3.4.2.1 Direct to consumer advertising and ethical prescribing

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Educational Objectives:

1. Evaluate evidence on the effects of direct-to-consumer advertising (DTCA) on patient requests and physician prescribing behaviour;

2. Describe current trends in pharmaceutical marketing, in order to critically evaluate patient information influenced or generated by DTCA;

3. Discuss practical and ethical strategies for managing patient requests generated by DTCA.

Background

Patients derive information from a variety of sources outside the medical encounter, including traditional media, internet and social media, and friends and family. Physicians have long faced the challenge of integrating patient values and beliefs with medical expertise to arrive at good shared decisions. In recent years, due to regulatory changes and marketing trends, the information patients gather from all these sources may derive directly or indirectly from direct-to-consumer advertising (DTCA) of prescription drugs by the pharmaceutical industry.

Most industrialized countries, including Canada, have laws prohibiting DTCA of prescription-only medicines on health protection grounds. The United States and New Zealand are the two exceptions. These laws represent a trade-off between commercial free speech and health protection. The rationale for restrictions is that prescription-only drugs generally treat more serious conditions and have greater potential toxicity than over-the-counter drugs. A physician’s advice is required in order to ensure appropriate care and prevent unnecessary exposure to medication adverse effects. DTCA has been found to lead to higher prescribing volumes and costs (Gilbody et al, 2005) and less appropriate prescribing (McKinlay et al, 2014; Spence et al, 2005; Nierdeppe et al, 2013).

Spending on DTCA has risen rapidly in the US since the early 1990’s, reaching US $4.2 billion in 2010. (Mintzes, 2012) In Canada, although DTCA is prohibited in the Food & Drugs Act, two administrative policies introduced in 1996 and 2001 allow some forms of DTCA. These policies allow manufacturers to advertise conditions treated by their products in ‘disease-awareness ads’, as long as neither the brand nor manufacturer is stated, and allow ‘reminder advertising’, in which a brand name is mentioned but not the condition the product aims to treat. (Gardner et al, 2003) Additionally, Canadians are exposed to U.S. advertising through cross-border media and the Internet, including social media campaigns. On average, Americans see around 16 hours of DTCA a year on television, far outweighing time spent with a doctor. (Brownfield et al, 2007) Law et al (2008) estimated that English-speaking Canadians see one-third this volume in cross-border US advertising. Per capita spending on “made-in-Canada” DTCA is around 5% of US levels. (Mintzes et al, 2009a)

Law et al (2008) compared prescribing rates in English-speaking provinces and Quebec pre- and post- three US DTCA campaigns, using differences in cross-border US television viewing as a natural experiment. They found that DTCA increased prescribing of tegaserod for irritable bowel syndrome, a drug later withdrawn for safety reasons. Prescribing of two other
drugs was not affected, etanercept, provided only in specialty care, and mometasone, fully only reimbursed in Quebec. This study showed that effects of DTCA can differ by drug and reimbursement status, and that a poor safety profile failed to prevent effects of DTCA on sales.

Two particular areas of concern are engaged by allowable DTCA in Canada.

The permission Canada extends to disease awareness campaigns matches industry’s shift to marketing diseases rather than drugs. (Mintzes, 2006) Brody and Light (2011) propose that a set of marketing strategies, including “medicalization” (creation of new diseases) and “indication creep” (shifting the threshold for treatment) contribute to what they call the “inverse benefit law,” as drugs with reasonably clinical utility for narrow patient populations are used in broader populations, where they may cause net harm. For example, there is RCT evidence that patient requests for advertised medicines can lead to inappropriate prescribing. Kravitz et al. (2005) randomized standardized patients to scenarios representing major depression or ‘adjustment disorder’, temporary distress due to relocation and unemployment. The standardized patients were also randomized to request an advertised antidepressant, Paxil (paroxetine), no request, or a general query about an antidepressant. If they requested Paxil, they were equally likely to receive an antidepressant whether they presented with depression or adjustment disorder. Antidepressants are not approved nor shown to be effective for the latter.

Furthermore, the safety profiles of medicines promoted in Canadian ‘reminder’ advertising raise concerns. Eight medicines were heavily advertised on television from 2001 to 2006, representing 59% of Canadian DTCA spending. Six of these were subject to Health Canada safety advisories, and four to US FDA ‘black box’ warnings. (Mintzes et al, 2009a) No risk information is provided in reminder ads. In the US, reminder advertising is prohibited for drugs with ‘black box’ warnings.

DTCA is typically part of larger marketing campaigns aimed primarily at physicians, through sales visits, free samples, educational events, and journal advertising. Funding of clinical practice guidelines, cultivating key opinion leaders, and supporting patient groups are also synergistic marketing activities. (Fugh-Berman & Ahari, 2007)

According to a 2004 survey, US physicians often view DTCA negatively, with most saying that DTCA shifts patients’ expectations of prescribing and increases medication use, and that better regulation is needed. (Robinson, 2004) In focus groups, physicians noted that it can be hard to refuse patient requests (Tentler et al, 2007). One comment made was that it seemed better to err on the side of overtreatment in the face of uncertainty. Physicians often comply with requests although they might not have chosen the same treatment otherwise. (Mintzes et al, 2003) However, providing a brief explanation and/or treatment alternatives helps to mitigate negative effects of a refusal, (Blose and Mack, 2009) as does exploring the patient context for the request (Kravitz, 2013; Paterniti, 2010).
Case

Dr. Persadie attends a talk at his annual urology conference with Dr. McKenzie, a prominent expert in testosterone insufficiency. Apart from his clinical update on conditions that cause inadequate testosterone production (e.g. Klinefelter’s syndrome, other congenital abnormalities, pituitary tumours), Dr. McKenzie outlined his own recent research into age-related testosterone insufficiency.

