

Bladder cancer: diagnosis and management

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline is the basis of QS106.

Overview

This guideline covers diagnosing and managing bladder cancer in people 18 and above referred from primary care with suspected bladder cancer, and those with newly diagnosed or recurrent bladder (urothelial carcinoma, adenocarcinoma, squamous-cell carcinoma or small-cell carcinoma) or urethral cancer.

A [table of NHS England interim treatment regimens](#) gives possible alternative treatment options for use during the COVID-19 pandemic to reduce infection risk. This may affect decisions for patients with bladder cancer. See the [COVID-19 rapid guideline: delivery of systemic anticancer treatments](#) for more details.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- Adults with bladder cancer and their families and carers

Introduction

Bladder cancer is the seventh most common cancer in the UK. It is 3 to 4 times more common in men than in women. In the UK in 2011, it was the fourth most common cancer in men and the thirteenth most common in women. There were 10,399 people diagnosed with bladder cancer and 5081 deaths from bladder cancer in 2011. The majority of cases occur in people aged over 60. The main risk factor for bladder cancer is increasing age, but smoking and exposure to some industrial chemicals also increase risk.

Bladder cancer is usually identified on the basis of visible blood in the urine or blood found on urine testing, but emergency admission is a common way for bladder cancer to present, and is often associated with a poor prognosis.

Most bladder cancers (75 to 80%) do not involve the muscle wall of the bladder and are usually treated by telescopic removal of the cancer (transurethral resection of bladder tumour [TURBT]). This is often followed by instillation of chemotherapy or vaccine-based therapy into the bladder, with prolonged telescopic checking of the bladder (cystoscopy) as follow-up. Some people in this group who are at higher risk are treated with major surgery to remove the bladder (cystectomy). People with cancer in or through the bladder muscle wall may be treated with intent to cure using chemotherapy, cystectomy or radiotherapy, and those who have cancer too advanced to cure may have radiotherapy and chemotherapy.

The involvement of the urogenital tract and the nature of the treatments give this cancer a strong psychological impact, in addition to the physical impact of the disease and its treatments, which is often profound. The prevalence of the condition and the nature of its management make bladder cancer one of the most expensive cancers for the NHS.

There is thought to be considerable variation across the NHS in the diagnosis and management of bladder cancer and the provision of care to people who have it. There is evidence that the patient experience for people with bladder cancer is worse than that for people with other cancers.

This guideline covers adults (18 years and older) referred from primary care with suspected bladder cancer and those with newly diagnosed or recurrent bladder (urothelial carcinoma, adenocarcinoma, squamous-cell carcinoma or small-cell carcinoma) or urethral cancer. There was insufficient high-quality evidence on which to make specific recommendations for non-urothelial bladder cancer (adenocarcinoma, squamous-cell carcinoma or small-cell carcinoma).

It does not cover people aged under 18 or adults with bladder sarcoma, urothelial cancer of the upper urinary tract, or secondary bladder or urethral cancer (for example, bowel or cervix cancer spreading into the bladder).

Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in [section 1](#).

Information and support for people with bladder cancer

- Use a holistic needs assessment to identify an individualised package of information and support for people with bladder cancer and, if they wish, their partners, families or carers, at key points in their care such as:
 - when they are first diagnosed
 - after they have had their first treatment
 - if their bladder cancer recurs or progresses
 - if their treatment is changed
 - if palliative or end of life care is being discussed.

Diagnosing and staging bladder cancer

Diagnosis

- Consider CT or MRI staging before transurethral resection of bladder tumour (TURBT) if muscle-invasive bladder cancer is suspected at cystoscopy.
- Offer white-light-guided TURBT with one of photodynamic diagnosis, narrow-band imaging, cytology or a urinary biomarker test (such as UroVysion using fluorescence in-situ hybridization [FISH], ImmunoCyt or a nuclear matrix protein 22 [NMP22] test) to people with suspected bladder cancer. This should be carried out or supervised by a urologist experienced in TURBT.
- Offer people with suspected bladder cancer a single dose of intravesical mitomycin C given at the same time as the first TURBT.

Treating non-muscle-invasive bladder cancer

Prognostic markers and risk classification

- Ensure that for people with non-muscle-invasive bladder cancer all of the following are recorded and used to guide discussions, both within multidisciplinary team meetings and with the person, about prognosis and treatment options:
 - recurrence history
 - size and number of cancers
 - histological type, grade, stage and presence (or absence) of flat urothelium, detrusor muscle (muscularis propria), and carcinoma in situ
 - the risk category of the person's cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#))
 - predicted risk of recurrence and progression, estimated using a risk prediction tool.

