Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries Ltd., Cephalon, Inc., and Actavis Generic Defendants'

Direct Examination of Pradeep Chintagunta, Ph.D.

June 13, 2022

Pradeep K. Chintagunta, Ph.D.

Northwestern University

IIM AHMEDABAD

CHICAGO BOOTH

Education

- Ph.D., Marketing, Northwestern University (1990)
- Post Graduate Diploma in Management, Indian Institute of Management, Ahmedabad, India (1986)
- Bachelor of Technology in Mechanical Engineering, Indian Institute of Technology, Banaras Hindu University, India (1984)

Professional Highlights

- Professor of Marketing, Booth School of Business, University of Chicago, 1995 – present
- Member, Editorial Board: International Journal of Research in Marketing, Journal of Business-to-Business Marketing, Journal of the Academy of Marketing Science, present
- Director, Ph.D. program, Booth School of Business, University of Chicago, 2004 – 2013
- Gilbert A. Churchill, Jr. Award for Lifetime Achievement awarded by the AMA's Marketing Research SIG

Courses Taught

- Foundations of Advanced Quantitative Marketing
- Marketing Management
- Marketing Strategy Simulation
- Global Senior Management Program - Chicago and Madrid (Executive Education)
- The Accelerated Development Program (Executive Education)

Pradeep K. Chintagunta, Ph.D.

Research and Publications

- Empirical analysis of the causal impact of firms' marketing efforts on various outcomes of interest (e.g., prescriptions)
- Research on pharmaceutical markets, with a focus on the impact of marketing on physician prescribing behavior.
- Relevant Examples:
  - "Responsiveness of Physician Prescription Behavior to Salesforce Effort: An Individual Level Analysis," *Marketing Letters*, 2004
  - "Response Modeling with Nonrandom Marketing-Mix Variables," *Journal of Marketing Research*, 2004
  - "Information, Learning, and Drug Diffusion: The Case of Cox-2 Inhibitors," *Quantitative Marketing and Economics*, 2009
  - "New Drug Diffusion When Forward-Looking Physicians Learn from Patient Feedback and Detailing," *Journal of Marketing Research*, 2012

Summary of Opinions

There are three types of pharmaceutical marketing: Branded, Unbranded ("Disease-Awareness" or "Help-Seeking"), and Generic

Dr. Perri's opinions on a "heightened standard" and "aggressive marketing" with respect to pharmaceutical marketing are subjective

There are certain methodological requirements for assessing the causal impact, if any, of marketing on an increase in prescribing

The People's experts failed to conduct a valid causal assessment of the impact, if any, of marketing on an increase in prescribing consistent with these methodological requirements

The People have not determined the impact, if any, of allegedly false, misleading or fraudulent marketing by Cephalon, Teva USA, or any Actavis Generic Entity on opioid prescribing, medically inappropriate or otherwise

Opinion # 1: Types of Marketing

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Types of Pharmaceutical Marketing

Branded Marketing	Unbranded "Disease-Awareness" Marketing	Generics "Marketing"
Promotion of brand-name medicines for which the manufacturer has patent rights	**Not specific to a brand** **Exempt from FDA regulation**	**Promotion begins once generic is approved after the expiration of the brand's patent rights.**
Content: Typically discusses efficacy, safety, and dosing of the branded drug	**Content**: Typically focuses on disease state awareness and providing information about the medicine category and other available treatments	**Content**: Does not discuss drug's safety or efficacy, instead focuses on product availability and pricing
Audience: Prescribers, via detailing to physicians, journal advertising and other programs.	**Audience**: Consumer or prescribers	**Audience**: Pharmacies and wholesalers, typically not physicians
Time: Early- to mid- product life cycle	**Time**: Early- to mid- product life cycle	**Time**: Late product life cycle
FDA Standard: Fair balance	**FDA Standard**: Unregulated/Exempt	**FDA Standard**: Fair Balance Not Required

Opinion # 2: Dr. Perri's "Standards" Are Subjective

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The People's Witness: "Heightened Standard" for Marketing

Dr. Matthew Perri

The People's Expert Marketing/Causation

(May 25, 2022 Trial Tr. 1640:9-23)

Q. Okay. Is there a heightened standard for pharmaceutical marketing versus other types of marketing?

A. I mean, let's not forget what we're talking about here. We're -- you know, pharmaceutical drugs are not widgets and opioids are not aspirin; so there's definitely a heightened standard.

