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Ethnicity and age as factors in sildenafil treatment of erectile dysfunction

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Abstract

Introduction: Sildenafil has been evaluated in >16 000 men with erectile dysfunction (ED) in double-blind, placebo-controlled trials.

Aim: To assess efficacy and safety of sildenafil in ED by ethnicity (white, black Asian) and age (≤45, 46-60, ≥61 years).

Methods: Data were pooled from 38 double-blind, placebo-controlled, flexible-dose trials. Most had starting sildenafil doses of 50 mg once daily, ~1 hour before sexual activity, with adjustment to 100 or 25 mg as needed.

Main Outcome Measures: Change from baseline in International Index of Erectile Function erectile function (IIEF-EF) domain score assessed with analysis of covariance and a Global Assessment Question (GAQ; "Did the treatment improve your erections?") at endpoint assessed with logistic regression analysis.

Results: 4120 and 3714 men received sildenafil and placebo, respectively (2740 and 2671 White; 407 and 385 Black; 973 and 658 Asian). For sildenafil vs. placebo groups, overall treatment differences for IIEF-EF domain and GAQ were significant for each ethnic and age group ($P<.0001$); significant treatment-by-ethnicity and treatment-by-age interactions were also observed for change in IIEF-EF domain scores ($P<.05$), with differences significantly greater for White vs. Black ($P<.0001$), White vs. Asian ($P=.0163$), and Asian vs. Black ($P=.0036$) men. A significant treatment-by-ethnicity interaction was observed for GAQ ($P=.0004$). The OR comparison for GAQ was significantly greater ($P=.0001$) with sildenafil vs. placebo in White (OR=11.2) or Asian (OR=12.4) men vs. Black men (OR=5.1). Adverse-event rates were generally similar, with some age variations.

Conclusions: Sildenafil is effective and well-tolerated regardless of ethnicity or age; however, treatment effects can vary.

1 | INTRODUCTION

Erectile dysfunction (ED), the persistent inability to achieve and/or maintain erections sufficient for satisfactory sexual performance,[1] is a multifactorial condition that is associated with age, comorbid systemic diseases (eg, cardiovascular disease [CVD], hypertension [HTN], diabetes and depression), certain therapeutic medications (eg, antihypertensives, antidepressants and vasodilators) and various endocrine, neurological and psychological factors.[2] With the availability in 1998 of sildenafil, the first oral medication for the treatment of ED, the management of ED entered a new era. Sildenafil is an effective and well-tolerated oral agent that is recommended as a first-line therapy for ED [3,4] based on data from extensive double-blind, placebo (PBO)-controlled trials in more than >16 000 men with ED and nearly 20 years of use in clinical practice. The efficacy and safety data collected during the clinical trials of sildenafil provide a database for investigating factors that may influence and aid in the management of ED in clinical practice. For example, the efficacy and

safety of sildenafil vs. placebo according to patient age recently were assessed in 11 364 men with ED using data from 48 randomised, double-blind, placebo-controlled, flexible-dose sildenafil trials.[5] The results of this pooled analysis indicated that sildenafil is a clinically effective and well-tolerated treatment for ED regardless of patient age, including those aged ≥75 years. In the current article, data from 38 randomised, double-blind, placebo-controlled, flexible-dose, sildenafil trials were used to evaluate the effects of patient ethnicity and age on the efficacy and safety of sildenafil for the treatment of ED.

What's known

Sildenafil is a well-tolerated and effective first-line therapy for erectile dysfunction, as evidenced by its almost two decades of use in clinical practice. A large body of sildenafil clinical trial data provides important information that can be used to facilitate the clinical management of patients with erectile dysfunction. Pooled analyses from 48 randomised, double-blind, placebo-controlled, flexible-dose sildenafil trials showed the efficacy and tolerability of sildenafil are unaffected by age.

