# Conflits d'intérêts: Un danger pour l'intégrité scientifique

Pr. Didier Dreyfuss
Réanimation médico-chirurgicale
Hôpital Louis Mourier, Colombes
UFR Médecine Paris-Diderot

Ex-secrétaire de la Commission d'Ethique SRLF

# Liens d'intérêts

https://www.transparence.sante.gouv.fr

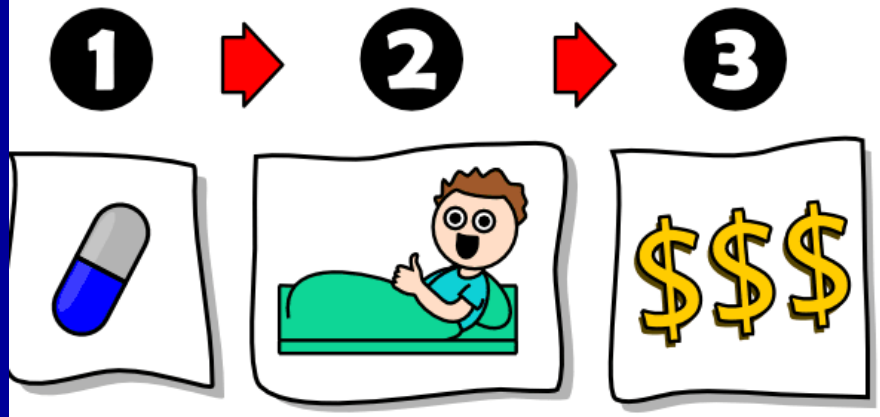
- Conventions: aucune
- Avantages: aucun
- Rémunérations: aucune
- Membre du FORMINDEP. Mes propos n'engagent néanmoins que moi-même

**http://lepharmachien.com/industrie-pharmaceutique/**

http://lepharmachien.com/industrie-pharmaceutique/

« Si nous fabriquons d'excellents médicaments qui améliorent la santé des gens, nous serons incroyablement riches »

Ce qui se résume par l'équation suivante :



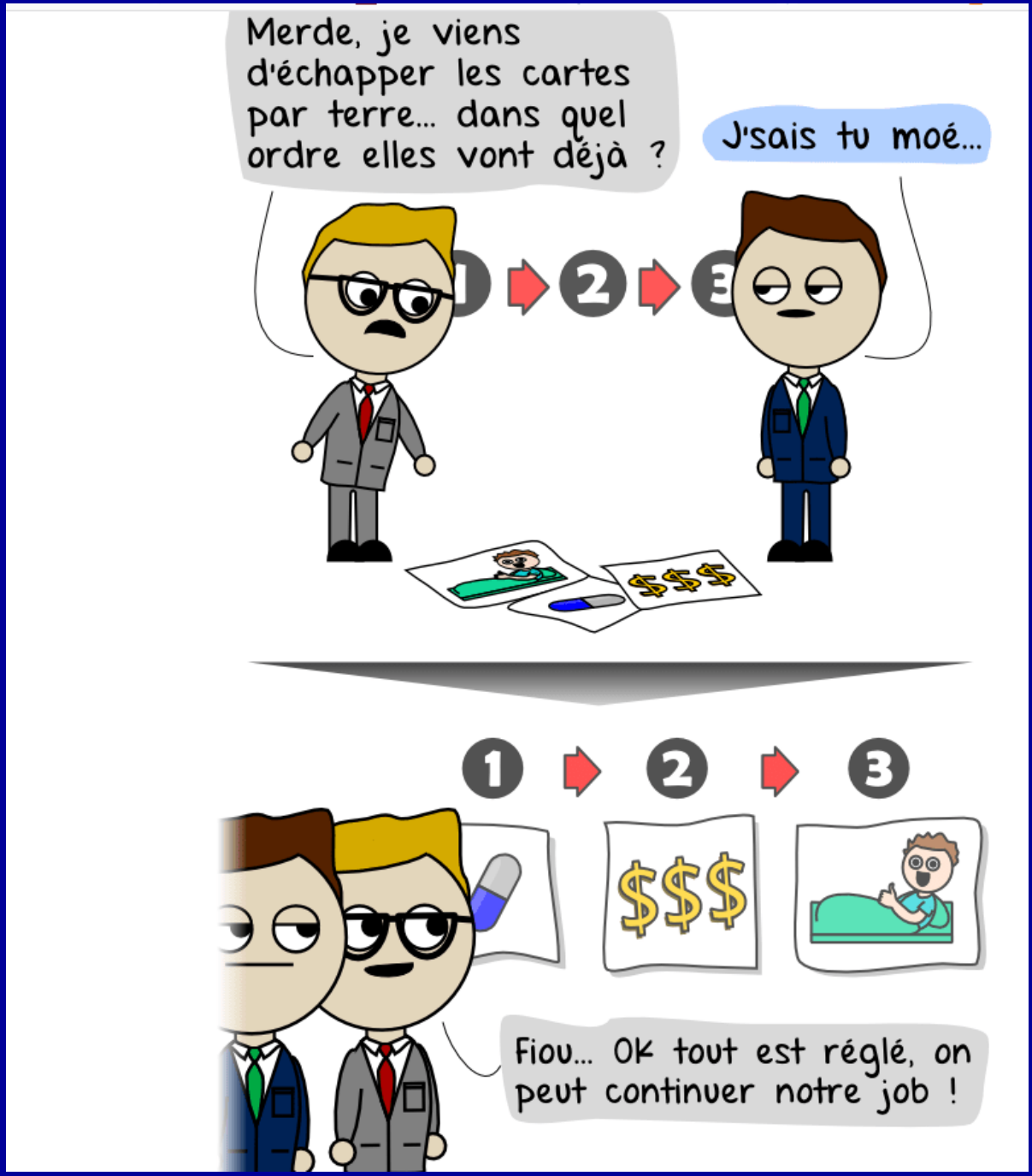

Soyons clairs dès le départ : il n'y a

**ABSOLUMENT RIEN**

de mal dans une telle mission.

