

## Personal and professional use of menopausal hormone therapy among gynecologists: A multinational study (REDLINC VII)

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### ABSTRACT

**Background:** Previously, the REDLINC VI study showed that the main reason for the low use of menopausal hormone therapy (MHT) was its low rate of prescription by doctors.

**Objective:** To determine the use of MHT and perceived related risks among gynecologists.

**Methods:** A self-administered and anonymous questionnaire was delivered to certified gynecologists in 11 Latin American countries.

**Results:** A total of 2154 gynecologists were contacted, of whom 85.3% responded to the survey ( $n = 1837$ ). Mean age was  $48.1 \pm 11.4$  years; 55.5% were male, 20.3% were faculty members and 85% had a partner. Overall, 85.4% of gynecologists responded that they would use MHT if they had menopausal symptoms (81.8% in the case of female gynecologists) or prescribe it to their partner (88.2% in the case of male gynecologists;  $p < 0.001$ ). Perceived risk related to MHT use (on a scale from 0 to 10) was higher among female than among male gynecologists ( $4.06 \pm 2.09$  vs.  $3.83 \pm 2.11$ ,  $p < 0.02$ ). The top two perceived reported risks were thromboembolism (women 33.6% vs. men 41.4%,  $p < 0.009$ ) and breast cancer (women 38.5% vs. men 33.9%,  $p < 0.03$ ). Overall, gynecologists reported prescribing MHT to 48.9% of their symptomatic patients (women 47.3% vs. men 50.2%,  $p < 0.03$ ) and 86.8% currently prescribed non-hormonal remedies and 83.8% alternative therapies for the management of the menopause. Gynecologists who were older and academic professionals prescribed MHT more often.

**Conclusion:** Although this Latin American survey showed that gynecologists are mostly supporters of MHT use (for themselves or their partners), this is not necessarily reflected in their clinical practice.

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### 1. Introduction

Menopause can impair quality of life and is associated with an increase in the incidence of chronic diseases such as osteoporosis and cardiovascular disease [1–3]. Menopausal hormone therapy (MHT) and the adoption of healthy lifestyles are important

strategies to counteract these negative effects [4]. However, MHT use, which achieved great popularity among doctors and women some decades ago, dropped massively after 2002, as a result of the publication of the results of the Women's Health Initiative study (WHI), which demonstrated that the risks related to MHT use outweighed the benefits [5,6]. Despite this, several subsequent WHI sub-analyses have shown that these risks are mainly observed in older postmenopausal women and that even the risk of breast cancer (a risk of major concern) decreased among hysterectomized women receiving estrogen alone [7]. Not only have the reported implications of the WHI changed over time, but several different

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publications have criticized the conclusions drawn [8]. Moreover, a recent report indicates that the study had serious methodological flaws that would invalidate its results (e.g., the Cox proportional hazards model was applied without fulfilling the necessary criteria for its use) [9].

As a direct or indirect effect of the WHI results, many women worldwide abandoned their MHT, consequently losing its benefits (i.e., over menopausal symptoms), and perhaps even increasing their mortality. Indeed, Sarrel et al. [10] estimated that between 18,601 and 91,610 women have died in the US because they avoided MHT. These data are consistent with a study in Finland which estimated that mortality among MHT users decreased between 12% and 38%, in a nearly linear relationship with duration of treatment [11].

Despite the aforementioned facts, and although the results of the WHI study are currently better interpreted, the percentage of women using MHT continues to be extremely low [5]. A previous study by our research group (REDLINC Study VI) found that the main reason for the low take-up of MHT was its low rate of prescription by doctors [12]. Bearing this in mind, the present study aimed to analyze the use of MHT among gynecologists. We hypothesized that gynecologists would behave differently in prescribing MHT to their patients or for themselves or their partner. In addition, we explored their perceived risks related to MHT use and the prescription of non-hormonal and/or alternative therapies for the menopause.

