

# Medical Marketing in the United States, 1997-2016

Lisa M. Schwartz, MD, MS; Steven Woloshin, MD, MS

**IMPORTANCE** Manufacturers, companies, and health care professionals and organizations use an array of promotional activities to sell and increase market share of their products and services. These activities seek to shape public and clinician beliefs about laboratory testing, the benefits and harms of prescription drugs, and some disease definitions.

**OBJECTIVE** To review the marketing of prescription drugs, disease awareness campaigns, health services, and laboratory tests and the related consequences and regulation in the United States over a 20-year period (1997-2016).

**EVIDENCE** Analysis (1997-2016) of consumer advertising (Kantar Media data for spending and number of ads); professional marketing (IQVIA Institute for Human Data Science, Open Payments Data [Centers for Medicare & Medicaid Services]); regulations and legal actions of the US Food and Drug Administration (FDA), Federal Trade Commission (FTC), state attorneys general, and US Department of Justice; and searches (1975-2018) of peer-reviewed medical literature (PubMed), business journals (Business Source Ultimate), and news media (Lexis Nexis) for articles about expenditures, content, and consequences and regulation of consumer and professional medical marketing. Spending is reported in 2016 dollars.

**FINDINGS** From 1997 through 2016, spending on medical marketing of drugs, disease awareness campaigns, health services, and laboratory testing increased from \$17.7 to \$29.9 billion. The most rapid increase was in direct-to-consumer (DTC) advertising, which increased from \$2.1 billion (11.9%) of total spending in 1997 to \$9.6 billion (32.0%) of total spending in 2016. DTC prescription drug advertising increased from \$1.3 billion (79 000 ads) to \$6 billion (4.6 million ads [including 663 000 TV commercials]), with a shift toward advertising high-cost biologics and cancer immunotherapies. Pharmaceutical companies increased DTC marketing about diseases treated by their drugs with increases in disease awareness campaigns from 44 to 401 and in spending from \$177 million to \$430 million. DTC advertising for health services increased from \$542 million to \$2.9 billion, with the largest spending increases by hospitals, dental centers, cancer centers, mental health and addiction clinics, and medical services (eg, home health). DTC spending on advertising for laboratory tests (such as genetic testing) increased from \$75.4 million to \$82.6 million, although the number of ads increased more substantially (from 14 100 to 255 300), reflecting an increase in less expensive electronic media advertising. Marketing to health care professionals by pharmaceutical companies accounted for most promotional spending and increased from \$15.6 billion to \$20.3 billion, including \$5.6 billion for prescriber detailing, \$13.5 billion for free samples, \$979 million for direct physician payments (eg, speaking fees, meals) related to specific drugs, and \$59 million for disease education. Manufacturers of FDA-approved laboratory tests paid \$12.9 million to professionals in 2016. From 1997 through 2016, the number of consumer and professional drug promotional materials that companies submitted for FDA review increased from 34 182 to 97 252, while FDA violation letters for misleading drug marketing decreased from 156 to 11. Since 1997, 103 financial settlements between drug companies and federal and state governments resulted in more than \$11 billion in fines for off-label or deceptive marketing practices. The FTC has acted against misleading marketing by a single for-profit cancer center.

**CONCLUSIONS AND RELEVANCE** Medical marketing increased substantially from 1997 through 2016, especially DTC advertising for prescription drugs and health services. Pharmaceutical marketing to health professionals accounted for most spending and remains high even with new policies to limit industry influence. Despite the increase in marketing over 20 years, regulatory oversight remains limited.

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**Author Affiliations:** The Center for Medicine in the Media, Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, New Hampshire.

**Corresponding Author:** Steven Woloshin, MD, MS, Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, 1 Medical Center Dr, WRTB, Level 5, Lebanon, NH 03756 ([steven.woloshin@dartmouth.edu](mailto:steven.woloshin@dartmouth.edu)).

**H**ealth care spending in the United States is the highest in the world, totaling \$3.3 trillion—17.8% of the gross domestic product in 2016.<sup>1</sup> To capture market share and to expand the potential market, drug manufacturers, companies that manufacture clinical and home-based laboratory tests, and health care organizations use an array of promotional activities to sell their products and services. These activities seek to shape public and clinician perceptions about the benefits and harms of health care, prescription drugs, laboratory tests, and specific diseases and their definitions. Medical marketing influences behaviors and choices that can have important health consequences and also may adversely influence efforts to control unsustainable health care spending.

The marketing of medicine involves a complex interaction involving industry, organizations, and individuals involved in health care. Pharmaceutical and device manufacturers target health care professionals and health care organizations, and these companies, along with those that manufacture other clinical products and consumer-based products, target various health care organizations and audiences to generate sales directly (such as with marketing toward consumers, clinicians, pharmacy benefit managers, insurers, and employers) and indirectly (by funding patient advocacy organizations and opinion leaders who in turn generate interest in drugs, devices, testing, and other services).

This Special Communication reviews marketing of prescription drugs, disease awareness campaigns, health services, and laboratory tests to consumers and professionals, and examines the consequences and regulation of medical marketing in the United States over a 20-year period, from 1997 through 2016.

## Methods

Direct-to-consumer (DTC) and professional medical marketing for prescription drugs, disease awareness campaigns, health services, and laboratory tests in the United States from 1997 through 2016 were analyzed. Prescription drug marketing included DTC and professional branded advertising, detailing visits, free drug samples, direct physician and hospital payments (eg, speaker fees, food, travel); disease awareness marketing included unbranded DTC advertising and direct physician and hospital payments for disease education; health services included DTC advertising for hospitals, clinics, practices and services such as home health care; and laboratory testing included DTC advertising for commercial tests and home test kits and direct physician and hospital payments by laboratory manufacturers. Trends in medical marketing expenditures were analyzed with adjustment of all spending to 2016 dollars.<sup>2</sup> Overall spending on marketing for drugs and health services as a proportion of total US health care spending was determined, and regulatory oversight and legal actions related to medical marketing were assessed.

### DTC Marketing

For DTC advertising, data were obtained from Kantar Media, which monitors major media in national and local markets, for advertising running in 1997, 2004, 2008, 2012 and 2016 (selected to provide 4-year intervals for the more recent years and one 7-year interval to include the base year, 1997).

## Key Points

**Question** How has the marketing of prescription drugs, disease awareness, health services, and laboratory tests in the United States changed from 1997 through 2016?

**Findings** From 1997 through 2016, medical marketing expanded substantially, and spending increased from \$17.7 to \$29.9 billion, with direct-to-consumer advertising for prescription drugs and health services accounting for the most rapid growth, and pharmaceutical marketing to health professionals accounting for most promotional spending.

**Meaning** There has been marked growth in expenditures on and extent of medical marketing in the United States from 1997 through 2016.

## Marketing to Professionals

Annual professional drug promotion data (medical journal advertising, detailing, and free samples) from 1997 through 2016 were obtained from IQVIA Institute for Human Data Science. Because disease and drug promotion cannot be distinguished, all spending was counted toward drug promotion because these products likely represent the majority of spending.

Physician and teaching hospital nonresearch payments were determined using the Open Payments 2016 general payment data set, excluding nonmarketing payments (royalties, and licenses). These data were not available for 1997. Company websites and products associated with payments (when available) were used to identify pharmaceutical and laboratory test manufacturers. Consistent with company explanations,<sup>3</sup> only payments for speaker fees, honoraria, and education not related to a specific drug (ie, unbranded disease education) were counted toward disease awareness marketing.

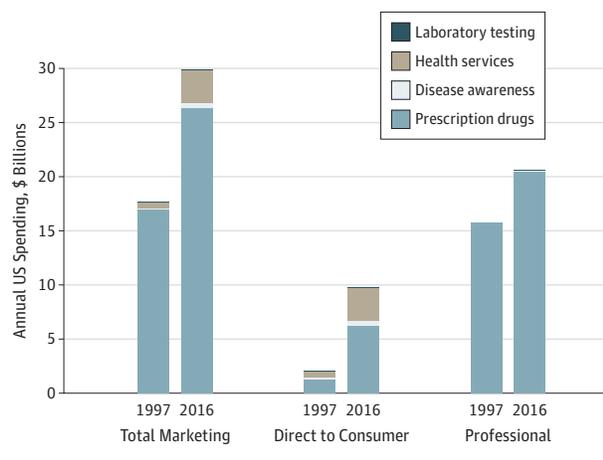
## Regulatory Oversight of Medical Marketing

To determine regulatory and legal actions, the US Food and Drug Administration (FDA), the Federal Trade Commission (FTC), and all state attorneys general websites were searched, and staff were contacted by phone and email at the FDA Office of Prescription Drug Promotion (OPDP) and Center for Devices and Radiologic Health [which regulates laboratory testing], the FTC Bureau of Consumer Protection, and Public Citizen (which provided data from its analyses of major financial settlements between drug companies and federal and state governments).

