

# A holistic approach to mature women's health and aging

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## INTRODUCTION

The health and aging of middle-aged women are nowadays the subject of many challenging strategies in view of recent important progress in preventive medicine.

Women are cells of a 'social body'. As such, one should study them both in their macrosocial and in their microsocial context, without forgetting that 'everything should be made as simple as possible . . . but not simpler', as said by Albert Einstein.

### Holism

A holistic approach seems to be more realistic and meaningful. Holism is 'the approach to the study of a phenomenon through the analysis of the phenomenon as a complete entity in itself'<sup>1</sup>. It permits one to see 'an individual as a complex system'<sup>2</sup>, arising in the body, the psychological life, the ecosocial environment, and the health-care system.

The World Health Organization (WHO) has defined health as a 'state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity'. In itself, this definition is holistic, meaning that the individual is seen as a complex system, as indicated above.

As a matter of fact, 'the *climacteric* is a complex, multifaceted process that responds to the interaction of different *biopsychosocial factors*'<sup>3</sup>. This is, therefore, a very judicious counsel as to how to manage the mature women who come to their doctors seeking advice and help.

### Health

One of the most difficult tasks facing the attending physician is the diagnosis of 'health'. It is far simpler to diagnose a disease. 'It is politically less

threatening to view women's health only through the biomedical model but *this denies* the roles social, political and economic circumstances have in shaping and influencing everyone's health'. 'Conflicts over the best approach to women's health arise in large part because *there is no agreed upon, universal definition* of women's health'<sup>4</sup>.

Women's health and men's health are different. Heart disease kills 19% more women than men, but 10 years later. Depression is two to three times more common in women than in men. Of those suffering from osteoporosis, 80% are women. Of those with autoimmune disease, 75% are women.

The 2002 WHO World Health Report focused on reducing risks to health in developed countries; the leading risk factors are: 'tobacco, blood pressure, alcohol, cholesterol, overweight, low fruit and vegetable intake, physical inactivity, illicit drugs, unsafe sex, iron deficiency'<sup>5</sup>.

### Aging

Aging is another very complex problem. 'It is the most pressing problem of our age'. 'One of the curious features of aging is its *unpredictability* at the individual level.' 'Aging is not a disease; it is a normal part of the life cycle'<sup>6</sup>. There are many theories that try to explain it, including free radicals, metabolic error catastrophe, DNA damage, glycosylation of cross-linkage, finite cell division, immune dysfunction, and neuroendocrine dysregulation.

'The fact that *genes* explain only 25% of individual variability in aging means that 75% *must be accounted for by other factors*, such as life-style variables (nutrition, exercise) and powerful effects of the environment (effects on older age).' 'We can always delay aging but we can never avoid it . . .'<sup>6</sup>.

The promotion of health for the elderly is focused on active aging – physically, socially and mentally. Active aging has several determinants: health and social services, behavioral determinants, personal determinants, physical environment, social determinants, and economic determinants<sup>7</sup>. The purpose of all interventions is ‘the compression of morbidity’<sup>8</sup> in the last years of one’s life.

Following the holistic model based on the WHO definition of health, women’s health must be analyzed in its components.

### SOCIAL HEALTH

‘In the developed world, the percentage of women over 50 years of age has *tripled* in the last 100 years’<sup>9</sup>. In Japan and Canada, the percentage of population aged 65 and older will increase from 2000 to 2020 by 53.7% and 42.9%, respectively. In Australia, New Zealand, United States and Germany the respective increases will be 39.2%, 33.7%, 32.8% and 31.9%<sup>10</sup>. ‘In more developed regions, the proportion of older people already exceeds that of children; by 2050 it will double’<sup>11</sup>.

In 1998, the health status of women (45–64 years of age) was such that 57% had one chronic condition and 23% had a disability or limiting illness. After age 65, the percentages were, respectively, 80% and 31%<sup>12</sup>. It is dramatic that the percentage of the population aged 65 and older living alone in 1990 was 41% in Germany, 38% in the United Kingdom and approximately 30% in the United States, New Zealand, France, Canada and Australia. Nevertheless, the number was much lower in Japan (14%), indicating the influence of sociocultural conditions<sup>13</sup>.

### MENTAL HEALTH

During the transition from the reproductive to the non-reproductive years, women are usually more perceptive of their mental health. It is, thus, not surprising that emotions and feelings may play an important role in their behaviors and coping and that many of their complaints may be of a psychosomatic nature. Psychosomatics is not a new specialty; it is the true perspective of human medicine.