Dr. McKenzie highlighted the need for men over 45 to get their testosterone checked regularly, suggesting that timely diagnosis and treatment of low testosterone can help improve men’s quality of life, fitness and muscle strength, sex drive, and is potentially cardioprotective, especially when combined with exercise. Although regular testing is beneficial for everyone, he highlighted its importance for men with type II diabetes and obesity, two high-risk groups for “Low-T”. Early diagnosis and treatment of Low-T to normalize these men’s hormone levels is expected to have substantial effects on quality of life and may have broader health benefits, according to Dr. McKenzie, such as prevention of cardiovascular complications. Hence, he spoke both about Health Canada-approved indications and off-label prescribing for Androgel, in the context of other possible clinical approaches.

Dr. Persadie is somewhat sceptical. An article in *JAMA Internal Medicine* on Low-T as a “template for selling a disease” (Schwartz and Woloshin, 2013) highlighted the lack of consensus on a threshold for low testosterone levels, or any real link to symptoms. He recalls basic physiology: testosterone levels are highest when men are in their 20s and then gradually decline. He has also seen media reports on a study showing that testosterone supplements can cause heart attacks, stroke and death. (Vigen et al, 2013) This risk has brought the question of Androgel’s labeling back before the FDA. (Thompson, 2014)

Dr. Persadie’s 52-year-old patient, Tom Jones, comes with a referral from his family physician reporting symptoms of lowered sexual desire, depressed mood and fatigue. Mr. Jones asks directly about having his testosterone tested and says that he thinks he may have Low-T. He has the classic symptoms, he says, feeling tired, grumpiness, “falling asleep after dinner,” pretty tired after a long day at work, a lot less interest in sex than he used to have, and trouble with performance. He also asks directly about Androgel: does Dr Persadie think it might help? He says that his family doctor didn’t want to prescribe it without a more thorough work-up.

Questions

Q1. What are the likely sources of Mr. Jones’s and Dr. Persadie’s information? How reliable are these?

Mr. Jones may have seen the results of disease-awareness campaigns. This could have been traditional advertising, or media appearances of patient spokespersons, websites.

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1 Although the scenario is based in a case that might be seen in urology or endocrinology, details of the hypothetical advertising campaign are an amalgam of observed or documented marketing strategies across specialties, and do not represent any one company or campaign. This framework may be used for specialty-specific scenarios, such as the request for particular pain medications in rheumatology or psychotherapeutics in psychiatry. Choosing an example drawn from your specialty will assist in reinforce clinical expertise and the role of critical thinking and evidence-based practice.
“Reminder ads” using the brand name may have been linked to disease awareness ads through visual cues (similar design, proximal placement).

Dr. Persadie has scientific information, some of which is produced with and some without funding by the manufacturers of Androgel. Dr. McKenzie, in his scientific presentation, was able to speak about his research and clinical experience prescribing for off-label indications, which the company is otherwise not permitted to do in its marketing.

**Q2. Mr. Jones’s family physician sent Mr. Jones to you for further testing. How appropriate is this referral?**

Some family physicians may be using “referral for further testing” as an approach to managing requests for inappropriate treatment driven by DTCA. This may be better than acquiescing to patient requests, but it may have resource implications.

**Q3. Should Dr. Persadie send Mr. Jones for testosterone testing? Is testing useful or not in this situation?**

Are results likely to lead to better management and patient health?

Consider the risks of overdiagnosis and overtreatment raised by screening tests. What are the test characteristics: sensitivity and specificity; test-retest reliability (e.g. is multiple testing needed, does testosterone fluctuate over time)?

How do you balance the risks of over-testing with patient-centred care?

Would testing have been considered in the absence of an Androgel promotional campaign?

**Q4. What should Dr. Persadie say to Mr. Jones? How should s/he approach requests for non-medically indicated tests and treatment in general, and as driven by DTCA in specific?**

Kravitz 2013 and Paterniti 2010 are sources of ideas for specific clinical approaches.

Observed options included changing the topic, refusal, or further testing and referral. You now are the “referral,” and may be in a position to address the risks of overtreatment and overtreatment more directly with the patient.

Evidence supports patient-centred responses that include exploring context—“Where did you see the ad? What rang true for you?”—while offering alternative diagnosis and/or seeking consultation/advice from relevant other providers, on an agreed timeline to address the symptoms and revisit the prescription request.
References


Hafemeister TL, Gulbrandsen RM. The fiduciary obligation of physicians to "just say no" if an "informed" patient demands services that are not medically indicated. Seton Hall Law Rev 2009; 39:335-86.