## Literature Search

The peer-reviewed medical literature (PubMed), business journals (Business Source Ultimate), and news media (Lexis Nexis) were searched from January 1975 to June 2018 for articles about expenditures, content, consequences, and regulation of DTC or professional medical marketing (or advertising) for prescription drugs, disease (ie, disease awareness), health services from hospitals, academic medical or cancer centers or practices, and laboratory testing, including genetic tests (see eAppendix in the Supplement for search strategy and specific search terms). Web of Science searches were performed for key articles. Search results are presented for marketing characteristics (eg, strategies or content) and influence of marketing (eg, utilization, prescribing) if identified.

Figure 1. Medical Marketing 1997 vs 2016



When multiple studies of similar quality were available, the most current evidence was reported.

## Results

From 1997 through 2016, total annual spending on the marketing of prescription drugs, disease awareness campaigns, health services, and laboratory testing increased from \$17.7 billion to \$29.9 billion. Marketing to medical professionals accounted for the highest proportion of spending, increasing from \$15.6 billion in 1997 (88% of total spending) to \$20.3 billion in 2016 (68% of total spending), with most spending for marketing of prescription drugs. The most rapid change in spending was for DTC advertising, which increased from \$2.1 billion (11.9% of total spending) to \$9.6 billion (32.1% of total spending) (Figure 1).

Overall prescription drug marketing investment increased more slowly than corresponding US spending (eTable in the Supplement). From 1997 through 2016, marketing for prescription drugs and disease awareness campaigns increased from \$17.1 billion to \$26.9 billion (60% increase), whereas total US drug spending increased from \$116.5 billion to \$328.6 billion (180% increase). Drug marketing as a proportion of total US drug spending decreased from 14.7% to 8.2%.

For health services, spending on marketing increased faster than corresponding total US spending. Marketing spending increased from \$542 million to \$2.9 billion (430% increase), whereas spending on health services increased from \$1.2 trillion to \$2.2 trillion (90% increase). Health services marketing as a proportion of total US health services spending increased from 0.05% to 0.13%.

### DTC Marketing

#### Prescription Drugs

Spending on DTC advertising increased from \$1.3 billion in 1997 to \$6 billion in 2016. The number advertisements (occurrences, not unique advertisements) increased from 79 000 (including 72 000 television commercials) in 1997 to 4.6 million (663 000 television commercials) in 2016. The spending increase paralleled a shift to more costly television commercials, which exceeded spending for print ad-

vertising in the late 1990s. Annual spending increased in the early 2000s, then declined until around 2012, then increased again (Figure 2).

Advertising spending for prescription drugs increased across all therapeutic categories, with 3 exceptions. There were substantial declines for allergy and cholesterol drugs, and a smaller decline for osteoporosis drugs (Figure 3). In each case for these 3 categories of drugs, the larger advertising campaigns in 1997 ended as top-selling products lost patent protection (statins and bisphosphonates) or became available over-the-counter (antihistamines), without replacement by equally large advertising campaigns for new drugs in the category. Spending increases from 1997 through 2016 were greatest for drugs for diabetes/endocrine diseases (from \$22 million to \$725 million), dermatology conditions (\$67 million to \$605 million), pain/central nervous system disorders (\$56 million to \$542 million), arthritis (\$27 million to \$484 million), cardiac diseases (\$0 to \$379 million) and cancer (\$3 million to \$274 million), largely reflecting competition among expensive new biologics and cancer therapies. Figure 3 highlights spending changes for the top 10 therapeutic categories in 1997 and 2016.

#### Disease Awareness Campaigns

From 1997 through 2016, the number of DTC awareness campaigns—unbranded advertising promoting a disease without mentioning the drug or indication—increased from 44 to 401, and spending increased from \$177 million to \$430 million (Table 1). The leading issues covered in these campaigns were public health concerns (smoking cessation, hepatitis C), symptom diagnoses (insomnia, migraine), mental health disorders (attention-deficit-hyperactivity-disorder, depression), and conditions not conventionally considered medical problems (low testosterone, dry eye disease). A notable change in 2016 was the promotion of highly specialized conditions (eg, exocrine pancreatic insufficiency, pseudobulbar affect).

#### Health Services

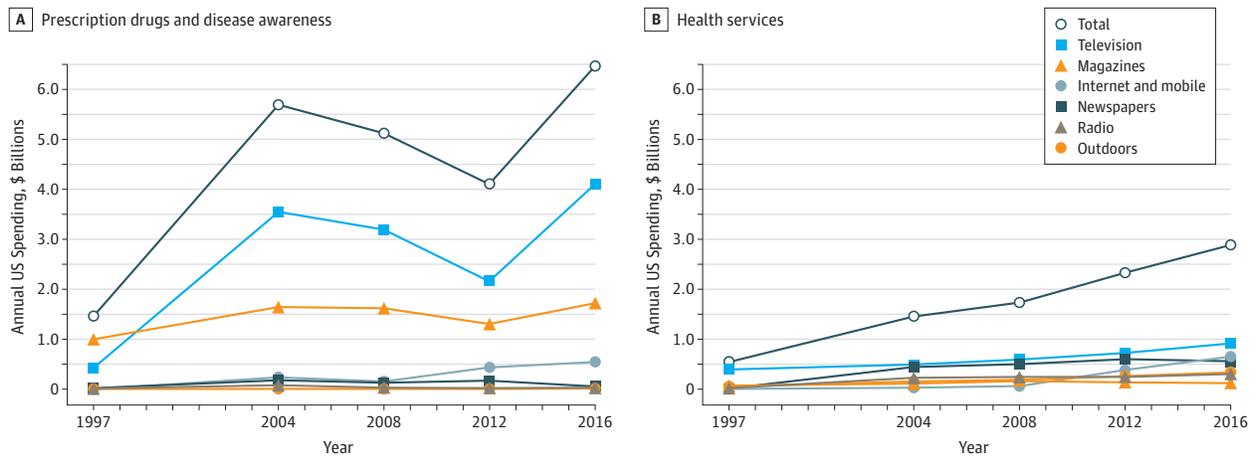
From 1997 through 2016, DTC health service advertising increased from \$542 million to \$2.89 billion (Table 2). The number of advertisements increased from 912 000 (including 909 000 television commercials) to 17.6 million (3 555 000 television commercials).

Health services advertising appeared mostly on television or in newspapers (Figure 2). Electronic advertising increased since 2000 (from \$0 in 1997 to \$653 million in 2016), exceeding newspaper advertising in 2016. Outdoor advertising, including billboards, transit banners, and transit posters, increased from \$55 million in 1997 to \$333 million in 2016, representing 96% of all medical-related DTC outdoor advertising.

Hospitals and health care systems accounted for most DTC health services advertising, with the largest proportional increases for cancer centers (from \$18 million to \$200 million), mental health and addiction services (from \$2 million to \$162 million), cosmetic surgery (from \$6 million to \$93 million), and back and neck pain (from \$3 million to \$89 million). In 2016, hospitals, health and medical services (eg, physical therapy), dental, and cancer centers accounted for the highest amount of advertising spending for health services. Clinician practice advertising increased from \$11 million in 1997 to \$61 million in 2016.

