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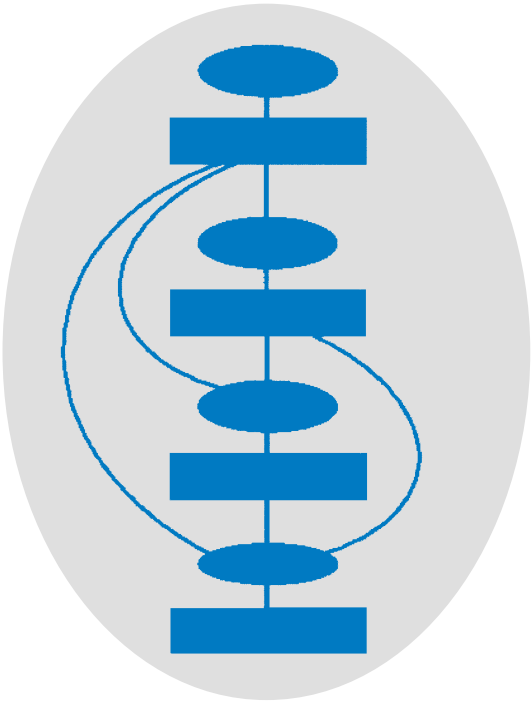
National Institute for Clinical Excellence

Guidance on Cancer Services

Improving Outcomes in Urological Cancers

The Manual



Urological cancer service guidance

Cancer service guidance supports the implementation of *The NHS Cancer Plan* for England,[1] and the NHS Plan for Wales *Improving Health in Wales.*[2] The service guidance programme was initiated in 1995 to follow on from the Calman and Hine Report, *A Policy Framework for Commissioning Cancer Services.*[3] The focus of the cancer service guidance is to guide the commissioning of services and is therefore different from clinical practice guidelines. Health services in England and Wales have organisational arrangements in place for securing improvements in cancer services and those responsible for their operation should take this guidance into account when planning, commissioning and organising services for cancer patients. The recommendations in the guidance concentrate on aspects of services that are likely to have significant impact on health outcomes. Both the anticipated benefits and the resource implications of implementing the recommendations are considered. This guidance can be used to identify gaps in local provision and to check the appropriateness of existing services.

References

1. Department of Health (2001) *The NHS Cancer Plan.* Available from: www.doh.gov.uk/cancer/cancerplan.htm

2. National Assembly for Wales (2001) *Improving Health in Wales: A Plan for the NHS and its Partners.* Available from: www.wales.gov.uk/healthplanonline/health_plan/content/nhsplan-e.pdf

3. *A Policy Framework for Commissioning Cancer Services*: *A Report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales* (1995). Available from: http://www.doh.gov.uk/cancer/pdfs/calman-hine.pdf

This guidance is written in the following context:

This guidance is a part of the Institute's inherited work programme. It was commissioned by the Department of Health before the Institute was formed in April 1999. The developers have worked with the Institute to ensure that the guidance has been subjected to validation and consultation with stakeholders. The recommendations are based on the research evidence that addresses clinical effectiveness and service delivery. While cost impact has been calculated for the main recommendations, formal cost-effectiveness studies have not been performed.

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Copies of this document can be obtained from the NHS Response Line by telephoning 0870 1555455 and quoting reference N0138. Bilingual information for the public has been published, reference N0139, and a CD with all documentation including the research evidence on which the guidance is based is also available.

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Guidance on Cancer Services

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Contents

Foreword

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Chairman, National Cancer Guidance Steering Group

This is the sixth new title in the series of national guidance documents on the organisation and delivery of cancer services, and the first to be published under the auspices of the National Institute for Clinical Excellence. It deals with a relatively frequent group of cancers, one of which (prostate cancer) has become the subject of increasing patient group and political interest. This is seen by some as a prime men's health issue and it has become a focus for increasing awareness among men of the possibility of cancer.

To those members of the National Cancer Guidance Steering Group who have been in this venture from the beginning, the experience of preparing each successive guidance document has revealed something of a pattern in the way cancer site-specific services develop over time. Familiar issues arise with each cancer site, issues on which the Group has already published recommendations in guidance on services for other cancer sites. It seems that new patterns of practice, adopted by services for one cancer, may not be actively considered by those involved in delivering services for different cancers.

The widely accepted features of modern cancer care were set out in the Calman-Hine report, and those principles have been influential in the most recent statement of national policy in England, the NHS *Cancer Plan*, and in the *Cameron Report* in Wales. Most of the recommendations in Calman-Hine were first applied to breast cancer services, and have subsequently been adapted in developing services for other common cancers such as colorectal and lung.

Whilst there are honourable exceptions, urological cancer services in general have lagged behind in adopting these principles, although there are encouraging signs that this has begun to change. For example, properly constituted multidisciplinary clinical teams (MDTs) are less common in urology than in some other areas. In both surgery and non-surgical oncology for urological malignancies, care is often fragmented, with most individuals handling cases outside formal MDTs. This guidance provides the impetus to change this state of affairs.

So what are these predictable common themes? The first can best be described as an 'awakening': a growing recognition, often expressed by patient groups as well as influential professionals in the field

concerned, of the variability and deficiencies in current organisation and delivery of clinical care to patients. Awareness that the delivery of services needs to become more consistent and coherent opens the way to change.

The second is the crucial importance of the diagnostic and referral process. Reliable and thorough diagnosis is the cornerstone of good clinical cancer care. Optimum decisions on management depend on the accurate, reliable, and comprehensive diagnosis and staging of disease. Without all the relevant information, of a quality that can be relied on, those involved in decisions on clinical management are disadvantaged, as are their patients. Important weaknesses have been found in urological cancer diagnostics - as there were in diagnostic services for breast and other common cancers. Site-specific cancer services need the involvement of diagnostic specialists working carefully to modern protocols. Improvements in services for specific cancers require diagnostic specialisation and professional continuity, with the full involvement of these individuals in multidisciplinary working. Urological malignancies are no exception. Putting this emphasis on the importance of the diagnostic contribution is justifiable notwithstanding an acknowledged and serious shortfall in the supply of qualified individuals in the relevant disciplines. Addressing this will inevitably take time, but it remains a critical objective.

The next recurring theme is the way in which decisions on the management of individual patients are best taken. Multidisciplinary teams which involve all the different professions and disciplines required for each group of cancers need to be assembled. Getting these teams to work together effectively, and supporting their activities, is the key to doing this well. The skills of all the members are important to clinical decision-making, which then becomes a collective process.

Another common strand is the importance of defining the natural sequence of events in the organisation and delivery of care. The processes from first referral through to arrangements to manage recurrent and advanced disease have to reflect the needs of the patient at various stages. This is a major driver to shape the way services are organised and delivered. Such ideas are not by any means the sole province of this guidance. There has been huge interest in defining pathways of care and thinking through patient journeys. The Cancer Services Collaborative in England has encouraged fresh thinking on many of the logistic and organisational issues which professionals face in delivering care to their patients.

The final theme that occurs remorselessly is the need to determine whether there are any aspects of service - often, but not exclusively, dealing with rare forms of disease or complex procedures - which would be best provided for larger populations and caseloads than can

be managed by local services. This has proved to be a crucial factor in shaping the service pattern for cancers of intermediate frequency. There are inevitably vested interests amongst the clinical communities concerned, and sometimes tensions between those who favour one model or another. Whilst evidence on these matters is not always profuse, it does exist, and has to be carefully considered for each group of cancers. We have been struck by the consistency between results of studies on different cancers.

The evidence base for managing urological malignancies is less comprehensive and in some important clinical areas, less clear, than for many other cancers. This has made the task of reviewing evidence particularly difficult. It is an appropriate point to gratefully acknowledge the huge contribution made by external reviewers to these guidance documents.

A new and important feature of the implementation process is the recent advent of National Cancer Standards in England and the Minimum Standards for Cancer Services in Wales. Key features of each guidance document will be incorporated in future revisions of these standards, expanding the range of the accompanying peer reviews. Implementation is the prime function of cancer networks, too, supported by the rollout of the Cancer Services Collaborative in England. This Guidance uses the results from some Collaborative projects as evidence; it is the first time this has been available to us.

Taken together, the service context for implementing guidance has advanced very considerably since the early years following publication of Calman-Hine. There is now systematic support for the implementation of the *Cancer Plan* in England and the *Cameron Report* in Wales, of which this guidance is only one element. Together these will help to realise one of the original goals of Calman-Hine, which was (and remains) arguably the single most crucial objective:-

> ***'All patients should have access to a uniformly high quality of care in the community or hospital wherever they may live to ensure the maximum possible cure rates and best quality of life. Care should be provided as close to the patient's home as is compatible with high quality, safe and effective treatment'.***

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Key recommendations

The key recommendations highlight the main organisational issues specific to urological cancers that are central to implementing the guidance. As such, they may involve major changes to current practice.

- All patients with urological cancers should be managed by multidisciplinary urological cancer teams. These teams should function in the context of dedicated specialist services, with working arrangements and protocols agreed throughout each cancer network. Patients should be specifically assured of:
  - Streamlined services, designed to minimise delays;
  - Balanced information about management options for their condition;
  - Improved management for progressive and recurrent disease.
- Members of urological cancer teams should have specialised skills appropriate for their roles at each level of the service. Within each network, multidisciplinary teams should be formed in local hospitals (cancer units); at cancer centres, with the possibility in larger networks of additional specialist teams serving populations of at least one million; and at supra-network level to provide specialist management for some male genital cancers.
- Radical surgery for prostate and bladder cancer should be provided by teams typically serving populations of one million or more and carrying out a cumulative total of at least 50 such operations per annum. Whilst these teams are being established, surgeons carrying out small numbers (five or fewer per annum) of either operation should make arrangements within their network to pass this work on to more specialised colleagues.
- Major improvements are required in information and support services for patients and carers. Nurse specialist members of urological cancer teams will have key roles in these services.
- There are many areas of uncertainty about the optimum form of treatment for patients with urological cancers. High-quality research studies should be supported, with encouragement of greater rates of participation in clinical trials.

Background

Incidence and mortality

The group of diseases with which this Manual deals – cancers of the prostate, testis, penis, kidney and bladder – account for 16.5% of all new cases of cancer (excluding non-melanoma skin cancer) and 11.7% of cancer deaths.[1,2] Prostate cancer is the second most frequently diagnosed cancer among men of all ages; testicular cancer, although relatively infrequent, is nevertheless the most common cancer in men under 45 years of age. Cancer of the penis, by contrast, is rare. Cancers of the kidney and bladder may develop in people of either sex but are roughly twice as common among men (Table 1). Numbers of deaths and mortality rates are shown in Table 2.

Table 1. Urological cancers and cancers of the male genital system: registrations and incidence, 1998, England and Wales

Cancer site	ICD10 code	England			Wales		
		Registrations	Incidence: rate per 100,000		Registrations	Incidence: rate per 100,000	
		Total	Men	Women	Total	Men	Women
Prostate	C61	19,335	79.3	-	1,264	87.9	-
Testis	C62	1,541	6.3	-	89	6.2	-
Penis	C60	315	1.3	-	23	1.6	-
Bladder	C67	11,528	30.9	11.9	847	42.1	16.1
Kidney	C64-66	4,653	11.8	6.8	327	12.9	9.5

Source: Data for England downloaded from www.statistics.gov.uk, May 2002; data for Wales provided on request by the Welsh Cancer Intelligence & Surveillance Unit, Cardiff, May 2002.

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1 Office for National Statistics. *Mortality statistics - cause, England and Wales, 1999.* London: Stationery Office, 2000.

2 Office for National Statistics. *Cancer statistics - registrations, England, 1995-1997.* London: Stationery Office, 2001.

Table 2. Urological cancers and cancers of the male genital system: number of deaths and mortality rates, 2000, England and Wales

Cancer site	ICD10 code	England			Wales		
		Deaths	Mortality: crude rate per 100,000		Deaths	Mortality: crude rate per 100,000	
		Total	Men	Women	Total	Men	Women
Prostate	C61	7,785	31.5	-	492	34.0	-
Testis	C62	63	0.3	-	6	0.4	-
Penis	C60	83	0.3	-	12	0.8	-
Bladder	C67	4,173	11.0	5.7	152	10.5	5.6
Kidney	C64-66	2,548	6.3	3.9	92	6.4	4.8

Source: Data provided on request by the Office of National Statistics, London, and the Welsh Cancer Intelligence & Surveillance Unit, Cardiff, May 2002.

Considered as a group, these cancers are slightly more common in the population as a whole than breast cancer (37,000 new cases of urological and male genital cancers, 33,350 of breast cancer in 1997; both sexes, England and Wales). But whilst it may be useful for service planning to lump together all the cancers considered in this Manual, the patterns of care required for each cancer site vary widely because these cancers are very different in nature and characteristics.

Prostate cancer is particularly common among elderly men; two thirds of those who die from prostate cancer are over the age of 75.[3] Autopsy studies reveal that the majority of men over 80 years old have areas of malignant tissue in their prostate glands; most die *with* it, not *of* it.[4] Prostate cancer may be identified as a result of investigations or intervention for symptoms related to benign prostate disease, also a very common condition in elderly men. However, when prostate cancer develops in younger men, it seems to have a more aggressive nature. Relatively few of the 40-49 age-group are affected, but these men have the highest mortality rate.[3]

[3] Quinn M, Babb P, Brock A, *et al. Cancer trends in England and Wales 1950-1999.* London: Stationery Office, 2001.

[4] Selley S, Donovan J, Faulkner A, *et al.* Diagnosis, management and screening of early localised prostate cancer. *Health Technol Assess* 1997;**1**.

Testicular cancer is very different. It is predominantly found in young men, with a modal age at diagnosis of about 30.[5] It may be associated with developmental abnormalities of the urogenital system.

Cancers of the kidney, bladder and associated urinary organs are neither especially common nor rare. They are most likely to occur in men aged between 60 and 80 years. Penis cancer tends to affect the same age-group.[2]

In a single year, the average GP, with a list of 2,000 patients, is likely to see one or two new patients with one of these cancers per year. A notional average district general hospital (DGH), serving a population of 200,000, deals with roughly 70 men with prostate cancer, 6 with testicular cancer, perhaps 20 people with kidney and 50 with bladder cancer – a total of around 150 new patients per year with urological cancers. Figures for prostate cancer incidence show particularly wide geographical variations because more cases are identified when patients and clinicians search more aggressively for it.

Five-year survival rates are shown in Table 3. Although there has been little overall change in these rates between patient groups diagnosed in 1986-90 and 1991-93, the significant improvement for men with testicular cancer – a rise in five-year survival rates from 91.2% to 94.5% – is notable in view of the small amount of room for such improvement. The 7% improvement in prostate cancer survival rates is, however, likely to be due more to lead time and length time biases associated with increasing use of prostate specific antigen (PSA) testing than to improvements in treatment.[2]

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[5] United Kingdom Testicular Cancer Study Group. Aetiology of testicular cancer: association with congenital abnormalities, age at puberty, infertility and exercise. *BMJ* 1994;**308**:1393-9.

Table 3. Urological cancers and cancers of the male genital system: five-year relative survival rates (age-standardised), England and Wales*[2]

Cancer site	ICD10 code	Five-year survival rates by year of diagnosis					
		1986-90		1991-3		1993-5[a]	
		Men	Women	Men	Women	Men	Women
Prostate	C61	42.2	-	48.9	-	54.9	-
Testis	C62	91.2	-	94.5	-	N/A	-
Penis	C60	69.0	-	63.1[b]	-	N/A	-
Bladder	C67	65.2	57.9	65.7	57.6	66.2	57.9
Kidney	C64-66	39.6	35.6	40.5	37.3	N/A	N/A

* All stages of disease are combined in tables 1-3; thus bladder cancer, for example, includes both superficial and invasive tumours.

[a] England only; data downloaded from ONS online, May 2002.

[b] Northern, Yorkshire and Humberside only; data from the Northern and Yorkshire Cancer Registry and Information Service.

For testicular and bladder cancers, age-standardised survival rates in England are similar to the European average, but for cancers of the kidney and prostate, survival rates in England are significantly lower than in many European countries (Table 4).[6] This evidence is not, however, sufficient to determine the cause or importance of these differences. It is possible that they are associated with earlier diagnosis in some parts of Europe, where greater use of imaging will tend to increase the rate of detection of small (incidental) kidney tumours and widespread PSA testing will reveal more early prostate cancers. The apparent survival differences could therefore be due, at least in part, to length and lead-time biases.

[6] Berrino F, Sant M, Verdecchia A, *et al. Survival of cancer patients in Europe: the EUROCARE study.* Lyon: International Agency for Research on Cancer, 1995.

Table 4. Urological cancers and cancers of the male genital system: five-year relative survival rates (age-standardised), England and Europe, 1985-9.[6]

Cancer site	Five-year survival rates, % England		Five-year survival rates, % (95% CI) European average	
	Men	Women	Men	Women
Prostate	44.3	-	55.7 (54.3-57.1)	-
Testis	90.0	-	89.5 (87.4-91.7)	-
Penis	70.2	-	73.7 (67.6-80.4)	-
Bladder	65.6	59.4	65.2 (63.8-66.6)	59.7 (57.5-61.9)
Kidney	39.4	36.9	47.7 (45.6-49.9)	49.8 (47.1-51.6)

Symptoms and presentation

Most patients with urological cancers are referred to urologists by their GPs. Some present with symptoms such as bone pain, which may not be immediately recognised as due to metastatic urological cancer, and some are referred by geriatricians.

The main presenting symptoms of primary urological tumours fall into three groups: lower urinary tract symptoms, haematuria, and suspicious lumps. Lower urinary tract symptoms are relatively common. In older men, they are often due to benign prostatic hyperplasia, which is at least four times as common as prostate cancer and may co-exist with it.[4,7] Cancer is very unlikely to be the cause of such symptoms in younger men or women, but persistent problems that fail to respond to antibiotics are occasionally due to bladder cancer.

