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Hair Diseases

Is the Safety of Finasteride Correlated With Its Route of Administration: Topical Versus Oral? A Pharmacovigilance Study With Data From the United States Food and Drug Administration Adverse Event Reporting System

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ABSTRACT

Background: The United States Food and Drug Administration (FDA) approved oral finasteride for androgenetic alopecia. In 2022, approximately 2.6 million U.S. men used it for hair loss and prostate conditions. Post-finasteride syndrome (PFS), proposed in 2012, involves persistent sexual and neuropsychiatric adverse events (AEs) after cessation. These AEs are controversial and often lack assessment of contributing risk factors. We analyzed FDA Adverse Event Reporting System (FAERS) data to explore finasteride's administration route and PFS-like AEs.

Methods: Using the information component (IC) method for disproportionality analyses, we assessed signals for 13 PFS-related AEs with topical and oral finasteride and dutasteride across two periods: 2006–2011 (pre-PFS reporting) and 2019–2024 (post-PFS reporting). These periods reflect times before and after formal PFS reporting in 2012. Eight analyses per AE were conducted based on agent, route, and era.

Results: Fewer signals for PFS-like AEs were detected with topical finasteride compared to oral finasteride in both eras. No signals were found for topical dutasteride, possibly because its use is very limited. Many reported AEs, such as erectile dysfunction and depression, may be influenced by age, stress, or comorbidities.

Conclusions: Signals for PFS-like AEs were detected with topical finasteride, but were less frequent than with oral finasteride. The high prevalence of these AEs in the general population and the influence of confounding factors, such as psychological stress or nocebo effects, combined with the lack of genotyping, hormonal assessments, or family history data in most reports, suggest caution in attributing causality to finasteride. Topical finasteride may pose a lower risk, but robust evidence is needed to clarify its safety profile.

1 | Introduction

Androgenetic alopecia (AGA), a common form of hair loss, is associated with psychosocial distress [1]. Finasteride, a 5- α -reductase inhibitor (5-ARI), inhibits testosterone

conversion to dihydrotestosterone (DHT), a key contributor to AGA. The United States Food and Drug Administration (FDA) approved oral finasteride (1 mg/day) for AGA in 1997 [2, 3]. Finasteride is widely used globally, with approximately 2.6 million U.S. men prescribed it in 2022 for AGA and benign prostatic

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hyperplasia (BPH), suggesting millions more use it worldwide, though exact global figures are unavailable [4].

The safety of finasteride, particularly topical formulations, has sparked debate due to reports of sexual and neuropsychiatric United States Food and Drug Administration (FDA) approved, often labeled as post-finasteride syndrome (PFS) [3, 5]. PFS describes a group of sexual and neuropsychiatric AEs reported to persist after finasteride cessation, unlike accepted side effects such as mild sexual dysfunction that typically resolve after the medication is stopped [3]. Most PFS reports do not take into consideration confounding factors by genotyping for conditions like Klinefelter's syndrome, hypogonadism, or family history/preexisting history of depression, limiting the accuracy of causal inference [6]. These symptoms are highly prevalent in the general population, with erectile dysfunction affecting 20–40% of men over 40 years, depression occurring in 10–20% of adults, and suicidal ideation reported in 2–5% annually, driven by factors like age, comorbidities, and psychological stress [7–11]. Reports of PFS-like AEs with topical finasteride, such as gynecomastia or libido loss, have added to the controversy [5, 12, 13]. However, the evidence is mixed: some trials report no sexual or neuropsychiatric AEs with topical finasteride, while others note them [12–16].

Topical finasteride's potential transdermal absorption, bypassing hepatic metabolism, may increase bioavailability, but patient factors like skin permeability or psychological predisposition could also explain AE variability [17, 18]. Critics argue that the lack of standardized formulations and high baseline rates of these symptoms in the general population create an unclear clinical platform and undermine claims of causality [19]. Table 1 presents the indications and recommended dosages for oral finasteride, topical finasteride, and oral dutasteride [12, 20, 21].

This study uses FDA Adverse Event Reporting System (FAERS) data to compare PFS-like AEs between topical and oral finasteride and dutasteride, emphasizing that many reported AEs are non-specific and may reflect background rates or confounding factors rather than drug-specific effects.

2 | Materials and Methods

The conduct of our work was in accordance with guidelines of the reporting of a disproportionality analysis for drug safety

signal detection using individual case safety reports in pharmacovigilance (READUS-PV) collaborative [22]. No research ethics board approval was required, as human participants were not directly involved.