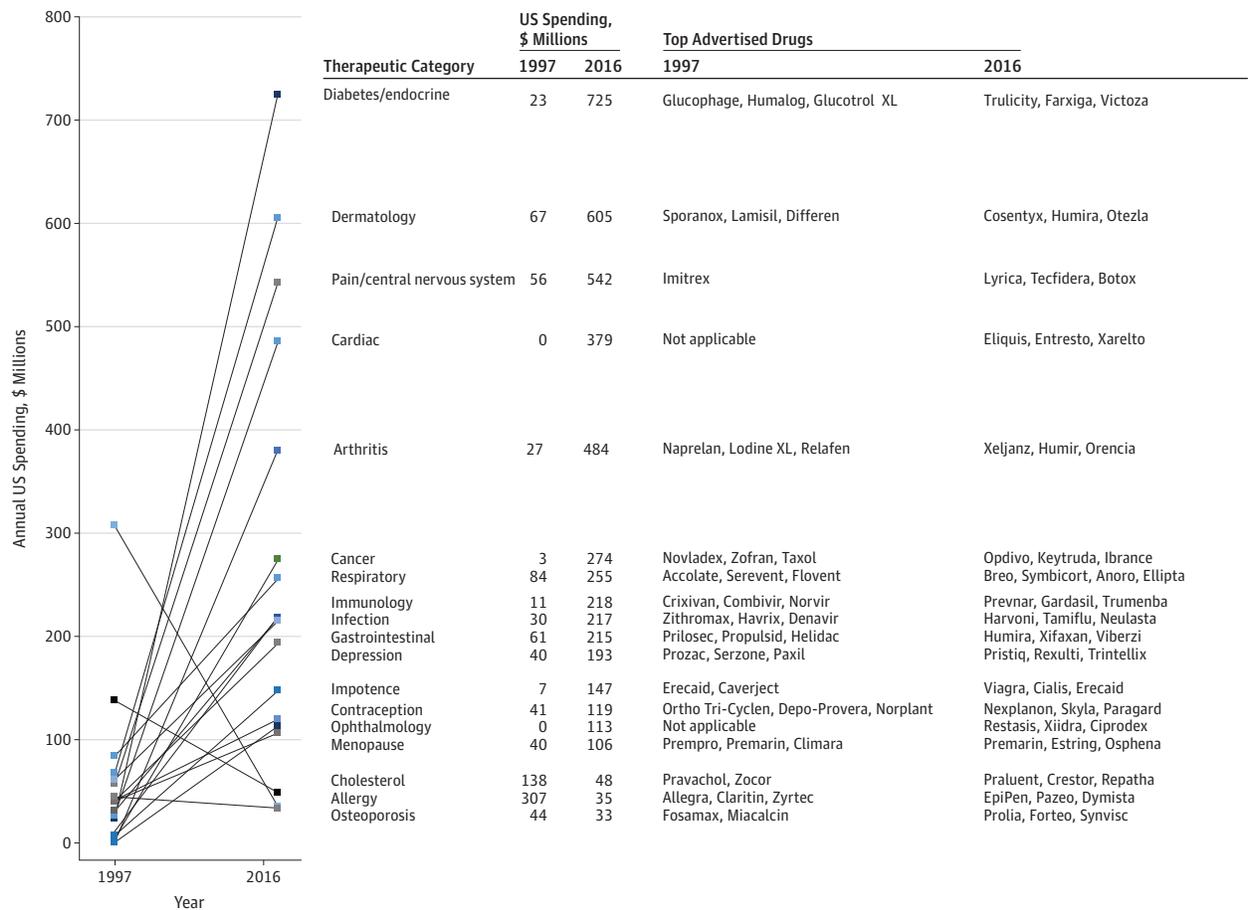
Advertising also increased for 2 experimental or controversial services: stem cell clinic advertising increased from \$0.9 million in

Figure 2. Direct-to-Consumer Advertising for Drugs and Health Services



The outdoor category includes billboards and mass transit posters and banners.

Figure 3. Direct-to-Consumer Drug Advertising by Therapeutic Category



Box colors vary for differentiation purposes only, to assist with viewing.

2012 to \$11.3 million in 2016, and mobile screening services increased from \$1.4 million in 2004, peaking at \$8.4 million in 2012, and declining to \$4.1 million in 2016.

**Laboratory Testing**

DTC laboratory test advertising varied over the time period, from \$75.4 million in 1997, peaking at \$157.8 million in 2004, and declining

**Table 1. Direct-to-Consumer Pharmaceutical Company Disease Awareness Advertising Campaigns for 1997, 2004, 2008, 2012, and 2016<sup>a</sup>**

Year	No. of Campaigns	Condition	Advertising Spending, \$ Millions	Linked Drugs <sup>b</sup>
1997	44		177	
		Smoking cessation	27	Bupropion (Zyban)
		Migraine headache	17	Naratriptan (Amerge)
		<i>H pylori</i> (duodenal ulcer)	17	Omeprazole (Prilosec)/Clarithromycin (Biaxin)
		Osteoporosis	13	Raloxifene (Evista)
2004	115	Insomnia	14	Zolpidem (Ambien)
			286	
		High blood pressure	65	Valsartan (Diovan)
		Deep vein thrombosis	35	Enoxaparin (Lovenox)
		Migraine headache	20	Almotriptan (Axert); Topiramate (Topamax)
2008	179	Peripheral artery disease	15	Clopidogrel (Plavix)
		Insomnia	13	Zolpidem (Ambien)
			238	
		Smoking cessation	88	Varenicline (Chantix)
		Peripheral artery disease	20	Clopidogrel (Plavix)
2012	223	Diabetes	13	Insulin glargine injection (Lantus)
		Migraine headache	12	Sumatriptan (Imitrex); Sumatriptan/naproxen (Treximet)
		Attention-deficit-hyperactivity-disorder	9	Guanfacine extended-release (Intuniv)
			265	
		Shingles	66	Zoster vaccine live (Zostavax)
2016	401	Migraine	19	OnabotulinumtoxinA (Botox)
		Chronic obstructive pulmonary disease	19	Fluticasone/salmeterol (Advair)
		Insomnia	17	Eszopiclone (Lunesta)
		Low testosterone	17	Testosterone (Androgel)
			430	
Chronic dry eye	40	Lifitegrast ophthalmic (Xiidra)		
Opioid-induced constipation	37	Naloxegol (Movantik)		
Exocrine pancreatic insufficiency	36	Pancrelipase (Creon)		
Hepatitis C	35	Sofosbuvir (Sovaldi)		
Diabetic neuropathy	28	Pregabalin (Lyrica)		

<sup>a</sup> Years were selected to provide 4-year intervals for the more recent time frames and one 7-year interval to include the base year (1997). Reported conditions indicate the 5 highest spending campaigns for each time frame, for which reason, advertising spending subcategories will not sum to the total for the year. Source: Kantar Media.

<sup>b</sup> Listed by nonproprietary drug name (brand name, sponsor of the awareness campaign for the condition).

to \$82.6 million in 2016 (Table 3). The number of advertisements increased from 14 100 to 255 300, with the proportion of electronic media increasing from 0% to 82%.

In 1997, DTC advertising spending for laboratory testing was almost exclusively for pregnancy/fertility tests, HIV tests, and glucose monitors, whereas by 2016, 64% of DTC advertising spending was for genetic tests. AncestryDNA, the highest advertiser, spent \$38 million in 2016, largely for commercials promoting genealogy and ethnicity DNA tests.<sup>5</sup> Other advertised genetic tests were for cellular age, based on telomere length; statin-related muscle adverse effects; personalized diet or exercise recommendations; and food intolerance. In 2016, companies spent \$3.8 million on mostly electronic advertising for direct access testing.

### Professional Marketing

#### Prescription Drugs

Spending on product detailing to professionals (typically face-to-face office and hospital visits by more than 70 000 pharmaceuti-

cal company sales representatives), was similar in 1997 and 2016: approximately \$5 billion (Figure 4) with an estimated return on investment, based on a 2001 analysis, of 2 to 1 overall and 10 to 1 for new branded drugs.<sup>7</sup> Spending on free drug samples, distributed by sales representatives (including online request), increased from \$8.9 billion in 1997 to \$13.5 billion in 2016. Medical journal advertising declined from \$744 million in 1997 to \$119 million in 2016.

In 2016, companies paid physicians and teaching hospitals \$978.96 million for nonresearch activities (Table 4), including \$381.13 million to serve as faculty or speakers presenting company-developed materials during lunch or dinner talks. Other payments were for consulting (\$210.05), food and beverages (\$164.21 million), travel and lodging (\$96.9 million), and honoraria (14.64 million).