## 2. Method

### 2.1. Study design and participants

In this cross-sectional study, certified gynecologists working in Latin American cities with more than 500,000 inhabitants were invited to complete a survey. Researchers and their corresponding cities are detailed in Appendix A. Due to the low response rate observed in similar studies carried out electronically, the invitation to participate was made personally by academics, heads of gynecology and obstetrics services or other medical opinion leaders who were REDLINC members and co-authors of this study. That is, these leaders asked gynecologists working in their hospitals, units, departments, services or professional societies to participate in the study.

To calculate the sample size required for this study we asked the pharmaceutical industry to estimate the number of certified obstetricians and gynecologists practicing in a given city or place. Therefore, according to the records of Recalcine Laboratory (Santiago, Chile) there are nearly 1400 of these certified professionals in Lima (Peru) and Buenos Aires (Argentina); about 1000 in Rosario (Argentina), Guayaquil (Ecuador), Caracas (Venezuela), Bogota (Colombia) and Santiago (Chile); and fewer than 500 in San José (Costa Rica), Panama City (Panama), Mendoza (Argentina) and

Medellin (Colombia). Based on these numbers and Buhling et al. [13] estimate that 97% of German gynecologists supported MHT use for themselves or their partners, we estimated that in Latin America 80% of professionals would support MHT use. Assuming an error of 10% with a 95% confidence level, the number of respondents required ranged from 55 in places with 500 gynecologists to 59 in places with 1500 of these specialists. In cities with fewer than 500 certified specialists, 50 doctors were asked to fill out the survey.

The research protocol was reviewed and approved by the Scientific Ethics Committee of the Servicio de Salud Metropolitano Sur, Santiago de Chile, Chile. Informed consent was obtained from each professional before they filled out the survey.

### 2.2. Tool

A self-administered and anonymous survey was used. It covered personal data such as age, sex, partner status, and place of work. Prior to implementation, the questionnaire was validated at each site. The survey assessed: (a) the use of MHT among female gynecologists or the partners of male professionals, if menopausal symptoms were present; (b) the perceived level of risk related to MHT use (evaluated from 0 to 10, with 0 being no risk and 10 the highest risk); (c) the specific perceived risks of using MHT; (d) the percentage of women with menopausal symptoms for whom each doctor prescribed MHT; and (e) the prescription frequency of non-hormonal and/or alternative therapies to treat menopausal symptoms.

### 2.3. Statistical analysis

Data analysis was performed using the statistical program EPI-INFO (Version 7.1.5, 2015, Centers for Disease Control and Prevention, Atlanta, GA, USA). Results are presented as mean  $\pm$  standard deviations, percentages (95% confidence intervals, CI). The Kolmogorov-Smirnov test was used to assess the normality of data distribution and the Bartlett test to evaluate the homogeneity of the measured variance. Accordingly, group comparisons were performed with Student's *T* test (parametric continuous data) or the Mann-Whitney *U* test (non-parametric continuous data). Percentages were compared with the chi-square test. A *p* value of  $<0.05$  was considered statistically significant.

## 3. Results

A total of 2154 certified gynecologists from 28 health centers in 11 Latin American countries were invited to participate. Of these, 1837 (85.3%) responded to the survey, of whom 1019 (55.5%) were men. The mean age of the whole sample was  $48.1 \pm 11.4$  years; the women were on average younger than the men ( $45.0 \pm 10.7$

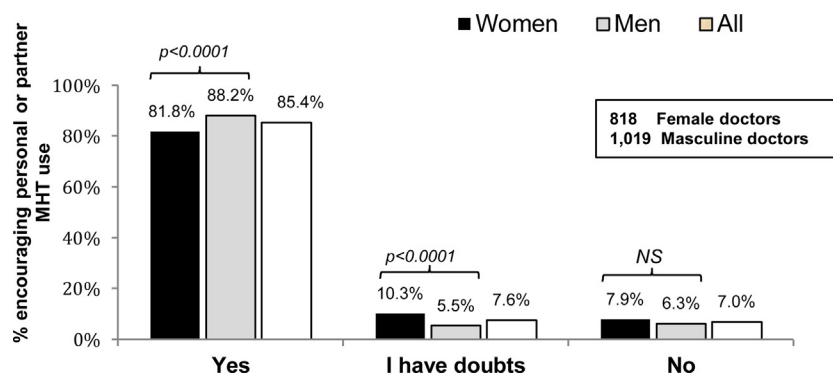


Fig. 1. Would you personally use MHT or prescribe it to your partner, if menopausal symptoms are present?

