



Complete Summary

GUIDELINE TITLE

Investigation of post-menopausal bleeding. A national clinical guideline.

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Investigation of post-menopausal bleeding. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Sep. 25 p. (SIGN publication; no. 61). [68 references]

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SCOPE

DISEASE/CONDITION(S)

- Post-menopausal bleeding (PMB)
- Endometrial cancer (Diagnosis; Risk Assessment)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based recommendations for the investigation of post-menopausal bleeding (PMB) with focus on the detection of endometrial cancer

TARGET POPULATION

Women with post-menopausal bleeding

INTERVENTIONS AND PRACTICES CONSIDERED

1. Risk assessment for endometrial cancer
2. Referral to specialist for investigation of post-menopausal bleeding (PMB)
3. Clinical inquiry and pelvic examination
4. Investigation techniques
 - Transvaginal ultrasonography (TVUS)
 - Transabdominal ultrasound
 - Dilatation and curettage (D&C)
 - Endometrial biopsy
 - Hysteroscopy

Note: Guideline developers considered, but did not recommend, other ultrasonographic techniques (i.e. transvaginal Doppler ultrasonography, three-dimensional ultrasonography, saline enhanced transvaginal ultrasonography and endometrial texture and margin analysis) for routine investigation.

MAJOR OUTCOMES CONSIDERED

- Risk and rate of endometrial cancer
- Transvaginal ultrasonography (TVUS) test performance (i.e. sensitivity and specificity)
- Pre-test and post-test probability estimates of transvaginal ultrasonography for endometrial cancer
- Accuracy and patient acceptability of investigative techniques

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were restricted to systematic reviews, meta-analyses, randomised controlled trials, and longitudinal studies. Internet searches were carried out on

the Web sites of the Canadian Practice Guidelines Infobase, the United Kingdom (UK) Health Technology Assessment Programme, the United States (US) National Guideline Clearinghouse, and the United States National Institutes of Health. Searches were also carried out on the search engines Northern Light and OMNI, and all suitable links followed up. Database searches were carried out on Cochrane Library, Embase 1985-May 1999, Healthstar 1975-May 1999, and Medline 1966-May 1999. Search strategies were reviewed by an independent information specialist. The Medline version of the search strategy can be viewed on the Scottish Intercollegiate Guidelines Network (SIGN) web site.

The main searches were supplemented by material identified by individual members of the development group and were updated in the course of development. All selected papers were evaluated using standard methodological checklists before conclusions were considered as evidence.

NUMBER OF SOURCE DOCUMENTS

Not stated

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

Levels of Evidence

1++

High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+

Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-

Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++

High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+

Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-

Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3

Non-analytic studies, e.g. case reports, case series

4

Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Scottish Intercollegiate Guidelines Network (SIGN) carries out comprehensive systematic reviews of the literature using customized search strategies applied to a number of electronic databases and the Internet. This is often an iterative process whereby the guideline development group will carry out a search for existing guidelines and systematic reviews in the first instance and, after the results of this search have been evaluated, the questions driving the search may be redefined and focused before proceeding to identify lower levels of evidence.

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. SIGN has developed checklists to aid guideline developers to critically evaluate the methodology of different types of study design. The result of this assessment will affect the level of evidence allocated to the paper, which in turn will influence the grade of recommendation it supports.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the [SIGN Web site](#).)

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The process for synthesizing the evidence base to form graded guideline recommendations is illustrated in the companion document titled "SIGN 50: A Guideline Developer's Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN website.

Evidence tables should be compiled, summarizing all the validated studies identified from the systematic literature review relating to each key question. These evidence tables form an important part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

In order to address how the guideline developer was able to arrive at their recommendations given the evidence they had to base them on, SIGN has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups are expected to summarise their view of the total body of evidence covered by each evidence table. This summary view is expected to cover the following aspects:

- Quantity, quality, and consistency of evidence
- Generalisability of study findings
- Applicability to the target population of the guideline
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources need to treat them.)

Guideline development groups are provided with a pro forma in which to record the main points from their considered judgement. Once they have considered these issues, the group are asked to summarise their view of the evidence and assign a level of evidence to it, before going on to derive a graded recommendation.

The assignment of a level of evidence should involve all those on a particular guideline development group or subgroup involved with reviewing the evidence in relation to each specific question. The allocation of the associated grade of recommendation should involve participation of all members of the guideline development group. Where the guideline development group is unable to agree a unanimous recommendation, the difference of opinion should be formally recorded and the reason for dissent noted.

The recommendation grading system is intended to place greater weight on the quality of the evidence supporting each recommendation, and to emphasise that the body of evidence should be considered as a whole, and not rely on a single study to support each recommendation. It is also intended to allow more weight to be given to recommendations supported by good quality observational studies where randomised controlled trials (RCTs) are not available for practical or ethical reasons. Through the considered judgement process guideline developers are also able to downgrade a recommendation where they think the evidence is not generalisable, not directly applicable to the target population, or for other reasons is perceived as being weaker than a simple evaluation of the methodology would suggest.

