
Menopause Management Roundtable on Quality of Life (QOL)

Recently published analyses from data collected in the Women's Health Initiative seem to suggest that combined estrogen-progestin therapy (EPT) does not improve quality of life (QOL) compared with placebo. However, like many other studies, the WHI did not use a scientifically validated QOL measure. Which of these measures are best? Which have been researched most thoroughly? How applicable are they to various menopausal populations? Menopause Management posed these and other questions to three experts in the field.

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In your opinion, what is the contemporary definition of QOL as it relates to menopausal women?

Pinkerton: Quality of life as it relates to menopausal women is best described as health-related quality of life and includes physical health and functioning, emotional functioning, role limitations, and social functioning. Unfortunately, the term "quality of life" is often used simply to refer to menopausal symptoms such as presence of significant hot flashes, night sweats, vaginal dryness or pain, and loss of well-being. These climacteric symptoms may negatively affect quality of life for symptomatic menopausal women and often improve with EPT. However, it is important to recognize these symptoms—along with other more global aspects of quality of life including health status, life satisfaction, coping, and psychological functioning.

Alder: There are many definitions of QOL, and they depend on the theoretical perspective taken. A health/illness model looks at the effect of ill health on a number of dimensions such as those measured in the SF-36. If a symptom approach is taken, then these need to be

measured. However, menopause is not a disease; and QOL is related to more than health. The WHO 1993 definition of an individual perception of their position of life in the context of the culture and value systems in which they live and in relation to their goals, standards, and concerns can be applied to menopausal women.

Utian: The term "quality of life" is no longer acceptable as a loose cliché. Rather, it must be defined by measurable domains. Moreover, these domains should be evaluable independent of the presence or absence of disease or symptoms, although, of course, these might influence QOL. Thus, QOL refers to a global sense of well-being and self-satisfaction beyond the presence or absence of symptoms. It also determines how the peri- or postmenopausal woman feels generally and, specifically, regarding interest in life, ability to complete a day's work with satisfaction, maintenance of good interpersonal relationships, sexuality, and a general feeling of wellness.

Are contemporary instruments capable of adequately measuring and tracking

QOL? If not, please explain. Describe which instruments work best or have been researched most thoroughly.

Pinkerton: To adequately measure QOL, an instrument needs to be modern, applicable, and reliable, with normal values for different populations. It also must show change over time, or with different interventions. It should be comparable to other validated instruments and be responsive to changes in clinical symptoms over time. The failure to use adequately validated rating scales has been a major problem in menopause research.

The best current instruments, according to Schneider, are the Greene Climacteric Scale, the Women's Health Questionnaire, the Menopausal Symptom List, the Menopause Rating Scale, which is self-administered, and the Utian QOL Scale.

Simply using a checklist of symptoms can introduce bias since many will respond positively to symptoms on a checklist, but the reporting rate will decrease if frequency or bothersomeness of symptoms are included.

The Kupperman Menopausal Index is a summation of menopausal complaints derived from clinical experience in New York in the 1950s. It is a classic scale that, while widely used, is not considered very sensitive. Kupperman included 11 symptoms (vasomotor, paresthesia, insomnia, nervousness, melancholia, vertigo, weakness/fatigue, arthralgia/myalgia, headaches, palpitations, and formication) on a four-point scale. It overrates neurovegetative symptoms while neglecting measurement of sexuality, including vaginal dryness, dyspareunia, and breast tenderness.

Standardized menopause-specific instruments that measure symptoms of climacteric need to satisfy criteria of factor analysis, include subscales measuring different aspects of symptomatology, as well as sound psychometric properties, and be standardized across populations of women.

Menopause-specific scales that

measure the symptoms of climacteric women include:

- *The Greene Climacteric Scale* uses factor analysis as the basis to categorize symptoms into three factors (vasomotor, somatic, and psychological) and currently consists of 21 symptoms, each rated on a four-point scale of severity. Test-retest reliability coefficients of subscales achieved a satisfactory level. Validity has been proven over time.
- *The Women's Health Questionnaire* is based on a factor analysis of 36 symptoms reported by a general population sample from southeast England. There are eight subscales; four are identical to the Greene Climacteric Scale with 32 symptoms, each rated on a binary scale 0/1. Satisfactory test-retest reliability was good. It is used as a comparative measure, demonstrating its construct validity.
- *The Menopausal Symptom List* is based on factor analysis of 56 symptoms from a general population sample of Australian women. There are three subscales (vaso-somatic, general somatic, and psychological). The psychological subscale includes the anxiety and depression subscales of the Greene Climacteric Scale and the Women's Health Questionnaire. The final version has 25 symptoms, each rated on a six-point scale of frequency and severity. Test-retest reliability is satisfactory, but the validation is limited.
- *The Menopause Rating Scale* is based on factor analysis of three dimensions of severity (somatic, psychological, and urogenital symptoms) from a sample of German women. The final scale consists of 11 symptoms, each rated on a five-point severity scale. The women were retested over 1.5 years with a high degree of stability of all three subscales.
- *The Utian Menopause Quality of Life Score* is based on a two-stage factorial process. A principal component analysis was followed by a factor