What's new

The treatment of erectile dysfunction with a flexible-dose of sildenafil was effective and well-tolerated vs. placebo treatment in white, black and Asian men, regardless of their ethnic background. Although men of all ages and ethnicities achieve a significant treatment effect with sildenafil vs. placebo, there are some variations in the efficacy and safety of sildenafil vs. placebo as a result of treatment-by-ethnicity and treatment-by-age interactions.

2 | METHODS

Of the 74 double-blinded, placebo-controlled, sildenafil clinical trials included in a Pfizer clinical data repository, 38 trials had a flexible-dose design, included the self-reported ethnicity of the enrolled men, and collected baseline and endpoint data for the International Index of Erectile Function (IIEF) [6] for men with ED who were randomised to sildenafil or placebo; 37 of these 38 flexible-dose trials collected Global Assessment Question (GAQ; "Did the treatment improve your erections?") data at endpoint. In the present post hoc analysis, data were pooled from these 38 double-blind, placebo-controlled, flexible-dose trials to assess the efficacy and safety of sildenafil according to ethnicity and age. The starting sildenafil dose was 50 mg, to be taken approximately 1 hour before sexual activity but not more than once daily, with subsequent dose adjustment to 100 mg or 25 mg as needed. The majority of the trials included a 12-week treatment period and enrolled men with ED of 3-6-months' duration who were in a stable heterosexual relationship. Men taking nitrate therapy or nitric oxide donors and those with severe cardiac failure, unstable angina, or recent stroke or myocardial infarction were excluded from enrolment. Each study was conducted in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki. All trial protocols were approved by appropriate local ethics committees or institutional review boards. Each subject provided written informed consent before trial enrolment.

The data were pooled for the overall population and also stratified by self-reported ethnicity (white, black, and Asian) and by age at baseline (≤45, 46-60, and ≥61 years). Efficacy analyses included all men with ED who were randomised to treatment and had baseline and ≥1 postbaseline assessment of the IIEF efficacy outcome or a response to the GAQ at endpoint. Safety analyses (ie, treatment-related adverse events) included all randomised men who received at least one dose of study medication. Treatment efficacy was assessed based on patient-reported scores for the IIEF erectile function (IIEF-EF) domain (score range: 1-30, with lower scores indicating greater ED severity), IIEF question 3 (Q3: achieving erection; score range: 0-5) and IIEF question 4 (Q4; maintenance of erection; score range: 0-5) at baseline and endpoint (38 trials),[6] and a Global Assessment Question (GAQ: "Did the treatment improve your erections?") at endpoint (37 trials). Adverse events occurring during each study and up to 7 days after the last dose of study medication were reported.

For each IIEF outcome, an analysis of covariance (ANCOVA) model was applied to the change from baseline to endpoint (or termination with last-observation-carried-forward [LOCF] method). The ANCOVA model included baseline value, study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression, and diabetes), interaction of treatment by age group, interaction of treatment by ethnic group, and interaction of treatment by ethnic and age group. For each IIEF outcome, the least squares (LS) mean, the standard error (SE) of the LS mean, and *P* values for the treatment comparison between sildenafil and PBO and a type 3 test for main effects and the interaction of treatment by age and/or ethnic group were reported. In addition, the treatment difference was compared between age groups and between ethnic groups separately. For the GAQ, a logistic regression model was applied. The logistic regression analysis included study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression and diabetes), interaction of treatment by age group, interaction of treatment by ethnic group, and interaction of treatment by ethnic and age group. The odds ratio (OR; exponentiated estimate) for sildenafil vs. PBO, the 95% confidence interval (CI) of the OR, the *P* value for the treatment comparison, and the likelihood-ratio statistic for the type 3 test for main effects and interactions were assessed. In addition, the treatment difference OR was compared between age groups and between ethnic groups separately. All statistical tests were 2-sided with a 5% level of significance. No adjustment was made for multiple comparisons.

3 | MAIN OUTCOME MEASURES

Patient-reported quantitative scores for the IIEF erectile function domain, Q3 (achieving erection), and Q4 (maintenance of erection)

at baseline and endpoint, together with the qualitative yes or no response to the GAQ at endpoint, were the main outcome measures.