Haematuria, or blood in the urine, is the most common symptom of both bladder and kidney cancer. Around one patient in five who develops visible haematuria is likely to have urological – usually bladder – cancer.[8,9] Whilst population studies suggest that

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7 Chamberlain J, Melia J, Moss S, *et al*. Report prepared for the Health Technology Assessment panel of the NHS Executive on the diagnosis, management, treatment and costs of prostate cancer in England and Wales. *BJU Int* 1997;**79 (Suppl 3)**:1-32.

8 Buntinx F, Wauters H. The diagnostic value of macroscopic haematuria in diagnosing urological cancers: a meta-analysis. *Fam Pract* 1997;**14**:63-8.

9 Lynch TH, Waymont B, Dunn JA, *et al*. Rapid diagnostic service for patients with haematuria. *Br J Urol* 1994;**73**:147-51.

microscopic haematuria, on its own, rarely signifies malignant disease,[10,11] studies carried out in hospital haematuria clinics tend to find higher cancer rates among patients with microscopic haematuria;[12] this difference could reflect other, unmeasured, criteria which GPs consider when they make the decision to refer.

Whilst the most common presenting symptom of kidney cancer is haematuria, this disease is often asymptomatic until it reaches a late stage. It is diagnosed increasingly frequently when imaging, carried out for some other reason, reveals a mass in the kidney. A recent (unpublished) audit in north west England reported that in 37% of patients with kidney cancer, the tumour was an incidental finding.[13]

Most patients with testicular cancers present with a lump in the scrotum, usually detected initially by the man himself or by his partner.

Epidemiology, trends and treatment

Prostate cancer

Registration and mortality rates for prostate cancer have been increasing (Figure 1), although how great the true increase in incidence may be is not clear because early, asymptomatic disease is more likely to be diagnosed than in previous decades. The main reason for this is the use of PSA testing, which became commonplace during the last decade. Despite this, about a quarter of patients in the UK have advanced disease at the time of diagnosis (Table 5); in these cases, bone pain caused by metastatic cancer may prompt the initial consultation.

Both diagnosis and mortality rates began to fall again after 1995 (see Figure 1). Current trends in diagnosis rates are unclear, but even if these do not rise, the ageing of the population means that the number of men with prostate cancer can be expected to increase to around 22,000 by 2011 (figures extrapolated from Chamberlain *et al*, 1997[7]). The scale of the problem and increasing public concern has led to the initiation of a range of measures such as the NHS Prostate

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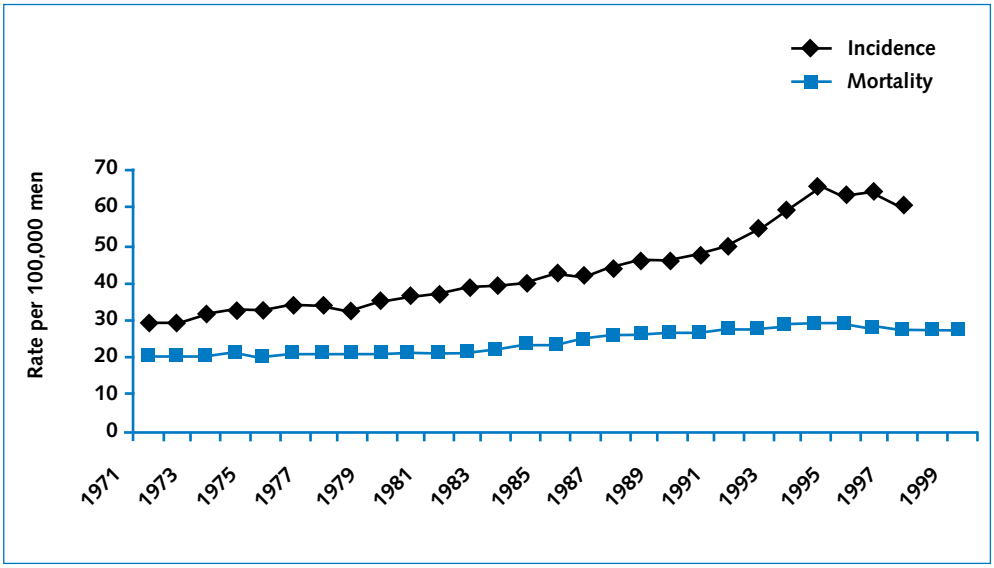
[10] Froom P, Froom J, Ribak J. Asymptomatic microscopic hematuria - is investigation necessary. *J Clin Epidemiol* 1997;**50**:1197-200.

[11] Froom P, Ribak J, Benbassat J. Significance of microhaematuria in young adults. *BMJ* 1984;**288**:20-2.

[12] Khadra M, Pickard M, Charlton P. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. *J Urol* 2000;**163**:524-7.

[13] Clarke N. Personal communication. 2001.

Figure 1. Prostate cancer: incidence and mortality rates (age-standardised), England and Wales, 1971-1999



Source: Data provided on request by the Office of National Statistics, London

Table 5. Prostate cancer: stage at diagnosis

Clinical stage[a]	Classification	Description	Proportion of new cases
Organ-confined (Stage I or II)	T1 or T2, N0 M0	Cancer confined to prostate	52%
Extra-capsular (Stage III)	T3 N0 M0	Tumour extends through prostate capsule	26%
Locally advanced (Stage IV)	T4 N0 M0 Any T, N≥1	Tumour in lymph nodes or tissues close to prostate	22%
Metastatic (Stage IV)	Any T, M≥1	Metastatic disease, usually in bones	

Source: Figures derived from British Association of Urological Surgeons (BAUS) data for 1999. This database includes about 60% of cases and may not accurately reflect the population as a whole.

[a] Clinical staging is used in decision-making about management but this is not always clearly related to pathological staging.

Cancer Programme and a Prostate Cancer Risk Management Programme. One recent change to policy was the decision that PSA tests should be available to men who request them, but that they should first be provided with clear information about the test and the uncertainty about the balance of benefits and risks of screening for prostate cancer. This information is now available on the National electronic Library for Prostate Cancer.[14]

Neither the causes of prostate cancer nor the reasons for the increase in mortality rate over the past thirty years are known, although some risk factors have been identified. Hormones are important; meta-analysis of cohort and case-control studies show that men with serum testosterone levels in the highest quartile are 2.3 (95% CI: 1.3 to 4.2) times as likely to develop prostate cancer as those in the lowest quartile. High levels of insulin-like growth factor (IGF-1) are associated with a similar increase in risk.[15]

Genetic factors are important in about 9% of cases, particularly when the disease develops at a young age. The risk is doubled when a man has one close relative with this cancer and it increases with the number of relatives affected.[16] Increased risk has also been linked with a family history of breast cancer.

A suggested association between vasectomy and prostate cancer was not confirmed by a thorough systematic review and meta-analysis of research evidence.[17]

There are wide international variations in the incidence of clinically-evident prostate cancer. The highest rates – over 100 per 100,000 – are found among African-Americans, and the lowest among Asians, with fewer than 10 men per 100,000 affected. European men fall into an intermediate position.[18]

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[14] See http://www.nelh.nhs.uk/psatesting

[15] Shaneyfelt T, Husein R, Bubley G, *et al*. Hormonal predictors of prostate cancer: A meta-analysis. *J Clin Oncol* 2000;**18**:847-53.

[16] McLellan DL, Norman RW. Hereditary aspects of prostate cancer. *Can Med Assoc J* 1995;**153**:895 900.

[17] Bernal-Delgado E, Latour-Perez J, Pradas-Arnal F, *et al*. The association between vasectomy and prostate cancer: a systematic review of the literature. *Fertil Steril* 1998;**70**:191-200.

[18] Dijkman GA, Debruyne FM. Epidemiology of prostate cancer. *Eur Urol* 1996;**30**:281-95.

One reason for this variation between ethnic groups is likely to be differences in diet, and a variety of relationships have been found between prostate cancer risk and specific types of food. Decreased risk is associated with a high intake of vegetables rich in carotenoids, particularly tomatoes.[18,19,20,21] Fish also seems to be protective.[22]

Increased risk is associated with diets high in animal fat;[19] this might be linked with bio-concentration in animal fat of agricultural chemicals which affect hormone levels.[23] Evidence that high consumption of dairy products can double the risk of prostate cancer (especially advanced disease), even after controlling for fat intake, has led to the development of a yet another hypothesis: that high calcium intake may promote these tumours.[24] The true reasons for the higher risk associated with dietary patterns of northern Europe, North America and Australasia remain unknown.

Prostate cancer may be detected by PSA testing, digital rectal examination (DRE), and trans-rectal ultrasound (TRUS) guided biopsy. Tumour may also be found by pathological examination of tissue samples after trans-urethral resection of the prostrate (TURP) carried out to relieve urinary obstruction.

The disease usually progresses slowly, but prognosis depends heavily on the grade of the tumour. This is assessed using the Gleason scoring system. Gleason scores range from 2 to 10; more aggressive cancers, which spread faster beyond the prostate, have higher scores. Audit data from north west England (unpublished) suggests that two-thirds of new patients have moderately differentiated tumours, with Gleason scores of 5 to 7; the remainder are roughly equally divided between the lower and higher ranges of the scale.[13] The Gleason score is used in combination with PSA level and information on local tumour spread gained from DRE and TRUS to assess prognosis.

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[19] World Cancer Research Fund. *Food, nutrition and the prevention of cancer: a global perspective*. Washington DC: American Institute for Cancer Research, 1997.

[20] Cohen J, Kristal A, Stanford J. Fruit and vegetable intakes and prostate cancer risk. *J Natl Cancer Inst* 2000;**92**:61-8.

[21] Giovannucci E. Tomatoes, tomato-based products, lycopene, and cancer: Review of the epidemiologic literature. *J Natl Cancer Inst* 1999;**91**:317-31.

[22] Terry P, Lichtenstein P, Feychting M, *et al*. Fatty fish consumption and risk of prostate cancer. *Lancet* 2001;**357**:1764-6.

[23] Kellerbyrne JE, Khuder SA, Schaub EA. Meta-analyses of prostate cancer and farming. *Am J Ind Med* 1997;**31**:580-6.

[24] Chan J, Giovannucci E, Andersson S, *et al*. Dairy products, calcium, phosphorus, vitamin D, and risk of prostate cancer. *Cancer Causes Control* 1998;**9**:559-66.

Data from a large US study suggest that 10-year disease-specific survival rates are over 90% among men with early, low grade tumours, and over 75% among those with intermediate grade tumours, whatever form of treatment is used.[25] Death-rates are, as would be expected, higher among patients with higher grade tumours.

Approaches to treatment range from active monitoring and conservative treatment of symptoms (also known as "watchful waiting") to radical surgery (prostatectomy), radical radiotherapy (external beam or implantation of radioactive seeds – brachytherapy) and hormone treatment. Radical treatment is associated with significant complications, particularly impotence and incontinence; and whilst it can control local symptoms, there is no clear evidence showing whether it improves survival. Hormone treatment reduces the rate of progression of the cancer and may be used in combination with other forms of treatment or as the primary intervention; however, it also causes loss of libido and impotence. Active monitoring is particularly appropriate for men whose tumours are not expected to cause problems in their lifetime, either because their life-expectancy is relatively short or because the cancer is small and growing only slowly.[4]

The main problems in advanced prostate cancer are lower urinary tract symptoms and pain due to metastatic disease, predominantly in bones. Palliative interventions include hormone treatment, radiotherapy and analgesia.

Testicular cancer

There has been a continuous rise in the incidence of testicular cancer over the past few decades. A large case-control study in England and Wales has elucidated some aspects of the aetiology of this disease; it revealed significant associations with congenital abnormalities, particularly undescended testes, early age at puberty, and sedentary lifestyle.[5] The incidence of undescended testes – linked with a four-fold increase in risk (odds ratio 3.82, 95% CI: 2.24 to 6.52) – has also been increasing. Family members of men with testicular cancer are at increased risk; the probability that a brother of an affected man will develop the disease by the age of 50 is around 2% - 10 times the general population risk.[26] The majority of cases are identified at an early stage, however, (Table 6) and this form of cancer can usually be cured even when it has spread beyond the testis.

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[25] Lu-Yao G, Yao S. Population based study of long term survival in patients with clinically localised prostate cancer. *Lancet* 1997;**349**:906-10.

[26] Forman D, Oliver RT, Brett AR, *et al*. Familial testicular cancer: a report of the UK family register, estimation of risk and an HLA class 1 sib-pair analysis. *Br J Cancer* 1992;**65**:255-62.

There is a widespread belief among health professionals that young men should be educated to examine their testes for lumps in order that any cancer might be treated as quickly as possible. But young men are notoriously disinterested in health. Few examine themselves even after specific teaching, and there is no evidence that educational interventions intended to encourage them to do so are effective.[27]

There are two main types of testicular tumour, seminoma and non-seminoma. Surgery is used to treat both types and may be sufficient to control the disease, but patients with seminoma may be treated with post-operative radiotherapy, whilst chemotherapy is more appropriate for patients with non-seminomas. Success rates are high – fewer than 10% of patients die from testicular cancer – but the problem may recur: up to 5% of men develop cancer in the remaining testis within 25 years of the initial diagnosis.[28]

Table 6. Testicular cancer: stage at diagnosis (1980-94)

Clinical stage (Royal Marsden Stage)	Proportion of new cases
Early (stage I)	55%
Lymph node metastases (stage II – III)	28%
Distant metastases (stage IV)	17%

Source: Figures derived from data on 1,600 patients from The Royal Marsden Hospital Testicular Tumour Unit, 1980-1994.

Penile cancer

Penile cancer is rare in developed countries, particularly in men who were circumcised as babies, and there have been few reliable studies of risk factors or potential causes. However, there is accumulating evidence suggesting that infection with human papillomavirus (HPV or genital warts) may be involved in many cases.[29] A North American case-control study found that the risk for men with a history of such infection was six times that in age-matched controls, and that 49% of tumours contained HPV genetic material.[30] Other factors which increased risk three-fold or more were smoking; lack of, or late, circumcision; and a history of penile rash or tear.

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[27] Rosella JD. Testicular cancer health education: an integrative review. *J Adv Nurs* 1994;**20**:666-71.

[28] Colls BM, Harvey VJ, Skelton L, *et al*. Bilateral germ cell testicular tumors in New Zealand: experience in Auckland and Christchurch 1978-1994. *J Clin Oncol* 1996;**14**:2061-5.

[29] Holly EP, Palefsky JM. Factors related to risk of penile cancer. *J Natl Cancer Inst* 1993;**85**:2-3.

[30] Maden C, Sherman KJ, Beckmann AM, *et al*. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. *J Natl Cancer Inst* 1993;**85**:19-24.

These cancers tend to be fairly obvious and can be diagnosed before the tumour has progressed to an advanced stage, so survival rates are fairly high (around 65-70% at five years). Usually, there is a painless ulcer or growth, most often on the glans or foreskin, but some men develop a rash, bumps or flat growths on the penis and there may be foul-smelling discharge under the foreskin. Diagnosis is by biopsy. The most common treatment is surgery but radiotherapy may be an option. Topical chemotherapy or laser treatment can be used for superficial tumours (carcinoma in situ). Radiotherapy or systemic chemotherapy can be used for palliation in metastatic disease.

Bladder cancer

The most common causes of bladder cancer are carcinogenic chemicals – particularly aromatic amines – in urine. An important source of such carcinogens is cigarette smoke, and there is a significant dose-response relationship between the lifetime number of cigarettes smoked and the risk of bladder cancer. Meta-analysis of data from 43 studies reveals that, compared with non-smokers, current smokers face three times the risk of developing urinary tract cancers (odds ratio 3.33; 95% CI: 2.63 to 4.21), whilst for ex-smokers, the risk is doubled (odds ratio 1.98; 95% CI: 1.72 to 2.29).[31] Current cigarette smokers are two to five times more likely to develop bladder cancer than non-smokers, the level of risk increasing among heavier smokers; but quitting leads to a 30-60% fall in risk within four years.[32,33] Since rates of smoking have been falling faster among men than women, it is possible that the difference between the sexes in bladder cancer rates could decrease, as with lung cancer.

Up to 20% of bladder cancers may be caused by exposure to chemicals in the workplace.[34] These can cause bladder cancer five to 50 (typically, 10-15) years later. The highest risk is again associated with aromatic amines, which used to be commonplace in dyes, paints and plastics and are currently found in diesel exhaust fumes and other industrial by-products.

Occupations associated with increased risk include work in textile, dyestuffs, chemical or plastics industries; tyre and rubber manufacture; truck and taxi driving; painting and printing; metalwork; work in the cable industry; leather work and hairdressing.[32,34]

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[31] Zeegers M, Tan F, Dorant E, *et al*. The impact of characteristics of cigarette smoking on urinary tract cancer risk: a meta-analysis of epidemiologic studies. *Cancer* 2000;**89**:630-9.

[32] Silverman DT, Hartge P, Morrison AS, *et al*. Epidemiology of bladder cancer. *Hematol Oncol Clin North Am* 1992;**6**:1-30.

[33] Hartge P, Silverman D, Hoover R, *et al*. Changing cigarette habits and bladder cancer risk: a case-control study. *J Natl Cancer Inst* 1987;**78**:1119-25.

[34] Vineis P, Simonato L. Proportion of lung and bladder cancers in males resulting from occupation: a systematic approach. *Arch Environ Health* 1991;**46**:6-15.

Bladder cancer in places such as Egypt is often associated with infection with the water-borne parasite *Schistosoma* (bilharzia). Other causes include previous treatment for cancer – in particular, radiotherapy to the pelvis and some forms of chemotherapy. Long-term use of chlorinated drinking water may increase the risk up to two-fold.[32]

95% of patients present with haematuria and cancer can be detected using a cystoscope to view the inside of the bladder. The staging system for bladder cancer is summarised in Table 7.

In about three quarters of new cases, the cancers are superficial and can be removed by surgery carried out through the urethra (trans-urethral resection, or TUR). Irrigation of the bladder with immunotherapeutic or chemotherapeutic agents may be used to reduce the probability of recurrence of superficial cancers. Surgery, radiotherapy and, increasingly, chemotherapy, are used to treat invasive tumours. Metastatic disease may be widespread, affecting lymph nodes, liver, lungs and bones.