High-risk non-muscle-invasive bladder cancer

- Offer the choice of intravesical BCG (Bacille Calmette-Guérin) or radical cystectomy to people with [high-risk non-muscle-invasive bladder cancer](#) (see the [section on risk classification in non-muscle-invasive bladder cancer](#)), and base the choice on a full discussion with the person, the clinical nurse specialist and a urologist who performs both intravesical BCG and radical cystectomy. Include in your discussion:
 - the type, stage and grade of the cancer, the presence of carcinoma in situ, the presence of variant pathology, prostatic urethral or bladder neck status and the number of tumours
 - risk of progression to muscle invasion, metastases and death
 - risk of understaging
 - benefits of both treatments, including survival rates and the likelihood of further treatment
 - risks of both treatments
 - factors that affect outcomes (for example, comorbidities and life expectancy)
 - impact on quality of life, body image, and sexual and urinary function.

Follow-up after treatment for non-muscle-invasive bladder cancer

Low-risk non-muscle-invasive bladder cancer

- Discharge to primary care people who have had low-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) and who have no recurrence of the bladder cancer within 12 months.

Intermediate-risk non-muscle-invasive bladder cancer

- Offer people with intermediate-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) non-muscle-invasive bladder cancer cystoscopic follow-up at 3, 9 and 18 months, and once a year thereafter.

Treating muscle-invasive bladder cancer

Neoadjuvant chemotherapy for newly diagnosed muscle-invasive urothelial bladder cancer

- Offer neoadjuvant chemotherapy using a cisplatin combination regimen before radical cystectomy or radical radiotherapy to people with newly diagnosed muscle-invasive urothelial bladder cancer for whom cisplatin-based chemotherapy is suitable. Ensure that they have an opportunity to discuss the risks and benefits with an oncologist who treats bladder cancer.

Radical therapy for muscle-invasive urothelial bladder cancer

- Offer a choice of radical cystectomy or radiotherapy with a radiosensitiser to people with muscle-invasive urothelial bladder cancer for whom radical therapy is suitable. Ensure that the choice is based on a full discussion between the person and a urologist who performs radical cystectomy, a clinical oncologist and a clinical nurse specialist. Include in the discussion:
 - the prognosis with or without treatment
 - the limited evidence about whether surgery or radiotherapy with a radiosensitiser is the most effective cancer treatment
 - the benefits and risks of surgery and radiotherapy with a radiosensitiser, including the impact on sexual and bowel function and the risk of death as a result of the treatment.

1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

People have the right to be involved in discussions and make informed decisions about their care, as described in [NICE's information on making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Information and support for people with bladder cancer

- 1.1.1 Follow the recommendations on communication and patient-centred care in [NICE's guideline on patient experience in adult NHS services](#) and the advice in [NICE's guidelines on improving outcomes in urological cancers and improving supportive and palliative care for adults with cancer](#) throughout the person's care.
- 1.1.2 Offer clinical nurse specialist support to people with bladder cancer and give them the clinical nurse specialist's contact details.
- 1.1.3 Ensure that the clinical nurse specialist:
- acts as the key worker to address the person's information and care needs
 - has experience and training in bladder cancer care.
- 1.1.4 Use a holistic needs assessment to identify an individualised package of information and support for people with bladder cancer and, if they wish, their partners, families or carers, at key points in their care such as:
- when they are first diagnosed

- after they have had their first treatment
- if their bladder cancer recurs or progresses
- if their treatment is changed
- if palliative or end of life care is being discussed.

1.1.5 When carrying out a holistic needs assessment, recognise that many of the symptoms, investigations and treatments for bladder cancer affect the urogenital organs and may be distressing and intrusive. Discuss with the person:

- the type, stage and grade of their cancer and likely prognosis
- treatment and follow-up options
- the potential complications of intrusive procedures, including urinary retention, urinary infection, pain, bleeding or need for a catheter
- the impact of treatment on their sexual health and body image, including how to find support and information relevant to their gender
- diet and lifestyle, including physical activity
- smoking cessation for people who smoke
- how to find information about bladder cancer, for example through information prescriptions, sources of written information, websites or DVDs
- how to find support groups and survivorship programmes
- how to find information about returning to work after treatment for cancer
- how to find information about financial support (such as free prescriptions and industrial compensation schemes).

