



Metastatic malignant disease of unknown primary origin: Evidence Update February 2012

A summary of selected new evidence relevant to NICE clinical guideline 104 'Diagnosis and management of metastatic malignant disease of unknown primary origin' (2010)



Evidence Update 7

Evidence Updates provide a regular, often annual, summary of selected new evidence published since the literature search was last conducted for the accredited guidance they update. They reduce the need for individuals, managers and commissioners to search for new evidence and inform guidance developers of new evidence in their field. In particular, Evidence Updates highlight any new evidence that might reinforce or generate future change to the practice described in the most recent, accredited guidance, and provide a commentary on the potential impact. Any new evidence that may impact current guidance will be notified to the appropriate NICE guidance development centres. For contextual information, Evidence Updates should be read in conjunction with the relevant clinical guideline, available from www.nice.org.uk/guidance/CG104. NHS Evidence is a service provided by NICE to improve use of, and access to, evidence-based information about health and social care.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

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Introduction

This Evidence Update identifies new evidence that might reinforce or generate future change to the practice laid out in the following reference guidance:

 ¹ **Metastatic malignant disease of unknown primary origin. NICE clinical guideline 104 (2010). Available from www.nice.org.uk/guidance/CG104**

A comprehensive search was undertaken, and five pieces of new evidence were selected for discussion (see appendix A for details of the evidence search and selection process). The Evidence Update Advisory Group, comprised of subject experts, reviewed the prioritised evidence and provided a commentary on the one paper deemed to be of limited interest.

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

¹ NICE-accredited guidance is denoted by the Accreditation Mark 

1 New evidence

After the evidence search and selection procedure (outlined in Appendix A) had been carried out, the Evidence Update Advisory Group (EUAG) decided that of the five studies identified for discussion, one piece of evidence was sufficiently aligned to the scope of the guidance to warrant commentary. The remaining four papers were excluded from commentary as they covered therapeutic areas outside the scope of the NICE guidance, with some also having methodological weaknesses.

As only one piece of evidence was located, it was decided that this was insufficient evidence to produce a full Evidence Update at the present time. This document is therefore a statement of process, describing the steps that were undertaken, and providing brief commentary on the one piece of limited evidence that was found.

1.1 Organisation of services and support

No new key evidence was found for this section.

1.2 Diagnosis

Immunohistochemistry

[Anderson and Weiss \(2010\)](#) performed a meta-analysis of five studies to quantify the performance of immunohistochemistry (IHC) panels used to identify the site of the tissue of origin for metastatic tumours, especially those of unknown or uncertain origin. The included studies looked at metastatic tumours only (n = 368 specimens) or a combination of primary and metastatic tumours (n = 289 specimens).

It was found that IHC panels correctly identified the tissue in 82.3% (95% confidence interval [CI] 77.4 to 86.3%) of the combined primary and metastatic tumour studies, and in 65.6% (95% CI 60.1 to 70.7%) of the metastatic only studies. Interpretation of these results should take into account a number of limitations to the study. Only one database (PubMed) was searched for the literature review, few details of the literature search and review were provided, no quality assurance measures were described, and details of how the studies were combined were lacking.

Within the study limitations, the percentage values for correct identification of tissue from the meta-analysis may suggest a potential minimum diagnostic accuracy requirement for new tests designed to distinguish tissue of origin in metastatic tumours of unknown origin.

Key reference

Anderson GG, Weiss LM (2010) Determining tissue of origin for metastatic cancers: Meta-analysis and literature review of immunohistochemistry performance. *Applied Immunohistochemistry and Molecular Morphology* 18: 3–8

Abstract: www.journals.lww.com/appliedimmunohist/Abstract/2010/01000/Determining_Tissue_of_Origin_for_Metastatic.2.aspx

1.3 Factors influencing management decisions

No new key evidence was found for this section.

1.4 Managing specific presentations

No new key evidence was found for this section.

2 New evidence uncertainties

No new evidence uncertainties were identified during the Evidence Update process, however any uncertainties that may be identified in future for metastatic malignant disease of unknown primary origin will be added to the NHS Evidence UK Database of Uncertainties about the Effects of Treatments (DUETs) at www.library.nhs.uk/duets/.

DUETs has been established in the UK to publish uncertainties about the effects of treatment which cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Other uncertainties can be found in the NICE research recommendations database at www.nice.org.uk/research/index.jsp?action=rr.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Metastatic malignant disease of unknown primary origin. NICE clinical guideline 104 (2010). Available from www.nice.org.uk/guidance/CG104

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 1 January 2009 to 21 June 2011:

- CINAHL
- Cochrane Database of Systematic Reviews – Cochrane Library
- Embase
- MEDLINE
- PreMEDLINE
- PsycINFO

Although the end of the search period of NICE clinical guideline 104 was September 2009, an earlier search date was used for the Evidence Update to confirm that all relevant information was previously included in the clinical guideline.