Table 7. Bladder cancer: stage at diagnosis

Clinical stage	Classification	Description	Proportion of new cases
Lower-risk superficial cancer	PTa G1 or G2	Non-invasive tumours	45%
	pT1 G1 pT1 G2	Low-grade invasive tumours, no muscle invasion; G2 tumours are more likely to progress than G1	
High-risk superficial cancer	PTa G3 or pT1 G3	High-grade tumours, no muscle invasion; likely to recur and progress	23%
Muscle invasive	pT2	Tumour in muscular wall of bladder	18%
Locally advanced	pT3	Tumour in perivesical fat	9%
	pT4	Tumour in pelvic organs	5%
Metastatic	M	Tumour in distant tissues such as bones	

Source: Figures derived from British Association of Urological Surgeons (BAUS) data for 1999.[35] This database may not accurately reflect the population as a whole.

[35] British Association of Urological Surgeons: Section of Oncology. *Analyses of minimum data set for Urological cancers, January 1st to December 31st, 1999.* British Association of Urological Surgeons, 2000. Available from: http://www.baus.org.uk

Kidney cancer

Kidney cancer is less common than bladder or prostate cancer (Table 1) although both incidence and mortality rates are rising steadily in developed countries. The most common form is renal cell cancer, which accounts for over 80% of cases in England and Wales. The other main form of kidney cancer (transitional cell carcinoma) affects the renal pelvis; similar tumours can also develop in the ureters. Where this Manual refers to kidney cancer without further specification, it should be assumed to mean renal cell cancer.

Over two decades from the mid-1970s to the mid-1990s, the incidence of renal cell cancer rose by about 3% per annum in the US[36] and 2.5% per annum in northern England.[37] The English data show an 86% age-standardised increase between 1978 and 1997. Whilst part of this rise is likely to be due to increased detection of early, pre-symptomatic tumours by imaging, this does not account for much of the change in incidence.

A quarter of kidney cancers are believed to be directly attributable to smoking; smokers are more than twice as likely to develop renal cell cancer and four times as likely to develop cancer of the renal pelvis as non-smokers.[38] Renal cell cancer is more common in obese people, and is independently associated with hypertension.[39] In Minnesota, these three risk factors together account for half of all cases.[40] Whilst there are other known risk factors, such as exposure to cadmium and the once-popular analgesic phenacetin,[38,41] their impact on kidney cancer incidence in the population as a whole is much less than that of obesity, hypertension and smoking.

Some kidney cancers are due to genetic influences. Two rare conditions associated with specific mutations are von Hippel-Lindau syndrome, which increases the risk of kidney and other cancers, and Wilms' Tumour, which affects children. In addition, a family history of renal cell cancer is associated with increased risk.

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[36] Chow WH, Devesa SS, Warren JL, *et al*. Rising incidence of renal cell cancer in the United States. *JAMA* 1999;**281**:1628-31.

[37] Tate R, *et al*. Increased Incidence of Renal Parenchymal Carcinoma in the Northern and Yorkshire region of England, 1978-1997. (submitted for publication).

[38] McCredie M, Stewart JH. Risk factors for kidney cancer in New South Wales. *Br J Ind Me* 1993;**50**:349-54.

[39] McLaughlin JK, Mandel JS, Blot WJ, *et al*. A population-based case-control study of renal cell carcinoma. *J Natl Cancer Inst* 1984;**72**:275-84.

[40] Benichou J, Chow W, McLaughlin J, *et al*. Population attributable risk of renal cell cancer in Minnesota. *Am J Epidemiol* 1998;**148**:424-30.

[41] Sali D, Boffetta P. Kidney cancer and occupational exposure to asbestos: a meta-analysis of occupational cohort studies. *Cancer Causes Control* 2000;**11**:37-47.

Early kidney cancer produces no symptoms and is most likely to be discovered incidentally by ultrasound or computed tomography (CT) imaging carried out for some other reason. More advanced tumours can cause haematuria, back pain, and an abdominal mass. Renal cell cancers may also cause fever.

Treatment is primarily surgical. These cancers tend not to respond to chemotherapy although immunotherapy is sometimes effective. Metastatic spread may involve lymph nodes, bones, liver, lungs, brain and other organs.

Prevention

The evidence on risk factors for this group of cancers suggests that there is substantial scope for prevention. Population-wide initiatives aimed at reducing smoking and improving diet are highlighted as government priorities. These could lead to substantial reductions in the number of people who develop urological cancers.

Half the cases of urinary tract (bladder or kidney) cancer in men and a third of cases in women are likely to be due to smoking.[31] Effective interventions for reducing smoking are described in the document on lung cancer in this series (*Improving Outcomes in Lung Cancer: The Manual)*. It is unlikely, however, that prostate cancer rates would be affected significantly by action against smoking.[42] Dietary improvements – specifically, increased consumption of vegetables and fish, and decreased consumption of dairy produce and meat – might reduce the prevalence of symptomatic prostate cancer.[19,43] Increased fruit and vegetable consumption is also likely to reduce the risk of other urological cancers.[19,44] Finally, interventions to reduce obesity and hypertension could reduce the prevalence of kidney cancer.[40]

There is no reliable evidence showing that population screening reduces mortality rates from any form of urological cancer. Systematic reviews have concluded that screening for prostate cancer using PSA testing cannot be justified on the basis of current evidence.[4,7]

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[42] Lumey LH. Prostate cancer and smoking - a review of case-control and cohort studies. *Prostate* 1996;**29**:249-60.

[43] Working Group on Diet and Cancer, Committee on Medical Aspects of Food and Nutrition Policy. *Nutritional aspects of the development of cancer*. London: Department of Health, 1998.

[44] La Vecchia C, Negri E. Nutrition and bladder cancer. *Cancer Causes Control* 1996;**7**:95-100.

Current services in the NHS

One of the problems that has been highlighted in urological cancer services is the delay between referral and diagnosis. Long delays are relatively common, particularly for patients with cancers of the prostate, bladder, renal pelvis and ureter. 33% of patients referred by GPs to urologists have to wait for more than 12 weeks between referral and diagnosis; 12% wait more than 24 weeks. Table 8 shows the length of delay for 15,543 patients after referral to urologists.[35] These figures suggest that there are major problems with urological diagnostic services.

Table 8. Time between referral to urologist and diagnosis (excluding patients diagnosed before referral)

Organ	Mean (days)	Median (days)
Prostate	115	60
Bladder	83	54
Kidney	67	38
Testis	27	13
Kidney pelvis/ ureter	117	64
Penis	52	33

Structure and quality of current services

Patients with the more common urological cancers are managed by urologists working in local district general hospitals, sometimes in collaboration with oncologists. Co-ordinated multidisciplinary team structures are not common in urology.

There is little information on the quality of current services but there is evidence that delays in diagnosis and treatment are greater for patients with prostate and bladder cancers than for those with other common cancers. Both time to first out-patient appointment and time to first definitive treatment are, in general, substantially longer for prostate and bladder cancer than for breast, colorectal, lung, gynaecological, or upper gastro-intestinal cancers. A study of waiting times for all patients newly diagnosed with cancer in 1997 found that men with prostate cancer endured the longest delays - 53 days (median) to first definitive treatment for cases referred as urgent, 111 days for non-urgent cases.[45]

[45] Spurgeon P, Barwell F, Kerr D. Waiting times for cancer patients in England after general practitioners' referrals: retrospective national survey. *BMJ* 2000;**320**:838-9.

The fragmentation of services for patients with urological cancers is reflected in the low numbers of radical operations for prostate and bladder cancers performed each year in most NHS Trusts (Table 9). (See also, the evidence section of Topic 1, *The urological cancer network and multidisciplinary teams.*)

Table 9. Radical surgery for prostate and bladder cancer in NHS hospitals: activity by region, 1999-2000

Region	Population (millions)	Number of radical prostate-ctomies + cystectomies	Number of Trusts	Number of Trusts doing 50+	Number of Trusts doing <6
Northern & Yorkshire	6.4	322	17	2	4
Trent	5.1	195	14	0	3
West Midlands	5.3	243	21	0	9
North West	6.6	271	24	0	8
Eastern	5.4	284	17	0	1
London	7.2	384	25	0	6
South East	8.6	392	24	1	4
South West	4.9	267	17	0	5
English Subtotals	**49.5**	**2358**	**159**	**3**	**40**
Wales	2.9	135	10	0	4
Overall Totals	**52.4**	**2493**	**169**	**3**	**44**

Source: Hospital episode statistics (HES) data for England; Patient episode data for Wales (PEDW).

Provisional NHS service configuration

Most patients with urological cancer will be treated locally, in district general hospitals which have both urology services and cancer units. These hospitals will form part of wider networks designed to provide co-ordinated services at many levels. Local hospitals will need to collaborate to generate the workload necessary to support increased specialisation among urologists, a minority of whom will develop expertise in the management of urological cancers.

Each network will include the following key parts:

- GPs/primary care teams. The management of patients with prostate cancer, in particular, requires considerable primary care involvement since many of the men affected live with slowly advancing cancer for years.

- Dedicated clinics in local district general hospitals which have both urology services and cancer units; these will be responsible for rapid diagnosis and initial assessment.

- Treatment and palliative care services at local hospitals, where patients will be managed by multidisciplinary teams.

- Support and information services for patients and carers. These will be linked with social services, particularly services for the elderly.

- Specialised palliative care services and facilities such as hospices, which may be provided in partnership with the voluntary sector.

- Specialist multidisciplinary teams, most of which will be based in cancer centres, providing more technically challenging forms of treatment for selected patients. Most networks will have one such team; larger networks may have two.

- Specialist services at supra-network level which will manage patients with testicular, penile, and complicated kidney cancers.

Representatives from the whole network will work with members of specialist urological cancer teams to develop treatment and referral protocols and ensure that the service works in a co-ordinated way. Non-surgical oncologists will work across networks, providing services at the local level.

The urological cancer network and multidisciplinary teams

A. Recommendations

The network

Each cancer network provides and co-ordinates a wide range of services for patients with urological cancers within a defined geographical area. Different degrees of specialisation are required to deal with the various types of cancer, and multidisciplinary teams (MDTs) should be established in cancer units, cancer centres, and at supra-network level; these will be distinct teams, although there is likely to be overlap between their members. All teams should participate fully in the urological cancer network, and all members of teams should be involved in discussions on local policy decisions and in auditing adherence to them.

All patients with urological cancer – both new and existing – should be managed by appropriate MDTs. Documented clinical policies for referral and treatment should be agreed between cancer leads in primary care and lead clinicians representing urological, oncology and palliative care services throughout the network, and signed off by the lead clinician for the network. Effective systems will be required to ensure rapid communication and efficient co-ordination between teams.

Local urological cancer teams should be established in cancer units at district general hospitals. Specialist urological cancer teams should be based in larger hospitals, usually cancer centres. There are various possible ways of providing local services which meet the criteria defined in this Manual; local teams may be set up by individual Trusts; two or more Trusts may work in partnership; and some services could be provided by mobile teams. Although there should not be more than one MDT of any specific type working in a single hospital, a centre serving a large population may have teams at different levels of specialisation.

Substantial changes in working practice will be required to create the form of service described here. Each network should decide how it will establish the specialist teams which are central to these recommendations. Some clinicians working in cancer units may wish

to join a specialist urological cancer team based in another hospital; where this pattern of practice is adopted, all such individuals should participate fully in team meetings. All teams should include sufficient members to allow for adequate cover for the absence of any individuals and all members should meet the attendance criterion (attending more than half of the meetings of the team in which they work).

It is recognised that a period of transition will be required before the new pattern of service provision is established. In the meantime, all surgeons who carry out fewer than five radical prostatectomies or fewer than five cystectomies per year should pass this work to more specialised colleagues.

The local urological cancer team

In general, local urological cancer teams should serve populations of 250,000 to 500,000, but the minimum figure may be closer to 200,000 in large sparsely populated areas. Core teams should include, at a minimum, the members specified below. All members of each team should have a particular interest in urological cancer and treatment should be provided by these designated individuals.

Those who are directly involved in treating patients (in particular, urologists, oncologists and cancer care nurses) should recognise that they have responsibility for good communication with patients and carers, and should receive specific training in communication skills.

Members of the local urological cancer team

- Designated lead clinician (normally a consultant urologist) who will take overall responsibility for the service.

- Urologists. The team should include a minimum of two designated urologists with a special interest in cancer.

- Designated nurse who will provide information and support for patients. This nurse may, if suitably trained, carry out a range of interventions such as digital rectal examination, flexible cystoscopy, and intravesical treatment for patients with resected superficial bladder cancer.

- Radiologist with expertise in urological cancers. All imaging investigations should be carried out in accordance with Royal College of Radiologists Guidelines.[46]

[46] The following guidelines are available from the Royal College of Radiologists: Johnson R, Husband JE (Eds) *Guidelines for the use of CT scanning in the investigation of common malignancies* (1995); Husband JE, Johnson RJ, Reznek RH. *A guide to the practical use of MRI in oncology* (1999); RCR Working Party. *Making the best use of a Department of Clinical Radiology: Guidelines for Doctors (Fourth Edition)*. London: The Royal College of Radiologists, 1998. A fifth edition of this booklet is due to be published in 2002.

- Pathologist. Pathology reports should include all the information required by the current Royal College of Pathologists' minimum dataset for the relevant cancer.[47] A national histopathology quality assurance (EQA) scheme should be established along the lines of the EQA scheme for breast cancer, to be run by those directly involved in this work.

- Oncologist with expertise in radiotherapy and chemotherapy for patients with urological cancers. The oncologist, who is likely to be a member of the specialist urological cancer team from a linked cancer centre, should co-operate with other specialist oncologists in the network.

- Palliative care specialist (physician or nurse).

- Team co-ordinator (see below, *Organisation of MDT meetings,* for discussion of this role).

- Team secretary who will provide clerical support for the MDT. The secretary should record all decisions made by the team and communicate appropriate information promptly to all those (such as GPs) who may require it. The roles of secretary and co-ordinator overlap and one person may be able to cover both functions in smaller teams.

The role of the local urological cancer team

This team will:

- Provide a rapid diagnostic and assessment service;

- Identify and manage all patients with urological cancers, including those cared for elsewhere in the hospital;

- Be responsible for the provision of information, advice and support for all patients and their carers throughout the course of the illness; this should include those who are receiving most of their care from clinicians who are not members of the urological cancer team, such as physicians for care of the elderly;

- Provide treatment and follow-up for these patients and ensure that every patient with urological cancer receives multidisciplinary management with appropriate oncological input;

- Provide a rapid referral service for patients who require specialist management;

[47] The Royal College of Pathologists' minimum datasets for specific cancers are available on http://www.rcpath.org/activities/publications.

- Liaise with primary care teams, specialist teams, services for the elderly and voluntary organisations such as hospices;
- Ensure that GPs are given prompt and full information about any changes in their patients' illness or treatment;
- Collect data for network-wide audit.

The team must maintain close contact with all other professionals who are actively involved in treating or supporting patients. These will include the following:

- Stoma nurse;
- Liaison psychiatrist;
- Clinical psychologist trained in psychotherapy and cognitive behaviour therapy;
- Trained counsellor with expertise in cancer and psychosexual problems;
- Social worker;
- Occupational therapist;
- GPs/primary health care teams;
- Palliative care teams;
- Clinical geneticist/genetics counsellor.

Arrangements should be made to alert an appropriate member of the core team whenever a patient managed by that team is admitted to hospital for any reason, both so that the team may contribute to decision-making about diagnosis or treatment and to ensure that it has up-to-date information about such patients.

The team should meet weekly and should assume responsibility for all patients with urological cancers. All team members should attend the majority of meetings and all should participate in collaborative decision-making.

Decisions about management and standards for therapy should follow documented clinical policy which has been agreed throughout the network. This policy should be demonstrably evidence-based and should be produced jointly by members of all the teams in the network which deal with patients with urological cancer.

One member of the team (usually the lead clinician) should take managerial responsibility for the service as a whole. Audit of processes and outcomes, and action stimulated by audit findings, should be discussed in team meetings. Data collection systems should be compatible with those used at the cancer centre to facilitate network-wide audit.

Specialist urological cancer teams

Patients with cancers which are less common or require complex treatment should be managed by specialist multidisciplinary urological cancer teams. These teams should be established in large hospitals or cancer centres, and each team should carry out a cumulative total of at least 50 radical operations for prostate or bladder cancer per year. All operations carried out by any particular team should be carried out in a single hospital, which should also provide post-operative care and host the MDT meetings.

In larger cancer networks (those providing services for urological malignancies for populations of two million or more), a second specialist team may be established, provided the population served by each of the teams is no less than one million. Any non-centre teams should be capable of the full range of activities required of specialist teams and must be able to demonstrate strong clinical links to the radiotherapy centre and associated non-surgical oncology services at the cancer centre.

Where two specialist teams are established within one network, there should be strong links between them. They should jointly establish common clinical policies across the network as a whole, and for the audit of all aspects of their work. Each team should appoint a lead clinician who will take an active role in the co-ordination of urological cancer services provided by the network as a whole.

Specialist urological cancer teams should manage the following types of patient. The figures given in brackets for each category of patients are the numbers likely to require complex or radical surgery each year in a population of one million.

- Men with early-stage prostate cancer for whom surgery is considered appropriate and who elect to undergo radical prostatectomy (25-50).

- Patients with muscle-invasive bladder cancer (50). Patients with high-risk superficial tumours should be formally discussed with the specialist team; some of these will require referral for management by the specialist team. There should be specific local protocols which define these patients and give details of appropriate referral and management.

- Patients with kidney cancer who fall into the following categories (20-30):
    - Those with tumours which have, or may have, invaded major blood vessels;
    - Patients who might benefit from resection of metastases;
    - Patients with bilateral disease or who will require dialysis;
    - Patients with small tumours for whom nephron-sparing surgery may be possible;
    - Patients with von Hippel-Lindau disease or hereditary papillary tumours.