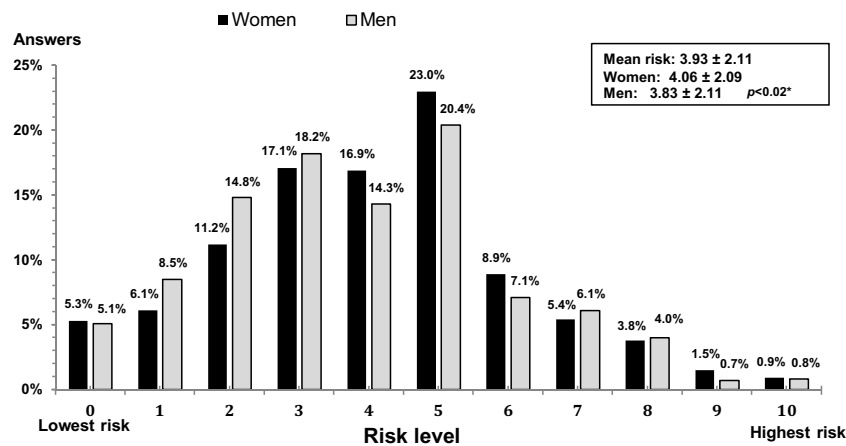


Fig. 2. How would you grade your perceived level of risk (0 to 10) related to MHT use? \*p value determined with the Student's T test.

Table 1

Influence of age and academic working status over perceptions and behaviors related to MHT use.

Perceptions and behaviors	University member <sup>+</sup>		Age (years)		
	Yes (n = 373)	No (n = 1464)	<40 (n = 490)	40–59 (n = 1044)	≥60 (n = 303)
% Favors personal or partner MHT use if symptoms are present	89.8 (86.2–92.6)	84.2 (82.2–86.0)**	82.4 (78.7–85.7)	86.8 (84.5–88.7) <sup>†</sup>	85.1 (80.5–88.9) <sup>NS</sup>
Perceived risk level related to MHT use (scale 0–10)	4.1 ± 1.9	3.9 ± 2.1 <sup>†</sup>	4.1 ± 2.1	3.9 ± 2.1 <sup>NS</sup>	3.9 ± 2.1 <sup>NS</sup>
Top two perceived risks (% replies):					
Thromboembolism	43.2 (38.1–48.4)	36.6 (34.1–39.1) <sup>NS</sup>	36.9 (32.7–41.4)	38.2 (35.3–41.3) <sup>NS</sup>	38.6 (33.1–44.4) <sup>NS</sup>
Breast cancer	36.5 (31.6–41.6)	35.8 (33.3–38.3) <sup>NS</sup>	34.5 (30.3–38.9)	36.4 (33.5–39.4) <sup>NS</sup>	36.6 (31.2–42.4) <sup>NS</sup>
% of symptomatic women that doctors <sup>1</sup> prescribe MHT	55.9 ± 27.7	47.1 ± 29.8***	47.7 ± 29.5	49.0 ± 29.6 <sup>NS</sup>	50.70 ± 29.5 <sup>NS</sup>
% of doctors <sup>1</sup> prescribing					
Non hormonal drugs	86.9 (82.9–90.0)	86.7 (84.9–88.4) <sup>NS</sup>	86.1 (82.7–89.0)	87.7 (85.6–89.6) <sup>NS</sup>	84.5 (79.8–88.3) <sup>NS</sup>
Alternative therapies	81.8 (77.4–85.5)	84.4 (82.4–86.2) <sup>NS</sup>	83.9 (80.3–87.0)	85.4 (83.2–87.5) <sup>NS</sup>	78.2 (73.1–82.6) <sup>†</sup>