#### Disease Awareness Marketing

In 2016, pharmaceutical companies paid physicians and teaching hospitals \$58.95 million for disease awareness education, including speaker fees at company events (\$51.18 million), honoraria

Table 2. Direct-to-Consumer Advertising of Health Services From 1997 through 2016<sup>a</sup>

	Annual Advertising, \$ Millions				
	1997	2004	2008	2012	2016
Total	542	1453	1733	2336	2887
No. of advertisements (%) <sup>b</sup>	912 000	2 195 000	6 165 000	15 300 000	17 600 000
Television	909 000 (99)	1 367 000 (62)	2 009 000 (33)	2 769 000 (18)	3 555 000 (20)
Internet and mobile	0	569 000 (26)	1 929 000 (31)	9 515 000 (62)	9 915 000 (56)
Hospitals and clinics	482	1166	1394	1877	2375
Hospitals and health care systems	396	813	915	1156	1418
Dental centers	29	72	114	202	254
Cancer centers	18	52	74	165	200
Mental health and addiction	2	5	7	62	162
Cosmetic surgery	6	40	55	77	93
Back or neck pain	3	10	13	43	89
Eye surgery	3	81	83	68	55
Chiropractor	6	18	17	18	25
Fertility and sexual medicine	0.6	8	5	12	12
Pediatric	3	5	8	9	11
Women's health and gynecology	0.6	3	3	12	10
Hair restoration	9	26	62	11	8
Imaging	3	11	6	6	8
Blood banks	0.2	7	9	4	7
Asthma and allergy	0.2	2	2	2	6
Podiatry	0.7	5	7	9	5
Experimental or controversial services					
Stem cell clinics <sup>c</sup>	0	0.3	0.2	0.9	11.3
Mobile screening (Life Line, HealthFair)	0	1.4	1.2	8.4	4.1
Clinician practices (physicians, nurses, chiropractors, dentists)	11	76	77	86	61
Health and medical services (eg, physical therapy, home health)	49	211	261	373	451

<sup>a</sup> Advertising data for all reported years are from Kantar Media. Numbers may not sum to totals because of rounding and miscellaneous categories.

<sup>b</sup> Includes television, radio, newspaper, magazine, internet, and mobile advertising. Data were not available for outdoor and cinema advertising.

<sup>c</sup> Includes all clinics with stem cell in name of provider except for 2016, which also includes clinics marketing stem cell therapies in 2016 identified by Turner and Knoepfler.<sup>4</sup>

(\$2.04 million), and education (\$4.13 million) not related to specific products (Table 4). Some manufacturers acknowledged that they fund "unbranded informational presentations to promote disease state awareness to health care professionals."<sup>3</sup> Almost all speaker fees were for company events (97%) rather than accredited continuing medical education.

#### Laboratory Testing

Manufacturers of FDA-approved laboratory tests made \$12.9 million in nonresearch payments to physicians and teaching hospitals in 2016 (Table 4), including speaker fees for company-sponsored education (\$2.04 million), food and beverages (\$2.54 million), and consulting (\$4.06 million).

#### Regulation

Key regulatory activities are summarized in Table 5, and the regulatory process for each type of marketing is shown in eFigure 1 in the Supplement.

#### Prescription Drugs

The OPDP, which regulates consumer and professional promotional materials<sup>13</sup> received an increasingly high volume of submissions from 1997 (34 182) through 2016 (97 252) (Figure 5; Table 5). At the same time, violation letters issued for prescription drug advertising decreased from 156 to 11. Violation letters prior to 2007 mostly involved marketing unapproved doses and uses,<sup>17</sup> but by 2014-2015, most letters involved inadequate risk information, including an increasing proportion addressing websites, sponsored links, or social media platforms.<sup>18</sup> In 2016, the FDA reviewed 41% of core materials (ie, key messages, important risk disclosures) for new drugs or indications prior to launch—a critically important institutional performance measure.<sup>8</sup>

In response to complaints or initiating civil legal actions, the Consumer Protection Branch of the US Department of Justice and State attorneys general offices reached 103 settlements, 91% (n=94) since 2007, resulting in more than \$10.5 billion in financial penalties for unlawful (most commonly off-label) promotion.

Table 3. Direct-to-Consumer Advertising for Laboratory Testing From 1997 through 2016

	Annual Advertising, \$ Millions <sup>a</sup>				
	1997	2004	2008	2012	2016
Laboratory tests (total)	75.4	157.8	125.3	102.2	82.6
No. of advertisements <sup>b</sup>	14 100	101 900	112 300	339 000	255 300
Television	14 000 (99)	96 400 (95)	63 000 (56)	106 700 (31)	36 200 (14)
Internet and mobile	0	5200 (5)	29 500 (27)	190 300 (56)	209 400 (82)
Home test kits <sup>b</sup>	75.4	157.8	125.3	99.4	78.8
No. of advertised tests	20	46	65	78	97
Top 3 advertised tests <sup>c</sup>	EPT pregnancy; Confide HIV; Fact Plus pregnancy	One Touch Ultra glucose; Accu-Chek Compact glucose; First Response pregnancy	Freestyle glucose; First Response pregnancy; Contour glucose	Onetouch Verioiq glucose; First Response pregnancy; Accu-Chek Nano glucose	AncestryDNA; 23andMe; First Response pregnancy
Top 3 categories <sup>c</sup>	Pregnancy, fertility; HIV; glucose meters	Glucose meters; pregnancy, fertility; breast self-exam kit	Glucose meters; pregnancy, fertility; drug testing kit	Glucose meters; genetic; pregnancy, fertility	Genetic; pregnancy; glucose
Tests by category					
Genetic	0	0	1.4	3.8	52.6
Ancestry, traits, carrier, health	0	0	0.2	0.7	52.1
Paternity	0	0	1.2	3.1	0.5
Pregnancy, fertility, ovulation	55.7	47.9	38.7	28.7	14.3
Glucose monitors	2.8	108	81.2	64.1	10.4
HIV tests	16.4	0.3	0.001	0.7	0.02
Breath tests (eg, <i>H pylori</i> )	0	0	0.2	0.2	0.5
Drugs of abuse testing	0	0	2.1	0.7	0.1
Tests completed at laboratory (direct access testing) <sup>d</sup>	NA	NA	NA	2.8	3.8

Abbreviation: NA, not applicable.

<sup>a</sup> Advertising data for all reported years are from Kantar Media. Data are reported as No. or as No. (%).

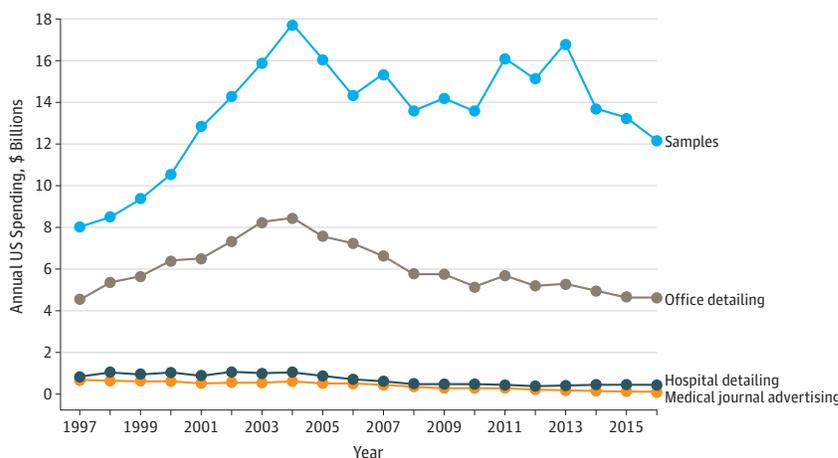
<sup>b</sup> Home test kits identified as Kantar's category "in-home tests."

<sup>c</sup> Listed categories and individual tests indicate those with the highest

advertising spending, and include television, radio, newspaper, magazine, internet, and mobile advertising. Data were not available for outdoor, cinema.

<sup>d</sup> Tests done at laboratory identified from industry report of top 20 companies and first 10 pages of Google searches ("order my own blood tests" and "order labs").

Figure 4. Professional Marketing for Prescription Drugs and Disease



IQVIA provided the yearly data, based on monthly, nationally representative audits of approximately 4000 office physicians in 19 specialties. Sample spending used suggested retail prices except for hospital detailing from 1997 to 2000 (IMS data reported by Kaiser Foundation). Spending for meetings and events was not included (reported to have declined from \$2.1 million to \$0.8 million between 2001 and 2010; data from Kornfield et al<sup>9</sup>).

Disease Awareness Campaigns

The FDA 2004 guidance for industry on awareness advertising, which included standards such as unbranded campaigns not visually resembling branded campaigns, and avoiding encouragement of self-diagnosis

and self-treatment,<sup>9,10</sup> was withdrawn in 2015 and has not been replaced. The FTC has jurisdiction to ensure that unbranded advertising is not misleading, but it has not taken any regulatory action. Whether the FDA has requested any FTC investigations is unknown.