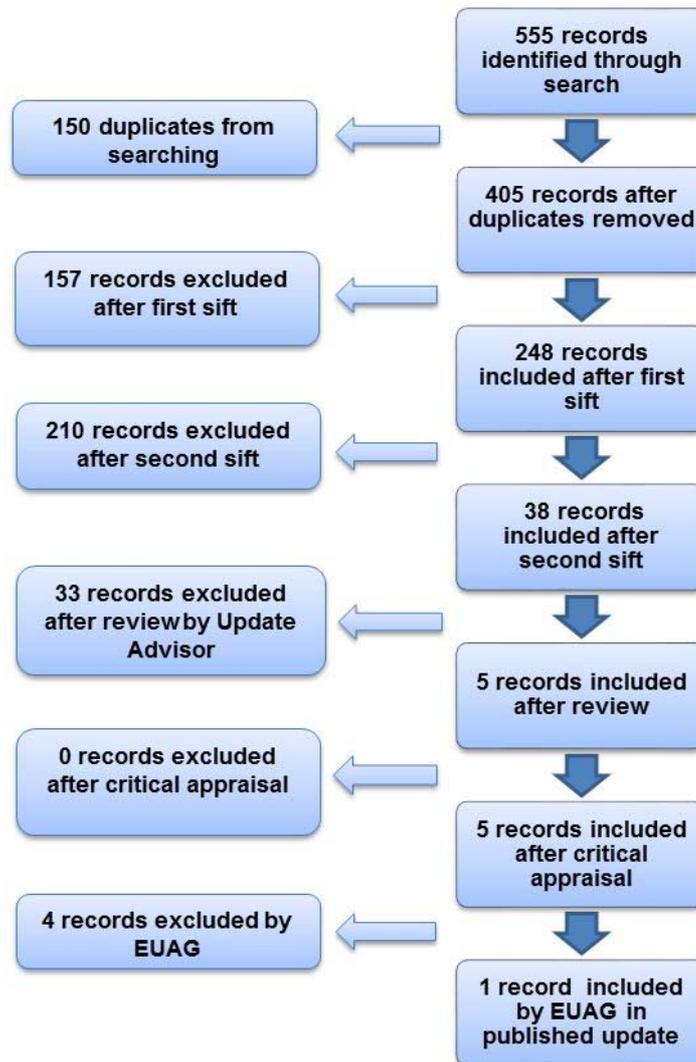
Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The clinical guideline used separate search strategies to answer 28 clinical questions. This Evidence Update used more general terms to identify significant evidence published for Metastatic malignant disease of unknown primary origin. Terminology for the Evidence Update search strategy was taken from the clinical guideline but is indicative of one general search. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews (www.sign.ac.uk/methodology/filters.html).

Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Update Adviser (the chair of the EUAG), and the full search strategies, are available on request from contactus@evidence.nhs.uk.

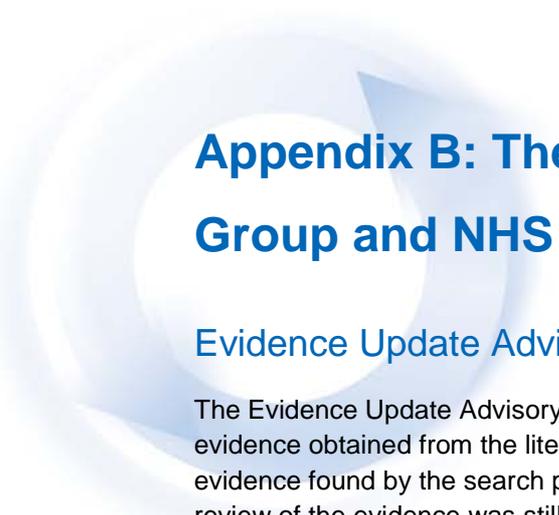
Table 1 MEDLINE search strategy (adapted for individual databases)

1	Neoplasms, Unknown Primary
2	((Unknown primar\$ or unknown origin\$1) and (cancer\$ or neoplas\$ or tumor\$ or carcinoma\$ or adeno\$ or metasta\$ or micrometasta\$ or malignan\$ or lymphoma\$ or sarcoma\$ or melanoma\$)).tw
3	(Occult adj5 (cancer\$ or neoplas\$ or tumor\$ or carcinoma\$ or adeno\$ or metasta\$ or micrometasta\$ or malignan\$ or lymphoma\$ or sarcoma\$ or melanoma\$)).tw
4	((Undetermined primar\$ or undetermined origin\$1) adj5 (cancer\$ or neoplas\$ or tumor\$ or carcinoma\$ or adeno\$ or metasta\$ or micrometasta\$ or malignan\$ or lymphoma\$ or sarcoma\$ or melanoma\$)).tw
5	((Unidentifi\$ primar\$ or unidentifi\$ origin\$1) adj5 (cancer\$ or neoplas\$ or tumor\$ or carcinoma\$ or adeno\$ or metasta\$ or micrometasta\$ or malignan\$ or lymphoma\$ or sarcoma\$ or melanoma\$)).tw
6	((Undefined primar\$ or undefined origin\$1) adj5 (cancer\$ or neoplas\$ or tumor\$ or carcinoma\$ or adeno\$ or metasta\$ or micrometasta\$ or malignan\$ or lymphoma\$ or sarcoma\$ or melanoma\$)).tw
7	Or/1-6

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group



Appendix B: The Evidence Update Advisory Group and NHS Evidence project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of subject experts who review the prioritised evidence obtained from the literature search. Due to the limited volume and quality of evidence found by the search process, the group did not meet in person, however a thorough review of the evidence was still undertaken.

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