## Post Finasteride Syndrome (PFS)

**What is PFS ?**

According to the Post-Finasteride Syndrome Foundation[1] Post-finasteride syndrome (PFS) describes persistent sexual, neurological, physical and mental adverse reactions in patients who have taken finasteride, a 5-alpha reductase type II enzyme inhibitor used to treat hair loss or enlarged prostate.

Unfortunately, PFS is a condition with no known cure and few, if any, effective treatments. As an increasing number of men report their persistent side effects to health and regulatory agencies worldwide, medical and scientific communities are only beginning to realize the scope of the problem.

**Does it really exist?**

In an article in Healhnewsreview.org "*Advocacy group spin may skew discussion on finasteride side effects*"[2] Dr Richard Hoffman writes:

> Until recently, however, I had never heard of the "Post-Finasteride Syndrome" (PFS). I received an e-mailed advisory — essentially a news release — from Dr. John Santmann, described as an emergency medicine-trained physician and health informaticist, who is the CEO of the Post-Finasteride Syndrome Foundation. (The document emailed to me was nearly identical to this "Global Public Health Advisory" on the PFS Foundation website.) Santmann alerted me that PFS is a condition that "often has a life-altering impact on victims and their families, such as job loss and the breakup of marriages and romantic relationships, while also being linked to suicides." The advisory was timed to coincide with the apparent addition of PFS to the NIH's Genetics and Rare Diseases Information Center (GARD) and because a meta-analysis just published in *JAMA Dermatology* (not the more prestigious *JAMA*, as erroneously reported by the advisory) noted the seemingly biased and poor quality of reporting on the sexual adverse harms of low-dose finasteride for androgenic alopecia (male-pattern baldness).
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> This alert raises some interesting issues. The sexual adverse harms of finasteride for BPH are well documented; I was not aware of any long-term harms following discontinuation of the drug. **The average age of men in the BPH treatment trials was about 65, so aging is also contributing to declining sexual function—thus confounding efforts to attribute harms to the medication.** However, many of the men enrolled in the hair-loss trials were in their 20s or 30s. Hair loss is not exactly a life-threatening condition, and sexual dysfunction certainly adversely affects quality of life. Expecting more rigorous efforts to determine the incidence and severity of important side effects of pharmacotherapy is reasonable—a point raised by an editorialist of the meta-analysis.
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> Nonetheless, **the advisory seems rather hyperbolic** in admonishing physicians to be vigilantly looking out for "symptoms in adverse drug reaction reports, suicide post-mortems, suicide-prevention services, and other patient records" and to alert the general population of this newly recognized condition. **These appeals strike me as**

[1] https://www.pfsfoundation.org/
[2] https://www.healthnewsreview.org/2015/08/advocacy-group-spins-harms-from-post-finasteride-syndrome/

**uncomfortably reminiscent of late-night TV and billboard pitches for malpractice attorneys.**

In highlighting the growing concerns about this condition, the Foundation cites ongoing studies at prominent institutions–implying that this has become a priority research issue. However, **these studies were actually funded by the Foundation**, in part to **"help establish PFS as a bona fide condition."** An announcement describing one of these studies and providing patient recruitment details refers to those suffering from finasteride-related side effects as "victims."

The NIH has also expressed concerned about the quality of media communications on this topic. The PFS Foundation advisory referenced above was headlined, "U.S. National Institutes of Health Recognizes Post-Finasteride Syndrome" — suggesting that the NIH had given its imprimatur to classify PFS as a rare disease. However, inquiries from HealthNewsReview.org suggest that the agency interprets things differently. Bobbi Gardner, a public affairs specialist at NIH, wrote that the purpose of the NIH Genetics and Rare Diseases Information Center is to distribute information about conditions or syndromes, "not to determine or proclaim something a rare disease." She emphasized that the page has a primary name "Adverse events of 5-alpha-reductase inhibitors" and was added in response to an outside inquiry. "The statement by the Post Finasteride Foundation you referenced therefore is not accurate and was not determined by us," she said.

Why is this important? While I applaud efforts to obtain better evidence about the possible side effects of finasteride and communicate that information to patients, **the public discussion about this issue seems to be troublingly skewed toward worst-case scenarios and personal stories highlighting speculative harms of the drug**. The *JAMA Dermatology* **meta-analysis did not find any evidence for a life-altering impact of finasteride, just that studies consistently failed to provide sufficient data to adequately characterize the potential harms of the drug. And yet the media coverage of the topic, based on these individual stories, presents an extremely dire portrait**.