1.1.6 Offer smoking cessation support to all people with bladder cancer who smoke, in line with [NICE's guideline on stop smoking interventions and services](#).

1.1.7 Offer people with bladder cancer and, if they wish, their partners, families or carers, opportunities to have discussions at any stage during their treatment and care with:

- a range of specialist healthcare professionals, including those who can provide psychological support
 - other people with bladder cancer who have had similar treatments.
- 1.1.8 Clinicians caring for people with bladder cancer should ensure that there is close liaison between secondary and primary care with respect to ongoing and community-based support.
- 1.1.9 Trusts should consider conducting annual bladder cancer patient satisfaction surveys developed by their urology multidisciplinary team and people with bladder cancer, and use the results to guide a programme of quality improvement.

1.2 Diagnosing and staging bladder cancer

Diagnosis

- 1.2.1 Do not substitute urinary biomarkers for cystoscopy to investigate suspected bladder cancer or for follow-up after treatment for bladder cancer, except in the context of a clinical research study.
- 1.2.2 Consider CT or MRI staging before transurethral resection of bladder tumour (TURBT) if muscle-invasive bladder cancer is suspected at cystoscopy.
- 1.2.3 Offer white-light-guided TURBT with one of photodynamic diagnosis, narrow-band imaging, cytology or a urinary biomarker test (such as UroVysion using fluorescence in-situ hybridization [FISH], ImmunoCyt or a nuclear matrix protein 22 [NMP22] test) to people with suspected bladder cancer. This should be carried out or supervised by a urologist experienced in TURBT.
- 1.2.4 Obtain detrusor muscle during TURBT.
- 1.2.5 Do not take random biopsies of normal-looking urothelium during TURBT unless there is a specific clinical indication (for example, investigation of positive cytology not otherwise explained).
- 1.2.6 Record the size and number of tumours during TURBT.

- 1.2.7 Offer people with suspected bladder cancer a single dose of intravesical mitomycin C given at the same time as the first TURBT.

Staging

- 1.2.8 Consider further TURBT within 6 weeks if the first specimen does not include detrusor muscle.
- 1.2.9 Offer CT or MRI staging to people diagnosed with muscle-invasive bladder cancer or high-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) that is being assessed for radical treatment.
- 1.2.10 Consider CT urography, carried out with other planned CT imaging if possible, to detect upper tract involvement in people with new or recurrent high-risk non-muscle-invasive or muscle-invasive bladder cancer.
- 1.2.11 Consider CT of the thorax, carried out with other planned CT imaging if possible, to detect thoracic malignancy in people with muscle-invasive bladder cancer.
- 1.2.12 Consider fluorodeoxyglucose positron emission tomography (FDG PET)-CT for people with muscle-invasive bladder cancer or high-risk non-muscle-invasive bladder cancer before radical treatment if there are indeterminate findings on CT or MRI, or a high risk of metastatic disease (for example, T3b disease).

1.3 Treating non-muscle-invasive bladder cancer

Risk classification in non-muscle-invasive bladder cancer

There is no widely accepted classification of risk in non-muscle-invasive bladder cancer. To make clear recommendations for management, the Guideline Development Group developed the consensus classification in table 1, based on the evidence reviewed and clinical opinion.

Table 1 Risk categories in non-muscle-invasive bladder cancer

Low risk	<p>Urothelial cancer with any of:</p> <ul style="list-style-type: none"> solitary pTaG1 with a diameter of less than 3 cm solitary pTaG2 (low grade) with a diameter of less than 3 cm any papillary urothelial neoplasm of low malignant potential
Intermediate risk	<p>Urothelial cancer that is not low risk or high risk, including:</p> <ul style="list-style-type: none"> solitary pTaG1 with a diameter of more than 3 cm multifocal pTaG1 solitary pTaG2 (low grade) with a diameter of more than 3 cm multifocal pTaG2 (low grade) pTaG2 (high grade) any pTaG2 (grade not further specified) any low-risk non-muscle-invasive bladder cancer recurring within 12 months of last tumour occurrence
High risk	<p>Urothelial cancer with any of:</p> <ul style="list-style-type: none"> pTaG3 pT1G2 pT1G3 pTis (Cis) aggressive variants of urothelial carcinoma, for example micropapillary or nested variants

Prognostic markers and risk classification

1.3.1 Ensure that for people with non-muscle-invasive bladder cancer all of the

following are recorded and used to guide discussions, both within multidisciplinary team meetings and with the person, about prognosis and treatment options:

- recurrence history
- size and number of cancers
- histological type, grade, stage and presence (or absence) of flat urothelium, detrusor muscle (muscularis propria), and carcinoma in situ
- the risk category of the person's cancer
- predicted risk of recurrence and progression, estimated using a risk prediction tool.

