

Conflict of interest: “Be rigorous in judging ourselves and gracious in judging others”

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The recent *New York Times* article with the banner headline Top Cancer Researcher Fails to Disclose Corporate Financial Ties in Major Research Journals and the subsequent discussion about Dr. Jose Baselga, demands the attention of the medical community^{1,2}. The story not only illuminates conflict of interest (coi) involving health care professionals, but more importantly, how the public will respond if they know that physicians are receiving money or gifts from pharmaceutical companies. In this commentary, we reflect less on the failure to declare coi and more on the existence of coi and how it can influence physician behaviour and public perception.

The *New York Times* article focuses on Dr. Baselga's relationship with a broad range of institutions—drug companies, scientific organizations, and international journals—in his roles as board member, consultant or advisor, and founder or president. The article notes his “positive spin” on the results of the industry-sponsored APHINITY trial (for which he was the senior author and which evaluated the addition of pertuzumab to trastuzumab in adjuvant therapy for women with HER2-positive breast cancer) in contrast to the more “disappointing” editorial on the study in the *New England Journal of Medicine*^{3,4}. The *New York Times* article points to his having received “more than 3 million dollars” in various types of compensation⁵.

We recommend caution in assuming that a financial interest was behind Dr. Baselga's support for pertuzumab. He was deeply involved in the development of pertuzumab from early clinical efforts to the definitive CLEOPATRA study⁶, and researchers often put a positive spin on their own research. In addition, he is not alone in his enthusiasm; the discussant at American Society of Clinical Oncology meetings, and other thought leaders in the field of breast cancer, hold the opinion that pertuzumab represents a clinical breakthrough for the adjuvant treatment of breast cancer. For those and other reasons, we have used John Wesley's quote in the title of our commentary.

Response to the failure to declare apparent coi has been swift: comments in the *New York Times* have expressed disgust not only with nondisclosure, but with the coi that existed in the first place. In response, Memorial Sloan Kettering Cancer Center released a statement urging their staff to “do better,” which was followed by the resignation of Dr. Baselga as their chief medical officer⁷. Subsequent editorials from patients, physicians, journal editors, key members of organizations, and ethicists have renewed the

call for transparent, universal, and drastic reforms². From the patient point of view, the existence of coi is important whether conflicts are declared or not. That feeling is understandable, given that it is difficult to defend the idea that simply declaring receipt of money or any other advantage from a vested interest makes receipt of the consideration acceptable.

It is almost impossible in medical oncology to conduct drug development research without an interaction with industry, but if we are not rigorous in refusing personal gifts, we should not be surprised if better standards are demanded of us. Public perception can lead rapidly to uncontrolled public shaming. That such a circumstance has befallen Dr. Baselga should be warning to us all.

Many changes can be made to improve public perception of our ties to industry. Ample literature has demonstrated that physicians who see company representatives are less likely to follow evidence-based practice guidelines⁸. The pharmaceutical industry extensively supports physician travel to conferences, and such support changes the prescribing behavior of practitioners⁹. It has been shown that pharmaceutical support of continuing medical education leads to poorer prescribing habits, which are less adherent to guidelines. One disastrous example is the growing opioid crisis in the United States, which is largely attributable to the creation of a speakers' bureau and sponsorship of more than 20,000 educational programs to support the use of OxyContin (Purdue Pharma, Stamford, CT, U.S.A.) for benign causes of pain. It has subsequently been shown that those education efforts misrepresented the compound's risk for addiction and abuse¹⁰. As a result, sales of that specific opioid grew from US\$48 million in 1996 to almost US\$1.1 billion by 2000, and many people became addicted¹¹. Even the receipt of pharmaceutical industry-paid meals or small gifts, which are provided at sponsored events, can influence clinical practice^{12,13}. Furthermore, a recent editorial has suggested that these practices “purchase the silence” of physicians in relation to the exorbitant rise in drug prices, with little public outcry from most individual physicians or their learned societies¹⁴.

Senior and well-published physicians (also known as thought leaders) could contribute to improving the current environment. In many oral presentations at medical conferences, coi statements are often displayed too briefly to be read and understood, are not discussed or explained by the presenter, or are sometimes missing. A prospective

delegate-based observational study that sampled 201 oral presentations at five medical conferences in 2016 found that slides containing coi statements were displayed for a median of two seconds¹⁵. Most importantly, coi has to be declared by developers of consensus statements and clinical practice guidelines. A study evaluating consensus statements and clinical practice guidelines published in *Current Oncology*, the *European Journal of Cancer*, and the *Journal of Clinical Oncology* found that 65% of consensus statements and 45% of clinical practice guidelines did not declare their funding source¹⁶. Given the interactions with industry required during the development of novel therapeutics, it is unrealistic to expect no coi among thought leaders. Nevertheless, physicians who participate in guideline panels and consensus statements likely have to make better efforts to minimize coi so as to maintain public confidence in their recommendations.

Health care professionals hold a unique and privileged place in society. Our patients, often at their most vulnerable, trust us to act in their best interest. We must be rigorous in judging ourselves, and we must resist the temptation to accept benefits that lead to coi. As authors, we also note that we are not exempt from this reality.

