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Conflicts of Interest in Medicine

Presentation before
 10th Annual Medwatcher Symposium
 Tokyo
 June 8, 2008

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Outline

- Varieties of conflict of interest
- Financial vs. intellectual conflicts of interest
- Framework for addressing conflict of interest
- Conclusions

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Varieties of Conflict of Interest

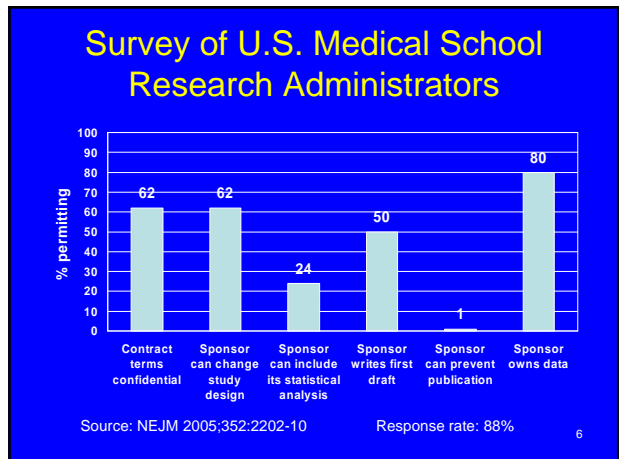
- Research
- Clinical practice
- Education
- Public advisory committees

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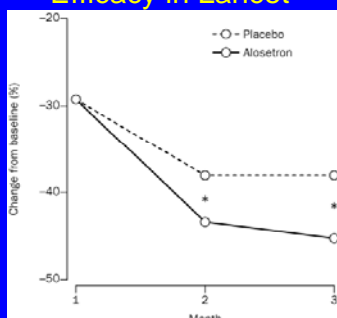
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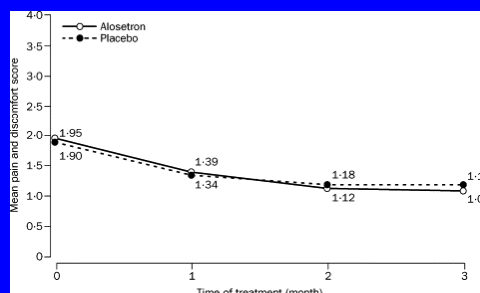
Depiction of Alosetron (Lotronex) Efficacy in Lancet



Source: Lancet 2000;355:1035-40

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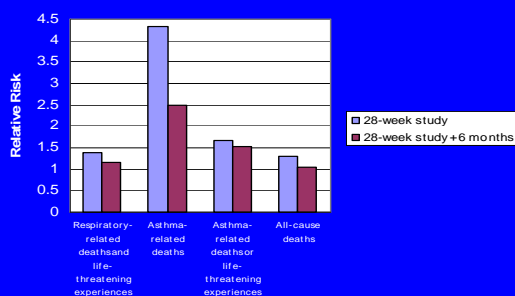
Public Citizen Depiction of alosetron (Lotronex) Efficacy



Source: Lancet 2000;356:2009

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Salmeterol Postmarketing Study (SMART)



Source: Lurie and Wolfe, Lancet 2005;366:1261-2

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RCT of Funding Disclosure

- BMA members randomised to receive papers with and without competing interest statements
- Scale of 1-5 (lowest-highest)

	Statement	None
Interest (NS)	3.06	3.21
Importance	3.03	3.29
Relevance	3.13	3.44
Validity	2.82	3.16
Believability	3.20	3.49

Source: BMJ 2004;328:742-3

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Non-disclosure Continues

- Statin trials published 1999 – 2005 – 37% no funding disclosure
- Vagus nerve stimulator review in Neuropsychopharmacology – No disclosure of conflicts by all 8 academics – First author is editor of the journal – Editor forced to resign

Sources: PLOS Medicine 2007;4:e184; Neuropsychopharmacology 2006;31:1345-55

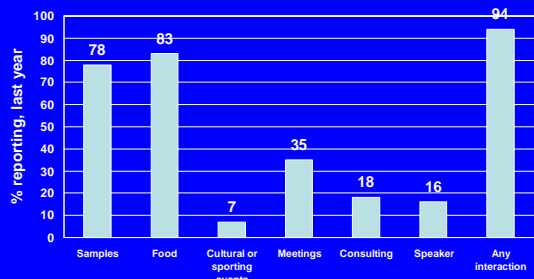
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Survey of U.S. Physicians



Source: NEJM 2007;356:1742-50

Weighted response rate: 58%

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Statement by American College of Physicians

“What would my patients think about this arrangement? What would the public think? How would I feel if the relationship was disclosed through the media?”

