

Investigation of Suicidality and Psychological Adverse Events in Patients Treated With Finasteride

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Editorial

IMPORTANCE There is ongoing controversy about the adverse events of finasteride, a drug used in the management of alopecia and benign prostatic hyperplasia (BPH). In 2012, reports started emerging on men who had used finasteride and either attempted or completed suicide.

OBJECTIVE To investigate the association of suicidality (ideation, attempt, and completed suicide) and psychological adverse events (depression and anxiety) with finasteride use.

DESIGN, SETTING, AND PARTICIPANTS This pharmacovigilance case-noncase study used disproportionality analysis (case-noncase design) to detect signals of adverse reaction of interest reported with finasteride in Vigibase, the World Health Organization's global database of individual case safety reports. To explore the strength of association, the reporting odds ratio (ROR), a surrogate measure of association used in disproportionality analysis, was used. Extensive sensitivity analyses included stratifying by indication (BPH and alopecia) and age (≤ 45 and >45 years); comparing finasteride signals with those of drugs with different mechanisms but used for similar indications (minoxidil for alopecia and tamsulosin hydrochloride for BPH); comparing finasteride with a drug with a similar mechanism of action and adverse event profile (dutasteride); and comparing reports of suicidality before and after 2012. Data were obtained in June 2019 and analyzed from January 25 to February 28, 2020.

EXPOSURES Reported finasteride use.

MAIN OUTCOMES AND MEASURES Suicidality and psychological adverse events.

RESULTS Vigibase contained 356 reports of suicidality and 2926 reports of psychological adverse events (total of 3282 adverse events of interest) in finasteride users (3206 male [98.9%]; 615 of 868 [70.9%] with data available aged 18-44 years). A significant disproportionality signal for suicidality (ROR, 1.63; 95% CI, 1.47-1.81) and psychological adverse events (ROR, 4.33; 95% CI, 4.17-4.49) in finasteride was identified. In sensitivity analyses, younger patients (ROR, 3.47; 95% CI, 2.90-4.15) and those with alopecia (ROR, 2.06; 95% CI, 1.81-2.34) had significant disproportionality signals for increased suicidality; such signals were not detected in older patients with BPH. Sensitivity analyses also showed that the reports of these adverse events significantly increased after 2012 (ROR, 2.13; 95% CI, 1.91-2.39).

CONCLUSIONS AND RELEVANCE In this pharmacovigilance case-noncase study, significant RORs of suicidality and psychological adverse events were associated with finasteride use in patients younger than 45 years who used finasteride for alopecia. The sensitivity analyses suggest that these disproportional signals of adverse events may be due to stimulated reporting and/or younger patients being more vulnerable to finasteride's adverse effects.

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Concerns have emerged about the adverse effects of finasteride, a drug indicated for the management of both male-pattern baldness (androgenetic alopecia)^{1,2} and benign prostatic hyperplasia (BPH).³⁻⁵ Reports of suicidality and psychological adverse events related to finasteride have led to coining of the term *postfinasteride syndrome* and the creation of organizations such as the Post-Finasteride Syndrome Foundation.⁶⁻¹⁰ In 2011, a postmarketing report was sent to the US Food and Drug Administration suggesting that finasteride may be linked to depression, self-harm, and suicide.¹¹ In the last 5 years, health authorities in Canada, Korea, New Zealand, and the United Kingdom have also acknowledged these potential adverse effects and issued warnings for finasteride.¹²⁻¹⁵

There is a plausible biological basis linking finasteride, a 5 α -reductase inhibitor (5ARI), with depression and anxiety. Some reports suggest that men with depression have lower levels of the neurosteroid allopregnanolone, which is produced by the 5 α -reductase enzyme and has antidepressant and anxiolytic effects.¹⁶⁻¹⁸ Broader clinical context, however, is lacking for this association. At the population level, studies have found an increased risk of depression associated with finasteride use among patients with BPH.¹⁹⁻²¹ Most of these studies relied on claims data,²² although 1 study that used a validated screening tool for depression²³ found an association between finasteride exposure and depression.

