Awareness and clinical impact of the revised FDA warning on menopausal hormone therapy among Latin American physicians. REDLINC XIV

Juan E. Blümel, MD, PhD,[1] María S. Vallejo, MD,[2] Peter Chedraui, MD, MSc, PhD,[3] Hugo Salinas, MD, PhD,[4] Sócrates Aedo, MSc,[5] Alejandra Schüle, MD,[6] Ana L. Ribeiro Valadares, MD, PhD,[7] Ascanio Bencosme, MD,[8] Carlos Escalante, MD, MSc,[9] Carlos Salinas, MD, MSc,[10] Claudia Rey, MD, MSc,[11] Daysi A. Navarro-Despaigne, MD, PhD,[12] Doris Rodríguez-Vidal, MD,[13] Eliana Ojeda, MD,[14] Erik González, MD, MSc,[15] Eugenio Arteaga, MD,[16] Félix Ayala, MD,[17] Flory Morera, MD,[18] Gabriela Ayala, MD,[19] Gladys Fernández, MD,[20] Greta Solis, MD,[21] Hugo Gutiérrez-Crespo, MD,[22] Humberto Izaguirre, MD,[23] Ircania Garcia, MD,[24] José Moreno, MD,[25] Juan Matzumura-Kasano, MD, PhD,[26] Konstantinos Tserotas, MD,[27] Lucia Costa-Paiva, MD,[28] Luis R. Hernández, MD,[29] María A. Basavilvazo, MD,[30] Mabel Martino, MD,[31] Marcela López, MD,[32] Marcela S. Aguirre, MD,[33] Marcio A.H. Rodrigues, MD, PhD,[34] José Mendes Aldrighi, MD, PhD, MSCP,[35] Maribel Dextre, MD, MSCP,[36] Mónica Ñañez, MD,[37] Nilson R. de Melo, MD, MSCP,[38] Pablo Carpintero, MD, PhD,[39] Patricio Barriga, MD,[40] and Rogerio B. Machado, MD[41]

Received for publication June 1, 2026; accepted July 2, 2026.

From the [1]Department of Internal Medicine South, Faculty of Medicine, University of Chile, Santiago de Chile, Chile; [2]Obstetrics and Gynecology, University of Chile, Clinical Hospital, Santiago de Chile, Chile; [3]Postgraduate School of Health, Holy Spirit University (UEES), Samborondón, Ecuador; [4]Obstetrics and Gynecology, Clinical Hospital, University of Chile, Santiago de Chile, Chile; [5]School of Medicine, Finis Terrae University, Santiago de Chile, Chile; [6]Gynecology Service, Second Chair of Gynecology, Faculty of Medical Sciences, National University of Córdoba, University Hospital of Maternity and Neonatology, Córdoba, Argentina; [7]Department of Obstetrics and Gynecology, School of Medicine, State University of Campinas (UNICAMP), Campinas, Sao Paulo, Brazil; [8]Department of Medicine, Faculty of Health Sciences, Pontifical Catholic University Mother and Teacher, Santiago de los Caballeros, Dominican Republic; [9]Department of Gynecology, Faculty of Medicine, University of Costa Rica, San José, Costa Rica; [10]Obstetrics and Gynecology Service, Ángeles Hospital, Puebla, México; [11]Argentinian Association for the Study of Menopause, Buenos Aires, Argentina; [12]Institute of Endocrinology, Medical Sciences University of the Habana, Habana, Cuba; [13]University of Buenos Aires, José de San Martín Clinical Hospital, Buenos Aires, Argentina; [14]Academic Department of Human Medicine, Health Sciences Faculty, Andean University of Cusco, Cusco, Peru; [15]Gynecology and Obstetrics Service, Hospital Angeles Ciudad Juarez, México; [16]Department of Endocrinology and CETREN, Faculty of Medicine, Pontifical Catholic University of Chile, Santiago, Chile; [17]Department of Gynecology and Obstetrics, Faculty of Medicine, National University of San Marcos, Lima, Peru; [18]Department of Gynecology, Faculty of Medicine, University of Costa Rica, San José, Costa Rica; [19]Obstetrics and Gynecology, Metropolitan Hospital, Quito, Ecuador; [20]Gynecological Endocrinology and Climacteric, Hospital de Clínicas José de San Martín, University of Buenos Aires (UBA), Buenos Aires, Argentina; [21]Obstetrics and Gynecology, Vivian Pellas Hospital, Managua, Nicaragua; [22]Faculty of Medicine, National University of San Marcos, Lima, Peru; [23]Gynecology Service, National Maternal Perinatal Institute, Lima, Peru; [24]Modern Medical Center, Santo Domingo, Dominican Republic; [25]El Avila Clinic, Caracas, Venezuela; [26]Research Unit, Faculty of Medicine, National University of San Marcos, Lima, Peru; [27]Department of Gynecology and Obstetrics, Tserotas's Clinic, Paitilla Hospital, Panama City, Panama; [28]Department of Obstetrics and Gynecology, State University of Campina (UNICAMP) Campinas, Sao Paulo, Brazil; [29]Department of Gynecology and Obstetrics, Herrera Llerandi Hospital, Guatemala City, Guatemala; [30]Mexican Social Security Institute, Mexico City, Mexico; [31]Rosario Association of Obstetrics and Gynecology (ASOGIR), Rosario, Argentina; [32]Gynecologic Endocrinology and Menopause Unit, Clínica Alemana de Santiago, Santiago, Chile; [33]Department of Climacteric Medicine, Eva Perón Teaching Hospital, Granadero Baigorria, Santa Fe, Argentina; [34]Department of Gynecology and Obstetrics, Federal University of Minas Gerais, Belo Horizonte, Brazil; [35]Public Health Faculty, Sao Paolo University, Sao Paolo, Brazil; [36]Ginecología Obstetricia, Clínica Internacional, Lima, Perú; [37]Gynecology Service, Second Chair of Gynecology, Faculty of Medical Sciences, National University of Córdoba, University Hospital of Maternity and Neonatology, Córdoba, Argentina; [38]Department of Obstetrics and Gynecology, São Paulo University Medical School, São Paulo, Brazil; [39]Buenos Aires Gynecological Institute (IGBA), Buenos Aires, Argentina; [40]Professor Clinic Hospital, Santiago de Chile, Chile; and [41]Obstetrics and Gynecology Department, Jundiaí Medical School, Jundiaí, Brazil.