Data are presented as mean ± standard deviations or % (95% confidence intervals); NS; non significant; \*p < 0.05, \*\* p < 0.01 or \*\*\* p < 0.001 as compared to the first column of each analyzed category; <sup>†</sup> Indicating that he/she works as a professor at the University; <sup>1</sup> Refers to all surveyed doctors: men and women.

vs. 50.6 ± 11.5 years,  $p < 0.0001$ ). Overall, 20.3% ( $n = 373$ ) were faculty members (women 17.6% vs. men 22.5%,  $p < 0.009$ ) and 85% had a partner (women 75.3% vs. men 92.7%,  $p < 0.0001$ ). If menopausal symptoms were present, 85.4% of gynecologists would use MHT for themselves or their partner. Overall, 7.6% stated they had doubts about using MHT and 7.0% stated that they would not encourage its use or would not be willing to use it (Fig. 1). The proportion of female gynecologists who favored MHT use was higher than the proportion of male gynecologists who would prescribe MHT for their partner (81.8% vs. 88.2%,  $p < 0.001$ ).

The gynecologists' graded perceived level of risk regarding the use of MHT is presented in Fig. 2. Overall, 5.2% perceived that the use of MHT had no risk (score 0), 21.7% considered it to carry an intermediate risk (score 5) and less than 1% estimated that there is an extreme risk (score 10). The perceived level of risk related to MHT use was higher among female than among male gynecologists (average scores:  $4.06 \pm 2.09$  vs.  $3.83 \pm 2.11$ ,  $p < 0.02$ ).

The main perceived risks related to MHT use are presented in Fig. 3. Overall, the top two perceived risks among surveyed professionals were thromboembolism and breast cancer. A greater proportion of female gynecologists than of male gynecologists perceived breast cancer to be a risk (38.5% vs. 33.9%,  $p < 0.03$ ), whereas a greater proportion of male gynecologists perceived thromboembolism to be a risk (41.4% vs. 33.6%,  $p < 0.009$ ). Overall, 7.7% perceived that the main risk related to MHT use was stroke, with no gender differences observed; and only 2.9% considered myocardial infarction to be a risk related to MHT use.

Regarding MHT prescription behavior, overall, gynecologists reported prescribing MHT to 48.9% of their symptomatic patients; the rate was higher for male than for female gynecologists (50.2% vs. 47.3%,  $p < 0.03$ ). Overall, 86.8% of respondents currently prescribed

non-hormonal remedies and 83.8% alternative therapies for the management of the menopause; in neither case was a significant gender difference observed. Table 1 shows the influence of doctors' age and academic level on perception behaviors regarding MHT use. Academic professionals (university staff member or professorship) tended to favor more personal/partner MHT use than non-academic professionals; however, they had a higher perceived level of risk related to MHT use (higher scores). No significant differences were observed between academic and non-academic professionals in terms of the two top perceived risks (thromboembolism and breast cancer). Academic gynecologists prescribed MHT to a higher percentage of their symptomatic patients than non-academic ones (55.9% vs. 47.1%,  $p < 0.001$ ) but had a similar prescription rate for non-hormonal and alternative therapies. Regarding age, gynecologists under 40 were less in favor MHT use by themselves or their partner, but no differences were observed between age groups in terms of the perceived risk level or specific perceived risks related to MHT use. There was a non-significant trend for younger gynecologists to prescribe MHT to a smaller percentage of their symptomatic patients and a significantly larger proportion of them prescribed alternative therapies for the menopause.