Studies on the association between suicidality and finasteride use are limited. In a large cohort of men 66 years or older with BPH, Welk et al¹⁹ found no increased risk of completed suicide with finasteride but did identify an increased risk of self-harm compared with unexposed men. To the contrary, an analysis of the US Food and Drug Administration's Adverse Event Reporting System database found disproportional reporting of suicidal ideation among men using finasteride for alopecia, but the sample size was limited to 39 men.²⁴ Given the limited evidence, we performed a pharmacovigilance study to further investigate the association between finasteride use and suicidality (ideation, attempt, and completed suicide) and psychological adverse events (depression and/or anxiety) using VigiBase, the World Health Organization's international database of individual case safety reports.²⁵

Methods

Data Source

VigiBase collects data from 153 countries on all drug-adverse reaction pairs. It is managed by the Uppsala Monitoring Centre, the World Health Organization Collaborating Centre for International Drug Monitoring. It is the largest database of its kind and contains more than 20 million safety reports of suspected medication adverse events, dating from 1967 to 2019. These reports originate from a variety of sources, including physicians, other health care professionals, patients, and pharmaceutical companies.²⁵ Data abstracted include patient demographic characteristics, drug dosage, reported reaction, and Medical Dictionary for Regulatory Activities (MedRA) classification terms. A waiver of institutional review board

Key Points

Question Is finasteride use associated with more spontaneous reports of suicidality, depression, and/or anxiety?

Findings This pharmacovigilance case-noncase study of 3282 users of finasteride used VigiBase, the World Health Organization's global database of individual case safety reports, and found a disproportional signal of suicidality, depression, and anxiety associated with finasteride use for alopecia in patients younger than 45 years. No such signal was associated with drugs that had different mechanisms of action but similar indications or with drugs that had similar mechanisms and adverse effect profiles.

Meaning This study's findings suggest that the risk of suicidality, depression, and anxiety should be considered when prescribing finasteride to younger patients with alopecia who may be more vulnerable to the drug's adverse effects; this association may be biased by stimulated reporting and should be further investigated.

approval was obtained from the institutional review boards of Brigham and Women's Hospital and Massachusetts General Hospital before the start of the study, owing to the use of deidentified data.

Inclusion and Exclusion Criteria

VigiBase includes spontaneous reports of adult patients receiving finasteride for any indication, at any dose, and reporting any adverse event, all of whom we included. Except for duplicate reports, no patients were excluded from the analysis to ensure that any bias of finasteride reports, such as misclassification, was similar to bias present in the rest of the database, which was used as the comparator.²⁶⁻³⁰ To identify duplicate reports, we used a published record-linkage strategy that groups the records by 8 fields: country, sex, age-reaction, reported outcome variable (reoutcome), preferred base name, reported term, onset date, and start date. If there was overlap in at least 7 of the 8 fields, the records were considered duplicates and removed.³¹

End Points

The primary end point was any suicide-related adverse event, commonly described as suicidality. Suicidality was subcategorized into suicidal ideation, attempted suicide, and completed suicide. Secondary end points were depression or anxiety. Because the more granular MedRA descriptors for the psychological adverse events (depression and anxiety) significantly overlapped, we did not further subcategorize them and will refer to them as psychological adverse events from this point. All adverse event end points were defined and identified using standardized MedRA terminology.

Statistical Analysis

Data were obtained in June 2019 and analyzed from January 25 to February 28, 2020. Descriptive statistics were calculated for patient demographics. Means and SDs were generated for continuous variables. Frequencies and proportions were generated for categorical variables.

Disproportionality analysis, a validated case-noncase method in drug safety research, was used to assess whether

suicidality or psychological adverse events were more frequently reported than would be expected by chance alone with finasteride compared with suicidality and psychological adverse events reported for all the other drugs in VigiBase.²⁶⁻³⁰ Because there is no control group consisting of individuals taking the drug of interest but not experiencing an adverse event, pharmacovigilance uses all other reports of adverse events in the database (with drugs other than the drug of interest) as comparators. If the proportion of a specific adverse event is significantly higher for finasteride than it is for any other drug in the database, a disproportionality signal suggests that there is an association between finasteride and the specific adverse event.²⁶⁻³⁰

Two common methods to report findings from a disproportionality analysis are the reporting odds ratio (ROR) and empirical Bayes estimator (EBE). The ROR is a frequentist measure of association, derived from the contingency table of the drug and counts of adverse events. If the lower bound of the ROR's 95% CI is greater than 1.00, this indicates a disproportionality signal and can be interpreted as significantly more adverse events observed for the drug of interest than one would expect by chance alone.³²⁻³⁴ A limitation of using the ROR is not being robust to sampling variability when events are rare. Alternatively, the EBE is more robust to variability when event counts are low but lacks interpretability. The EBE assumes a Poisson distribution for every cell count with an unknown true mean. It fits prior and posterior distributions for each ratio, allowing the calculation of posterior values. Because the EBE is a more conservative measure, we calculated the 5th percentile value of the EBE for all adverse events of interest and used it as a conservative threshold for signal detection.²⁶ If a signal was detected based on the EBE, we would only then obtain and report the ROR with 95% CI.³⁵ In addition, we examined the dose-response association by evaluating whether higher doses led to greater signals of end points of interest.

