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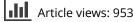
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#### **ORIGINAL ARTICLE**

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# An analysis of online content related to testosterone supplementation

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#### ABSTRACT

**Objective:** To describe the quality of online information on testosterone replacement therapy (TRT) in men.

**Methods:** A quantitative content analysis was conducted on websites providing patient-directed information on TRT for the purpose of treating late onset hypogonadism (LOH). Websites were identified through Google in March 2017. The DISCERN instrument was used to determine the quality of health information.

**Results:** A total of 20 websites met inclusion criteria. Websites were primarily from the United States (45%), United Kingdom (25%), and Australia (15%). Sources of information were cited by 40% of websites. Several websites (40%) claimed that TRT had benefits, with 25% claiming that TRT was effective for treating LOH. TRT was described as a safe therapy by one website (5%), with gynecomastia (35%) and increased hematocrit (35%) representing the most commonly described side effects. Prostate specific antigen (35%) and serum testosterone monitoring (30%) were the most commonly described monitoring parameters. The mean DISCERN score was 46.4, indicating fair guality information. The Flesh–Kincaid Grade Level was 12.2.

**Conclusion:** Online TRT information is incomplete, often failing to describe important safety information and the need for regular monitoring.

#### **ARTICLE HISTORY**

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#### **KEYWORDS**

Testosterone; men's health; hypogonadism; consumer health information; internet

# Introduction

Classic male hypogonadism (often referred to as testosterone deficiency) develops when the testis fail to produce physiological levels of testosterone due to a disruption in the hypothalamic-pituitary-testicular axis (HPTA). Disruptions to the HPTA at the testicular level cause primary testosterone deficiency, whereas central defects in the hypothalamus or pituitary cause secondary testosterone deficiency [1,2]. Testosterone deficiency can also develop secondary to aging, with serum levels decreasing by 1-2% per year [3,4], often referred to as late-onset hypogonadism (LOH) [5]. Other terms used to describe LOH include "low-T", "andropause", and "male menopause" [2]. Testosterone deficiency is associated with low sex drive, erectile dysfunction, impotence, fatigue, reduced muscle mass and strength, loss of body hair, depression, osteoporosis, metabolic syndrome, and anemia [1,2,5]. However, many of these signs and symptoms may also be due to other common comorbidities [6]. The serum testosterone threshold required to cause deficiency symptoms is highly variable between men, further complicating the diagnosis [7].

Administration of exogenous testosterone (known as testosterone replacement therapy or "TRT") is considered the standard of care for classic male hypogonadism [8]. TRT is associated with several side effects including gynecomastia, increased hematocrit, changes in lipid levels (increased LDL, lowered HDL), sleep apnea, and reduced fertility [9]. However, testosterone supplementation for treatment of LOH is riddled with controversy and uncertainty. Recent systematic reviews have reported minimal to no clinically meaningful improvements in guality of life, erectile dysfunction, mood, physical function, and cognition with TRT [10,11]. Uncertainty around the cardiovascular safety of TRT has also sparked debate, with some studies showing an increase in cardiovascular events [12-14], and others showing a neutral [15-19] or protective effect [20,21]. The United States Food and Drug Administration approved TRT for testosterone deficiency due to disorders of the testicles, pituitary gland, or brain, outlining that a lack of definitive efficacy and safety data precludes its approval for LOH [22]. Other regulatory agencies (Health Canada, and the European Medicines Agency) have taken a more liberal stance,

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approving TRT for men with clinical manifestations of testosterone deficiency and low testosterone levels [23,24].

The global sales of testosterone is estimated to have increased 12 fold, from \$150 million to \$1.8 billion, over an 11-year period (2000–2011) with the largest increase occurring in Canada [25]. A recent review found that there were various patient, provider, and healthcare system factors that have increased prescribing, including aggressive marketing, establishment of specialty clinics, online sales, and ambiguous guidelines [26]. Other possible contributors include directto-consumer advertising, creation of clinics dedicated to prescribing testosterone, mail-order internet pharmacies, and the improved ease of use with new transdermal formulations [24].