We mined FAERS to detect signals for 13 PFS-related AEs (e.g., erectile dysfunction, libido decreased, suicidal ideation) using the information component (IC) method for disproportionality analysis [23]. AEs were identified per Medical Dictionary for Regulatory Activities (MedDRA) version 27.0 terms. We analyzed topical and oral finasteride and dutasteride across two periods: 2006–2011 (pre-PFS reporting) and 2019–2024 (post-PFS reporting), reflecting times before and after PFS reporting in 2012. Eight analyses per AE were conducted based on agent, route, and era. We also characterized drug-level and patient-level factors across reports.

The FAERS database is comprised of seven data files (i.e., the 'DEMO', 'DRUG', 'INDI', 'OUTC', 'REAC', RPSR and 'THER' datasets) that—since 1969—are published quarterly. Our objectives required data from only the 'DEMO', 'DRUG' and 'REAC' datasets. As alluded to earlier, we used the IC method to conduct case/non-case disproportionality analysis for each of the 13 PFS AEs. Given that we investigated two agents (finasteride, dutasteride) and two routes of administration (topical, oral), we conducted a set of eight analyses for each PFS AE. We used the literature [24, 25] to inform our data mining approach, which involved deduplicating the data files.

For each IC disproportionality analysis, a signal is detected when the lower bound of the 95% confidence interval (CI) for IC exceeded 0. The IC and its 95% CI were calculated as per the following equations: Contingency table for count data used for the computation of IC and its 95% CI

$$IC = \log_2((a \times (a + b + c + d)) / ((a + c) \times (a + b)))$$

Lower bound of 95% confidence interval for IC =

$$\exp. ((\log(IC)) - 1.96 \times (((1/a) + (1/b) + (1/c) + (1/d))^{0.5}))$$

Upper bound of 95% confidence interval for IC =

$$\exp. ((\log(IC)) + 1.96 \times (((1/a) + (1/b) + (1/c) + (1/d))^{0.5}))$$

	Intervention of interest	All other drugs
Adverse effect of interest	a	c
All other adverse effects	b	d

TABLE 1 | Indications and recommended dosages for 5-ARIs.

Drug	Indications	Typical dosage	Approval status
Finasteride (oral)	Male androgenetic alopecia	1 mg once daily	FDA-approved
	Benign prostatic hyperplasia	5 mg once daily	FDA-approved
Finasteride (topical)	Male androgenetic alopecia	50–200 µL of 0.25% (w/w) solution	Not FDA-approved; however, approved in Italy, Germany, Luxembourg and Portugal
Dutasteride (oral)	Male androgenetic alopecia	0.5 mg once daily	Not FDA-approved; however, approved in South Korea and Japan
	Benign prostatic hyperplasia	0.5 mg once daily	FDA-approved

Abbreviation: 5-ARIs, 5-alpha-reductase inhibitors.

