Promotion of Prescription Drugs to Consumers and Providers, 2001–2010

Rachel Kornfield¹, Julie Donohue²,³, Ernst R. Berndt⁴,⁵, G. Caleb Alexander¹,⁶,⁷,⁸*

¹ Section of General Internal Medicine, Department of Medicine, University of Chicago, Chicago, Illinois, United States of America, ² Department of Health Policy and Management, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, ³ Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, ⁴ Alfred P. Sloan School of Management, Massachusetts Institute of Technology, Cambridge, Massachusetts, United States of America, ⁵ National Bureau of Economic Research, Cambridge, Massachusetts, United States of America, ⁶ Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America, ⁷ Department of Medicine, Johns Hopkins Medicine, Baltimore, Maryland, United States of America, ⁸ Department of Pharmacy Practice, University of Illinois at Chicago School of Pharmacy, Chicago, Illinois, United States of America

Abstract

**Background:** Pharmaceutical firms heavily promote their products and may have changed marketing strategies in response to reductions in new product approvals, restrictions on some forms of promotion, and the expanding role of biologic therapies.

**Methods:** We used descriptive analyses of annual cross-sectional data from 2001 through 2010 to examine direct-to-consumer advertising (DTCA) (Kantar Media) and provider-targeted promotion (IMS Health and SDI), including: (1) inflation-adjusted total promotion spending ($ and percent of sales); (2) distribution by channel (consumer v. provider); and (3) provider specialty both for the industry as a whole and for top-selling biologic and small molecule therapies.

**Results:** Total promotion peaked in 2004 at US$36.1 billion (13.4% of sales). By 2010 it had declined to $27.7 billion (9.0% of sales). Between 2006 and 2010, similar declines were seen for promotion to providers and DTCA (both by 25%). DTCA’s share of total promotion increased from 12% in 2002 to 18% in 2006, but then declined to 16% and remains highly concentrated. Number of products promoted to providers peaked in 2004 at over 3000, and then declined 20% by 2010. In contrast to top-selling small molecule therapies having an average of $370 million (8.8% of sales) spent on promotion, top biologics were promoted less, with only $33 million (1.4% of sales) spent per product. Little change occurred in the composition of promotion between primary care physicians and specialists from 2001–2010.

**Conclusions:** These findings suggest that pharmaceutical companies have reduced promotion following changes in the pharmaceutical pipeline and patent expiry for several blockbuster drugs. Promotional strategies for biologic drugs differ substantially from small molecule therapies.

Citation: Kornfield R, Donohue J, Berndt ER, Alexander GC (2013) Promotion of Prescription Drugs to Consumers and Providers, 2001–2010. PLoS ONE 8(3): e55504. doi:10.1371/journal.pone.0055504

Received: October 19, 2012; Accepted: December 23, 2012; Published: March 4, 2013

Copyright: © 2013 Kornfield et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: Ms. Kornfield and Dr. Alexander were supported by the Agency for Healthcare Research and Quality (RO1 HS0189960). The funding sources had no role in study design or conduct; collection, management, analysis, or interpretation of the data; or preparation, review, or final manuscript approval.

Competing Interests: Ms. Kornfield and Dr. Alexander were supported by the Agency for Healthcare Research and Quality (RO1 HS0189960). Dr. Alexander has served as an ad-hoc member of the Food and Drug Administration’s Drug Safety and Risk Management Advisory Committee (DSARM) and Ms. Kornfield and Dr. Alexander are consultants for IMS Health, one of the three sources of data for our report. The funding sources had no role in study design or conduct; collection, management, analysis, or interpretation of the data; or preparation, review, or final manuscript approval. This does not alter the authors’ adherence to all the PLOS ONE policies on sharing data and materials.

* E-mail: galexand@jhsph.edu

**Introduction**

In the United States, pharmaceuticals are heavily promoted to providers and patients. The pharmaceutical industry spent nearly $30 billion dollars in 2005 on marketing and promotion, of which 84% went toward physician detailing and free samples, with less devoted to professional advertising and direct-to-consumer advertising (DTCA) [1,2]. Spending varied considerably by product, although both detailing and DTCA tended to favor drugs with broader clinical indications for use [3]. Pharmaceutical promotion can influence demand for prescription drugs [4], increase physician visits for conditions treated by heavily advertised drugs [5] and affect physician prescribing [6].

Little is known about how pharmaceutical companies have altered promotional spending in response to major health care changes. First, during the past decade there has been a slowdown in new drug introductions. During the second half of the 1990s, the FDA approved a large number of small molecule therapies for common conditions, including many drugs that were the first of their kind. These “blockbuster” drugs were heavily marketed, resulting in a 162% increase in total promotional spending between 1996 and 2005 [1]. In recent years, however, blockbuster drugs have faced increasing competition from generics, as well as branded rivals, with the generic share of total prescriptions increasing markedly from 63% in 2006 to nearly 80% in 2010 [7]. Fewer new drugs have been approved annually in recent years [8],...
and a greater proportion of those introduced have been for orphan conditions [9]. Second, drugs manufactured using biologic processes, or “biologics”, represent an increasing proportion of newly approved products and drugs sales [10,11]. Biologics comprised over 40% of products in late stage research and development in 2009, suggesting that they may account for an increasing proportion of new products launched in the near future [10]. Since these products are often used by a smaller number of patients, administered parenterally by providers, and sold at much higher prices, the promotional strategies may differ substantially compared to small molecule therapies. Finally, in response to mounting empirical evidence as well as legal challenges, media scrutiny [12], and the recommendations of professional societies [13], numerous medical centers have limited pharmaceutical sales representatives access to physicians [14–16]. Furthermore, certain states now require disclosure of gifts from pharmaceutical companies to providers [17]. While there is some evidence of decreases in industry interaction with office-based physicians [18,19], it is unclear how industry practices have changed in response to these provisions.