Funding/Support: None reported.

Financial disclosures/Conflicts of interest: G.A. has past relationships with Gedeon Richter, Chalver Laboratories, and ELEA. K.T. has an ongoing relationship with Abbott and Procaps. L. C.-P. has a past relationship with Astellas and a current relationship with Theramex. The other authors have nothing to disclose.

The research protocol of the study from which this analysis derives was reviewed and approved by the Ethics Committee of the Clinical Hospital, University of Chile, Santiago de Chile, Chile (Memorandum 022, 2026) and was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the study objectives and assessment tool and subsequently provided written consent prior to participation.

Abstract

Objective: To evaluate Latin American physicians' awareness regarding the recent revised statement of the US Food and Drug Administration (FDA) "black box warning" on menopausal hormone therapy (MHT) and to analyze its self-reported impact on clinical practice.

Methods: A multicenter cross-sectional study was conducted in thirteen Latin American countries. Physicians caring for peri- and postmenopausal women completed an anonymous survey assessing awareness of the revised FDA communication, perceived clarity, self-reported impact on clinical practice, and MHT prescribing patterns. Bivariate analyses and multivariable logistic regression were performed.

Results: A total of 2,166 physicians participated, mainly obstetrician-gynecologists (75.7%) and endocrinologists (9.0%). Overall, 80.7% were aware of the FDA revised statement. In addition, 90.5% considered that the previous warning had overestimated breast cancer risk, and 78.9% believed that the revised communication provides a more balanced view of risks and benefits. Changes in clinical practice were reported by 59.4% of participants, whereas 18.7% reported increased MHT prescribing. Furthermore, 53.3% modified the way they explain breast cancer risk, and 40.4% reported spending more time on patient education and shared decision-making. Physicians with ≤20 years of professional experience and those from specialties other than obstetrics and gynecology or endocrinology were more likely to report that the FDA revised statement would influence their therapeutic conduct.

Conclusions: The revised FDA communication appears to have influenced Latin American physicians' views and self-reported clinical practice, promoting a more balanced view of MHT and encouraging patient education and shared decision-making. However, the increase in MHT prescribing rates was relatively modest, and overall findings should be interpreted cautiously given the cross-sectional design, self-reported nature of the data, and potential selection bias.

Key Words: U.S. food and drug administration, Black box, Menopausal hormone therapy, MHT, Breast cancer.

(*Menopause* 2027;34:000–000)

Since the early 2000s, menopausal hormone therapy (MHT) products have carried a US Food and Drug Administration (FDA)[1] boxed warning largely based on findings from the Women's Health Initiative, highlighting potential risks such as cardiovascular disease, breast cancer, and dementia.[2] This boxed warning represented the highest level of safety alert required by the FDA for a medication and had a major impact on both clinical practice and risk perception among patients and health care professionals.[3] In November 2025, the FDA announced the removal of this specific warning related to breast cancer and other risks from most hormonal products, arguing that the information was based on outdated evidence and no longer accurately reflected current scientific knowledge.[4] This decision represents a major shift in the communication of risks associated with MHT and may have important clinical and epidemiological implications.

MHT has consistently demonstrated efficacy in relieving vasomotor symptoms, improving quality of life, preventing bone loss, and reducing the risk of osteoporotic fractures.[5] However, despite these benefits, its global use remains low. In the United States, MHT use has been estimated to have declined from 26.9% to 4.7% over the past two decades, reflecting a substantial change in clinical practice following the dissemination of studies warning about potential risks.[6] This trend partly reflects the long-lasting impact of regulatory warnings and the medical community's interpretation of the evidence.

In Latin America, MHT use is also limited. In 2014, a multicenter study including 6,731 healthy women aged 45-59 years from 15 cities in 11 countries across the region reported an MHT prevalence of 12.5%.[7] In that study, the main reason for not using MHT was lack of medical prescription (28%), followed by absence of symptoms (27.8%). Fear of cancer or other adverse effects was reported in fewer than 10% of cases, suggesting that factors related to medical practice and clinical decision-making may play a more important role than patient risk perception.

In this context, recent changes in FDA risk communication raise important questions regarding their impact on clinical practice. Modification of a boxed warning, historically considered a key element in drug safety regulation, may influence prescribing behavior, perceptions of MHT safety, and ultimately treatment utilization. However, how physicians interpret and adopt these changes has not been sufficiently explored, particularly outside the United States.

The aim of the present study was to explore how physicians caring for women during the climacteric period

This manuscript was originally drafted in Spanish and subsequently edited using Grammarly (Grammarly Inc., San Francisco, CA), an artificial intelligence–based writing assistance tool, to improve grammar, language, and style. All content, interpretations, and conclusions remain the responsibility of the authors.