And when we look at it, the Schedule II narcotics, opioids, they have very serious side effects, potentials for abuse; and that leads to what I would refer to, and I have referred to over time, as a distortion in the demand. And what I mean by that is when you take opioids because of tolerance and dependence and addiction, you -- in the future down the road, you may need or will likely need more opioids; so the demand for opioids perpetuates itself. And that's a distortion in the demand. It goes beyond what would normally be used.

The People's Witness: "Aggressive" Marketing

Dr. Matthew Perri

The People's Expert Marketing/Causation

(May 25, 2022 Trial Tr. 1641:17-1642:12)

17 **Q.** And let's drill down on that. First of all, what do you
18 mean when you say "aggressive marketing"?
19 **A.** Well, I've been asked that a lot of times; and I've
20 consistently said that aggressive marketing, from a marketer's
21 perspective, is just marketing that is very fervently designed,
22 vigorously executed. It's marketing that is sophisticated.
23 It's -- it's persistent, pervasive. It's got the
24 characteristics of something that's been very carefully
25 integrated and well-developed, and that's a marketer's view of
1 it.
2 You know, aggressive marketing also has other
3 implications. Certainly some of the word "aggressive" has the
4 negative connotation to it, but defendants' marketing plans and
5 other opioid marketers commonly referred to their marketing
6 materials as aggressive or that they were going to pursue these
7 things aggressively. So it wasn't just, you know, my
8 definition. It was also the defendants' own terminology.
9 And in addition to that, I would say that, you know,
10 because case study allow us to look at things in the context of
11 the real world, if you looked at the lay media, lay media
12 frequently referred to opioid marketing as aggressive.

TCA_Defendants_Court_Exhibit_00008

Opinion # 3: Requirements To Assess Causal Impact

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Tenets of Causal Analysis (Quantitative AND Qualitative)

1. Causal analysis needs to precisely **define the intervention and outcome**
2. Causal analysis needs to **define a causal model**
   - Must account for other influencing factors
   - Must allow and empirically test alternative hypotheses
3. Using its causal model, causal analysis needs to **isolate the impact** of the intervention on the outcome
4. Causal analysis needs to use **data that are representative** of the population of interest
5. Reliable causal analyses needs to be **reproducible**

Establishing a causal link between alleged false and misleading marketing by Cephalon, Teva USA, or Actavis Generic Defendants and any increase in opioid prescribing **REQUIRES**:

1. Distinguishing alleged false and misleading marketing from truthful and non-misleading marketing.

2. Distinguishing marketing by Cephalon, Teva USA, or Actavis Generic Defendants from marketing by other opioid manufacturers.

3. Distinguishing medically inappropriate prescribing from medically appropriate prescribing.

4. Properly accounting for the impact of the various factors other than alleged false and misleading marketing that may influence prescribing decisions.

Opinion # 4: People's Experts Failed To Conduct Valid Causal Assessment of Marketing Impact

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Selected Factors Affecting Prescriber Decisions