4 | RESULTS

4.1 | Patients

A total of 7834 men were included in the present post hoc analysis, with 4120 men treated with sildenafil (white: 2740; black: 407; Asian: 973) and 3714 men treated with PBO (white: 2671 black: 385; Asian: 658). The mean age and IIEF scores at baseline within each ethnicity group and within each age group were comparable for men treated with sildenafil and men treated with PBO (Table 1). The mean duration of ED at baseline was 4-5 years across the three ethnicity groups. The mean scores at baseline for the IIEF-EF domain, IIEF Q3 and IIEF Q4 generally decreased with increasing age in each ethnic group. The modal dose of sildenafil during these flexible-dose trials was predominantly 100 mg in each ethnic group (white: 64%; black: 62%; Asian: 58%) and in each age group (≤45 years: 49% to 61%; 46-60 years: 56%-69%; ≥61 years: 56%-65%).

4.2 | Efficacy outcomes

Based on type 3 tests from the ANCOVA model analysing quantitative IIEF outcomes, significant treatment-by-age and treatment-by-ethnicity interactions were observed for the change from baseline in IIEF-EF domain, Q3 (achieving erection), and Q4 (maintenance of erection) scores (all $P<.05$; Table 2). In addition, significant treatment differences were observed in the change from baseline in the IIEF-EF domain, Q3, and Q4 scores between men with vs. men without CVD/HTN ($P<.05$) and men with vs. men without diabetes ($P<.0001$), but not between men with vs. men without depression ($P\geq.2463$). Treatment differences were highest in men aged ≥61 years and lowest in men aged ≤45 years. The treatment difference was the greatest in white men and the lowest in black men.

All treatment differences significantly favoured sildenafil vs. PBO in the change from baseline to endpoint in the IIEF-EF domain score for each ethnic, age and ethnic-age group (all P values <.02; Table 3). Within the three ethnic groups, the treatment comparison for sildenafil vs. PBO in IIEF-EF domain scores was significantly greater for white

TABLE 1 Patient characteristics at baseline according to ethnic and age groups

	Placebo			Sildenafil		
	White	Black	Asian	White	Black	Asian
Mean (SD) age, years Range	n=2671 55.9 (11.0) 18-89	n=385 52.7 (10.8) 23-81	n=658 52.2 (11.3) 24-78	n=2740 56.3 (10.9) 19-87	n=407 53.4 (9.5) 21-78	n=973 50.6 (11.9) 24-86
≤45 years	n=450 38.7 (5.7) 18-45	n=94 8.4 (5.7) 23-45	n=190 38.2 (5.3) 24-45	n=419 38.6 (5.7) 19-45	n=77 39.2 (5.0) 21-45	n=350 37.7 (5.7) 24-45
46-60 years	n=1245 53.4 (4.2) 46-60	n=204 53.2 (4.2) 46-60	n=300 43.4 (4.3) 46-60	n=1299 53.5 (4.2) 46-60	n=234 53.1 (4.1) 46–60	n=401 53.3 (4.4) 46-60
≥61 years	n=976 67.1 (4.8) 61-89	n=87 66.8 (4.8) 61-81	n=168 66.0 (4.2) 61-78	n=1022 67.2 (4.8) 61-87	n=96 65.5 (3.4) 61-78	n=222 66.1 (4.6) 61-86
Mean (SD) ED duration, y	4.7 (4.6)	4.6 (5.3)	4.1 (4.0)	4.6 (4.3)	4.1 (4.0)	4.1 (4.2)
Mean (SD) IIEF score at baseline[a]						
EF domain[a]						
≤45 years	14.6 (6.9)	14.4 (6.0)	14.2 (4.6)	14.3 (7.0)	16.3 (6.2)	15.0 (4.2)
46-60 years	12.6 (6.8)	13.8 (6.4)	12.6 (5.3)	12.7 (6.9)	13.1 (6.5)	13.5 (4.8)
≥61 years	10.9 (6.8)	11.6 (7.1)	12.2 (6.3)	10.9 (6.7)	12.0 (7.5)	12.2 (5.7)
Q3[a]						
≤45 years	2.7 (1.6)	2.6 (1.5)	2.5 (1.3)	2.6 (1.6)	3.0 (1.5)	2.6 (1.3)
46-60 years	2.3 (1.5)	2.6 (1.4)	2.1 (1.3)	2.3 (1.5)	2.3 (1.5)	2.3 (1.3)
≥61 years	1.9 (1.5)	1.9 (1.5)	2.0 (1.4)	1.9 (1.5)	2.0 (1.6)	1.9 (1.3)
Q4[a]						
≤45 years	2.3 (1.4)	2.1 (1.3)	2.0 (1.1)	2.2 (1.5)	2.6 (1.2)	2.1 (1.1)
46-60 years	1.9 (1.4)	2.2 (1.3)	1.8 (1.1)	1.9 (1.3)	2.1 (1.3)	1.9 (1.1)
≥61 years	1.6 (1.3)	1.8 (1.5)	1.8 (1.2)	1.6 (1.3)	1.8 (1.5)	1.8 (1.2)

