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Menopause research in Latin America

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ABSTRACT
For 15 years, the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) has been conducting research on several topics including age of menopause, metabolic syndrome, quality of life and climacteric symptoms, sexual dysfunction, poor quality of sleep and insomnia, and use of menopausal hormone therapy (MHT) in the general population and among gynecologists. Examples of data to have emerged for this region include the age of menopause (49 years), a high prevalence of metabolic syndrome (42.9%), and a new waist circumference cut-off value for the Latin American population (88 cm). Sexual dysfunction, poor quality of life, and sleep disorders have a prevalence of over 50%, with obesity and sedentary lifestyles affected importantly. MHT use is still low (12.5%), lack of prescription the most important reason for not using it, and gynecologists use MHT for themselves but do not recommend it often to their patients. The prevalence of alternative therapy use, recommended by physicians, is high.

Introduction
In 2004, the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) was formed by a group of physicians, mostly gynecologists, who themselves had a background in research and education and who were eager to join together to produce data specific to Latin America and thus more precisely helpful to local communities and women. REDLINC was officially announced at the Regional Congress on Menopause in Lima, Peru in May 2004.

Latin America is a subcontinent with 654 million people (as of September 2018), divided into 20 countries and 13 dependencies, with five cities of over 10 million inhabitants (Mexico City, Sao Paolo, Buenos Aires, Rio de Janeiro, and Lima) and a total population of 43 million women older than 60 years of age 1.

Dr Juan Enrique Blümel, an endocrinologist from Chile, and Dr Luis Danckers, a gynecologist from Lima, Peru, presented REDLINC to the Congress floor. Fifty-one physicians from 15 countries of Latin America joined the Collaboration, which received great support from international experts on the menopause present at the Lima meeting including Dr Leon Speroff, Dr Hermann Schneider, Dr Andrea Genazzani, and Dr Santiago Palacios. Despite having no funding or institutional support, our first study protocol ‘REDLINC I – Age of Menopause in Latin America’ was presented. Since then, seven investigation projects have been developed, resulting in 18 publications (Table 1).

REDLINC I: Age of menopause
‘Age of Menopause’ was our first publication. We studied age of menopause in Latin America and factors that could modify it. A total of 17,850 women aged 40–59 years (49.4 ± 5.5 years) from 51 centers in 15 countries were studied 2. The median age of menopause for the entire sample using logit analysis was 48.6 years. Logistic regression analysis determined that women aged 49 years living in cities at 2000 m or more above sea level (odds ratio [OR] 2.0; 95% confidence interval [CI] 1.4–2.9, p < 0.001) and those with lower educational level (OR 1.9; 95% CI 1.3–2.8, p < 0.001) or living in countries with low gross national product (OR 2.1; 95% CI 1.5–2.9, p < 0.001) were more prone to an earlier onset of menopause 2.

REDLINC II: Metabolic syndrome
In our second study, on metabolic syndrome (METS), we enrolled a total of 3965 postmenopausal women, aged 45–64 years, seeking health care at 12 gynecological centers in major Latin American cities 3. The prevalence of METS was 35.1%, increasing from 28.1% (age 40–44 years) to 42.9% (age 60–64 years). The risk of METS (multivariate analysis) increased with obesity (OR 13.01; 95% CI 10.94–15.49), hypertension (OR 9.30; 95% CI 7.91–10.94), smoking cigarettes (OR 1.40; 95% CI 1.19–1.65), age (OR 1.22; 95% CI 1.03–1.43), and time elapsed since menopause >5 years (OR 1.18; 95% CI 1.00–1.38). In contrast, hormone therapy reduced this risk (OR 0.59; 95% CI 0.51–0.70) 3.

In a reanalysis of data, a waist circumference cut-off value of 88 cm was determined as optimal for defining the METS among postmenopausal Latin American woman. This cut-off value is the same as that set for occidental women and not...
similar to that set for Asian women (range 80–85 cm) as was previously thought.