Low-risk non-muscle-invasive bladder cancer

1.3.2 For the treatment of low-risk non-muscle-invasive bladder cancer, see [recommendations 1.2.3 to 1.2.8](#).

Intermediate-risk non-muscle-invasive bladder cancer

1.3.3 Offer people with newly diagnosed intermediate-risk non-muscle-invasive bladder cancer a course of at least 6 doses of intravesical mitomycin C.

1.3.4 If intermediate-risk non-muscle-invasive bladder cancer recurs after a course of intravesical mitomycin C, refer the person's care to a specialist urology multidisciplinary team.

High-risk non-muscle-invasive bladder cancer

1.3.5 If the first TURBT shows high-risk non-muscle-invasive bladder cancer, offer another TURBT as soon as possible and no later than 6 weeks after the first resection.

1.3.6 Offer the choice of intravesical BCG (Bacille Calmette-Guérin) or radical cystectomy to people with high-risk non-muscle-invasive bladder cancer, and base the choice on a full discussion with the person, the clinical nurse specialist and a urologist who performs both intravesical BCG and radical cystectomy. Include in your discussion:

- the type, stage and grade of the cancer, the presence of carcinoma in situ, the presence of variant pathology, prostatic urethral or bladder neck status and the number of tumours
- risk of progression to muscle invasion, metastases and death
- risk of understaging
- benefits of both treatments, including survival rates and the likelihood of further treatment
- risks of both treatments
- factors that affect outcomes (for example, comorbidities and life expectancy)
- impact on quality of life, body image, and sexual and urinary function.

Intravesical BCG

- 1.3.7 Offer induction and maintenance intravesical BCG to people having treatment with intravesical BCG.
- 1.3.8 If induction BCG fails (because it is not tolerated, or bladder cancer persists or recurs after treatment with BCG), refer the person's care to a specialist urology multidisciplinary team.
- 1.3.9 For people in whom induction BCG has failed, the specialist urology multidisciplinary team should assess the suitability of radical cystectomy, or further intravesical therapy if radical cystectomy is unsuitable or declined by the person, or if the bladder cancer that recurs is intermediate- or low-risk.

Radical cystectomy

- 1.3.10 See [recommendations 1.5.4 to 1.5.7 for people who have chosen radical cystectomy](#).

Recurrent non-muscle-invasive bladder cancer

- 1.3.11 Consider fulguration without biopsy for people with recurrent non-muscle-invasive bladder cancer if they have all of the following:

- no previous bladder cancer that was intermediate- or high-risk
- a disease-free interval of at least 6 months
- solitary papillary recurrence
- a tumour diameter of 3 mm or less.

Managing side effects of treatment

- 1.3.12 Do not offer primary prophylaxis to prevent BCG-related bladder toxicity except as part of a clinical trial.
- 1.3.13 Seek advice from a specialist urology multidisciplinary team if symptoms of bladder toxicity after BCG cannot be controlled with antispasmodics or non-opiate analgesia and other causes have been excluded by cystoscopy.

1.4 Follow-up after treatment for non-muscle-invasive bladder cancer

- 1.4.1 Refer people urgently to urological services if they have haematuria or other urinary symptoms and a history of non-muscle-invasive bladder cancer.
- 1.4.2 See [recommendation 1.2.1 on the use of urinary biomarkers for follow up after treatment for bladder cancer](#).

Low-risk non-muscle-invasive bladder cancer

- 1.4.3 Offer people with low-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) cystoscopic follow-up 3 months and 12 months after diagnosis.
- 1.4.4 Do not use urinary biomarkers or cytology in addition to cystoscopy for follow-up after treatment for low-risk bladder cancer.
- 1.4.5 Discharge to primary care people who have had low-risk non-muscle-invasive bladder cancer and who have no recurrence of the bladder cancer within 12 months.
- 1.4.6 Do not offer routine urinary cytology or prolonged cystoscopic follow-up after

12 months for people with low-risk non-muscle-invasive bladder cancer.