We examined trends in promotion to consumers and providers over the last decade. We hypothesized decreases in absolute spending on promotion to providers and DTCA, with an increasing share of detailing devoted to specialists given the expanding role of biologics. In addition to trends for the pharmaceutical industry overall, we compared the promotional strategies of top-selling small molecule and biologic therapies. Finally, to determine whether trends in promotion were correlated with changes in the pharmaceutical pipeline, we examined the number of products and spending per product promoted.

**Methods**

**Data**

We used the IMS Health Integrated Promotional Services™ to obtain data on detailing, free samples dispensed to providers, and journal advertisements. We obtained data from SDI on spending for electronic promotion (e.g., Internet) targeting providers and for meetings and conferences. IMS Health detailing estimates are derived from a nationally representative audit of office- and hospital-based providers as well as pharmacy directors. Office-based detailing includes spending on service visits associated with sample distribution. Estimates of units of free samples dispensed to physicians are derived from an audit of office-based physician practices, while their retail value is calculated based on suggested retail prices. Journal advertising data is collected through a census of all medical journals. Using directory information from the American Medical Association, IMS also reports detailing expenditures by physician specialty. SDI spending is based on

### Table 1. Pharmaceutical promotion to consumers and providers 2001–2010.

| Direct-to-consumer advertising (millions of 2010 dollars) | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 |
|----------------------------------------------------------|------|------|------|------|------|------|------|------|------|------|
| Television                                               | 2,184 | 2,061 | 2,367 | 3,213 | 3,150 | 3,270 | 3,194 | 2,951 | 2,919 | 2,375 |
| Print                                                    | 1,242 | 1,242 | 1,606 | 1,651 | 1,823 | 2,291 | 2,132 | 1,617 | 1,587 | 1,747 |
| Internet                                                 | 27    | 42    | 72    | 214   | 181   | 230   | 105   | 141   | 312   | 202   |
| Radio                                                    | 46    | 51    | 73    | 67    | 68    | 87    | 48    | 24    | 43    | 44    |
| Outdoor                                                  | 2     | 6     | 6     | 6     | 8     | 13    | 4     | 3     | 6     | 3     |
| Total                                                    | 3,500 | 3,402 | 4,124 | 5,151 | 5,231 | 5,891 | 5,483 | 4,738 | 4,868 | 4,371 |
| As percentage of sales                                   | 1.7   | 1.6   | 1.6   | 1.9   | 1.9   | 2.0   | 1.9   | 1.6   | 1.6   | 1.4   |

| Promotion to providers (millions of 2010 dollars)         | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 |
|----------------------------------------------------------|------|------|------|------|------|------|------|------|------|------|
| Office-based promotion                                   | 5,897 | 6,450 | 7,442 | 7,621 | 6,892 | 6,780 | 6,147 | 6,043 | 5,906 | 5,306 |
| Hospital-based promotion                                 | 864   | 1,071 | 1,005 | 1,059 | 881   | 718   | 620   | 490   | 491   | 479   |
| Journal advertising                                      | 523   | 578   | 582   | 628   | 531   | 570   | 494   | 392   | 320   | 326   |
| Free samples (retail value)                              | 12,884 | 14,455 | 16,057 | 18,056 | 16,318 | 14,970 | 15,614 | 14,193 | 14,416 | 13,850 |
| E-promotion (SDI)                                        | –     | –     | 251   | 255   | 314   | 356   | 415   | 497   | 532   | 525   |
| Conferences and meetings (SDI)                           | 2,605 | 2,644 | 2,890 | 3,295 | 3,027 | 2,851 | 2,910 | 2,993 | 2,952 | 2,840 |
| Total                                                    | 22,773 | 25,197 | 28,229 | 30,915 | 27,963 | 26,242 | 26,201 | 24,609 | 24,616 | 23,326 |
| As percentage of sales                                   | 10.8  | 10.7  | 10.9  | 11.4  | 10.1  | 9.0   | 8.9   | 8.5   | 8.1   | 7.6   |

| All DTCA and promotion to providers ($2010 millions)      | 26,274 | 28,599 | 32,352 | 36,065 | 33,194 | 32,133 | 31,685 | 29,347 | 29,484 | 27,697 |
| All sales ($2010 billions)                               | 212    | 236    | 260    | 270    | 276    | 292    | 296    | 290    | 305    | 307    |
| As percentage of sales                                   | 12.4  | 12.1  | 12.5  | 13.4  | 12.0  | 11.0  | 10.7  | 10.1  | 9.7    | 9.0    |
| Number of new molecular entities launched                | 31     | 28     | 30     | 21     | 20     | 27     | 21     | 19     | 26     | 21     |
| Number of products marketed and promoted                 | 2,920  | 3,087  | 3,056  | 3,105  | 3,094  | 2,680  | 2,730  | 2,660  | 2,576  | 2,474  |
| Average promotion per product (millions)                 | 9.0    | 9.3    | 10.6   | 11.6   | 10.7   | 12.0   | 11.6   | 11.0   | 11.4   | 11.2   |