Supra-network specialist teams

Patients with testicular or penile cancer should be managed by specialist testicular cancer or penile cancer teams working at the supra-network level. Such teams should serve up to four networks, with a combined population base of at least two million for testicular cancer and four million for penile cancer. (See Topic 6, *Testicular cancer*, and Topic 7, *Penile cancer.*) These teams should liase closely with local urological cancer teams which will be responsible for some aspects of the diagnosis and treatment of these cancers.

Members of specialist urological cancer teams

The MDT described below should be regarded as a generic form; additional members are required for teams treating male genital cancers at the supra-network level, as specified in Topic 6, *Testicular cancer* and Topic 7, *Penile cancer*. Each member of a specialist urological cancer team should have a specialist interest in urological cancer and all team members must attend a majority of meetings. The team should carry out a cumulative total of at least 50 radical operations for prostate or bladder cancer per year.

The specialist urological cancer team should include one or more of each of the following individuals:

- Urologists. There should be at least two urologists in the team.
- Clinical oncologist.
- Medical oncologist, except where the clinical oncologist has specific expertise in systemic treatment for urological cancers.
- Radiologist with expertise in urological cancers. All imaging investigations should be carried out in accordance with Royal College of Radiologists Guidelines. [46]

- Pathologist. Pathology reports should include all the information required by the current Royal College of Pathologists' minimum dataset for the relevant cancer.[47] The pathologist should participate in a national histopathology quality assurance (EQA) scheme.

- Clinical nurse specialist. This role is similar to that of a breast care nurse. The nurse must have a high level of skill in communication because patient advocacy and provision of information and support for patients and carers are crucial aspects of the role. (See Topic 3, *Patient-centred care*.)

- Pain management and palliative care specialist(s). Some palliative care specialists may be nurses but consultant input and advice will be necessary.

- Team co-ordinator, who will organise meetings and ensure that all documentation (such as patient lists and case notes) that may be required to inform discussion is available at each meeting.

- Team secretary, who should provide clerical support for the MDT, record decisions, and communicate information generated by the MDT to all those who may require it.

The team should have access to critical care facilities. It should maintain close contact with other professionals who may be actively involved in supporting patients or carrying out the management strategy decided by the team, so that rapid access to their services can be provided when required. These include the following:

- GPs/primary health care teams;

- Local urological cancer teams at linked cancer units;

- Plastic surgeon;

- Thoracic surgeon;

- Liaison psychiatrist;

- Clinical psychologist trained in psychotherapy and cognitive behaviour therapy;

- Counsellor with expertise in treating psychosexual problems;

- Stoma care nurse;

- Lymphoedema specialist;

- Occupational therapist;

- Social worker;
- Palliative care teams.

Organisation of MDT meetings (local and specialist teams)

Meetings should be arranged by the team co-ordinator, who should ensure that information necessary for effective team functioning is available at each meeting. This will include a list of patients to be discussed and copies of their case notes, along with diagnostic, staging, and pathology information.

Preparation and attendance at meetings should be recognised as clinical commitments and time should be allocated accordingly. Team members should be adequately prepared for each meeting, so that they can discuss each case without delay.

All new patients should be discussed, along with any other patients whose cases are thought to require discussion as their condition or treatment progresses. Straightforward cases may need very little discussion but they should nevertheless be included.

Audit, clinical trials, and other issues of relevance to the network should also be discussed at MDT meetings.

Suitable facilities should be provided to support effective and efficient team working. In addition to the basic physical facilities such as adequate room and table space, these are likely to include, for example, appropriate equipment to allow the whole group to review large numbers of radiographic images and pathology slides. Teams may consider taking formal training to facilitate effective group working.

Co-ordination between teams

Close co-ordination is required between primary care teams, diagnostic and treatment teams at cancer units and cancer centres, palliative care teams, and patients and their families. There should be a designated individual in each team who has responsibility for communication and information provision, and adequate support must be provided to ensure that all decisions about patient management are recorded. (See the role of team secretary/co-ordinator, above.)

Clearly defined arrangements should be made to ensure that appropriate information (including the name of the clinician and nurse specialist who are directly responsible for each patient) is communicated promptly to patients and others (such as GPs) who may require, or may benefit from, information about decisions concerning particular patients. GPs should be given sufficient information about each patient's cancer and management for them to advise and support patients and their carers.

Trusts should produce patient-held information packs. These should contain details of the patient's disease and treatment, relevant MDT(s), clinical appointments, and a diary in which patients can record symptoms and other potentially useful information about their condition, both for the patients' own use and to help clinicians who may see them out of hours to respond appropriately to their needs.

B. Anticipated benefits

Re-structuring services for urological cancers to increase specialisation and establish multidisciplinary team working is expected to produce wide-ranging benefits for patients and the NHS.

A co-ordinated cancer network should be capable of delivering consistent, efficient and effective care to all patients in the region it covers. Within each level of the service, team working will facilitate co-ordinated care. Patients managed by teams which function effectively are more likely to be offered appropriate information and guidance, to receive continuity of care through all stages of their disease, and to be treated in accordance with locally-agreed protocols and clinical guidelines.

Increasing specialisation will tend to refine surgical expertise, provide the necessary conditions for training in uro-oncology for specialist registrars and newly appointed consultants, and permit meaningful audit of individual outcomes. This will enhance the level of skill available within the NHS.

Discussion of every patient by multidisciplinary teams will improve patient-centred care by ensuring that psychosocial, as well as clinical, issues are considered; these issues tend to be raised by nurse specialists and others who bring different perspectives from those of urologists and oncologists. It provides an opportunity for pathology and radiology results to be discussed and allows the team as a whole to check that everything necessary is done for the patient.

It is anticipated that these changes, implemented together, will lead to significant improvements in outcomes for patients with urological cancers.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Multidisciplinary teamwork

There is little direct research evidence for the effectiveness of multidisciplinary teamwork in the management of patients with urological cancer. Nevertheless, there are a number of strands of evidence which, considered together, point to the value of this model of working.

In prostate cancer, in particular, patients are faced with difficult decisions about treatment options. As the evidence summarised in Topic 5, *Prostate cancer* shows, there is often no convincing evidence for the overall superiority of any particular approach to treatment over others. Uncertain benefits of treatment have to be balanced against potentially deleterious effects on quality of life. In this situation, specialists have a natural tendency to prefer, and to recommend, active treatment using the modality in which they specialise. Most tend to under-value conservative options such as active monitoring.

These biases have been documented in studies of the attitudes and behaviour of urologists and oncologists treating men with prostate cancer.(B) They have also been reported by patients, who find the experience of hearing conflicting recommendations from different specialists distressing.(C)

Insights from the Cancer Services Collaborative

Two case studies of action to improve the effectiveness of MDT meetings discussing patients with prostate cancer have been reported by the Cancer Services Collaborative in England.(C) The initial problems – poor attendance by team members and failure to discuss all the patients who should have been discussed – were common to both and were solved by similar strategies.

These strategies had two main elements. The first was improved team-building, with involvement of all team members in discussions about meetings. The second was the introduction of effective systems to ensure that all new patients were discussed and that necessary information (such as case notes and results of diagnostic investigations) was available for each patient at the meeting. Documentation was improved using, in one case, a *pro forma* developed specifically for these meetings, and in the other, an information sheet designed to aid communication.

Both case studies reported improvements in attendance rates and the effectiveness of meetings. The proportion of patients discussed by the teams also rose. One study reported a dramatic increase in the percentage of patients managed in accordance with clinical guidelines, from 10% before the introduction of the MDT *pro forma* and action to ensure the availability of patients' notes, to 100% eight months later.

Further information can be obtained from the Cancer Services Collaborative Service Improvement Guide on Multidisciplinary teamworking at www.nhs.uk/npat.

Specialist management

It is rarely possible to separate the effects on outcomes of specialist management and high patient throughput; in practice, the former is not achievable without the latter – although it is conceivable that, in some hospitals, large numbers of patients may be treated by relatively unspecialised clinicians.

There is consistent evidence showing the benefits of either higher patient throughput or higher levels of institutional specialisation in both prostate and testicular cancer. Systematic reviews and individual studies which examine relationships between the number of patients treated and the quality of treatment received show that care in high volume institutions is associated with significantly better outcomes.(B)

For radical surgery for prostate cancer, the cut-off points for high and low volumes vary between studies, but all show a progressive improvement in outcomes from the smallest centres (25 or fewer prostatectomies per year) to the largest (over 140 per year). Hospitals which manage larger numbers of these patients report lower complication and mortality rates and lower resource use.

In one review of outcomes after radical prostatectomy, in-hospital mortality rates were almost identical in low and medium volume hospitals (<25 or 25-54 prostatectomies per year), and significantly poorer than in higher volume hospitals (>54 prostatectomies per year); odds ratios 1.8 and 1.7 for low and medium volumes (95% CI: 1.2 to 2.7 and 1.2 to 2.6, respectively), compared with higher volumes. Serious complications and re-admissions showed the same pattern: the highest patient numbers were associated with the lowest risk. Compared with hospitals which carried out more than 140 prostatectomies per year, the risk of serious complications was 43% greater (95% CI: 37% to 48%) in hospitals which carried out 39 or fewer prostatectomies, 25% greater (19% to 31%) for a volume range of 39-74, and 9% greater (3% to 15%) when volumes were between 75 and 140. However, simply increasing the throughput of patients managed by established institutions may not be sufficient to improve outcomes.(B)

In testicular cancer, too, there is a clear relationship between patient numbers treated and the quality of care provided. Patients treated in institutions which deal with larger numbers of such cases are significantly more likely to survive.(B) (See also Research Evidence for Topic 6, *Testicular cancer*.)

Further evidence supporting concentration of services comes from a review focusing on specialisation, which reported reduced mortality rates among patients treated for urological cancers by specialists, or in hospitals linked with universities.(B)

Studies of pathology services in prostate and testicular cancer have found that specialised centres produce more accurate reports on

biopsy specimens. Histopathological review by experts can result in crucial changes in management; for example, a study of testicular tumour pathology found that expert review led to a major change in diagnosis in 6% of cases.(B)

Current services in the NHS

NHS services for the more common forms of urological cancer are fragmented, with most hospitals treating small numbers of these patients. Hospital episode statistics (HES) show that about two-thirds of the hospitals which carry out prostatectomy, and over three-quarters of those which carry out cystectomy, do 10 or fewer of each operation per year. Table 10 and Figure 2, below, show frequency distributions of Trust workload for radical surgery for prostate and bladder cancer in England between 1995 and 2000.

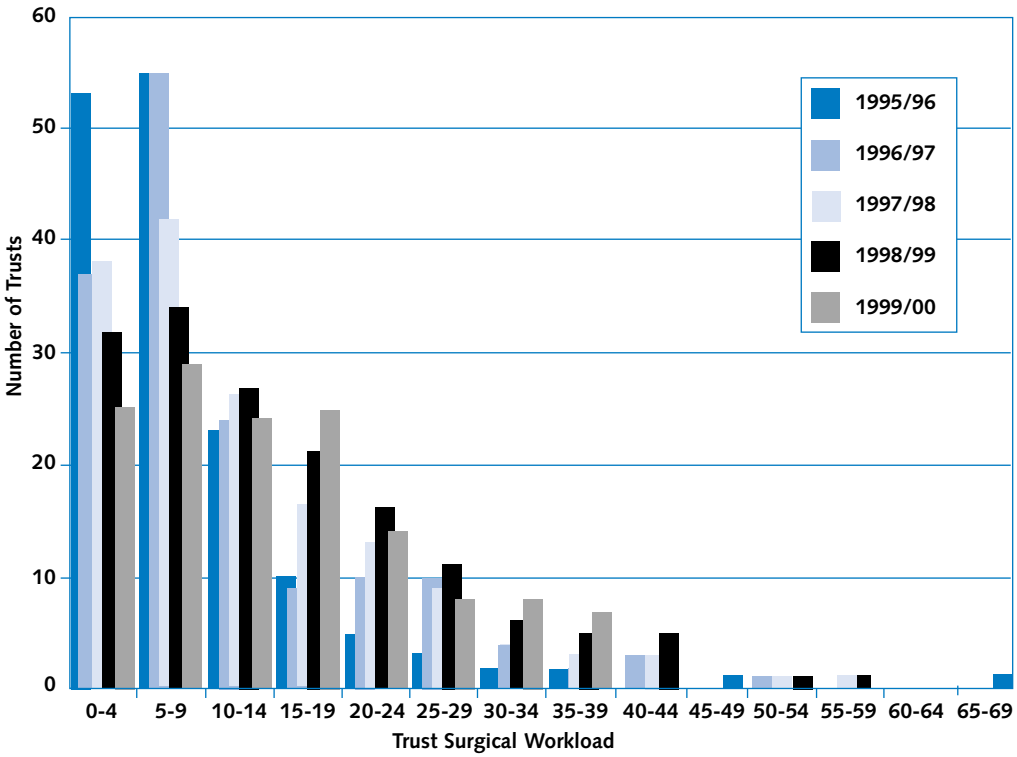
Table 10. Frequency distribution of Trust workload for prostatectomy and cystectomy combined (England)

Number of operations per Trust*	1995/96	1996/97	1997/98	1998/99	1999/00
0-4	53	37	38	32	25
5-9	55	55	42	34	29
10-14	23	24	26	27	24
15-19	10	9	16	21	25
20-24	5	10	13	16	14
25-29	3	10	9	11	8
30-34	2	4	4	6	8
35-39	2	2	3	5	7
40-44		3		3	5
45-49					1
50-54	1		1		1
55-59			1	1	
60-64					
65-69					1
Grand Total	**154**	**154**	**153**	**156**	**148**

* "Operations" refers to the combined total of radical prostatectomies and cystectomies carried out for cancer treatment by individual Trusts in a specified year.

Whilst it is clear that workload patterns are changing in the direction of higher volumes and, presumably, greater specialisation, there is a long way to go before the criteria recommended in this Manual can be met. Just two hospitals in England provided 50 or more radical operations (prostatectomies plus cystectomies) for prostate or bladder cancer in 1999-2000, 7.4% of the total number done (2,358 operations).

Figure 2. Frequency distribution of Trust workload for prostatectomy and cystectomy combined (England)



Although HES data provides a fair picture of the general situation in the NHS, HES figures are not precisely correct. The accuracy of HES data depends on the quality of coding, both for disease and procedure, and errors occur when patients with cancer are not identified or the nature of surgery is incorrectly described. In addition, recent Trust mergers mean that data for more than one treating hospital may be included in a single figure, overstating hospital workload. Despite these limitations in the data, there is no reason to doubt the overall picture of low rates of radical urological surgery in individual NHS hospitals.

D. Measurement

Accreditation standards for multidisciplinary teams to deal with urological cancers will be published in the NHS *Manual of Cancer Service Standards* in England and in the Minimum Standards for Cancer Services in Wales.

Structure

- A network in which the roles of hospitals which offer services for patients with urological cancer are specified.
- Systems to link and co-ordinate the activities of hospitals within the network.
- Appropriate teams in place in each hospital in the network.
- Adequate systems and support for rapid communication between teams within the network.
- Evidence-based assessment, treatment and referral guidelines, agreed by specialist teams throughout the network.
- Systems for network-wide audit of procedures and outcomes.
- Provision of adequate and appropriate facilities for surgery and post-operative care.

Process

- Evidence of weekly MDT meetings at both cancer units and centres.
- Records showing that every individual member of each MDT is present at a majority of meetings.
- Evidence that every patient with cancer has been discussed in an MDT meeting.
- Comparison of total number of patients diagnosed in each Trust with number reviewed by relevant MDTs.
- Use of locally agreed clinical policies and guidelines.
- Number of patients managed annually by each team.
- Number of cystectomies and radical prostatectomies carried out by each team; the sum total of these operations should come to more than 50 per year.
- Audit of time taken to communicate essential information about individual patients (e.g. diagnosis and treatment plan) between hospital staff and primary care teams.
- Number of patients choosing each form of treatment.

Outcome

- One, two and five-year survival rates for each type of cancer, adjusted for case-mix.

- Audit of outcomes of treatment, including detailed information on case-mix.

E. Resource implications

At the time of writing, there are few genuine MDTs in urological cancer. Implementing these recommendations will require far-reaching changes in working practices and establishment of new staff posts within the team. For example, a larger number of clinical nurse specialists and team co-ordinators will be required than are currently in post, and time has to be set aside by all those involved to attend team meetings. Increased resources will be required over a considerable period for re-structuring of urological services, for training, and to achieve sufficient numbers of professionals to work in these teams.

- The additional annual costs of ensuring that all MDTs have a co-ordinator, an additional consultant session, and additional staff time for MDT meetings are estimated at £6.4 million (see Appendix 1, *Economic implications of the guidance*).

- The cost consequences of the centralisation of radical surgery for bladder and prostate cancers to teams in specialist centres is between £3.8 and £5.0 million (see Appendix 1, *Economic implications of the guidance*).

Diagnosis and assessment

2

The following guidelines for urgent referral (within two weeks) have been published by the Department of Health:[48] Similar guidelines for patients at high risk of urological cancer have been published in Wales.[49]

- Macroscopic haematuria in adults.
- Microscopic haematuria in adults over 50 years.
- Swellings in the body of the testis.
- Palpable renal masses.
- Solid renal masses found on imaging.
- Elevated age-specific prostate specific antigen (PSA) in men with a 10 year life expectancy.
- A high PSA (>20ng/ml) in men with a clinically malignant prostate or bone pain.
- Any suspected penile cancer.

A. Recommendations

Diagnostic investigations in primary care

GPs within each network should work with members of specialist urological cancer teams to develop and circulate locally agreed guidelines on appropriate referral for patients with suspected urological cancer. Compliance with these guidelines should be audited.

[48] Department of Health. *Referral Guidelines for Suspected Cancer*. Available on http://www.doh.gov.uk/cancer.