analysis using 40 questions from a sample of Americans living in the east and Midwest. The final scale consists of 23 items, each rated on a five-point Likert scale. It should be used with a standardized measure of climacteric symptoms.

Alder: There is no 'correct' or 'adequate' measure—it depends entirely on the question asked. If the concern is the effect of symptoms on quality of life, then a measure such as the Menopause Rating Scale (MRS) is appropriate. Alternatively, if the individual woman's view of her own quality of life is the concern, a patient-centered scale such as the Patient Generated Index (PGI) can be used. If the question is to compare menopausal women with other groups, then a standardized generic measure such as the The MOS 36-item short-form health survey (SF-36) would be appropriate.

Utian: Instruments have been and are being developed for multiple situations. In the area of menopause-related QOL, the first generation instruments were unvalidated symptom profiles (eg, the discredited Kupperman index). Second-generation instruments tended to rely heavily on symptom-evaluation and be light, if mentioned at all, on domains of QOL (eg, the Menopause Specific Quality of Life, or MENQOL questionnaire). The latest third-generation focuses exclusively on measuring QOL domains and not symptoms (eg, UQOL).

Are all these instruments applicable to peri- and postmenopausal populations? Please specify.

Pinkerton: It is important to distinguish menopause-related changes from those of age or disease and to recognize that there is a transition from premenopause through perimenopause to postmenopause.

It is difficult to identify the perimenopausal population because it is a

time of transition, and there are no definable blood tests or other activities to make inclusion criteria easy. Therefore, perimenopausal women will vary on these scales over time because of the fluctuations seen in their hormonal levels, climacteric symptoms, and moods. In studying the perimenopausal process, it would probably be best to pick an age range of 45-55 and then do longitudinal evaluation over time.

In contrast, postmenopausal populations can be best defined as those reporting more than one year since their last period (one year of amenorrhea) and showing a follicle-stimulating hormone (FSH) level of >30. This population can then be compared over time and with different interventions and in different cross-cultural analyses.

In addition, if a specific group is being studied, such as symptomatic menopausal women, that group should have a strict definition such as moderate-severe (eg, 7 hot flashes per day or 50 hot flashes per week) to be included in analysis of quality of life measures for symptomatic women.

Alder: The applicability depends on the question. Not all have been validated on menopausal populations.

Utian: Only those instruments that have been validated for specific populations or circumstances can be appropriately utilized. Thus, the MENQOL or the UQOL apply to the peri- and postmenopausal populations. An ideal profile can best be generated by combination of a validated menopause symptom profile (eg, Greene) in combination with a QOL instrument (eg, UQOL). This allows a clarification of the relationship between each and change or progress over time.

Does the recent publication of the Women's Health Initiative's QOL data test the correct population and utilize satisfactory instruments?

Pinkerton: The WHI publication on QOL benefits found no significant clinical QOL benefit on any of the QOL outcomes including general health, vitality, mental health depressive symptoms, or sexual satisfactions. It did find EPT use associated with a statistically significant, but not clinically significant, benefit in sleep disturbance, physical functioning, and body pain at one year, but not at three years. It was comparable to the Heart-Estrogen/progestin Replacement Study (HERS), where no improvement in QOL was seen in older, asymptomatic postmenopausal women.

However, it is important to note that women were dissuaded from entering the WHI trial if they had significant vasomotor symptoms because of the possibility of placebo. In addition, women self-defined if they had moderate to severe hot flashes relying on self-recall to complete questionnaires at one and three years. Hot flash diaries would be more methodologically sound along with strict definition of moderate-severe hot flash intensity, such as 7 hot flashes per day or 49 per week. Thus, the WHI study did not answer the question of whether EPT improves QOL in women with moderate-severe symptoms or how important that QOL benefit is to a symptomatic individual in comparison to the small increased risks found with EPT.

