Appendix: Revisions To Recommendations

CANADIAN CONSENSUS ON MENOPAUSE AND OSTEOPOROSIS

PERIMENOPAUSE – SIGNS AND SYMPTOMS

RECOMMENDATIONS:

A1. Health care providers should not use random serum markers of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol E_2 for the purpose of predicting menopause since clear markers for predicting menopause are yet to be identified. **(II-2)**

A2. In addition to providing effective contraception, low-dose oral contraceptives are an effective treatment for symptomatic, healthy, non-smoking perimenopausal women. **(I)**

A3. Using the data from studies in postmenopausal women and clinical expertise as a guide, estrogen replacement therapy (ERT) or hormone replacement therapy (HRT) may be considered as a treatment option for those perimenopausal women whose symptoms are disruptive. **(III)**

SUMMARY OF KEY POINTS:

A4. Perimenopause is characterized by fluctuating hormone levels, irregular menstrual cycles, and the onset of symptoms that may increase in number and severity as menopause approaches. **(II-2)**

A5. The perimenopause is an optimal period for preventive health care based on an individualized assessment, adoption of a healthy lifestyle, and involvement of the woman in decisions regarding treatment options and their risk-benefit assessment. **(III)**

MENOPAUSE AND HEALTHY LIVING

RECOMMENDATIONS:

B1. Health care providers should encourage patients to consider lifestyle modifications such as exercise, optimal diet, and smoking cessation, as these lifestyle changes can reduce the risk of cardiovascular disease and osteoporosis. **(I, II-2)**

B2. The principles of health promotion and disease prevention should be encouraged in all perimenopausal and postmenopausal women. **(III)**

MENOPAUSE AND SEXUAL FUNCTION

RECOMMENDATIONS:

C1. All health care providers dealing with menopausal women should be versed in the appropriate counselling and management of menopause and related sexual health issues. **(III)**

C2. In women with vaginal atrophy, health care providers may consider the use of local estrogen therapy as an effective mode of treatment or consider vaginal moisturizers as effective alternatives. **(I, II-1)**

C3. In women with decreased libido who have undergone bilateral oophorectomy, adding androgen to estrogen therapy has been shown to be effective in increasing libido **(I)**. Androgen therapy may be administered to estrogen-treated postmenopausal women who have decreased libido not explained by any other factors. A risk-benefit profile has not been determined from studies with sufficiently large patient numbers. **(III)**

C4. Routine evaluation of hormone levels (specifically measuring serum androgen levels) in postmenopausal women with psychosexual problems is not recommended. **(III)**

C5. Sildenafil citrate does not appear to improve sexual response in estrogenized women **(III)**. However, it may do so in women with decreased libido associated with use of selective serotonin re-uptake inhibitors (SSRIs) **(III)**.

HORMONE REPLACEMENT THERAPY AND CARDIOVASCULAR DISEASE

RECOMMENDATIONS:

D1. Hormone replacement therapy (oral continuous-combined conjugated equine estrogens [CEE] and medroxyprogesterone acetate [MPA]) **(I)** or other regimens **(III)** should not be initiated or continued for the sole purpose of preventing future cardiovascular events (primary and secondary prevention). **(I)**

D2. All women should be counselled about the beneficial effects of lifestyle modifications on reducing the risk of future cardiovascular events. Appropriate modifications include consumption of a heart-healthy diet, cessation of smoking, moderate daily exercise, and maintenance of healthy body weight. **(II)**

D3. To prevent future cardiovascular events, women should be prescribed therapies for which there is abundant scientific evidence, such as antihypertensive and lipid-lowering medications, β-adrenergic blockers, antiplatelet agents, and angiotensin-converting enzyme (ACE) inhibitors, with due attention to the potential risks or adverse effects of any of these therapies. **(I)**

OSTEOPOROSIS

RECOMMENDATIONS:

E1. Evaluation of fracture risk in postmenopausal women should include the assessment of risk factors, with bone mineral density measurement for those at increased risk.

a) Central (hip and spine) measurements by dual energy X-ray absorptiometry (DEXA) are the most accurate and precise measurements of bone density

available, making them useful for both risk assessment and follow-up. **(I)**

b) Peripheral bone mass measurements (e.g., ultrasound or DEXA measurements in the radius, phalanx, or heel) is useful for fracture risk assessment, but cannot be used for follow-up. **(I)**

E2. Physicians should be aware that a prevalent vertebral or non-vertebral fragility fracture markedly increases the risk of future fracture. **(I)**

E3. Markers of bone resorption, while useful in documenting group responses in large clinical trials, have no clear place in the evaluation of follow-up of individual patients. **(II)**

E4. Women should be encouraged to have adequate intake of calcium and vitamin D, good nutrition and exercise, avoidance of negative lifestyle habits (smoking, alcohol). A normal exposure to estrogen during reproductive life and exercise contribute to optimal achievement and maintenance of genetically determined peak bone mass. These recommendations are applicable to all women **(II)**; for early postmenopausal women, adequate calcium and vitamin D intake alone is not sufficient to maintain bone mass. **(I)**

E5. Although combination of antiresorptive therapies may be synergistic in increasing bone mineral density, their effect on fracture has not been proven. Combination therapy should be reserved for patients not responding to single-agent antiresorptive therapy. **(I)**

SUMMARY OF KEY POINTS:

E6. The goal of osteoporosis management is the prevention of fracture. This may or may not be associated with significant increases in bone mineral density. **(I)**

E7. Postmenopausal bone loss can be effectively prevented by antiresorptive therapy such as estrogen replacement, selective estrogen receptor modulator, or bisphosphonate therapy. **(I)**

E8. Treatment with alendronate or risedronate has been demonstrated to decrease both vertebral and non-vertebral fractures including hip fractures **(I)**; treatment with raloxifene, or calcitonin, has been demonstated to reduce vertebral fractures **(I)**; treatment with estrogen or etidronate appears to reduce vertebral fracture **(II)**. Physicians should consider a range of treatment options for osteoporosis.