J.E.B., M.S.V., P.C.: study conception and design, text revision and reading of the final version. J.E.B. and S.A.: statistical analysis. All other authors: data collection, text revision and approval of the final version.

There are no linked research datasets associated with this article. The data generated and analyzed during the current study are not publicly available; however, they may be made available upon reasonable request for research collaboration purposes, subject to ethical approval, privacy considerations, and applicable legal regulations.

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.menopause.org.

Address correspondence to: Juan E. Blümel, MD, PhD, Departamento de Medicina Interna Sur, Facultad de Medicina, Universidad de Chile, Orquídeas 1068, Departamento 302, P.O. BOX 7510258, Providencia, Santiago de Chile, Chile. E-mail: jeblumelm@gmail.com.

© 2026 by The Menopause Society

eISSN: 1530-0374
DOI: 10.1097/GME.0000000000002893

perceived the FDA communication regarding the modification of the boxed warning and to evaluate its self-reported impact on clinical practice. This analysis seeks to provide evidence that may improve understanding of the determinants of MHT prescribing in real-world practice and guide future medical education and risk communication strategies in this field.

METHODS

Study design and participants

In this cross-sectional study, board-certified physicians working in major Latin American urban centers (cities with population > 500,000 inhabitants) were invited to complete a survey. This criterion was selected because these cities concentrate most referral hospitals, specialty clinics, academic institutions, and physicians actively involved in menopause care. Recruitment was coordinated by academic investigators in each participating country, who identified eligible participants through professional networks, hospitals, outpatient clinics, universities, and scientific societies involved in women's health. Eligible participants were board-certified physicians involved in the care of peri- and postmenopausal women, including obstetrician-gynecologists (OB-GYNs), endocrinologists, general practitioners, internists, family physicians, psychiatrists, cardiologists, and other clinicians participating in women's health care.

The survey was distributed either in person or electronically, depending on local logistics. In-person distribution occurred in clinical and academic settings, including hospitals, outpatient clinics, departmental meetings, continuing medical education activities, and scientific meetings when available. Recruitment was coordinated through established academic leaders and professional networks in each participating country. Participation was voluntary and anonymous, and no incentives were provided. To maximize geographic representation, investigators were encouraged to recruit clinicians from different practice settings and regions within their respective countries.

Given the low response rates commonly reported in electronic physician surveys, particularly web-based studies,[8] invitations were delivered through academic leaders, heads of obstetrics and gynecology departments, and other opinion leaders affiliated with REDLINC who served as study coauthors. This strategy was intended to facilitate survey dissemination and enhance participation across participating countries.

The sample size was considered adequate to detect clinically meaningful changes in MHT prescribing patterns following the FDA communication. Assuming a minimum expected difference of 10%-15%, a sample of approximately 150-200 physicians would provide 80% power at a 5% significance level.[9] The final sample substantially exceeded this requirement, ensuring high statistical power for the primary analysis.

The research protocol of the study was reviewed and approved by the Ethics Committee of the Clinical Hospital, University of Chile, Santiago de Chile, Chile (Memorandum 022-2026), and was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the study objectives and assessment tool and subsequently provided written consent before participation.

Instrument

Because no internationally validated instrument was available to assess barriers to MHT use, a study-specific self-administered anonymous questionnaire was developed by the REDLINC/Latin American Federation of Menopause and Climacteric Societies (FLASCYM) research group. An initial version was pilot-tested in 30 physicians from different Latin American countries to assess content relevance, clarity, and wording, leading to item refinement based on their feedback. The revised instrument was subsequently reviewed by a panel of seven FLASCYM-appointed experts, who reached consensus on the final version. The survey was administered in Spanish and Portuguese using equivalent terminology commonly used in menopause care across participating countries. Responses were collected using predefined categorical options according to the nature of each item.

The survey collected participants' demographic and professional characteristics, including workplace setting, as well as their awareness of the FDA communication and the sources from which they obtained this information. It also assessed physicians' perceptions of the communication, including its clarity, interpretation, and content, as well as its self-reported impact on prescribing behavior, confidence in prescribing MHT, shared decision-making with patients, and perceived effects on patients' risk perception, treatment acceptance, and willingness to use MHT.

Statistical analysis

All analyses were performed using IBM SPSS Statistics for Window, version 21.0 (IBM Corp., Armonk, NY, USA). Categorical variables were described using absolute frequencies and percentages. Group comparisons were performed using Pearson χ^2 test, and crude odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs) were calculated in bivariate analyses. Subsequently, binary logistic regression analysis was performed to identify factors independently associated with the perception that the FDA statement influenced or will influence physicians' therapeutic behavior.

Given the large sample size and the number of outcome events, the study had sufficient statistical power to perform multivariable logistic regression analyses. The number of events per variable exceeded the recommended minimum (10 cases per variable), ensuring model stability. Variables associated with the outcome in the bivariate analyses at a significance level of $P < 0.05$ were entered into the multivariable logistic regression models using the enter method. Model results were expressed as adjusted odds ratios (aOR) with 95% CIs. Model fit was assessed using the Hosmer-Lemeshow test, and overall significance

© 2026 by The Menopause Society

TABLE 1. Specialty of participating physicians

Specialty	Frequency	Percentage	Cumulative Percentage
OB-GYN	1,640	75.7	75.7
Endocrinology	194	9.0	84.7
General practice	163	7.5	92.2
Internal medicine	55	2.5	94.7
Other specialties	114	5.3	100.0
Total	2,166	100.0	100.0

was evaluated using the Omnibus test of model coefficients. Collinearity among independent variables was explored using the variance inflation factor (VIF). A P value < 0.05 was considered statistically significant.

