General

Guideline Title

Recommendations on screening for cervical cancer.

Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.


A complete list of planned reviews, updates and revisions is available under the What's New section at the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

Recommendations

Major Recommendations

The grades of recommendations (strong, weak) and grades of evidence (high, moderate, low, very low) are defined at the end of the "Major Recommendations" field.

Recommendations are presented for the use of cervical cytology (Papanicolaou [Pap] tests) for women with no symptoms of cervical cancer who are or have been sexually active, regardless of sexual orientation. The recommendations do not apply to women with symptoms of cervical cancer (e.g., abnormal vaginal bleeding), women with previous abnormal results on screening (unless they have been cleared to return to normal screening), women who do not have a cervix (because of hysterectomy), women who are immunosuppressed (e.g., as a result of organ transplantation, chemotherapy, chronic corticosteroid treatment, HIV infection) or women who have limited life expectancy such that they would not benefit from screening.

The recommendations do not address screening with human papilloma virus (HPV) testing (alone or in combination with Pap testing). In our judgment, such a recommendation would be premature until the evidence in this area is further developed.

Cytology (conventional or liquid-based, manual or computer-assisted)

- For women aged less than 20 years, the Task Force recommends not routinely screening for cervical cancer. (Strong recommendation;
For women aged 20–24 years, the Task Force recommends not routinely screening for cervical cancer. (Weak recommendation; moderate-quality evidence)

For women aged 25–29 years, the Task Force recommends routine screening for cervical cancer every 3 years. (Weak recommendation; moderate-quality evidence)

For women aged 30–69 years, the Task Force recommends routine screening for cervical cancer every 3 years. (Strong recommendation; high-quality evidence)

For women 70 years of age or older who have undergone adequate screening (i.e., 3 successive negative Pap test results in the last 10 years), the Task Force recommends that routine screening may stop. For all other women 70 years of age or older, the Task Force recommends continued screening until 3 negative test results have been obtained. (Weak recommendation; low-quality evidence)

Definitions:

Grading of Recommendations

- **Strong recommendations** are those for which the task force is confident that the desirable effects of an intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention). A strong recommendation implies that most people will be best served by the recommended course of action.

- **Weak recommendations** are those for which the desirable effects probably outweigh the undesirable effects (weak recommendation for an intervention) or undesirable effects probably outweigh the desirable effects (weak recommendation against an intervention) but appreciable uncertainty exists. A weak recommendation implies that most people would want the recommended course of action, but many would not. For clinicians, this means they must recognize that different choices will be appropriate for individual women, and they must help each woman arrive at a management decision consistent with her own values and preferences. Policy-making will require substantial debate and involvement of various stakeholders. Weak recommendations result when the balance between desirable and undesirable effects is small, the quality of evidence is lower, and there is more variability in the values and preferences of patients.

Grading of Recommendation Assessment, Development and Evaluation (GRADE) Working Group Grades of Evidence

- **High quality**: Further research is very unlikely to change the Task Force's confidence in the estimate of effect.

- **Moderate quality**: Further research is likely to have an important impact on the Task Force's confidence in the estimate of effect and may change the estimate.

- **Low quality**: Further research is very likely to have an important impact on the Task Force's confidence in the estimate of effect and is likely to change the estimate.

- **Very low quality**: The Task Force is very uncertain about the estimate.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Cervical cancer

Guideline Category

Prevention

Screening
Clinical Specialty
Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Pathology

Intended Users
Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants
Physicians

Guideline Objective(s)
To provide updated recommendations for screening for cervical cancer in Canada

Target Population
Asymptomatic women who are or have been sexually active

Note: The guideline does not apply to women:
- With symptoms of cervical cancer or previous abnormal test results on cervical screening (unless they have been cleared to resume normal screening)
- Who have had complete surgical removal of the cervix
- Who are immunosuppressed by human immunodeficiency virus (HIV), organ transplantation, chemotherapy or chronic use of corticosteroids
- Who have limited life expectancy such that they would not benefit from screening

Interventions and Practices Considered
Screening for cervical cancer with Papanicolaou (Pap) cytology testing

Major Outcomes Considered
- Incidence of invasive cervical cancer
- Mortality

Methodology

Methods Used to Collect/Select the Evidence
Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by McMaster University and the Canadian Task Force on Preventive Health Care (CTFPHC) (see the "Availability of Companion Documents" field).

Search Strategies

Three separate search strategies were conducted using Medline, EMBASE and Cochrane Central databases. For Key Question (KQ) 1 the search focused generally on cervical cancer screening, included both randomized controlled trials (RCTs) and observational studies, and covered the period from 1995 to April 2012 (see Appendix 1 of the systematic review document [see the "Availability of Companion Documents" field]).