Intermediate-risk non-muscle-invasive bladder cancer

- 1.4.7 Offer people with intermediate-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) cystoscopic follow-up at 3, 9 and 18 months, and once a year thereafter.
- 1.4.8 Consider discharging people who have had intermediate-risk non-muscle-invasive bladder cancer to primary care after 5 years of disease-free follow-up.

High-risk non-muscle-invasive bladder cancer

- 1.4.9 Offer people with high-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive bladder cancer](#)) cystoscopic follow-up:
- every 3 months for the first 2 years then
 - every 6 months for the next 2 years then
 - once a year thereafter.
- 1.4.10 For people who have had radical cystectomy for high-risk non-muscle-invasive bladder cancer, see [recommendations 1.6.1 and 1.6.2](#).

1.5 Treating muscle-invasive bladder cancer

- 1.5.1 Ensure that a specialist urology multidisciplinary team reviews all cases of muscle-invasive bladder cancer, including adenocarcinoma, squamous cell carcinoma and neuroendocrine carcinoma, and that the review includes histopathology, imaging and discussion of treatment options.

Neoadjuvant chemotherapy for newly diagnosed muscle-invasive urothelial bladder cancer

- 1.5.2 Offer neoadjuvant chemotherapy using a cisplatin combination regimen before radical cystectomy or radical radiotherapy to people with newly diagnosed muscle-invasive urothelial bladder cancer for whom cisplatin-based

chemotherapy is suitable. Ensure that they have an opportunity to discuss the risks and benefits with an oncologist who treats bladder cancer.

Radical therapy for muscle-invasive urothelial bladder cancer

- 1.5.3 Offer a choice of radical cystectomy or radiotherapy with a radiosensitiser to people with muscle-invasive urothelial bladder cancer for whom radical therapy is suitable. Ensure that the choice is based on a full discussion between the person and a urologist who performs radical cystectomy, a clinical oncologist and a clinical nurse specialist. Include in the discussion:
- the prognosis with or without treatment
 - the limited evidence about whether surgery or radiotherapy with a radiosensitiser is the most effective cancer treatment
 - the benefits and risks of surgery and radiotherapy with a radiosensitiser, including the impact on sexual and bowel function and the risk of death as a result of the treatment.

Radical cystectomy

- 1.5.4 Offer people who have chosen radical cystectomy a urinary stoma, or a continent urinary diversion (bladder substitution or a catheterisable reservoir) if there are no strong contraindications to continent urinary diversion such as cognitive impairment, impaired renal function or significant bowel disease.
- 1.5.5 Members of the specialist urology multidisciplinary team (including the bladder cancer specialist urological surgeon, stoma care nurse and clinical nurse specialist) should discuss with the person whether to have a urinary stoma or continent urinary diversion, and provide opportunities for the person to talk with people who have had these procedures.
- 1.5.6 Offer people with bladder cancer and, if they wish, their partners, families or carers, opportunities to have discussions with a stoma care nurse before and after radical cystectomy as needed.

Adjuvant chemotherapy after radical cystectomy for muscle-invasive or lymph-node-positive urothelial bladder cancer

- 1.5.7 Consider adjuvant cisplatin combination chemotherapy after radical

cystectomy for people with a diagnosis of muscle-invasive or lymph-node-positive urothelial bladder cancer for whom neoadjuvant chemotherapy was not suitable (because muscle invasion was not shown on biopsies before cystectomy). Ensure that the person has an opportunity to discuss the risks and benefits with an oncologist who treats bladder cancer.

Radical radiotherapy

- 1.5.8 Use a radiosensitiser (such as mitomycin in combination with fluorouracil [5-FU] or carbogen in combination with nicotinamide) when giving radical radiotherapy (for example, 64 Gy in 32 fractions over 6.5 weeks or 55 Gy in 20 fractions over 4 weeks) for muscle-invasive urothelial bladder cancer.

In February 2015, this was an off-label use of mitomycin in combination with fluorouracil and carbogen in combination with nicotinamide. See [NICE's information on prescribing medicines](#).

Managing side effects of treatment

- 1.5.9 Seek advice from a specialist urology multidisciplinary team if symptoms of bladder toxicity after radiotherapy cannot be controlled with antispasmodics or non-opiate analgesia and other causes have been excluded by cystoscopy.