The woman’s perception of her own existence and identity is not only an act of thought, as Descartes put it in his famous ‘I think, therefore I am’. Recent research in human models led Damasio (1994) to challenge Descartes and to rephrase his sentence into ‘I feel, therefore I am’. This is very important, as exemplified in the effect of a psychosocial treatment on the survival of patients with metastatic breast cancer<sup>14</sup>. The survival time from time of randomization and onset of intervention was a mean 36.6 (standard deviation (SD) 37.6) months in the *intervention group*, compared with 18.9 (SD 10.8) months in the *control group*.

Depression also influences components of immune function that may affect cancer surveillance. ‘Life stress situations, depression and social isolation have been linked to increased risk of myocardial infarction in women’<sup>15</sup>. Therefore, mental health is an important determinant of physical health.

### PHYSICAL HEALTH

Across all ages, the most frequent causes of death among women are diseases of the circulatory system (accounting for 43% of all deaths), cancer (26%), diseases of the respiratory system (6%), suicide and accidents (5%)<sup>16</sup>.

Cardiovascular diseases are the major cause of women’s death after age 50. For every 10-year increase in age, their risk for heart disease increases about three times. A family history of premature coronary heart disease (myocardial infarction, 65 in women) increases the risk for myocardial infarction about two times<sup>15</sup>.

The role of female hormones in the primary prevention of cardiovascular diseases has recently been much contested. However, ‘It appears that half of the benefits in the prevention of cardiovascular diseases *are not* hormone-related’<sup>17</sup>!

The major concerns about hormonal treatments are related to cardiovascular and breast cancer risks. But . . . will hormones provide benefit or harm? Menopausal hormonal treatments are very good, but treatments without hormones may also be very good for a woman’s health<sup>18,19</sup>.

And, should one say HRT (hormone replacement therapy) or MHT (menopausal hormonal

therapy)<sup>19-22?</sup> This discussion is important because there is a tendency to consider that there is nothing but estrogens to offer to a postmenopausal woman, and that such treatment is obligatory for every woman and for a very long time. This is wrong<sup>20</sup>.

In fact, 'there are no really 'safe' biological active drugs. There are only 'safe' physicians'. 'Science . . . is an art of probability. Medicine . . . is an art of uncertainty'<sup>23</sup>.

The alarm that was spread all over the world in recent years is the consequence of several well-known clinical trials and of their interpretation in the light of evidence-based medicine. Yet, 'Not everything that can be counted counts; and not everything that counts can be counted' (Albert Einstein).

If one extrapolates the relative risks shown in the trials into NNH (number needed to harm), the reciprocal of relative risk, it becomes apparent that the absolute risks are rather insignificant. 'As with the WHI reports, much emphasis has been given to the relative risks of percentage increases of 30-200%, whereas absolute figures provide a more suitable perspective of the risk. The additional cancers associated with estrogen-only therapy are 1.5 after 5 years and 5 after 10 years, and for combined estrogen-progestin therapy the figures are 6 and 19, respectively per 1000 women by the age of 65 years. Or, put in another way, a doctor would need to give combined estrogen-progestin therapy to 116 women for 5 years or 53 women for 10 years to see one extra case of breast cancer'<sup>24</sup>.

In the Heart and Estrogen/progestin Replacement Study (HERS)<sup>25,26</sup>, for a relative risk of 26%, the NNH is 833/1 year, whereas, in the WHI trial, for an increase in relative risk of 26%, the NNH is 1250/1 year. Other risks accepted by women and doctors, like obesity<sup>15</sup> - or two alcoholic drinks/day, are indeed far more important than female hormones.

This alarm has caused an enormous drop in hormonal treatments given to postmenopausal women after July 2002<sup>27</sup>.

Recent research has emphasized that every medical treatment should be based on evidence. 'It is therefore worrisome if the decline in the use of HRT is followed by an increased use of alternative medicines, with mostly undocumented

effects'<sup>28</sup>. We have recently critically reviewed all these alarmist trials. The conclusions of these studies suggest that the 'safe woman' (NNH between 600 and 1000) to *initiate* HT is between 50 and 59 years of age, with vasomotor symptoms, less than 10 years after the menopause, being treated with statins, with a good lipid profile, and with a body mass index  $\geq 30$ . This is precisely the profile of the great majority of women who come for consultation after their menopause.

Therefore it seems that what most gynecologists are doing for their predominant population of patients is not unsafe and contributes not only to a good quality of life but to prevention, as well<sup>29</sup>.

The interpretation of what should and should not be done to preserve women's health (quality of life, prevention of diseases) is nowadays strongly influenced by the rules of evidence-based medicine and their application to the results of the clinical trials published in the last decade. It is appropriate, therefore, to discuss these problems in the light of their applicability to good clinical practice.

