Elective and Risk-Reducing Salpingo-oophorectomy

In the United States, 600,000 hysterectomies are performed annually, of which one half include salpingo-oophorectomy (1). Salpingo-oophorectomy is performed electively at the time of hysterectomy to decrease the risk of ovarian cancer and to avoid possible morbidities and future surgery related to benign ovarian neoplasms, endometriosis, and pelvic pain.

There is a subset of women with an elevated risk of ovarian carcinoma and breast carcinoma recurrence who are candidates for risk-reducing salpingo-oophorectomy performed for the primary purpose of reducing breast, ovarian, and fallopian tube carcinoma risks. The purpose of this document is to provide a framework for counseling women about the benefits and risks of elective salpingo-oophorectomy at the time of hysterectomy and to provide some guidelines for risk-reducing salpingo-oophorectomy.

Background

Risk-reducing and elective salpingo-oophorectomies are the removal of the ovaries for the potential benefit of preventing long-term morbidity and mortality. The term risk-reducing salpingo-oophorectomy implies that the ovaries are normal at the time of removal. Salpingo-oophorectomy can be performed either alone as a planned surgical procedure or in conjunction with other planned surgical procedures such as hysterectomy or colectomy. Elective salpingo-oophorectomy is a term commonly used when the ovaries are removed at the time of another indicated surgical procedure, and this term should not be used interchangeably with risk-reducing salpingo-oophorectomy.
Ovarian Physiology in Premenopause and Natural and Surgical Menopause

The mean age at which menopause occurs in developed countries is 51.4 years (2). After menopause, estradiol production decreases by 90% (3, 4) because of follicular atresia, and estrone becomes the dominant estrogen. Estrone produced after menopause comes primarily from peripheral conversion of adrenal androstenedione by aromatase, primarily in adipose tissues. After menopause, small concentrations of progesterone continue to be produced by the adrenal gland. However, with natural menopause, the transition from a premenopausal profile to postmenopausal profile occurs over 4 years, on average (5).

As reproductive aging progresses, serum levels of androgens decrease, but not to the extent that estrogen levels diminish. Androstenedione levels decrease by approximately 50% because of declines in ovarian production (3, 6, 7) while adrenal output remains relatively constant. Testosterone continues to be secreted by the ovarian stroma but decreases by approximately 30% (3, 6, 7). Serum concentrations of the adrenal androgen precursor dehydroepiandrosterone (DHEA) decrease with biological aging, beginning before the final menstrual period (7).

The reproductive hormone profile observed with surgical menopause is quite similar to that of a postmenopausal woman. In premenopausal women, the mean reductions in serum testosterone and estradiol concentrations following oophorectomy are 50% and 80%, respectively (8).

Cancer Prevention

The American Cancer Society estimates that 22,430 new cases of ovarian cancer will be diagnosed in 2007 in the United States, with an estimated 15,280 deaths from ovarian cancer (9). The lifetime risk of developing ovarian cancer in the general population is 1 in 70 or 1.4%. Current methods of ovarian cancer screening have not been found to enable early diagnosis of invasive ovarian carcinomas, much less decrease morbidity and mortality from ovarian cancer. Transvaginal ultrasonography and serum CA 125 measurement are not recommended for screening in the general population.

The most effective method of preventing ovarian cancer is surgical removal of the ovaries and fallopian tubes. It is estimated that approximately 1,000 cases of ovarian cancer could be prevented each year if elective salpingo-oophorectomy was performed in all women undergoing hysterectomy at 40 years or older in the United States (10). Approximately 5–10% of women with ovarian cancer have had a previous hysterectomy at age 40 years or older (11). The potential benefit in cancer risk reduction for premenopausal women at average risk of ovarian cancer must be balanced with the consequences of premature loss of estrogen production.

Identification of women with a genetically increased risk of ovarian carcinoma is important in identifying those who would benefit from risk-reducing salpingo-oophorectomy (see box “Oophorectomy Versus Ovarian Preservation at the Time of Hysterectomy”). Women with this increased risk account for 10–15% of all ovarian carcinomas that could be effectively prevented if risk were identified (12–14). Other factors that increase the risk of ovarian carcinoma include nulligravidity, decreased fertility, age, and family history of ovarian carcinoma (15). Data from the Women’s Health Initiative are not mature enough to determine if the risk of ovarian carcinoma is significantly increased by the use of estrogen therapy (16). The use of ovulation induction agents is not clearly linked to an increased risk of ovarian carcinoma (17).