1.6 Follow-up after treatment for muscle-invasive bladder cancer

- 1.6.1 Offer follow-up after radical cystectomy or radical radiotherapy.
- 1.6.2 After radical cystectomy consider using a follow-up protocol that consists of:
- monitoring of the upper tracts for hydronephrosis, stones and cancer using imaging and glomerular filtration rate (GFR) estimation at least annually and
 - monitoring for local and distant recurrence using CT of the abdomen, pelvis and chest, carried out together with other planned CT imaging if possible, 6, 12 and 24 months after radical cystectomy and
 - monitoring for metabolic acidosis and B12 and folate deficiency at least annually and

- for men with a defunctioned urethra, urethral washing for cytology and/or urethroscopy annually for 5 years to detect urethral recurrence.

1.6.3 After radical radiotherapy consider using a follow-up protocol that includes all of the following:

- rigid cystoscopy 3 months after radiotherapy has been completed, followed by either rigid or flexible cystoscopy:
 - every 3 months for the first 2 years then
 - every 6 months for the next 2 years then
 - every year thereafter, according to clinical judgement and the person's preference
- upper-tract imaging every year for 5 years
- monitoring for local and distant recurrence using CT of the abdomen, pelvis and chest, carried out with other planned CT imaging if possible, 6, 12 and 24 months after radical radiotherapy has finished.

1.6.4 See [recommendation 1.2.1 on the use of urinary biomarkers for follow up after treatment for bladder cancer](#).

1.7 Managing locally advanced or metastatic muscle-invasive bladder cancer

First-line chemotherapy

1.7.1 Discuss the role of first-line chemotherapy with people who have locally advanced or metastatic bladder cancer. Include in your discussion:

- prognosis of their cancer and
- advantages and disadvantages of the treatment options, including best supportive care.

1.7.2 Offer a cisplatin-based chemotherapy regimen (such as cisplatin in combination with gemcitabine, or accelerated [high-dose] methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] in combination with granulocyte-colony stimulating factor [G-CSF]) to people with locally advanced or metastatic

urothelial bladder cancer who are otherwise physically fit (have an [Eastern Cooperative Oncology Group \[ECOG\] performance status](#) of 0 or 1) and have adequate renal function (typically defined as a glomerular filtration rate [GFR] of 60 ml/min/1.73 m² or more).

- 1.7.3 Offer carboplatin in combination with gemcitabine to people with locally advanced or metastatic urothelial bladder cancer with an ECOG performance status of 0 to 2 if a cisplatin-based chemotherapy regimen is unsuitable, for example, because of ECOG performance status, inadequate renal function (typically defined as a GFR of less than 60 ml/min/1.73 m²) or comorbidity. Assess and discuss the risks and benefits with the person.

In February 2015 this was an off-label use of carboplatin in combination with gemcitabine. See [NICE's information on prescribing medicines](#).

- 1.7.4 For people having first-line chemotherapy for locally advanced or metastatic bladder cancer:
- carry out regular clinical and radiological monitoring and
 - actively manage symptoms of disease and treatment-related toxicity and
 - stop first-line chemotherapy if there is excessive toxicity or disease progression.

Second-line chemotherapy

- 1.7.5 Discuss second-line chemotherapy with people who have locally advanced or metastatic bladder cancer. Include in your discussion:
- the prognosis of their cancer
 - advantages and disadvantages of treatment options, including best supportive care.
- 1.7.6 Consider second-line chemotherapy with gemcitabine in combination with cisplatin, or accelerated (high-dose) MVAC in combination with G-CSF for people with incurable locally advanced or metastatic urothelial bladder cancer whose condition has progressed after first-line chemotherapy if:
- their renal function is adequate (typically defined as a GFR of 60 ml/min/1.73 m² or more) and

- they are otherwise physically fit (have an ECOG performance status of 0 or 1).

1.7.7 Consider second-line chemotherapy with carboplatin in combination with paclitaxel or gemcitabine in combination with paclitaxel for people with incurable locally advanced or metastatic urothelial bladder cancer for whom cisplatin-based chemotherapy is not suitable, or who choose not to have it. (Also see the [NICE Pathway on bladder cancer for all our technology appraisal guidance on this topic.](#))

In February 2015, this was an off-licence use of carboplatin in combination with gemcitabine and gemcitabine in combination with paclitaxel. See [NICE's information on prescribing medicines.](#)

1.7.8 For recommendations on vinflunine as second-line chemotherapy for people with incurable locally advanced or metastatic urothelial bladder cancer, see [NICE's technology appraisal guidance on vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract.](#)

1.7.9 For people having second-line chemotherapy for locally advanced or metastatic bladder cancer:

- carry out regular clinical and radiological monitoring and
- actively manage symptoms of disease and treatment-related toxicity and
- stop second-line chemotherapy if there is excessive toxicity or disease progression.