**REDLINC III: Sexual dysfunction**

The objective in our third study was to assess the prevalence of sexual dysfunction and associated risk factors in middle-aged women in Latin America using one validated instrument. The Female Sexual Function Index (FSFI) was applied to 7243 healthy women aged 40–59 years who were users of 19 health-care systems from 11 Latin American countries. We found that 56.8% of participating women presented with sexual dysfunction (FSFI total score ≤26.55). Risk factors were poor lubrication (OR 3.86; 95% CI 3.37–4.43), use of alternative menopausal therapies (OR 2.13; 95% CI 1.60–2.84), partner with sexual dysfunction (OR 1.89; 95% CI 1.36–2.20), older women (age >48 years), bladder problems, menopausal hormone therapy (MHT) use, negative perception of female health status, and being married. Protective factors were higher educational level, partner faithfulness, and access to private health care.

In an accompanying editorial, Dr Sheryl Kingsberg wrote: ‘These data provided information on sexuality in Latin America where, except for the use of alternative therapies, it indicates that Latin American women may share many of the same general risk factors for sexual problems as those of aging women in other countries and cultures.’ The second interesting parallel to research in female sexual function is the use of a single validated instrument, the FSFI. The FSFI results confirm that the most prevalent sexual problem among women, desire, was the most compromised sexual domain. In contrast, the least affected sexual domain from the FSFI was satisfaction. Lack of vaginal lubrication, the most significant risk factor related to sexual problems, can typically be easily resolved if brought to the attention of a health-care provider. However, many women still do not know that discomfort with sexual activity is a legitimate complaint and worry that it is not an appropriate problem to address with their health-care provider.

**REDLINC IV: Quality of life and climacteric symptoms**

The objective in our fourth study was to determine quality of life (QoL) using the Menopause Rating Scale (MRS) and to determine factors associated with severe menopausal symptoms (QoL impairment). This was a cross-sectional study of 8373 healthy women aged 40–59 years accompanying patients to medical appointments at 18 centers in 12 countries. Poor QoL was reported by 55.4% of women (moderate 30.5% [MRS score 9–16%] + severe 24.9% [MRS score ≥17%]). Associated risks were living at high altitude (OR 1.43; 95% CI 1.25–1.62), using alternative therapies for the menopause (OR 1.47; 95% CI 1.22–1.76), use of psychiatric drugs (OR 1.57; 95% CI 1.29–1.90), attending a psychiatrist (OR 1.66; 95% CI 1.41–1.96), being postmenopausal (OR 1.48; 95% CI 1.29–1.69), being age 49 years or older (OR 1.24; 95% CI 1.08–1.42), and having a partner with premature ejaculation (OR 1.34; 95% CI 1.16–1.55) or erectile dysfunction (OR 1.69; 95% CI 1.47–1.94). Protective measures were MHT use (OR 0.65; 95% CI 0.56–0.76) and engaging in healthy habits (OR 0.59; 95% CI 0.50–0.69).

Latin American women have higher scores in all three groups of symptoms on the MRS (psychological, somatic, and urogenital) compared to women from the USA, Europe.

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**Table 1. Menopause research in Latin America by the Collaborative Group for Research of the Climacteric in Latin America (REDLINC).**