**Table 4. Pharmaceutical and Laboratory Test Manufacturer Nonresearch Payments to Physicians and Teaching Hospitals in 2016<sup>a</sup>**

Payment Category	Payment, \$ Millions		
	Drugs	Disease <sup>b</sup>	Laboratory Tests
Faculty or speaker			
Company event, not CME	381.13	51.18	2.04
Unaccredited CME	10.29	0.83	0.09
Accredited CME	0.05	0.77	0.03
Honoraria	14.64	2.04	0.57
Education	4.61	4.13	0.95
Food and beverages	164.21	0	2.54
Travel and lodging	96.90	0	1.02
Grant	72.30	0	0.32
Consulting	210.05	0	4.06
Entertainment	0.02	0	0.003
Gift	0.55	0	1.07
Charitable contribution	7.38	0	0.11
Current or prospective ownership or investment interest	7.98	0	0
Space rental or facility fee	8.84	0	0.09
Total 2016 nonresearch payments	978.95	58.95	12.90

Abbreviation: CME, continuing medical education.

<sup>a</sup> Data from Open Payments 2016—Centers for Medicare & Medicaid Services. Individual categories may not sum to totals because of rounding.

<sup>b</sup> Indicates non-drug-related payments for unbranded disease state education (per open payment explanations from pharmaceutical companies). To avoid overcounting, non-drug-related payments for food and beverages (\$12.6 million), travel and lodging (\$20.9 million), and entertainment (\$3000) were counted toward drugs.

### Health Services

State attorneys general, who regulate nonprofit organizations, have not initiated any action against deceptive consumer advertising for health services. In 1996, the FTC, which regulates for-profit organizations, took its only action against Cancer Treatment Centers of America for unsubstantiated survival claims,<sup>11</sup> requiring unrepresentative patient testimonials to include a disclaimer “No case is typical. You should not expect these results.”

In 2018, after a number of patients had been harmed, the FDA ordered permanent closure of 2 stem cell clinics that offered unapproved and unproven products.<sup>19</sup>

### Laboratory Testing

The FTC has never acted against misleading laboratory test promotion, nor have state attorneys general, except for a 2016 settlement against DirectLabs and LabCorps for violating New York state law forbidding selling of direct access testing.<sup>12</sup>

The FDA Center for Devices and Radiological Health Division of Premarket and Labeling Compliance, which regulates promotion of prescription-only tests, has issued an increased number of violation letters regarding genetic test promotion (eFigure 2 in the [Supplement](#)). Prior to 2010, only 1 of 18 (5.6%) letters concerned promotion of unapproved genetic tests, compared with 36 of 38 (94.7%) from 2010 to 2017, including directing 23andMe to cease DTC marketing of genetic health tests. In 2017, the FDA approved DTC marketing by 23andMe of such tests to predict risk for 10 diseases (including late-onset Alzheimer disease) and *BRCA* testing for genetic mutations among persons of Ashkenazi Jewish ethnicity. The FDA also announced plans to exempt other 23andMe genetic health tests from review, as well as tests from other companies after first test approval,<sup>20</sup> essentially approving companies rather than tests.

No violation letters have mentioned misleading claims or concerns about companies marketing genetic tests without premarket approval provided the tests require a physician order, reflecting current FDA policy.

## Discussion

From 1997 through 2016, spending on medical marketing increased substantially from \$17.7 to \$29.9 billion. Although spending on DTC advertising for prescription drugs and health services increased the fastest, spending on pharmaceutical marketing to professionals consistently accounted for most promotional spending, despite efforts to limit industry entanglements. Although marketing expanded over 20 years, regulatory oversight remains relatively limited.

Increased medical marketing reflects a convergence of scientific, economic, legal, and social forces. As more drugs and devices and medical advances convert once-fatal diseases into chronic illnesses and with renewed interest in prevention for some diseases, the marketing of tests, treatments, and services has expanded. An aging more insured population, with Medicare Part D, the Affordable Care Act, and a receptivity to lifestyle interventions, has expanded the customer reservoir. More clinicians, health care centers, for-profit sector growth, and market consolidation have increased competition, stimulating marketing growth. The eBox in the [Supplement](#) summarizes strategies that support responsible marketing to reduce adverse consequences.

### DTC Marketing

#### Prescription Drugs

DTC prescription drug advertising, which began in the early 1980s, is only permitted in the United States and New Zealand.<sup>21</sup> The FDA required DTC advertisements that make product claims to include a brief summary of serious and common adverse effects, inhibiting proliferation of broadcast commercials because required air time added substantial expense. Subsequent FDA guidance (1997) allowed substitution of short spoken statements that covered important risks and referred consumers to other sources for complete information. This regulatory change sparked the modern era of DTC advertising.

**Table 5. Regulatory Activity for Misleading Promotion**

Regulator and Year	Activity
<b>Drugs</b>	
FDA OPDP <sup>a</sup>	
1997-2016	Promotional drug materials submitted by companies increased from 34 182 to 97 252 Violation letters for prescription drug advertising decreased from 156 to 11
2016	Reviewed 41% of core promotional materials (ie, key messages, important risk disclosures) for new drugs or indications prior to launch <sup>8</sup>
US Department of Justice Consumer Protection Branch; State attorneys general	
1997-2016	103 Settlements have resulted in >\$11 billion in financial penalties for unlawful promotion Nearly all settlements (90%) occurred in 2007 or later Highest penalties were for unlawful promotion (usually for off-label indications)
<b>Disease Awareness Campaigns</b>	
FDA OPDP	
1997-2016	No active rules for awareness advertising
2015	FDA withdrew its 2004 guidance <sup>9,10</sup> ; not reissued
FTC <sup>b</sup>	
1997-2016	No regulatory action for misleading advertising
<b>Health Services</b>	
State attorneys general (regulates nonprofit organizations)	
1997-2016	No regulatory action for misleading advertising
FTC <sup>b</sup>	
1996	Single action against the Cancer Treatment Centers of America for unsubstantiated higher survival claims <sup>11</sup>
FDA	
2018	Stopped 2 stem cell clinics from marketing unapproved products
<b>Laboratory Tests</b>	
FDA Center for Devices and Radiological Health Division of Premarket and Labeling Compliance	
2005-2009	1 of 18 Violation letters concerning the DTC promotion of genetic laboratory developed tests without premarket review
2010-2017	36 of 38 Violation letters concerning the DTC promotion of genetic laboratory developed tests without premarket review
1997-2016	No violation letters issued for misleading claims or marketing without premarket review if a physician order is required
FTC <sup>b</sup>	
1997-2016	No regulatory action for misleading advertising
State attorneys general	
2016	New York State attorneys general settlement against DirectLabs and LabCorps for violating state law by selling direct access testing <sup>12</sup>

Abbreviations: DTC, direct to consumer; FDA, US Food and Drug Administration; FTC, Federal Trade Commission; OPDP, FDA Office of Prescription Drug Promotion.

<sup>a</sup> Office has a staff of 72 reviewers.

<sup>b</sup> Regulates for-profit organizations.

**Marketing Characteristics** | Drug company advertisements increasingly offer coupons, rebates, or discounts to defray out-of-pocket costs particularly for expensive drugs and drugs with generic competition.<sup>22</sup> These strategies have been criticized for encouraging use of expensive drugs despite lower-cost options, undermining insurance design, diminishing competitive pressure to lower prices, and ultimately shifting higher costs back to payers.<sup>23</sup>

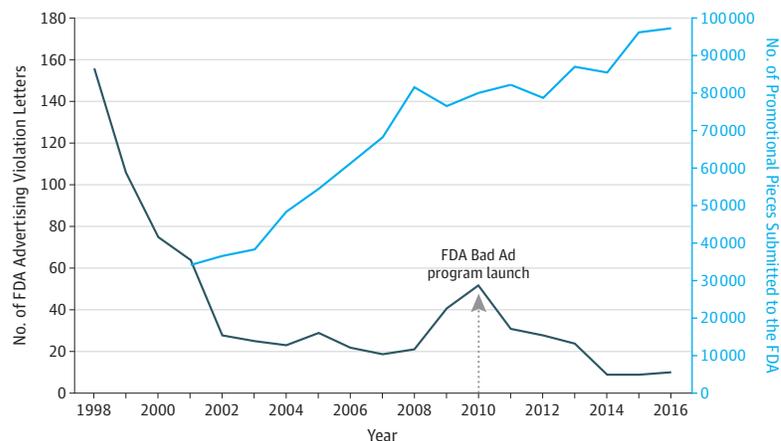
Recently, some companies have introduced find-a-doctor features in advertisements to help consumers locate prescribers, an approach that has raised ethical questions by creating a conflict of interest as to whether prescribers serve patients or companies. For example, websites for Contrave (weight loss) and Addyi (hypoactive sexual desire) encourage consumers to schedule telemedicine visits to “complete your doctor consultation from the privacy

of your own home,”<sup>24,25</sup> raising additional concern, such as whether care may be adversely affected because prescriber follow-up is either not allowed (Contrave) or not standard practice (Addyi).