1. Whether and degree to which the physician received the marketing messages

2. Physician characteristics and phsyican and patient experience with the medication

3. Patient characteristics (age, health background, other personal characteristics)

4. Scientific evidence

5. Medication characteristics (e.g., quality, effectiveness, risks/side effects)

6. Physician and patient specific factors (whether physicians discount manufacturers trials/marketing, etc.)

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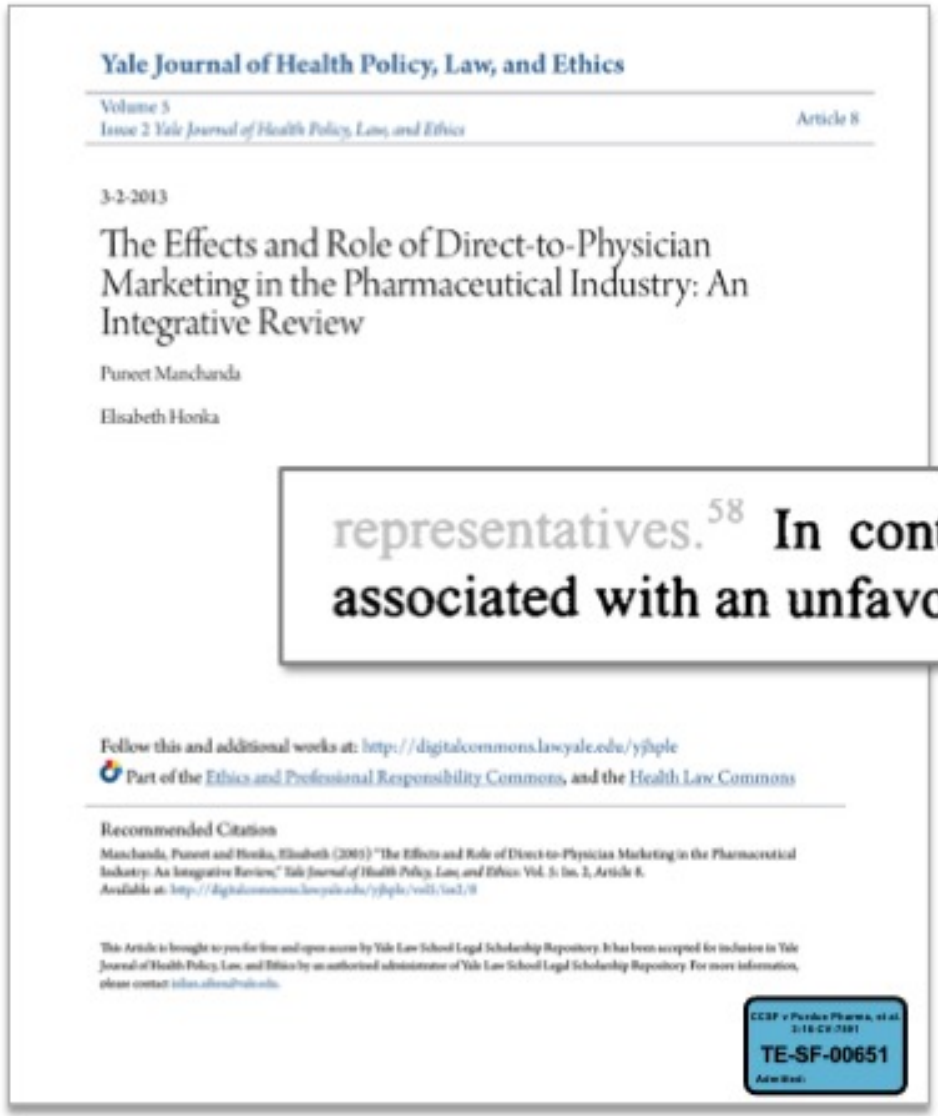

Yale Journal of Health Policy, Law, and Ethics

Volume 3
Issue 2 *Yale Journal of Health Policy, Law, and Ethics* Article 8

3-2-2013

The Effects and Role of Direct-to-Physician Marketing in the Pharmaceutical Industry: An Integrative Review

Puneet Manchanda

Elisabeth Honka

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Recommended Citation

Manchanda, Puneet and Honka, Elisabeth (2013) "The Effects and Role of Direct-to-Physician Marketing in the Pharmaceutical Industry: An Integrative Review," *Yale Journal of Health Policy, Law, and Ethics*: Vol. 3: Iss. 2, Article 8.
Available at: http://digitalcommons.lawyale.edu/yjhple/vol3/iss2/8