#### 4. Discussion

A high percentage of gynecologists agreed to participate in the study. Our response rate (85.3%) was much higher than the 26.6% agreeing to participate in the study by Buhling et al. [13]. In a study that analyzed attitudes to the self-use and prescription of hormone therapy among gynecologists in New York City the response rate was 12% [14]. We believe that our high response rate was achieved because gynecologists were invited to complete the survey by medical opinion leaders at their own institutions.

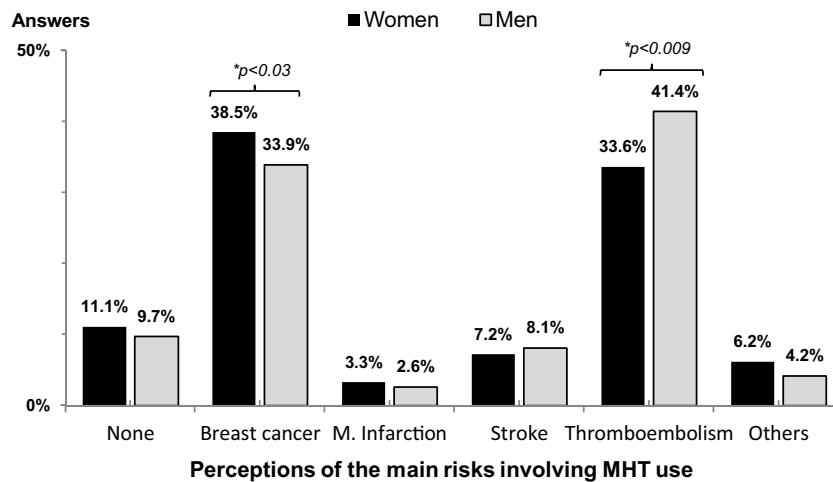


Fig. 3. Which are the main **perceived** risks related to MHT use? \**p* value determined with the chi square test.

Consistent with other studies, the gynecologists surveyed in our study were mostly supportive of MHT use (85.4%) if menopausal symptoms were present (i.e., among the female gynecologists themselves, or among the partners of the male professionals); only 7% indicated that they were not willing to use MHT. Our high rate is in agreement with the aforementioned German study by Buhling et al. [13], which found that 97.0% of gynecologists would use MHT [13]. Similarly, a study performed in 2007 reported that between 68% and 74% of Scandinavian gynecologists would prescribe MHT for themselves or their partners [15]. In the US and Europe an investigation covering six countries showed that 92% would prescribe MHT for themselves [16]. These figures suggest that not all physicians accept the reliability of the results of the WHI. This is in agreement with an Italian study which found that only 8% of female doctors and 4% of doctors' partners stopped MHT after the publication of the WHI data [17]. To the best of our knowledge, our study is the first to provide data from Latin America in relation to MHT self-prescription among gynecologists, evidencing a similar behavior as other worldwide studies.

Although personal MHT prescription is high among Latin American gynecologists, its use among women in these countries is low. Indeed, a previous multicenter study conducted in 11 Latin American countries showed that the overall prevalence of MHT use among women aged 45–59 was 12.5% in large cities [12]. This number may even be lower if smaller towns and rural areas are taken into account, in which women of lower socio-economic status live. In this sense, we have previously reported a lower rate of MHT use related to lower economic status [18]. As we have already reported [12], the main reason for the low rate of use of MHT in Latin American women is simply the lack of medical prescription. The present study shows a certain degree of concern among gynecologists regarding the possible risks related to MHT use, especially in terms of breast cancer and thromboembolism. Interestingly, and putting into perspective our previous report on MHT use in Latin America [12], although gynecologists seem to be concerned about the risk of MHT use, their rate of personal or partner use is high, whereas their patient prescription rate is low. The perception of thromboembolic disease as the main risk related to MHT use is striking, especially given that it is well known that transdermal MHT use has no thrombotic effects. Moreover, reports indicate that this route is also advantageous for women with diabetes, hypertension and other cardiovascular risk factors, and those of advanced age [19].