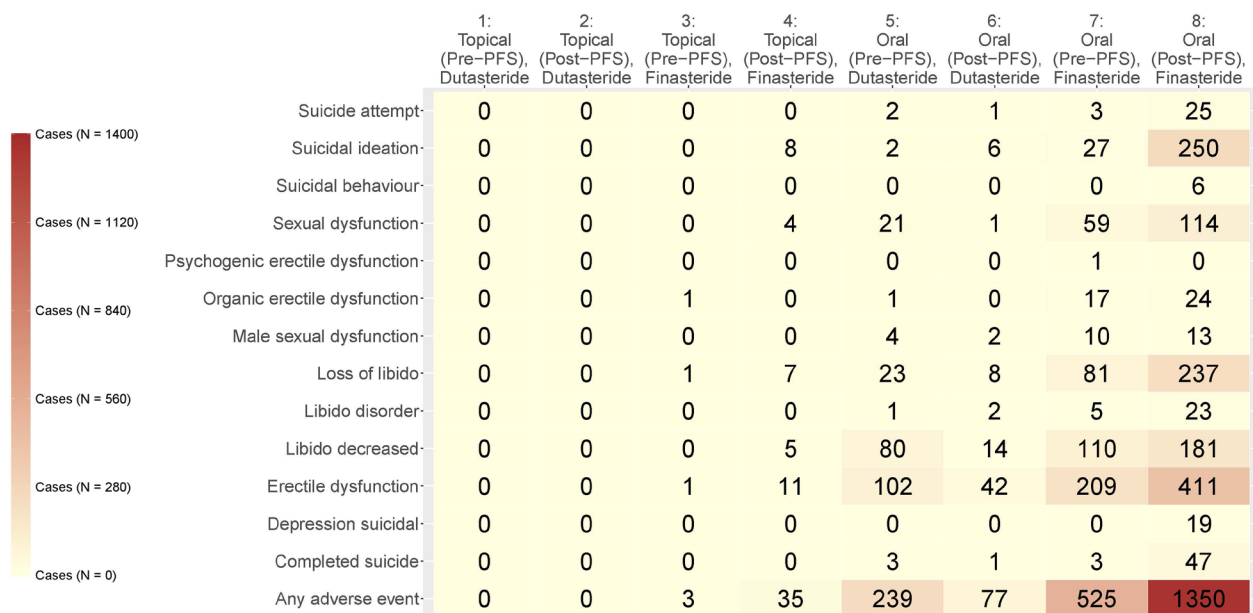


FIGURE 1 | Overall findings from disproportionality analyses. This Kilim plot depicts the number of reports of PFS-like AEs with topical and oral finasteride and dutasteride before and after PFS reporting in 2012. The darker the cell color, the more the number of reports for the respective route-agent-era group.

TABLE 2 | Association between finasteride use (topical vs. oral) and occurrence of adverse events (sexual and neuropsychiatric) between 2006 and 2011 (inclusive) and across men.

Adverse event	Topical finasteride		Oral finasteride	
	Number of cases	Lower bound of 95% CI of information component (IC)	No. of cases	Lower bound of 95% CI of information component (IC)
Sexual adverse events				
Erectile dysfunction	1	0.74	209	3.91
Libido decreased	0		110	4.74
Libido disorder	0		5	1.09
Loss of libido	1	1.22	81	5.4
Male sexual dysfunction	0		10	3.52
Sexual dysfunction	0		59	3.86
Organic erectile dysfunction	1	1.45	17	3.86
Psychogenic erectile dysfunction	0		1	0.87
Neuropsychiatric adverse events				
Completed suicide	0		3	—
Depression suicidal	0		0	
Suicidal behavior	0		0	
Suicidal ideation	0		27	0.99
Suicide attempt	0		3	—

Note: Information presented in this table is from disproportionality analyses—of FAERS—as per the Information Component (IC) method. Gray colored cells with bold text represent statistically significant ($p < 0.05$) associations as per the IC method.

Report characterization was performed such that summary information was provided across the eight ‘agent-route’ groups, namely, (1) Topical Dutasteride pre-PFS, (2) Topical Dutasteride post-PFS, (3) Topical Finasteride pre-PFS, (4) Topical Finasteride post-PFS, (5) Oral Dutasteride pre-PFS, (6) Oral Dutasteride post-PFS, (7) Oral Finasteride pre-PFS and (8) Oral Finasteride post-PFS. All analyses were conducted using RStudio [26].

3 | Results

The number of cases identified in the set of eight analyses, per PFS AE, are summarized in the Kilim plot in Figure 1; darker cells correspond to more reports (i.e., more cases). The number in each cell corresponds to the number of reports with the respective AE and agent-route modality (Figure 1). For example, under ‘3: Topical (pre-PFS) Finasteride’, the first cell (from the top) with the value of 1 means there was 1 report of organic erectile dysfunction with topical finasteride between 2006 and 2011 (inclusive). Insofar as a ‘big picture overview’ of the plot the color gradient is such that the cells under the orals are darker than those under topicals; per administrative route, the cells for finasteride are darker than the cells for dutasteride (Figure 1).

Tables 2–5 summarize findings from disproportionality analyses; the lower bound of the 95% CI for the respective IC is

presented with signals depicted in bold text and darkly colored gray cells. For instance, in Table 2, the 3 reports for completed suicide with oral finasteride (pre-PFS) did not constitute a signal. A signal was detected for erectile dysfunction with both routes of finasteride across both periods (Tables 2 and 3). Furthermore, erectile dysfunction constituted the greatest proportion of PFS AEs across all agent-route groups (Figure 1, Tables 2–5). There were no PFS AE reports with topical dutasteride. Table 6 summarizes drug-level and patient-level characteristics across the eight agent-route groups.