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representatives.[58] In contrast, a manipulative and aggressive selling style was associated with an unfavorable attitude.[59]

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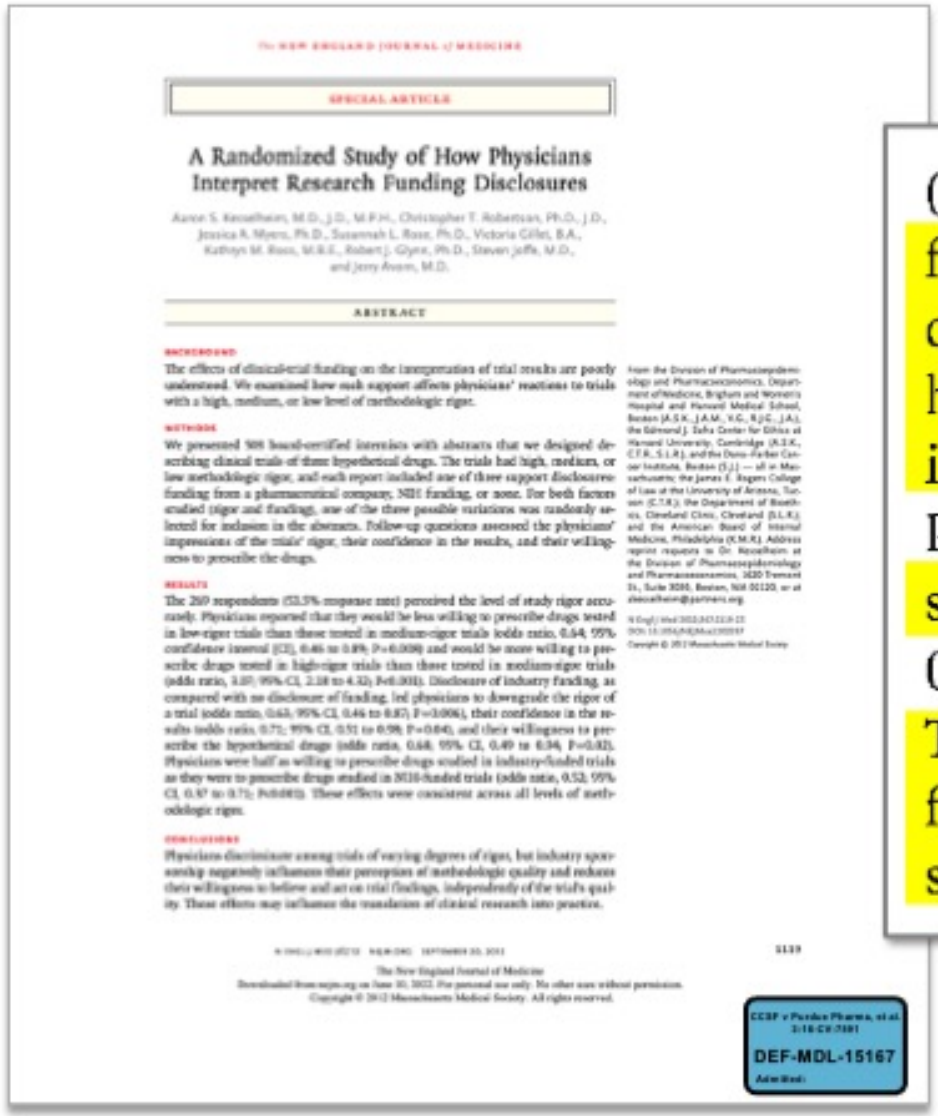
6. Physician and patient specific factors (whether physicians discount manufacturers trials/marketing, etc.)