ED, erectile dysfunction; IIEF, 15-item International Index of Erectile Function; SD, standard deviation. Data from 38 double-blind, placebo-controlled, flexible-dose trials. [a]Q3=IIEF question 3 (achieving erection; score range 0-5); Q4=IIEF question 4 (maintaining erection; score range 0-5); EF Domain=6-item erectile function domain (score range: 1-30).

TABLE 2 Change from baseline to endpoint in IIEF scores[a] and improved erections at endpoint for GAQ[b]

Outcome	Overall treatment difference (Sildenafil vs. PBO)	Overall age group difference	Overall ethnic group difference	Treatment-by-age group interaction	Treatment-by-ethnic group interaction	Comorbidity effect	Study effect
IIEF Erectile function domain	*P*<.0001	*P*<.0001	*P*<.0001	*P*=.0242	(*P*<.0001)	CVD/HTN: *P*=.0105 Diabetes: *P*<.0001 Depression: *P*=.2463	*P*<.0001
IIEF Q3 (achieving erection)	*P*<.0001	*P*<.0001	*P*=.0001	*P*=.0411	*P*=.0002	CVD/HTN: *P*=.0170 Diabetes: *P*<.0001 Depression: *P*=.6146	*P*<.0001
IIEF Q4 (maintaining erection)	*P*<.0001	*P*<.0001	*P*=.0231	*P*=.0439	*P*=.0003	CVD/HTN: *P*=.0004 Diabetes: *P*<.0001 Depression: *P*=.4884	*P*<.0001
GAQ ("Did the treatment improve your erections?")	*P*<.0001	*P*<.0001	*P*<.0001	*P*=.5331	*P*=.0004	CVD/HTN: *P*=.2049 Diabetes: *P*<.0001 Depression: *P*=.1368	*P*<.0001

ANCOVA, analysis of covariance; GAQ, global assessment question; IIEF, International Index of Erectile Function; CVD/HTN, cardiovascular disease and/or hypertension; PBO, placebo. Data from 38 (IIEF) or 37 (GAQ) double-blind, PBO-controlled, flexible-dose trials; includes only men with baseline and postbaseline IIEF scores or GAQ data. [a]Significance for IIEF outcomes based on *P* values for type 3 test from ANCOVA model with baseline value, study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression and diabetes), treatment-by-age group interaction, treatment-by-ethnic group interaction and treatment-by-age group-ethnic group interaction (2-sided at 5% significance level). [b]Significance for GAQ based on likelihood ratio *P* values for type 3 analysis from logistic regression model with study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression and diabetes), treatment-by-age group interaction, treatment-by-ethnic group interaction, and treatment-by-ethnic group and age group interaction (2-sided at 5% significance level).