The search for KQ2 focused on adverse events associated with cervical cancer screening, included any study design, and covered the period from 1995 to April 2012 (see Appendix 1 of the systematic review document [see the "Availability of Companion Documents" field]). The third search focused on the Contextual Questions, included any study design, and covered the period from 2005 to February 2011 (see Appendix 1 of the systematic review document [see the "Availability of Companion Documents" field]). All three search strategies combined subject heading and text word terms for cervical cancer and screening, adapted for each database. All citations were uploaded to a web-based systematic review software program for screening and data extraction. A fourth search of websites was conducted in February 2011 to find grey literature with relevant Canadian statistics (see Appendix 2 of the systematic review document [see the "Availability of Companion Documents" field]).

Study Selection

Eligible studies included women aged 15 to 70 years who were or had been sexually active. The cervical cancer screening methods of interest included conventional Papanicolaou (Pap) tests, liquid-based Pap tests and human papilloma virus (HPV) deoxyribonucleic acid (DNA) tests. For the effectiveness of screening for cervical cancer (KQ1) the study designs included systematic reviews, RCTs, and observational studies with comparison groups. Any study design was considered to answer the harms questions (KQ2) and the Contextual Questions. All included studies were in English or French. Grey literature was included if recent relevant national Canadian data were reported. The list of inclusion/exclusion criteria for this review is provided in Table 2 of the systematic review document (see the "Availability of Companion Documents" field).

Number of Source Documents

A total of 29 relevant studies (32 papers) were located and included to answer the Key Questions in the original guideline document. Some of the studies were used to answer more than one question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendation Assessment, Development and Evaluation (GRADE) Working Group Grades of Evidence

- High quality: Further research is very unlikely to change the Task Force's confidence in the estimate of effect.
- Moderate quality: Further research is likely to have an important impact on the Task Force's confidence in the estimate of effect and may change the estimate.
- Low quality: Further research is very likely to have an important impact on the Task Force's confidence in the estimate of effect and is likely to change the estimate.
- Very low quality: The Task Force is very uncertain about the estimate.
Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by McMaster University and the Canadian Task Force on Preventive Health Care (CTFPHC) (see the "Availability of Companion Documents" field).

Quality Assessment, Data Abstraction and Analysis

The titles and abstracts of papers considered for the Key Questions were reviewed in duplicate by members of the synthesis team; any article marked for inclusion by either team member went on to full text rating. Full text inclusion, quality assessment and data extraction were done by two people. All disagreements were resolved through discussions rather than relying on a particular level of kappa score to indicate when discussions were no longer necessary. The inclusion results were reviewed by a third person. Data were extracted by two people using a standard format. The exceptions to this process were studies related to the Contextual Questions and grey literature, for which title and abstract screening and data extraction was done by one person.

The strength of the evidence was determined based on the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system of rating the quality of evidence using GRADEpro software. This system of assessing evidence is widely used and is endorsed by over 40 major organizations including the World Health Organization, Centers for Disease Control and Prevention, and the Agency for Healthcare Research and Quality. The GRADE system rates the quality of a body of evidence as high, moderate, low or very low (see the "Rating Scheme for the Strength of the Evidence" field); each of the four levels reflects a different assessment of the likelihood that further research will impact the estimate of effect (e.g., high quality: further research is unlikely to change confidence in the estimate of effect). A GRADE quality rating is based on an assessment of five conditions: (1) limitations in study designs (risk of bias), (2) inconsistency (heterogeneity) in the direction and/or size of the estimates of effect, (3) indirectness of the body of evidence to the populations, interventions, comparators and/or outcomes of interest, (4) imprecision of results (few events/observations, wide confidence intervals), and (5) indications of reporting or publication bias. Grouped randomized controlled trials (RCTs) begin with a high quality rating which may be downgraded if there are serious or very serious concerns across the studies related to one or more of the five conditions. All groups of observational (e.g., case-control and cohort) studies begin with a low quality rating which may be further downgraded based on assessments of the same five criteria. All other types of evidence are assigned a very low quality rating. For this review, key data were entered into the GRADEpro software along with the quality assessment ratings to produce two analytic products, the GRADE Evidence Profile Tables and the GRADE Summary of Findings Tables (presented in the Evidence Sets of the systematic review document [see the "Availability of Companion Documents" field]).