It is estimated that 60% of adult internet users in North America and Europe seek out health information online [27]. A recent survey of health information seekers found that the internet was the preferred source of health information [28]. It is important that patients have access to accurate health information. The need for accurate information is especially important for TRT given the unclear efficacy and safety data with TRT, together with a rapid increase in testosterone sales. The objective of this study is to describe the quality of information on websites providing patient-directed information on testosterone supplementation in men.

# **Methods**

## Study design

A quantitative content analysis was conducted to assess the quality of health information about TRT found on websites.

## Website selection

Websites were identified using Google from 10th March 2017 to 17th March 2017. Google was chosen to conduct the search as research suggests 65% of internet searches are performed using this search engine [29]. A single researcher (CM) completed the search using the following search terms: "testosterone supplementation AND men"; "testosterone replacement therapy AND men"; "testosterone deficiency AND men." Prior to conducting the search, the browser history and cookies were erased and all existing website data were removed to avoid generating personalized results. The first 3 pages of consecutive websites from each search term were screened with the inclusion and exclusion criteria. Previous studies have shown

that 90% of internet users will not click on a webpage beyond the first 3 pages of results [30].

To be included, websites had to target male patients and provide health information regarding TRT for the purpose of treating LOH, or associated terms. Associated terms included male menopause, andropause, low T, and low testosterone. Websites had to provide information on testosterone supplementation, and be written in the English language. Websites were excluded if they were duplicates, blogs, forums, required users to become members, discussed bioidentical or compounded testosterone therapy, targeted healthcare professionals or females, or if they provided information regarding the use of testosterone primarily for purposes other than for treatment of LOH.

#### Data abstraction

Data abstraction was completed by two investigators (CM, ES) independently; any discrepancies were resolved via consensus. If a consensus could not be reached, a third coder (CS) resolved the discrepancy.

The coding scheme was developed by the study investigators based on currently available clinical practice guidelines for TRT [1,2,5,31]. Data categories included: general website characteristics, the website's description of testosterone supplementation, efficacy and safety claims, and monitoring parameters for patients using TRT. The presence of commonly used words to describe testosterone (e.g. vitality, energy, and vigor) was also abstracted.

General website characteristics that were captured included: the source of the website (e.g. commercial company, professional organization, nonprofit organizations, government website, or general information websites). Data regarding uniform resource locator (e.g. .com, .org, .gov, .ca, or .net), geographic region of publication, the use of citations, and the time of last update were also captured.

To assess the description of testosterone supplementation, websites were assessed for the presence/ absence of a formal definition of TRT. This definition had to explain that TRT was the practice of taking exogenous testosterone via one or more routes for the purpose of treating male hypogonadism. Data regarding the type of TRT product and route of administration were also extracted.

Efficacy claims about testosterone supplementation included claims regarding treatment of LOH, increasing muscle mass, hair loss, erectile dysfunction, and low energy. Safety claims about testosterone supplementation included side effects, abnormal lab values, contraindications, common drug interactions and monitoring parameters.

## **Quality assessment**

The quality of information on each webpage was analyzed using the DISCERN tool. The DISCERN tool is a 16-item validated instrument used to estimate the quality of health-related information by a lay-person [32]. Each item is rated on a scale of 1 to 5, with a higher number being assigned to higher quality information. A score of 5 is assigned to items where the answer is a definite yes. A score of 1 is assigned to items where the answer is a definite yes. A score of 1 is assigned to items where the answer is a definite no. A score of 2 to 4 is assigned if the webpage meets the criterion of the item to some extent. Total possible score for the DISCERN is 75. Scores were then categorized based on quality as excellent (a score between 63 and 75), good (51 to 62), fair (39 to 50), poor (27 to 38), and very poor (15 to 26) [33,34].

# Readability assessment

The readability of each website was determined using the Flesch–Kincaid Grade Level (FKGL) formula which assigned a U.S. school-grade reading level that the average student in that grade could read [35]. The Flesch reading-ease score (FRES) was also calculated for each website. From the FRES, websites were classified as very easy to read (a score between 90 and 100), easy to read (80 to 89), fairly easy to read (70 to 79), standard (60 to 69), fairly difficult to read (50 to 59), difficult to read (30 to 49), or very difficult ( $\leq$ 29). A score  $\geq$ 60 is considered acceptable for most documents [36].