4 | Discussion

Post-finasteride syndrome (PFS) remains controversial due to the lack of conclusive evidence substantiating that finasteride is the cause of persistent sexual and neuropsychiatric AEs [27], unlike recognized side effects that typically resolve when medication is discontinued. However, most reports lack genotyping for contributory clinical conditions like Klinefelter's syndrome (most are 47XXY) which affects an estimated 250,000 men in the US [28] or laboratory analysis to exclude, for example, other causes of hypogonadism or family history/preexisting history of anxiety, depression, or suicide, which may contribute to these AEs [6]. Given the widespread use of finasteride, with millions of men likely exposed annually, the

TABLE 3 | Association between finasteride use (topical vs. oral) and occurrence of adverse events (sexual and neuropsychiatric) between 2019 and 2024 (inclusive) and across men.

Adverse event	Topical finasteride		Oral finasteride	
	Number of cases	Lower bound of 95% CI of information component (IC)	No. of cases	Lower bound of 95% CI of information component (IC)
Sexual adverse events				
Erectile dysfunction	11	3.32	411	4.32
Libido decreased	5	2.83	181	4.76
Libido disorder	0		23	3.63
Loss of libido	7	3.75	237	5.71
Male sexual dysfunction	0		13	2.95
Sexual dysfunction	4	2.35	114	3.83
Organic erectile dysfunction	0		24	4.77
Psychogenic erectile dysfunction	0		0	
Neuropsychiatric adverse events				
Completed suicide	0		47	1.11
Depression suicidal	0		19	2.59
Suicidal behavior	0		6	1.03
Suicidal ideation	8	2.47	250	3.02
Suicide attempt	0		25	0.53

Note: Information presented in this table is from disproportionality analyses—of FAERS—as per the Information Component (IC) method. Gray colored cells with bold text represent statistically significant ($p < 0.05$) associations as per the IC method.

potential for coincidental overlap with common conditions is significant [4].

The present study found fewer PFS-like AE signals with topical finasteride compared to oral finasteride, and none with topical dutasteride. It is important to note that the use of topical dutasteride remains limited, though some studies have explored dutasteride mesotherapy. Mesotherapy with 0.01% dutasteride, administered every three months, commonly causes localized pain (reported in 45.5% of cases) but shows minimal systemic absorption [29]. This treatment is not FDA-approved, and no standardized protocol exists in North America.

However, the high prevalence of these AEs in the general population raises questions about causality. For example, erectile dysfunction affects 20–40% of men over 40 years, and depression is reported in 10–20% of adults [7, 8]. These rates suggest that AEs reported in finasteride users may reflect population incidence rather than drug-specific effects.

Confounding factors further complicate attribution. Age, a key risk factor for sexual dysfunction, aligns with AGA's typical onset (30–40 years), when men may naturally experience declining testosterone or increased stress [30, 31]. Comorbidities like diabetes, hypertension, and obesity, common in middle-aged men, are also linked to erectile dysfunction and mood disorders [31].

Psychological factors, including the nocebo effect, may amplify perceived AEs, particularly after heightened PFS reporting post-2012 [32, 33]. An additional factor identified with increased reporting is the impact of social media and common-hosted media sites [34]. Increased consumer reporting post-PFS reporting (70% for oral finasteride post-PFS reporting vs. 52% pre-PFS reporting) may reflect reporting bias rather than true AE incidence.

The low rate of positive rechallenge (e.g., 9.4% for topical finasteride post-PFS reporting) and missing data in FAERS reports weaken evidence for causality [35]. Randomized trials on topical finasteride, using validated tools like the International Index of Erectile Function, show inconsistent AE reporting, with some noting no sexual AEs [12, 15, 36]. This variability may stem from differences in patient populations, skin permeability, or psychological predispositions [18].

Postmarketing surveillance data, like FAERS, are prone to biases (e.g., underreporting, reporting bias), limiting causal inferences [27]. Randomized trials often fail to balance prognostic factors post-randomization, and early oral finasteride trials lacked validated AE assessment tools [27]. Recent transparency improvements, such as unsealed AE documents, confirm erectile dysfunction's frequency amongst some finasteride users; however, given the common population incidence of this finding, it does not indicate or establish causation [27].

TABLE 4 | Association between dutasteride use (topical vs. oral) and occurrence of adverse events (sexual and neuropsychiatric) between 2006 and 2011 (inclusive) and across men.