RESULTS

Participant characteristics

Table 1 shows that 2,166 physicians were included, the majority of whom were OB-GYNs (75.7%), followed by endocrinologists (9.0%) and general practitioners (7.5%). Data were obtained from 38 centers across 13 Latin American countries. Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/MENO/B614 shows the number of participating physicians from each country. Regarding professional experience, 50.1% had more than 20 years of clinical practice, whereas 13.2% had fewer than 5 years of experience. In terms of clinical practice, 77.3% of participants cared for peri- or postmenopausal women on a weekly or daily basis.

Awareness and sources of information regarding the FDA communication

Overall, 80.7% of physicians (95% CI: 79.0-82.4) being aware of the modification of the FDA "black box warning" (Fig. 1). Awareness was significantly higher among endocrinologists (87.6%; 95% CI: 83.0-92.3) and OB-GYNs (86.2%; 95% CI: 84.6-87.9) than among general practitioners (41.1%; 95% CI: 84.6-87.9). Internal medicine specialists and physicians from other specialties showed intermediate levels of awareness (58.2%, 95% CI: 44.7-71.6 and 57.0%, 95% CI: 47.8-66.2, respectively, $P < 0.001$). The main sources of information were scientific societies (32.5%), followed by social media (20.5%) and medical journals (16.9%). However, 13.4% of respondents reported not having been informed about the FDA communication.

Perception of the clarity and content of the FDA statement

Figure 2 shows an overall positive perception of the FDA communication, particularly regarding the possible previous overestimation of breast cancer risk. Overall, 70.3% of physicians considered the information to be clear or very clear, whereas 15.8% perceived it as unclear or confusing. Regarding the content, 90.5% agreed or strongly agreed that the previous warning had overestimated the breast cancer risk associated with MHT. Likewise, 86.9% considered the new communication appropriate or very appropriate, and 78.9% believed that it promotes a more balanced view of the risks and benefits of MHT.

Impact on clinical practice of the FDA statement

Table 2 shows that 18.7% of physicians reported increasing their prescribing of MHT following the FDA statement, whereas 65.6% indicated that it influenced the way they explain breast cancer risk, and 59.4% reported having modified their clinical practice. By specialty, general practitioners were more likely than OB-GYNs and endocrinologists to report changes in their overall clinical practice following the FDA statement (75.5%; 95% CI: 68.8-82.1 vs. 58.0%; 95% CI: 55.8-60.3, $P < 0.001$). However, general practitioners were less likely than OB-GYNs and endocrinologists to report modifying the way they communicated breast cancer risk to patients (45.4%; 95%

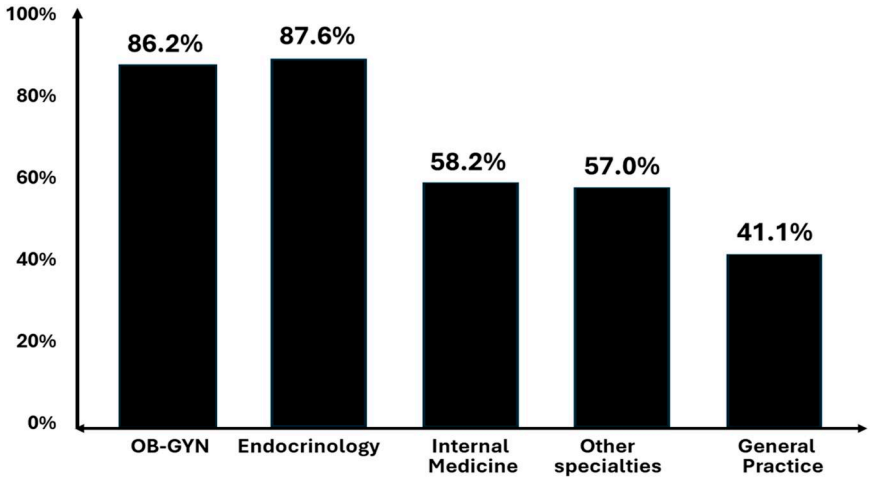


FIG. 1. Percentage of physicians aware of the removal of the FDA "black box warning" for MHT, according to specialty. MHT, menopausal hormone therapy.

© 2026 by The Menopause Society

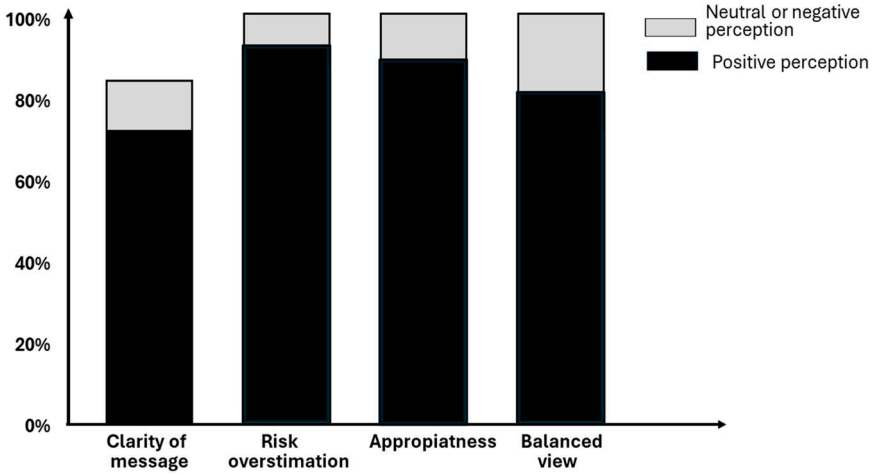


FIG. 2. Physicians' perceptions regarding the FDA statement on MHT. MHT, menopausal hormone therapy.