Faire de l'argent en aidant la société,

http://lepharmachien.com/industrie-pharmaceutique/



LES ENTREPRISES DU MÉDICAMENT

Ph Lamoureux
Directeur Général

« Un expert sans lien d'intérêt est un expert sans intérêt »

Fake news!!!!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

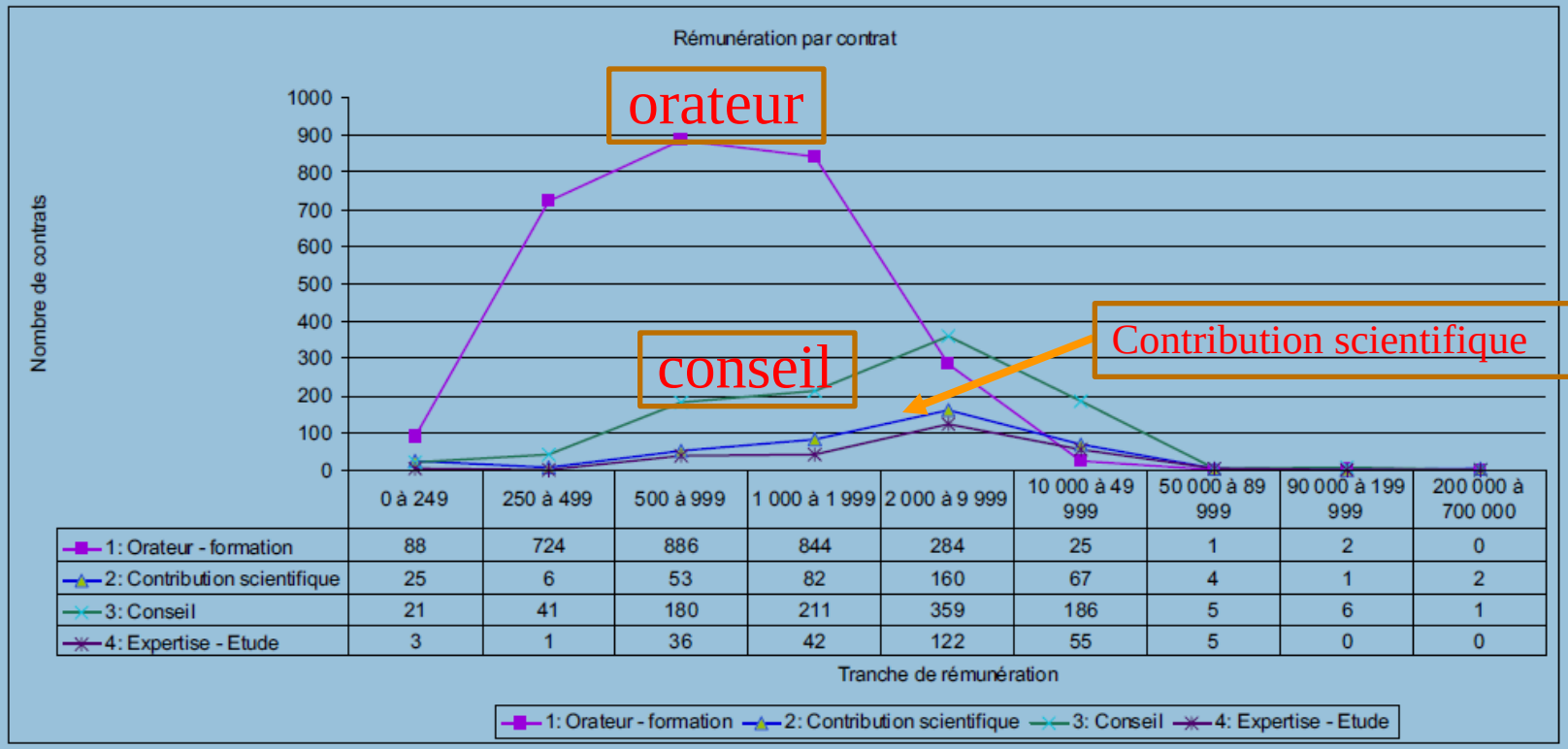
# Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

Stéphane Gaudry, M.D., David Hajage, M.D., Fréderique Schortgen, M.D., Laurent Martin-Lefevre, M.D., Bertrand Pons, M.D., Eric Boulet, M.D., Alexandre Boyer, M.D., Guillaume Chevrel, M.D., Nicolas Lerolle, M.D., Ph.D., Dorothée Carpentier, M.D., Nicolas de Prost, M.D., Ph.D., Alexandre Lautrette, M.D., Anne Bretagnol, M.D., Julien Mayaux, M.D., Saad Nseir, M.D., Ph.D., Bruno Megarbane, M.D., Ph.D., Marina Thirion, M.D., Jean-Marie Forel, M.D., Julien Maizel, M.D., Ph.D., Hodane Yonis, M.D., Philippe Markowicz, M.D., Guillaume Thiery, M.D., Florence Tubach, M.D., Ph.D., Jean-Damien Ricard, M.D., Ph.D., and Didier Dreyfuss, M.D., for the AKIKI Study Group*

N ENGL J MED 375;2 NEJM.ORG JULY 14, 2016

Moins de rein artificiel, c'est mieux….sauf pour l'industrie

Graphique 7 : Dispersion des honoraires versés au médecin par la firme selon la typologie de la prestation




| | 0 à 249 | 250 à 499 | 500 à 999 | 1 000 à 1 999 | 2 000 à 9 999 | 10 000 à 49 999 | 50 000 à 89 999 | 90 000 à 199 999 | 200 000 à 700 000 |
|---|---|---|---|---|---|---|---|---|---|
| 1: Orateur - formation | 88 | 724 | 886 | 844 | 284 | 25 | 1 | 2 | 0 |
| 2: Contribution scientifique | 25 | 6 | 53 | 82 | 160 | 67 | 4 | 1 | 2 |
| 3: Conseil | 21 | 41 | 180 | 211 | 359 | 186 | 5 | 6 | 1 |
| 4: Expertise - Etude | 3 | 1 | 36 | 42 | 122 | 55 | 5 | 0 | 0 |