Sensitivity Analyses

In sensitivity analyses, we examined finasteride signals by indication (alopecia vs BPH) and age group (<45 and ≥45 years). We expected finasteride use in the younger age group to be primarily for alopecia and in the older age group to be primarily for BPH. Because date of birth was a mandatory reporting field but indication was not, age was used as a proxy for indication.

To mitigate confounding by indication and to explore the association between finasteride's mechanism of action and the adverse events of interest, we compared the signals of cases using finasteride for either hair loss or enlarged prostate with that of patients using drugs with different mechanisms of action but similar indications. For patients using finasteride for BPH, we selected tamsulosin hydrochloride, an α -adrenergic blocker indicated for the treatment of lower urinary tract symptoms due to BPH. For patients using finasteride for alopecia, we selected minoxidil, a vasodilator indicated for the management of hair loss. We presented both overall signals and signals stratified by age and indication, similarly to the primary analysis of finasteride.

The adverse effects of finasteride have received media attention during the last few years, which could potentially lead to stimulated reporting and/or a placebo effect.^{36,37} To account for this possible bias, we examined the signals of dutasteride, another 5ARI with the same indications as finasteride. In terms of differences between the 2 drugs, finasteride selectively inhibits the type 2 isoenzyme of 5 α -reductase, whereas dutasteride inhibits both types 1 and 2, and dutasteride reduces serum dihydrotestosterone levels markedly more than finasteride.³⁸⁻⁴⁰ Therefore, considering the similarities of these 2 drugs, one would expect similar reporting of adverse events associated with dutasteride and finasteride. As such, examining dutasteride also evaluates potential reporting biases of finasteride. Again, we examined both overall signals and signals stratified by age and indication.

To further account for any reporting bias, we examined the signals of finasteride before and after 2012, with 2012 as a wash-out period. We compared these signals with those of all other drugs in the database for the same period. This is the only sensitivity analysis stratifying both the drug of interest and the comparator; all other sensitivity analyses compared stratified signals of the drug of interest with those of the rest of the database, as per standard practice. The rationale for stratifying the database by year is to adjust for any changes in reporting during these periods, such as policy changes and initiatives encouraging reporting. The year 2012 was chosen a priori for 3 reasons. First, the first clinical study indexed on PubMed from the search result *finasteride AND suicide* was published in 2012.⁴¹ This study garnered significant media attention at the time.^{9,10} Second, the Post-Finasteride Syndrome Foundation, an organization dedicated to raising funds for scientific and clinical research on postfinasteride syndrome, was founded in July 2012.⁴² Third, according to Google Trends, Google searches for "post-finasteride syndrome" started steadily rising around that time.⁴³

All analyses were performed using R, version 3.6.1 (R Foundation). Two-sided $P < .05$ indicated significance.

Results

Demographics

We identified 356 suicidality cases and 2926 psychological adverse events associated with finasteride use, for a total of 3282 cases (among those with data available, 3206 male [98.9%] and 17 female [0.5%] of 3241 with data available; aged 18-44 years, 615 of 868 [70.9%] with data available). Almost all suicidality and psychological adverse events reported by VigiBase originated in the Americas (226 [63.5%] reports of suicidality and 2437 [83.3%] psychological reports) and Europe (116 [32.6%] reports of suicidality and 423 [14.5%] psychological reports). Suicidality and psychological adverse event reports were highest in 2015 to 2019 (290 [81.5%] and 2306 [78.8%], respectively). Most cases with a recorded age were 18 to 44 years of age (122 of 145 with age data available [84.1%] for suicidality and 493 of 723 with age data available [68.2%] for psychological adverse events). Additional demographic information for

Table 1. Characteristics and Demographics of Finasteride Users With Associated Suicidality or Psychological Adverse Events^a