The Cervical Cancer Screening Working Group rated each of the outcomes and potential harms of screening using the GRADE process. GRADE suggests a nine point scale (1 to 9) to judge the importance of the outcomes and harms. The upper end of the scale (7 to 9) identifies outcomes of critical importance for clinical decision making. Rankings of 4 to 6 represent outcomes that are important but not critical, while low ranked items (1 to 3) are deemed of limited importance to decision making or to patients. This rating process identified cervical cancer incidence, cervical cancer mortality and all-cause mortality as critical primary outcomes and overdiagnosis as a critical harm associated with screening. Table 3 of the systematic review document lists the rankings for the outcomes and harms considered in this review in terms of their importance for clinical decision making.

Arriving at a GRADE rating for a body of evidence requires a preliminary assessment of the risk of bias or study limitations for the individual studies. The RCTs were assessed using the Cochrane Review Manager Risk of Bias tool. All case-control studies and the one cohort study with exposed and unexposed groups (a requirement embedded in the assessment tool) were quality appraised with the Newcastle-Ottawa Scale. Information to determine the quality of evidence was abstracted in duplicate from the primary methodology paper for each study. The two team members extracting the data were blind to each other's ratings. In cases of disagreement, final decisions were determined by consensus after consultation with a third reviewer. Tables 4 to 6 of the systematic review document summarize the results of these assessments.

For each study used to answer the Key Questions, review team members extracted data about the patient population, the study design, analysis and results. The characteristics of the included studies are reported by review question in Tables 7 to 12 of the systematic review document (see the "Availability of Companion Documents" field).

For consistency the risk ratios (RRs) and hazard ratios (HRs) are reported for the screened group(s) with the unscreened group as the referent. For the case-control studies, even though study authors reported odds ratios (ORs) for the incidence of cervical cancer, technically the estimates
of effect were for the participants' exposure to cervical screening. Consistent with how the committee reported the RRs and HRs, in this review all ORs are less than one which relates to the protective effect of screening. Some studies reported ORs in the opposite direction or provided ORs for the longest screening interval (KQ1d); in these cases the committee inverted the OR and the confidence interval (CI) to get results for the screened population or the group with the shortest interval. These data were used for calculations and presentation of the findings within the body of the review and the Evidence Sets.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by McMaster University and the Canadian Task Force on Preventive Health Care (CTFPHC) (see the "Availability of Companion Documents" field).

The Canadian Task Force on Preventive Health Care is an independent panel of clinicians and methodologists that makes recommendations about clinical manoeuvres aimed at primary and secondary prevention. Work on each set of recommendations is led by a workgroup of 2 to 6 members of the task force. Each workgroup establishes the research questions and analytical framework for the guideline.

The development of these recommendations was led by a workgroup of 5 members of the task force, in collaboration with 2 members of the Pan-Canadian Cervical Screening Initiative and supported by scientific officers from the Public Health Agency of Canada.

Analytic Framework and Key Questions

The workgroup established the research questions and analytical framework for the guideline (see Appendix 1 in the systematic review document [see "Availability of Companion Documents" field]), which were incorporated into the search protocol.

The Key Questions (KQ) considered for the systematic review include:

1. What is the effect of cervical cancer screening on incidence of and mortality from invasive cervical cancer?
   a. Do liquid-based methods of cytology reduce incidence of or mortality from invasive cervical cancer compared to slide-based techniques?
   b. Does either primary or reflex human papilloma virus (HPV) testing reduce incidence of or mortality from invasive cervical cancer compared to conventional cytology screening?
   c. Does computer-assisted screening reduce incidence of or mortality from invasive cervical cancer compared to conventional cytology screening?
   d. How does varying the screening interval affect incidence of or mortality from invasive cervical cancer?
   e. How does varying the age at which screening is started or stopped reduce incidence of or mortality from invasive cervical cancer?
2. What are the harms of cervical cancer screening (including colposcopy and biopsy procedures, anxiety/depression, sexual dysfunction, overdiagnosis and false-positives)?
   a. At what rates do these harms occur, by age, and with different screening intervals?
3. What is the effect of cervical cancer screening in subgroups: reduction in mortality and/or morbidity, and harms? Subgroups include: (a) Aboriginal populations, (b) rural populations, (c) immigrants, (d) pregnant women, (e) women who have sex with women, (f) immunocompromised women (e.g., with human immunodeficiency virus [HIV]), (g) women who had a hysterectomy, (h) women who received the HPV vaccination, and (i) women who have multiple partners or a change in partners. Is there evidence that women from any of these groups have a higher risk of invasive cervical cancer, or greater risk of harms (of screening), and if so, is there evidence that screening policies should be different for any of these groups: more or less frequent or with different starting/stopping rules?