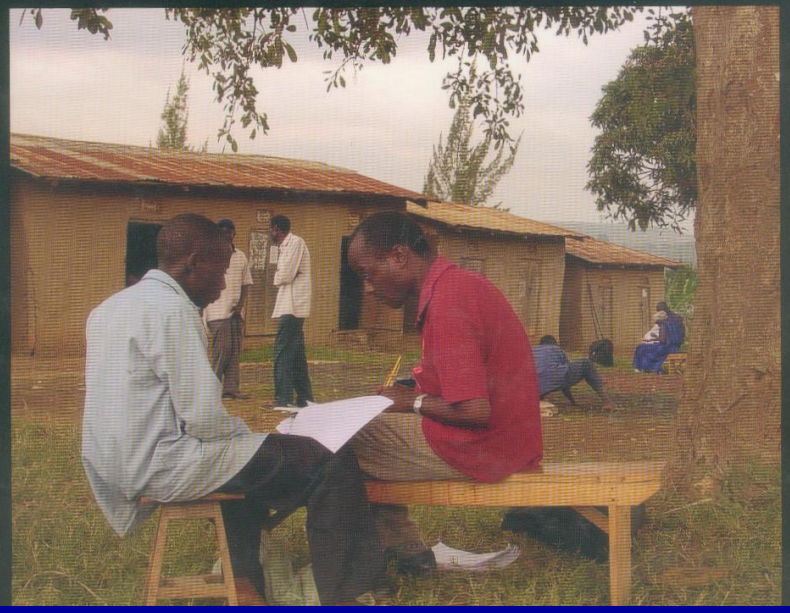
*Source : Mission Igas/Cges Exploitation de 6675 dossiers transmis au Conseil national de l'Ordre des médecins*

IGAS janvier 2009: rapport sur la rémunération des médecins et chirurgiens hospitaliers

# The Oxford Textbook of Clinical Research Ethics

EDITED BY

Ezekiel J. Emanuel
Christine Grady
Robert A. Crouch
Reidar K. Lie
Franklin G. Miller
David Wendler



- A conflict of interest is a set of circumstances or conditions in which professional judgment of a primary interest, such as the integrity and quality of research, tends to be unduly influenced by a secondary interest, such as personal financial gain

- A conflict of interest refers to a tendency, not an occurrence

- The secondary interest is usually not illegitimate in itself. The secondary interests are objectionable only under circumstances in which they tend to have greater weight than the primary interest

Citations from Emanuel EJ and Thompson DF
*In* The Oxford Textbook of Clinical Research Ethics (p. 760)

- “The classic case of a conflict of interest involves a researcher who owns stock in or consults for a pharmaceutical company, and who also serves as the principal investigator in a clinical trial evaluating whether a drug manufactured by that company is safe and effective”.

- “The common distinctions between potential or perceived conflicts and actual conflicts of interest are not helpful”

Ezekiel Emanuel *in The oxford textbook of clinical research ethics.*

- “One should be concerned not only about the financial ties of researchers involved in the trials themselves, but also about the financial interests of authors who synthesize or integrate existing data to make clinically relevant recommendations”

- “Data suggest that industry-funded clinical research leads to pro-industry results more frequently than does nonindustry-funded research”.

- “Data strongly suggest that financial conflicts can threaten the integrity of the research process”.

Hampson et al. *in The oxford textbook of clinical research ethics.*


- L'industrie peut demander à des cliniciens chercheurs de devenir consultants plus pour obtenir leur bienveillance que pour leur expertise
- Les voyages autour du monde pour apparaître dans des symposium financés par l'industrie s'apparentent plus à du marketing qu'à du transfert de technologie
- Les chercheurs peuvent entreprendre des études parce qu'elles sont financées par l'industrie et non parce qu'elles sont scientifiquement importantes

# Industry-Sponsored Clinical Research
## A Broken System

Marcia Angell, MD

(Reprinted) JAMA, September 3, 2008—Vol 300, No. 9 1069

- Clinical research that *is* published is often biased, usually by designing the studies in ways that will almost inevitably yield favorable results for the sponsor
- 200 practice guidelines: plus d'un tiers des auteurs avaient un lien d'intérêt avec le produit qu'ils recommandaient
- Sur les 170 contributeurs au DSM4, 95% avaient des liens financiers avec l'industrie pharmaceutique

*Open access, freely available online*

**Essay**

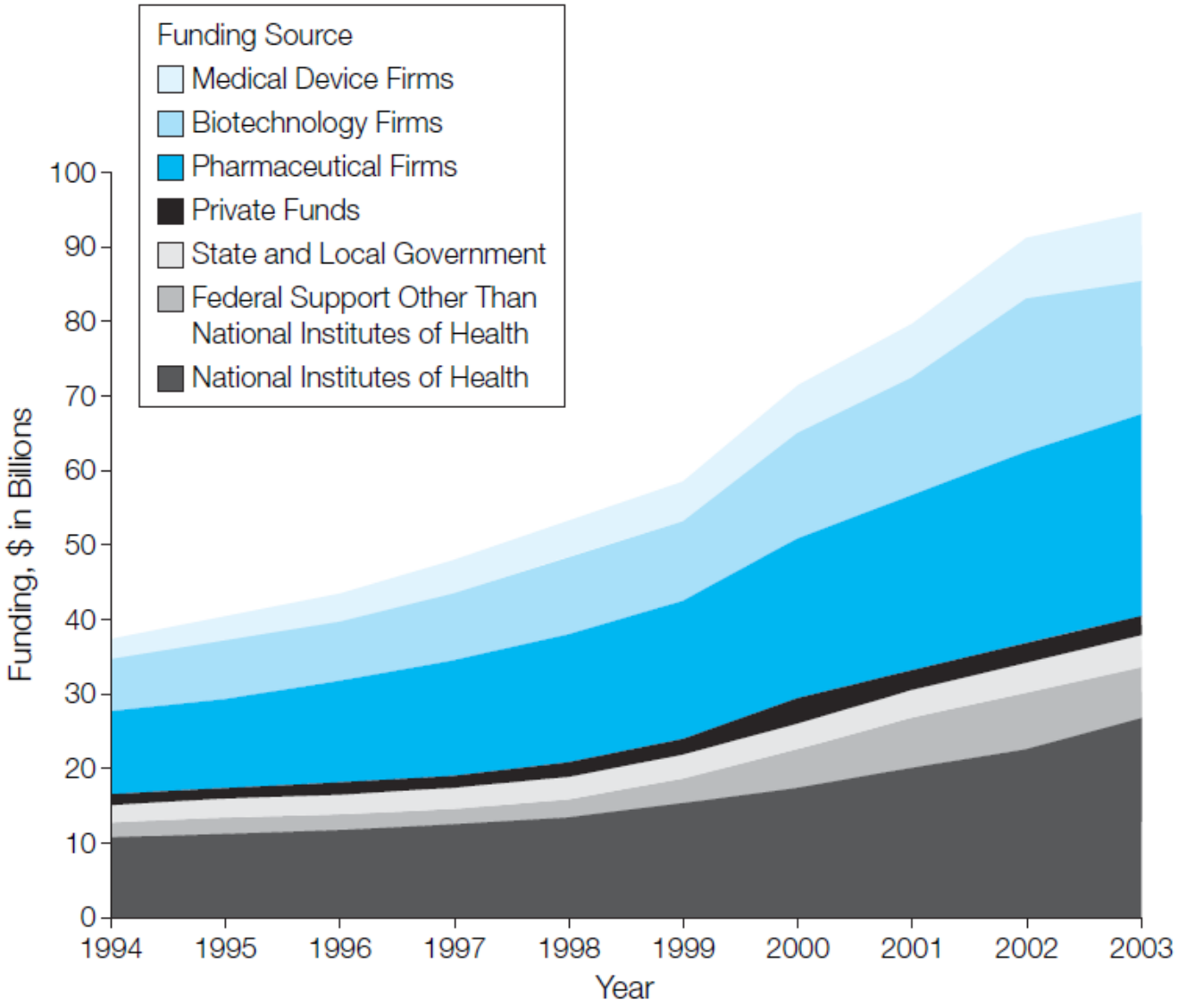
# Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies

**Richard Smith**

PLoS Medicine | www.plosmedicine.org 0364 May 2005 | Volume 2 | Issue 5 | e138

Richard Smith a été éditeur du BMJ de 1991 à 2004

**Figure 1.** Funding for Biomedical Research by Source, 1994-2003




Oxford Textxbook of Clinical Research Ethics (p. 759; reproduced from Moses et al JAMA 2005)

# Big pharma and the UK Government

*Joe Collier*

St George's (University of London), London SW17 0RE, UK
collier@sghms.ac.uk

JC has been an adviser to the UK House of Commons Health Select Committee since 1993 and served in this capacity on the inquiry into the influence of the pharmaceutical industry.

www.thelancet.com Vol 367 January 14, 2006

In March, 2005, the UK House of Commons Health Select Committee reported on the influence of the pharmaceutical industry.[1] The committee began its inquiry in June,

Its overall findings were clear: the influence of the pharmaceutical industry is enormous and out of control. The committee learned that while the industry's influence was traditionally targeted at health professionals, today, big pharma's tentacles penetrate much more widely, reaching patients, health departments, regulators, managers, researchers, and medical charities, and then on to academics, the media, carers, school children, and politicians. Other parallel issues also arose. Could patients be disadvantaged by the fact that the large multinationals design, sponsor, orchestrate, and control the publication of all the key drug trials; produce, market, and promote the medicines we take; and virtually determine how medicines are prescribed? Big pharma works hard and spends vast amounts to gain influence,

# Comprendre la promotion pharmaceutique et y répondre

## Un manuel pratique

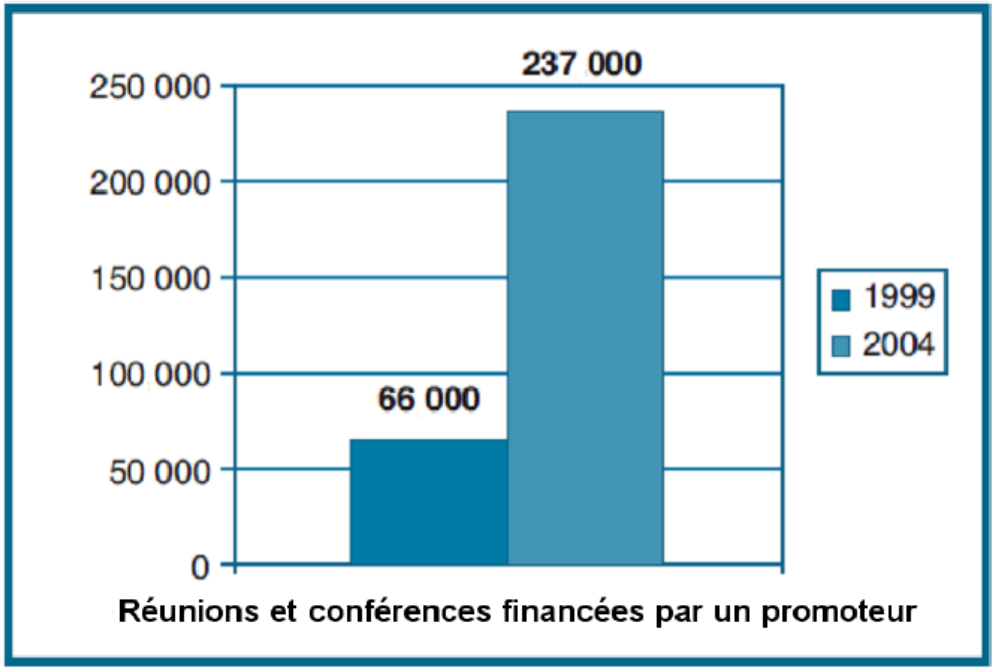
Edition originale 2009
Première version pour expérimentation et évaluation

Traduction française 2013

**Organisation Mondiale de la Santé et Action Internationale pour la Santé**
*Projet collaboratif*

https://www.has-sante.fr/portail/upload/docs/application/pdf/2013-04/comprendre_la_promotion_pharmaceutique_et_y_repondre_-_un_manuel_pratique.pdf

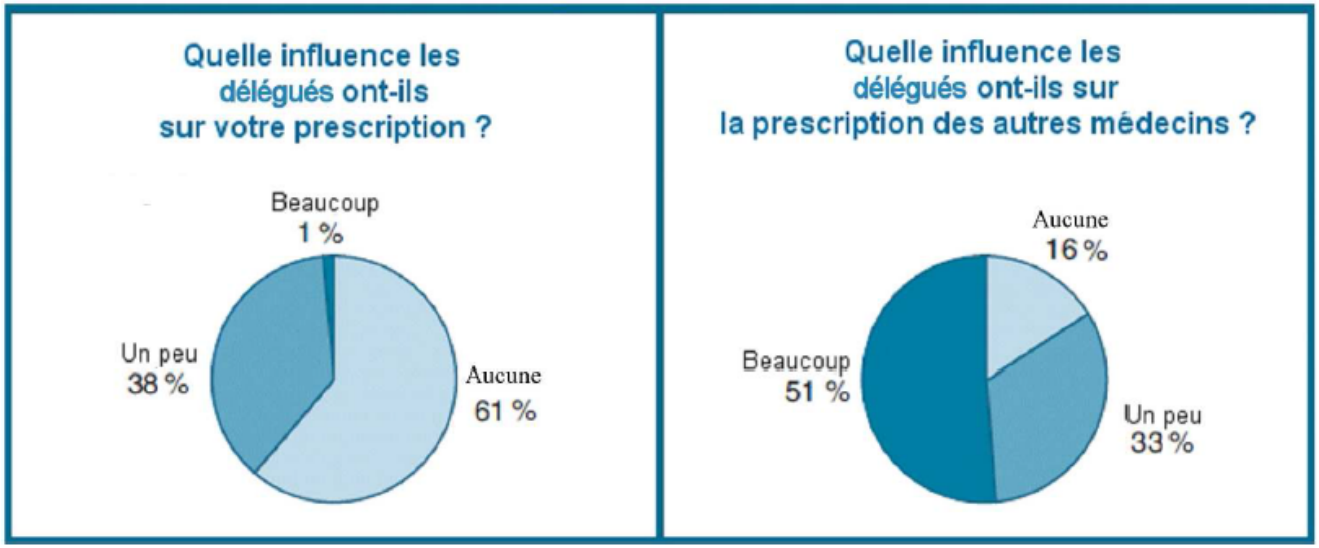
Figure 2 : nombre de réunions et de conférences financées par un promoteu
aux États-Unis, en 1999 et 2004