Adverse event	Topical dutasteride		Oral dutasteride	
	Number of cases	Lower bound of 95% CI of information component (IC)	No. of cases	Lower bound of 95% CI of information component (IC)
Sexual adverse events				
Erectile dysfunction	0		102	2.86
Libido decreased	0		80	4.24
Libido disorder	0		1	0.52
Loss of libido	0		23	3.29
Male sexual dysfunction	0		4	1.99
Sexual dysfunction	0		21	2.3
Organic erectile dysfunction	0		1	0.31
Psychogenic erectile dysfunction	0		0	
Neuropsychiatric adverse events				
Completed suicide	0		3	2.3
Depression suicidal	0		0	
Suicidal behavior	0		0	
Suicidal ideation	0		2	—
Suicide attempt	0		2	—

Note: Information presented in this table is from disproportionality analyses FAERS per the Information Component (IC) method. Gray colored cells with bold text represent statistically significant ($p < 0.05$) associations as per the IC method.

TABLE 5 | Association between dutasteride use (topical vs. oral) and occurrence of adverse events (sexual and neuropsychiatric) between 2019 and 2024 (inclusive) and across men.

Adverse event	Topical dutasteride		Oral dutasteride	
	Number of cases	Lower bound of 95% CI of information component (IC)	No. of cases	Lower bound of 95% CI of information component (IC)
Sexual adverse events				
Erectile dysfunction	0		42	3.83
Libido decreased	0		14	2.17
Libido disorder	0		2	0.95
Loss of libido	0		8	1.73
Male sexual dysfunction	0		2	1.06
Sexual dysfunction	0		1	—
Organic erectile dysfunction	0		0	
Psychogenic erectile dysfunction	0		0	
Neuropsychiatric adverse events				
Completed suicide	0		1	—
Depression suicidal	0		0	
Suicidal behavior	0		0	
Suicidal ideation	0		6	—
Suicide attempt	0		1	—

Note: Information presented in this table is from disproportionality analyses FAERS per the information component (IC) method. Gray colored cells with bold text represent statistically significant ($p < 0.05$) associations as per the IC method.

Topical finasteride's lower AE signals suggest a potentially safer profile, possibly due to reduced systemic exposure [3]. However, its transdermal potential and variability in skin absorption warrant further study [17]. The lack of standardized formulations in some regions adds complexity to safety assessments.

5 | Prevalence of PFS-Like Symptoms in the General Population

Many PFS-associated symptoms are non-specific and common. Erectile dysfunction affects 20–40% of men over 40 years, increasing with age, diabetes, hypertension, smoking, and psychological stress [7, 10]. Reduced libido is reported in 10–20% of men, often linked to stress, hormonal changes, or relationship issues [11]. Depression and anxiety have a lifetime prevalence of 10–20% and 15–30%, respectively, with higher rates in men with chronic conditions or genetic predispositions [8]. Between 30% and 55% of suicidal behavior in twin studies is heritable [37]. Additional factors include chronic stress, trauma, and substance abuse [34]. Suicidal ideation, while less common than anxiety and depression, occurs in 2–5% of adults annually and is associated with depression, social isolation, and economic stressors [9]. These baseline rates suggest that AEs reported in finasteride users may coincide with expected population trends, especially

in middle-aged men with AGA, who may face psychosocial stress [1].

6 | Confounding Factors

Confounders like age, comorbidities, and psychological factors likely contribute to reported AEs. Men with AGA, often in their 30s–40s, may experience natural declines in sexual function or mood, independent of finasteride [30]. Stress from hair loss itself is a known risk factor for anxiety and depression [1]. The placebo effect, heightened by PFS reporting, and fueled by social media posting, may lead to over-reporting of symptoms [32–34]. Skin conditions affecting absorption (e.g., psoriasis) could also explain variability in topical finasteride AEs [18]. These factors highlight the challenge of isolating and proving a causal link in finasteride's role in persistent AEs reported as PFS.

7 | Conclusions

This study detected fewer PFS-like AE signals with topical finasteride compared to oral finasteride, with no signals for topical dutasteride. Given the widespread use of finasteride, overlap with common conditions like sexual dysfunction and

TABLE 6 | Characterization of all reports.