All financial data were adjusted to 2010 dollars, utilizing the Consumer Price Index – All Urban. Sources: Direct-to-consumer advertising data provided by Kantar Media; promotion to professionals data derived from the IMS Health Integrated Promotional Services™, 2002–2010 with the exception of data regarding e-promotion and conferences and meetings which was derived from the SDI Physician Meeting and Event Audit and SDI ePromotion Audit; provider promotion for 2001 derived from reference #1; sales data derived from IMS Health Use of Medicines 2010 Report; newly launched molecular entities derived from reference #10; number of products marketed and promoted derived from IMS Health Integrated Promotional Services™ and includes products with any spending targeting providers.

doi:10.1371/journal.pone.0055504.t001
a monthly audit of approximately 4,000 office-based providers representing 19 specialties. Data are collected and projected by region and specialty to represent a universe of approximately 380,000 practicing providers. Finally, Kantar Media provided industry-wide and product-specific DTCA expenditures accounting for television, magazine, radio, outdoor, newspaper, and Internet promotion. These estimates are drawn from a sample of national media such as network TV and national newspapers as well as local media sampled at the Designated Media Area level.

We used IMS Health sales figures [7], supplemented for certain therapies with data from the IMS Health National Sales PerspectivesTM, in order to calculate promotion and marketing as a percentage of total sales. Estimates of the annual sales were calculated based on unit sales from both retail and non-retail channels and ex-manufacturer invoices (amount paid to wholesalers or manufacturers net of prompt payment discounts). We obtained data on the number of products on the market and, of these, the number promoted each year using IMS Health National Sales PerspectivesTM and Integrated Promotional ServicesTM. We used a data set of drug launches [10], supplemented for 2009 and 2010 with the number of new molecular entities approved by the Food and Drug Administration [20], to determine the number of new molecular entities per year.

Biologic therapies were defined as those manufactured using biologic processes [10], while the remainder of products were categorized as small molecules.

**Analyses**

We used descriptive statistics to characterize six aspects of promotion to providers: the retail value of free samples, office-based detailing, hospital-based detailing, journal advertising, epromotion and conferences and meetings. We quantified the absolute and relative magnitude of annual total promotional efforts towards providers. We also assessed the concentration of promotion for top-selling small molecules and biologic therapies.

We obtained a list of the top-selling U.S. and European biologics in 2010 [21]. We then identified additional biologics with high sales expenditures [22] and used the IMS Health National Sales PerspectivesTM to rank these therapies. Sales and promotional expenditures were aggregated across all formulations of a brand, and for the few molecules available both as mono-therapies and fixed-dose combinations, we excluded sales and

---

**Table 2. U.S. sales revenue and promotional spending for leading selling prescription medicines according to dollar sales in 2010.**