The WHI did not use a validated QOL instrument. The surrogate measures were not as specific for answering the question of QOL in symptomatic menopausal women. The lack of beneficial QOL in this study, therefore, could have been predicted.

According to Utian in the NAMS News 2003, "the population was an older asymptomatic population, not a general menopausal population. Biomedical measures were used to assess QOL. While these measures are a necessary component to determine health status, they are not sufficient to accurately reflect a sense of global well being. As no validated QOL instrument

was used, investigators had to rely on a series of surrogate tests to determine QOL, virtually all with severe limitations. For example, only one question was used to determine sexuality, a crude evaluation for cognitive benefit (the Modified Mini-Mental State Examination), and they used the RAND-36 Item Health Survey, which is designed to test more for health-related factors than for sense of well-being and QOL. Third, progestin is known to attenuate estrogenic effects, and this study involves the continuous administration of progestin with estrogen. The post hoc analysis was to determine the impact of estrogen-progestin therapy on QOL in a subset of younger, symptomatic women—a much more accurate subset to evaluate. However, this was based on an intent-to-treat analysis which is difficult to evaluate a mental benefit of women not taking an active drug and then comment on a lack of effect from that drug."

Alder: Sorry, can't answer this.

Utian: The WHI QOL publication is extraordinarily flawed. The wrong population (median age 63, mostly without moderate to severe menopause symptoms) was followed inadequately without validated instruments (unvalidated symptom profile, no hot flash score or diary, one question for sexuality, crude cognition and mental state measures, etc). The conclusions published, therefore, can only be regarded with a high degree of skepticism. This is unfortunate as, of course, they may or may not be correct.

Should clinicians consider routine measurement of QOL? If so, how often and in which populations?

Pinkerton: It is important to recognize that the menopause is an important transition that providers can help women navigate to maximize their quality of life and minimize negative

aspects. A well-defined menopausal complaint rating scale would help providers and patients choose the best treatment or lifestyle changes for their individual needs and allow follow-up at future visits to see if there has been significant improvement. In addition, we would learn more information about different populations of women.

Alder: No, most measures are devised for research studies in large populations and may not be applicable to individuals. The PGI is the most sensitive and could be used. I would expect that clinical judgment would be the best measure of improvement or deterioration in an individual if the clinician is trained to ask sensitive questions and address the patient's agenda. It is easy to make assumptions about QOL for others, but the research in disability suggests that individuals rate their QOL higher than others do and they often rate it relative to previous state of health.

Utian: A simple QOL score has clinical value if tracked longitudinally from visit to visit. If the score is decreasing, the medical history should focus on whether an existing problem has deteriorated or whether a new problem has developed.

What modalities exist for providers to enhance QOL in their peri- and postmenopausal patients?

Pinkerton: Modalities providers can use to enhance QOL for menopausal women include education about menopausal symptoms and the menopausal transition, improvements in lifestyle issues such as appropriate weight maintenance, calcium intake, and adequate physical activity. In addition, there are medications such as EPT, which may be very helpful for symptomatic menopausal women and alternatives for those who can't or won't take EPT. For example, there are local estrogen products for vaginal atrophy

and dyspareunia, bone-specific medications such as bisphosphonates, selective estrogen receptor modulators (SERMs) for those with bone loss and risk of breast cancer, selective serotonin reuptake inhibitors (SSRIs) for persistent hot flashes if estrogen is not used, and statins to lower cholesterol and prevent cardiac disease.

Understanding the impact of psychological stressors and asking about them is very important. For example, Dennerstein reports that overall life satisfaction is related to mood, predicted by earlier attitudes and affected by relationship to partner, current stress and lifestyle issues unrelated to menopause, hormone levels, or EPT use.

Alder: This is interesting because it depends on the definition. Clearly, climacteric symptoms can be very disabling. If, for example, hot flashes are alleviated and self-esteem and social confidence are improved, then there is a direct effect. Similarly, if night sweats are reduced, there may be less fatigue and more energy. Many studies show a domino effect on psychological state. The scales of the SF-36 measure health from the patients' point of view. Other aspects of QOL may be beyond the provider's ability unless there is social change.

Utian: The best approach is to determine existing problems and treat effectively. In particular, domains of health, emotional well-being, and sexuality can be addressed. Occupational issues, on the other hand, are difficult for the health provider to remedy. ■

Suggested Reading

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