<table>
<thead>
<tr>
<th>Study</th>
<th>Theme</th>
<th>Results</th>
<th>References</th>
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</thead>
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<tr>
<td>REDLINC I</td>
<td>Age of menopause</td>
<td>Age of menopause is 49.4 ± 5.5 years. Earlier age occurs with higher altitude, low national income, and lower education</td>
<td>2</td>
</tr>
<tr>
<td>REDLINC II</td>
<td>Prevalence of metabolic syndrome</td>
<td>Prevalence of 42.9% (age 60–64 years). Risk factors: obesity, hypertension, smoking cigarettes, age, and time elapsed since menopause &gt;5 years. Protective measures: MHT. New waist circumference cut-off value: 88 cm</td>
<td>3,4</td>
</tr>
<tr>
<td>REDLINC III</td>
<td>Sexual dysfunction</td>
<td>Prevalence: 56.8%. Risk factors: poor lubrication, use of alternative menopausal therapies, and partner with sexual dysfunction</td>
<td>5, 6</td>
</tr>
<tr>
<td>REDLINC IV</td>
<td>Quality of life</td>
<td>Prevalence: 55.4%. Risk factors: living at high altitude, using alternative therapies for the menopause, psychiatric drugs, postmenopausal, and having a partner with sexual dysfunction. Protective measures: MHT use and engaging in healthy habits</td>
<td>7–9</td>
</tr>
<tr>
<td>REDLINC V</td>
<td>Sleep disorders</td>
<td>Prevalence: 56.6%. Risk factors: age, presence of chronic disease, anxiety, depression, vasomotor symptoms, and drug use (hypnotics and hormone therapy). Protective measure: higher education</td>
<td>10–13</td>
</tr>
<tr>
<td>REDLINC VI</td>
<td>Menopausal hormone therapy use</td>
<td>Current use: 12.5%, mostly oral. MHT use associated with positive perceptions on therapy and better socioeconomic level. No prescription is the most important reason for not using MHT</td>
<td>14</td>
</tr>
<tr>
<td>REDLINC VII</td>
<td>Gynecologist’s use of and recommendation for MHT</td>
<td>High level of personal use but a lower level of patient recommendation (85% vs. 48%). Over 80% prescribe non-hormonal and/or alternative remedies. Postmenopausal female physicians prescribe more MHT than premenopausal female physicians</td>
<td>15,16</td>
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MHT, menopausal hormone therapy.
and Asia\(^7\). A hypothesis resulting from this observation was that the indigenous origin of our mestizo population could make a difference. A group of 573 naturally menopausal women aged 45–59 years (288 Quechua, Peru and 285 Zenú, Colombia) living in isolated communities were surveyed\(^17\). The total MRS score was higher among Quechua women as compared to Zenú women, but both were higher than in the Hispanic and European population. Quechua women presented more intense psychological and somatic symptoms as compared to Zenú women, but both had similar urogenital symptoms. More than 90% of indigenous women (Quechua and Zenú), in all age intervals, presented with severe urogenital scores, a much higher percentage than that described in the world literature. Higher altitude contributed to poor QoL in our study, and comparing Quechua (high altitude) vs. Zenú (lowlands) may explain some of their differences\(^17\).

To study whether the difference in menopausal symptoms between Quechua and Zenú women was due to altitude or their ethnic origin, a new investigation began comparing 376 ‘pure’ Quechuas with 395 ‘Hispanic-Mestizas’ (Quecha-Spaniard breeding) from Cuzco, Perú (same altitude)\(^18\). All three domains and all subsets had significant differences in the MRS score against Quechus, total score of 14.54 ± 7.51 vs. 9.87 ± 6.26 (p < 0.0001), respectively. Consequently, 46.5% of the ‘Quechus’ had deteriorated QoL due to severe climacteric symptomatology, compared to only 14.2% of ‘Hispanic-Mestizas’ women (p < 0.0001). Thus, it seems that indigenous women have more severe climacteric symptoms compared to mestizas who live at a comparable altitude\(^18\).

This suggests that ethnicity could be one of the factors that explain the augmented symptoms in Latin American climacteric women when compared to other societies seen on our REDLINC IV study\(^7\).

From this same database, an observation was made in relation to ‘muscle and joint aches (MJA)’. Higher risk for MJA was associated with vasomotor symptoms (OR 6.16; 95% CI 5.25–7.24), premature menopause (OR 1.58; 95% CI 1.02–2.45), postmenopausal status, psychiatric consultations, and use of psychotrophic drugs. Lower risk was associated with MHT use, private health-care access, and a perception of good health. In this large mid-aged sample, the prevalence of MJA was high, which was significantly associated with menopausal variables, especially vasomotor symptoms. This association may suggest a potential role of mid-life female hormonal changes in the pathogenesis of MJA\(^9\).

In another publication\(^9\) looking into the beginning of symptomatology, we found that severely rated menopausal symptoms occur early in the premenopause (12.9%), increasing to 26.4% in perimenopausal women, 31.6% in early postmenopausal women, and 29.9% among late postmenopausal women. With age and each menopausal phase, impaired QoL has an impact lasting 5 years beyond the menopause. Muscle and joint discomfort, physical and mental exhaustion, and depressive mood were highly prevalent and rated as severe–very severe at a higher rate than vasomotor symptoms (15.6%, 13.8%, and 13.7% vs. 9.6%, respectively). In this study, vasomotor symptoms ranked ninth in a list of menopausal complaints in contrast to the preeminent position of such symptoms in studies of western women. Nevertheless, the presence of hot flushes increased the risk of impairment of overall QoL in both premenopausal women (OR 12.67; 95% CI 9.53–16.83) and peri/postmenopausal women (OR 9.37; 95% CI 7.85–11.19)\(^9\).