Recent studies of DTC broadcast advertising deemed informational quality low, with drug benefit typically presented in testimonials rather than quantified (ie, only 9% of these advertisements presented absolute risk reductions) and adverse effects in long lists, often minimized by competing positive imagery, and never quantified.<sup>22,26,27</sup> Few advertisements (7%) included nondrug options.<sup>27</sup> No evidence has shown that DTC advertising improves patient adherence.<sup>28,29</sup>

**Influence of Marketing** | DTC advertising has been associated with increased patient requests and prescriptions (despite cost-effective

Figure 5. FDA Prescription Drug Advertising Violation Letters and Promotional Materials Submitted to the FDA



Data from Sullivan et al,<sup>14</sup> and the FDA (US Food and Drug Administration).<sup>15</sup> The FDA Bad Ad program teaches prescribers and the public to identify and report misleading promotion.<sup>16</sup>

alternatives) and higher costs through more patient visits.<sup>28-32</sup> In a 2005 trial,<sup>33</sup> standardized patients at primary care visits (n = 298 visits to 152 physicians) were randomized to make DTC-driven requests for a brand-name antidepressant ("I saw this ad about Paxil") or no requests. The former group received more prescriptions whether indicated or not, resulting in less underuse (more antidepressants for major depression, 53% vs 31%) and more overuse (more for adjustment disorder, 55% vs 10%).

**Regulatory Considerations** | In 2006, after Vioxx's DTC campaign and market withdrawal of the drug, the Institute of Medicine recommended 2 policies: adding a black triangle to advertisements to highlight inherent uncertainty of new drugs, and a DTC advertising ban during the first few years on the market.<sup>34</sup> However, the FDA did not adopt either policy.

Despite important uncertainties about efficacy and safety of some new products, DTC advertising is allowed for drugs with accelerated approval. The FDA requires professional labeling to note that approval is provisional, based on improved surrogate outcomes (eg, tumor response) but not patient outcomes (eg, survival).<sup>35</sup> The FDA does not require similar statements in DTC advertising, but should consider doing so.

In 2015, the American Medical Association (AMA) called for a ban on DTC advertising because of concerns that DTC advertising drove up drug costs without adding benefit.<sup>36</sup> Companies objected on First Amendment grounds and a ban is unlikely.

To better inform consumers, the FDA's Risk Communication Advisory Committee recommended adding tables (drug facts boxes) that quantify benefits and adverse effects in advertisements. Randomized clinical trials<sup>37</sup> replicated by the FDA<sup>38,39</sup> have shown that drug facts boxes improve hypothetical drug choices, although these have not been implemented in drug advertisements. In 2018, the FDA issued guidance recommending how companies should quantify benefit and risk information but did not mandate including this information in promotional materials.<sup>40</sup>

In addition, even though drug advertising accounted for the largest growth in DTC marketing, the corresponding decrease in FDA violation letters suggests the possibility of less oversight. Companies might be producing better materials but it is also possible that FDA

reviewers may be overwhelmed by the massive increase in promotional submissions (Figure 5).

#### Disease Awareness Campaigns

Companies can conduct disease awareness campaigns anywhere in the world, even before corresponding drug approval occurs. Since campaigns do not name or make claims about specific products, these campaigns are exempt from FDA's branded advertising fair balance requirements (ie, equal emphasis on benefits and risks). Raising awareness can be beneficial if it increases diagnosis and effective treatments of serious or debilitating diseases, or destigmatizes diseases (eg, HIV) or embarrassing symptoms (eg, impotence). But increasing disease awareness also can cause harms (such as those related to overdiagnosis, overtreatment, and wasted resources) by medicalizing ordinary experience and expanding disease definitions without evidence of net benefit.

**Marketing Characteristics** | Disease awareness campaigns have used several approaches to promote conditions: memorable destigmatizing acronyms (eg, ED for erectile dysfunction), quizzes to define the disease and allow self-diagnosis, and encouragement to "ask your doctor" (often including question scripts) about symptoms, disease, and treatment.<sup>41</sup> Industry reports identified awareness campaigns as particularly engaging social media topics and found that unbranded Facebook pages were more common than branded ones (44 vs 24 pages) and more popular (eg, the most popular unbranded page, Takeda's Lighter Blue [depression] had 1.1 million views vs 295 000 for the most popular branded page, Novartis' Gilenya.com [multiple sclerosis]).<sup>42</sup>

Companies also support patient advocacy organizations that shape disease conceptions: 83% of the 104 largest US patient advocacy organizations received funding from drug, device, or biotechnology companies,<sup>43</sup> and 14 pharmaceutical companies donated at least \$116 million to 594 patient groups in 2015.<sup>44</sup> Companies have worked with television scriptwriters to create disease-related story lines (without disclosing the collaboration).<sup>45,46</sup>

**Influence of Marketing** | A 2005 trial by Kravitz et al<sup>33</sup> provides the strongest evidence for disease campaigns' effect on prescribing.

Standardized patients who told the physician "I was watching this TV program about depression wondering if you thought a medicine might help me," compared with those who made no request, received more prescriptions for antidepressants (76% vs 31%) and for adjustment disorder (39% vs 10%).

A national ecological study demonstrated an association between regional exposure to DTC advertising for "low testosterone of aging," an off-label use, and increased testosterone prescriptions.<sup>47</sup> During the course of this campaign, testosterone sales increased from \$1.01 million (2009) and peaked at \$2.7 billion (2013).<sup>48</sup> Associations were nominally stronger for unbranded than branded advertisements. The FDA did not challenge the off-label claims.<sup>49,50</sup>

FDA research has documented another problem in that disease awareness efforts can cause people to falsely conflate disease information with drug benefit. Compared with people exposed only to drug information, people who also were exposed to disease information were more likely to falsely believe the drug had unproven benefits.<sup>51,52</sup>

**Regulatory Considerations |** Despite the growth in disease awareness campaigns, no official FDA rules governing this type of marketing exist. The FDA and FTC should establish and enforce standards for responsible disease awareness campaigns, including criteria to validate symptom quizzes (or banning them) and evidence-based strategies to minimize misconceptions that a drug can treat all symptoms of disease. Efforts by Google, Twitter, and Facebook to shift DTC advertising from television and print to social and digital media<sup>53</sup> underscore the need for new rules.<sup>54</sup>

#### Health Services

Health service advertising, relatively uncommon 20 years ago, is now ubiquitous. The AMA recommended banning physician advertising until the 1980s, when federal courts ruled that doing so violated protected commercial speech, inhibited competition, and prevented physicians from providing the public with important information about available services, quality, and prices.<sup>55</sup> These rulings also led the American Hospital Association to rescind its advertising ban.

**Marketing Characteristics |** Hospital marketing often highlights convenience, accommodations, or reputation, but rarely provides comparative data on quality.<sup>56</sup> In an older study that has not been updated, *US News & World Report's* 2005 honor roll of academic medical centers promoted institutional prestige, tests, and interventions (many unproven) using emotional appeals rather than data.<sup>57</sup> More recently, some advertisements for cancer centers have emphasized hope and fear without mentioning treatment harms or quantifying benefit; some advertisements have used survivor testimonials falsely implying patients live longer or have better outcomes when treated at those centers.<sup>58</sup>

Hospital websites have prominently advertised new technologies including stereotactic radiation surgery,<sup>59</sup> robotic prostatectomy,<sup>60</sup> or robotic gynecologic surgery,<sup>61</sup> often with unsubstantiated benefit claims without noting risks or alternatives, and, in the case of stereotactic radiation, use in cancers outside professional guidelines. Some medical centers may advertise advanced new technology to attract new patients, but the need to recoup the capital investment in the technology may stimulate advertising, creat-

ing a self-reinforcing cycle.<sup>62</sup> Many hospitals (including some academic centers) market "executive physicals," 1- to 2-day examinations including unproven advanced imaging (eg, full-body computed tomography scan) directly to consumers or indirectly through employers as an executive management benefit.<sup>63</sup>

The influence of health services advertising on consumers is largely unknown. Although this advertising may inform better choices, it may result in higher costs and overuse of new or unproven technology.