[49] National Assembly for Wales. *Urological Cancer Services All Wales Minimum Standards*. Available on http://www.wales.gov.uk/subihealth/content/cscg/index.htm

Prostate cancer
GPs should use digital rectal examination (DRE) to assess lower urinary tract symptoms (such as frequency, hesitation, poor stream) suggesting obstructive disease of the prostate or bladder neck. If the prostate feels normal, the option of PSA testing may be discussed with patients but appropriate counselling, including information about the reliability of PSA results and acknowledgement of uncertainty about the balance of risks and benefits, should be given before a PSA test is carried out. Patients should be offered material designed to promote informed choice about PSA tests, available through the National electronic Library for Prostate Cancer.[14] Any patient with a prostate that feels abnormal, or whose symptoms or test results suggest the possibility of prostate cancer, should be referred to a prostate assessment clinic (see below).

Testicular cancer
Only a small proportion of men with scrotal swellings have cancer; a GP may see only one case of testicular cancer every 20 years and is not likely, therefore, to be able to distinguish between tumours and non-malignant causes of symptoms. GPs should refer men with testicular masses or other unexplained testicular symptoms such as a sensation of scrotal heaviness or pain, to a testicular assessment clinic (see below).

Penile cancer
GPs should refer men with suspicious penile lesions such as growths, swelling at or near the glans, painless ulcers which do not appear to be due to infection, or other unexplained abnormalities such as plaques on the skin or foreskin of the penis, to a local urological cancer team.

Bladder and kidney cancer
Most patients with bladder or kidney cancer develop visible haematuria and they should be referred within two weeks to a dedicated haematuria clinic. Patients with kidney cancer may also present with persistent loin pain; such patients should be referred for imaging.

Patients (particularly those over 50 years of age) with persistent irritative urinary symptoms which do not respond to antibiotic treatment should be referred for further investigation.

Diagnostic services in district general hospitals

Prostate assessment clinics and haematuria clinics should be provided by urology departments of district general hospitals. These clinics should be staffed by diagnostic teams with members drawn from the local urological cancer multidisciplinary team (MDT), and should include a nurse with special responsibility for providing information and support for patients. Urologists and other clinic staff should give patients clear reasons for investigations and explain the implications of results. (See Topic 3, *Patient-centred care*.)

Diagnostic services should be organised, where possible, so that they can carry out sufficient tests to determine whether cancer is present during a single visit. The concept of a one-stop clinic should not be taken to imply that all diagnostic tests should be offered in a single location or necessarily carried out at the first visit. Ultrasonography, for example, may be carried out in a radiology department but the MDT should aim to synchronise imaging with other diagnostic investigations so that delays are minimised.[50]

When successive appointments are necessary, they should be pre-booked to minimise delay between investigations. An appointment to discuss results should be arranged for a date within two weeks of the initial investigation appointment. Patients should be encouraged to bring a close friend or relative to any meeting at which they are expected to receive news of a diagnosis of cancer.

Prostate assessment clinics should provide DRE and PSA testing, as well as trans-rectal ultrasound (TRUS) and needle biopsy, carried out by a suitably trained health professional.

Haematuria clinics should offer clinical examination, urine testing, flexible cystoscopy, and rapid access to ultrasound imaging and intravenous urography (IVU) when required. When an abnormality or growth in the bladder is apparent but the diagnosis is uncertain, patients should be told that a definite diagnosis cannot be given until pathology results are available.

Arrangements also need to be made for rapid assessment of scrotal swellings using ultrasound; this service may be provided as part of general urology or elsewhere, as judged appropriate locally. All diagnostic and assessment services should follow documented clinical policies which have been agreed throughout the network.

Staff who carry out diagnostic investigations such as biopsy should have received adequate and appropriate training in the techniques they use, to minimise the potentially high error rate. When prostate biopsy proves negative but there is strong suspicion that cancer is present (for example when the PSA level remains persistently high), re-biopsy is necessary. Local clinical protocols should include specific criteria to guide judgements in such cases.

[50] An appropriate model might be the one-stop clinic for diagnosis of breast cancer. Mammography is often carried out in a different part of the hospital from the breast clinic, but diagnostic investigations are integrated so that patients do not have to wait for long periods.

Diagnostic investigations in secondary and tertiary centres

Prostate cancer

TRUS and prostate biopsy may be carried out by a suitably trained health professional working in a prostate assessment clinic. Pathology reports should include all the information required by the current Royal College of Pathologists' minimum dataset for prostate cancer.[51] When biopsy samples suggest the presence of cancer and radical treatment is being considered, pathology results should be reviewed by the pathologist member of the specialist urological cancer team at the centre at which such treatment would be carried out. A national histopathology quality assurance (EQA) scheme should be established along the lines of the EQA scheme for breast cancer, to be run by those directly involved in this work.

Magnetic resonance imaging (MRI) may have a role in the pre-operative assessment of patients who are considered to be at intermediate or high risk (PSA above 10ng/ml, Gleason score 5 or more), who might benefit from radical treatment and whose cancer does not appear to have spread beyond the prostate. All images held by local MDTs should be forwarded to the appropriate specialist MDT if radical surgery is being considered.

Networks should agree and document clinical policies for the use of bone scans in urological cancers. Routine bone scanning is not necessary for all patients with prostate cancer. In particular, it is not likely to be useful for previously untreated men with PSA levels below 10ng/ml and Gleason scores below 8, who are free from bone pain. Such men are very unlikely to have metastatic disease.

Testicular cancer

Testicular cancer can be reliably confirmed or excluded by a combination of clinical examination and ultrasound imaging. Men with scrotal swellings should be assessed in regular clinics equipped with ultrasound facilities capable of producing precise images and staff who are skilled in interpreting ultrasound images of the scrotum.

If ultrasound and clinical examination suggest the presence of cancer, blood should be taken before surgery to assess levels of tumour markers including alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotrophin (βhCG). The results of these assays should be available within one week. Laboratory techniques for measuring these tumour markers should be agreed by the whole network, to ensure consistency across the network.

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[51] The Royal College of Pathologists. *Minimum dataset for prostate cancer histopathology reports*. Available on http://www.rcpath.org/activities/publications/prostate.html.

Most patients should undergo orchidectomy before referral to a specialist testicular cancer MDT at a designated cancer centre, except when there are clear signs or symptoms of metastatic germ cell cancer. These patients should be referred immediately to the specialist MDT.

The risk of cancer in the contralateral testis and the option of biopsy should be discussed with patients. Biopsy and surgical samples should be reviewed by a histopathologist member of the testicular cancer MDT.

Bladder and other urothelial cancers

The majority of patients will be assessed in haematuria clinics, described earlier in this section. Assessment of bladder cancer normally requires diagnostic resection. If initial assessment suggests that the patient has a low-grade superficial tumour, resection can be carried out by a urologist member of the local urological cancer MDT who has an interest in bladder cancer. This resection should be sufficiently deep to determine the depth of tumour invasion. Pathology reports should include all the information required by the current Royal College of Pathologists' minimum dataset for bladder cancer.[52]

About 50% of patients will have high-risk superficial tumours or muscle-invasive cancer (T2 or above). Patients with G2 or G3 tumours should be formally discussed with the specialist urological cancer team. Those who have pT2 or more advanced tumours should be referred to the specialist team; images produced at local hospital or unit level should be sent with the patient for review by the specialist team. MRI, or computed tomography (CT) if MRI is not available, should be used to assess the extent of invasive tumours before radical treatment. Patients with high-risk tumours should have the opportunity to discuss the implications of the results of staging investigations in a joint meeting with a surgeon and an oncologist.

Tumours of the upper urological tract are relatively unusual. These tumours are linked with bladder cancer and the same grading system is used. Assessment and staging requires urinary cytology, ureteroscopic biopsy, and CT imaging.

Kidney cancer

The diagnosis of kidney cancer is usually made by imaging. All patients with renal masses which could be malignant should be referred to the local urological cancer team.

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[52] The Royal College of Pathologists. *Minimum dataset for bladder cancer histopathology reports*. Available on http://www.rcpath.org/activities/publications/bladder.html.

CT is required to assess local invasion and spread to lymph nodes. The lungs should be scanned using CT to check for metastatic disease, except in patients with small tumours (up to 3cm), for whom chest x-ray may be sufficient. If it appears that tumour may have invaded the renal vein or inferior vena cava, or if nephron-sparing surgery might be possible, patients should be referred to the specialist urological cancer team, which should arrange further assessment including MRI. Biopsy is not normally necessary before surgery; it should be reserved for selected cases when imaging is unclear or surgery is not appropriate and biological treatment is being considered.

B. Anticipated benefits

The establishment of dedicated clinics for the assessment of haematuria and prostate-related symptoms is expected to reduce delays in diagnosis of the more common forms of urological cancer. Currently, many patients with urological cancers experience long delays before a definitive diagnosis is achieved and treatment begins. It is unclear whether such delays affect survival rates, but they can cause considerable distress to patients.

The Cancer Services Collaborative in England has demonstrated that a prostate assessment clinic with a pre-booked appointments system can reduce delays from as much as six months to less than one month. When diagnostic services are not only efficient, but sensitive and responsive to patients' needs, this tends to establish a pattern of harmonious relationships between patients, carers and service providers.

Accurate staging and pathology results are essential to inform decision-making about therapy.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Prostate cancer

Detection and initial diagnosis

Prostate cancer may produce no symptoms until it has reached an advanced stage, but early cancer can be detected by DRE, which is used to investigate lower urinary tract symptoms. In older men, these symptoms are often caused by benign prostatic hyperplasia, with which cancer may co-exist.

DRE is quick and minimally invasive and when negative, usually means the patient does not have prostate cancer (negative predictive value 0.99, 95% CI: 0.98 to 0.99). The positive predictive value of DRE is low in the context of primary care (0.28, 95% CI: 0.20 to 0.36), so a positive result cannot be used to make a diagnosis but does indicate a need for further investigation and/or referral.(B)

The most-studied diagnostic test for prostate cancer is the PSA assay. PSA rises with the burden of disease and is generally highest – often over 100ng/ml – in men with metastatic disease. Prospective screening studies have found that a quarter to a third of men with PSA over 10ng/ml have prostate cancer but PSA levels vary widely, both among men who do have cancer and those who do not. There is no criterion below which men may be reassured that they do not have cancer, nor an agreed level which is regarded as diagnostic. Different systems for measuring PSA can produce quite variable results and apparent changes in PSA levels can reflect the use of assay materials from different manufacturers. In addition, sexual activity, clinical investigation and some forms of treatment can affect PSA levels.(B)

TRUS is used to estimate prostate size, guide needle biopsy and stage tumours. Biopsy is necessary for histological confirmation of cancer, but this too can produce very variable results, depending on operator skill and the method used. Re-biopsy can be positive for cancer in a substantial proportion of cases when initial biopsy was negative but other investigations suggest the presence of cancer. Adverse effects of prostate biopsy include pain, bleeding and infection; they have been reported to occur in up to 13.5% of patients who receive antibiotic cover and up to 34% of those who do not.(B)

Assessment of stage and local spread

Information on the stage and spread of prostate cancer can be obtained from PSA, DRE, TRUS, CT and MRI, and accurate assessment requires an appropriate combination of these. Clinical assessment of early prostate cancer tends to underestimate the stage of the tumour, often failing to detect when tumour has spread beyond the capsule of the prostate. In a recent study, 13% (17 of 131) of men who were believed on the basis of clinical assessment (including DRE) to have organ-confined disease, actually had bone metastases.

Accurate imaging is essential to assess the extent of apparently localised prostate cancer if radical treatment is being considered, because surgery is not likely to be curative when the tumour has spread beyond the capsule. Ultrasound, although invaluable for guiding biopsy, is not adequate for informing decisions of this sort except in low-risk patients.

Two studies suggest that that MRI is more useful than CT for assessing extracapsular extension and invasion of seminal vesicles and lymph nodes.(B) However, these were poor quality studies and imaging technology has improved since they were carried out. MRI is however, recommended as the staging method of choice for prostate cancer by the Royal College of Radiologists.[53](C)

Metastatic disease

In the UK, about 20% of men have metastatic disease, usually affecting the bones, when their prostate cancer is first diagnosed. PSA level is the best biochemical marker for bone metastases, which are very rare in untreated men with PSA below 10ng/ml.(B) Only a minority of men with PSA levels between 10 and 50ng/ml have metastatic disease, and efforts have been made to find a criterion which offers the optimum compromise between sensitivity and specificity. Levels of 35 and 70ng/ml have been proposed on the basis of receiver operator characteristic (ROC) curves.(B)

Bone pain in men with prostate cancer is usually due to metastatic disease. In one study, all patients with bone pain and PSA levels over 20ng/ml had metastatic disease.(B) A US review of 288 patients who were classified as "at risk" of bone metastases if they had abnormal acid phosphatase, alkaline phosphatase or bone pain found that only 1.4% of men who had none of these had metastases (B). Poor overall functioning is also associated with metastatic disease.(B)

Bone scans are generally used as the "gold standard" to detect bone metastases but it is not clear from the research evidence that these, on their own, are actually more accurate than the combination of symptoms and appropriate blood tests. Bone scans are appropriate, however, for assessing men with bone pain, since they can be used to inform management.

Testicular cancer

Initial diagnosis

No review of research evidence was carried out to assess the effectiveness of ultrasound for the initial diagnosis of testicular cancer. There is consensus in the clinical community that this is the most appropriate form of investigation.(C)

Assessment of metastatic disease

CT is generally more accurate than plain film chest radiography (x-ray) for detection of lung metastases. The use of both chest radiography and CT is not justified.(B)

[53] Husband JE, Johnson RJ, Reznek RH. *A guide to the practical use of MRI in oncology.* London: The Royal College of Radiologists, 1999.

Bladder and kidney cancers

Detection and initial diagnosis

Most patients with cancers of the bladder or kidney present with visible haematuria. This may be intermittent but a single episode of haematuria can signal the presence of cancer. Clinic-based studies suggest that 15% to 37% of patients with visible haematuria may have cancer, with higher proportions in areas where substantial numbers of people work in hazardous industries (see *Background*).(B)

Microscopic haematuria is common in young men and is rarely associated with any pathology, but it is a better predictor of cancer in older men. A large study (n=1,930) based in a Newcastle hospital haematuria clinic found that 9.4% of patients with microscopic haematuria had cancer. Although the probability of cancer increased with age, it was found in a few men below the age of 40.(B)

Bladder and kidney cancers are unusual in people less than 40 years old. The incidence of both rises steeply with each decade between the ages of 40 and 60, rising from 9.2 per 100,000 in men aged 40-44 to 36.5 per 100,000 in men aged 50-54, and 109.5 in those aged 60-64. The incidence in women shows a similar rate of increase with age, but the proportion affected in each age-group is less than half the corresponding proportion of men.(B)

Assessment of tumour stage and spread

The Royal College of Radiologists states that "MRI is superior to CT for staging bladder cancer" and recommends that MRI should be the staging method of choice.[54] (C) Published comparative studies do not show a consistent advantage for MRI over CT but these studies are all rather old and the technology has improved.(B) In renal cell cancer, CT is adequate for assessing most tumours but MRI may be marginally more accurate for staging.(B)

Quality of current services

A study of the management of muscle-invasive bladder cancer in the South West Region in 1989 and 1993 revealed clear evidence of deficiencies. The median delay between GP referral and diagnostic cystoscopy was 59 days in 1989 and 52 days in 1993; there were then further delays of 55 days (1989) and 44 days (1993) between cystoscopy and treatment. This brings the total period for median delay to more than three months in both 1989 and 1993. Inadequacies were reported in diagnosis and staging, with poor recording of details of pathology and stage of tumours. Similar problems were found in all types of hospital.(B)

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[54] Husband JE, Johnson RJ, Reznek RH. *A guide to the practical use of MRI in oncology*. London: The Royal College of Radiologists, 1999, p 46.

More recent data shows that waiting times may be long in England as a whole. Median time before the first out-patient appointment for NHS patients newly diagnosed with bladder cancer in 1997 was 20 days for urgent cases, 33 days for those classified as non-urgent; time to first definitive treatment was 57 and 82 days for these groups, respectively. 10% of urgent patients had to wait four months or more before their treatment began.(B)

The situation is even worse for patients with prostate cancer. An audit of delays experienced by patients with localised prostate cancer in south west England in 1993 found that some men waited for more than a year after their first clinic appointment before treatment began. This study also reported serious deficiencies in assessment, staging, documentation, and communication between the various clinicians involved in patient care.(B) The study described in the previous paragraph found that for England as a whole, waiting times were longer for men with prostate cancer than for patients with any other common cancer.(B)

The Cancer Services Collaborative in England has reported on pilot studies of a variety of initiatives designed to reduce delays in diagnostic services for prostate cancer.(C) These studies provide information both on the situation that existed before the initiative was launched (November 1999), and on ways of streamlining services to improve the experience for patients.

The Collaborative found that the established pattern in the NHS was for diagnostic investigations to be undertaken in sequence, with each successive investigation arranged only when the results from the previous one became available. This creates built-in delays. The introduction of rapid-access and one-stop clinics, along with pre-booking systems for diagnostic appointments, led to impressive reductions in delay. Examples of successful initiatives in diagnostic services include the following:

- In Leicester General Hospital, waiting time from referral to diagnosis was cut from 36 weeks to 3-4 weeks by the establishment of a prostate assessment clinic.

- One-stop clinics in three Trusts in the Bristol area now allow patients to have counselling, examination and appropriate investigations on a single day, with a follow-up appointment for results 10 days later.

- In Liverpool, a wait of 6-18 weeks for a staging bone scan was reduced to two weeks for appropriate patients by the introduction of protocols.

- In Colchester, patients had to wait for up to three months before getting their prostate biopsy results. The delay was reduced to a maximum of two weeks by re-organising the appointments system.

- Patients in West London waited eight weeks for TRUS and biopsy, and a further two weeks to hear the results. Now, biopsy is done either the same day as the first consultant appointment or within a week, and it is pre-scheduled. The total delay has been reduced from 10 weeks to two or less.

Further information is given in the Prostate Cancer Service Improvement Guide, available from the Cancer Services Collaborative (www.nhs.uk/npat).

D. Measurement

Structure

- Establishment of rapid-access and one-stop clinics for assessment of patients with possible urological cancers.

- Efficient appointment systems designed to minimise delay between referral and diagnosis.

Process

- Completion of current form of Royal College of Pathologists' histopathology dataset for each patient, where appropriate. This represents a minimum standard for pathology.[55]

- Time between date of receipt of GP referral letter and first hospital appointment.