The Contextual Questions (CQ) considered for this review are:

1. What are the harms of cervical cancer screening for pre-cancer (i.e., overdiagnosis and false-positive rates, specificity)?
2. What are the harms of treatment of cervical cancer? Harms include: (a) harms of colposcopy, (b) harms of biopsy: cone biopsy (immediate and late; pre-term labour, miscarriage) and loop electrosurgical excision procedure/large loop excision of the transformation zone (LEEP/LEETZ) (immediate and late effects), (c) harms of treatment of cervical cancer: total hysterectomy (incontinence, infection, hospitalization) and radiotherapy.
3. What is the effect of cervical cancer screening in subgroups: reduction in mortality and/or morbidity, and harms? Subgroups include: (a) Aboriginal populations, (b) rural populations, (c) immigrants, (d) pregnant women, (e) women who have sex with women, (f) immunocompromised women (e.g., with human immunodeficiency virus [HIV]), (g) women who had a hysterectomy, (h) women who received the HPV vaccination, and (i) women who have multiple partners or a change in partners. Is there evidence that women from any of these groups have a higher risk of invasive cervical cancer, or greater risk of harms (of screening), and if so, is there evidence that screening policies should be different for any of these groups: more or less frequent or with different starting/stopping rules?
4. What are the resource implications and cost effectiveness of cervical cancer screening in Canada?
5. What are patients' values and preferences regarding cervical cancer screening?
6. What process and outcome performance measures or indicators have been identified in the literature to measure and monitor the impact of cervical screening?
7. What is the evidence of the value of organized programs for cervical cancer screening?
8. What is the evidence of using different categories of health care professionals to perform Papanicolaou (Pap) smears in medical or different settings?
9. What is the evidence of the value (acceptability, participation rates) of women self-sampling for HPV testing?

Grading of Recommendations

Recommendations are graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE offers 2 strengths of recommendation: strong and weak. The strength of recommendations is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether the intervention represents a wise use of resources.

Rating Scheme for the Strength of the Recommendations

Grading of Recommendations

- Strong recommendations are those for which the Task Force is confident that the desirable effects of an intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention). A strong recommendation implies that most people will be best served by the recommended course of action.
- Weak recommendations are those for which the desirable effects probably outweigh the undesirable effects (weak recommendation for an intervention) or undesirable effects probably outweigh the desirable effects (weak recommendation against an intervention) but appreciable uncertainty exists. A weak recommendation implies that most people would want the recommended course of action, but many would not. For clinicians, this means they must recognize that different choices will be appropriate for individual women, and they must help each woman arrive at a management decision consistent with her own values and preferences. Policy-making will require substantial debate and involvement of various stakeholders. Weak recommendations result when the balance between desirable and undesirable effects is small, the quality of evidence is lower, and there is more variability in the values and preferences of patients.

Cost Analysis

The systematic review identified six studies of costs related to cervical cancer screening; two of these, primarily assessing human papilloma virus (HPV) testing, were US-based and German-based; leaving four that contained Canadian information. Three relevant reports were found in a grey literature search for Canadian data; one of which was also in peer-reviewed form.

Economic Implications of Screening

Most of the economic studies reviewed did not assess the relative cost-effectiveness of cytologic or HPV testing alone. Available data from a Canadian economic modelling study suggest that screening with either cytology (every year or every 3 years) or HPV testing (every 3 years) is highly cost-effective compared with no screening.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

Description of Method of Guideline Validation

Table 1 of the original guideline document provides a comparison between the current and previous task force guidelines, as well as recommendations from other groups.
Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of screening for cervical cancer in asymptomatic women aged 15 to 70 years, which may lead to improved health

Potential Harms

- Additional follow-up tests for abnormal results
- Unnecessary treatment (e.g., owing to false-positives and overdiagnosis)

Qualifying Statements

Limitations

The findings of the systematic review are impacted by the biases and limitations of the literature and the included studies. For the question on the effect of cervical cancer screening on mortality, all of the data came from one randomized controlled trial (RCT) of a single lifetime screen offered to women in rural villages in India with follow-up limited to eight years. No studies reported on the outcome of all-cause mortality and there was no evidence that met our inclusion criteria for the effectiveness of liquid-based versus slide-based screening or reflex human papillomavirus (HPV) testing versus conventional cytology. The bulk of the evidence used to answer the other Key Questions was taken from low or very low Grading of Recommendations Assessment, Development and Evaluation (GRADE) quality case-controls, the results of which need to be considered with caution. Finally, we restricted our search to papers in English or French, thus the guideline developers may have missed the opportunity to analyze data from papers written in other languages.