**Regulatory Considerations |** The limited action by the FTC or state attorneys general speaks to the need for better consumer protection. The sheer volume of organizations and individuals engaging in health services marketing and the wide range of services that can be promoted prevent systematic monitoring, and no explicit guidance on when such advertising becomes deceptive exists. This gray zone is illustrated by the promotion of mobile screening units (Life Line and Health Fair) in which consumers may undergo multiple tests, many exceeding evidence-based guidelines (eg, the US Preventive Services Task Force recommends against population screening for carotid artery disease).<sup>64</sup> Given their social mission, academic medical centers could commit to better self-regulation, for example, requiring internal independent review of advertising, similar to institutional review board evaluation and approval of research proposals. The Joint Commission (JCAHO, formerly the Joint Commission on Accreditation of Healthcare Organizations) could add responsible advertising to accreditation checklists. The FTC or state attorneys general could replicate the FDA Bad Ad program to teach prescribers and the public to identify and report misleading promotion.<sup>16</sup> Regulators also could address loopholes that allow third parties, such as clinicians or health care organizations, to promote products in ways that the manufacturer could not (eg, ignoring the FDA's fair balance standards).

#### Laboratory Testing

Although historically focused on hospitals and physicians, laboratory test marketing now targets consumers. Sales of these products have increased substantially from \$15 million in 2010 to \$131 million in 2015, are projected to reach \$350 million by 2020, and have been spurred partly by substantial venture capital investment (eg, 23andMe reportedly raised more than \$400 million).<sup>65</sup>

**Marketing Characteristics |** Traditional commercial laboratory testing companies (eg, Quest) market direct access testing whereby consumers place online orders for traditional blood tests or panels (eg, wellness, cancer markers, hormone health).<sup>65</sup> Although direct access testing offers convenience, with laboratory samples drawn at the nearest facility without involving a physician, the appropriateness of this testing is questionable. A 2011 study of 92 marketed laboratory tests involving screening found that few tests were recommended by evidence-based guidelines (12% in targeted populations; none in the general population) and that guidelines recommended against testing for nearly one-quarter of the laboratory tests studied.<sup>66</sup>

Some companies market or allow consumers to purchase physician-ordered genetic tests for cancer genes, newborn screening, and pharmacogenetics. For example, Color Genomics allows consumers to purchase saliva home kits for 30 hereditary cancer genes

and familial hypercholesterolemia and submit their own physician's order at checkout or authorize an independent physician to order the test. Some consumers at Color Genomics and other companies may never have contact with or meet the ordering physician before or after testing.<sup>67</sup>

The most familiar DTC genetic testing involves consumers purchasing kits for ancestry, paternity, traits (eg, unbrow), wellness (eg, sleep), carrier status (eg, cystic fibrosis), and disease risk prediction (eg, Alzheimer disease) from the company, Amazon, or retailers such as pharmacies and big box stores. Some testing is marketed as a fun activity (eg, spitting parties), a thoughtful gift (eg, Christmas and Valentine's day), or as adventurous (LivingDNA—Start Your Ancestry Adventure Today).

However, genetic testing websites rarely provide information about the potential adverse consequences of testing (eg, genetic discrimination, emotional consequences), limitations (eg, genetics are only 1 component of risk), or offer pretest counseling. Some websites, such as those for tests that have not been reviewed by the FDA, have reportedly acted misleadingly by citing laboratory-quality certification that inferred the tests were FDA approved.<sup>68</sup>

**Influence of Marketing** | Myriad conducted the first large-scale campaign for physician-ordered *BRCA* testing in 2002. The campaign, which was criticized for overstating testing benefit to the general population, increased genetic counseling referrals at Kaiser Permanente Colorado from 144 patients to 499 patients vs no increase at a control hospital.<sup>69</sup> While more women with low risk were referred for counseling (from 31% to 52%), the number of women with low risk who were tested was unchanged.

The limited available research shows that testing causes minimal psychological harm to individuals with higher-risk variants,<sup>70</sup> and it does little to motivate behavior change.<sup>71</sup> In one study (N = 1026), only 27% of consumers actually shared results of personal genomic testing with their physician 6 months later.<sup>72</sup> Doing so was generally unsatisfying, and many patients questioned their physician's competency interpreting results. A pilot randomized trial of 100 patients found that adding whole-genome screening to family history review in primary care detected abnormalities of uncertain value; although most mutations were managed appropriately, some (18%) prompted inappropriate clinical actions.<sup>73</sup>

**Regulatory Considerations** | According to the Centers for Disease Control and Prevention (CDC) Office of Public Health Genomics, "consumer genetic testing is booming" with an estimated number of more than 12 million people in 2017 undergoing genetic health tests, often bundled with genealogy tests.<sup>74</sup> The CDC is concerned that many tests are performed without genetic counseling, and the balance of benefits and harms is largely unknown.

Genetic test regulation is in flux. Historically, the FDA treated these tests as simple laboratory developed tests (LDTs): one-off tests developed by single laboratories to address local needs, with limited commercial value and that did not need premarket review.<sup>75</sup> But over time, genetic tests have become technologically complex, commercially valuable, and broadly marketed, leading to calls for increased vigilance and premarket review.<sup>75,76</sup>

US General Accountability Office investigations in 2006 and 2010,<sup>77,78</sup> along with a 2015 FDA report,<sup>79</sup> have documented public health evidence of actual or possible harm related to high-risk LDTs

that were disseminated without premarket review, including false-positive results leading to overtreatment, false negatives resulting in suboptimal cancer treatment, and screening tests with no predictive value (eFigure 2 in the Supplement). The FDA issued a draft guidance in 2014 to phase in LDT premarket approval,<sup>80</sup> but plans for finalization are uncertain.

The FDA has increasingly acted against the DTC promotion of unapproved genetic LDTs, most notably requiring premarket review before granting 23andMe the first authorization for DTC marketing of genetic health risk tests. Establishing accuracy and predictive ability, approval does not, however, address clinical utility (ie, improved outcomes). Under the approval for 23andMe, the company is required to communicate warnings and limitations (eg, "the test does not mean you will ultimately develop a disease") and note professional guideline recommendations even when the guidelines do not support testing.

In 2018, the FDA approved the first DTC pharmacogenetic test. This test provides information about genetic variants that may be associated with how drugs are metabolized "to help inform discussions with a health care provider."<sup>81</sup> However, the standard for approval is problematic and was based only on assay reproducibility, not evidence of clinical usefulness. The FDA has warned that the test does not predict response to any drug and should not be used to make treatment decisions. One day after approval, the FDA issued a safety alert announcing that many pharmacogenetic tests (DTC or clinician ordered) claiming to predict response to specific medications have not been evaluated by the FDA or lack supporting evidence.<sup>82</sup> The FDA should not approve or permit promotion of such tests without premarket review establishing a meaningful clinical benefit.

Whether the FDA, FTC, or state attorneys general will enforce or raise standards or monitor promotion for unsupported claims of benefit is unclear. Similarly, regulatory attention to marketing claims for standard direct access laboratory testing is also needed because this testing is now allowed in all states except New York, New Jersey, Rhode Island, Maryland, and Massachusetts.

## Professional Marketing

### Prescription Drugs

Companies have consistently spent more on promoting free samples and providing detailing visits than other forms of medical marketing. Direct physician payments are also substantial for speaker fees and sponsored educational events, which are mostly company sponsored, rather than accredited continuing medical education (CME) programs that prohibit industry review of content.