CI: 37.7-53.1 vs. 69.0%; 95% CI: 66.9-71.1, $P < 0.001$). Likewise, reported increases in MHT prescribing were less frequent among general practitioners and other specialties than among OB-GYNs and endocrinologists (12.3%; 95% CI: 7.8-16.8 vs. 19.6%; 95% CI: 17.8-21.5, $P = 0.024$).

Safety and clinical decision-making

Following the FDA communication, 82.6% (95% CI: 81.0-84.2) of physicians reported feeling confident prescribing MHT, while 74.2% (95% CI: 72.4-76.0) indicated that they prescribed it to symptomatic women (Table 3). OB-GYNs and endocrinologists showed the highest levels of confidence (86.9% and 87.9%, respectively) and prescription rates among symptomatic women (80.5% and 80.4%). In contrast, general practitioners, internists, and other specialties demonstrated lower levels of both confidence and prescribing, with values close to or below 50% and 40%, respectively.

TABLE 2. Impact of the FDA statement on physicians' clinical practice according to specialty

Specialty	Response	Increased MHT Prescribing n (%)	Explaining Changes in Breast Cancer Risk n (%)	Changes in Clinical Practice n (%)
OB-GYN	Yes	303 (18.5)	1,137 (69.3)	942 (57.4)
(n = 1,640)	No	1,272 (77.6)	411 (25.1)	698 (42.6)
	Other[a]	65 (4.0)	92 (5.6)	
Endocrinology	Yes	57 (29.4)	128 (66.0)	122 (62.9)
(n = 194)	No	122 (62.9)	54 (27.8)	72 (37.1)
	Other	15 (7.7)	12 (6.2)	
General practice	Yes	22 (13.5)	74 (45.4)	123 (75.5)
(n = 163)	No	59 (36.2)	40 (24.5)	40(24.5)
	Other	82 (50.3)	49 (30.0)	
Internal medicine	Yes	12 (21.8)	26 (47.3)	33 (60.0)
(n = 55)	No	22 (40.0)	16 (29.1)	22 (40.0)
	Other	21 (38.2)	13 (23.6)	
Other specialties	Yes	12 (10.5)	55 (48.2)	66 (57.9)
(n = 114)	No	36 (31.5)	28 (24.6)	48 (42.1)
	Other	66 (57.9)	31 (27.2)	
Total	Yes	406 (18.7)	1,420 (65.6)	1,286 (59.4)
(n = 2,166)	No	1,436 (66.3)	549 (25.3)	880 (40.6)
	Other	324 (15.0)	197 (9.1)	

MHT, menopausal hormone therapy.
[a]Other: does not prescribe MHT, was unaware of the FDA statement, or unsure.

Impact of the FDA statement on patients

Only 21.5% of physicians believed that their patients were aware of the change in the "black box" warning, whereas 60.7% considered that patients were not informed and 17.8% reported being unsure (Table 4). Perceived patient awareness differed significantly across specialties ($P < 0.001$), ranging from 8.6% among general practitioners and 14.5% among internists to 22.7% among endocrinologists and 23.7% among OB-GYNs.

Regarding fear toward MHT, 36.9% of physicians believed that the FDA communication had reduced it, whereas 30.0% considered that it had no impact and 33.1% were unsure. Uncertainty was particularly high among internists compared with OB-GYNs and endocrinologists (56.4% vs. 29.9%, $P < 0.001$). Regarding clinical practice, 40.4% of physicians reported spending more time on patient education and shared decision-making, while 37.7% indicated that their practice had not changed in this regard.

Influence of the statement on physician's clinical practice and future perspectives

When analyzed by specialty, OB-GYNs showed a high perceived impact of the FDA statement on their clinical practice, with 30.5% reporting a strong influence and 48.9% a moderate influence. Similarly, among endocrinologists, the perception of substantial impact predominated, with 29.4% reporting a strong influence and 54.1% a moderate influence. Overall, 78.6% of physicians considered that the FDA statement had influenced their clinical practice.

© 2026 by The Menopause Society

TABLE 3. Impact of the FDA statement on physicians' clinical practice according to specialty

Specialty	Confident Prescribing MHT n (%)	Prescribes MHT to Symptomatic Women n (%)
OB-GYN (n = 1,640)	1,449 (88.4)	1,321 (80.5)
Endocrinology (n = 194)	177 (91.2)	156 (80.4)
General practice (n = 163)	83 (50.9)	66 (40.5)
Internal medicine (n = 55)	51 (54.5)	22 (40.0)
Other specialties (n = 114)	51 (44.7)	42 (36.8)
Total (n = 2,166)	1,790 (82.6)	1,607 (74.2)

MHT, menopausal hormone therapy.

Most physicians perceived that the FDA statement had a relevant impact on their clinical practice (Table 5). In the overall sample, 29.7% reported a strong influence and 48.9% a moderate influence.

By specialty, OB-GYNs and endocrinologists were more likely to report a strong perceived impact of the FDA statement on their clinical practice (30.4%), whereas general practitioners and internists more frequently reported a lower perceived impact (22.0%, $P = 0.022$).