# Data analysis

Summary statistics were used to describe the data. The mean score and standard deviation were calculated for continuous data (DISCERN, FRES, and FKGL scores). All analysis was conducted with Microsoft Excel 2007.

# Results

## Search results

The search yielded 91 websites, of which 20 met the inclusion criteria. The reasons for exclusion of websites included duplicates (5%), directed at health professionals (30%), did not provide information on testosterone for treatment of hypogonadism (26%), discussion forums or blogs (9%), required membership or subscription (4%), website was not available (2%), and websites focused on bioidentical or compounded testosterone supplementation (1%). Search results are included in Figure 1.

# **General website characteristics**

The majority of websites were general information websites (45%) and originated from the United States (45%) and United Kingdom (25%). The mean FRES was 40.37 ( $\pm$ 10.37) and written at a Flesch–Kincaid Grade level of 12.16 ( $\pm$ 1.99) indicating a grade 12 or higher

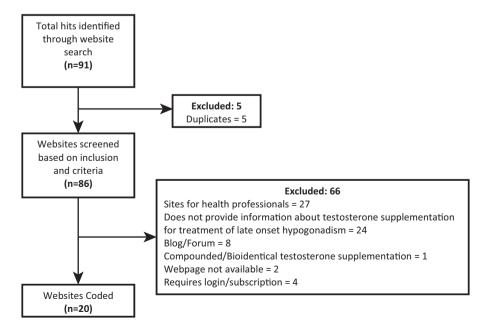


Figure 1. Inclusion and exclusion of websites identified through Google search.

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## Table 1. Website characteristics.

Characteristics	Websites $N = 20$ (%)
Source of website	
General information	9 (45)
Online magazine	2 (10)
Commercial company	2 (10)
Professional organization	2 (10)
Government	2 (10)
Non-profit organization	0 (0)
Other <sup>a</sup>	3 (15)
Website URL	
.com	10 (50)
.org	3 (15)
.gov	1 (5)
.ca	1 (5)
.net	0 (0)
Other <sup>b</sup>	5 (25)
Cites sources of information	12 (60)
Region	
United States	9 (45)
United Kingdom	5 (25)
Australia	3 (15)
Canada	1 (5)
Other	2 (10)
Time of last update	
Within 1 year	8 (40)
>2 years	7 (35)
Between 1 and 2 years	4 (20)
Unknown	1 (5)
Type of testosterone supplementation being described	Mean (SD)
General information	16 (80)
Commercial products	4 (20)
Grade and reading level	
Flesch reading ease score	40.37 (10.37)
Flesch–Kincaid grade level	12.16 (1.99)
<sup>a</sup> Other — educational institution, news provider	

<sup>a</sup>Other = educational institution, news provider.

<sup>b</sup>Other = .edu, .co.uk, .gov.au, .info.

reading level is required to read the text. Website characteristics are included in Table 1.

#### Description of testosterone supplementation

Most websites provided general information on testosterone (80%), with 20% describing a commercial testosterone product (Table 2). With respect to route of administration, 90% of websites described intramuscular, while 85% identified transdermal administration as a potential option. Oral testosterone was discussed by 60% of websites, while 40% discussed other testosterone formulations including implanted pellets, buccal tablets or patches, and intranasal sprays.

#### Efficacy of testosterone supplementation

Testosterone was claimed to have a general benefit in 40% of websites, while a benefit in LOH was mentioned in only 20% (Table 3). Specific efficacy claims made on websites included increased muscle mass (35%), increased energy (30%), erectile dysfunction (20%), and hair loss reversal (5%).