- Time between first clinic appointment and diagnosis.

Outcome

- Patients' satisfaction with services.

- Stage distribution at time of diagnosis.

[55] The Royal College of Pathologists. *Standards and minimum datasets for reporting cancers*. Currently published for adult renal, bladder, prostate and testicular tumours. Available on: http//www.rcpath.org/activities/publications/minimum datasets.

E. Resource implications

The direct resource implications specific to the recommendations in this topic are modest.

- They include £0.28 million for bladder cancer and between £0.23 million and £0.4 million for pre-operative MRI imaging for prostate cancer. These are offset by savings of £0.34 million to £0.58 million for bone scans (see Appendix 1, *Economic implications of the guidance*).

- However, the rising incidence of prostate cancer coupled with greater use of PSA testing will increase both diagnostic and treatment costs (see Topic 5, *Prostate cancer*).

Patient-centred care

A. Recommendations

The recommendations in this section call for major changes in the provision of care for patients with urological cancers. Nurse specialists will play a crucial part, both in ensuring that patients receive adequate support and information, and in shaping the way that urological cancer multidisciplinary teams (MDTs) work. These aspects of the nurse specialist's role, although relatively new to urology, are particularly well developed in services for patients with breast cancer.

Communication with patients

In urological cancer in general, and prostate cancer in particular, the appropriate management strategy for an individual patient may depend crucially on that individual's values and attitudes. Because of the nature of the disease and the unpredictable rate of progression, the optimum strategy is often unclear. Radical treatment carries the threat of incontinence and permanent damage to sexual function and enjoyment, which may be unacceptable to some patients – especially when there is uncertainty about the degree of survival benefit that such treatment may offer. Others may feel that such risks are of little significance compared with the prospect of living with cancer.

In this situation, shared decision-making is essential. This can only work if patients are sufficiently well informed to understand the choices they face, and have sufficient time to consider the options carefully.

Patients should be given as much information as they wish to have, in language they are likely to understand, and in both verbal and written forms. When English is not the patient's first language, somebody who speaks the patient's language should be available to facilitate communication. Providers should not expect members of the patient's family to act as interpreters.

Patients should be given written material in information packs (see Topic 1, *The urological cancer network and multidisciplinary teams*) to which additional material can be added as required. Each pack should contain up-to-date information about the patient's disease and treatment, the names of MDT members responsible for his or her care, and clear information about services, including the following:

- A description of the way the clinics and doctors function together, and their various responsibilities.

- The way the appointments system operates.

- Contact details for people with whom patients or carers can talk if they feel concerned about any aspect of the illness, its treatment, or the hospital service.

- A telephone number for the nurse specialist member of the MDT responsible for his or her care.

Information offered to patients should also include:

- Sufficient information about basic anatomy and pathology for patients and their carers to understand how the disease might affect them.

- Realistic information about the disease and the range of individual variation in its impact and rate of progression.

- Information about known causes of the patient's type of cancer, including occupational risk factors if relevant.

- The aims, risks and likely effects of proposed diagnostic procedures. Each procedure should be explained to the patient before it is undertaken.

- Balanced information about potential treatment options, including the probability of improved survival or symptom reduction (and uncertainties about benefits), known risks and potential short- and long-term adverse effects.

- The likelihood of long-term continuing contact with the urological cancer team.

- Reasons for not offering interventions which patients might anticipate.

- Information on action that patients can take to help themselves and sources of support for such action – e.g. quitting smoking, improving their diet.

Patients should receive individual support and guidance from members of the MDT, as well as well-produced information leaflets. When patients have a choice between different therapeutic modalities, they should be offered the opportunity to discuss treatment options in a joint meeting with their urologist, oncologist, and specialist nurse.

Providers should ask patients if they want additional information and seek to discover how much they wish to be involved in discussions about treatment. Patients should be encouraged to bring a close friend or relative to the "bad news" consultation.

Clinicians must be sensitive to potential problems with communication, and those who provide direct patient care – particularly senior clinical staff - should have training in communication skills. They need to be aware that patients often find it difficult to take in information given during the consultation, especially just after receiving bad news.

Sensitive communication of bad news is particularly important to patients. The "bad news" consultation should be carried out in a private room without interruptions. The diagnosis should be explained clearly by a senior clinician who must allow adequate time for explanation and a specialist nurse should be present. After the consultation, the specialist nurse should offer to remain with the patient to provide support and further information tailored to individual needs. The Mount Vernon guidelines on handling the communication of bad news[56] should be followed.

All health professionals involved with each patient should know what information has been given to the patient. A record of this, along with the patient's preferences for information and involvement in decision-making, should be included in the notes and given to the patient's GP, together with a comprehensive summary of the management plan, as quickly as possible, so that primary care staff can provide additional support for patients and carers.

Advice for smokers

Patients with bladder or kidney cancer should be asked if they smoke and smokers should be strongly advised to quit. The association between smoking and urological cancer should be explained, and the benefits of quitting explicitly linked with reduced risk of recurrence. Smokers should be given information about local initiatives designed to help them quit and encouraged to participate.

Psychological support, sexual issues, continence and fertility

From the time of diagnosis, each patient should have access to a specialist cancer nurse who can offer psychosocial support and continuity of care. Patients should, whenever possible, be offered contact details for others who have experienced similar cancers or treatments; this may be arranged through Patient Advocacy and Liaison Services (PALS). Appropriate patients should be given information about organisations which offer specific forms of support such as The Association to Aid the Sexual and Personal Relationships of People with a Disability (SPOD)[57].

The nurse specialist, or another member of each MDT, should be trained in counselling patients and couples who may have to live with impotence or other sexual problems, loss of fertility, incontinence or

[56] The Mount Vernon guidelines and a Patient Information Card can be obtained from the King's Fund by ringing 020 7307 2672. The King's Fund has also published a book, *Breaking Bad News* (ISBN 1-85717-135-7).

[57] Telephone number: 020 7607 8851; www.spod-uk.org.

stomas after treatment for cancer. Psychological and psychosexual issues should be discussed with every patient who may experience adverse effects in these areas before final decisions are made about treatment. Counselling should be available when required from an individual who has specific expertise in dealing with psychosexual and body-image issues; this should be available to help patients and their partners to cope with such problems after treatment and for as long as it is needed.

Patients who may have problems with urinary incontinence should be given information both about local continence services and the Continence Foundation.[58]

Arrangements for cryopreservation of sperm should be explained to men whose ability to father children could be reduced by treatment. This is likely to be particularly relevant to men with testicular cancer.

Practical and social support

Many patients, particularly those with prostate cancer, are over 70 years of age. They, and their carers, are likely to require long-term support. The primary and palliative care teams have particularly important roles in co-ordinating with social services and ensuring that the needs of both patients and carers are identified and met.

Patients should be given information about sources of help, such as local and national support groups and disability and benefits helplines, both verbally and in writing. Information about support groups of various kinds is provided by NHS Direct and by cancer charities.[59]

B. Anticipated benefits

Provision of clear and timely information can help patients to cope with their disease, enhance satisfaction with services, and reduce criticism and complaints. Sensitive delivery of bad news is particularly valued by patients.

Information has a variety of benefits for cancer patients, particularly anxiety reduction, improved ability to cope with treatment and better self-care. Effective communication tends to heighten awareness of the various needs - whether medical, practical or psychological - of patients and carers, and increase the probability that these needs can be met.

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[58] Information about the Continence Foundation can be found on www.continence-foundation.org.uk. The Foundation provides a helpline on 020 7831 9831.

[59] Websites which provide information on support groups for cancer patients and carers can be obtained from NHS Direct (Tel: 0845 4647)

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Communication and information

Insights from patients treated for urological cancer

Patient focus groups, convened to discuss services for urological cancers, emphasised the importance for decision-making of good information on adverse effects of treatment and long-term quality of life. The communication of bad news was specifically highlighted; the nature of this experience seems to influence patients' views about subsequent interactions with health services. In particular, patients value the following:

- Privacy and lack of interruption during the "bad news" interview;
- Diagnosis given by a senior clinician;
- Clarity; patients prefer clinicians to use the word "cancer", thus avoiding confusion when they explain the diagnosis;
- Appropriate timing and adequate time for explanation;
- Sensitive mode of communication;
- Immediate support and information after the interview, tailored to individual needs and provided by a specialist nurse.

Patients reported problems with inadequate information during and after treatment. Lack of information left them bewildered, fearful, and unable to cope with long-term adverse effects of treatment such as incontinence. Some reported conflicting information from different clinicians and a specific lack of information about brachytherapy, about which they learnt from the internet. They wanted more support in decision-making about treatment options and more information about known adverse effects of treatment.

Whilst patients did not expect clinicians to be able to predict the future – especially in metastatic disease – they did want to know what might happen to them, and what support services were available. In particular, they wanted advice and support to help prepare for whatever the future might hold. Contact with other patients who had undergone similar experiences was valued.

Research evidence

The review of research evidence did not identify any studies which specifically addressed communication and information needs of patients with urological cancers. The following conclusions have been drawn from studies which included patients with a variety of cancers.

Problems with communication between clinical staff and patients can cause unintended distress. Although some patients may not wish to take an active part in decision-making, there is consistent evidence that they value accurate information and that many feel they are not given sufficient information. Studies demonstrating both patients' desire for information and its beneficial effects are summarised in the Research Evidence for previous documents in this series, in particular *Improving Outcomes in Lung Cancer.*

The following strategies have been found to be effective for improving communication:

- Doctors asking patients directly, in a structured way, whether they would like to know about particular issues.(A)

- Providing patients with a questionnaire (using the word "illness", not "cancer"), to elicit their concerns.(A)

- A taped or written record of the consultation. Although a majority of patients find audiotapes helpful, they can increase distress in those whose prognosis is poor and some patients do not wish to receive them. It is important that staff check that the patient does want a record of the consultation before it is given.(A)

- Patient-held shared-care records or information folders which hold details of appointments, medication, strategies for symptom control, contact addresses and telephone numbers, and a diary of significant events.(B)

- Provision of specific, easily-understood information about the nature and effects of any treatment before it begins, and on the management of pain and other symptoms at home. Such information can reduce anxiety and lead to more effective symptom control and self-care.(A)

- Cancer information booklets, videos, tapes and telephone help-lines. Whether these provide specific information, for example on pain management or anti-cancer treatments, or more general information on cancer, they are appreciated by patients and carers alike.(A)

Training in communication skills can change the attitudes of health professionals, improve their methods of eliciting and offering information, and increase their confidence in their ability to deal with patients with cancer.(B) The benefits appear to be greatest for people who hold particularly negative attitudes before training.(B) Some studies suggest that improvements can be maintained for several years, but training which fails to address participants' concerns may not be effective, as the skills learnt will not be put into practice.(B)

Psychosocial interventions

Cancer has profound effects on the lives of patients and their families, touching them at every level. They may need psychotherapeutic help or social support at any point, from initial diagnosis to death and bereavement. Estimates of the prevalence of psychiatric morbidity in patients with advanced cancer range from 37% to 63%.(B)

The research evidence is consistent in showing that social support and psychotherapeutic or psycho-educational interventions can improve patients' quality of life. A wide range of psychological interventions can reduce anxiety, depression, nausea, vomiting and pain;(A) cognitive therapy designed specifically for patients with cancer is significantly more effective than supportive counselling.(A) Home support by an oncology nurse during periods of out-patient treatment may reduce anxiety and depression.(A)

One small study (n=73) of patients with newly diagnosed testicular cancer found that routine cognitive/behavioural treatment was ineffective for this group.(A) Such interventions may be more appropriate for patients who are experiencing difficulty in coping with their situation.

D. Measurement

Structure

- Evidence that patients are given appropriate and adequate verbal and written information about their cancer, proposed treatments and options, and sources of practical help.
- Training courses in communication skills for clinical and other staff.
- Clinical nurse specialists who have had training in counselling patients with cancer.
- Facilities and support for patients' mutual support groups.

Process

- Private rooms used for crucial meetings between health care staff and patients (in particular, consultations at which patients are given bad news).
- There should be evidence that patients receive information and support from the time of diagnosis from suitably trained staff.
- There should be evidence that every patient has access to a named nurse specialist who knows about his or her condition and who can offer advice and arrange meetings with appropriate health or social services staff when required.
- The proportion of staff involved in direct patient care who have had specific training in communication and counselling skills should be monitored.

Outcome

- Providers should carry out surveys of patients' experience to assess the adequacy of each component of patient-centred care, including patient knowledge about available resources and patients' views on the quantity of information and the manner in which it was given.

E. Resource implications

- Additional resources may be necessary for the provision of information and educational material for patients with urological cancers.
- Resources will be required to allow sufficient staff time for provision of help and support for patients.
- Adequate training in communication skills and psychosexual counselling for nurses and other clinical staff is likely to require additional resources.
- Expansion in the numbers of specialist nurses is recommended. These staff have a range of roles including patient support and improving communications. The overall cost of expanding numbers of specialist nurses is £2.68 million (see Appendix 1, *Economic implications of the guidance*).

Palliative care

Supportive and palliative care guidance is currently being developed under the auspices of the National Institute for Clinical Excellence (NICE). This section deals with the structure of palliative care services. Interventions for palliation of symptoms associated with advanced urological cancer are discussed in the context of specific cancers, in particular prostate cancer.

A. Recommendations

4

Palliative care should be an integral part of patient management. Specialist palliative care teams should be available to arrange the provision both of relief from symptoms and social and psychological support for patients and their carers when these needs cannot be met by primary care teams.

Patients with advanced urological cancer may require care from specialist cancer treatment teams, specialist palliative care teams and primary care teams. Palliative care teams should work closely with primary care teams and hospital services; rapid and effective communication and information-sharing between teams is essential.

Specific services should be established for patients with advanced urological cancers. The majority of these will be men with prostate cancer, who may live with slowly progressing disease for a decade or even more, but there will also be men and women with other forms of advanced urological cancer. All need care that evolves to fit their changing requirements. These services should be linked with other primary and palliative care services.

Criteria for referral for specialist care should be agreed and documented for the whole network by palliative care specialists and representatives from primary care and specialist treatment teams. Primary care teams should assess patients' needs regularly and accurately, to ensure that patients who require specialist palliative care or interventions (see below) are referred quickly and appropriately.

The specialist palliative care team

Palliative care is essentially a local service, and specialist palliative care teams should be based both in hospitals that manage patients with urological cancer, and in the community. The role of the specialist palliative care team includes both direct care for patients and families with complex problems, and the provision of advice, support and education for other health professionals. One member of the team should be responsible for ensuring co-ordination of palliative care services and rapid communication, both between professionals and with patients and their families.

The specialist palliative care team should be multidisciplinary, and should, as a minimum, include the following members:

- Palliative care physician.
- Palliative care nurse specialists.

The team should have close links with the following:

- Physiotherapist.
- Clinical psychologist.
- Liaison psychiatrist.
- Social worker.
- Occupational therapist.
- Chaplain/pastoral care worker who can offer counselling and spiritual guidance for patients with advanced incurable illness and their carers.
- Bereavement care worker.
- The primary care team.

Patients, their carers, GPs and hospital staff who care for these patients should have access to a member of the specialist palliative care team at any time of the day or night. A named member of the team should be responsible for ensuring effective co-ordination of palliative care services, continuity of care, and rapid communication, both between professionals and with patients and their families.

The team should endeavour to make it possible for patients to spend their remaining life in the place they prefer, whether this is home, hospital or hospice, but should be alert to the possibility that this preference may change as death approaches.

Management of patients with advanced disease

All patients with advanced cancer should be asked regularly if they have pain, so that prompt action may be taken to relieve it. Cancer pain can normally be controlled with oral or parenteral analgesics, usually opiates, in accordance with the World Health Organisation (WHO) 3-step method for control of cancer pain.[60] This requires regular and frequent assessment of pain, with titration of the dose of analgesia against pain severity.

There should be a system for rapid referral for radiotherapy for palliation of pain, particularly when it is associated with bone metastases. Urgent access to radiotherapy, orthopaedic and neurosurgical services should be available for patients at risk of fractures or spinal cord compression. (See Topic 5, *Prostate cancer*.)

B. Anticipated benefits

Prompt identification and appropriate action to manage problems experienced by patients is crucial to reduce their distress and disability and diminish strain on carers. High quality co-ordinated palliative care services can improve quality of life for people with advanced cancer, and effective home care can usually keep symptoms sufficiently well controlled to allow patients to stay at home for as long as they wish. This is preferred by most patients and may be the least expensive option for the NHS.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Patients' needs

Advanced urological cancer and its treatment can cause pain, fatigue, mobility problems, fractures, constipation, urinary retention or incontinence, impotence, psychological distress and problems with social relationships. Palliative care and support must be multi-faceted and responsive to the needs of individual patients; conventional care alone is not sufficient.

Patients with advanced disease can receive high quality care in a variety of settings, including hospitals, hospices, and their own homes, so long as there is adequate input from specialists who can offer pain and symptom control when required. Older primary

[60] World Health Organisation. *Cancer Pain Relief*. Geneva: World Health Organisation, 1996.

studies showed poorer management of pain for patients in their homes than in the institutional environment, but this appears to have improved in recent years.(B)

Palliative home care teams have small but positive effects on outcomes for both patients and carers. Pain, symptom control and levels of satisfaction can be improved by specialist home care team involvement.(B)

A systematic review of studies which compared "standard home care" with interventions based in hospitals, hospices or the community, suggests that standard care alone may not be sufficient. Additional interventions may be required for patients who remain at home, to control physical symptoms and reduce the need for re-admission. Favourable results were reported in studies of palliative home care teams when members held regular meetings and visited patients at home.(B)

Current NHS services

The Department of Health undertook a national stocktake of palliative care services across England in 1999. The results of this survey, mapped in collaboration with the Office of National Statistics, is available on the Department of Health cancer website (www.doh.gov.uk/cancer). For all categories of provision – day care, home care, hospice and specialist palliative in-patient care, and hospital support – a majority of health authorities in every region reported shortages. Only 14 of 99 health authorities were able to report adequate provision of all types of service.