In addition to pregnancy, factors that are protective against ovarian carcinoma include bilateral tubal ligation, hysterectomy with ovarian preservation, and use of oral contraceptives (15, 18–20).

Recognizing women with a genetically increased risk of ovarian cancer may provide the opportunity of preventing most hereditary ovarian carcinomas. This approach has the potential to prevent more total cases of

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ovarian carcinoma, with far fewer oophorectomies, than if elective oophorectomy were performed at the time of hysterectomy in all average-risk women older than 40 years.

Inherited susceptibility to ovarian cancer has the greatest impact of all ovarian cancer risk factors. Women with the highest risk of ovarian carcinoma are those with hereditary breast and ovarian cancer, followed by women with hereditary nonpolyposis colorectal cancer (HNPCC). Suggestive family histories of hereditary cancer risk include cancer occurring at young ages; cancer in first-degree relatives; cancer in multiple generations; bilateral, metachronous, or synchronous cancer in one individual; and clustering of cancer on one side of the family (see box “Criteria for Referral for BRCA Testing”).

The types of cancer suggestive of hereditary breast and ovarian cancer include early-onset (before age 50 years) or bilateral breast cancer, epithelial ovarian cancer (at any age), male breast cancer, pancreatic cancer, and early-onset prostate cancer. If a BRCA1 or BRCA2 mutation comes from the paternal side of the family or from a lineage containing few females, cancer histories may be subtle or absent (21). Most hereditary breast and ovarian cancer are caused by inherited mutations in the BRCA1 or BRCA2 genes, which lead to lifetime risks of ovarian cancer of 20–50% and of breast cancer of 60–85% (21, 22). Inherited mutations in BRCA1 and BRCA2 account for 10–15% of all ovarian carcinomas (12, 14). Mucinous and borderline ovarian neoplasms are not suggestive of BRCA1 or BRCA2 mutations. The BRCA mutation carrier rate is higher in certain populations because of the presence of founder mutations. Three founder mutations in BRCA1 and BRCA2 are present in 2–2.5% of Ashkenazi individuals (23, 24). Consequently, in Ashkenazim, a higher proportion of breast and ovarian cancers (12% and 40%, respectively) are associated with inherited mutations in BRCA1 or BRCA2 (21, 23, 25, 26).

Types of cancer associated with HNPCC include those of the colon or rectum, endometrium, biliary tract, stomach, brain, and urinary tract. Because HNPCC leads to cancer equally in both sexes, women with HNPCC are more likely to have a positive family history than are those women with hereditary breast and ovarian cancer. Criteria for diagnosis of HNPCC have been modified to include gynecologic and other noncolonic cancer (27) (see box “Criteria for Referral for BRCA Testing” and box “Revised Diagnostic Criteria for Hereditary Nonpolyposis Colorectal Cancer”). Hereditary nonpolyposis colorectal cancer or Lynch syndrome is caused by inherited mutations in the DNA mismatch repair genes MSH2, MLH1, PMS2, and MSH6. The most common types of cancer in women with HNPCC are colon and endometrial cancer. Women with HNPCC have a 40–60% lifetime risk of endometrial cancer and an 8–10% risk of ovarian cancer (28, 29).

### Criteria for Referral for BRCA Testing

**For non-Ashkenazi Jewish women:**
- Two first-degree relatives with breast cancer, one relative in whom breast cancer was diagnosed when younger than 50 years
- A combination of three or more first- or second-degree relatives with breast cancer at any age
- A combination of both breast and ovarian cancer among first- and second-degree relatives
- A first-degree relative with bilateral breast cancer
- A combination of two or more first- or second-degree relatives with ovarian cancer at any age
- A first- or second-degree relative with both breast and ovarian cancer at any age
- A male relative with breast cancer

**For women of Ashkenazi Jewish heritage:**
- Any first-degree relative with breast or ovarian cancer
- Two second-degree relatives on the same side of the family with breast or ovarian cancer


### Revised Diagnostic Criteria for Hereditary Nonpolyposis Colorectal Cancer

- Three or more relatives have an HNPPC-associated cancer, including cancer of the colon, endometrium, small bowel, ureter, or renal pelvis.
- Two or more successive generations are affected.
- Cancer is diagnosed in at least one individual who is younger than 50 years.
- Familial adenomatosus polyposis should be excluded in any colorectal cancers.

