

Metastatic Malignant Disease of Unknown Primary Origin

Clinical Guideline

Key Messages and Q&A

Key Messages

- The National Institute for Health and Clinical Excellence (NICE) has today (26 July) published a new guideline to help the NHS provide effective and tailored care for patients whose cancer has spread to other parts of the body from an unknown primary location.
- This type of cancer is known as metastatic malignant disease of unknown primary origin, more commonly referred to as Cancer (or Carcinoma) of Unknown Primary (CUP). This new guideline aims to support oncologists, nurses and other health professionals in the effective diagnosis, treatment and care of cancer patients with CUP. It seeks to provide a consistent, national approach to the management of this condition.
- It is thought over 10,000 people each year are diagnosed with metastatic malignant disease of unknown primary origin in England and Wales. These patients generally have a poor prognosis and little is known about which types of treatment work best for them. They also tend to miss out on medical and other benefits normally accessed by people with a site-specific cancer diagnosis (e.g. breast, prostate, liver, skin). This is because of a lack of information, specialised services and understanding of, and research into, the disease
- The guideline calls for dedicated teams to be established at local, regional and national level to help improve care for patients with CUP. Specifically, it recommends:
 - All hospitals with a cancer centre or unit should establish specialist CUP teams to support and manage the care of patients with this diagnosis. This team will be responsible for managing patients' care until they are referred to a site-specialist consultant, referred for palliative care alone or diagnosed with a non-malignant condition.
 - A network of CUP Multi Disciplinary Teams to be set up at regional level to review the treatment and care of patients with confirmed CUP, or with complex diagnostic or treatment issues.

- Every cancer network should establish a network site specific group responsible for managing all stages of CUP.
- The guideline makes recommendations to improve patients' experiences, particularly through the creation of these local CUP teams:
 - Inpatients should be seen by a dedicated member of the CUP team by the end of the next working day after referral. Outpatients should be seen within two weeks.
 - Patients should be given access to an identified CUP specialist nurse or key worker when this type of cancer is diagnosed.
 - Decision aids should be developed to help patients and their carers make informed decisions about continuing diagnostic investigations and using anticancer treatment after CUP has been diagnosed.
- The guideline also contains advice for those involved in the diagnosis and care of a patient with CUP, such as oncologists, pathologists and nurses. These recommendations include:
 - Take account of prognostic factors, in particular performance status, presence of liver metastases, lactate dehydrogenase levels and serum albumin, when making decisions about further diagnostic tests and treatment.
 - Explain to patients and carers if further investigations will not alter treatment options and provide appropriate emotional and psychological support.
 - Offer patients with CUP the opportunity to enter clinical trials.
 - If chemotherapy is given outside clinical trials, take into account the clinical and pathological characteristics of the tumour, the toxicity profile of the drugs, their ease of administration and response rate when choosing which treatment to use.
- The guideline also calls for more research to further our understanding of the disease and help ensure patients receive the most effective treatments available.

Q&A

What is 'metastatic malignant disease of unknown primary origin'?

Metastatic malignant disease of unknown primary origin is a type of cancer that has spread within a patient's body from an unknown primary location. It is commonly referred to as Cancer of Unknown Primary or Carcinoma of Unknown Primary (CUP). For the purposes of the guideline, this type of disease is categorised in three stages;

- ***Malignancy of undefined primary origin (MUO)***: Metastatic malignancy identified on the basis of a limited number of tests, without an obvious primary site, before comprehensive investigation.
- ***Provisional carcinoma of unknown primary (provisional CUP)***: Metastatic epithelial or neuroendocrine malignancy identified on the basis of histology/cytology, with no primary site detected despite a selected initial set of investigations, before specialist review and possible further specialised investigations.
- ***Confirmed carcinoma of unknown primary (confirmed CUP)***: Metastatic epithelial or neuroendocrine malignancy identified on the basis of final histology, with no primary site detected despite a selected initial set of investigations, specialist review, and further specialised investigations as appropriate.

It is thought over 10,000 people each year are diagnosed with metastatic malignant disease of unknown primary origin in England and Wales and it is the fourth most common cause of cancer death.