E9. According to the WHI study, continuous combined HRT was effective in reducing the risk of hip fractures (5 fewer cases per 10,000 women per year). Vertebral and other fractures were also reduced.

UROGENITAL HEALTH

RECOMMENDATIONS:

F1. Urodynamic studies should be performed prior to incontinence surgery or when there is mixed incontinence. **(II-3)**

SUMMARY OF KEY POINTS:

F2. Urogenital aging may result in urinary urge and stress incontinence, recurrent urinary tract infection, and pelvic organ prolapse.

F3. There is no objective benefit from estrogen replacement therapy for postmenopausal urinary stress incontinence. **(I)**

F4. There is neither objective nor subjective benefit from estrogen replacement therapy for postmenopausal urge incontinence. **(I)**

F5. Estrogen therapy decreases the incidence of recurrent urinary tract infections in postmenopausal women. **(I)**

HORMONES AND THE BRAIN

SUMMARY OF KEY POINTS:

H1. Estrogen positively influences brain structures and functions that are known to be critical for memory. **(I)**

H2. In healthy postmenopausal women, estrogen protects against the deterioration in short- and long-term memory that occurs with normal aging. **(I)**

H3. Estrogen replacement is associated with a reduction in the risk of developing Alzheimer's disease in postmenopausal women **(II-2)**, but does not affect the progression of deterioration in women with diagnosed Alzheimer's disease. **(I)**

H4. Estrogen effectively enhances mood in women with dysphoria or mood lability **(I)**, but there is no evidence that estrogen alone is an effective treatment for clinical depression. The addition of progestin may attenuate the beneficial effect of estrogen on mood and on cognition in some women. **(I)**

H5. At present, there is no evidence that raloxifene influences cognitive functioning or mood. **(I)**

PHARMACOTHERAPY

RECOMMENDATIONS:

I1. The route of estrogen delivery should be primarily determined by patient preference, with the objective of using the lowest effective dose. **(III)**

I2. Physicians should consider alternate routes of administration such as vaginal and transdermal administration. **(III)**

I3. Physicians should be aware that women who wish to use continuous combined HRT long term (five or more years) should be re-evaluated annually. **(III)**

HORMONE REPLACEMENT THERAPY AND CANCER

RECOMMENDATIONS:

J1. No estrogen-progestin regimen is completely protective against endometrial carcinoma, and all unscheduled uterine bleeding should be investigated. **(II-2)**

J2. Estrogen-progestin therapy should not be withheld from women with treated stage 1 and 2, grade 1 or 2 adenocarcinoma of the endometrium who have moderate to severe menopausal symptoms. **(II-3)**

J3. Physicians should inform patients that the use of estrogen-progestin treatment increases the risk of breast cancer but is not statistically significant until after four years of use. The risk returns to baseline five years after stopping therapy. **(I)**

J4. There should be increased breast surveillance for women who are at high risk of developing breast cancer when using estrogen-progestin therapy. **(III)**

J5. In very special circumstances, women at increased risk of developing breast cancer or who have been treated for breast cancer may be prescribed low dose estrogen-progestin therapy for severe symptoms unrelieved by effective alternative therapies, after risks and benefits have been extensively discussed. The duration of therapy should be regularly reviewed; there is no preventative role for estrogen therapy in this population. **(III)**

J6. Physicians should be aware that the reported effects of estrogen-progestin therapy on ovarian cancer have been inconsistent. A possible increased risk may occur in women on long-term estrogen-only therapy (10 or more years). **(I)**

SUMMARY OF KEY POINTS:

J7. Unopposed estrogen therapy substantially increases the risk of developing atypical endometrial hyperplasia **(I)** and endometrial carcinoma **(II-2)**. The appropriate dose and duration of progestin therapy will reduce these estrogen-associated risks.

J8. Continuous combined HRT was associated with a reduction in the risk of colorectal cancer, which failed to reach statistical significance (6 fewer cases per 10,000 women per year). **(I)**

COMPLEMENTARY APPROACHES

RECOMMENDATIONS:

K1. Physicians and their patients should be more aware of complementary therapies in order to effectively consider treatment options. **(III)**

K2. Patients should be informed that lifestyle changes, including dietary modifications, exercise **(I)**, reduction of stress, and cessation of smoking can benefit the emotional and physical health of women in midlife. **(II-1)**

EVALUATION, DECISION-MAKING, AND FOLLOW-UP

RECOMMENDATIONS:

L1. The assessments recommended by the Canadian Task Force on the Periodic Health Examination should be included in the evaluation and follow-up of perimenopausal and postmenopausal women. **(III)**

L2. Routine abdominal or transvaginal ultrasonography of the pelvis should not be used in healthy asymptomatic postmenopausal women. **(II-1)**

L3. Postmenopausal women with abnormal bleeding patterns should undergo a review of their estrogen-progestin therapy administration (where appropriate), a pelvic examination, and an endometrial biopsy **(II-1)**. Transvaginal ultrasonography is an alternative when endometrial sampling is not possible or the results are inconclusive. If the situation remains unclear, tissue sampling with or without hysteroscopy is recommended. **(II)**

L4. The majority of women wish to participate in the decision-making process, and health care providers should encourage them to do so. **(III)**

L5. Decisions should be based on an individual assessment of symptoms, risk factor analysis, and discussion of the risks and benefits of each option. The decision should be re-evaluated as new information becomes available. **(III)**

L6. Health care providers should actively advocate for public-funded educational programs to increase knowledge about menopause and osteoporosis for both women and their health care providers. **(III)**