| Rank | Therapy | Type of therapy | U.S. Sales (billions) | Promotion (millions) | Percentage of sales |
|------|---------|-----------------|-----------------------|----------------------|---------------------|
|     |         |                 |                       | DTCA | Office | Hospital | Samples | Journals | All Provider | Total |                      |
| 1    | Lipitor | Small molecule  | 7.2                   | 272.0 | 97.3   | 7.6      | 359.7   | 4.3      | 468.8        | 740.8 | 10.3%                  |
| 2    | Nexium  | Small molecule  | 6.4                   | 16.7  | 32.5   | 2.3      | 208.5   | 0.7      | 244.0        | 260.7 | 4.1%                   |
| 3    | Plavix  | Small molecule  | 6.1                   | 127.3 | 60.1   | 9.1      | 93.3    | 0.2      | 162.7        | 290.0 | 4.8%                   |
| 4    | Serquel | Small molecule  | 5.2                   | 80.6  | 51.2   | 11.8     | 91.0    | 0.0      | 153.9        | 234.5 | 4.5%                   |
| 5    | Advair Diskus | Small molecule | 4.7                 | 200.5 | 47.5   | 1.8      | 343.4   | 0.0      | 392.7        | 593.2 | 12.6%                  |
| 6    | Abilify | Small molecule  | 4.6                   | 155.7 | 49.7   | 6.1      | 412.7   | 0.0      | 468.5        | 624.2 | 13.6%                  |
| 7    | Singular | Small molecule | 4.1                   | 70.3  | 69.5   | 3.6      | 309.5   | 0.04     | 382.6        | 452.9 | 11.0%                  |
| 8    | Crestor | Small molecule  | 3.8                   | 95.3  | 101.5  | 7.0      | 389.7   | 1.0      | 499.2        | 594.5 | 15.6%                  |
| 9    | Actos  | Small molecule  | 3.5                   | 40.7  | 48.9   | 1.5      | 202.2   | 0.0      | 252.6        | 293.3 | 8.4%                   |
| 10   | Epogen | Biologic        | 3.3                   | 0     | 0.4    | 0.1      | 0.0     | 0.0      | 0.4          | 0.4   | 0.01%                  |
| 11   | Remicade | Biologic       | 3.3                   | 0     | 4.7    | 0.7      | 0.3     | 0.6      | 6.3          | 6.3   | 0.2%                   |
| 12   | Enbrel | Biologic        | 3.3                   | 71.5  | 9.9    | 0.9      | 8.1     | 1.2      | 20.1         | 91.6  | 2.8%                   |
| 13   | Zyprexa  | Small molecule | 3.3                   | 1.2   | 16.0   | 5.8      | 174.1   | 0.0      | 195.9        | 197.1 | 6.0%                   |
| 14   | Cymbalta | Small molecule | 3.2                   | 206.0 | 93.6   | 72.0     | 309.6   | 0.04     | 382.6        | 620.4 | 19.4%                  |
| 15   | Avastin  | Biologic       | 3.1                   | 0.0007 | 2.8   | 1.6      | 0.0     | 2.2      | 6.6          | 6.6   | 0.2%                   |
| 16   | Oxycontin | Small molecule | 3.1                   | 0.1   | 9.9    | 0.9      | 0.0     | 2.6      | 13.4         | 13.5  | 0.4%                   |
| 17   | Lantus  | Biologic       | 3.0                   | 46.5  | 37.2   | 4.7      | 58.3    | 8.3      | 108.5        | 154.9 | 5.1%                   |
| 18   | Neulasta | Biologic       | 3.0                   | 0.3   | 1.4    | 0.2      | 0.0     | 0.7      | 2.3          | 2.6   | 0.1%                   |
| 19   | Humira  | Biologic       | 2.9                   | 34.1  | 12.9   | 3.8      | 25.4    | 0.1      | 42.2         | 76.3  | 2.6%                   |
| 20   | Lexapro | Small molecule  | 2.8                   | 2.1   | 108.2  | 6.7      | 270.9   | 13.1     | 398.8        | 400.9 | 14.3%                  |
| 21   | Rituxan | Biologic       | 2.8                   | 0.05  | 4.3    | 0.2      | 0.0     | 2.3      | 6.8          | 6.9   | 0.2%                   |
| 22   | Aricept | Small molecule | 2.5                   | 34.3  | 25.5   | 2.6      | 154.1   | 2.2      | 184.5        | 218.8 | 8.8%                   |
| 23   | Lovenox | Small molecule | 2.3                   | 0.1   | 7.3    | 8.5      | 3.2     | 0.0      | 19.0         | 19.1  | 0.8%                   |
| 24   | Atripla | Small molecule | 2.2                   | 0.8   | 2.1    | 1.0      | 0.2     | 0.4      | 3.7          | 4.5   | 0.2%                   |
| 25   | Copaxone | Biologic    | 2.2                   | 0     | 4.0    | 0.7      | 2.3     | 0.2      | 7.2          | 7.2   | 0.3%                   |
| TOTAL | –      | –               | 91                    | 1,456 | 20%   | 2%       | 77%     | 1%       | 4,455        | 5,911 | 6.4%                  |

Sources: Direct-to-consumer advertising data provided by Kantar Media; promotion to professionals data derived from the IMS Health Integrated Promotional ServicesTM, 2010™ and excludes epromotion and expenditures for conferences and meetings depicted in Table 1; sales data derived from IMS Health Use of Medicines 2010.

doi:10.1371/journal.pone.0055504.t002
promotional spending associated with combination therapies. Except where otherwise noted, data on sales and promotional spending were adjusted to 2010 dollars using the Consumer Price Index – All Urban [23].

Results

Trends in Overall and Provider Promotion

Table 1 characterizes aggregate trends in marketing and promotion. Total inflation-adjusted promotional spending peaked in 2004 both in terms of absolute spending ($36.1 billion) and spending relative to sales (13.4%). Afterward, spending declined each year to $27.7B (9.0% of sales) by 2010. Nearly all forms of promotion saw declines beginning in 2005. The retail value of free samples declined 23%, or 11% when not adjusted for inflation, from $18.1 B in 2004 to $13.9B in 2010. The expenditure shares across the three major promotional categories were remarkably stable. Despite a more than two-fold relative increase in electronic promotion, this category accounted for less than 2% of provider promotion in 2010.

Trends in Direct-to-consumer Advertising (DTCA)

DTCA peaked at $5.9B in 2006 followed by a 25% decline to $4.4B by 2010. As a percentage of total promotional spending, DTCA increased from 12% in 2002 to 18% in 2006, but declined modestly to 16% by 2010. During this period, television accounted for a decreasing proportion of all DTCA, declining from 62% in 2001 to 54% by 2010. Print DTCA increased 84% 2001–2006, but then declined 24% by 2010. In 2010, internet promotion accounted for less than 5% of overall consumer promotion.

Drug Launches and Overall Number of Products Promoted

The number of new molecular entities launched ranged from 19 to 31 across the study period, with the greatest numbers of new molecular entities introduced between 2001 and 2003 (Table 1). Declines in the number of products promoted paralleled declines in promotional spending. The average promotional spending per product actually increased from $9.0M (2001) to $12.0M (2006), then declined modestly to $11.2M (2010).