(Source : Caplovitz, 2006)

Les chargés de marketing pharmaceutique appellent les porte-parole professionnels de santé rémunérés des « leaders d'opinion de premier plan ». « *Un nombre effrayant de médecins de l'auditoire ignorent que l'objectif de ces présentations est purement commercial* » commente Jerry Avorn de la Harvard Medical School, USA, (Hensley, 2005). Dans un État américain, le Minnesota, sur une année, plus de 20 % des médecins ont reçu des paiements de la part d'entreprises pharmaceutiques, et plus de 100 médecins ont reçu plus de 100 000 USD (Spurgeon, 2007).

Figure 1 : enquête menée auprès de praticiens hospitaliers relative à l'influence des délégués médicaux




(Source : Steinman, 2001)

Des psychologues ont constaté qu'il est normal de croire que seuls les *autres* sont vulnérables aux techniques promotionnelles et peuvent être induits en erreur. Cela s'appelle **l'illusion de l'unique invulnérabilité** (Sagarin et al., 2002).

Résultats analogues quand on demande si les COI influencent les articles qu'ils écrivent: les médecins répondent non pour la plupart . Si on leur demande si cela influence les autres, beaucoup plus répondent positivement

https://www.has-sante.fr/portail/upload/docs/application/pdf/2013-04/comprendre_la_promotion_pharmaceutique_et_y_repondre_-_un_manuel_pratique.pdf

Les entreprises dépensent une part significative de leurs budgets de marketing en déjeuners, cadeaux et divertissements pour les professionnels de santé parce qu'elles savent que ces dépenses génèrent des ventes supplémentaires. Il y a plus de deux décennies, Rawlins (1984) attirait déjà l'attention sur cette situation :

*«…peu de médecins reconnaissent qu'on ait pu les corrompre. La plupart des médecins pensent qu'ils sont à l'abri des moyens de séduction des spécialistes marketing de l'industrie pharmaceutique ; qu'ils ne sont pas influencés par la propagande promotionnelle reçue ; qu'ils peuvent profiter de la générosité d'une entreprise sous la forme de cadeaux et d'hébergement, sans prescrire ses produits. Le degré auquel la profession, composée principalement de personnes honorables et convenables, peut se cacher la face est extraordinaire. Aucune entreprise pharmaceutique ne dépense l'argent de ses actionnaires par générosité désintéressée. »*

https://www.has-sante.fr/portail/upload/docs/application/pdf/2013-04/comprendre_la_promotion_pharmaceutique_et_y_repondre_-_un_manuel_pratique.pdf

JAMA May 2, 2017 Volume 317, Number 17 1753

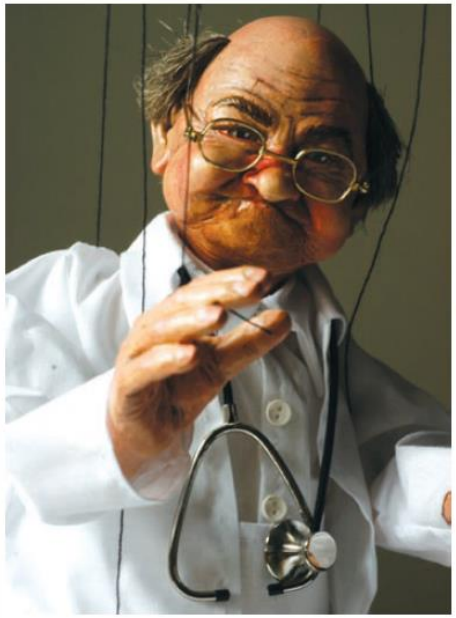
VIEWPOINT

# Physicians, Industry Payments for Food and Beverages, and Drug Prescribing

**Robert Steinbrook, MD**
Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut.

**In 2015,** the pharmaceutical industry and other health care companies reported to the Centers for Medicare & Medicaid Services through the Open Payments program a total of $235 million in food and beverage payments to physicians, accounting for approximately 12% of general payments.[1]

Using Open Payments data, a 2016 study found that receipt of industry-sponsored meals, even just a single meal, was associated with an increase in the rate of prescribing the brand-name drug that was being promoted.[7]



# KEY OPINION LEADERS Independent experts or drug representatives in disguise?

BMJ | 21 JUNE 2008 | VOLUME 336

**Ray Moynihan** examines the role of the influential experts paid by industry to help "educate" the profession and the public

Ray Moynihan is a visiting editor, *BMJ*
University of Newcastle, Newcastle, New South Wales, Australia
Ray.moynihan@newcastle.edu.au

Kimberly Elliott, who was a drug company sales representative for almost two decades in the United States, puts it directly. "Key opinion leaders were salespeople for us, and we would routinely measure the return on our investment, by tracking prescriptions before and after their presentations," she said. "If that speaker didn't make the impact the company was looking for, then you wouldn't invite them back."

# Quelques exemples….

Issus de ma discipline (Médecine Intensive – Réanimation)

Est-ce différent dans les autres disciplines ? ☺ ☹

## Surviving Sepsis — Practice Guidelines, Marketing Campaigns, and Eli Lilly

Peter Q. Eichacker, M.D., Charles Natanson, M.D., and Robert L. Danner, M.D.