On occasion, there is an important practical point that the guideline developer may wish to emphasise but for which there is not, nor is their likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. These are marked in the guideline as "good practice points." It must be emphasized that these are not an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

Grade A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or randomized controlled trial rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

Grade C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rate as 2++

Grade D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

Introduction

The development process for this guideline has included explicit consideration of economic issues at each stage, as part of a pilot study being run by the Scottish Intercollegiate Guidelines Network (SIGN) and the Scottish Health Economists' Network. This pilot study recognises that by taking account of the resource implications of guidelines the National Health Service (NHS) can ensure that the quality of services is improved, while contributing to the goal of efficient use of scarce resources.

Methodology

The first stage of the process of incorporating economic considerations is to review the economics literature in addition to the clinical literature. Where high quality information is obtained from this review it is incorporated into the clinical recommendations. The second stage involves consideration of the economic implications of the guideline where no economic evaluations are available. This involves considering the following questions:

- Are the resource implications of implementation of the guideline likely to be significant nationally or locally, such that they cannot be absorbed within existing resource allocation?
- Will the guideline affect outcomes or resource use in other areas of the NHS (such as primary care, other clinical specialties, support departments)?
- Will the guideline affect outcomes or resource use in partner organisations (e.g. social work departments; the voluntary sector, etc.)?
- Will the guideline affect costs to patients, for example will they face additional visits to hospital/general practitioner (GP) or have to spend longer in hospital?
- Will the guideline affect outcomes or resource use in future time periods?
- Will other groups benefit or be potentially disadvantaged by the recommendation / guideline?
- Are there disproportionate costs or outcomes for a particular group?

Results

The literature review found no high quality economic evaluations of the investigation of postmenopausal bleeding which could be used to inform the clinical recommendations. As a result, an economic analysis of the guideline was undertaken. Refer to the original guideline document for details.

METHOD OF GUIDELINE VALIDATION

External Peer Review

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development at which the guideline development group present their draft recommendations for the first time. The national open meeting for this guideline was held on 12 May 2000 attended by representatives of all key specialties. The draft guideline was also available on the SIGN web site for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

The guideline was also reviewed in draft form by independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline.

As a final quality control check, the guideline was reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the peer reviewers' comments had been addressed adequately and that any risk of bias in the guideline development process as a whole had been minimised.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

The strength of recommendation grading (A-D) and level of evidence (I++-4) are defined at the end of the "Major Recommendations" field.

Risk of Endometrial Cancer

Hormone Replacement Therapy (HRT)

C: Clinicians should be aware of the background incidence of endometrial cancer among users and non-users of HRT and in those who present with post-menopausal bleeding (PMB).

A: HRT should include a progestogen regime which is protective against the endometrial effects of unopposed oestrogen.

Tamoxifen

A: Clinicians should be aware that post-menopausal women receiving tamoxifen therapy, particularly for longer than five years, are at increased risk of endometrial cancer.

Referral for Assessment

When to Refer

D: The risk of endometrial cancer in non-HRT users complaining of PMB and in HRT users experiencing abnormal bleeding is sufficient to recommend referring all patients for investigation.

Investigative Techniques

Transvaginal Ultrasonography

B: Where sufficient local skills and capacity exist, transvaginal ultrasound is an appropriate first-line procedure to identify which women with PMB are at higher risk of endometrial cancer.

Transabdominal Ultrasound

D: Transabdominal ultrasound may be used as a complementary examination if the uterus is significantly enlarged or a wider view of the pelvis or abdomen is required. Transabdominal ultrasound may also be used in the small proportion of women in whom it proves technically impossible to perform a transvaginal ultrasound.

Dilatation and Curettage (D&C)

D: Dilatation and curettage should no longer be used as the first-line method of investigating PMB in most cases.

Endometrial Biopsy

C: Hysteroscopy and biopsy (curettage) is the preferred diagnostic technique to detect polyps and other benign lesions.

C: Histological specimens may be obtained either at the same time as inpatient or outpatient hysteroscopy with curettage or using an endometrium sampling device, e.g. Pipelle™.

Hysteroscopy

B: Outpatient techniques for hysteroscopy and suction sampling of the endometrium should be available in all diagnostic units.

B: Facilities to perform hysteroscopy and curettage under general anaesthetic should be available for when the outpatient procedure is not possible or the patient has a strong preference for a general anaesthetic.

Investigation of Women Using Tamoxifen

C: Endometrial investigation should only be carried out in post-menopausal women on tamoxifen who experience vaginal bleeding.

D: Hysteroscopy with biopsy is preferable as the first line of investigation in women taking tamoxifen who experience post-menopausal bleeding.

Interpretation of Transvaginal Ultrasound (TVUS)

B: A cut-off threshold of 3 mm or less should be used for TVUS in women with PMB or unscheduled bleeding who:

- have never used HRT
- have not used any form of HRT for a year or more
- are using continuous combined HRT

B: If the clinician and the woman judge that the level of reassurance and reduced risk are acceptable following a TVUS measurement of 3 mm or less, no further action need be taken. Further investigations should be carried out if symptoms recur.