Table 3. Therapies most heavily promoted through direct-to-consumer advertising, 2010.

| Ranking | Trade name | Type of drug | Spending in direct-to-consumer advertising (millions) |
|---------|------------|--------------|------------------------------------------------------|
| 1       | Lipitor    | Statin       | 272                                                  |
| 2       | Cialis     | Phosphodiesterase type 5 inhibitor | 216                                                |
| 3       | Cymbalta   | Serotonin-norepinephrine reuptake inhibitor | 206                                             |
| 4       | Advair     | Inhaled corticosteroid and long-acting beta-agonist | 200                                               |
| 5       | Abilify    | Atypical antipsychotic | 156                                               |
| 6       | Symbicort  | Inhaled corticosteroid and long-acting beta-agonist | 152                                               |
| 7       | Pristiq    | Serotonin-norepinephrine reuptake inhibitor | 127                                               |
| 8       | Plavix     | Oral thienopyridine antiplatelet | 127                                               |
| 9       | Lyrica     | Anticonvulsant | 112                                               |
| 10      | Chantix    | Nicotinic receptor partial agonist | 110                                               |
| 11      | Toviaz     | Muscarinic antagonist | 109                                               |
| 12      | Viagra     | PDE5 inhibitor | 100                                               |
| 13      | Crestor    | Statin       | 95                                                  |
| 14      | Boniva     | Oral bisphosphonate | 85                                               |
| 15      | Lovaza     | Omega-3 fatty acid | 81                                               |
| 16      | Seroquel   | Atypical antipsychotic | 81                                               |
| 17      | Enbrel*    | Tumor necrosis factor inhibitor | 72                                               |
| 18      | Simponi*   | Tumor necrosis factor inhibitor | 71                                               |
| 19      | Spiriva Handihaler | Anticholinergic bronchodilator | 71                                               |
| 20      | Singular   | Leukotriene receptor antagonists | 70                                               |
| 21      | Januvia    | Dipetidyle peptide-4 (DPP-4) inhibitor | 65                                               |
| 22      | Restasis   | Cyclosporin topical emulsion | 58                                               |
| 23      | Vyvanse    | Psychostimulant | 58                                               |
| 24      | Trilipix   | Fibrate      | 56                                                  |
| 25      | Lunesta    | Non-benzodiazepine hypnotic | 54                                               |
| All 25 combined |                     |             | 2,805                                               |
| Total percentage of industry DTCA spending |                     |             | 64                                                 |

Source: Data provided by Kantar Media.
*Biologics therapy.
doi:10.1371/journal.pone.0055504.t003
Table 4. U.S. sales revenue and promotional spending for leading selling biologics according to dollar sales in 2010.*

| Rank | Therapy | U.S. Sales (millions) | Promotion | Percentage of sales | Type of provider promotion (thousands) |
|------|---------|-----------------------|-----------|---------------------|--------------------------------------|
|      |         |                       | DTCA (thousands) | Provider (thousands) | Total (thousands) | Office | Hospital | Samples | Journals |
| 1    | Epogen  | 3,325                 | 0           | 447                 | 447                  | 0.01%  | 394      | 53       | 0        | 0        |
| 2    | Remicade | 3,303                 | 0           | 6,270               | 6,270               | 0.2%   | 4,682    | 679      | 277      | 632      |
| 3    | Enbrel   | 3,291                 | 71,507      | 20,129              | 91,636              | 2.8%   | 9,864    | 931      | 8,143    | 1,192    |
| 4    | Avastin  | 3,091                 | 1           | 6,643               | 6,644               | 0.2%   | 2,837    | 1,570    | 0        | 2,237    |
| 5    | Lantus   | 3,045                 | 46,461      | 108,474             | 154,935             | 5.1%   | 37,178   | 4,696    | 58,284   | 8,316    |
| 6    | Neulasta | 3,011                 | 252         | 2,291               | 2,543               | 0.1%   | 1,379    | 217      | 695      |
| 7    | Humira   | 2,929                 | 34,108      | 20,129              | 54,237              | 2.6%   | 12,894   | 531      | 653      | 144      |
| 8    | Rituxan  | 2,862                 | 45          | 6,780               | 6,825               | 0.2%   | 4,314    | 202      | 0        | 2,264    |
| 9    | Copaxone | 2,253                 | 0           | 7,177               | 7,177               | 0.3%   | 3,983    | 723      | 2,256    | 216      |
| 10   | NovoLog  | 2,097                 | 4,496       | 53,130              | 57,626              | 2.7%   | 11,261   | 890      | 39,566   | 1,413    |
| 11   | Humalog  | 1,608                 | 13,665      | 57,805              | 71,470              | 4.4%   | 13,075   | 1,037    | 35,671   | 8,022    |
| 12   | Herceptin| 1,537                 | 0           | 2,563               | 2,563               | 0.2%   | 1,644    | 267      | 0        | 115      |
| 13   | Procrit/Eprex | 1,466 | 13          | 2,277               | 2,290               | 0.2%   | 1,295    | 867      | 0        | 115      |
| 14   | Lucentis | 1,435                 | 2,053       | 666                 | 2,719               | 0.2%   | 274      | 53       | 0        | 339      |
| 15   | Avonex   | 1,424                 | 334         | 4,231               | 4,565               | 0.3%   | 2,965    | 487      | 258      | 521      |
| 16   | Aranesp  | 1,305                 | 0           | 3,470               | 3,470               | 0.3%   | 1,971    | 1,499    | 0        | 0        |
| 17   | Neupogem | 961                   | 0           | 83                  | 83                  | 0.01%  | 74       | 9        | 0        | 0        |
| 18   | Rebif    | 941                   | 2,053       | 666                 | 2,719               | 0.2%   | 274      | 53       | 0        | 339      |
| 19   | Prevnar-7| 829                   | 0           | 7,177               | 7,177               | 0.3%   | 3,983    | 723      | 2,256    | 216      |
| 20   | Betaseron| 862                   | 4           | 3,148               | 3,152               | 0.4%   | 2,857    | 20       | 0        | 271      |
| 21   | Synagis  | 735                   | 0           | 2,910               | 2,910               | 0.4%   | 2,181    | 728      | 0        | 0        |
| 22   | Erbitux  | 709                   | 0           | 3,640               | 3,640               | 0.5%   | 2,318    | 191      | 0        | 1,131    |
| 23   | Levmir   | 673                   | 144         | 82,889              | 83,033              | 12.3%  | 27,125   | 2,782    | 48,242   | 4,740    |
| 24   | Byetta   | 571                   | 42          | 113,461             | 113,503             | 19.9%  | 23,121   | 1,598    | 85,194   | 3,549    |
| 25   | Pegasys  | 512                   | 0           | 3,447               | 3,447               | 0.7%   | 3,016    | 431      | 0        | 0        |
| TOTAL|         | 44,639                | 189,494     | 545,427             | 734,921             | 1.6%   | 33%      | 4%       | 56%      | 7%       |