SPECIAL ARTICLES

A Randomized Study of How Physicians Interpret Research Funding Disclosures

Aaron S. Kesselheim, M.D., J.D., M.P.H., Christopher T. Robertson, Ph.D., J.D., Jessica A. Myers, Ph.D., Susannah L. Rose, Ph.D., Victoria Gillet, B.A., Kathryn M. Ross, M.P.H., Robert J. Glynn, Ph.D., Steven Joffe, M.D., and Jerry Avorn, M.D.

ABSTRACT

BACKGROUND

The effects of clinical-trial funding on the interpretation of trial results are poorly understood. We examined how such support affects physicians' reactions to trials with a high, medium, or low level of methodologic rigor.

METHODS

We presented 359 board-certified internists with abstracts that we designed describing clinical trials of three hypothetical drugs. The trials had high, medium, or low methodologic rigor, and each report included one of three support disclosures: funding from a pharmaceutical company, NIH funding, or none. For both factors studied (rigor and funding), one of the three possible variations was randomly selected for inclusion in the abstracts. Follow-up questions assessed the physicians' impressions of the trials' rigor, their confidence in the results, and their willingness to prescribe the drugs.

RESULTS

The 269 respondents (53.5% response rate) perceived the level of study rigor accurately. Physicians reported that they would be less willing to prescribe drugs tested in low-rigor trials than those tested in medium-rigor trials (odds ratio, 0.64; 95% confidence interval [CI], 0.46 to 0.89; P=0.008) and would be more willing to prescribe drugs tested in high-rigor trials than those tested in medium-rigor trials (odds ratio, 3.07; 95% CI, 2.18 to 4.32; P<0.001). Disclosure of industry funding, as compared with no disclosure of funding, led physicians to downgrade the rigor of a trial (odds ratio, 0.63; 95% CI, 0.46 to 0.87; P=0.006), their confidence in the results (odds ratio, 0.71; 95% CI, 0.51 to 0.98; P=0.04), and their willingness to prescribe the hypothetical drugs (odds ratio, 0.68; 95% CI, 0.49 to 0.94; P=0.02). Physicians were half as willing to prescribe drugs studied in industry-funded trials as they were to prescribe drugs studied in NIH-funded trials (odds ratio, 0.52; 95% CI, 0.37 to 0.71; P<0.001). These effects were consistent across all levels of methodologic rigor.

CONCLUSIONS

Physicians discriminate among trials of varying degrees of rigor, but industry sponsorship negatively influences their perception of methodologic quality and reduces their willingness to believe and act on trial findings, independently of the trial's quality. These effects may influence the translation of clinical research into practice.

From the Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston (A.S.K., J.A.M., Y.G., R.J.G., J.A.); the Edmond J. Safra Center for Ethics at Harvard University, Cambridge (A.S.K., C.T.R., S.L.R.), and the Dana–Farber Cancer Institute, Boston (S.J.) — all in Massachusetts; the James E. Rogers College of Law at the University of Arizona, Tucson (C.T.R.); the Department of Bioethics, Cleveland Clinic, Cleveland (S.L.R.); and the American Board of Internal Medicine, Philadelphia (K.M.R.). Address reprint requests to Dr. Kesselheim at the Division of Pharmacoepidemiology and Pharmacoeconomics, 1620 Tremont St., Suite 3030, Boston, MA 02120, or at akesselheim@partners.org.

N Engl J Med 2012;367:1119-27.
DOI: 10.1056/NEJMsa1202397

(Fig. 2A). Similarly, in comparisons with trials for which no funding was listed and regardless of the study design, physicians were less likely to have confidence in the results of trials funded by industry (odds ratio, 0.71; 95% CI, 0.51 to 0.98; P=0.04) (Fig. 2B) and were less willing to prescribe drugs described in such trials (odds ratio, 0.68; 95% CI, 0.49 to 0.94; P=0.02) (Fig. 2C). These effects were even greater when industry-funded trials were compared with trials described as having NIH support.

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Summary of Opinions

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