Implementation of the Guideline

Description of Implementation Strategy

Considerations for Implementation

Evidence from countries that begin screening at an older age and with a longer interval between screens than is usual in Canada suggests that organized screening is more effective than opportunistic screening. Some Canadian provinces have established such programs, and the rest are developing them. Most provinces have recently revised their guidelines. Previously, some provinces recommended annual screening starting at early ages, but all have now increased the starting age and intervals between screens. Doctors in each province will need to consider their population and resources in applying the task force’s recommendations.

One randomized trial found no significant differences in the incidence of or mortality due to cervical cancer between women undergoing conventional cytologic screening (manual reading of screens) and computer-assisted screening (computer-assisted reading of screens). Based on this evidence, either reading technique may be used for women of any age for whom Papanicolaou (Pap) tests are recommended. Although no identified studies compared liquid-based to conventional cytology in terms of incidence of and mortality due to cervical cancer, the sensitivity and
specificity of liquid-based and conventional cytology are similar.

Increased or decreased screening may be appropriate for women with different risk profiles. Women who have had a complete hysterectomy for benign disorders no longer need to undergo screening, whereas women who are immunocompromised may benefit from more frequent screening. There is very limited evidence available as to the benefits of screening among women who have sex with women; however, because this group is at risk for cervical cancer, they should be advised to undergo screening according to these recommendations. The guideline workgroup found no evidence to recommend a specific interval between first sexual activity (with potential for human papilloma virus [HPV] infection) and first need for screening, nor for more frequent screening for women at increased risk owing to multiple sexual partners.

Practitioners should be aware of women's values, preferences and beliefs about screening and discuss these in the context of the potential benefits and harms of the screening process. Certain subgroups of women are less likely to receive adequate screening, including immigrant groups, Aboriginal women and women with very low socioeconomic status. Many women prefer female health care providers to perform screening. In addition, cultural views on screening may affect a woman's willingness to undergo the procedure as might misconceptions regarding Pap testing. Other factors affecting the willingness to undergo screening include fear, fatalistic attitudes, embarrassment, fear of pain or discomfort, anxiety and stress related to diagnosis, distrust of the health care system and the belief that screening is not necessary without illness.

The limited evidence regarding patient preferences for screening intervals suggests that women who are used to undergoing frequent screening prefer the feeling of security provided by shorter rather than longer screening intervals, and that they are concerned that recommendations for longer intervals between screens are primarily a means to save costs. Therefore, the potential harms and benefits should be discussed between patient and provider for informed decision-making.

Evidence concerning the performance of Pap tests by different types of health care professionals was limited. The guideline workgroup's search found only 1 case–control study, which reported that nongynecologist physicians were twice as likely as gynecologists to collect unsatisfactory cervical specimens in a US teaching hospital. However, results at this centre may not be generalizable. In the UK, where practice nurses obtain cervical specimens, better training improved both the quality of the specimens and policy adherence.

**Suggested Performance Measures for Implementation**

Recommended indicators are designed to measure Pap testing at the level of individual primary care practices. Suggested performance measures include rates of discussion about cervical cancer screening, actual rates of testing and subsequent follow-up (Appendix 7 of the systematic review document [see “Availability of Companion Documents” field]). The incidence of and mortality due to cervical cancer should continue to be monitored at the provincial, territorial and national levels.

**Implementation Tools**

Audit Criteria/Indicators

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

**Institute of Medicine (IOM) National Healthcare Quality Report Categories**

**IOM Care Need**

Staying Healthy
IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1994 (revised 2013 Jan 8)

Guideline Developer(s)

Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]

Source(s) of Funding

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Guideline Committee

Canadian Task Force on Preventive Health Care (CTFPHC) Writing Group

Composition of Group That Authored the Guideline


Financial Disclosures/Conflicts of Interest

The views of the funding body have not influenced the content of the guideline; competing interests have been recorded and addressed. None of the members of the guidelines writing group have declared competing interests.

Guideline Endorser(s)

College of Family Physicians of Canada - Professional Association
Guideline Status

This is the current release of the guideline.


A complete list of planned reviews, updates and revisions is available under the What's New section at the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

Guideline Availability


Availability of Companion Documents

The following are available:


There is a CTFPHC mobile app for primary care practitioners available for download from the CTFPHC Web site.

In addition, suggested performance measures are available in the original guideline document.

Patient Resources

The following are available:


Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.