**In a paper by Raymond Fertig et al *"Investigation of the Plausibility of 5-Alpha-Reductase Syndrome"*[3] it is noted:**

> Postfinasteride syndrome (PFS) is a term recently coined to characterize a constellation of reported undesirable side effects described in postmarketing reports and **small uncontrolled studies** that developed during or after stopping finasteride treatment, and persisted after drug discontinuation. Symptoms included decreased libido, erectile dysfunction, sexual anhedonia, decreased sperm count, gynecomastia, skin changes, cognitive impairment, fatigue, anxiety, depression, and suicidal ideation.
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> A literature review of adverse side effects associated with 5αRIs shows that persistent sexual side effects were **only documented in low-quality studies with strong bias selection as participants were part of an Internet blog.** The only high-quality study documenting persistent sexual side effects showed that these were **more frequent in the placebo than in the treatment group**, implying that the effects were not necessarily related to the treatment. A significant placebo/nocebo effect has been documented among patients informed about possible side effects of finasteride and this may explain the high prevalence of reported sexual dysfunction including persistent dysfunction in subjects participating in Internet groups and blogs. **Psychiatric side effects were only documented in moderate- or low-quality studies** including studies performed on patients with sexual side effects, which could influence patient's mood. Most of these studies recruited patients through the same Internet patient website.
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> Is the PFS a reality or not? Up to now, this question has gone unanswered. **The addition of PFS to the NIH's GARD database does not officially recognize PFS by the NIH**, but rather serves as a resource to find more information regarding reported adverse events.
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> **Persistent sexual and psychiatric side effects after 5αRIs are not documented by high-quality studies**, and prospective studies to establish true incidence and frequency of the problem are really needed. The NIH is currently funding a large epidemiological study, and we hope that the PFS Foundation will start to involve dermatologists in their advisory board in order to generate data from prospective and not retrospective studies. As dermatologist dealing with hair loss patients, we need to keep in mind that finasteride 1 mg is an improved medication and that [redacted](finasteride) labeling includes warnings of possible sexual dysfunction including persistent sexual dysfunction (such as difficulty in achieving an erection after discontinuing the medication), depression, breast tenderness, breast enlargement, and male breast cancer.

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6369643/

**In an article titled *"A Comment on the Post-Finasteride Syndrome"*[4] Rezende et al state:**

> The post-Finasteride syndrome (PFS) has been claimed to occur in men who have taken oral finasteride to treat hair loss or benign prostatic hyperplasia. While the incidence of persistent sexual, mental, and physical side effects despite quitting finasteride is unknown, **and the condition is not recognized by the scientific community,** individuals who suffer from PFS do present with very distinctive and homogenous symptoms. **The concept has emerged from reports of nondermatologists, neuroendocrinological research, case reports, and uncontrolled studies**. These have been scrutinized by hair experts who found that persistent sexual side effects were **only documented in low-quality studies with a strong bias selection and a significant nocebo effect.** Others totally dispute the credibility of the PFS.
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> In any case, the PFS is a problem that has to be dealt with. **Low-quality studies neither confirm nor refute the condition as a valid nosologic entity**. Therefore, it is as inappropriate to dismiss the condition, as it would be to demonize finasteride for the treatment of male pattern hair loss. Whether the PFS represents a nocebo reaction or a real drug adverse event is irrelevant, while **the best way to alleviate the emotional distress related to hair loss is to effectively treat the condition causing the problem.** It is not sufficient to only discuss the plausibility of the PFS. There is a need for practical recommendations to include such important issues as patient selection and risk assessment, appropriate patient information, how to react in case of drug-related adverse events, issues of fertility and malignancy, management of the PFS, and alternatives, specifically the use of topical finasteride.
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> The concept of the PFS has emerged from reports primarily of nondermatologists, neuroendocrinological research and considerations, case reports, and uncontrolled studies. These have recently been scrutinized by a group of hair experts. Their investigations into the plausibility of the syndrome were based on a comprehensive review of the respective medical literature. **The authors found that persistent sexual side effects were only documented in low-quality studies with strong bias selection, while a significant nocebo effect has been documented among patients** informed about the possible side effects of finasteride. Since the PFS has received disproportionate attention, especially of the nonmedical community, and legal action has been taken against the manufacturer of [redacted] (Merck), reinforcing the common belief in the authenticity of the condition, the authors concluded that prospective studies to establish the true incidence and frequency of the problem are mandatory, and that dermatologists need to be included in further investigations and the advisory board of the Post-Finasteride Syndrome Foundation, as they represent the major primary prescribers of finasteride for treatment of hair loss