We imagine that the dichotomic behavior of Latin American gynecologists (and perhaps of those worldwide) could be influenced by their level of medical knowledge regarding the

menopause and MHT use. Indeed, the present study found that academic gynecologists were more supportive of personal/partner and patient MHT use than were their non-academic colleagues. Another factor that we believe may influence the low rate of prescription to symptomatic women is a lack of knowledge among doctors regarding the symptoms related to menopause. Reports show that the main reasons for gynecologists to prescribe MHT to menopausal women are vasomotor and genitourinary symptoms [13,20]. Few studies have cited musculoskeletal discomfort and mood disorders as indications for MHT. These menopausal symptoms are the earliest in presentation and most prevalent [21]. If these symptoms are not taken into consideration upon evaluation, fewer women will receive the benefits of MHT. We found a correlation between the doctor's age and prescription behavior. A smaller proportion of gynecologists under 40 prescribe MHT to themselves or their partners (if menopausal symptoms are present) and they prescribe alternative therapies for a larger proportion of their symptomatic patients. This is understandable, since the prevalence of menopausal symptoms is lower among women under 40 years of age; hence their position is to favor less risky interventions or therapies.

In our opinion the main weakness of the present study is that the invitation to participate was made by medical opinion leaders who are involved in the care of menopausal women and are REDLINC members and co-authors of this study. Although this helped us to achieve a very high response rate, respondents may have been influenced by the position of these leaders, and recorded more favorable behaviors toward MHT in the care of their menopausal patients than was really the case. We acknowledge this bias as a limitation and that it would have been better to obtain a complete list of certified gynecologists in each country in order to perform random sampling. Nevertheless, we chose to take advantage of our network, a well known and well established group of investigators in many Latin American countries, and in this case, as in many other REDLINC studies, it allowed the recruitment of a large sample. This in fact may be seen as a potential strength of the study.

In conclusion, the present study found that Latin American gynecologists are mostly supporters of MHT use (for themselves or their partners). However, this behavior does not translate into clinical practice with their patients.

### Contributors

L.D. and J.E.B. conceived and designed the study. All authors apart from JEB were involved in data collection. Statistical analysis was undertaken by J.E.B. and P.C.

L.D., J.E.B. and P.C. drafted and revised the text. All authors have seen and approved the final manuscript.

### Conflicts of interest

None declared.

### Funding

No funding was received for this study.

### Ethical approval

The study was reviewed and approved by the Scientific Ethics Committee of the Servicio de Salud Metropolitano Sur (Ministry of Health), Santiago, Chile. Informed consent was obtained from all participants.

### Provenance and peer review

This article has undergone peer review.

### Appendix A.

*List of participating countries, investigators (city).*

**Argentina:** Mabel Martino (Rosario), Blanca Campostrini (La Plata) and Silvina Witis (Buenos Aires); **Bolivia:** María T. Espinoza (Cochabamba), Desireé Mostajo (Santa Cruz), Nelva Meruvia (La Paz) and Javier Saavedra (Sucre); **Chile:** Juan E. Blümel (Santiago de Chile), Jaime Martínez (La Serena), Eugenio Arteaga (Viña del Mar), and María S. Vallejo (Santiago de Chile); **Colombia:** Gustavo Gómez (Cali), Alvaro Monterrosa (Cartagena), and William Onatra (Bogotá); **Costa Rica:** Flory Morera (San José) and Gerardo Broutin (San José); **Ecuador:** Peter Chedraui (Guayaquil), Andrés Calle (Quito) and Hugo Sánchez (Machala); **México:** Erik González (Juárez), Armando Montañón (México, DF) and Carlos Salinas (Puebla); **Panamá:** Konstantino Tserotas (Panamá); **Perú:** Félix Ayala (Lima), Luis Danckers (Lima), Eliana Ojeda (Cuzco), Olivia Castillo (Arequipa) and José A. Rojas (Lima); **República Dominicana:** Ascanio Bencosme (Santiago de los Caballeros); **Uruguay:** Selva Lima (Montevideo).

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