Clinical Considerations and Recommendations

What factors should be considered when deciding on elective salpingo-oophorectomy versus ovarian preservation at the time of hysterectomy?

Multiple factors should be considered, including the age of the woman, genetic risk of ovarian carcinoma (see boxes, “Criteria for Referral for BRCA Testing” and “Revised Diagnostic Criteria for Hereditary Nonpolyposis Colorectal Cancer”), atherosclerosis, osteoporosis predisposition, risk of subsequent ovarian surgery if the ovaries are retained, and issues related to quality of life. Age is probably the most important factor to consider. Only approximately 4% of women who are ovulatory at age 40 years become menopausal by age 45 years (30); consequently, the positive effects of ongoing production of estrogen by the ovaries versus potential nonadherence with estrogen therapy should be considered before removal of the ovaries in premenopausal women. Strong consideration should be given to retaining normal ovaries in premenopausal women who are not at increased genetic risk of ovarian cancer. However, given the risk of ovarian cancer in postmenopausal women, ovarian removal at the time of hysterectomy should be considered for these women. There are no studies evaluating differences in surgical complications with the addition of salpingo-oophorectomy to abdominal or laparoscopic hysterectomy.

What is the effect of salpingo-oophorectomy on long-term survival?

Epidemiologic studies have suggested that premature menopause (natural or surgical) without estrogen therapy is associated with a subsequent increased risk of heart disease, fractures, cognitive impairment, dementia, parkinsonism, and decreased long-term survival (31–38). Prospective population-based studies show that age of menopause, either natural or surgical (without subsequent use of estrogen therapy), is the most important determinant of long-term survival (31, 34, 39, 40). The findings of these studies showed that in general, women with menopause after age 50 years have a lower all-cause mortality rate than do women age 50 years or younger. In one study, the overall survival was determined predominantly by the decreased risk for ischemic heart disease (hazard ratio = 0.98 per year [95% confidence interval, 0.97–0.99]) and less so by the increased risk for fatal uterine and ovarian cancer (hazard ratio = 1.07 per year [95% confidence interval, 1.01–1.12]) (34).

A study using decision analysis to calculate the optimal age for elective salpingo-oophorectomy at hysterectomy for benign disease concluded that ovarian conservation through age 65 years benefited long-term survival in women who had an average risk of ovarian carcinoma (41). The results of this decision analysis are controversial and are not supported by evidence from large prospective cohort studies (31, 40, 42).

How often will ovarian preservation result in reoperation?

The frequency of repeat surgery for ovarian pathology is reported to be twice as high in women who had one ovary retained versus both (7.6% versus 3.6%). Most of these repeat surgical procedures are performed because of pelvic pain or a pelvic mass and occur within 5 years of the hysterectomy. Women with endometriosis, pelvic inflammatory disease, and chronic pelvic pain are at higher risk of reoperation if the ovaries are retained. The risk of subsequent ovarian surgery should be weighed against the benefit of ovarian retention in these patients.

Should estrogen therapy be recommended for women undergoing oophorectomy?

Use of estrogen therapy in women younger than 50 years has not been examined in randomized controlled trials. In women ages 50–79 years (average age, 63 years) who have had a hysterectomy, use of estrogen therapy has shown no increased risk of breast cancer or heart disease with up to 7.2 years of use (42, 43). However, an increased risk of thromboembolic disease and stroke was observed (42, 43).

How will salpingo-oophorectomy or ovarian preservation affect the patient’s quality of life?