B: If the clinician, the patient or both are not satisfied with this level of reassurance, further investigation is justified. This should include an endometrial biopsy to obtain a histological assessment.

B: For women on sequential combined HRT presenting with unscheduled bleeding, TVUS using a cut-off point of 5 mm or less should be used to exclude endometrial cancer.

Definitions:

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A

At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.

B

A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+.

C

A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++.

D

Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+.

Levels of Evidence

1++

High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+

Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1–

Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++

High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+

Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-

Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3

Non-analytic studies, e.g. case reports, case series

4

Expert opinion

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The specific type of supporting evidence is explicitly identified in each section of the guideline.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

- Identification of patients at risk for endometrial cancer
- Appropriate investigation of post-menopausal bleeding (PMB) and subsequent identification or exclusion of endometrial pathology
- Early detection of endometrial cancer

Specific Benefits of Transvaginal Ultrasonography (TVUS)

- TVUS can reliably assess thickness and morphology of the endometrium and can thus identify a group of women with post-menopausal bleeding who have a thin endometrium and are therefore unlikely to have significant endometrial disease.
- The relatively non-invasive nature of TVUS may make it more acceptable than other investigations, especially to elderly women.
- TVUS helps to identify those women with post-menopausal bleeding at higher risk of endometrial cancer who require further investigation.
- TVUS is an effective means of excluding endometrial cancer.

Subgroups Most Likely to Benefit:

Patients at higher risk of endometrial cancer, such as women receiving tamoxifen therapy, are more likely to benefit from investigation of post-menopausal bleeding (PMB).

POTENTIAL HARMS

False negative or positive investigative test results

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made in light of the clinical data presented by the patient and the diagnostic and treatment options available. However, it is advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- The sequence of investigation of post-menopausal bleeding (PMB) will depend on clinical judgement, local resources and expertise, and patient preference.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Trust and is an essential part of clinical governance. It is acknowledged that every Trust cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

Key points for audit are identified in the original guideline document.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Investigation of post-menopausal bleeding. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Sep. 25 p. (SIGN publication; no. 61). [68 references]

ADAPTATION

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

DATE RELEASED

2002 Sep

GUIDELINE DEVELOPER(S)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Scottish Executive Health Department

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Guideline Development Group: Dr Jo Davis (chairman); Dr Robbie Foy (methodologist); Dr Simon Crawford (secretary); Dr Alison Bigrigg; Dr Lucy Caird; Professor Hilary Critchley; Dr Heather Deans; Dr Eleanor Guthrie; Mr Robin Harbour; Sister Jacqueline McConville; Dr Rod Muir; Dr Moray Naim; Dr Shelagh Neil; Mrs Winnie Sherry; Mrs Pamela Warner

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Scottish Intercollegiate Guidelines Network (SIGN) guideline development groups are required to complete a declaration of interests, both personal and non-personal. A personal interest involves payment to the individual concerned, e.g., consultancies or other fee-paid work commissioned by or shareholdings in the pharmaceutical industry; a non-personal interest involves payment which benefits any group, unit or department for which the individual is responsible, e.g., endowed fellowships or other pharmaceutical industry support. SIGN guideline group members should be able to act as independently of external commercial influences as possible, therefore, individuals who declare considerable personal interests may be asked to withdraw from the group. Details of the declarations of interest of any guideline development group member(s) are available from the SIGN executive.

GUIDELINE STATUS

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

GUIDELINE AVAILABILITY

Electronic copies: Available from the Scottish Intercollegiate Guidelines Network (SIGN) Web site:

- [HTML Format](#)
- [Portable Document Format \(PDF\)](#)

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Quick reference guide: Investigation of post-menopausal bleeding, Scottish Intercollegiate Guidelines Network, 2002. 2 p. Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).
- SIGN 50: a guideline developers' handbook. Edinburgh (UK): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the [SIGN Web site](#).
- Appraising the quality of clinical guidelines. The SIGN guide to the AGREE (Appraisal of Guidelines Research & Evaluation) guideline appraisal instrument. Edinburgh (UK): Scottish Intercollegiate Guidelines Network, 2001. Available from the [SIGN Web site](#).
- Additional supporting documentation regarding existing facilities for investigation of postmenopausal bleeding, female consultation and incidence rates, background to transvaginal ultrasonography, and option appraisal on use of transvaginal ultrasonography, is available from the [SIGN Web site](#).

PATIENT RESOURCES

The following is available:

- Information for patients. In: Investigation of post-menopausal bleeding. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2002 Sep. 25 p. (SIGN publication; no. 61).

Electronic copies: Available from the Scottish Intercollegiate Guidelines Network (SIGN) Web site:

- [HTML Format](#)
- [Portable Document Format \(PDF\)](#)

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.

NGC STATUS

This NGC summary was completed by ECRI on February 21, 2003. The information was verified by the guideline developer on March 12, 2003.

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