
This supplementary material has been provided by the authors to give readers additional information about their work.
### eAppendix. Search Strategy and Terms

#### 1. Medical Literature

**Source:** PubMed (1975-2018, English Language)

<table>
<thead>
<tr>
<th>Concept</th>
<th>MeSH</th>
<th>Keyword</th>
</tr>
</thead>
<tbody>
<tr>
<td>Money being spent</td>
<td>&quot;Advertising as Topic/economics&quot;[Majr] OR &quot;Marketing of Health Services/economics&quot;[Majr]</td>
<td>Expenditure* [tiab] OR</td>
</tr>
<tr>
<td>Regulation</td>
<td>&quot;Advertising as Topic/legislation and jurisprudence&quot;[MAJR] OR &quot;marketing of health services/legislation and jurisprudence&quot;[majr]</td>
<td>Regulation [tiab]</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td></td>
<td>Pharmaceutical* [tiab] OR</td>
</tr>
</tbody>
</table>

Web of science searches for citations of key articles

#### 2. Business literature

**Source:** Business Source Ultimate (1975-2018)

(direct AND "to" AND consumer AND advertising AND "of" AND prescription AND drugs) OR (direct to consumer advertising healthcare) OR (advertising AND medicine) OR ((hospital OR health facilities) AND advertising) OR (medical laboratories AND marketing)

#### 3. News media

**Source:** LexisNexis (1997-2018)

Direct to consumer advertising, direct access laboratory testing, genetic testing AND advertising, prescription drug promotion, hospital advertising, drug company AND disease awareness
Grey boxes indicate that FDA enforcement actions occur through the Department of Justice.

**Television ads required to be submitted (but not approved) prior to dissemination include: initial ads for any prescription drug or a new indication, ads for drugs with a Risk Evaluation and Mitigation Strategy (REMS) with elements to ensure safe use, all ads for Schedule II controlled substances, and first ads following safety labeling update (e.g. Boxed warning, Contraindications, Warnings & Precautions) and enforcement letters.**
eFigure 2. FDA Violation Letters and Associated Policy and Investigations
**eTable.** Comparison of Growth in Marketing to Total US Spending From 1997 Through 2016 for Prescription Drugs and Health Services*

<table>
<thead>
<tr>
<th></th>
<th>Annual spending (millions)</th>
<th>Relative change</th>
<th>% of Total spending</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prescription drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marketing spending</td>
<td>$17,082</td>
<td>$26,872</td>
<td>1.6</td>
</tr>
<tr>
<td>Total US spending</td>
<td>$116,454</td>
<td>$328,588</td>
<td>2.8</td>
</tr>
<tr>
<td><strong>Health services</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marketing spending</td>
<td>$542</td>
<td>$2,887</td>
<td>5.3</td>
</tr>
<tr>
<td>Total US spending</td>
<td>$1,157,928</td>
<td>$2,162,536</td>
<td>1.9</td>
</tr>
</tbody>
</table>

* Source: Kantar Media, IQVIA, Open Payments (marketing spending); and CMS National Health Expenditure Historical Data and OECD Health Expenditure Indicators (total U.S. spending). 1997 spending is reported in 2016 dollars.

**Marketing spending includes prescription drugs and disease. Total US spending on prescription drugs from CMS National Health Expenditure Historical Data

† Total US spending on health services estimated from the proportion of total health spending from inpatient, outpatient and home care (OECD Health Expenditure Indicators) and total US health spending (CMS National Health Expenditure Historical data).
**Prescription drugs**

**Strengthen FDA regulation of promotion**

Maintain FDA's jurisdiction over off-label promotion

Prohibit DTC advertising and limit detailing of: highly-addictive drugs, accelerated approvals prior to confirmation of clinical benefit and new drugs during the first few years on the market, institute "black triangle" for new drugs

Require advertising to highlight uncertainties and negative results

Consider banning company sponsored telemedicine visits to prescribe advertised drug

**Limit industry influence on prescribing and increase transparency**

Establish state** and institution restrictions or bans on pharmaceutical company detailing visits and gifts to clinicians, and prohibit faculty participation on company speaker bureaus.

Accelerate public reporting of industry payments to physician assistants, nurse practitioners, nurses, pharmacists and patient assistance charities – not mandated to begin until 2022.

**Disease awareness campaigns**

**Clarify regulation of disease awareness campaigns**

Coordinate FDA and FTC processes and issue joint guidance for disease awareness campaigns addressing issues such as permissibility of symptom quizzes and scientific standards, fair balance – mention treatment harms, evidence standards for disease prevalence estimates, prominence of company sponsorship.

Reliably tagging awareness websites with “Ad” in search engines.

**Establish criteria for trustworthy disease definitions**

Adopt National Academy of Medicine and Guidelines International Network\(^{109}\) principles for trustworthy guidelines in setting quality criteria for new or modified disease definitions by experts without financial conflicts of interest

**Health services**

**Increase awareness of – and surveillance for - “Bad Ads”**

Initiate programs such as FDA's Bad Ad initiative for drugs to encourage clinicians and consumers to report misleading health services (or laboratory test) advertisements to FTC and state Attorneys General

Establish proactive review of hospital advertisements by the Joint Commission

Better self-regulation by academic medical centers and hospitals

Encourage “Truth in advertising” pledges by marketing departments and require submission of advertisements (including co-branded ads) to the local IRB or a third-party reviewer for independent assessment prior to dissemination

**Laboratory tests**

**Clarify and enforce regulations about laboratory test approval**

Finalize and implement new FDA policy for premarket approval of moderate-to-high risk LDTs to establish reproducibility and predictive value, and monitor for serious adverse events.

Approve individual tests not laboratories (i.e., do not grant "precertification" exemptions after first test approved).

**Set and enforce promotional standards**

Issue FDA guidance establishing standards for promotional materials including mention of supporting evidence (e.g. "[Test] approved by FDA based on accuracy – not been shown to improve outcomes"), harms (e.g., false positives or negatives), extent of FDA review, major evidence-based guideline recommendations (e.g. Preventive Services Task Force), and substantiating clinical utility - for tests making health claims.

Enforce regulations forbidding promotional materials for pharmacogenetic tests to claim or imply a clinical benefit unless supported by sufficient evidence noted in the approved label.

Require companies promoting unapproved physician-ordered LDTs to disclose clinician or hospital payments

Professional organizations should discourage physicians from being paid to prescribe advertised tests and require physicians identified through companies to disclose to patients how they are being paid