## EVIDENCE-BASED MEDICINE

Since evidence-based medicine is in fashion and considered by most physicians to be the only law to obey, it is pertinent to meditate on some statements and facts. 'Evidence-based medicine and/or medicine-based evidence?'<sup>20</sup>. 'Without clinical expertise, practice risks becoming tyrannized by evidence'. 'Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients'<sup>30</sup>. 'Evidence alone does not make decisions'. 'The new look of evidence-based medicine should be research-enhanced health care'<sup>31</sup>. In fact, evidence-based medicine can be used *to do . . . and not to do*.

Here are some astonishing examples of contradictions:

- (1) The 'annual physical check-up may be an empty ritual' . . . 'Many tests that are useful, like cholesterol and blood pressure checks, *need not be done every year*, it is said in reports to doctors, policy makers and the public'. There is 'no evidence', it is said, 'that routine pelvic, rectal and testicular exams made any difference in overall survival rates for those with no

- symptoms of illness<sup>31</sup>. Is this a wise economic recommendation?
- (2) For estrogen and memory in postmenopausal women: 'New data provide further positive evidence that estrogen treatment might provide positive long-term effects on memory and learning in postmenopausal women.' 'Doctors may be 'throwing the baby out with the bath water' by having their patients stop taking estrogen replacement.' Studies recently published in the *Journal of the American Medical Association* 'have a lot of problems with their methodology'<sup>32</sup>. 'Low physiological levels of estradiol replacement exert dramatic protective effects in the brain. Using an animal model of stroke, we found that estradiol dramatically decreases the degree of brain injury in adult female rats and mice and in the aging female rats'<sup>33</sup>.
- (3) Coronary heart disease prevention:
- (a) A cost-effective prevention strategy would offer aspirin and initial antihypertensive treatment to all patients at greater than 75% 5-year coronary risk<sup>34</sup>. But . . . 'Women who take an aspirin a day - which millions do to prevent heart attack and stroke as well as to treat headaches - may raise their risk of getting deadly pancreatic cancer'<sup>35</sup>.
- (b) High-fat, no-starch diets do not raise cholesterol . . . 'Patients with atherosclerosis lose weight on a high-fat, no-starch Atkins-style diet, without increasing their blood fat (lipid) levels'<sup>36</sup>. Is this not the opposite of what one recommends?
- (c) 'Postmenopausal women who have undergone bilateral salpingo-oophorectomy have a decreased risk of coronary artery disease'<sup>37</sup>. However, 'Hormone replacement therapy is associated with less coronary atherosclerosis in postmenopausal women'<sup>38</sup>, although some say that . . . 'Estrogen-only/estrogen-progestin therapy does not appear to increase or decrease atherosclerosis rate'<sup>39</sup>.
- (d) WHI women have an 81% higher risk of heart attack during the first year of hormone therapy.' But, the same study concludes later<sup>40</sup> that 'women who were less than 10 years postmenopause had an overall hazard ratio of 0.89, while women 20 or more years postmenopause had a hazard ratio of 1.7' and that 'Estrogen-progestin therapy use for 6 years was associated with a 30% decrease in coronary heart disease.'
- However, 'Hormone therapy is not risky for heart disease in the first year.' These findings would suggest that the results of early coronary heart disease risk observed in the Women's Health Initiative (trial) might not be applicable to healthy, younger postmenopausal women who seek treatment for menopausal symptoms' and 'healthy women within 5 years of menopause do not experience early harm'<sup>41</sup>. Furthermore, a recent study concludes that HRT given for 13-60 months 'was associated with a small reduction in acute myocardial infarction, but, when used for more than 60 months, there was a substantial risk reduction'<sup>42</sup>.
- The fact is that 'WHI was very much a study about older women'<sup>43</sup>. Therefore, it is mandatory to meditate, serenely, without passion, on the data that are available in order to merge them, wisely, in each one's experience as contributions for good clinical practice. 'You cannot create experience. You must undergo it' (Albert Camus). 'He who *learns*, but does *not think* is *lost*. He who *thinks*, but does *not learn* is *dangerous*' (Confucius). 'If we both learn and think . . . *we will neither be lost . . . nor dangerous . . .* to our postmenopausal women patients'<sup>44</sup>. It is regrettably true that, after all 'Common sense is not so common' (Voltaire).
- Thus, the important questions are: what do we *know* today? And, to know . . . What is it? To know is the selective and critical acquisition of information and its concerted integration in one's mind. Are we being well informed, or well misinformed?