Table 6 shows the factors associated with the perception that the FDA statement influenced or will influence physicians' therapeutic behavior, based on bivariate analysis. Physicians from specialties other than obstetrics-gynecology/endocrinology reported a greater influence of the statement compared with OB-GYNs and endocrinologists (66.9% vs. 58.0%; OR = 1.15; 95% CI: 1.06-1.26; $P = 0.003$). Likewise, physicians with ≤20 years of experience reported greater influence than those with more than 20 years of professional practice (64.3% vs. 54.5%; OR = 1.18; 95% CI: 1.10-1.26; $P = 0.001$).

Awareness of the FDA updated statement and the perception that it was clearly communicated were not significantly associated with therapeutic influence ($P = 0.725$ and $P = 0.687$, respectively). Physicians who considered that the "black box warning" overestimated the risks showed a nonsignificant trend toward greater influence of the statement (60.0% vs. 53.4%; OR = 1.31; 95% CI: 0.98-1.75; $P = 0.069$). Finally, those who perceived that the statement presented a more balanced risk-benefit profile were more likely to report an influence on their therapeutic behavior (61.6% vs. 50.9%; OR = 1.55; 95% CI: 1.26-1.91; $P = 0.001$).

Variables that were significantly associated with the outcome in the bivariate analysis (Table 6) were entered into a multivariable logistic regression model. In the multivariate logistic regression analysis, physicians from specialties other than obstetrics-gynecology/endocrinology were more likely to consider that the FDA statement influences or will influence their therapeutic behavior (aOR = 2.01; 95% CI: 1.45-2.78; $P < 0.001$). Likewise, physicians with ≤20 years of experience were more likely to report an influence of the statement compared with those with more than 20 years of professional practice (aOR = 1.51; 95% CI: 1.25-1.83; $P < 0.001$). Similarly, perceiving that the updated FDA statement presents a better risk-benefit balance was significantly associated with a greater influence on therapeutic behavior (aOR = 1.84; 95% CI: 1.43-2.37; $P < 0.001$). The model showed adequate fit according to the Hosmer-Lemeshow test ($P = 0.606$), was globally significant based on the Omnibus test ($\chi^2 = 51.7$; df = 3; $P < 0.001$), and showed no relevant collinearity issues (VIF: 1.03-1.24).

TABLE 4. According to physicians' perception, are patients aware of the FDA change regarding the "black box" warning on menopausal hormone therapy?

Specialty	Yes (%)	No (%)	Unsure (%)
OB-GYN (n = 1,640)	388 (23.7)	1,000 (61.0)	252 (15.3)
Endocrinology (n = 194)	44 (22.7)	96 (49.5)	54 (27.8)
General Practice (n = 163)	14 (8.6)	107 (65.6)	42 (25.8)
Internal Medicine (n = 55)	8 (14.5)	37 (67.3)	10 (18.2)
Other specialties (n = 114)	12 (10.5)	74 (64.9)	28 (24.6)
Total (n = 2,166)	466 (21.5)	1,314 (60.7)	386 (17.8)

DISCUSSION

The present study shows that the revised FDA boxed warning statement on MHT has had an important impact on the views and self-reported practice of Latin American physicians, particularly OB-GYNs and endocrinologists. More than 80% of participants were aware of the revised FDA communication, and nearly 60% reported changes in their clinical practice.

These findings should be interpreted within the historical context generated by the initial publication of the WHI study in 2002, an event that profoundly changed the perception of MHT safety worldwide.[10] Following the dissemination of the first WHI results, multiple studies have demonstrated a sharp decline in MHT prescribing, accompanied by increased fear among both physicians and patients regarding the risks of breast cancer and cardiovascular disease.[11,12] In this context, the revised FDA communication appears to represent an attempt to partially correct a perception of risk considered excessive by a large part of the international scientific community.

In our study, 90.5% of physicians considered that the previous warning overestimated the risk of breast cancer associated with MHT. This finding is consistent with contemporary reviews indicating that the initial interpretation of the WHI was frequently oversimplified and extrapolated to all menopausal women, without considering age, time since menopause, type of hormone

© 2026 by The Menopause Society

TABLE 5. Do you consider that the FDA statement strongly influences your clinical practice?

Specialty	Strongly (%)	Moderately (%)	Slightly (%)	Not at All (%)
OB-GYN	501 (30.5)	802 (48.9)	248 (15.1)	89 (5.4)
Endocrinology	57 (29.4)	105 (54.1)	26 (13.4)	6 (3.1)
General Practice	36 (22.1)	83 (50.9)	29 (17.8)	15 (9.2)
Internal Medicine	12 (21.8)	25 (45.5)	16 (29.1)	2 (3.6)
Other specialties	37 (32.5)	44 (38.6)	24 (21.1)	9 (7.9)
Total	643 (29.7)	1,059 (48.9)	343 (15.8)	120 (5.5)

therapy, or baseline risk profile.[13] Several scientific societies, including The Menopause Society (formerly The North American Menopause Society) and the International Menopause Society,[5,14] have subsequently emphasized that, in women younger than 60 years or within the first 10 years after menopause, the benefits of MHT generally outweigh risks when there is an appropriate clinical indication.

