

funded continuing medical education–accredited lectures on the subject at conferences or other types of professional meetings. This is common practice, although, I believe, fundamentally problematic. Physician education programs (regardless of funding source) have been shown to influence physicians' prescribing behavior, even though the physicians who attend such symposia often deny such influence.¹⁰ And the more objective and less obviously biased a program appears, the greater its potential impact because the messages more easily slip through the skepticism that would be aroused by more ham-handed presentations. "Speakers who sound like drug reps alienate physician audiences and thus work against industry interests," noted the authors of a 2006 article on the subject.^{11(p413)}

Conclusions

In this article I have described how drug companies can pay for the creation of apparently objective physician or consumer education media products while obscuring or minimizing their role and/or the identity of the actual writers or producers of the products. I have also described how industry influence may skew content even when funding sources are nominally identified or acknowledged. I be-

lieve that these dynamics are widespread and deserve closer scrutiny by physicians, consumers, and regulators.

Despite progress in raising the level of transparency about funding, conflicts of interest, and ghostwriting, drug companies remain free to pursue subtle—and, therefore, effective—means of marketing. They can continue to hire public relations firms that, in turn, place articles or ideas in popular media with no mention of the funding source. Continuing medical education programs and consensus panels continue to be funded by companies selling products directly tied to the messages being conveyed by the resulting "educational" materials. And patient education materials continue to be created that, although factually accurate, subtly shift attitudes by including only selected facts and omitting (intentionally or unintentionally) ideas that would undermine the funder's preferred paradigm.

Everyone involved in the creation of drug company–sponsored educational materials for physicians or consumers—myself most certainly included—must constantly guard against these kinds of influences. We must do our own research, ask hard questions, be skeptical about all claims, and question whether our judgment and our words are being subtly skewed by the knowledge that the funder is watching. Physicians, for their part, must be equally vigilant, skeptical, and independent.

ARTICLE INFORMATION

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Invited Commentary

Low "T" as in "Template" How to Sell Disease

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A man on TV is selling me a miracle cure that will keep me young forever. It's called AndroGel...for treating something called Low T, a pharmaceutical company-recognized condition affecting millions of men with low testosterone, previously known as getting older.

The Colbert Report, December 2012

Mr Ferguson, a healthy 55-year-old man without active problems, is in your office for his annual checkup. He tells you that he has no problems and feels fine.

"Well," his wife chimes in, "he has been a little grumpy. Especially since Sammy—our son—starting beating Shaun here in their one-on-one basketball games."

"Of course, I'm grumpy. We bet on a game and now I have to do the lawn," Shaun says, shaking his head. "Takes forever, and it's exhausting."

"I understand," you reply, laughing. "So, are you still off cigarettes?"

"Wait," his wife blurts out before Shaun answers. She stares. "Don't you think he needs a blood test? Could this

be...Low T?" She hands you a paper—Shaun has completed the Low T question quiz from the Is It [Low T]? website.²

Testosterone usually brings sex to mind. Curiously, only 2 of 10 quiz questions are about sex: Decreased libido? Erections less strong? Your patient did not check either. But he checked 3 about energy, mood, and sports performance, enough for the quiz to suggest asking his doctor about "Low T" (low testosterone level, aka hypogonadism).

The site also offers strategies for spouses to "motivate the men in their lives to talk to their doctors." For example, if the man says "I don't have much energy anymore," "[his spouse might think] he's



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just making excuses." But the site tells her that Low T may be the real issue because it *can* affect energy levels—never suggest-

ing other explanations such as stress, depression, or other medical problems.

The Low T website is part of a broader disease awareness campaign run by Abbott Laboratories, maker of Androgel, the leading testosterone replacement product (>3 million prescriptions and >\$1 billion in sales in the United States in 2012³).

Whereas traditional drug promotion such as direct-to-consumer ads, physician samples, gifts, and detailing has received much attention, far less is known about disease awareness campaigns—much broader efforts to influence how physicians and the public think about what constitutes disease and when drugs are needed. These well-coordinated campaigns are more subtle than drug-specific campaigns, and they blur the line between public health or professional education and marketing.

The article by Braun⁴ on the promotion of Low T is a fascinating and troubling first-hand look inside the kitchen of industry disease awareness campaigns. Braun exposes how industry used ghost-written magazine articles under a celebrity physician's byline. This is on top of educational campaigns, television and magazine ads, and mobilizing industry-funded advocacy groups. The campaigns also target physicians through special journal supplements, consensus statements, and continuing medical education, as Braun also highlights.

The Low T campaign provides a template for understanding how disease awareness campaigns work. Like other campaigns (eg, Bipolar Disorder and Restless Legs Syndrome), the Low T campaign uses 3 basic strategies: lower the bar for diagnosis (turning ordinary life experiences into conditions that require medical diagnoses), raise the stakes so that people want to get tested, and spin the evidence about drug benefits and harms.

