 282: 1453, 1998



Efeito terapêutico. A notícia da promessa terapêutica das estatinas faz subir o preço das acções da WEntreMed



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Sirolimus-Eluting Stents versus Standard Stents in Patients with Stenosis in a Native Coronary Artery

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ABSTRACT

BACKGROUND

Preliminary reports of studies involving simple coronary lesions indicate that a sirolimus-eluting stent significantly reduces the risk of restenosis after percutaneous coronary revascularization.

METHODS

We conducted a randomized, double-blind trial comparing a sirolimus-eluting stent with a standard stent in 1058 patients at 53 centers in the United States who had a newly diagnosed lesion in a native coronary artery. The coronary disease in these patients was complex because of the frequent presence of diabetes (in 26 percent of patients), the high percentage of patients with longer lesions (mean, 14.4 mm), and small vessels (mean, 2.80 mm). The primary end point was failure of the target vessel (a composite of death from cardiac causes, myocardial infarction, and repeated percutaneous or surgical revascularization of the target vessel) within 270 days.

RESULTS

The rate of failure of the target vessel was reduced from 21.0 percent with a standard stent to 8.6 percent with a sirolimus-eluting stent ($P<0.001$) — a reduction that was driven largely by a decrease in the frequency of the need for revascularization of the target lesion (16.6 percent in the standard-stent group vs. 4.1 percent in the sirolimus-stent group, $P<0.001$). The frequency of neointimal hyperplasia within the stent was also decreased in the group that received sirolimus-eluting stents, as assessed by both angiography and intravascular ultrasonography. Subgroup analyses revealed a reduction in the rates of angiographic restenosis and target-lesion revascularization in all subgroups examined.

CONCLUSIONS

In this randomized clinical trial involving patients with complex coronary lesions, the use of a sirolimus-eluting stent had a consistent treatment effect, reducing the rates of restenosis and associated clinical events in all subgroups analyzed.

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*The SIRIUS investigators are listed in the Appendix.

N Engl J Med 2003;349:1315-23.

	Consultor	Palestrante	Financiamento	Accionista
Moses	+	+		+
Leon	+	+		+
Popma	+	+	+	
Fitzgerald	+	+	+	
Kereiakes		+	+	
Williams	+		+	
Teirstein	+	+		+

O que está em causa?

- O interesse do público
  - Verdade não contaminada
  - Descoberta com potencial beneficio rapidamente transferida para a clínica
  - Participação com consentimento esclarecido
- O interesse do investigador
  - Progresso na carreira
  - Recompensa financeira
  - Financiamento de projectos
- O interesse da indústria
  - Aprovação e comercialização
  - A importância da publicação

Conflitos na comunicação

- Resistência à publicação de resultados negativos ou desfavoráveis
- Limitar acesso dos participantes
- “Ghost Writers”
- Não revelação de conflitos de interesse
- A necessidade de “guidelines”

Lancet, JAMA, N Engl JM, Annals Int Med, etc

Conflito de interesse

- "Does declaration of competing interests affect reader's perceptions? A randomized trial"*

  Results of study on impact of pain in herpes were found less interesting , important, relevant, valid and believable when the authors were employees of fictitious pharmaceutical company than with ambulatory care centers.

* Chaudhry et al. B M J 325:1391, 2002

Financiamento e autonomia

(The Editors of Ann Int Med, JAMA, New England J Med, Canad MAJ, J Danish M A, Lancet, Medline, etc, Sep 2001)

- When authors submit manuscript they are responsible for disclosing all financial and personal relationships that might bias their work
- Researchers should not enter in agreements that interfere
    - Their access to the data
    - Ability to analyze data independently
    - Prepare manuscripts
    - Publish them

Rules for authorship

The International Committee of Medical Journal Editors (Vancouver Group)

- Authorship credit

  1. Substantial collaboration to conception and design, or acquisition of data, or analysis and interpretation of data.
  2. Drafting the article or revising it critically for important intellectual content
  3. Final approval of the version to be published

- Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship
- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.
- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

thermore, we assume that trialists would have been more likely to respond if their outcome reporting was more complete and less biased. Any response bias would thus result in conservative estimates of reporting deficiencies in our cohort.

Implications for Practice and Research

Outcome reporting bias acts in addition to the selective publication of entire studies and has widespread implications. It increases the prevalence of spurious results, and reviews of the literature will therefore tend to overestimate the effects of interventions. The worst possible situation for patients, health care professionals, and policy-makers occurs when ineffective or harmful interventions are promoted, but it is also a problem when expensive therapies, which are thought to be better than cheaper alternatives, are not truly superior.