vs. black men (*P*<.0001), white vs. Asian men (*P*=.0163) and Asian vs. black men (*P*=.0036). Within the three age groups, the comparison for sildenafil vs. PBO in IIEF-EF domain scores was significantly greater for men aged ≥61 years vs. men aged ≤45 years (*P*=.0103) and for men aged 46-60 years vs. men aged ≤45 years (*P*=.0217). Similar significant results were observed for comparisons in IIEF Q3 and Q4 scores for sildenafil vs. PBO within the ethnicity and age groups (data not shown), except the treatment comparison between white vs. Asian men was not significant (Q3: *P*=.8561; Q4: *P*=.8400).

The results of type 3 tests from the logistic regression analysis of the qualitative GAQ indicated a significant treatment-by-ethnicity interaction (*P*=.0004) and a non-significant treatment-by-age interaction (*P*=.5331) (Table 2). Significant differences were observed for the GAQ between men with vs. men without diabetes (*P*<.0001), but not between men with vs. men without CVD/HTN (*P*=.2049) or depression (*P*=.1368).

The OR for sildenafil vs. PBO on the GAQ at endpoint was significant in each ethnic group and in each age group (all *P*<.0001; Table 4). The ORs for sildenafil vs. PBO were similar in men aged ≤45 years (OR=7.9), 46-60 years (OR=8.9), and ≥61 years (OR=10.1). Each comparison between age groups was not significant. The ORs for sildenafil vs. PBO in white men (OR=11.2) and Asian men (OR=12.4) were greater than the OR for black men (OR=5.1). Treatment comparisons between ethnic groups were significant for white vs. black men (*P*=.0001) and for Asian vs. black men (*P*=.0001).

4.3 | Adverse events

Treatment with sildenafil was well tolerated in each ethnic and age group. The most common treatment-related adverse events (ie, ≥3% incidence in either treatment group and with a greater incidence with sildenafil than with placebo) are listed in Table 5. Overall, treatment-related adverse events were predominantly mild in severity. Headache was the most common treatment-related adverse event in white and black men, whereas flushing was the most common treatment-related adverse event in Asian men. In men aged ≤45 years, the incidence of treatment-related headache was higher in black men (20.8%) than in white (13.4%) or Asian (12.6%) men. The incidence of headache was slightly higher in white men than in black or Asian men in the 46-60-year and ≥61-year age groups. Of note, flushing was not a common treatment-related adverse event among black men in any age group.

TABLE 3 Treatment difference (sildenafil vs. PBO) for the change from baseline to endpoint in IIEF-EF domain score in ethnic, age and ethnic-age groups

Comparison (Sildenafil vs. PBO)	LS mean (SE) treatment difference	95% CI	*P* Value[a]
Overall	6.4 (0.2)	6.0-6.9	<.0001
Ethnic groups			
White	7.8 (0.2)	7.3-8.2	<.0001
Black	4.8 (0.6)	3.8-5.9	<.0001
Asian	6.7 (0.4)	6.0-7.5	<.0001
Between ethnic groups			
White vs. Black	2.9 (0.6)	1.8-4.1	<.0001
White vs. Asian	1.0 (0.4)	0.2-1.8	.0163
Black vs. Asian	−1.9 (0.7)	−3.2–−0.6	.0036
Age groups			
≤45 years	5.5 (0.5)	4.6-6.4	<.0001
46-60 years	6.7 (0.3)	6.2-7.3	<.0001
≥61 years	7.1 (0.4)	6.3-7.9	<.0001
Between age groups			
≤45 vs. 46–60 years	−1.2 (0.5)	−2.3–−0.2	.0217
≤45 vs. ≥61 years	−1.6 (0.6)	−2.8–−0.4	.0103
46–60 vs. ≥61 years	−0.3 (0.5)	−1.4-0.7	.6645
Ethnic-age groups			
White ≤45 years	8.5 (0.5)	7.6-9.5	<.0001
White 46-60 years	7.5 (0.3)	6.9-8.0	<.0001
White ≥61 years	7.3 (0.3)	6.6-7.9	<.0001
Black ≤45 years	2.7 (1.1)	0.6-4.9	.0139
Black 46-60 years	5.2 (0.7)	3.9-6.5	<.0001
Black ≥61 years	6.6 (1.0)	4.6-8.6	<.0001
Asian ≤45 years	5.2 (0.6)	4.0-6.5	<.0001
Asian 46-60 years	7.6 (0.5)	6.5-8.6	<.0001
Asian ≥61 years	7.4 (0.7)	6.0-8.8	<.0001