Characteristic	Suicidality, No. (%)				P value ^b	Psychological adverse events, No. (%) (n = 2926)
	Overall (n = 356)	Ideation (n = 274)	Attempted (n = 37)	Completed (n = 45)		
Reporting region						
Africa	0	0	0	0	<.001	0
Eastern Mediterranean	0	0	0	0		1 (0.03)
Europe	116 (32.6)	94 (34.3)	13 (35.1)	9 (20.0)		423 (14.5)
Americas	226 (63.5)	175 (63.9)	22 (59.5)	29 (64.4)		2437 (83.3)
South-East Asia	0	0	0	0		0
Western Pacific	14 (3.9)	5 (1.8)	2 (5.4)	7 (15.6)		65 (2.2)
Reporting year						
1993-1999	2 (0.6)	0	1 (2.7)	1 (2.2)	.001	78 (2.7)
2000-2004	5 (1.4)	2 (0.7)	2 (5.4)	1 (2.2)		60 (2.1)
2005-2009	2 (0.6)	1 (0.4)	1 (2.7)	0		37 (1.3)
2010-2014	57 (16.0)	45 (16.4)	5 (13.5)	7 (15.6)		445 (15.2)
2015-2019	290 (81.5)	226 (82.5)	28 (75.7)	36 (80.0)		2306 (78.8)
Sex ^c						
Male	340 (95.5)	263 (96.0)	34 (91.9)	43 (95.6)	.65	2866 (97.9)
Female	3 (0.8)	3 (1.1)	0	0		14 (0.5)
Unknown	13 (3.7)	8 (2.9)	3 (8.1)	2 (4.4)		5 (0.2)
Age, y ^d						
<18	2 (0.6)	2 (0.7)	0	0	<.001	7 (0.2)
18-44	122 (34.3)	91 (33.2)	9 (24.3)	22 (48.9)		493 (16.8)
45-64	9 (2.5)	4 (1.5)	0	5 (11.1)		136 (4.6)
65-74	3 (0.8)	0	0	3 (6.7)		44 (1.5)
≥75	9 (2.5)	2 (0.7)	3 (8.1)	4 (8.9)		43 (1.5)
Indication						
Benign prostatic hyperplasia	10 (2.8)	9 (3.3)	0	1 (2.2)	<.001	141 (4.8)
Alopecia	232 (65.2)	200 (73.0)	18 (48.6)	14 (31.1)		2058 (70.3)
Unknown or ambiguous	114 (32.0)	65 (23.7)	19 (51.4)	30 (66.7)		727 (24.8)

^a Percentages have been rounded and may not total 100.^b Calculated as distribution across suicidality subgroups.^c Data were available for 2885 cases with psychological adverse events.^d Data were available for 145 cases with suicidality and 723 with psychological adverse events.

Table 2. Disproportionality Analysis of Finasteride

Adverse event	No. of cases	Expected count	EBE (5th percentile)	ROR (95% CI)
Suicidality	356	219	1.48	1.63 (1.47-1.81)
Suicidal ideation	274	62.7	3.90	4.39 (3.90-4.95)
Attempted suicide	37	70.3	0.39	NA ^a
Completed suicide	45	84.5	0.41	NA ^a
Psychological	2926	709	3.99	4.33 (4.17-4.49)

Abbreviations: EBE, empirical Bayes estimator; NA, not applicable; ROR, reporting odds ratio.

^a Did not meet EBE threshold. As such, no ROR was calculated.

finasteride, stratified by suicidality, suicidality subcategories, and psychological adverse events, can be found in **Table 1**.

Adverse Event Signals and Dose-Response Association

We identified a significant disproportionality signal for suicidality in finasteride users (ROR, 1.63; 95% CI, 1.47-1.81). These signals were driven by suicidal ideation reports (ROR, 4.39; 95% CI, 3.90-4.95); there was no signal for attempted or completed suicide. We also identified a significant disproportionality signal for psychological adverse events in finasteride users (ROR, 4.33; 95% CI, 4.17-4.49). Additional information on

the disproportionality analysis for finasteride can be found in **Table 2**. We did not observe a dose-response association (ROR for 1-mg dose, 1.64 [95% CI, 1.41-1.91]; ROR for unknown dose, 1.97 [95% CI, 1.68-2.30]) (**Table 3**). The ROR for the 5-mg dose did not meet the EBE threshold.

Sensitivity Analyses

In sensitivity analyses stratified by indication and age, younger patients (ROR, 3.47; 95% CI, 2.90-4.15) and patients with alopecia (ROR, 2.06; 95% CI, 1.81-2.34) had a significant disproportionality signal for suicide; no signal was present in older

Table 3. ROR of Suicidality by Finasteride Dose

Dose	No. of cases	Expected count	EBE (5th percentile)	ROR (95% CI)
1 mg	171	104.4	1.43	1.64 (1.41-1.91)
5 mg	30	53.3	0.40	NA ^a
Unknown	155	80.7	1.70	1.97 (1.68-2.30)

Abbreviations: EBE, empirical Bayes estimator; NA, not applicable; ROR, reporting odds ratio.