#### Table 2. Testosterone description.

Testosterone description	Websites <i>N</i> = 20 (%)
Definition of testosterone supplementation is provided	4 (20)
Route of administration	
Intramuscular	18 (90)
Transdermal/topical	17 (85)
Oral	12 (60)
Implanted subcutaneous pellets	7 (35)
Not Specified	2 (10)
Buccal tablet/patch	3 (15)

#### Table 3. Efficacy, safety, and monitoring claims of testosterone supplementation.

Efficacy of testosterone supplementation	Websites $N = 20$ (%)
General claim made stating testosterone has benefits	8 (40)
Testosterone claimed to be effective for late onset	5 (25)
hypogonadism or associated terms	
Testosterone claimed to be effective for signs	
and symptoms of hypogonadism	
Increased muscle mass	7 (35)
Low energy/fatigue	6 (30)
Erectile dysfunction	4 (20)
Hair loss	1 (5)
Other <sup>a</sup>	10 (50)
Safety of testosterone supplementation	
General claim made stating testosterone is safe	1 (5)
Discusses serious risks	
Prostate cancer	13 (65)
Cardiovascular (MI/stroke)	11 (55)
Side effects	
Gynecomastia	7 (35)
Mood disturbances	3 (15)
Insomnia	0 (0)
Abnormal lab values	
Increased hematocrit	7 (35)
Risk of abnormal lab values	3 (15)
Increased hemoglobin	1 (5)
Abnormal cholesterol/lipids	1 (5)
Absolute contraindications	
Prostate cancer	8 (40)
Male breast cancer	4 (20)
Prolactinoma	0 (0)
Monitoring of testosterone therapy	
Need for regular PSA testing	7 (35)
Need for regular testosterone levels	6 (30)
Need for yearly DRE	3 (15)
Need for regular liver function tests	1 (5)
Other <sup>b</sup>	2 (10)

<sup>a</sup>Other = Increased bone density, reduced insulin resistance, improved mood, improved immune function, improved endothelial function, reduced coronary heart disease, improved low urinary tract symptoms, improved prostate health, improved cognition, weight loss, increased libido, reduced risk of dementia, reduced risk of anemia, deepens voice <sup>b</sup>Other = BMD, estradiol, LUTS, sleep apnea, edema, breast growth.

#### Safety of testosterone supplementation

Testosterone was claimed to be safe by only 1 website (5%) (Table 3). Specific risks and side effects described by websites included prostate cancer (75%), cardiovascular risks (65%), gynecomastia (35%), increased hematocrit (35%), and mood disturbances (15%). Absolute contraindications include prostate cancer (40%) and male breast cancer (20%). None of the websites discussed drug interactions with testosterone. Specific monitoring parameters mentioned included regular serum testosterone levels (30%), prostate specific antigen (PSA) (35%), digital rectal exam (DRE) (15%), and liver function tests (LFT) (5%).

## **Other claims**

In addition to efficacy claims, the words energy, vitality, younger, and vigor were found on 65%, 30%, 25%, and 10% of websites, respectively (Figure 2). Other words or phrases found on websites included happiness, bloom, second adolescence, and longevity.

# **Quality of information**

The mean overall DISCERN score was  $46.4 \pm 10.81$  (Table 4). The highest mean score was for "does it describe the benefits of each treatment"  $(4.25 \pm 1.29)$ , and the lowest mean score was for "does it describe

what would happen if no treatment is used"  $(1 \pm 0.0)$ . In this analysis, 10% of websites were of very poor quality, 10% were poor quality, 40% were fair quality, and 40% were good quality. None of the websites were excellent quality (Figure 3).

# Discussion

#### Findings and implications

Our findings indicate that the majority (60%) of websites describing patient specific information on testosterone supplementation were "very poor" to "fair" quality. Although most websites provided information on the different routes of administration, our findings suggest that online information on TRT is inadequate, with minimal information on side effects, contraindications, drug interactions, or the need for monitoring. Recent studies indicate that aggressive direct-toconsumer advertising is associated with recent

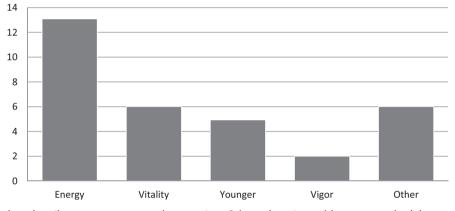


Figure 2. Words used to describe testosterone supplementation. Other = happiness, bloom, second adolescence, longevity.