ANCOVA, analysis of covariance; CI, confidence interval; IIEF-EF domain, International Index of Erectile Function erectile function domain; LS, least squares; PBO, placebo. Data from 38 double-blind. PBO-controlled, flexible-dose trials; includes only men with baseline and postbaseline IIEF-EF scores. [a]*P* value from ANCOVA model with baseline value, study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression and diabetes), treatment-by-age group interaction, treatment-by-ethnic group interaction, and treatment-by-ethnic group and age group interaction (2-sided at 5% significance level).

5 | DISCUSSION

In the current analyses, data for 7834 men from 38 randomised, double-blind, placebo-controlled, flexible-dose, sildenafil trials were used to evaluate the effects of patient ethnicity (white, black or Asian) and age (≤45, 46-60, or ≥61 years) on the efficacy and safety of sildenafil for the treatment of ED. The results of this pooled analysis demonstrated that overall treatment differences for sildenafil vs. PBO for the IIEF-EF domain and the GAQ were significant for each ethnic and each age group (all *P* <.0001). However, significant treatment-by-ethnicity and treatment-by-age interactions were observed for the change from baseline in quantitative IIEF-EF domain scores with sildenafil vs. PBO (all *P*<.05). A significant treatment-by-ethnicity interaction also was observed for the treatment difference in the qualitative GAQ (*P*=.0004). The types and incidences of treatment-related adverse events were generally similar in white, black and Asian men, with some variations among the three age groups. Overall, these results demonstrate the efficacy and safety of sildenafil in white, black and Asian men in all three age groups, with some variations in treatment effects according to ethnicity and age.

The strengths of the current analyses of the efficacy of sildenafil are that the statistical models included a treatment-by-ethnicity interaction and also adjusted for various ED-associated comorbidities [2] that may have an effect on ED treatment responsiveness.[7] The efficacy and safety data also were collected during trials with a similar double-blind, PBO-controlled, flexible-dose design. Furthermore, efficacy results were assessed with both the quantitative change from

TABLE 4 Treatment difference (sildenafil vs. PBO) for the percentage of men with improved erections on GAQ in ethnic, age and ethnic-age groups

Comparison (Sildenafil vs. PBO)	Odds ratio for treatment difference	95% CI	*P* value
Overall	8.9	7.6-10.5	<.0001
Ethnic groups[a]			
White	11.2	9.5-13.2	<.0001
Black	5.1	3.5-7.4	<.0001
Asian	12.4	9.5-16.1	<.0001
Between ethnic groups[b]			
White vs. Black	2.2	1.5-3.3	.0001
White vs. Asian	0.9	0.7-1.2	.5354
Black vs. Asian	0.4	0.3-0.7	.0001
Age groups[a]			
≤45 years	7.9	5.7-10.8	<.0001
46-60 years	8.9	7.2-11.0	<.0001
≥61 years	10.1	7.5-13.6	<.0001
Between age groups[b]			
≤45 vs. 46-60 years	0.9	0.6-1.3	.5219
≤45 vs. ≥61 years	0.8	0.5-1.2	.2624
46-60 vs. ≥61 years	0.9	0.6-1.3	.5032
Ethnic-age groups[a]			
White ≤45 years	16.7	11.5-24.3	<.0001
White 46-60 years	10.0	8.2-12.2	<.0001
White ≥61 years	8.5	6.8-10.7	<.0001
Black ≤45 years	3.2	1.5-6.8	.0024
Black 46-60 years	5.4	3.4-8.6	<.0001
Black ≥61 years	7.6	3.7-15.3	<.0001
Asian ≤45 years	9.1	5.9-14.0	<.0001
Asian 46-60 years	13.0	8.8-19.2	<.0001
Asian ≥61 years	16.0	9.5-26.9	<.0001