N ENGL J MED 355;16 WWW.NEJM.ORG OCTOBER 19, 2006

- Protéine C activée: médicament miracle du choc septique??
- Campagne menée par des « leaders d'opinion » et subventionnée par Eli Lilly
- Dénonciation d'un « rationnement » des dépenses dans le sepsis sévère
- Augmentation des ventes de protéine C activée sous l'effet de cette campagne
- Démonstration ultérieure de son inefficacité: n'est plus commercialisée dans cette indication

Special Articles

Crit Care Med 2004 Vol. 32, No. 3

# Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

R. Phillip Dellinger, MD; Jean M. Carlet, MD; Henry Masur, MD; Herwig Gerlach, MD, PhD; Thierry Calandra, MD; Jonathan Cohen, MD; Juan Gea-Banacloche, MD, PhD; Didier Keh, MD; John C. Marshall, MD; Margaret M. Parker, MD; Graham Ramsay, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; Mitchell M. Levy, MD; for the Surviving Sepsis Campaign Management Guidelines Committee

## I. Recombinant Human Activated Protein C (rhAPC)

1. rhAPC is recommended in patients at high risk of death (Acute Physiology and Chronic Health Evaluation II ≥25, sepsis-induced multiple organ failure, septic shock, or sepsis-induced acute respiratory distress

**Grade B**

## C. Antibiotic Therapy

1. Intravenous antibiotic therapy should be started within the first hour of recognition of severe sepsis, after appropriate cultures have been obtained.

**Grade E**

Intensive Care Med (2012) 38:1258–1271
DOI 10.1007/s00134-012-2614-0

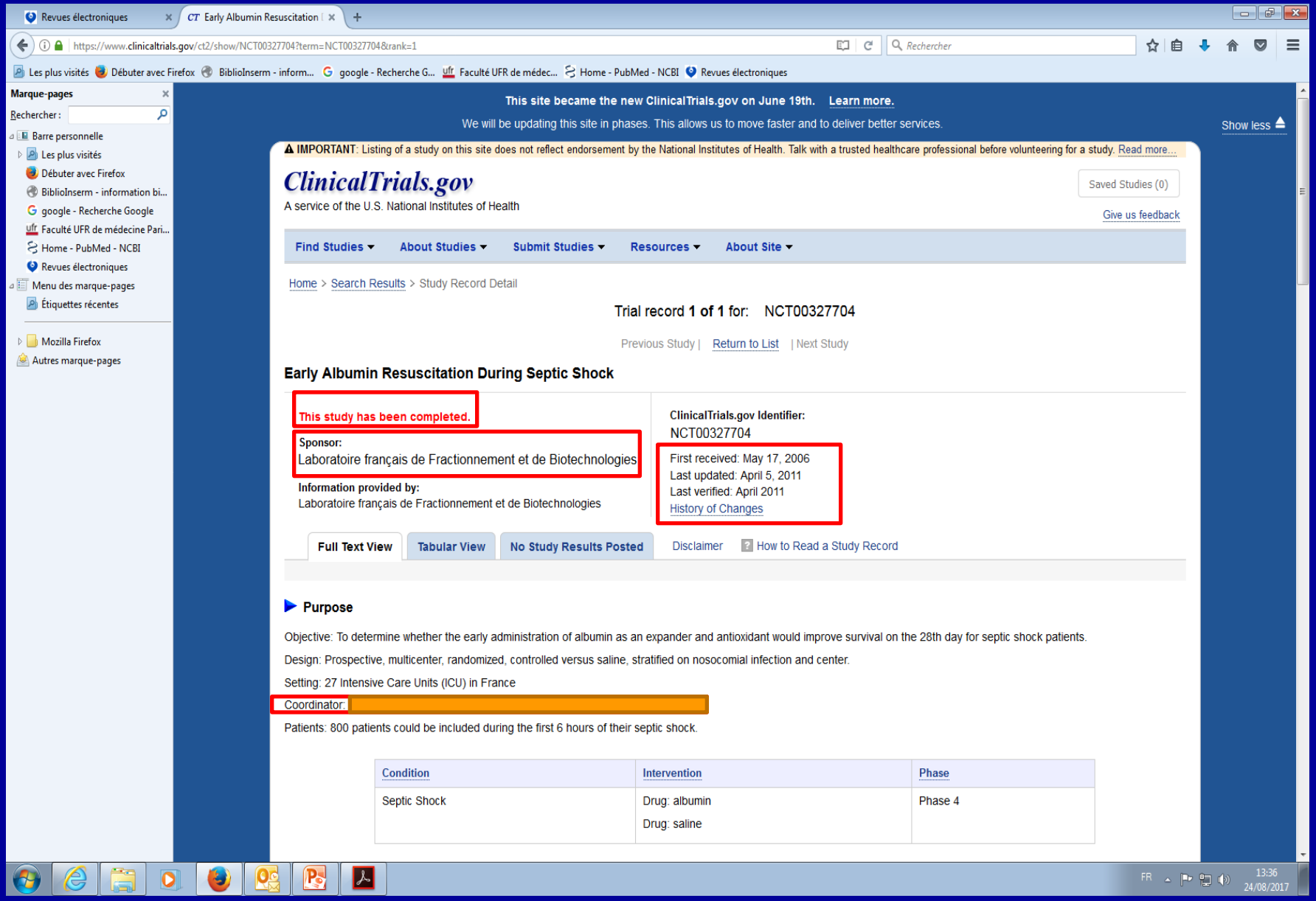
SYSTEMATIC REVIEW

Christiane S. Hartog
Helga Skupin
Charles Natanson
Junfeng Sun
Konrad Reinhart

# Systematic analysis of hydroxyethyl starch (HES) reviews: proliferation of low-quality reviews overwhelms the results of well-performed meta-analyses

Overall, most guidelines did not specifically recommend HES use, but those that did were written by authors who had or eventually developed ties to HES manufacturers [54, 61].

# Un célèbre réanimateur français



Présenté en abstract au congrès européen de réanimation en 2011…et jamais publié en article

Ne pas publier une connaissance acquise grâce au dévouement des malades est à la fois non éthique du point de vue de la recherche et irrespectueux pour les malades

**0438**

**EFFICACY AND TOLERANCE OF HYPERONCOTIC ALBUMIN ADMINISTRATION IN SEPTIC SHOCK PATIENTS: THE EARSS STUDY**

J
T

**INTRODUCTION.** Albumin administration during hypovolemia and particularly in septic shock patients remains controversial. Despite its numerous potentially beneficial properties, albumin is considered as a costly blood product with a potential risk of renal and pulmonary toxicity.