In Table 1, we present some (non-exhaustive) suggestions as a starting point for broader discussion. Before embarking on any activity that relates to the pharmaceutical industry, we should ask ourselves if discomfort would ensue should that activity become publicly known. As a consequence, before saying “These considerations do not apply to me,” we should all remember the experience of the gifted Dr. Baselga.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare the following interests: BB has attended advisor board meetings for Roche, Amgen, and Novartis; AA has attended advisor boards for Novartis; JFH has served as an advisory consultant for Bristol–Myers Squibb, Eli Lilly, Merck, Novartis, Roche, Pfizer, and as a member of a data monitoring committee for Bristol–Myers Squibb; MC has served as an advisory board member for Helsinn.

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REFERENCES

- Ornstein C, Thomas K. Top Cancer Researcher Fails to Disclose Corporate Financial Ties in Major Research Journals [Web article]. *The New York Times* 2018; 8 September. [Available at: <https://www.nytimes.com/2018/09/08/health/jose-baselga-cancer-memorial-sloan-kettering.html>; cited 20 September 2018].
- Angell M. Transparency Hasn't Stopped Drug Companies from Corrupting Medical Research [Web article]. *The New York Times* 2018; 14 September. [Available at: <https://www.nytimes.com/2018/09/14/opinion/jose-baselga-research-disclosure-bias.html>; cited 20 September 2018].
- von Minckwitz G, Procter M, de Azambuja E, *et al.* Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. *N Engl J Med* 2017;377:122–31.
- Miller KD. Questioning our APHINITY for more. *N Engl J Med* 2017;377:186–7.
- Baselga J, Gelmon KA, Verma S, *et al.* Phase II trial of pertuzumab and trastuzumab in patients with human epidermal growth factor receptor 2–positive metastatic breast cancer

TABLE 1 Potential suggestions to limit conflict of interest (COI)

Health care professionals	<ul style="list-style-type: none"> ■ Increase awareness that COIs exist. ■ Limit or abolish privately funded continuing medical education and conference activities. ■ Limit or abolish personal funding from private sources that represents more than what is reasonable compensation for time spent. ■ Limit or abolish acceptance of pharmaceutical industry–paid meals or small gifts.
Health care institutions	<ul style="list-style-type: none"> ■ Prioritize and campaign for increased awareness of COI in the health care professions. ■ Publicize efforts made to limit COI so as to assure patients that the issue is taken seriously. ■ Identify limits to personal compensation from private sources.
Professional associations	<ul style="list-style-type: none"> ■ Develop a transparent, independent universal body (rather than journals or institutions) that records, develops, and monitors standards for COI. ■ Move away from private conference funding and adapt less costly, more environmental-friendly methods of disseminating new knowledge.
Medical journals	<ul style="list-style-type: none"> ■ Ensure complete disclosure and consider greater transparency (more precise information about author engagement and how it might affect the presented work). ■ Implement stricter consequences for nondisclosure.
Funding agency and governmental bodies	<ul style="list-style-type: none"> ■ Increase funding for patient-centred research (study design, interventions, outcomes, and independent pharmacoeconomic analyses).
Patient advocacy	<ul style="list-style-type: none"> ■ Continue to advocate for the rights of patients in receiving care that is patient-centred. ■ Increase the group's voice or lobby for professionals and organizations that are accountable for implementing changes thoroughly and rapidly. ■ Prioritize fundraising methods for patient-centred research.

- that progressed during prior trastuzumab therapy. *J Clin Oncol* 2010;28:1138–44.
6. Swain SM, Baselga J, Kim SB, *et al.* on behalf of the CLEOPATRA study group. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med* 2015;372:724–34.
 7. Thomas K, Ornstein C. MSK Cancer Center Orders Staff to “Do a Better Job” of Disclosing Industry Ties [Web article]. *The New York Times* 2018; 9 September. [Available at: <https://www.nytimes.com/2018/09/09/health/cancer-memorial-sloan-kettering-disclosure.html>]; cited 20 September 2018].
 8. Lurie N, Rich EC, Simpson DE, *et al.* Pharmaceutical representatives in academic medical centers: interaction with faculty and housestaff. *J Gen Intern Med* 1990;5:240–3.
 9. Orlowski JP, Wateska L. The effects of pharmaceutical firm enticements on physician prescribing patterns; there’s no such thing as a free lunch. *Chest* 1992;102:270–3.
 10. Meier B. In Guilty Plea, OxyContin to Pay \$600 Million [Web article]. *The New York Times* 2007; 10 May. [Available online at: <http://www.nytimes.com/2007/05/10/business/11drug-web.html>]; cited 20 September 2018].
 11. Van Zee A. The promotion and marketing of OxyContin: commercial triumph, public health tragedy. *Am J Public Health* 2009;99:221–7.
 12. DeJong C, Aguilar T, Tseng CW, Lin GA, Boscardin WJ, Dudley RA. Pharmaceutical industry-sponsored meals and physician prescribing patterns for Medicare beneficiaries. *JAMA Intern Med* 2016;176:1114–22.
 13. Katz D, Caplan AL, Merz JF. All gifts large and small: toward an understanding of the ethics of pharmaceutical industry gift giving all gifts large and small toward an understanding of the ethics of pharmaceutical industry gift-giving. *Am J Bioeth* 2003;3:39–46.
 14. Tannock IF, Joshua AM. Purchasing silence. *Ann Oncol* 2018;29:1339–40.
 15. Grey A, Avenell A, Dalbeth N, Stewart F, Bolland MJ. Reporting of conflicts of interest in oral presentations at medical conferences: a delegate-based prospective observational study. *BMJ Open* 2017;7:e017019.
 16. Jacobs C, Graham ID, Makarski J, *et al.* Clinical practice guidelines and consensus statements in oncology—an assessment of their methodological quality. *PLoS One* 2014;9:e110469.