The primary disadvantage of salpingo-oophorectomy is loss of natural ovarian hormone secretion. Estrogen therapy may relieve most of the clinical symptoms related to oophorectomy (eg, hot flushes, vaginal dryness, irritability, mood swings). Other possible disadvantages include changes in self-image and decreased libido attributed to loss of ovarian androgen production, but androgen replacement has been shown to improve mood, libido, and bone mineral density (44–48). Several studies performed in general populations of premenopausal women show overall sexual function was unaltered after oophorectomy, despite lower concentrations of ovarian sex steroids (49).

Potential benefits of testosterone therapy need to be weighed against possible increased risk for breast cancer.
and cardiovascular disease. Studies to date suggest that testosterone therapy and progestin therapy may be the determining factor in breast cancer risk with post-menopausal hormone therapy (50, 51).

**What are contraindications to ovarian preservation?**

Women at very high risk of ovarian carcinoma—specifically, women with documented hereditary breast and ovarian cancer susceptibility or hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome)—are not candidates for ovarian preservation. Referral to a certified genetic counselor can help clarify risk of ovarian cancer in women with suggestive personal or family histories. Other contraindications to ovarian preservation include invasive ovarian or endometrial carcinomas. Malignant germ cell tumors, stromal tumors, and borderline ovarian tumors do not mandate bilateral salpingo-oophorectomy in women desiring fertility preservation.

**What is the role of genetic counseling and testing for women who are considering risk-reducing salpingo-oophorectomy?**

The U.S. Preventive Services Task Force has recommended that women with family histories suggestive of BRCA1 and BRCA2 mutations be referred for genetic counseling and evaluation for BRCA testing (52) (see box “Criteria for Referral for BRCA Testing”). Both maternal and paternal family histories are important. Approximately 2% of U.S. women would meet these criteria for referral, and obstetrician–gynecologists play a critical role in identifying these women before their peak age of cancer risk.

Genetic testing can clarify ovarian carcinoma risk as well as risk of cancer to other organs. Women with an increased risk of ovarian carcinoma secondary to hereditary breast and ovarian cancer or HNPCC are at risk of cancer in other organs and qualify for more intensive surveillance or prevention measures. Women with hereditary breast and ovarian cancer should be offered surveillance for breast cancer with breast magnetic resonance imaging in addition to mammography and should be counseled about the option of prophylactic mastectomy (53–57). Women with HNPCC should have annual colonoscopies with removal of any polyps (57). Ovarian cancer risk should not be addressed in isolation without consideration of other cancer risks.

Genetic testing also provides the opportunity to clarify risk to other unaffected family members, targeting truly high-risk individuals for intensive surveillance or prevention measures and freeing relatives who have not inherited the familial risk from additional interventions.

**How effective is risk-reducing salpingo-oophorectomy?**

Carriers of the BRCA1 and BRCA2 mutations who undergo salpingo-oophorectomy achieve an 80–90% ovarian cancer risk reduction (13, 58), as well as an approximate 50–60% decrease in breast cancer risk if surgery is performed before menopause. Therefore, bilateral salpingo-oophorectomy should be offered to women with BRCA1 and BRCA2 mutations after completion of childbearing, preferably by age 40 years. After salpingo-oophorectomy, women remain at risk of primary peritoneal carcinoma. Findings of a large registry study indicated a 4.3% risk of primary peritoneal cancer at 20 years after risk-reducing salpingo-oophorectomy in BRCA1 mutation carriers. Many cases of primary peritoneal cancer occur within 2 years of risk-reducing salpingo-oophorectomy, suggesting that an occult cancer may have been missed at the time of risk-reducing salpingo-oophorectomy (58). Additionally, primary peritoneal cancer risk appears to be higher after risk-reducing salpingo-oophorectomy when salpingectomy is not performed, suggesting that occult cancer in fallopian tubes may seed the peritoneal cavity (59).

Hysterectomy with bilateral salpingo-oophorectomy effectively reduces endometrial and ovarian cancer risk in women with HNPCC and should be offered after completion of childbearing (57, 60).