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6369643/

**In a paper by Maksym et al *"Post-finasteride syndrome- does it really exist?"*[5] it is noted:**

> Testosterone (T) is a prohormone for androgen target cells and is converted in the endoplasmatic reticulum into dihydrotestosterone (DHT). DHT is the most potent natural ligand for the androgen receptor (AR). The transformation of T to DHT is conducted through the steroid 5a-reductase enzyme. DHT takes part in the pathogenesis of a number of human diseases, which include acne, hirsutism, androgenic alopecia, benign prostate hyperplasia (BPH), and prostate cancer. The search for treatment options for DHT-related disorders resulted in the development of a number of 5a-reductase inhibitors (5ARIs). The ideal 5ARI would selectively bind to different 5a-reductases with negligible or no affinity to the AR or other steroid receptors. Its low affinity for the AR protects against undesirable anti-androgen effects, such as impotence, impaired muscle growth or gynecomastia.
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> The recommended dose of finasteride that almost completely block reductase is usually 1mg or 5mg per day, but studies have shown, that even doses of 80 mg/day for 3 months did not reveal any severe adverse effects
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> Surprisingly, **the effect of finasteride on the DHT pharmacokinetic is not dose-dependent**, namely all daily finasteride doses between 0.4mg and 100mg lead to steady-state plasma levels of DHT between 0.1 and 0.15 ng/ml. The discontinuation of treatment results in a normalization of DHT levels within 2 weeks, irrespectively of the finasteride dose.
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> Data from the [redacted] Safety Plus Efficacy Canadian Two year study (PROSPECT) revealed that even placebo treatment was characterized by an unexpected high proportion of site effect (>40%), and **13.2% of the patients discontinued the placebo therapy due to adverse effects** [14], and a longer exposition to finasteride was relatively safe and did not cause the occurrence of new adverse effects.
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> This indicates that the high proportion of adverse event reports was an integral trait of the studied group of patients with BPH. **Another study showed that the administration of a small dose of finasteride (1 mg/day) did not cause any effects on erectile and orgasmic function, sexual desire, and sexual satisfaction evaluated by the IIEF-5 questionnaire**. The studied group includes males with androgenic alopecia evaluated after 4–6 months of therapy.
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> An analysis of data from a double-blind randomized [redacted] Long Term Efficacy and Safety Study (PLESS) on males with BPH showed a high adverse effect rate of 22%. Only 4% of the finasteride-treated group discontinued the treatment because of sexual side effects. In comparison, **2% of the placebo group ended the study because of sexual adverse effects**. However, the adverse event rate was similar to those reported in the placebo group after 2–4 years of treatment.
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> The adverse effects in the finasteride group were resolved only in 50% of the affected patients after discontinuation, **but the resolution rate was even lower (41%) in the placebo group**. **Interestingly, when patients were treated with finasteride and informed about a possible sexual dysfunction caused by the therapy, the nocebo effect was relatively significant. The fact of information being given at the beginning of the treatment caused a 14.3% increase in the reported sexual side effects to 43.6% .**

[5] https://www.ncbi.nlm.nih.gov/pubmed/30651009

Use of finasteride in a wide cohort of otherwise healthy and asymptomatic patients led to the description of more subtle adverse events that are observed less often, after longer times of use, or are less obvious and not easy to be self-reported. Post-finasteride syndrome (PFS) is usually described as the occurrence of persistent adverse events, including sexual dysfunction and depression, in a subset of men that used a 5a-reductase inhibitor. **Noteworthy is that these two symptoms commonly coexist also in subjects who are not exposed to finasteride.**

As meta-analysis has shown, the risk of sexual dysfunction is increased in the group of patients with depression (relative risk 1.52–1.71). The risk of depression is even more escalated in the group of patients with a sexual dysfunction (relative risk 1.69–3.12). **A similar persistent sexual dysfunction syndrome to PFS was observed in patients treated with selective serotonin reuptake inhibitors (SSRI) for depression. Moreover, the multifactorial background of adverse events, the subjective criteria of diagnosis and the variable reporting fraction in different health-care settings, make the problem hard to evaluate.**

The structure of the studies does not allow the relationship between these associations to be shown. 5ARI can potentially induce a brain disorder. **This association can also be an outcome of a higher prevalence of psychological disturbances in males who decided to use finasteride as a drug.**

**Controversies have surrounded the permanent effect that 5ARI has on sexual dysfunction since the first studies showed complete reversibility**. A review from 2008 reports that erectile dysfunction or a loss of libido affects less than 10%. Finasteride and dutasteride in high doses caused a dysfunction that was completely resolved when treatment was discontinued. **Moreover, treatment was discontinued due to sexual side effects only in 4% of patients. Further, a study on 3177 Japanese patients treated with small doses of finasteride for 41 months failed to reveal any sexual side effects**.

A current analysis of an unbiased population showed a rather low frequency of side effects. Among finasteride patients, only 22.7 in 100,000 (0.0227%) discontinued treatment due to sexual dysfunction.

**Conclusion**

Could it be that Post Finasteride Syndrome is something that is not based on clinical evidence and may well be an example of mass hysteria by a group of patients who have been self-selected to suffer from this ‘debilitating’ condition?

If Post Finasteride Syndrome was real would the TGA not have already removed this product from the ARTG?

The fact that the TGA have not removed finasteride from the ARTG would suggest that it is a safe and efficacious medicine.