But surely a cancer has to start growing somewhere?

In the majority of cases, cancer patients do receive a specific diagnosis because oncologists and pathologists are able to identify whereabouts in the body the tumour began growing. However, despite scientific advances in diagnostic methods, this is not always possible.

Patients with a provisional CUP diagnosis tend to be subjected to numerous tests and scans in an effort to find the primary location of their tumour. If this site cannot be found, cancer of unknown primary will be confirmed.

What is this type of cancer like?

Because of the nature of CUP, little is known about which treatments work best for patients. As a result, patients tend to have a poor prognosis. It is the fourth most common cause of cancer death.

What kind of care can CUP patients currently expect to receive from the NHS?

Currently, the clinical management of CUP varies widely across the NHS. Patients tend to miss out on medical and other benefits normally accessed by people with a site-specific cancer diagnosis (e.g. breast, prostate, liver, skin). This is because of a lack of information, specialised services and understanding of, and research into, the disease.

Some of the problems in current clinical practice, as identified in the guideline, include:

- No referral guidelines for suspected CUP and no system to rapidly identify patients to ensure early specialist involvement
- Uncertainty about appropriate diagnostic tests, including the use of new technologies, and optimal treatment
- Lack of both an overall organisational structure and a team structure to ensure high-quality care
- Insufficient specialist oncology expertise and dedicated key workers or specialist nurses.
- Lack of support and information for patients

This guideline seeks to end these inequalities and ensure all patients receive the same standard of care experienced by patients with other cancers.

What kinds of things are covered in the guideline?

This guideline focuses on areas that are known to be controversial or uncertain, where there are identifiable variations in clinical practice, where there is a lack of high quality evidence or where NICE guidelines are likely to have the most impact.

What are the guideline's key recommendations?

The guideline makes a series of recommendations to improve the care of CUP patients, which are aimed at various healthcare professionals.

Importantly, the guideline calls for all hospitals with a cancer centre or unit to establish specialist CUP teams to support and manage the care of patients with this diagnosis.

This team should comprise an oncologist, a palliative care physician and a CUP specialist nurse or key worker as a minimum. They should be given administrative support and sufficient designated time in their job plans for this specialist role. The team should also have a named lead clinician.

The guideline also recommends that:

- Specialist CUP Multi Disciplinary Teams should be set up at Network level to review the treatment and care of patients with confirmed CUP, or with complex diagnostic issues.
- Every cancer network should establish a network site specific group responsible for managing all stages of CUP.

In addition, the guideline outlines ways in which oncologists, pathologists and nurses can provide patient-centred care from the point of diagnosis onwards. It also calls for more research to further our understanding of the disease and help ensure patients receive the most effective treatments available

What would be the point of CUP teams at regional and national levels? What would they do?

The role of regional CUP network multidisciplinary teams would be to review the treatment and care of patients with confirmed or suspected CUP, or with complex diagnostic issues. This team should carry out established specialist multidisciplinary team responsibilities.

Nationally, every cancer network should establish a network site-specific group to define and oversee policies for managing CUP. The group should:

- ensure that every CUP team in the network is properly set up
- ensure that the local care pathway for diagnosing and managing CUP is in line with this guideline
- be aware of the variety of routes by which newly diagnosed patients present
- advise the cancer network on all matters related to CUP, recognising that many healthcare professionals have limited experience of CUP
- maintain a network-wide audit of the incidence of CUP, its timely management, and patient outcomes
- arrange and hold regular meetings for the group to report patient outcomes and review the local care pathway.

How will this guideline improve care for these patients?

All recommendations have been developed with the patient in mind and with the aim of ensuring everyone diagnosed with CUP receives the highest standard of care possible.

The local, hospital-based CUP teams will particularly provide patients with good quality one-on-one care such by putting into place practices including:

- Making sure inpatients are seen by a dedicated member of the CUP team by the end of the next working day after referral, with outpatients being seen within two weeks.
- Guaranteeing patients access to an identified CUP specialist nurse or key worker as soon as possible after diagnosis
- Developing decision aids to help patients and their carers make informed decisions about continuing diagnostic investigations and using anticancer treatment after CUP has been diagnosed.