Genomic biomarker-based treatment

The point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain. See [managing locally advanced or metastatic disease in the NICE Pathway on bladder cancer.](#)

Managing symptoms of locally advanced or metastatic bladder cancer

Bladder symptoms

1.7.10 Offer palliative hypofractionated radiotherapy to people with symptoms of haematuria, dysuria, urinary frequency or nocturia caused by advanced bladder

cancer that is unsuitable for potentially curative treatment.

Loin pain and symptoms of renal failure

- 1.7.11 Discuss treatment options with people who have locally advanced or metastatic bladder cancer with ureteric obstruction. Include in your discussion:
- prognosis of their cancer and
 - advantages and disadvantages of the treatment options, including best supportive care.
- 1.7.12 Consider percutaneous nephrostomy or retrograde stenting (if technically feasible) for people with locally advanced or metastatic bladder cancer and ureteric obstruction who need treatment to relieve pain, treat acute kidney injury or improve renal function before further treatment.
- 1.7.13 If facilities for percutaneous nephrostomy or retrograde stenting are not available at the local hospital, or if these procedures are unsuccessful, discuss the options with a specialist urology multidisciplinary team for people with bladder cancer and ureteric obstruction.

Intractable bleeding

- 1.7.14 Evaluate the cause of intractable bleeding with the local urology team.
- 1.7.15 Consider hypofractionated radiotherapy or embolisation for people with intractable bleeding caused by incurable bladder cancer.
- 1.7.16 If a person has intractable bleeding caused by bladder cancer and radiotherapy or embolisation are not suitable treatments, discuss further management with a specialist urology multidisciplinary team.

Pelvic pain

- 1.7.17 Evaluate the cause of pelvic pain with the local urology team.
- 1.7.18 Consider, in addition to best supportive care, 1 or more of the following to treat pelvic pain caused by incurable bladder cancer:

- hypofractionated radiotherapy if the person has not had pelvic radiotherapy
- nerve block
- palliative chemotherapy.

1.8 Specialist palliative care for people with incurable bladder cancer

- 1.8.1 A member of the treating team should offer people with incurable bladder cancer a sensitive explanation that their disease cannot be cured and refer them to the urology multidisciplinary team.
- 1.8.2 Tell the primary care team that the person has been given a diagnosis of incurable bladder cancer within 24 hours of telling the person.
- 1.8.3 A member of the urology multidisciplinary team should discuss the prognosis and management options with people with incurable bladder cancer.
- 1.8.4 Discuss palliative care services with people with incurable bladder cancer and, if needed and they agree, refer them to a specialist palliative care team (for more information, see [recommendation 1.1.4 on holistic needs assessment](#) and [NICE's guidelines on improving supportive and palliative care for adults with cancer and improving outcomes in urological cancers](#)).
- 1.8.5 Offer people with symptomatic incurable bladder cancer access to a urological team with the full range of options for managing symptoms.

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the [full guideline](#).

2.1 Patient satisfaction

What are the causative and contributory factors underlying the persistently very low levels of reported patient satisfaction for bladder cancer?

Why this is important

The urological cancers grouping (which includes bladder cancer but excludes prostate cancer) has consistently appeared near the bottom of the table of patient satisfaction comparisons of all cancer types in national patient experience surveys. Prostate cancer (which is also managed in urological services) is recorded separately and has continued to appear near the top of the tables.

It is uncertain why this is the case, except that there is now an accepted link between the level of clinical nurse specialist allocation, information and support provision and patient satisfaction. The urological cancers grouping has the lowest level of clinical nurse specialist allocation in comparison with all other cancer types or groupings (including prostate cancer). The prolonged pattern of intrusive procedures that dominate investigation, treatment and follow-up regimens for bladder cancer may also contribute to this position. Additionally, there is concern that people with bladder cancer at or near the end of life, who are by that stage often quite frail and elderly, may not always have access to the full range of palliative and urological support and may, at times, be treated in general wards in hospital and experience significant symptoms of pain and bleeding (haematuria).

To explore this research question bladder cancer patients need to be identified separately from the generic group of urological cancer patients in nationally collected data sets.