**When is salpingo-oophorectomy indicated in women with breast cancer?**

Salpingo-oophorectomy may be indicated for breast cancer survivors who have a high risk of ovarian cancer. Less than 5% of women with breast cancer harbor a germline BRCA1 mutation, but BRCA1 mutations are more frequently observed in younger women with breast cancer and those with family histories of breast and ovarian cancer. Families that are affected only by breast cancer and that test negative for BRCA1 and BRCA2 mutations do not have an appreciable increased risk of ovarian cancer (61). Those women with breast cancer who are identified with a BRCA1 or BRCA2 mutation have a 20–50% lifetime risk of ovarian cancer and a 40–60% risk of developing a second breast cancer (62, 63). For this reason, genetic counseling with consideration of genetic testing should be offered to all Ashkenazi women with breast cancer at any age, non-Ashkenazi women with invasive breast cancer younger than 40 years, and women with breast cancer and significant maternal or paternal family histories of breast or ovarian cancer.

Salpingo-oophorectomy also may be indicated for hormonal therapy of breast cancer. Salpingo-oophorectomy appears to be more effective than tamoxifen alone.
as adjuvant therapy in premenopausal women with hormone-sensitive breast cancer (64). Whether there is an added benefit to salpingo-oophorectomy in premenopausal women undergoing chemotherapy is less certain (64). In premenopausal women who are undergoing chemotherapy and are older than 40 years, induced menopause may negate any additional benefit of salpingo-oophorectomy (65). Ovarian ablation may be beneficial in women younger than 35 years who are treated with chemotherapy for hormone-sensitive breast cancer (66).

Estrogen receptor-positive metastatic breast cancer is treated first with aggressive hormonal therapy that may include suppressing the ovaries either medically or surgically (67, 68). Increasingly, aromatase inhibitors are used in the adjuvant therapy of estrogen-sensitive breast cancer (69). Aromatase inhibitors stimulate ovarian function in premenopausal women, resulting in high circulating estradiol levels. Premenopausal women taking aromatase inhibitors for breast cancer need concurrent suppression of ovarian function, and salpingo-oophorectomy may be a cost-effective alternative to long-term ovarian suppression using gonadotropin-releasing hormone (GnRH) agonists. In premenopausal women who become amenorrheic during chemotherapy, aromatase inhibitors may stimulate residual ovarian function. Monitoring serum estradiol levels in these women is important in recognizing ovarian stimulation and identifying the possible need for ovarian suppression or ablation.

**Can women who undergo risk-reducing salpingo-oophorectomy for hereditary breast and ovarian cancer use postmenopausal estrogen therapy?**

The use of short-term estrogen without progestins does not mitigate the sharp reduction in breast cancer risk achieved by premenopausal women with BRCA1 and BRCA2 mutations who undergo risk-reducing salpingo-oophorectomy (70). However, the ideal dose, duration of therapy, estrogen compound, and delivery method that maximizes quality of life while minimizing breast cancer risk in women with mutations in BRCA1 and BRCA2 have not been determined. The safety of progestins in this population has not been established. Because estrogen and progestin combination therapy is less favorable than estrogen alone for breast cancer risk in the general population (42, 50), it seems prudent to minimize combination hormone therapy in BRCA mutation carriers with intact breast tissue.

**At what age should risk-reducing salpingo-oophorectomy be performed?**

Ovarian cancer diagnoses are rare before age 40 years in women with hereditary breast and ovarian cancer (12, 14, 71, 72). The average age of ovarian cancer diagnosis is 52 years for women with BRCA1 mutations and 60 years for those with BRCA2 mutations (12, 14, 71). It is recommended that women with BRCA1 or BRCA2 mutations consider risk-reducing salpingo-oophorectomy between ages 35 years and 40 years if they have completed their childbearing. When risk-reducing salpingo-oophorectomy is performed before age 40 years in BRCA1 mutation carriers, there is a 64% reduction in breast cancer risk, compared with a 50% reduction if performed between ages 40 years and 50 years (73).

There are no established guidelines for age of risk-reducing surgery in women with HNPCC mutations. In women with HNPCC, the average age of ovarian cancer diagnosis is 42 years and the average age of endometrial cancer diagnosis is 50 years (28, 29, 74). Thus, it is also reasonable to consider prophylactic surgery in women with HNPCC between ages 35 and 40 years if childbearing is no longer desired (57).