**Marketing Characteristics** | The most heavily promoted drugs to physicians are less likely first-line treatments recommended in national guidelines compared with the most-prescribed or top-selling drugs,<sup>83</sup> facts generally not evident in medical journal advertisements. A 2008 study of advertising in 9 high-impact journals (N = 83 unique ads) found that 58% (48) did not quantify serious risks, 48% (40) lacked verifiable references, and 29% (24) did not quantify efficacy.<sup>84</sup>

Key opinion leaders feature prominently in professional marketing as consultants and speakers across a drug's lifecycle, developing commercialization strategies and serving as *product champions*.<sup>85</sup> These opinion leaders exert influence through research publications, presentations, media presence, and contributions to editorial

boards, guideline committees, and professional societies.<sup>86</sup> Payments to key opinion leaders, a function of reputation and specialty, reportedly account for approximately one-third of company marketing budgets.<sup>87</sup>

Other indirect industry promotion can be influential but difficult to quantify such as marketing or “seeding” trials in which a primary function is not research but to encourage physicians to start using a specific drug.

**Influence of Marketing** | Observational studies suggest that detailing and samples influence prescribing and raise costs by promoting expensive newer brand-name drugs rather than equally effective, less-expensive alternative products or nondrug choices.<sup>88-92</sup> Gifts such as travel, lodging, and meals also appear to stimulate physicians to prescribe the promoted drug; even small gifts promote increased prescribing, although larger gifts are associated with larger effects.<sup>93-98</sup> Because high prescribers may be predisposed to accept gifts or samples or to participate in detailing visits, these studies cannot prove causality.

**Regulatory Considerations** | Less exposure to detailing during medical school, residency, or practice is associated with less use of new costly drugs, and higher generic use.<sup>99</sup> State policies restricting or banning gifts were associated with less prescribing of new costly drugs,<sup>100</sup> and health care systems such as Kaiser Permanente and some academic medical centers now prohibit or limit speaker’s fees, nonresearch consulting, and meals.<sup>101</sup> In 2018, New Jersey adopted the first gift restrictions linked to licensure, capping annual consulting and speaking payments to \$10 000 and meals to \$15.<sup>102</sup> High-quality evidence supports academic counter-detailing programs as improving prescribing.<sup>103</sup>

Better oversight of detailing and education is needed. The OPDP monitors promotional exhibits and activities at major medical meetings and conventions but not detailing visits, lunch or dinner presentations, or speaker trainings. Experience with Oxycontin highlights potential detailing harms; drug representatives, minimizing abuse potential and promoting off-label use for chronic pain, helped contribute to the current opioid crisis,<sup>104</sup> although Oxycontin detailing ceased in 2018.<sup>105</sup> If OPDP cannot monitor promotional activities for drugs with important public health risks, a detailing ban might need to be considered.

In addition, while the Sunshine Act of 2010 required reporting of payments from industry to physicians, Congress recently enacted a law that closes an important gap involving these payments by expanding mandatory Sunshine Act disclosures, beginning in 2022, from industry to physician assistants, nurse practitioners, nurses, pharmacists, and dieticians.<sup>106</sup>

#### **Disease Awareness Campaigns**

Companies often pay physicians to talk or learn about disease diagnosis or treatment. The opioid crisis highlights the potential risks of entangling industry in disease education. Company-sponsored disease awareness fostered an aggressive approach to chronic pain treatment including lower thresholds for opioid use in noncancer pain. In 1996, without supporting evidence, the American Academy of Pain Medicine and the American Pain Society, both substantially funded by opioid manufacturers,<sup>107</sup> issued a consensus statement endorsing opioids for chronic noncancer pain, describing

addiction risk as low.<sup>108</sup> The American Pain Society also introduced pain as a fifth vital sign, which was adopted by the Department of Veterans Affairs and endorsed by the JCAHO, encouraging clinicians to screen all patients for pain along with measuring traditional vital signs.<sup>108</sup> Between 1996 and 2001, Purdue Pharma (the manufacturer of Oxycontin) paid more than 5000 physicians, pharmacists, and nurses to attend speaker training conferences and sponsored more than 20 000 pain education programs.<sup>109</sup> Opioid prescription sales and deaths quadrupled from 2000 to 2015.<sup>110</sup>

Even accredited CME disease education can induce inappropriate diagnosis and treatment. For example, a Medscape-accredited CME program, “Unmasking ADHD in Adults,” funded by Shire (the manufacturer of Adderall), taught primary care physicians that diagnosis can be made in 6 minutes.<sup>111</sup> After questioning, the psychiatrist who created the program reconsidered and repudiated the claim.<sup>111</sup>

Disease promotion also occurs through physician consultants on advisory boards that design awareness campaigns, develop disease management programs, or participate in company-funded workshops defining diagnostic criteria and treatment thresholds<sup>112</sup> (eg, International Restless Legs Syndrome Study Group, Chronic Dry Eyes Workshop). To address possible industry bias, the National Academy of Medicine and the Guideline International Network have developed quality criteria emphasizing that definition-setting panels should consist of experts without financial conflicts of interest.<sup>113,114</sup>

#### **Laboratory Testing**

Manufacturers of FDA-approved tests must report physician payments to Centers for Medicare & Medicaid Services; however, LDT manufacturers are exempt. These payments may be substantial because many LDT tests are marketed to clinicians. For example, Assurex, which markets GeneSight pharmacogenetic tests to optimize medications for depression, anxiety, or pain, hosts educational dinners for psychiatrists,<sup>115</sup> Other genetic testing companies have offered payments to physicians for each test ordered as part of research studies with unclear scientific merit (ie, seeding trials).<sup>116</sup>

**Regulatory Considerations** | The FDA could improve laboratory test promotion to physicians by requiring premarket review of physician-ordered tests to substantiate clinical claims. For example, a DTC genetic testing company, Kailos Genetics, which received an FDA violation letter for lack of premarket review, can sell the same unapproved pharmacogenetic LDT because a physician order is now required.<sup>117</sup>

#### **Limitations**

This review has several limitations. First, spending on medical marketing is underestimated. Data on professional marketing (eg, detailing) of laboratory tests, health services or devices, and pharmaceutical company spending on coupons or rebates, online promotion, and meetings and events could not be obtained. Also, the Centers for Medicare & Medicaid Services’ Open Payments system does not collect promotional payments by LDT companies for unapproved tests or speaker fees for accredited CME if the activity is supported by an unrestricted grant or a nonprofit society. Disease marketing to professionals is underestimated because detailing, medical journal advertising, and most direct payments were attributed to drug marketing. In addition, spending estimates vary based on the data

source and methodology. For example, in 2004, the amount of spending for detailing to physicians was estimated at \$10.6 billion (IQVIA present data) vs \$20 billion (reported by Cegedim).<sup>118</sup>

Second, company marketing budgets typically include numerous other activities and expenses that may not be captured by available data sources, such as the cost of marketing employees, training sales representatives, research to guide marketing efforts, analytics to assess return on investment from marketing choices, monies paid to advertising agencies, medical communication companies, public relations firms, unmonitored promotion (eg, patient assistance charities and advocacy groups, rebates, promotion to payers), and lobbying and campaign contributions.

Third, the published literature analyzing the return on investment of medical marketing or the related effects on health costs,

utilization, and outcomes, particularly for health service, laboratory testing advertising, and for newer media (eg, social media, online ads), is limited and largely based on observational data and therefore precludes drawing strong conclusions.

## Conclusions

Medical marketing increased substantially from 1997 through 2016, especially DTC advertising for drugs and health services. Pharmaceutical marketing to health professionals accounted for most spending and remains high even with new policies to limit industry influence. Despite the increase in marketing over 20 years, regulatory oversight remains limited.

### ARTICLE INFORMATION

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## Editor's Note

# A Tribute to Lisa M. Schwartz, MD, MS

Howard Bauchner, MD

**On a personal note**, one of the joys of my position as Editor in Chief of *JAMA* and the *JAMA* Network is to meet and talk with individuals whom I have admired my entire academic career.

Such was the case in meeting and discussing this article with Lisa and Steven. They clearly had boundless energy and enthusiasm for the topic. I had followed and known of their remarkable work for

decades—a powerful team, a couple of enormous intellectual talent. Sadly, Lisa passed away in November 2018. Steven informed us of her death shortly after the manuscript had been accepted, informing us that one of Lisa's last academic goals was to finish this manuscript and to know that it would be published. It is our privilege to publish this Special Communication<sup>1</sup> from Drs Schwartz and Woloshin. We offer our condolences to Steven and to Lisa and Steven's family.

**Author Affiliation:** Editor in Chief, *JAMA*.

**Corresponding Author:** Howard Bauchner, MD ([howard.bauchner@jamanetwork.org](mailto:howard.bauchner@jamanetwork.org)).

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