Lower the Bar

Health exists along a spectrum. At one end, people are clearly well; at the other, clearly sick. What about the big gray zone in between? When do bothersome experiences become symptoms? Where do you draw the line? For Low T, the location of the line is implausible. Everyone feels a little tired—or sad or grumpy—sometimes. And everyone slows down a bit over time (it is called aging). Recent US endocrinology⁵ and European urology⁶ guidelines actually recommend against using such Low T-type quizzes because they are unreliable and unvalidated. The Endocrine Society guideline goes even further, recommending against general population screening for Low T "because of the lack of consensus on a case definition and the

extent to which androgen deficiency is an important health problem."^{5(p2543)}

Interpreting laboratory values is all about lines—often determined statistically: lines are typically drawn, for example, 2 standard deviations beyond the mean, defining 5% of the population as abnormal. If the lines are drawn closer to the mean of normally distributed values, the proportion defined as abnormal expands rapidly. For testosterone, a serum level of 230 ng/dL (to convert to nanomoles per liter, multiply by 0.0347) defines 7% of men 50 years and older as abnormal; moving the line to 350 ng/dL (the cutoff for "normal" used in the consensus recommendation coauthored by Braun⁴) increases the abnormal proportion to 26%.

Ideally, the line would be drawn to maximize benefit and minimize harm. Unfortunately, lines are often drawn not because of evidence but to expand the market. Whether or not broad disease definitions are in the public's interest, they do serve the financial and professional interests of industry, specialists, and advocacy groups.

Raise the Stakes

It is one thing to tell men that Low T can make them grumpy; it is another to say that it can kill them. Messages raising the stakes about Low

Table. Claims and Supporting Evidence About Testosterone Therapy for Low T

Claims From isitlowt.com ⁹	Randomized Trial Evidence of TT ^a	Unknown Effect ^a
"Unwanted Body Changes: If you have Low T, you may feel that your body is changing. You may notice reduced muscle mass, an increase in body fat, or decreased bone strength. Testosterone helps increase muscle mass and strength, and maintain bone strength."	Increased lean body mass (2.7 kg), decreased fat mass (-2.0 kg), and no change in body weight vs placebo; increased bone density in lumbar spine -2%; No change in femoral neck; Increased grip strength (3.3 kg) and inconsistent effect on lower extremity strength or physical function	Effect on fractures or falls
"Decreased Energy: Some men may think loss of energy is just a part of aging. However, low energy may not just be a sign of getting older—it may also be a symptom of Low T. Some men with Low T may experience daily fatigue. Men who lack energy due to Low T may even find it difficult to do routine tasks."	No trials identified specifically assessed energy or fatigue	Meaningful improvement in energy level or ability to do routine tasks
"Mood Changes: Changes in mood, such as depressed mood and increased irritability may be a sign of Low T."	Inconsistent effect on depressive symptoms	Meaningful improvement in depressive symptoms
"Reduced Sex Drive: Low T can cause low libido (decreased sex drive), which is a lack of desire for sex that may lead to reduced sexual activity."	Moderate increase in libido; Possible small increase in overall sexual satisfaction	Meaningful improvement in overall sexual satisfaction
"Sexual Dysfunction: If you're having difficulty maintaining erections, it may be more than erectile dysfunction (ED), it may be a sign that you have Low T. Although the majority of men with ED do not have Low T, ED can sometimes be due to low testosterone."	Small increase in satisfaction with erectile function	Meaningful change in erectile dysfunction

Abbreviations: Low T, low testosterone level; TT, testosterone therapy.

^aRandomized trial evidence from systematic reviews and evidence summaries from the Endocrine Society Guideline.⁵

T have appeared regularly in scientific meeting reports and journal articles⁷ and often make their way into the news ("Low testosterone could kill you," according to ABC News⁸).

Because Low T becomes more common with aging, associations with death are inevitable. But these associations come from inherently weak observational studies that cannot exclude residual confounding or establish causality. To his credit, Braun⁴ was able to highlight these fundamental limitations in the consensus recommendations that he coauthored. Ironically, the same report asserts that Low T increases the risk of heart disease even though this finding is based on similarly limited research (in fact, a randomized trial of testosterone therapy in elderly men was stopped early because it *increased* the risk of cardiovascular disease⁹).

Spin the Evidence

The implicit message of the Low T awareness campaign is that testosterone therapy will improve men's energy, mood, and sex life. Neither the Low T website, nor the consensus recommendation, nor the magazine articles published using unnamed ghostwriters⁴ tell readers which outcomes are likely to improve with testosterone therapy—let alone the magnitude of the changes. The focus is on getting a diagnosis and on which form of treatment to take.

Physicians and patients who assume that treatment has an important effect on all or most symptoms may be surprised by the evidence from randomized trials (**Table**): Testosterone therapy

results in only small improvements in lean body mass and body fat, libido, and sexual satisfaction, and has inconsistent (or no) effect on weight, depression, and lower extremity strength. Whether these effects are big enough to matter to patients is unknown. Nor is it known whether they are big enough to outweigh the harms of testosterone therapy, ie, polycythemia that may increase thromboembolic events, edema, serious hepatotoxic effects, gynecomastia, worsening of sleep apnea, prostate enlargement, and rise in prostate-specific antigen level (and potential increased risk of prostate cancer).¹⁰

There are a lot of American men. Some are grumpy. Some are tired. Some may not even be interested in sex at the moment. And all of them are aging. This is the intended audience for the Low T campaign. Whether the campaign is motivated by a sincere desire to help men or simply by greed, we should recognize it for what it is: a mass, uncontrolled experiment that invites men to expose themselves to the harms of a treatment unlikely to fix problems that may be wholly unrelated to testosterone levels.

We agree with Braun that there is a strong analogy between the marketing of testosterone therapy for men and estrogen therapy for menopausal women. Ignoring the lessons of estrogen therapy is scandalous. Before anyone makes millions of men aware of Low T, they should be required to do a large-scale randomized trial to demonstrate that testosterone therapy for healthy aging men does more good than harm.

ARTICLE INFORMATION

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