**REDLINC V: Sleep disorders**

In our fifth study, our objective was to determine the prevalence of sleep disturbances in mid-aged women using validated tools. Assessment of determinants capable of influencing the prevalence of insomnia and poor-quality sleep was also performed. A total of 6079 women aged 40–59 years in 11 countries of Latin America were evaluated using the Athens Insomnia Scale, the Pittsburgh Sleep Quality Index, the Goldberg Anxiety and Depression Scale, the MRS, the Brief Scale of Abnormal Drinking, and a general sociodemographic questionnaire\(^10\).

In our study, 56.6% of surveyed women suffered either insomnia, poor sleep quality, or both. Specifically, 43.6% and 46.2% presented with insomnia and poor sleep quality. The prevalence of insomnia increased with female age (from 39.7% in those aged 40–44 years to 45.2% in those aged 55–59 years, p < 0.0001) and menopausal stage (from 39.5% in premenopausal women aged 40–44 years to 46.3% in late postmenopausal women, p < 0.0001). ‘Awakening during the night’ was the most highly rated of all items and contributed in a higher degree to the total score of the scale in all menopausal phases\(^10\).

In our population, anxiety and depression affected 59.7% and 46.5% of women, respectively. ORs for insomnia and poor sleep quality also displayed an increasing trend, nearly 8-fold to 10-fold in relation to higher depressive and/or anxiety score. Women presenting with sleep disturbances displayed a 2-fold increase in the severity of menopausal symptoms which translated into a 6–8 times higher risk of impaired QoL. Logistic regression analysis determined that female age, the presence of chronic disease, troublesome drinking, anxiety, depression, vasomotor symptoms, and drug use (hypnotics and hormone therapy) were significant risk factors for sleep disturbances. Higher educational level was related to less insomnia and better sleep quality\(^10\).

In a reanalysis of this database considering obesity\(^11\), we found that significant factors associated with obesity included arterial hypertension (OR = 1.87), depressive symptoms (OR = 1.57), sedentary lifestyle (OR = 1.50), diabetes mellitus (OR = 1.34), higher number of individuals living at home (OR = 1.31), sleep problems (OR = 1.22), anxiety (OR = 1.21), having a stable partner (OR = 1.20), parity (OR = 1.16), and vasomotor symptoms (OR = 1.14). A lower risk for obesity was found among women using hormonal contraceptives (OR = 0.69). We concluded that obesity in middle-aged women is the consequence of the interaction of multiple factors. It was associated with hypertension, depressive symptoms, sedentary lifestyle, climacteric symptoms, and other factors\(^11\).

In another publication from the viewpoint of ‘sedentary women’\(^12\), analysis showed that both obesity (OR 1.52; 95%
CI 1.32–1.76) and severe menopausal symptoms (OR 1.28; 95% CI 1.06–1.53), including insomnia and depressive mood, were positively associated with a sedentary lifestyle. Having a stable partner (OR 0.85; 95% CI 0.76–0.96), using hormone therapy (OR 0.75; 95% CI 0.64–0.87), and having a higher educational level (OR 0.66; 95% CI 0.60–0.74) were negatively related to a sedentary lifestyle. In an editorial in Menopause, Dr Antonio Cano mentioned our results and the added value of the use of specific and validated scales to assess menopausal symptoms19.

When looking directly at type II diabetes mellitus13, the prevalence was 6.7%. It was associated with arterial hypertension (OR 4.49; 95% CI 3.47–5.31), the use of psychotropic drugs (OR 1.54; 95% CI 1.22–1.94), hormonal therapy (OR 1.46; 95% CI 1.11–1.92), age (50 years and older) (OR 1.48; 95% CI 1.17–1.86), overweight or obese (OR 1.47; 95% CI 1.15–1.89), and waist circumference ≥88 cm (OR 1.32; 95% CI 1.06–1.65). Diabetes tripled the risk of menopause in women <45 years of age. Menopause does not increase the risk of type II diabetes mellitus13.