### The information

The information is supplied by clinical trials. 'Researchers from the University of California, at Davis, claim clinical trials are reported with misleading statistics.' 'Most randomized trials of new treatments published in leading medical journals (*Ann Intern Me, BMJ, JAMA, Lancet*) are reported in a potentially misleading way.' 'Most of the trials report results based on relative risk reduction!' 'Only 18 of the papers reviewed considered absolute risk reduction!' 'Only eight of the 359 trials reported the number needed to treat'<sup>45</sup>!

Concerning clinical trials, how were they performed, what similarities do they have with our clinical practice, and how do we interpret them? 'The popular belief that only randomized, controlled trials produce trustworthy results and that all observational studies are misleading *does a disservice* to patient care, clinical investigation, and the education of health-care professionals'<sup>46</sup>. 'Which clinical studies provide the best evidence?' 'An earlier systematic review also found no consistent difference between randomized controlled trials and observational studies in estimates of the effects of treatment in 22 areas'<sup>47</sup>.

'The new studies do not justify a major revision of the hierarchy of evidence, but they do support a flexible approach in which randomized controlled trials and observational studies are complementary'<sup>47</sup>.

'... the news media generally did a poor job of communicating a basic point about the data from the trial: that there was a considerable difference between the relative and absolute risks of combination hormone therapy'. 'Most articles and broadcast segments tended to focus exclusively on either the small absolute risks or the large relative risks, neglecting the more even-handed picture that presented both'. 'Since the sharply increased relative risks got the most play, news coverage about the trial's findings had an alarming cast'<sup>48</sup>.

Based on sound *information*, one must acquire the *knowledge* to find the *truth*.

### The truth?

'The objective of both basic and clinical science is to know the truth.' 'Every epidemiologic study, no

matter how good or how large, gives only one view of the truth.' 'It takes many views to come close to seeing the truth'<sup>49</sup>.

Which treatments were investigated? Only 'hormone replacement therapy'! Thus, studies based *only* on the use of hormones *do not reflect good clinical practice*! 'We are drawing in information, but starved for knowledge' (John Naisbitt).

Evidence-based medicine, to be clinically useful, must contribute to *know* the *truth*, based on reliable *information*.

### CONCLUSION

Since WHO defined *health* as 'a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity', one must take into consideration social health, mental health and physical health. Physicians are the health-care providers of *mental* health, *social* health, and *physical* health. As *physicians* and *citizens*, we have *civic* responsibilities, *political* responsibilities, and *medical* responsibilities at both the national and the international level.

### Final reminders

'Menopausal hormone therapy aptly fits the metaphor of the blind men describing the elephant: each touches a part, ear, trunk, tail, body, and draws a different conclusion. We are the blind men. The elephant is the data published in a half-century of medical literature that now includes the report from the Women's Health Initiative.' 'Biased opinions, be they pro or con, dishonor the profession and harm our patients'<sup>30</sup>.

It is regrettable that some epidemiologists, with no clinical experience, feel entitled to set the rules for clinical practice as if they were 'hormone legislators'!

It is very true that 'Each time we learn something new, the astonishment comes from the recognition that we were wrong before'. 'In truth, whenever we discover a new fact, it involves the elimination of old ones. *We are always*, as it turns out, fundamentally *in error*' (Lewis Thomas, *English Biologist*, 1913-1993).

Medical judgment requires: 'The application of accumulated knowledge and understanding

acquired not only through our appraisal of the literature but also from our education and experience.' 'The final impact on a patient is never the result of a single, solitary fact or one scientific study'<sup>50</sup>.

'Preventing a woman from the benefits of a sound postmenopausal hormone therapy because of the fear of rare side-effects does not seem to be satisfactory medicine'<sup>51</sup>.

'And, now that the dust has settled . . .' (about WHI): 'To publish data that may or may not be entirely true or certainly premature is a *disservice to the medical profession and, most important, to our patients.*' The majority of the data that were published are not statistically significant even at the nominal level'<sup>52</sup>.

### The message

The message is that we should prescribe postmenopausal hormonal treatments *when clinically indicated*, if not contraindicated. *No answers from ongoing clinical trials are indispensable* to practice today Good Medicine'<sup>29</sup>. Which is the winner - menopause (based) medicine, climacteric (based) medicine, sex (based) medicine, gender (based) medicine, or women's medicine?!

'There is only one medicine'<sup>50</sup>. Therefore, what one must learn is how to practice *good medicine*<sup>20</sup>! Let us not medicalize the Menopause. Instead, let us holistically approach the climacteric and the aging women.

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