D. Measurement

Structure

- Documented local clinical policies to guide referral for palliative care.
- Evidence that appropriate palliative care services are available in hospitals, hospices and the community, and that their resource and staff levels are adequate.
- Appropriate facilities for rehabilitation and palliative care.
- Specialist palliative care teams which meet specifications given in the NHS *Manual of Cancer Service Standards* in England, and the Minimum Standards for Specialist Palliative Care as applied to Cancer Services in Wales.
- Systems to permit 24-hour access to specialist advice on palliative care.

- Arrangements to facilitate prompt access to specialist interventions, including specialist pain control.
- Availability of rapid access to radiotherapy and orthopaedic services.
- Evidence of effective communication systems for information-sharing between all levels of the service and all those involved in individual patient management.

Process

- Audit of home visits made by palliative care team members.
- Evidence of regular meetings of palliative care teams.
- Audit of time to provision of specialist palliative interventions.
- Audit of speed of provision and appropriateness of equipment supplied by occupational therapists to patients in the community.

Outcome

- Audit of symptom control.
- Proportion of patients who suffer bone fractures or spinal cord compression.

E. Resource implications

Improved co-ordination of care could reduce costs per patient, but improving access to specialist palliative care services is likely to require increased resources in many areas. These changes are not specific to patients with any particular type of cancer.

Prostate cancer

Profound changes are anticipated in services for prostate cancer and it is recognised that, for many Trusts, establishing the structures described in this Manual will be a gradual process. Full implementation of the recommendations below may only be possible when other components of the service, in particular the multidisciplinary team (MDT) structure, have been set up. These recommendations, therefore, describe services towards which networks should work.

A. Recommendations

Early (organ-confined) prostate cancer

The prostate cancer service should be capable of providing active monitoring, radical surgery, radiotherapy, or hormone treatment for men whose cancer is believed to be confined to the prostate. All possible management options should be discussed with patients.

There is no consensus on the optimum form of management for these patients. Although observational studies suggest that radical treatment can improve long term survival rates in particular patient groups, this evidence is by its nature subject to bias. In addition, the uncertain benefits of radical interventions must be balanced against the risk of lasting adverse effects. Research – both randomised controlled trials and audit of outcomes outside the context of clinical trials – is essential to clarify the role of each form of treatment and should be supported.

Different men vary greatly in the value they ascribe to potential outcomes. The treatment each patient receives should be tailored to fit his individual values and situation, so it is essential that patients are actively involved in decision-making. This requires that they receive adequate and accurate information, both through meetings with members of the MDT, and in published forms that they can study at home. Patients should be given sufficient time to consider all the options available to them. (See Topic 3, *Patient-centred care*.)

Active monitoring

Active monitoring aims to detect disease progression as early as possible. This allows intervention to be avoided when the patient's condition is stable, whilst permitting prompt action to control symptoms and reduce the risk of serious problems when the cancer is progressing.

The option of active monitoring should be discussed with all men whose tumours are believed to be confined to the prostate. This form of management is particularly suitable for those who, because of advanced age or poor general health, have a life expectation of less than 10 years. Monitoring should involve regular clinical review and assessment of the prostate using prostate specific antigen (PSA) and digital rectal examination (DRE). When symptoms or rising PSA levels suggest that the cancer is progressing, the case should be reviewed by the MDT and treatment options again discussed with the patient. Patients who are considering active monitoring should be encouraged to participate in EORTC trial 30991, which is randomly allocating men with early prostate cancer to hormone therapy or "watchful waiting".

This strategy requires well co-ordinated shared care involving urological services, palliative care, and primary care teams. Patients should be managed in accordance with protocols which should be agreed by all relevant MDTs in the network and disseminated to all those who are likely to be responsible for their care.

Hormone therapy

The possibility of hormone treatment – orchidectomy (surgical castration) or treatment with an anti-androgen or Luteinising hormone-releasing hormone (LHRH) agonist – should be discussed with these patients.

Surgery

Radical prostatectomy should be discussed with men whose tumours are confined to the prostate and who would be expected to live for more than 10 years if they did not have prostate cancer.

Patients for whom surgery is being considered should be treated by specialist multidisciplinary urological cancer teams, normally based at cancer centres. (See Topic 1, *The urological cancer network and multidisciplinary teams.*) Ideally, all radical prostatectomies undertaken in each network should be carried out by a single team. Radical prostatectomy should not be carried out by teams which carry out fewer than 50 radical operations (prostatectomies and cystectomies) for prostate or bladder cancers per year.

This level of work-load is currently unusual in the UK and a transition period is likely to be required for re-organisation of services before the criterion of 50 operations can be met. In the meantime, surgeons who currently carry out fewer than five radical prostatectomies per year should refer patients to designated surgeons who will become more specialised in this type of surgery.

Laparoscopic prostatectomy is not recommended outside the context of well-designed clinical trials supervised by experienced surgeons. Proficiency in this procedure requires considerable practice and inexperienced surgeons can cause serious harm.

Radiotherapy

The option of radiotherapy (external beam or brachytherapy) should also be discussed with men with early disease. Conformal radiotherapy, using multileaf collimators which allow treatment using an irregularly shaped beam, is the optimum mode of delivery and all centres should aim to provide this form of treatment. Radiotherapy should be given by specialist clinical oncologists from, or in, the centre. Outcomes, including adverse effects, should be carefully monitored.

As with other forms of radical treatment for prostate cancer, the place of brachytherapy is uncertain. However, it offers the advantages of speed and convenience and there is demand from some patients for this form of treatment. Centres which offer brachytherapy should evaluate their outcomes with particular care. A large scale, nationally or internationally co-ordinated, research project is necessary to assess the effectiveness of brachytherapy for localised prostate cancer. A randomised intergroup trial comparing brachytherapy with radical surgery is being organised by the National Cancer Institute of Canada and the American College of Surgeons Oncology Group (NCIC CTG Study PR.10/ACOSOG Z0070). This will evaluate the advantages (equivalent disease control with reduced morbidity) in patients with localised disease (T1c or T2a N0 M0), claimed by enthusiasts for brachytherapy. UK participation in this study should be strongly encouraged through the appropriate National Cancer Research Institute (NCRI) Clinical Studies Groups and clinical research networks.

Continuing care

There should be documented clinical policies for shared care for men with prostate cancer managed in the community. These policies should specify criteria for referral back to the local urological cancer team. Telephone follow-up by the specialist nurse in the urological cancer team who is familiar with the patient's case should be offered to appropriate patients.

Primary care teams, patients and carers should have access to the specialist nurse, who should provide telephone advice and arrange rapid referral to the treatment team when required.

Locally advanced disease

Hormone therapy, with or without external beam radiotherapy, should be discussed with men whose tumours extend beyond the confines of the prostate. Suitable patients should be encouraged to enter the MRC PRO7 trial of hormone treatment with or without radiotherapy.

Metastatic disease

Hormone therapy

Men with advanced or metastatic prostate cancer should be offered orchidectomy (surgical castration) or treatment with an anti-androgen or LHRH agonist. All these options should be discussed with patients, who should be encouraged to make a choice based on their personal values and the likely balance of benefits and adverse effects. Hormone treatment should not be deferred if there is a risk of spinal cord compression. Maximum androgen blockade is not normally recommended.

Patients with metastatic disease in remission should remain under careful observation so that treatment can be provided promptly when further symptoms develop.

Treatment for bone metastases

For some patients with prostate cancer, bone pain is the first symptom. Short courses of radiotherapy should be available for patients with bone metastases. Treatment with radioisotopes should be considered for men with bone pain at multiple sites. There is growing evidence that bisphosphonates may be beneficial for men with prostate cancer but no definite recommendations can yet be made.

Severe backache should be regarded as a warning of possible spinal cord compression. Patients should be informed about this risk and about the importance of contacting the MDT if they experience new or worsening backache. There should be systems to permit rapid access to diagnosis and treatment for patients who could be at risk of fracture or spinal cord compression.

Other palliative interventions

Chemotherapy should be considered for men with symptomatic hormone-refractory prostate cancer and trials of this form of therapy should be supported. Palliative radiotherapy should also be available.

B. Anticipated benefits

Appropriate management of prostate cancer should maximise patients' quality of life and may improve their life expectancy. Well-designed research studies and better routine monitoring of outcomes will help to provide the information necessary to judge which forms of treatment are most suitable for individual patients.

Concentration of services for patients with early tumours in the hands of highly-skilled specialists is likely to increase the probability of appropriate treatment and decrease the frequency and severity of

adverse effects. Wider use of conformal radiotherapy will permit better disease control with lower levels of adverse effects among men who undergo radiotherapy.

Improved access to treatment for metastatic prostate cancer is likely to reduce both patients' suffering and the burden on the health service of catastrophic fractures and spinal cord compression.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Early prostate cancer

Radical interventions compared with active monitoring

Radical treatment – prostatectomy or radiotherapy – can control local symptoms of prostate cancer but can also cause significant complications, particularly impotence, proctitis and incontinence. There is no reliable evidence showing whether or not it improves survival. Large-scale prospective randomised trials are essential to resolve uncertainty about the relative effectiveness of different forms of treatment.

A new trial, ProtecT, has been set up by the Health Technology Assessment programme to compare outcomes in men with screen-detected prostate cancer treated with radiotherapy, radical prostatectomy or active monitoring. This is expected to produce important data and should be supported. As its starting point, the ProtecT trial assumes absolute equipoise between active monitoring, radical prostatectomy and radical radiotherapy, for all patients irrespective of age or tumour grade.

Other RCTs comparing active monitoring with radical treatment are in progress outside the UK, but these will not produce useful data on survival rates for some years.

Many non-randomised studies suggest that prostate cancer-specific survival rates are higher among men who undergo radical prostatectomy, but a variety of sources of bias – all of which tend to exaggerate the possible survival benefit associated with surgery – have been identified. First, there is selection bias: the fittest men tend to be selected for surgery. Second, studies have generally been analysed according to treatment received rather than intention to treat; consequently, the benefits of radical prostatectomy have been over-estimated. Finally, there is evidence of bias in reporting cause of death, such that deaths among patients who have undergone radical treatment for prostate cancer are significantly more likely to be

ascribed to other forms of cancer than would be expected in this population.(B) This would create the illusion of improved prostate cancer-specific survival rates even if radical treatment had no effect at all.

A US population-based study using information on almost 60,000 men in the Surveillance, Epidemiology, and End Results (SEER) database has assessed the effects of different management strategies on survival. Although this is weak evidence, it is the best currently available. Outcomes were sub-divided by tumour grade, which is the most important predictor of progression in prostate cancer. Overall, the risk of dying from prostate cancer was 10 times higher among men with high-grade tumours (Gleason score 8-10) than those with low-grade tumours (Gleason score 2-4).(B) This pattern is consistent with results reported in other studies.

The effectiveness of radical treatment varied with tumour grade. There was no difference in the 10-year prostate cancer-specific survivals for men with low-grade tumours, whether they elected to undergo radical prostatectomy or were managed conservatively. However, for men with high-grade tumours, survival rates were higher among those in the radical surgery group. Outcomes for men with intermediate grade tumours fell roughly mid-way between these extremes. Survival benefits were also reported for radical radiotherapy, but only among men with higher-grade tumours, and the effect diminished after five years.(B)

These results are only suggestive, not conclusive. They are not derived from randomised data and there are potential sources of bias. For example, the treatment given to patients who relapsed is not recorded: many probably had radiotherapy; and prostate cancer-specific death rates may not be reliable (see above). In addition, there was no adjustment for co-morbidity. Higher levels of co-morbidity would be expected in the conservative management group. Finally, there have been improvements in radiotherapy techniques, which may produce better outcomes in men who receive this form of treatment today.

Comparisons between radical treatment modalities: adverse effects

Studies of the impact of radical treatment on urinary and sexual function are consistent in reporting that surgery is more likely to lead to incontinence and/or impotence than radiotherapy.(B) Men who undergo surgery are less likely to be incontinent or impotent before treatment than those treated by radiotherapy, but are significantly more likely to become so afterwards. Bowel problems (proctitis) are common after external beam radiotherapy (EBRT), but are less severe with conformal radiotherapy than older methods of delivery.(A)

Surgery
Reported peri-operative mortality rates for radical prostatectomy range from 0.2% to 1.2%.(B) Reported rates for other adverse effects vary widely, but in general, they are considerably lower in case-series than in population studies.

A study of 1,291 men identified from the SEER registry revealed that only 32% of men had total urinary control (compared with 78% at baseline) and 44% were impotent (baseline 5%) two years after radical prostatectomy.(B) Much better results have been reported by expert surgeons, but it must be acknowledged that the patients included in such series may be carefully selected. Neither figures from case-series nor data derived from clinical trials can be regarded as realistic guides to outcomes in wider clinical practice.

Radiotherapy
Radiotherapy for localised prostate cancer can be delivered either by implantation of radioactive seeds (brachytherapy) or external beam. There is growing evidence that higher radiotherapy doses lead to better progression-free survival rates than lower doses, although the impact on overall survival is as yet unknown.(A) Two randomised studies have shown that conformal radiotherapy is associated with lower treatment morbidity than conventional radiotherapy; higher doses of radiotherapy can only be given when conformal radiotherapy is used.

Brachytherapy causes similar complications to external beam treatment and although adverse effects are believed to be less common, there have been no randomised trials to confirm this. Recent reports suggesting excellent outcomes are based on case-series and as such, may be seriously biased.

A US study of treatment given under Medicare two to three years after brachytherapy suggests that urinary obstruction was fairly common; 8.3% of the 2,124 men identified received surgery (usually trans-urethral resection of the prostate (TURP)) for bladder outlet obstruction.(B) Current techniques deliver lower doses of radiation to the urethra so this problem may occur less often; however, reliable information on outcomes is not available. The risk of incontinence associated with brachytherapy depends on previous surgery: TURP increases the incontinence rate from 1% to 12.5%,(B) and previous TURP is now regarded as a contra-indication to brachytherapy; but it is not clear whether brachytherapy increases the risk of incontinence if TURP is carried out subsequently. Reported impotence rates vary from zero to 38% and increase with time after treatment.(B)

Hormone therapy
The rate of progression of prostate cancer depends, in part, on the level of male hormones (androgens). This is the rationale for treatment with hormone manipulation using drugs, surgery

(orchidectomy), or both. Table 11 shows the main methods used, with the names of the drugs of each type available in the UK. There have been several meta-analyses of RCTs of different methods of manipulating androgen levels; these are consistent in showing that no form of medical treatment is more effective for disease control than orchidectomy.(A)

Table 11. Methods and agents used for hormone manipulation in prostate cancer

Method	Drug names	Advantages	Disadvantages
Surgical castration – orchidectomy	n/a	Low cost in long term. No treatment is more effective.	Irreversible; unacceptable to some men. Leads to loss of libido and symptoms similar to those of female menopause, such as hot flushes and osteoporosis.
"Medical castration" with LHRH or gonadorelin analogues	buserelin, goserelin, leuprorelin, triptorelin	Reversible. Probably as effective as orchidectomy	Loss of libido and hot flushes – adverse effects generally similar to surgery but wider range of symptoms. Initial stimulation of testosterone production can cause "tumour flare".
Anti-androgen treatment	bicalutamide, flutamide, cyproterone acetate (CPA)	Can be used with gonadorelin analogue to reduce tumour flare. Less depression of libido, fewer hot flushes than with other forms of treatment.	Loss of libido and hot flushes – adverse effects generally similar to surgery but wider range of symptoms. May be less effective than orchidectomy or LHRH analogues when used alone. Common adverse effects include breast pain and swelling (gynaecomastia) and risk of liver damage.

Hormone therapy begun immediately after diagnosis of locally advanced disease significantly reduces the rate of tumour progression and delays the onset of metastatic disease.(A) Hormone treatment can improve local disease control when used in combination with surgery when the cancer has invaded lymph nodes.(A) There is also accumulating evidence that adjuvant or neo-adjuvant hormone therapy, given with radiotherapy, can delay the progression of locally advanced disease. Some studies have reported survival benefits, but these may only be significant in specific sub-sets of patients.(A) It is not clear whether hormone therapy alone might be as effective as hormone treatment plus radiotherapy.

The first results of a very large study (n=8,113), assessing the effectiveness of adjuvant hormone therapy in combination with surgery, radiotherapy or watchful waiting, suggest that bicalutamide can significantly reduce the rate of tumour progression and delay the development of metastatic disease.(A) Survival data will not be available for some years.

This form of treatment can produce significant adverse effects, particularly loss of libido, impotence and hot flushes (see Table 11). Fewer patients withdraw from treatment because of adverse events with LHRH analogues than with non-steroidal anti-androgens (0-4% versus 4-10%). Treatment with an anti-androgen alone seems to have the least impact on libido and is least likely to cause hot flushes. Mono-therapy with an anti-androgen may be less effective for controlling the cancer and this type of drug can cause a variety of other adverse effects, particularly breast swelling and pain.(A)

Recent meta-analyses suggest that maximum androgen blockade – treatment with anti-androgens in addition to surgical castration or androgen suppression by pharmacological means – is unlikely to produce clinically significant survival benefits.(A) Maximum androgen blockade causes more severe adverse effects than monotherapy.(A)

Advanced disease

Radiotherapy for locally advanced and metastatic disease

External beam radiotherapy (EBRT) can help to relieve the symptoms of locally very advanced prostate cancer.(B) In addition, EBRT can reduce pain caused by bone metastases. Over 40% of patients experience at least 50% pain relief, and just under 30% can expect complete pain relief after one month. A single fraction is often effective; there appears to be little difference in efficacy between different fractionation schedules and doses.(A)

Strontium-89, a radioactive isotope which is taken up preferentially by bone, can reduce pain in men who have multiple painful bone metastases. It is as effective as EBRT for pain relief and may be more effective than local field EBRT for delaying the onset of pain at new sites, albeit at the expense of haematological toxicity.(A) One study suggests that it may improve survival when given with chemotherapy, but further research is needed to confirm this finding. Samarium-153 appears to offer similar benefits to Strontium-89 (A) but the two have not been directly compared in an RCT.