^a Did not meet EBE threshold. As such, no ROR was calculated.

Table 4. Summary of Sensitivity Analyses

Sensitivity analysis	Rationale	Finding	Implications
Indication	Evaluate whether different indications of finasteride (BPH and alopecia) confound the association with suicidality.	Significant signal for alopecia; no signal for BPH	The association may be confounded by use for alopecia.
Age group	Considering that age group (<45 and ≥45 y) is closely associated with indication, further evaluate if indication for finasteride confounds the association with suicidality.	Significant signal for young; no signal for old	Further supports the possibility of confounding by indication (use for alopecia in the young).
Tamsulosin	Tamsulosin is another drug used to manage BPH but is pharmacodynamically different from finasteride.	No signal for both overall and stratified analyses	Further confirms that finasteride used for BPH is not associated with suicidality.
Minoxidil	Minoxidil is another drug used to manage alopecia but is pharmacodynamically different from finasteride.	No signal for both overall and stratified analyses	Suggests that differences in signal observed in analyses stratifying by age and indication may be due to characteristics of finasteride unique to the younger population of users.
Dutasteride	Dutasteride is a drug similar to finasteride, sharing both indication and mechanism of action.	No signal for both overall and stratified analyses	Suggests that observed signals in finasteride may be due to characteristics of finasteride or that there is a reporting bias.
Before and after 2012	2012 is the year when the first clinical study finding an association between suicidality and finasteride was published and highly publicized. It is also the year the Post-Finasteride Syndrome society was founded. Google Trends show an increase in postfinasteride syndrome searches starting in 2012.	When stratifying both finasteride and the database by year, a significant signal after 2012, but no signal before 2012	Supports the hypothesis that suicidality signal associated with finasteride may be due to a reporting bias or stimulated reporting.

Abbreviation: BPH, benign prostatic hyperplasia.

patients and those with BPH. There was no disproportional signal for suicidality or psychological adverse events in patients using tamsulosin, minoxidil, and dutasteride for both overall and stratified analyses.

In analyses stratifying both finasteride use and the rest of the database by year, there was no signal of suicidality associated with finasteride use before 2012, but a disproportional signal of reporting after 2012 (ROR, 2.13; 95% CI, 1.91-2.39) was present. A summary of sensitivity analyses findings and implications can be found in Table 4. As described in the Methods section, we do not present RORs of associations that do not meet the EBE threshold.

Discussion

Increasing concerns over fatal outcomes linked to finasteride use have caught the attention of media and regulators alike.^{6,8,12,15,44} In light of this and the limited literature on this association, we sought to investigate psychological adverse events and suicidality associated with postfinasteride syndrome. Using validated pharmacovigilance methods, we identified disproportional signals for both psychological adverse events and suicidality associated with finasteride use in an international World Health Organization database.

To further test the validity of our findings and investigate different hypotheses, we performed several sensitivity analyses. The disproportional signal for suicidality was only present among younger patients using finasteride for alopecia and not in older patients prescribed finasteride for BPH. Suicidality signals were not observed for tamsulosin, another medication used in the management of BPH. This differential association of finasteride with suicidality by age and indication suggests that characteristics unique to the younger population with alopecia might explain suicidality.

These findings could raise concern that younger men with alopecia may be especially at risk for suicidality compared with the general population (ie, confounding by indication); however, the findings of our sensitivity analysis for minoxidil, another drug used for the treatment of alopecia but pharmacodynamically different from finasteride, did not find any disproportional reporting of suicidality. Taken together, our findings suggest that the disproportional reporting of suicidality and psychological adverse events in association with finasteride use could potentially be attributed to unique characteristics of the drug in young patients with alopecia. For example, the disproportional signals of adverse events in association with finasteride use could result from adverse effects, such as persistent sexual dysfunction, having a greater toll on younger patients using finasteride to treat a nonuro-

logic condition.^{18,45,46} This hypothesis is supported by a small postmarketing case series of 6 suicide completers who took finasteride for the treatment of androgenic alopecia.⁴⁷ Among all 6 cases, investigators found evidence of persistent sexual dysfunction after discontinuation of finasteride treatment. Alternatively, there may either be differential pharmacodynamic effects of finasteride or different patterns of use among younger or older populations; this could be addressed in a future study.