Discern Instrument	Mean Rating (SD)	
Are the aims clear?	1.4 (0.60)	
Does it achieve its aims?	1.5 (2.11)	
Is it relevant?	3.95 (1.05)	
Is it clear what sources of information were used to compile the publication (other than the author or producer)?	2.4 (1.23)	
Is it clear when the information used or reported in the publication was produced?	3.2 (1.36)	
Is it balanced and unbiased?	3.3 (1.17)	
Does it provide details of additional sources of support and information?	3.15 (1.46)	
Does it refer to areas of uncertainty?	3.75 (1.74)	
Does it describe how each treatment works?	3.0 (1.03)	
Does it describe the benefits of each treatment?	4.25 (1.29)	
Does it describe the risks of each treatment?	3.55 (1.61)	
Does it describe what would happen if no treatment is used?	1 (0)	
Does it describe how the treatment choices affect overall quality of life?	3.2 (0.95)	
Is it clear that there may be more than one treatment choice?	3.55 (1.23)	
Does it provide support for shared decision making?	2.65 (0.75)	
Based on the answers to all of the above questions, rate the overall quality of the publication as a source of information about treatment choices?	2.65 (0.81)	
Total discern score (out of 75)	46.4 (10.81)	

Table	4.	Discern	instrument.
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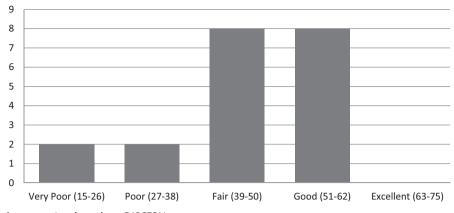


Figure 3. Overall webpage rating based on DISCERN score.

increases in testosterone use [37–39]. Given these marketing strategies, it is important that men have access to quality information on TRT.

There are a few encouraging findings to take from this analysis. One positive finding was that only a few websites made general claims of testosterone being effective for late onset hypogonadism, with fewer websites claiming testosterone as being a generally safe treatment. Findings indicate the majority of websites made an effort to describe the uncertainties surrounding testosterone therapy, with few websites making unfounded general claims of efficacy or safety. However, although the information on the websites was accurate, there were many missing details to help men make informed decisions about testosterone therapy. Another encouraging finding was that almost all the websites mentioned intramuscular or transdermal routes of administration, which is appropriate given that research indicates these are the two most commonly used routes [40,41]. However, few websites went into detail regarding the specific pros and cons associated with each formulation.

The overall lack of higher quality websites is concerning, as only 40% of the websites were rated as "good" quality. Studies have shown that majority of patients who use the internet to find health information do not have the background to enable them to accurately discern the credibility of a website [42-44]. Additionally, websites did not provide adequate safety information. Details outlining how testosterone may cause an increase in hematocrit and theoretical increased risk of venous thromboembolism were lacking on most websites [45]. None of the websites mentioned common drug interactions. For example, testosterone can increase insulin sensitivity, leading to a decreased need for insulin. If insulin doses are not adjusted, there is an increased risk of hypoglycemia [45]. Testosterone can also interact with anticoagulants such as warfarin [45]. It is important that men are aware of these interactions.

Our results are consistent with other studies published looking at online information. McBride et al. found that the majority of websites providing patientcentered information on TRT were of poor or sub-optimal quality, as only 30% of websites described at least 2 of 3 undefined risks and most were written at a high reading grade level [46]. Another study evaluating the quality of TRT focused patient information provided on healthcare provider websites found that less than half of the websites discussed the risks of TRT, and only 27% described any side effect [47].