Sources: Direct-to-consumer advertising data provided by Kantar Media; promotion to professionals data derived from the IMS Health Integrated Promotional Services™, 2010 and excludes epromotion and expenditures for conferences and meetings depicted in Table 1; sales data derived from IMS National Sales Perspectives™.
doi:10.1371/journal.pone.0055504.t004

Table 5. Detailing spending and number contacts with primary care providers and specialists 2001–2010.

| Year | Spending on Office-Based Detailing | Office-based Contacts |
|------|-----------------------------------|-----------------------|
|      | Primary Care, %                    | Specialty, %          |
|      |                                   | Total (millions)      |
|      | 2001                              | 2002                  |
|      | 2003                              | 2004                  |
|      | 2005                              | 2006                  |
|      | 2007                              | 2008                  |
|      | 2009                              | 2010                  |

Spending on Office-Based Detailing

Primary Care, %
- 62.0
- 62.3
61.9
61.0
60.9
60.5
60.6
60.3

Specialty, %
- 38.0
- 37.7
38.1
39.0
39.1
39.5
39.4
39.7

Total (millions $2010)
5,897
6,450
7,442
7,621
6,892
6,780
6,147
6,043
5,906
5,306

Office-based Contacts

Primary Care, %
69.3
68.6
68.5
67.7
63.2
63.1
62.4
62.8
62.6

Specialty, %
30.7
31.4
31.5
32.3
36.7
36.9
37.5
37.2
37.3

Total (millions)
50.8
53.6
67.7
69.0
60.1
58.8
54.0
51.9
48.9
44.6

All data were adjusted to 2010 dollars, utilizing the Consumer Price Index. Primary care providers include those trained in family practice, general practice, internal medicine, osteopathic medicine or pediatrics. Specialty providers were defined as all other provider types, including those trained in subspecialties of internal medicine such as cardiology or gastroenterology.

"--" indicates years when data was not available.

Source: IMS Health Integrated Promotional Services™, 2001–2010.
doi:10.1371/journal.pone.0055504.t005
Promotion of Top-selling Agents

Among the 25 top-selling products of 2010 listed in Table 2, 16 were small molecule therapies and the remaining nine were biologics.

Levels and intensities of provider and consumer-directed promotion were generally lower for biologics than small molecule therapies. The top 15 small molecule therapies had an average total promotional spending of $570 million in 2010 (8.8% of sales) compared to only $33 million for the top 15 biologics (1.4% of sales).

Products Most Heavily Promoted to Consumers

Table 3 displays the 25 drugs most heavily promoted to consumers via DTCA. The drug most heavily promoted to consumers in 2010 was Lipitor with $272M devoted to DTCA alone followed by Cialis ($216M) and Cymbalta ($206M). DTCA was concentrated in a small number of products. Only two of the top 25 consumer-promoted products, etanercept (Enbrel) and golimumab (Simponi), were biologic therapies, whereas biologics accounted for 9 of the 25 top-selling products.

Promotion of Biologics

Table 4 reports top US-selling biologics along with product-specific expenditures and promotional spending toward consumers and providers. In 2010, epoetin alfa (Epogen), infliximab (Remicade) and etanercept (Enbrel) led in biologic sales, each with $3.3B. Among top-selling biologic therapies, 2010 promotion was greatest for exenatide (Byetta) with 22% of its $571M in US sales dedicated to promotion, followed by insulin detemir (Levemir) with 12% and insulin glargine (Lantus) with 5% of its $3.0B in US sales dedicated to promotion. Promotion for 17 of the other top-selling 25 biologics was less than 1% of sales.