Source: Ann Intern Med 2002;136:396-402

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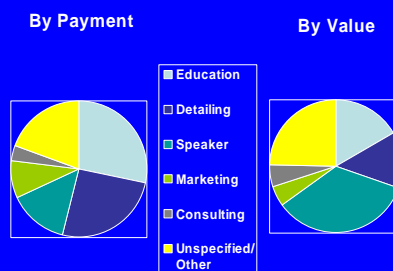
Public Disclosure of Pharmaceutical Company Gifts to Physicians, 2002-2004

	Vermont	Minnesota
Threshold	\$25	\$100
Trade secret exemption?	Yes	No
Electronic?	Yes	No
Reporting period	2 years	3 years
Median physician gift >\$100 (maximum)	\$177 (\$20,000)	\$1000 (\$922,239)
Total physician gifts	\$1.01 million	\$22.4 million

Source: JAMA 2007;297:1216-23

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Purpose of Payments >\$100 to Physicians in Vermont, 2002-4



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Public Disclosure of Pharmaceutical Company Gifts to Physicians, 2002-2004

- High rates of underreporting
 - Companies report \$millions one year, nothing the next
- Responses non-standardized
 - Aggregation by physician and by gift
- Exemptions
 - Samples
 - Research studies
- Limited accessibility
 - Lack of online submissions or reports
 - Need to file lawsuit in Vermont

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Medical Education Services Suppliers (MESSs)

- Analysis of survey of 123 MESSs in Medical Marketing and Media
- 80 responses (65%) total; 42 (53%) with financial data
- 1999 revenue: \$643m (19% up from 1998)
- 1999: grand rounds, \$115m; symposia, \$114m; publications-related activities, \$60m
- 76% of clients are drug companies

Available at: <http://www.citizen.org/publications/release.cfm?ID=7142> 19

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Disclosure of Conflicts of Interest of FDA AC Members

- 1997: Food and Drug Administration Modernization Act requires more extensive public disclosure of COIs
- September 2001: Public Citizen threatens the FDA with a lawsuit for failure to adequately disclose the COIs of AC members and consultants
- January 2002: the FDA drafts a guidance document with provisions for more detailed COI disclosure
- March 2007: FDA announces new draft guidance on conflict of interest
 - Recusal of members with total conflicts >\$50K
 - Members with conflicts <\$50K cannot vote
- September 2007: Congress requires 5% annual reduction in rate of COIs on FDA ACs

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Lancet Editorial

“Defenders of FDA policy say that it is difficult to find experts free of conflicts of interest. But it is hard to believe that in a country with 125 medical schools—not to mention the pool of international experts—the FDA cannot find experts who do not have financial ties with companies whose products are under review.”

Source: Lancet 2005;365:1664

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Disclosed Conflict Rates for FDA AC Members, 2001-4

	Through January 2002	After January 2002	Total
Per meeting COI rate*	77%	72%	73%
Per person-meeting COI rate**	28%	28%	28%

Recusal rate: 1%

*Percentage of 221 meetings where at least 1 COI was disclosed
 **Percentage of 2947 AC member or consultant person-meetings disclosing a COI

Source: JAMA 2006;295:1921-8

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Relationship between Conflict Type and Voting Behavior

	Index Conflict	Competitor Conflict	Any Conflict
Continuous outcome	NS	NS	NS
Dichotomous	NS	NS	NS
Exclusions lead to less favorable vote	64%	77%	72%
Exclusions change vote outcome	No	No	No
Mantel-Haenszel	0.74 (0.39-1.39)	1.20 (1.12-1.28)	1.10 (1.03-1.17)
Monte Carlo	NS	P<0.05	NS

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COX-2 Advisory Committee Meeting, 2005

- Considered Vioxx (already removed), Celebrex, Bextra
- Sales of all three endorsed
- Votes favoring the drugs
 - 93% of consultants
 - 56% of non-consultants
- If conflicted members excluded,
 - Vioxx not recommended to return
 - Bextra recommended for removal

Sources: NY Times, 2/25/05; NEJM 2005;353:116-8

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Financial vs. Intellectual Conflicts of Interest

Financial Conflicts	Intellectual Conflicts
Extrinsic	Intrinsic
Variable levels	Ubiquitous
Quantifiable	Not quantifiable
Unlikely to emerge	Likely to emerge
Remediable	Non-remediable
Distinguished legally	Not distinguished legally

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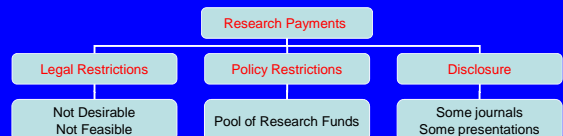
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Framework for Addressing Conflict of Interest



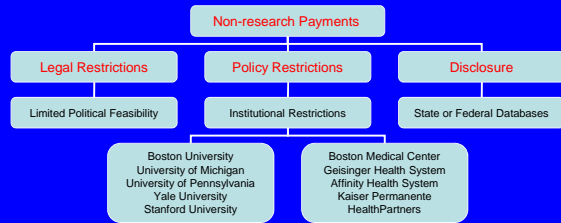
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Research Payments to Physicians



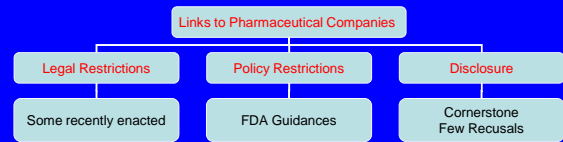
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Non-research Payments to Physicians



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FDA Advisory Committees



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Conclusions

- There is a limited research actually linking the conflicts with the outcomes of interest
- Financial conflicts are of particular concern and merit specific attention
- In general, committees/reviewers with low or no conflicts can be assembled
- Disclosure is no substitute for prevention of conflicts when this is feasible and legal

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