Characteristic	1: Topical Dutasteride pre-PFS (N=0)	2: Topical Dutasteride post-PFS (N=0)	3: Topical Finasteride pre-PFS (N=3)	4: Topical Finasteride post-PFS (N=35)	5: Oral Dutasteride pre-PFS (N=239)	6: Oral Dutasteride post-PFS (N=77)	7: Oral Finasteride pre-PFS (N=525)	8: Oral Finasteride post-PFS (N=1350)	p-value
Age, years									<0.001
Missing	—	—	0	2	33	11	79	233	
Mean (SD)	—	—	24.0 (0.0)	31.1 (9.6)	64.0 (11.6)	46.1 (23.8)	35.9 (12.9)	35.0 (13.7)	
Range	—	—	24.0–24.0	16.0–56.0	20.0–84.0	21.0–96.0	17.0–75.0	15.0–96.0	
Weight, kilograms									0.124
Missing	—	—	3	3	218	30	352	367	
Mean (SD)	—	—	NA	77.3 (10.3)	88.8 (12.0)	81.6 (15.6)	80.3 (12.1)	80.1 (17.2)	
Range	—	—	NA	61.6–99.9	70.0–117.0	54.9–107.0	56.0–124.7	44.5–165.5	
Rechallenge									<0.001
Rechallenge refers to planned re-introduction of a drug after its discontinuation due to suspected AEs linked to it									
• Positive rechallenge means AE reappears after the re-introduction									
• Negative rechallenge means AE does not appear after the re-introduction									
Missing	—	—	3	3	236	49	342	889	
D → Does not apply	—	—	0	28 (87.5%)	2 (66.7%)	13 (46.4%)	168 (91.8%)	248 (53.8%)	
N → Negative rechallenge	—	—	0	0 (0.0%)	1 (33.3%)	7 (25.0%)	4 (2.2%)	9 (2.0%)	
U → Unknown	—	—	0	1 (3.1%)	0 (0.0%)	8 (28.6%)	2 (1.1%)	168 (36.4%)	
Y → Positive rechallenge	—	—	0	3 (9.4%)	0 (0.0%)	0 (0.0%)	9 (4.9%)	36 (7.8%)	
Drug's reported role									0.004
Concomitant	—	—	0 (0.0%)	0 (0.0%)	6 (2.5%)	1 (1.3%)	13 (2.5%)	23 (1.7%)	
Primary Suspect Drug	—	—	3 (100.0%)	30 (85.7%)	229 (95.8%)	69 (89.6%)	476 (90.7%)	1186 (87.9%)	

(Continues)

TABLE 6 | (Continued)

Characteristic	1: Topical Dutasteride pre-PFS (N=0)	2: Topical Dutasteride post-PFS (N=0)	3: Topical Finasteride pre-PFS (N=3)	4: Topical Finasteride post-PFS (N=35)	5: Oral Dutasteride pre- PFS (N=239)	6: Oral Dutasteride post-PFS (N=77)	7: Oral Finasteride pre- PFS (N=525)	8: Oral Finasteride post-PFS (N=1350)	p-value
Secondary Suspect Drug	—	—	0 (0.0%)	5 (14.3%)	4 (1.7%)	7 (9.1%)	36 (6.9%)	141 (10.4%)	
Reporter's occupation									<0.001
Missing	—	—	0	0	2	6	76	14	
Consumer	—	—	3 (100.0%)	35 (100.0%)	209 (88.2%)	56 (78.9%)	233 (51.9%)	930 (69.6%)	
Health Professional	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (11.3%)	0 (0.0%)	121 (9.1%)	
Lawyer	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	50 (11.1%)	23 (1.7%)	
Physician	—	—	0 (0.0%)	0 (0.0%)	16 (6.8%)	6 (8.5%)	95 (21.2%)	201 (15.0%)	
Other	—	—	0 (0.0%)	0 (0.0%)	11 (4.6%)	0 (0.0%)	62 (13.8%)	31 (2.3%)	
Pharmacist	—	—	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (1.4%)	9 (2.0%)	30 (2.2%)	
Country that reported AE									<0.001
Missing	—	—	0	0	0	0	4	0	
AR → Argentina	—	—	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	6 (0.4%)	
AT → Austria	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	
AU → Australia	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.8%)	4 (0.3%)	
BE → Belgium	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
BG → Bulgaria	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
BR → Brazil	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (0.1%)	
CA → Canada	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (6.5%)	20 (3.8%)	68 (5.0%)	
CH → Switzerland	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
CN → China	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (0.7%)	
Not specified	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	
CZ → Czech Republic	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.2%)	
DE → Germany	—	—	0 (0.0%)	0 (0.0%)	5 (2.1%)	1 (1.3%)	8 (1.5%)	179 (13.3%)	