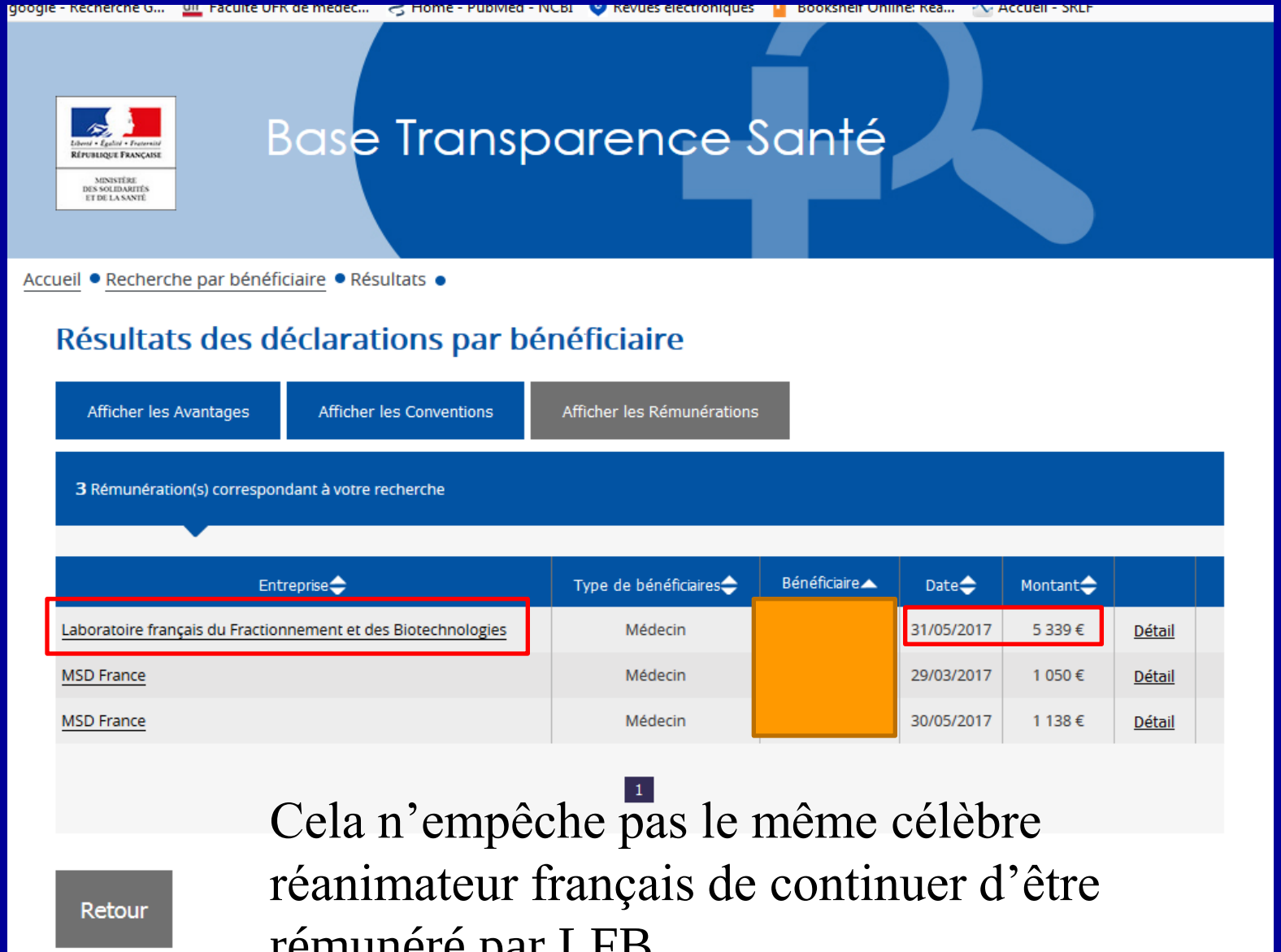
**OBJECTIVES.** The EARSS study investigates if early administration of hyperoncotic albumin reduces septic shock mortality and analyses the safety of this infusion in this high-risk population.

**METHODS.** Prospective open randomized multicenter study in 29 French centres. After informed consent, any patient with septic shock could be included within 6 h after catecholamine introduction. Patients with overweight, previous severe heart failure, neutropenia, cirrhosis and primary peritonitis and severe burns were excluded. Patients were randomized to receive either 100 ml of 20% albumin (LFB) (Albumin group) or 100 ml 0.9% NaCl (Control group) every 8 h for 3 days. The primary endpoint was all-cause mortality at D28. Secondary objectives were the evolution of the SOFA score, length of stay in ICU and in hospital and the number of days without assistance. The safety of albumin administration was evaluated on kidney failure and acute pulmonary oedema incidence.

**RESULTS.** Between July 2006 and March 2010, 798 patients were included. At inclusion, patient characteristics were comparable between the 2 groups; age: 66 years [IQR: 55, 76], M/F %: 67/33, medical/surgical admission %: 75/25; SAPS2 = 51 [IQR: 40, 65], SOFA D1 = 10 [8, 12], lactate = 2.2 mg/dL [IQR: 1.4, 3.8]. Infection origin was mainly pulmonary (45%) and a bacteriological documentation was present in 73% of cases. At baseline, hypoalbuminemia was almost constant and severe (17.96 [IQR: 14.1, 21.6] g/L). The ICU management was similar between the 2 groups and assessed the severity of the population (RRT: 23%). There was no difference in fluid loading between the 2 groups within 12 h before inclusion but also in the following days.

The mortality rate was not significantly different between the 2 groups: 24.1 vs 26.3% for the Albumin and the control group respectively. The number of days without catecholamine was significantly higher in the Albumin group. However resolution of other organ dysfunction, duration in ICU or hospital LOS were not significantly different between the groups. Similarly, renal and pulmonary tolerance was comparable in the 2 groups.

**CONCLUSION.** Septic shock is frequently associated with severe hypoalbuminemia that has been partially corrected by the administration of hyperoncotic albumin. Renal and pulmonary tolerance and safety was good, but albumin did not change significantly the mortality rate of septic shock.