CI, confidence interval; GAQ, Global assessment question; PBO, placebo. Data from 37 double-blind. PBO-controlled, flexible-dose trials; includes only men with GAQ data at endpoint. [a]Liklihood ratio *P* value for type 3 analysis from logistic regression model with study, treatment, age group, ethnic group, three comorbidity indicators (CVD/HTN, depression, and diabetes), treatment-by-age group interaction, treatment-by-ethnic group interaction and treatment-by-ethnic group and age group interaction (2-sided at 5% significance level). [b]Within-group *P* value based on a ratio of the odds ratios for treatment difference (sildenafil vs. PBO).

baseline in IIEF scores and the qualitative GAQ. Possible limitations include that the 38 clinical trials enrolled only men with ED who did not have certain prespecified concomitant diseases and those who were in a stable heterosexual relationship. Therefore, the results may not reflect those for all men with ED.

It is important to evaluate the efficacy and safety of treatments for ED in men from various ethnic and age populations because different ethnic and age groups have different prevalence rates of ED-associated comorbid diseases and other risk factors for ED. For example, in the United States, the age-adjusted prevalence of HTN is greater in blacks than in whites [8] and the age-adjusted prevalence of diabetes is higher in blacks or Asians than in whites.[9] Furthermore, the cultural and religious beliefs of different ethnic groups can have an impact on the diagnosis and treatment-seeking behaviour of men with ED.

Several small-scale, PBO-controlled studies of the efficacy and safety of sildenafil previously were conducted in black men [10] and in Asian men [11–15] with ED. In 246 black American men with ED evaluated by Young et al. in a double-blind, PBO-controlled, flexible-dose trial, approximately 60% reported HTN and 28% reported diabetes.[10] After 6 weeks of treatment, IIEF-EF domain, Q3, and Q4 scores and the percentage of men indicating improved erections on the GAQ were significantly greater with sildenafil vs. PBO. Treatment with sildenafil was well-tolerated in black men, with only 22 (18%) men experiencing treatment-related adverse events.[10] Four PBO-controlled studies assessing flexible-dose sildenafil for the treatment of ED in Asian men from Malaysia/Singapore/the Philippines, Thailand, Taiwan, or Korea (sample size range: 125-254 men) demonstrated significant improvements in IIEF-EF domain, Q3, and Q4 scores and significantly improved erections on the GAQ with sildenafil vs. PBO after 8-12 weeks of treatment.[11–14] The incidence of treatment-related adverse events in these four studies ranged from 23% to 56% in the sildenafil group and from 10% to 21% in the PBO group; all or most adverse events in the sildenafil group were mild in nature. Another small-scale, 6-week, PBO-controlled, flexible-dose study evaluated the efficacy and safety of sildenafil in 155 men from Malaysia, Thailand and Singapore with ED and 1 or more comorbidities (ie, mild-moderate HTN, diabetes and dyslipidaemia).[15] Despite the increased cardiovascular risk associated with one or more comorbidities, Asian men with ED treated with sildenafil for 6 weeks demonstrated significant improvements in IIEF-EF, Q3 and Q4 scores and a significantly greater percentage reported improved erections on the GAQ compared with PBO. The incidence of treatment-related adverse events was 10% in the sildenafil group and 10% in the PBO group.[15]

The results of the present analysis of 7834 men provide strong validation of the efficacy and safety of sildenafil vs. PBO in the treatment of ED in white, black and Asian men, regardless of age. Comparisons between different ethnic and age groups indicate some variations in efficacy outcomes and adverse events, but each group demonstrates a significant treatment difference favouring sildenafil vs. PBO. Although individual patients may have different ethnic backgrounds, different ages and different concomitant diseases, the clinical evidence indicates that sildenafil significantly improves erectile function and is a well-tolerated treatment option for men with ED.