**REDLINC VI: Use of hormone therapy**

Our objective in the sixth study was to determine the prevalence of current MHT use among mid-aged women and describe the characteristics of those who have never used, have abandoned, or are currently using MHT. This was a cross-sectional study that analyzed a total of 6731 otherwise healthy women (45–59 years old) from 15 cities in 11 Latin American countries14.

We found that current use of MHT was 12.5%, oral MHT being the most used (43.7%). The main factors related to current use included positive perceptions regarding MHT (OR = 11.53), being postmenopausal (OR = 3.47), and having a better socioeconomic level. A total of 48.8% of surveyed women had used MHT in the past but had abandoned it due to improvement of symptoms or being unconcerned. Among women who had never used MHT, 28% mentioned the lack of medical prescription as the main reason followed by absence of symptoms (27.8%). Among those reporting lack of prescription as the main reason for not using MHT, 30.6% currently had severe menopausal symptoms (total MRS score >16); 19.5% of women were using alternative ‘natural’ therapies, with 35.1% of them displaying severe menopausal symptoms as compared to 22.5% observed among current MHT users. We concluded that use of MHT has not regained the rates observed a decade ago. Positive perceptions regarding MHT were related to higher use. Lack of medical prescription was the main reason for not using MHT among non-users, many of whom were currently displaying severe menopausal symptoms14.

**REDLINC VII: Professional use of MHT**

The objective of our seventh study was to determine the use of MHT and perceived related risks among gynecologists15. A total of 1837 gynecologists were surveyed; 55.5% were male. Most gynecologists (85.4%) would use MHT if they had menopausal symptoms (81.8% female) or prescribe it to their partner (88.2% male gynecologists; p < 0.001). Perceived risk was higher among female than male gynecologists (4.06 ± 2.09 vs. 3.83 ± 2.11, p < 0.02). Of the two perceived risks, men were more concerned about venous thromboembolism (men 41.4% vs. women 33.6%, p < 0.009) and women about breast cancer (38.5% vs. men 33.9%, p < 0.03). Gynecologists reported prescribing MHT to 48.9% of their symptomatic patients. Gynecologists who were older and academic professionals prescribed MHT more often. Gynecologists prescribe MHT more to themselves than to their patients. Over 80% prescribe non-hormonal and/or alternative remedies15.

Amongst a subgroup of female gynecologists, most would use MHT if menopausal symptoms were present. Postmenopausal physicians use MHT and prescribe it to their symptomatic patients at a much higher rate than premenopausal physicians16.

**What do we have in the pipeline?**

Planned studies for the future are REDLINC VIII, ‘Menopause and sarcopenia’; REDLINC IX, ‘Use of metformin and bone aging’ (using as reference the Targeting Aging with Metformin Study); and REDLINC X, ‘Cognition/ovary status/MHT’.

**Game-changing data**

Some data for Latin America have emerged from the REDLINC studies to date:

- The age of menopause is 49 years.
- Differences in menopausal symptoms are seen with low education, poverty, and altitude of the city.
- There is a high incidence of METS in Latin American women and a waist circumference cut-off value of 88 cm was determined as optimal for defining the METS.
- There are many problems in sexual health (the most important being lubrication).
- QoL is affected by severe vasomotor symptoms, depression, anxiety, and obesity.
- Obesity affects all!
- Patient and medical education is the basis for good use of MHT.
- Obstetricians/gynecologists need to treat patients more as they treat themselves, especially female obstetricians/gynecologists.

**Final thoughts**

During the past 15 years, a group of physicians and friends, with the sole interest of evaluating and treating their patients better, formed REDLINC, with no budget but great personal interest. After 15 years, seven investigation projects have been completed and 50,000 patients and 1837 professionals have been surveyed. Eighteen papers have been
published in peer-reviewed journals and there have been several spin-off publications on national data.

We have proven that commitment and dedication using scientific methods and validated tools can produce great data, allowing us to understand our population a little better and thus train our doctors more effectively.

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