Despite the widespread awareness of the FDA statement, only 18.7% reported increasing MHT prescribing, suggesting persistent clinical inertia resulting from years of risk-related messages following the WHI. Previous studies have shown that negative perceptions regarding MHT may persist for decades, even after the emergence of new scientific evidence.[10,15] Furthermore, the relatively high proportion of physicians reporting MHT prescription should be interpreted as a measure of prescribing behavior rather than treatment volume. Consequently, these data cannot be directly compared with national MHT utilization rates or sales figures.

Likewise, the fact that more than 50% of physicians reported changes in the way they explain breast cancer risk reflects a transition from a model focused exclusively on risks toward a more balanced approach based on shared decision-making. This is consistent with recent recommendations emphasizing individualized therapy and the contextualized communication of absolute rather than relative risk.[16,17] In this regard, the reported increase in time devoted to patient education and shared decision-making represents a clinically important finding.

OB-GYNs and endocrinologists demonstrated higher levels of awareness, confidence, and MHT prescribing than general practitioners and internists, likely reflecting their greater expertise in menopause care. In contrast, physicians from other specialties were more likely to report that the FDA statement influenced their therapeutic behavior, possibly because they rely more on regulatory guidance when updating their clinical practice.

Similarly, physicians with fewer years of professional experience were more likely to report that the FDA statement influenced their practice. This finding is consistent with studies showing that younger physicians tend to be more receptive to new clinical recommendations and regulatory changes, whereas those with greater experience may maintain more stable therapeutic patterns.[18]

Another relevant aspect observed in our study is the persistent perception of misinformation among patients. Only one in five physicians believed that women are aware of the revision of the FDA warning. This suggests that much of the corrective information remains confined to the medical setting and does not necessarily reach the general population. Previous studies have shown that fear of breast cancer continues

TABLE 6. Factors associated with the influence of the FDA statement on physicians' therapeutic behavior (bivariate analysis)

Characteristic	Total Physicians	Influences % (95% CI)	p	OR[a] (95% CI)
Specialty				
Obstetrics-Gynecology/endocrinology	1,834	58.0 (55.8-60.3)		
Other specialties	332	66.9 (61.8-72.0)	0.003	1.15 (1.06-1.26)
Years of physician experience				
> 20 y	1,085	54.5 (51.5-57.4)		
≤ 20 y	1,081	64.3 (61.4-67.2)	0.001	1.18 (1.10-1.26)
Awareness of the current FDA statement				
Unaware of the FDA statement	418	58.6 (53.9-63.4)		
Aware of the FDA statement	1,748	59.6 (57.3-61.9)	0.725	1.04 (0.84-1.29)
Clarity of the current FDA statement[b]				
Perceive clarity	1,523	60.4 (55.2-65.6)		
Do not perceive clarity	341	59.2 (56.8-61.7)	0.687	0.97 (0.84-1.12)
Perception of the previous FDA "black box warning"				
Did not overestimate the risks	204	53.4 (46.5-60.3)		
Overestimated the risks	1,962	60.0 (57.8-62.2)	0.069	1.31 (0.98-1.75)
Current perception of the risk-benefit balance following the FDA statement				
Not sure it is more balanced	456	50.9 (46.3-55.5)		
Consider it more balanced	1,710	61.6 (59.3-63.9)	0.001	1.55 (1.26-1.91)

[a]Unadjusted OR (bivariate analysis), using the second category of each variable as the reference category.
[b]A total of 312 physicians did not know the statement sufficiently to provide an opinion.

© 2026 by The Menopause Society

to be one of the main barriers to MHT use, even among women with severe vasomotor symptoms and poor quality of life.[11] The persistence of negative perceptions may explain why many physicians reported uncertainty regarding the real impact of the new communication on patients' fear of MHT.

Our findings have important clinical and public health implications for Latin America. Menopause represents a growing challenge due to regional population aging, and menopausal symptoms significantly affect quality of life,[19] work productivity,[20] and mental health.[21] An exaggerated perception of risk may lead to undertreatment of symptomatic women. In this context, regulatory updates, promoting a more balanced assessment of the risk-benefit profile, could help improve access to effective, evidence-based therapies.

Among the strengths of this study are its large sample size, the participation of physicians from 13 Latin American countries, the inclusion of multiple medical specialties, and the comprehensive assessment of awareness, perceptions, clinical practice, and patient-related views. These features provide a broad regional perspective on the impact of the revised FDA statement in real-world clinical practice.

However, several limitations should be acknowledged. First, the cross-sectional design precludes causal inferences. Second, the findings were based on self-reported data and may therefore be subject to social desirability bias or overestimation of the actual clinical impact. Moreover, the study did not objectively assess whether reported changes translated into actual prescribing behavior. Third, most participants were OB-GYNs or endocrinologists, and many had extensive clinical experience, which may have influenced the reported levels of awareness and perceptions and may limit the generalizability of the findings to other specialties. In addition, physicians from nongynecology and nonendocrinology specialties were fewer and more heterogeneous, limiting specialty-specific comparisons. Fourth, participants were recruited through professional and academic networks, including hospitals, outpatient clinics, universities, scientific societies, and educational activities. Consequently, selection bias cannot be excluded, as physicians more engaged in academic activities may have been more likely both to participate and to be up to date on menopause management. Recruitment was also concentrated in large urban centers, and country representation was not proportional to the size of each national physician workforce, limiting generalizability.

Finally, participants received a brief description of the revised FDA communication during the informed consent process. This may have reduced differences between physicians with and without prior awareness and partly explains the lack of association between awareness and perceived influence observed in the multivariable analysis. In addition, the questionnaire was specifically developed for this study because no internationally validated instrument is available to assess barriers to menopausal hormone therapy prescribing. Although it underwent pilot testing in 30 physicians from different Latin American countries and review by seven FLASCYM experts, formal psychometric validation was not performed. Therefore, measurement bias cannot be excluded, although the findings provide useful preliminary evidence and support the need for validated instruments to assess barriers to evidence-based menopause care.