**Are surgical techniques for risk-reducing salpingo-oophorectomy different from standard techniques?**

Performing risk-reducing salpingo-oophorectomy in women at an increased risk of ovarian cancer necessitates complete removal of the ovaries and fallopian tubes. Risk-reducing salpingo-oophorectomy for these women should include careful inspection of the peritoneal cavity, pelvic washings, removal of the fallopian tubes, and ligation of the ovarian vessels at the pelvic brim. If hysterectomy is not performed, care must be taken to completely remove the fallopian tubes to the level of the cornu.

In women with BRCA1 and BRCA2 mutations, 5–12% will have an occult neoplasm of the ovary, peritoneum, or fallopian tube identified at risk-reducing salpingo-oophorectomy if thorough pathologic evaluation is performed (75–79). Appropriate evaluation includes serial sectioning at 2–3-mm intervals of the entire ovaries and fallopian tubes. Most of the earliest microscopic neoplasms originate in the fallopian tube when careful sectioning is performed (77, 79, 80). Both age and mutation status are predictors of occult neoplasm, and women with BRCA1 mutations who are 45 years or older have a 20% risk of occult neoplasm (77, 79).

**Should hysterectomy be performed at the time of risk-reducing salpingo-oophorectomy for hereditary breast and ovarian cancer?**

When salpingo-oophorectomy is performed primarily for prevention of ovarian cancer or for the hormonal therapy of breast cancer, hysterectomy is not required. Women
with *BRCA1* or *BRCA2* mutations do not have a known increased risk of endometrial cancer (81). Theoretically, hysterectomy allows more complete removal of the fallopian tube, a target of neoplasia in *BRCA1* or *BRCA2* mutation carriers. However, the interstitial component of the fallopian tube is not a known location of tubal cancer, and its removal may not be essential (82). Furthermore, there are no data to suggest that uterine preservation results in higher cancer risks in *BRCA1* or *BRCA2* mutation carriers. Careful consideration of the benefits and risks of elective hysterectomy in conjunction with risk-reducing salpingo-oophorectomy should be made with each woman, including individual risk factors for endometrial and cervical cancer, such as tamoxifen use, body mass index, and history of cervical dysplasia. In younger women undergoing risk-reducing salpingo-oophorectomy who want to use hormones after surgery, hysterectomy allows the use of estrogen without progestins, a regimen shown to be safe in high-risk women for short-term therapy (70).

### Summary of Recommendations and Conclusions

**The following conclusion is based on good and consistent scientific evidence (Level A):**

- In women ages 50–79 years who have had a hysterectomy, use of estrogen therapy has shown no increased risk of breast cancer or heart disease with up to 7.2 years of use.

**The following recommendation is based on limited or inconsistent scientific evidence (Level B):**

- Bilateral salpingo-oophorectomy should be offered to women with *BRCA1* and *BRCA2* mutations after completion of childbearing.

**The following recommendations are based primarily on consensus and expert opinion (Level C):**

- Women with family histories suggestive of *BRCA1* and *BRCA2* mutations should be referred for genetic counseling and evaluation for *BRCA* testing.

- For women with an increased risk of ovarian cancer, risk-reducing salpingo-oophorectomy should include careful inspection of the peritoneal cavity, pelvic washings, removal of the fallopian tubes, and ligation of the ovarian vessels at the pelvic brim.

- Strong consideration should be made for retaining normal ovaries in premenopausal women who are not at increased genetic risk of ovarian cancer.

- Given the risk of ovarian cancer in postmenopausal women, ovarian removal at the time of hysterectomy should be considered for these women.

- Women with endometriosis, pelvic inflammatory disease, and chronic pelvic pain are at higher risk of reoperation; consequently, the risk of subsequent ovarian surgery if the ovaries are retained should be weighed against the benefit of ovarian retention in these patients.

### References


68. Pritchard KI. Endocrine therapy of advanced disease: analysis and implications of the existing data. Clin Cancer Res 2003;9(suppl):460S–7S. (Level III)


The MEDLINE database, the Cochrane Library, and ACOG’s own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and June 2007. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I  Evidence obtained from at least one properly designed randomized controlled trial.
II-1 Evidence obtained from well-designed controlled trials without randomization.
II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III  Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.
Level B—Recommendations are based on limited or inconsistent scientific evidence.
Level C—Recommendations are based primarily on consensus and expert opinion.