2.2 BCG or primary cystectomy in high-risk non-muscle-invasive bladder cancer

Is primary radical cystectomy more effective than primary intravesical BCG in high-risk non-muscle-invasive bladder cancer (see the [section on risk classification in non-muscle-invasive](#)

bladder cancer), in terms of quality of life and cancer-specific outcomes?

Why this is important

Options for people with high-risk non-muscle-invasive bladder cancer include cystoscopy surveillance, BCG immunotherapy or radical surgery. To date, these have not been directly compared across the same population to understand their relative benefits.

Bladder-sparing approaches avoid major surgery, but have a greater risk of cancer progression. The potential advantage of bladder-sparing approaches compared with cystectomy in maintaining quality of life may be offset by continuing concern about cancer progression and morbidity from treatment. Primary cystectomy may improve survival; however, it has high short-term risks and life-changing consequences. It will be overtreatment for those people whose cancer would not have progressed.

2.3 Follow-up of high-risk non-muscle-invasive bladder cancer

In people with high-risk non-muscle-invasive bladder cancer, are these follow-up regimens equally effective in terms of identification of progression, cost effectiveness and health-related quality of life?

- Cystoscopic follow-up at 3, 6, 12, 18, 24, 36 and 48 months, and then annually, interspersed with non-invasive urinary tests.
- Cystoscopic follow-up at 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42 and 48 months, and then annually thereafter.

Why this is important

Cystoscopy is currently the standard of care for follow-up of people with high-risk non-muscle-invasive bladder cancer. Regular cystoscopy may be associated with anxiety, procedural discomfort to the person and significant costs to the NHS.

Urine tests based on a variety of technologies (including cytology, fluorescence in-situ hybridization [FISH] and proteomic platforms) can detect high-grade recurrence, raising the possibility that 1 or more of these tests could be used to reduce the frequency of cystoscopy. This could improve acceptability to patients and reduce costs to the NHS without increasing the risk of disease progression.

There is a lack of evidence on the optimal frequency of follow-up and whether the frequency of cystoscopy follow-up can safely be reduced by substitution of urinary tests.

2.4 Biomarkers for treatment selection

In patients with muscle-invasive bladder cancer suitable for radical treatment, does the use of biomarkers enable patients to select more effective treatment, and improve their outcomes, compared with treatment selected without biomarkers?

Why this is important

Response to surgery or radiotherapy is difficult to predict for individuals. There is variation not only in the cure rates for patients with muscle-invasive bladder cancer treated with either surgery or radiotherapy, but also in the side effects experienced during and after treatment. The usefulness of current biomarkers in predicting treatment outcomes for individual patients has not been clearly established. Currently treatment decisions are based on patient-related factors, and patient and clinician preference. Research into biomarkers that can predict the response of the patient's muscle-invasive bladder cancer to either radiotherapy or surgery could help individual patients and clinicians decide which treatment is more suitable and is considered an important step toward individualised treatment.

2.5 Follow-up after radical treatment for organ-confined muscle-invasive bladder cancer

Is symptom-based review as effective as scheduled follow-up for people treated with radical cystectomy or radical radiotherapy for organ-confined, muscle-invasive bladder cancer? Outcomes of interest are overall survival, health-related quality of life, resource use and cost.

Why this is important

Standard care after treatment for organ-confined, muscle-invasive bladder cancer is scheduled follow-up at intervals set out by the treating team. Although this can be reassuring for both the patient and the treating team, it is not known whether scheduled follow-up offers clinical benefit compared with symptom-based review, which is increasingly used for people with other cancers. Moreover, there are significant costs associated with follow-up. The current evidence about follow-up is confined to cystectomy. There is no evidence concerning follow-up after radiotherapy. In addition, the evidence on radiological follow-up uses mainly outdated imaging techniques.

Finding more information and committee details

You can see everything NICE says about this topic in the [NICE Pathway on bladder cancer](#).

NICE guidance on related topics, including guidance in development, see the [NICE webpage on bladder cancer](#).

For full details of the evidence and the guideline committee's discussions, see the [full guideline and evidence review](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources to help you put this guideline into practice](#). For general help and advice on putting our guidelines into practice, see [resources to help you put NICE guidance into practice](#).

Update information

May 2021: We added a link to the NICE Pathway on bladder cancer for information on genomic biomarker-based therapy in solid tumour treatment pathways.

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Accreditation