6 | CONCLUSIONS

Sildenafil is an effective and well-tolerated treatment for ED regardless of ethnicity or age. However, sildenafil treatment effects can vary with patient ethnicity and age.

TABLE 5 Most common treatment-related adverse events[a] in ethnic and ethnic-age groups

	Adverse event, n (%)	
Group	**PBO**	**Sildenafil**
Ethnic groups		
White	n=2671 Headache: 70 (2.6) Flushing: 23 (0.9) Dyspepsia: 9 (0.3)	n=2740 Headache: 323 (11.8) Flushing: 266 (9.7) Dyspepsia: 100 (3.6)
Black	n=385 Headache: 8 (2.1)	n=407 Headache: 46 (11.3)
Asian	n=658 Flushing: 20 (3.0) Headache: 26 (4.0) Dizziness: 19 (2.9) Nasal congestion: 4 (0.6)	n=973 Flushing: 124 (12.7) Headache: 69 (7.1) Dizziness: 55 (5.7) Nasal congestion: 31 (3.2)
Ethnic-age groups		
White ≤45 years	n=450 Headache: 14 (3.1) Flushing: 7 (1.6) Dyspepsia: 4 (0.9) Nasal congestion: 1 (0.2)	n=419 Headache: 56 (13.4) Flushing: 40 (9.5) Dyspepsia: 20 (4.8) Nasal congestion: 14 (3.3)
Black ≤45 years	n=94 Headache: 2 (2.1) Dyspepsia: 0	n=77 Headache: 16 (20.8) Dyspepsia: 3 (3.9)
Asian ≤45 years	n=190 Flushing: 5 (2.6) Headache: 8 (4.2) Dizziness: 7 (3.7)	n=350 Flushing: 44 (12.6) Headache: 23 (6.6) Dizziness: 20 (5.7)
White 46–60 years	n=1245 Headache: 33 (2.7) Flushing: 10 (0.8) Dyspepsia: 1 (<0.1)	n=1299 Headache: 161 (12.4) Flushing: 125 (9.6) Dyspepsia: 47 (3.6)
Black 46–60 years	n=204 Headache: 4 (2.0)	n=234 Headache: 23 (9.8)
Asian 46–60 years	n=300 Headache: 9 (3.0) Dizziness: 6 (2.0) Nasal congestion: 3 (1.0)	n=401 Headache: 29 (7.2) Dizziness: 20 (5.0) Nasal congestion: 14 (3.5)
White ≥61 years	n=976 Headache: 23 (2.4) Flushing: 6 (0.6) Dyspepsia: 4 (0.4)	n=1022 Headache: 106 (10.4) Flushing: 101 (9.9) Dyspepsia: 33 (3.2)
Black ≥61 years	n=87 Headache: 2 (2.3)	n=96 Headache: 7 (7.3)
Asian ≥61 years	n=168 Headache: 9 (5.4) Dizziness: 6 (3.6) Palpitations: 1 (0.6)	n=222 Headache: 17 (7.7) Dizziness: 15 (6.8) Palpitations: 7 (3.2)

PBO,placebo. Data from 38 double-blind, PBO-controlled, flexible-dose trials. [a]Treatment-related adverse events occurring in ≥3% of men in either treatment group and with a greater incidence with sildenafil than with placebo.

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AUTHOR CONTRIBUTIONS

All authors contributed to this manuscript as follows: study conception and design, analysis and interpretation of data, and drafting of the manuscript or revising critically for intellectual content.

DISCLOSURES

Dana A Ohl: Pfizer Sildenafil Advisory Board; Consultant/Surgical Trainer for Coloplast Corporation; Consultant for American Medical Systems. Vera Stecher: Employee of Pfizer Inc. Li-Jung Tseng: Employee of Pfizer Inc.

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