Spending on promotion to providers varied widely across the biologics examined, ranging from only $83,000 (filgrastim [Neupogen]) to more than $100 million (insulin glargine [Lantus] and exenatide [Byetta]). For the majority of therapies, office-based detailing accounted for the largest expenditures; however, among the minority of biologics that had any spending on free samples (e.g., Byetta, Lantus, Levemir), this was generally the dominant form of promotion. DTCA for biologics was limited to approximately two-thirds of the 25 therapies examined.

Promotion to Primary Care Physicians and Specialists

Table 5 summarizes trends in detailing and contacts directed at primary care providers and specialists (excluding free samples). The proportion of office-based detailing directed at primary care providers declined modestly from 69% of contacts in 2002 to 63% in 2010. However, smaller decreases were evident in the share of office-based detailing spending targeting primary care physicians.

Discussion

After steady increases in pharmaceutical marketing and promotion to consumers and providers during the first half of the last decade, since 2004 pharmaceutical firms have decreased both the absolute value of spending as well as the share of sales devoted to promotion. These declines in promotional spending do not seem to primarily reflect waning consumer purchasing power, since promotion has been declining in the context of rising sales [7]. Spending on meetings and electronic promotion has increased, yet these channels still account for only a small fraction of provider promotion. Despite anecdotal reports [26,27] and calls from stakeholders [27–29], we did not find evidence of substantial changes in the proportion of provider-targeted promotion accounted for by office-based detailing. In addition, we saw no substantial shifts in the proportion of expenditures targeting primary care providers.

DTCA remains highly concentrated among a small number of products and continues to account for a minority of promotional spending [30]. Declines in DTCA may accelerate as biologics make up a greater share of new therapies. Although relative increases in DTCA through media such as the Internet and social networking have occurred, these expenditures remain a small fraction of overall consumer-targeted promotion.

Our study has several limitations. First, our analyses were not designed to examine promotional content nor the causal effect of promotional expenditures [31–33]. Second, some biologics have unique distribution channels and thus our data capture may be incomplete. The difficulty in measuring the extended units for infused and injected therapies also prohibits us from estimating the ratio of promotion to units of utilization. Third, while there are a variety of methods of estimating promotion costs [34], we have used a conventional commercial definition and have considered only expenditures that are clearly directed at marketing rather than attempting to approximate unmonitored promotion and the R&D proportion that is promotional. Our estimates are similar to those of Donohue et al [1] although here we include estimates of expenditures for conferences and meetings as well as Epromotion to providers. As with prior investigations [1], our estimations of promotion devoted to free samples are based on their approximate retail value and thus may overstate manufacturers’ costs. Finally, to the extent medical care prices have increased more rapidly than non-medical care prices, our use of the Consumer Price Index – All Urban may underestimate the magnitude of the reduction in inflation-adjusted drug spending since 2006.

Manufacturers of branded pharmaceuticals continue to expend considerable sums on promotion to consumers and providers. However, in the context of marketplace changes, firms are decreasing spending but changing little about how expenditures are allocated across types of promotion. An increasing role for biologics to the market may cause more substantial shifts in future promotional patterns.

Acknowledgments

The statements, findings, conclusions, views, and opinions contained and expressed in this article are based in part on data obtained under license from the following IMS Health Incorporated information service(s): Integrated Promotional Services™, 2001–2010 and IMS Health Incorporated and National Sales Perspectives™, 2001–2010. All Rights Reserved.
References