We did not observe a signal for dutasteride, also a 5ARI, on suicidality or psychological adverse events. This finding is at odds with the findings of Welk et al,¹⁹ who found no significant differences in suicidality based on the type of 5ARI. Considering that dutasteride has similar pharmacologic properties and adverse effects as finasteride,⁴⁸ is prescribed for the same indications, but has received far less attention from the media or any organization, the disproportional reporting of suicidality associated with finasteride use could be owing to reporting bias. A similar reporting bias was observed in a previous study on the effect of publications about and mass media attention on antihistamine-induced arrhythmias.⁴⁹ Highly publicized studies reported in the media around 2012^{9,10,41} and efforts by organizations such as the Post-Finasteride Syndrome Foundation⁴² (founded in 2012) may have led to greater attention to and reporting of depression and suicidality suspected to be associated with finasteride use by health care professionals (ie, stimulated reporting) or induced a placebo effect in patients.^{36,37,50,51} As such, stimulated reporting is expected to be greater with finasteride than with minoxidil or dutasteride. This hypothesis is further supported by sensitivity analyses identifying disproportional reporting of suicidality associated with finasteride after 2012, even when accounting for any changes associated with reporting in VigiBase in the same period.

This is the first analysis, to our knowledge, of suicidality and psychological adverse events in association with finasteride in VigiBase, an international pharmacovigilance database, with comprehensive sensitivity analyses examining pharmacodynamically different drugs prescribed for similar indications (minoxidil and tamsulosin) as well as a drug with similar mechanisms of action (dutasteride). In the context of increased scrutiny of postfinasteride syndrome, our exploratory findings highlight the need to further investigate the adverse events of finasteride use among young patients treated with the drug for alopecia, the cohort driving the disproportionality signal. Clinicians should pay greater attention to the psychological adverse effects of finasteride when prescribing them, especially in the younger population using the drug for hair loss. In addition, our sensitivity analyses shed light on potential biases that may confound the association between finasteride use and suicidality, namely, stimulated reporting, which should be further investigated.

Limitations

A limitation of our study is that some adverse events are likely not reported to national authorities for inclusion in VigiBase. This limitation is mitigated by the breadth of data collection (153 countries) and high volumes of reports. Con-

founding is also a concern. For example, we did not account for social support, socioeconomic status, and other factors associated with depression and suicidality.^{52,53} Although concomitant psychiatric drug use could be abstracted from the data, it is challenging to determine with certainty the sequence of medication use owing to missing data and temporality being associated with an adverse event rather than a drug. In other words, it is difficult to know whether a psychiatric drug was initiated before finasteride use or after finasteride use to manage associated symptoms; as such, conducting this sensitivity analysis may lead to overcontrolling. Regardless, sensitivity analyses examining drugs used for similar indications, age groups, and/or mechanisms of action were limited in the same way. For example, although one could hypothesize that younger patients seeking hair loss treatments may be more vulnerable to suicidality and psychological adverse events (and as such more likely to use psychiatric drugs), one would expect to observe similar confounding for minoxidil (which did not have disproportional reporting in young patients with alopecia). However, these sensitivity analyses are also limited; although these drugs may share clinical indications with finasteride, their use in the clinical setting may slightly differ. For example, finasteride and minoxidil are often prescribed to patients with different severity of alopecia. For similar reasons as concomitant drug use, the duration of finasteride exposure could not be assessed. Future studies are needed to estimate the association of length of drug use with suicidality and psychological adverse events. Finally, inherent limitations to spontaneous reporting (eg, underreporting or the lack of a denominator) exist. However, despite its flaws, the analysis of pharmacovigilance databases remains a cornerstone for the study of adverse drug reactions and contributes to the convergence of proof of an association.²⁸

Conclusions

Using validated pharmacovigilance methods, we found significant disproportional signals for suicidality associated with finasteride use. In stratified analyses, these signals were not present in older patients prescribed finasteride for BPH but were only present among younger patients using finasteride for alopecia. In sensitivity analyses, drugs with similar indications but different mechanisms of action and drugs with similar mechanisms of action and adverse effect profiles did not have disproportional reporting of suicidality nor psychological adverse events. Disproportional reporting of suicidality associated with finasteride use was observed after 2012. In light of these exploratory findings, disproportional signals associated with finasteride may be attributed to reporting biases, namely, stimulated reporting, or to greater repercussions of adverse effects and/or inherent psychological morbidities among younger men. Suicidality and psychological adverse events associated with finasteride use by young patients undergoing treatment for alopecia and potential biases confounding this association merit further investigation.

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