This guideline has received the support of the National Cancer Peer Review Programme in England, which is studying the recommendations to develop a number of peer review measures. These are 'quality measures' that hospitals are assessed against with the aim of improving care for cancer patients and their families.

Which recommendations are being turned into peer review measures?

The National Cancer Peer Review Programme in England is currently studying the guideline and looking to develop an as yet unspecified number of peer review measures from those recommendations where clinical outcomes can be measured.

Who makes sure these peer review measures are followed?

Peer Review Measures are quality measures as set out by the National Cancer Peer Review Programme, a national quality assurance programme for NHS cancer services in England. This programme uses nationally agreed 'quality measures' which cancer services are assessed against. This involves self-assessment by cancer service teams and also external reviews of teams conducted by professional peers.

So will the NHS have to follow these guidelines?

Normally clinical guidelines are not statutory, but their recommendations are regarded as best practice. However, peer review measures are mandatory so the NHS in England will be expected to follow these.

This guideline is relevant to the NHS in England, Wales and Northern Ireland. Scotland has its own arrangements for managing healthcare.

You recommend the setting up of specialised CUP teams to help care for patients, but surely setting up new teams will place a heavy burden on already stretched NHS budgets?

The guideline does not necessarily advocate the creation of new teams who solely look after this group of patients. NICE anticipates teams who already look after other types of cancer patients, to also take on the specialist responsibility for CUP.

Members of the CUP team would not be expected to work full time in this specialist role, but would spend a proportion of their time on other cancer-related activities.

This will mean an increase in workload, but hospitals should ensure these teams are supported to ensure they have sufficient time in their job plans for this specialist role and any training that may be needed.

How much will it cost to establish these teams at a local, regional and national level like NICE suggests?

Local health communities are encouraged to assess the cost impact of implementing the guideline locally because there may be regional variation depending on local circumstances. The varied nature of this type of cancer means that it is difficult to estimate the cost impact of implementing the guideline nationally.

Although it is likely that there will be costs involved in the implementation of the guideline, there should also be savings from the more rational management of patients passing through the system with improved pathways of care and decreased length of hospital stays.

The Coalition Government have committed to achieving “cancer survival rates among the best in the world” by 2015. The CUP guideline is a step forward on this path

Who is the guideline aimed at?

This guideline is relevant to all healthcare professionals who come into contact with patients with metastatic malignant disease of unknown primary origin, as well as to the patients themselves and their carers. Commissioners and others involved in clinical governance in primary and secondary care may also find the guideline useful in helping to ensure that arrangements are in place to deliver appropriate care to this group of patients.

How does NICE expect healthcare professionals to make all the changes to clinical practice that are being recommended in this guideline?

NICE has developed a range of implementation tools to help healthcare professionals put this guidance into practice. These include a slideset to help inform staff and an audit tool, and are available to download from the NICE website; www.nice.org.uk.

NICE also has a team who works with the NHS and other organisations to put the Institute's guidance into practice at a local level for the benefit of patients.

FOR REACTIVE USE ONLY:

Wouldn't NHS money be better spent looking after and treating patients with more common cancers like breast, prostate or lung? Those types of cancers affect many tens of thousands of people every year...

Metastatic malignant disease of unknown primary origin is not a rare cancer – it is thought that over 10,000 people are diagnosed with this disease in England and Wales each year. It is also the fourth most common cause of cancer death.

Every cancer patient has a right to receive the same level of treatment and care, regardless of the type of cancer they have. CUP has been a neglected disease for too long already.

How sure can you be sure that this framework will still be working in the post-white paper NHS?

We would hope that the Government's white paper on NHS reform will not affect the way cancer services are run as they have a real impact on clinical outcomes and are highly valued by patients. The Coalition Government have committed to achieving "cancer survival rates among the best in the world" by 2015. The CUP guideline is a step forward on this path

Also, at a time when the Health Secretary is looking to make £20 billion of efficiency savings, NICE guidelines make cost-efficient and evidence-based recommendations to ensure patients receive the best care possible.