In light of our findings, major improvements remain to be made in the reporting of outcomes in randomized trials as published. First, protocols should be made publicly available—not only to enable the identification of unreported outcomes and post hoc amendments[30,31,34] but also to deter bias. Ideally, protocols should be published online after initial trial registration and prior to trial completion. Although journals constitute one obvious modality for protocol publication, academic and funding institutions should also take responsibility in providing further venues for disseminating research information.[35]

Second, deviations from trial protocols must be described in the published articles so that readers can assess the potential for bias. Third, journal editors should not only consider routinely demanding that original protocols and any amendments be submitted with the trial manuscript but that this material should also be provided to peer reviewers and preferably be made available at the journal's Web site.[20,21,36]

Finally, trialists and journal editors should bear in mind that most individual trials may well be incorporated into subsequent reviews. Outcomes that are mentioned in published articles, but are reported with insufficient data, may not always matter when interpreting a single trial report, but they can have an important impact on meta-analyses. Unreported outcomes are even more problematic for both trials and reviews. It is therefore crucial that adequate data be reported for prespecified outcomes independent of their results. The increasing use of the Internet by journals may help to provide the space needed to accommodate such data.[36]

In summary, we found that the reporting of trial outcomes in journals is frequently inadequate to provide sufficient data for interpretation and meta-analysis, is biased to favor statistical significance, and is inconsistent with primary outcomes specified in trial protocols. These deficiencies in outcome reporting pose a threat to the reliability of the randomized trial literature.

Author Contributions: Dr Chan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.
Study concept and design; analysis and interpretation of data: Chan, Hróbjartsson, Gøtzsche, Altman.
Acquisition of data: Chan, Hróbjartsson, Haahr, Gøtzsche.
Drafting of the manuscript: Chan, Gøtzsche, Altman.
Critical revision of the manuscript for important intellectual content: Chan, Hróbjartsson, Haahr, Gøtzsche, Altman.
Statistical expertise; study supervision: Altman.
Obtained funding: Chan, Gøtzsche.
Administrative, technical, or material support: Haahr, Gøtzsche, Altman.
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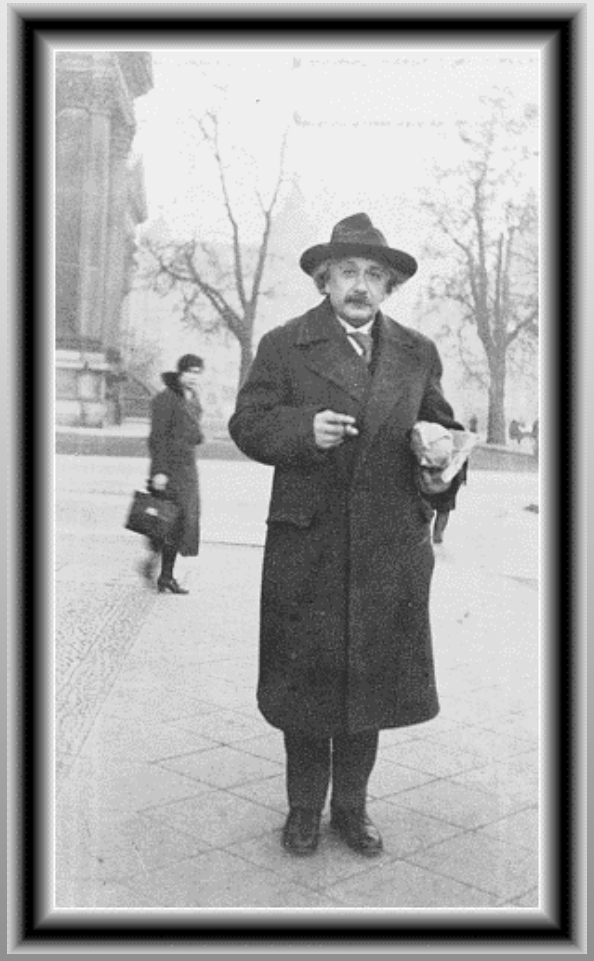
Como melhorar

- Investigação – bolsas de investigação para estudar integridade em ciência
- Compromisso institucional
- Educação – programas educacionais
- Auto-avaliação – promoção de auto-avaliação e auditoria.

[Adaptado de: “Integrity in Scientific Research.” Institute of Medicine. National Research Council, 2002]



“Many people say that is the intellect which makes a great scientist.

They are wrong: it is character”.