1. Donohue JM, Cevasco M, Rosenthal MB (2007) A decade of direct-to-consumer advertising of prescription drugs. N Engl J Med 357: 673–681.
2. Rosenthal MB, Berndt ER, Donohue JM, Frank RG, Epstein AM (2002) Promotion of prescription drugs to consumers. N Engl J Med 346: 498–505.
3. Campbell S (2009) Promotional Spending for Prescription Drugs. Congressional Budget Office Economic and Budget Issue Brief. Available: http://www.cbo.gov/ftpdocs/103xx/doc1022/12-02-DrugPromo_Brief.pdf. Accessed: 2012 Sep 5.
4. Rosenthal MB, Berndt ER, Donohue JM, Epstein AM, Frank RG (2003) Demand effects of recent changes in prescription drug promotion. Frontiers Health Policy Res 6: 1–26.
5. Izuka T, Jin GZ (2005) The effect of prescription drug advertising on drug visits. J Econ Manag Strategy 14: 701–727.
6. Donohue JM, Berndt ER (2004) Effects of Direct-to-Consumer Advertising on Medication Choice: The Case of Antidepressants. Journal of Public Policy and Marketing 23: 115–127.
7. IMS Institute for Healthcare Informatics (2011) The Use of Medicines in the United States: Review of 2010. Available: www.theimsinstitute.org. Accessed: 2012 Age 27.
8. Aitken ML, Berndt ER, Cutler DM (2009) Prescription Drug Spending Trends in the US: Looking Beyond the Turning Point. Health Aff (Milwood) 28: 151–160.
9. Generic Pharmaceutical Association (GPhA) (2012) Savings: $1 Trillion Over 10 Years – Generic Drugs Save the U.S. 4th Ed. Available: http://democrats.energycommerce.house.gov/sites/default/files/documents/IMS%20Study%20Generic%20Drugs%201%20Trillion%208.2.12.pdf. Accessed 2012 Sep 5.
10. Trusheim MR, Aitken ML, Berndt ER (2010) Characterizing markets for biopharmaceutical innovation: Do biologics differ from small molecules? National Bureau of Economic Research Working Paper No. 16014. Available: http://www.nber.org/papers/w16014. Accessed 2013 Jan 11.
11. Mullins CD, DeVries AR, Hsu YD, Meng F, Palumbo FB (2005) Variability and growth in spending for outpatient specialty pharmaceuticals. Health Aff (Milwood) 24: 1117–1127.
12. Henley S, Martinez B (15 July 2005) To sell their drugs, companies increasingly rely on doctors. The Wall Street Journal: A1. Available: http://online.wsj.com/article/SB1121230815452186385.html. Accessed: 2013 Jan 10.
13. American Board of Internal Medicine Foundation; American College of Physicians-American Society of Internal Medicine Foundation; European Federation of Internal Medicine (2002) Medical professionalism in the new millennium: a physician charter. Ann Intern Med 136: 243–246.
14. Rothman DJ, Chimonas SC (2008) New developments in managing physician-industry relationships. JAMA 300: 1067–1069.
15. Rothman DJ, Chimonas SC (2010) Academic medical centers’ conflict of interest industry policies. JAMA 304: 2294–2295.
16. Fugh-Berman A, Brown SR, Trippett R, Bell AM, Clark P, et al. (2011) Closing the door on pharma? A national survey of family medicine residencies regarding industry interactions. Acad Med 86: 649–654.
17. Chimonas S, Rozario NM, Rothman DJ (2010) Show us the money: lessons in industry interactions. Acad Med 86: 649–654.
18. O’Reilly K (23 March 2009) Doctors increasingly close doors to drug reps, while pharma cuts ranks. American Medical News. Available: http://www.crutchfielddermatology.com/news/images/amednews.pdf. Accessed: 2011 Oct 25.
19. O’Reilly K (23 March 2009) Doctors increasingly close doors to drug reps, while pharma cuts ranks. American Medical News. Available: http://www.crutchfielddermatology.com/news/images/amednews.pdf. Accessed: 2011 Oct 25.
20. United States Food and Drug Administration (2011) Center for Drug Evaluation and Research drug and biologic approval report. Available: http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM242695.pdf. Accessed: 2011 Dec 13.
21. Rader RA (2011) The top 50 biopharma products. Biotechnology Information Institute. Available: www.contractpharma.com/issues/2011-07/view_features/the-top-50-biopharma-products. Accessed: 2011 Dec 13.
22. Aggarwal A (2010) What’s fueling the biotech engine – 2009–2010. Nat Biotechnol 28: 1165–1171.
23. United States Department of Labor Bureau of Labor Statistics. Available at: http://www.bls.gov/cpi/. Accessed: 2011 Dec 21.
24. United States Food and Drug Administration (2011) Summary of NDA approvals & receipts, 1938 to the present. Available: http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothePresent/default.htm. Accessed: 2012 Sep 5.
25. Kolata G, Pollack A (6 July 2008) Costly cancer drug offers hope, but also a dilemma. The New York Times. Available: http://www.nytimes.com/2008/07/06/health/06avastin.html. Accessed: 2011 Dec 13.
26. Groves KEM, Sketris I, Tett SE (2003) Prescription drug samples—Does this marketing strategy counteract policies for quality use of medicines? J Clin Pharm Ther 28: 259–271.
27. Brennan TA, Rothman DJ, Blank L, Blumenthal D, Chimonas SC, et al. (2006) Health industry practices that create conflicts of interest: a policy proposal for academic medical centers. JAMA 295: 429–433.
28. American Association of Medical Colleges (2008) Protecting patients, preserving integrity, advancing health: Accelerating the implementation of COI policies in human subject research. Available: http://www.aamc.org/adovcacy/research/coi/. Accessed: 2011 Nov 29.
29. Institute of Medicine (2009) Conflict of interest in medical research, education, and practice. Available: http://books.nap.edu/openbook.php?record_id=12958. Accessed: 2009 Dec 15.
30. Eichler HG, Pignatti F, Flamion B, Leufkens H, Breckenridge A (2008) Biotechnological innovations: Do biologics differ from small molecules? Biotechnology Information. Available: crutchfielddermatology.com/news/images/amednews.pdf. Accessed: 2011 Oct 25.
31. Liang BA, Mackey T (2011) Direct-to-consumer advertising with interactive internet media. JAMA 305: 824–825.
32. Othman N, Vitry A, Roughead EE (2009) Quality of pharmaceutical advertisements in medical journals: a systematic review. PLoS One 4: e6350. doi:10.1371/journal.pone.0006350.
33. Kornstein D, Keyhani S, Mendelson A (2011) Adherence of pharmaceutical advertisements in medical journals to FDA guidelines and content for safe prescribing. PLoS One 6: e2336. doi:10.1371/journal.pone.0023336.
34. Gagnon MA, Leuchin J (2008) The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States. PLoS Med 5: e1. doi:10.1371/journal.pmed.0050001.

Author Contributions

Supervision: GCA. Conceived and designed the experiments: RK JD EB GCA. Performed the experiments: RK GCA. Analyzed the data: RK JD EB GCA. Contributed reagents/materials/analysis tools: RK JD EB GCA. Wrote the paper: RK.