CONCLUSION

The revised FDA communication regarding the "black box warning" on MHT appears to have fostered a more balanced understanding of the risks and benefits of MHT among Latin American physicians, particularly influencing self-reported clinical communication and therapeutic decision-making. Nevertheless, important knowledge gaps persist across specialties, as well as a considerable perception of misinformation among patients, underscoring the need to strengthen educational strategies for both health care professionals and menopausal women. However, these findings should be interpreted cautiously given the cross-sectional design, self-reported nature of the data, and potential selection bias.

REFERENCES

1. Food and Drug Administration US. FDA requires new boxed warning for estrogen and estrogen-progestin products. 2003. Accessed April 8, 2026. https://www.fda.gov/
2. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al.; Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-333. doi:10.1001/jama.288.3.321
3. Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy: annual trends and response to recent evidence. *JAMA* 2004;291:47-53. doi:10.1001/jama.291.1.47
4. Food and Drug Administration US. FDA approves labeling changes to menopausal hormone therapy products. 2026. Accessed April 8, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-labeling-changes-menopausal-hormone-therapy-products
5. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause* 2022;29:767-794. doi:10.1097/GME.0000000000002028
6. Yang L, Toriola AT. Menopausal hormone therapy use among postmenopausal women. *JAMA Health Forum* 2024;5:e243128. doi:10.1001/jamahealthforum.2024.3128
7. Blümel JE, Chedraui P, Barón G, Benítez Z, Flores D, Espinoza MT, et al.; Collaborative Group for Research of the Climacteric in Latin America (REDLINC). A multicentric study regarding the use of hormone therapy during female mid-age (REDLINC VI). *Climacteric* 2014;17:433-441. doi:10.3109/13697137.2014.882305
8. Cunningham CT, Quan H, Hemmelgarn B, Noseworthy T, Beck CA, Dixon E, et al. Exploring physician specialist response rates to web-based surveys. *BMC Med Res Methodol* 2015;15:32. doi:10.1186/s12874-015-0016-z
9. Machin D, Campbell MJ, Tan SB, Tan SH. *Sample Size Tables for Clinical Studies*, 3rd ed. Chichester (UK): Wiley-Blackwell; 2009.
10. Langer RD, Hodis HN, Lobo RA, Allison MA. Hormone replacement therapy - where are we now? *Climacteric* 2021;24:3-10. doi:10.1080/13697137.2020.1851183
11. Tan DA, Dayu ARB. Menopausal hormone therapy: why we should no longer be afraid of the breast cancer risk. *Climacteric* 2022;25:362-368. doi:10.1080/13697137.2022.2035711
12. Vickers MR, MacLennan AH, Lawton B, Ford D, Martin J, Meredith SK, et al.; WISDOM group. Main morbidities recorded in the women's international study of long duration oestrogen after menopause (WISDOM): a randomised controlled trial of hormone

© 2026 by The Menopause Society

replacement therapy in postmenopausal women. *Brit Med J* 2007; 335:239. doi:10.1136/bmj.39266.425069.AD
13. Manson JE. Menopausal hormone therapy and health outcomes: is timing everything? *Clin Chem* 2021;67:317-318. doi:10.1093/clinchem/hvaa286
14. Baber RJ, Panay N, Fenton A, IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. *Climacteric* 2016;19:109-150. doi:10.3109/13697137.2015.1129166
15. Manson JE, Kaunitz AM. Menopause management–getting clinical care back on track. *N Engl J Med* 2016;374:803-806. doi:10.1056/NEJMp1514242
16. El Khoudary SR, Aggarwal B, Beckie TM, Hodis HN, Johnson AE, Langer RD, et al. Menopause transition and cardiovascular disease risk: implications for timing of early prevention. A scientific statement from the American Heart Association. *Circulation* 2020; 142:e506-e532. doi:10.1161/CIR.0000000000000912
17. Gigerenzer G, Gaissmaier W, Kurz-Milcke E, Schwartz LM, Woloshin S. Helping doctors and patients make sense of health statistics. *Psychol Sci Public Interest* 2007;8:53-96. doi:10.1111/j.1539-6053.2008.00033.x
18. Huang H, Cai Y, Miao S, Luo L. Meta-synthesis of qualitative research on comfort experiences of family caregivers in hospice care: a systematic review. *Front Public Health* 2026;14:1819762. doi:10.3389/fpubh.2026.1819762
19. Chedraui P, Blümel JE, Baron G, Belzares E, Bencosme A, Calle A, et al. Impaired quality of life among middle aged women: a multicentre Latin American study. *Maturitas* 2008;61:323-329. doi:10.1016/j.maturitas.2008.09.026
20. D'Angelo S, Bevilacqua G, Hammond J, Zaballa E, Dennison EM, Walker-Bone K. Impact of Menopausal Symptoms on Work: Findings from Women in the Health and Employment after Fifty (HEAF) Study. *Int J Environ Res Public Health* 2022;20:295. doi:10.3390/ijerph20010295
21. Soares CN. Depression and Menopause: An Update on Current Knowledge and Clinical Management for this Critical Window. *Med Clin North Am* 2019;103:651-667. doi:10.1016/j.mcna.2019.03.001

© 2026 by The Menopause Society