#### Internet seeking behaviour

One reason men may turn to the internet for health information is that studies have shown that men feel their gender identity is threatened by seeking help from healthcare professionals [48]. Similarly, other research suggests patients feel empowered and more involved with their health decisions by seeking out information online [49,50]. A recent survey of 312 men with hypogonadism found that 82-89% of men obtained their health information from a healthcare professional, with  $\sim$ 20–30% obtaining information from online blogs/chats [51]. Although overall trends in health information seeking behavior show the internet as the most used source of information, hypogonadal men may be an exception. The use of the internet for disseminating information is a rational approach in engaging men, which is also supported by a recent study that used the internet in the UK to survey over 10,000 men internationally. They linked the survey regarding LOH symptoms to the Andropause Society and two other men's health websites [52]. The robust response indicates that men are accessing web-based information, and are willing to engage in online activities for research and to gather information.

## Readability

The readability of the websites was at a much higher grade level (12.1) compared to what the American Medical Association and the National Institutes on Health recommend for patient health information (no higher than a sixth-grade reading level) [53,54]. This is due in part to the fact that the average American reads at a grade 8 level [55,56]. Strategies to improve readability include reducing the number of syllables per word, reducing the number of words per sentence, avoiding the use of medical jargon, and utilizing bullet points.

## Limitations

Limitations of the study included a small sample size of websites (n = 20); however, these numbers are consistent with other studies of online health information [46,57]. Another limitation is the dynamic nature of the internet, as websites may have been updated or changed since the search was conducted. Our search strategy utilized the most popular search engine as well as simple search terms in an effort to emulate what a male would do when searching for TRT information; however, it is difficult to predict exactly how a man would search for this information. Although our study enabled us to capture what type of information is presented online, it does not speak to how this information affects men's opinion of TRT. Additionally, our study does not speak to the accuracy of online TRT information as there is currently no validated tool available to facilitate such an assessment. The DISCERN tool was validated in the 1990s for written information, and does not take into account how information is presented or organized on a website. Additionally, one question (does it describe what would happen if no treatment was used?) is not well suited to medical conditions that do not have dichotomous outcomes. All websites scored low on this question which may have been due to the non-dichotomous nature of LOH rather than the quality of the websites. In addition, we did not review all information that would impact decision making, such as duration of treatment. Addressing the duration of treatment and continuous versus intermittent use is important, particularly in light of research demonstrating that those with continuous exposure to treatment fared far better in terms of generalized symptoms, prostate symptom scores, obesity, and bladder function [58]. Future research is necessary to identify the ideal timing and duration of testosterone treatment in men with LOH. Future research efforts should assess how men may be impacted by online information on TRT.

## Conclusion

Information about TRT on the internet is not comprehensive, often failing to adequately describe important safety information and the need for regular monitoring and follow up. Most websites do not describe the various routes of administration in enough detail to support patients with their decision making. Additionally, websites are written at a higher readability level than what is currently recommended for patient health information. More effort is required to improve the quality of patient focused online TRT information.

#### **Disclosure statement**

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#### Notes on contributors

**Dr. Sehn** is a recent graduate from the pharmacy program at the University of Alberta. He currently practices in community pharmacy, providing pharmaceutical care for hypogonadal men on a daily basis. He has an interest in geriatrics and men's health and has also coauthored evidence based-medicine summaries, answering common questions in primary care.

*Cassidy Mozak* is a recent graduate of the pharmacy program at the University of Alberta. She currently practices in the community pharmacy setting. She has an interest in research and men's and women's health.

*Nese Yuksel* is a Professor at the University of Alberta and specializes in the area of women's health. She has a clinical practice in a mature women's health clinic, and conducts research on related topics, including osteoporosis, hormone therapy, and decision making for women. She also teaches on topics related to women's health (including hormonal contraception, menopause, menstrual related disorders, etc.). She has won numerous pharmacy practice and teaching awards in her career. She is also a NAMS Certified Menopause Practitioner (NCMP).

**Cheryl Sadowski** is a Professor at the University of Alberta and specializes in the area of geriatrics. She has a clinical practice in an interprofessional geriatric outpatient assessment clinic. She conducts research on geriatric syndromes, interprofessional education, and pharmacy practice change. She teaches geriatrics, men's health, and topics related to vulnerable populations, including those with disabilities. She has won pharmacy practice awards for her work in geriatrics, and teaching awards for innovation and team-based teaching. She is also a board certified geriatrics pharmacist.

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