(Continues)

TABLE 6 | (Continued)

Characteristic	1: Topical Dutasteride pre-PFS (N=0)	2: Topical Dutasteride post-PFS (N=0)	3: Topical Finasteride pre-PFS (N=3)	4: Topical Finasteride post-PFS (N=35)	5: Oral Dutasteride pre- PFS (N=239)	6: Oral Dutasteride post-PFS (N=77)	7: Oral Finasteride pre- PFS (N=525)	8: Oral Finasteride post-PFS (N=1350)	p-value
DK → Denmark	—	—	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	2 (0.4%)	3 (0.2%)	
EC → Ecuador	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	
ES → Spain	—	—	0 (0.0%)	0 (0.0%)	1 (0.4%)	17 (22.1%)	0 (0.0%)	42 (3.1%)	
FI → Finland	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	2 (0.1%)	
FR → France	—	—	0 (0.0%)	0 (0.0%)	2 (0.8%)	0 (0.0%)	1 (0.2%)	166 (12.3%)	
GB → United Kingdom	—	—	0 (0.0%)	1 (2.9%)	0 (0.0%)	10 (13.0%)	42 (8.1%)	188 (13.9%)	
GR → Greece	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
HR → Croatia	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
HU → Hungary	—	—	0 (0.0%)	0 (0.0%)	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
IE → Ireland	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	4 (0.8%)	3 (0.2%)	
IL → Israel	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.6%)	8 (0.6%)	
IN → India	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.2%)	
IT → Italy	—	—	0 (0.0%)	1 (2.9%)	0 (0.0%)	2 (2.6%)	6 (1.2%)	93 (6.9%)	
JP → Japan	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (9.1%)	6 (1.2%)	3 (0.2%)	
KR → South Korea	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.6%)	0 (0.0%)	1 (0.1%)	
MY → Malaysia	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	4 (0.3%)	
NL → Netherlands	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (5.2%)	0 (0.0%)	11 (0.8%)	
NO → Norway	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.8%)	11 (0.8%)	
PE → Peru	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	
PK → Pakistan	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.4%)	
PL → Poland	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (5.2%)	0 (0.0%)	0 (0.0%)	
PR → Puerto Rico	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	
PT → Portugal	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	
RO → Romania	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	

(Continues)

TABLE 6 | (Continued)

Characteristic	1: Topical Dutasteride pre-PFS (N=0)	2: Topical Dutasteride post-PFS (N=0)	3: Topical Finasteride pre-PFS (N=3)	4: Topical Finasteride post-PFS (N=35)	5: Oral Dutasteride pre-PFS (N=239)	6: Oral Dutasteride post-PFS (N=77)	7: Oral Finasteride pre-PFS (N=525)	8: Oral Finasteride post-PFS (N=1350)	p-value
SE → Sweden	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)	3 (0.2%)	
SG → Singapore	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	
SI → Slovenia	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	4 (0.3%)	
TR → Turkey	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	
US → United States	—	—	3 (100.0%)	33 (94.3%)	227 (95.0%)	21 (27.3%)	416 (79.8%)	495 (36.7%)	
ZA → South Africa	—	—	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	

depression is expected [4]. However, the high prevalence of sexual and neuropsychiatric AEs in the general population, along with confounding factors such as age, stress, and comorbidities, suggests that persistent symptoms may not be causally linked to finasteride. The placebo effect and increased reporting post-2012 likely contributed to reporting biases.

The study suggests that topical finasteride may have a lower risk profile due to reduced systemic exposure, but further investigation through robust clinical trials is needed. PFS remains a controversial diagnosis, with regulatory bodies (e.g., FDA, United Kingdom Medicines and Health care products porting agency, and Health Canada) acknowledging safety concerns but not validating it as a distinct syndrome. For most patients, AEs associated with finasteride are minimal or resolve upon discontinuation. Advocacy groups could advance patient safety by funding research to identify potential risk factors for AEs. Overall, finasteride remains an effective treatment for AGA-related hair loss. Healthcare providers should inform patients about potential AEs and clarify that some symptoms often attributed to PFS are common in individuals not using finasteride.

Ethics Statement

Given that human subjects were not involved, approval from a research ethics board was not required.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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