Cela n'empêche pas le même célèbre réanimateur français de continuer d'être rémunéré par LFB

# Invasive candidiasis

- Recommandations by experts (IDSA, ESCMID, prestigious european intensivists) with financial ties strongly advocate against conventional amphotericin B (CAMB) (strong incentive for echinocandins)
- ATS recommandations: first, last and corresponding authors have no financial ties: CAMB acceptable as first-line treatment
- Considerable savings might be obtained by VERY (24-48h) short use of CAMB (pending susceptibility results)

**Amphotericin B Deoxycholate for Candidiasis in Intensive Care Unit Patients Revisited: Medical, Ethical, and Financial Implications**

Correspondence

**Continuous Infusion of Amphotericin B Deoxycholate for the Treatment of Life-Threatening *Candida* Infections**

Dreyfuss et al. AJRCCM 2013

*BMJ* 2018;360:k1118 doi: 10.1136/bmj.k1118 (Published 8 March 2018)


NEWS

# Medical textbook authors received £11m in undisclosed payments from drug and device makers

Nigel Hawkes

AJOB EMPIRICAL BIOETHICS
https://doi.org/10.1080/23294515.2018.1436095

ARTICLE

# Undisclosed conflicts of interest among biomedical textbook authors

Brian J. Piper [a,b], Drew A. Lambert[c], Ryan C. Keefe[d], Phoebe U. Smukler[e], Nicolas A. Selemon[e,f], and Zachary R. Duperry[g]

**Conclusion:** An appreciable subset of biomedical authors have patents and have received remuneration from medical product companies and this information is not disclosed to readers. These findings indicate that full transparency of financial pCoI should become a standard practice among the authors of biomedical educational materials.

JAMA May 2, 2017 Volume 317, Number 17 1739



VIEWPOINT

# Conflict of Interest in Practice Guidelines Panels

**Harold C. Sox, MD**
Patient-Centered Outcomes Research Institute, Washington, DC.

The principles of management of COI include (1) avoiding panelists with conflicts; (2) using panelists without conflicts to draft the guideline; (3) involving experts in the discussion of the draft guideline; and (4) restricting the final revisions and voting to panelists without conflicts. Policies based on these principles should be easy to implement and monitor, but guideline sponsors have been slow to adopt them. The public deserves more responsible conduct.

VOLUME 31 · NUMBER 16 · JUNE 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

# American Society of Clinical Oncology: Policy for Relationships With Companies

*American Society of Clinical Oncology*

## *B. Original Research in ASCO Journals*

Manuscripts (including articles and abstracts) concerning ***original research*** are not eligible for publication in *JCO* or *JOP* if the ***first, last, or corresponding author*** has:

1. participated in a speakers' bureau (on any subject) on behalf of the Company sponsor of that research at any time during the 2 years before submission of the manuscript;
2. held an employment relationship with the Company sponsor of that research at any time during the 2 years before submission of the manuscript; or

## *F. Conflict of Interest Policy Implementation for Clinical Practice Guidelines*

. Among other requirements, the majority of panel members, including the panel chair, must not hold relevant relationships with Affected Companies.

thebmj

*BMJ* 2014;349:g7197 doi: 10.1136/bmj.g7197 (Published 28 November 2014)



## EDITORIALS

# Medical journals and industry ties

Zero tolerance on education articles with financial links to industry

Mabel Chew *practice editor*, Catherine Brizzell *head of education*, Kamran Abbasi *international editor*, Fiona Godlee *editor in chief*

The governing principle has been that transparency is a panacea.[1] We placed faith in this principle, but mounting experience and evidence tell us that we were only half right.[2] Transparency remains essential, but it isn't sufficient to eliminate bias or perception of bias.

We believe this risk of bias is particularly important for clinical educational articles that are designed to guide patient care, when authors' biases may be less visible to general medical readers.

From next year our clinical education articles will be authored by experts without financial ties to industry

# POURQUOI GARDER SON INDÉPENDANCE FACE AUX LABORATOIRES PHARMACEUTIQUES ?


Une initiative de La TROUPE DU RIRE - Collectif d'étudiant·e·s en médecine

Carlat et al. BMC Medical Education (2016) 16:202
DOI 10.1186/s12909-016-0725-y

BMC Medical Education

RESEARCH ARTICLE Open Access

# The updated AMSA scorecard of conflict-of-interest policies: a survey of U.S. medical schools

Daniel J. Carlat[1,6*], Teddy Fagrelius[2], Reshma Ramachandran[3], Joseph S. Ross[4] and Sallyann Bergh[5]

**Background:** Best practices for conflict-of-interest (COI) policies in medical schools have evolved rapidly over the past decade, in part motivated by the American Medical Student Association (AMSA) scorecard that has publicly graded schools since 2007. This report describes the methodological update and impact of revisions to the scorecard in 2014.

**Conclusions:** The revised 2014 AMSA scorecard, with its more stringent criteria for evaluating COI policies, assigned fewer As and more Bs and Cs than in years past. This was the first study to identify schools with COI policies stronger than those recommended in 2008 by the Association of American Medical Colleges. Developing more stringent COI policies should be helpful in reducing the influence of pharmaceutical and device industry marketing on both trainees and faculty in American medical schools.

PLOS ONE | DOI:10.1371/journal.pone.0168258 January 9, 2017

RESEARCH ARTICLE

# Conflict of Interest Policies at French Medical Schools: Starting from the Bottom

**Paul Scheffer[1]*, Christian Guy-Coichard[2], David Outh-Gauer[3], Zoéline Calet-Froissart[4], Mathilde Boursier[5], Barbara Mintzes[6], Jean-Sébastien Borde[7]**

**1** Sciences of Education Department, Paris 8 University, Saint-Denis France, **2** Saint-Antoine Hospital, Paris, France, **3** Faculty of Medicine Purpan, Toulouse 3 University, Toulouse, France, **4** Faculty of Medicine Aix-Marseille, Marseille, France, **5** Faculty of Medicine Rennes1, Rennes, France, **6** Faculty of Pharmacy, Charles Perkins Centre, The University of Sydney, Sydney, Australia, **7** Saintonge Hospital, Saintes, France

* classement.facultes@gmail.com

## Conclusion

This is the first survey in France to examine COI policies at medical faculties. We found little evidence that protection of medical students from undue commercial influence is a priority, either through institutional policies or education. This is despite national transparency

# Charte éthique et déontologique des Facultés de médecine et d'odontologie

Pour :

La Conférence nationale des Doyens de facultés de médecine et de santé:

Pr. Jean-Luc Dubois Randé

La Conférence nationale des Doyens de facultés de chirurgie dentaire

Pr. Corinne Taddei-Gross

Novembre 2017

Ce n'est qu'un début….

#BalanceTonConflitDinteret!