Palliative chemotherapy

The evidence on chemotherapy for men with advanced prostate cancer is poor, but it seems that some patients do benefit. This issue is being addressed by a number of ongoing trials using a range of agents including taxanes. One RCT found reduced pain scores after mitoxantrone/prednisolone chemotherapy in men with hormone-

refractory disease, and a second study suggested small but significant improvements in time to progression, with a trend towards improved quality of life.

There is some evidence suggesting that bisphosphonates may also be beneficial, but no definite conclusions can yet be drawn.

Current practice in the NHS

A survey of consultant urologists and general surgeons with an interest in urology was carried out in 1996 to gather information on the treatment of prostate cancer in the UK. Despite reminders, fewer than half responded, so the sample cannot be considered representative. Nevertheless, the findings give cause for concern for three main reasons: first, they suggest that many clinicians appear to hold exaggerated views of the value of radical treatment and are unduly reluctant to recommend active monitoring (observation); second, they reveal that some clinicians were giving ineffective forms of treatment; and third, few respondents referred symptomatic patients with metastatic disease to oncologists or palliative care specialists.

Radical treatment, usually radiotherapy, was favoured by consultants for the majority of patients – including those with T1 (localised) tumours and patients with asymptomatic disease. Observation was only the preferred option for patients aged 70 or more with well-differentiated early-stage disease. Even in this situation, 31% of respondents thought radical treatment would be more appropriate.

Taken as a whole, this survey suggests that radical treatments are recommended for many patients despite the paucity of evidence for their effectiveness or appropriateness.

D. Measurement

Structure

- Availability of access to brachytherapy at specified facilities.
- Availability of conformal radiotherapy.
- Systems for rapid access to treatment for potential spinal cord compression or fractures due to bone metastases.

Process

- Evidence that MDTs offer patients full information about treatment options and that they involve patients in decision-making about treatment, except if patients refuse opportunities for such involvement or suffer from such severe cognitive impairment that they are unable to understand treatment options.

- Evidence that patients with localised prostate cancer are given even-handed advice by the MDT on all treatment options.

- Evidence that the total annual number of radical prostatectomies plus cystectomies carried out for cancer by any team offering radical surgery is at least 50.

- Markers of quality of radical surgery, including the proportion of excised specimens with clear margins and blood transfusion requirements.

- Evidence that all forms of hormone therapy, including surgical castration, are discussed with patients.

- Evidence that patients given long-term hormone treatment are regularly reviewed by the treatment team.

- Evidence that patients have continuing access to a specialist nurse.

- Time between referral for palliative radiotherapy and treatment.

- Evidence that active monitoring includes regular PSA measurement.

- Evidence that men under active monitoring whose PSA levels show a sustained increase are given an opportunity to discuss treatment options with their MDT.

Outcome

- Short, medium and long-term survival rates of patients who undergo radical surgery, with information on cancer stage, co-morbidity, age and other features of case-mix. These data should be recorded for each surgeon.

- Short, medium and long-term survival rates of patients who undergo other types of treatment (including active monitoring), with information on case-mix.

- Major complication rates after surgery, radiotherapy or brachytherapy.

- Audit of quality of life, impotence, incontinence, bowel problems and hospital admissions one year after treatment (including patients under active monitoring).

- Audit of short-term and long-term adverse effects of treatment.

E. Resource implications

The resource consequences of the recommendations for the diagnosis and treatment of prostate cancer come under the Topic Areas for *Diagnosis and assessment* and *MDTs*. In addition, and not as a result of this guidance, the rising numbers of prostate cancer patients are likely to cost between £15.4 million and £43.8 million (see Appendix 1, *Economic implications of the guidance*), depending on the scale of the increase in incidence and the rate of PSA testing in the population at risk.

Testicular cancer

There are already specialist NHS services for the management of men with testicular cancer and outcomes are generally good, with 95% five-year survival rates even in metastatic disease. This is the only solid tumour type for which the vast majority of patients are cured. The recommendations below therefore define services which will build on, and improve, current practice.

A. Recommendations

A centralised service, described in outline in Topic 1 (*The urological cancer network and multidisciplinary teams*), is particularly appropriate for testicular cancer. Small and medium sized cancer networks should combine to offer a specialist service for a population base of two to four million. This supra-network service, based in selected cancer centres, would be expected to manage around 50-100 new patients each year.

Initial diagnosis and treatment (orchidectomy) should normally be carried out by a local urological cancer team; exceptions are discussed below. A full range of testicular prostheses should be available. All patients should be referred within 24 hours of surgery to designated specialist testicular cancer multidisciplinary teams (MDTs) for further assessment, and pathology should be reviewed by the specialist pathologist at the centre to which the patient is referred.

All patients should have computed tomography (CT) scans of the abdomen and pelvis. A CT scan of the chest is also necessary for patients with teratoma.

The following patients should be referred immediately (before orchidectomy) to the specialist MDT: those with obvious metastatic disease and very high tumour markers, lung metastases, or germ cell tumours in the mediastinum, lower abdomen (retroperitoneum) or brain.

Treatment of early stage and locally advanced disease

Seminoma

Adjuvant radiotherapy to the para-aortic region is standard practice in most UK centres, and should be discussed with all patients with stage I seminoma.

Alternative options, such as a single cycle of chemotherapy or surveillance (i.e. further treatment only if there is evidence of recurrence), should not be offered unless outcomes are meticulously monitored and patients receive careful counselling about the importance of early detection of recurrence.

Chemotherapy should be available for patients with more advanced disease, but radiotherapy may be appropriate when metastatic spread is confined to abdominal nodes of less than 5cm diameter.

Non-seminomatous germ cell tumours
After orchidectomy, patients with stage I malignant teratoma or mixed seminoma/teratoma without high risk features should normally be managed by surveillance by the specialist team, following a strict protocol. These patients should be selected after review of tumour pathology by the specialist pathologist who deals with testicular tumours at the centre. Surveillance is only appropriate if the patient is well motivated to return for follow-up and an effective service is provided.

Adjuvant chemotherapy, normally two courses of bleomycin/etoposide/cisplatin (BEP), should be discussed with patients when high risk features such as blood vessel or lymphatic invasion are found. However, as three cycles of BEP are usually adequate to treat patients who relapse, surveillance is an appropriate option. The specialist testicular cancer team should review every case when treatment has been completed.

Metastatic disease (seminoma or non-seminoma)

Chemotherapy
Men with metastatic testicular cancer should normally receive BEP chemotherapy. Those with intermediate or poor prognosis disease should be encouraged to participate in large multi-centre studies designed to help define the optimum treatment for this group of patients.

Management of residual masses
A substantial proportion of men who have undergone chemotherapy for metastatic tumours will have residual masses after treatment. Specialist review of radiology and pathology results is important to assess these masses, which may require surgical excision. This surgery should be undertaken in specialist centres where designated thoracic surgeons are available when needed. About 150 patients per year require highly specialised surgery, which is currently undertaken in at least 12 centres in England and Wales. This should be reviewed. It is doubtful whether centres which carry out fewer than 10 procedures per year have the necessary expertise to continue.

Sexual issues and fertility

The potential impact of testicular cancer on sexual function and fertility should be discussed with patients at the time of diagnosis. The treatment team should be alert to the possibility of psychosexual and body image problems and allow adequate time for discussion of such issues.

Sperm storage (cryopreservation) should be offered to all patients who may wish to father children. This should be available before chemotherapy or radiotherapy to the contralateral testis.

B. Anticipated benefits

Survival rates are currently high and the form of service described here is designed to maintain these good outcomes. The main focus of ongoing research into the management of testicular cancer is to identify treatment regimes that produce minimum toxicity whilst still achieving high cure rates.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Specialised treatment

There is consistent evidence that institutions that treat larger numbers of patients achieve better outcomes in testicular cancer (B) (see Topic 1, *The urological cancer network and multidisciplinary teams*). This suggests that specialised management is important for all forms of this disease.

Stage I seminoma

Reported cure rates for stage I seminoma are over 96%, irrespective of whether patients are managed by adjuvant radiotherapy or surveillance.(B)

Adjuvant radiotherapy

Prophylactic radiotherapy to the retroperitoneum and pelvis can be used to reduce the probability of relapse after orchidectomy. This can cause significant gastro-intestinal adverse effects, including pain, diarrhoea, nausea and vomiting, especially when delivered to a dogleg field.(A) In the longer term, patients who undergo radiotherapy face an increased risk of second malignancies, cardiovascular and renal disease. Radiotherapy to a smaller (para-

aortic) field is less toxic than dogleg radiotherapy and just as effective.(A) Treatment-related nausea and vomiting can be largely controlled with $5HT_3$ antagonists.(A)

Early results of a large (n=1,600) MRC study comparing one cycle of carboplatin chemotherapy with radiotherapy are expected to become available in 2003.

Stage I non-seminoma

Surveillance after orchidectomy

About a quarter of patients managed by surveillance will relapse and require salvage treatment; this is normally sufficient to eliminate the disease.(B)

Chemotherapy for advanced testicular cancer (seminoma and non-seminoma)

Prior to the introduction of platinum-based chemotherapy in the mid 1970s, most patients with metastatic testicular cancer died of the disease. Now, almost all are cured with combination chemotherapy (usually BEP), but these drugs can cause severe adverse effects. Recent research aimed to clarify the optimum chemotherapy regime and identify that which would maximise survival rates whilst minimising toxicity.

Three questions have dominated recent trials. The first was the necessity for bleomycin, which, although effective, can cause serious, sometimes fatal, lung damage; the second was whether carboplatin is an effective substitute for the more toxic cisplatin; and the third concerns the value of high-dose or high-intensity chemotherapy.

1. How important is bleomycin?

An ongoing systematic review of randomised controlled trials (RCTs) has concluded that bleomycin is beneficial despite its toxicity. Drug combinations which included bleomycin led to higher remission and survival rates than similar combinations without bleomycin ($p<0.01$).(A)

Some other drug combinations seem to be as effective as BEP and offer alternative options when necessary, but no combination has yet been demonstrated to be significantly more effective. Ifosfamide appears to be as effective as bleomycin but is also toxic.(A)

2. Is carboplatin an effective substitute for cisplatin?

Carboplatin and cisplatin are different forms of platinum chemotherapy, but cisplatin is the more toxic of the two. Studies comparing these drugs have found that cisplatin is more effective, reducing both relapse and deaths due to testicular cancer.(A)

3. Is more chemotherapy better?

Studies designed to establish which regimes offer the highest survival rates with least toxicity have defined the most effective range of doses and delivery periods. Maximising the effectiveness of chemotherapy requires the use of optimum doses over the optimum time-period (achieving optimum dose-intensity). Although some non-randomised studies have suggested that higher doses of drugs or the addition of extra chemotherapeutic agents may improve outcomes, there is no convincing evidence from randomised trials that high-dose chemotherapy is actually more effective than doses of BEP currently used in Europe.(A) Maintenance chemotherapy does not improve survival, it merely increases toxicity.(A)

Surgery for residual masses

A study of long-term outcomes among men treated with chemotherapy at the Royal Marsden Hospital between 1979 and 1986 reported that 31% of men were left with residual masses, 15% of which contained active cancer.(B) Surgery to remove such masses can lead to long-term survival, but may require complex procedures such as combined thoraco-abdominal surgery.(C)

Sexual issues and fertility

Testicular cancer is usually diagnosed when men are in the most sexually active phase of their lives, when many still look forward to fatherhood. Some have impaired semen quality before treatment, but cryopreservation of sperm before chemotherapy, radiotherapy or surgery for residual masses offers the chance of fatherhood after treatment.

Around a third of men who have been treated for testicular cancer suffer loss of desire or problems with sexual function.(B) The cause appears to be more often psychological than physical, although problems with ejaculation ("dry ejaculation") are reported most frequently in the research literature.(B)

D. Measurement

Structure

- Quality criteria for specialist germ cell tumour services have been defined by the Tri-Regional Germ Cell Tumour Working Group.

- Facilities for sperm banking.

Process

- Evidence that patients are fully informed and involved in decision-making about treatment.
- Time between diagnosis and initial treatment.

Outcome

- Five-year survival rates of patients who undergo radical treatment, with information on cancer stage, co-morbidity, age and other features of case-mix.
- Audit of short-term and long-term adverse effects of treatment.

E. Resource implications

No resource implications specific to the recommendations in this topic have been identified.

Penile cancer

A. Recommendations

Because penile cancer is so uncommon, its management should be formalised, with a degree of specialisation similar to that for testicular cancer. Specialised penis cancer multidisciplinary teams (MDTs) should be established jointly by two to four neighbouring networks. Each of these teams should serve a population base of four million or more and expect to manage a minimum of 25 new patients each year. The team should include members of the specialist urological cancer team who work in the cancer centre within which it is based, and it should also have access to expertise in plastic surgery.

Networks should agree referral protocols for patients with penile cancer. These should ensure that each new case is reviewed by a specialist penis cancer team, and that men who are likely to require lymph node dissection or reconstruction of the penis are treated by this team. Other forms of treatment may be carried out by specialist urological cancer teams which do not specialise in penile cancer, but the penis cancer MDT which reviews the case should remain responsible for overall management.

Surgery or radiotherapy may be used to treat early (stage I) penile cancer. The choice of treatment should be discussed with the patient in a meeting that includes a surgeon, clinical oncologist and specialist nurse.

The role of chemotherapy in the treatment of penile cancer is currently uncertain, but a trial of palliative chemotherapy should be considered for patients with metastatic disease.

B. Anticipated benefits

It is anticipated that increasing specialisation in the management of penile cancer will enhance the probability that patients receive appropriate treatment. At present, patients with early disease may be treated more aggressively than necessary, whilst those with more advanced disease and affected lymph nodes may not receive adequate treatment. This is important because men with lymphatic metastases can sometimes be cured by lymph node dissection.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

No randomised trials of any aspect of the management of penile cancer have been identified. All the studies in this field are observational in design and most are retrospective, so the research evidence is weak.

Amputation is the most common form of treatment used for penile cancer, but penis conserving therapy, using conservative surgery, radiotherapy (sometimes in combination with chemotherapy), brachytherapy, or laser treatment, is used for selected patients with localised tumours. Local failure rates may be higher than with amputation, but prompt use of salvage therapy for recurrence seems to produce similar survival rates.(B) Similarly, it is not known whether prophylactic lymph node dissection or radiotherapy is better than surveillance and salvage treatment for patients who develop recurrence. Randomised trials are needed to compare these ways of treating penile cancer.

The prognosis is poor for patients with metastatic penile cancer. Non-randomised studies suggest that the disease may respond to chemotherapy but it is not clear what the optimum therapeutic regime or schedule might be.(B)

D. Measurement

Structure

- Systems to ensure that patients are promptly referred to a penile cancer MDT.
- Effective links between the penile cancer MDT and local MDTs which may provide treatment for these patients.
- Availability of appropriate expertise in penis reconstruction.

Process

- Evidence that patients are fully informed and involved in decision-making about treatment.
- Use of lymph node dissection in patients at high risk of lymph node metastasis.

Outcome

- Five-year survival rates for all patients, with information on cancer grade and stage, co-morbidity, age and other features of case-mix.

- Audit of short-term and long-term adverse effects of treatment.

E. Resource implications

No resource implications specific to the recommendations in this topic have been identified. There may be some support costs associated with the formalisation of supra-network MDTs. These have not been calculated, as the numbers involved are small.

Bladder cancer

A. Recommendations

Superficial tumours

Patients with newly diagnosed, apparently superficial, tumours should be treated by complete trans-urethral resection (TUR), which should be carried out by designated urologists in local district general hospitals (DGHs). After recovery from resection, these patients should normally have a single instillation of chemotherapy (mitomycin or epirubicin) or glycine into the bladder (intravesical therapy). They should be allocated to one of the groups described below when the results of pathological review are available.

Lower-risk superficial cancer (pTa G1 or G2 or T1, G1 or G2)

About 50% of newly diagnosed patients have superficial tumours which carry a relatively low risk of progression after treatment but the majority of tumours will recur locally in the bladder. Guidelines for the frequency and timing of follow-up cystoscopy should be agreed and adopted throughout each network.

High-risk superficial cancer (pTa G3, or T1 G3 tumours, extensive, recurrent or multifocal G2 tumours, and carcinoma in situ)

These tumours are associated with higher risk of progression and death, and many patients are not receiving adequate treatment at present. Protocols for treatment and follow-up of patients with high-risk superficial tumours should be jointly agreed by the urological cancer multidisciplinary teams (MDTs) of each network and adopted throughout the network.

Although these patients may be treated – at least initially – by urologists who are members of local urological cancer teams, the options should be discussed with each patient in a joint meeting which includes a urologist, an oncologist and a nurse specialist who are also members of the MDT. The range of appropriate options may include intravesical treatment with bacillus Calmette-Guerin (BCG) or referral to the specialist urological cancer team for possible radical treatment. If the tumour fails to respond to BCG or recurs within a short time, radical treatment (normally cystectomy) should be offered. Patients with high-risk tumours should be encouraged, when

appropriate, to participate in randomised trials such as the MRC BS06 trial comparing radical radiotherapy with intravesical therapy.[61]

Muscle invasive tumours and locally advanced disease

All patients with invasive disease (pT2 and above) should be offered a joint meeting with a surgeon, oncologist, clinical nurse specialist, and palliative care specialist if appropriate, to discuss treatment options.

There is no clear-cut evidence for the overall superiority of surgery or radiotherapy; although surgery appears to offer better disease control, it has more severe adverse effects. There is an urgent need for a randomised trial comparing these treatment modalities.

Radical surgery

Radical surgery (cystectomy) should be available for patients with muscle-invasive tumours confined to the bladder. Although patients' general fitness should always be taken into account when radical treatment is being considered, age should not, of itself, be a bar to surgery.

Each network should agree clear guidelines on treatment and follow-up of bladder cancer which ensure that cystectomy is considered for patients with muscle-invasive or high-risk recurrent disease. Cystectomy is a complex operation which should be undertaken only by specialist surgeons working in cancer centres (see Topic 1, *The urological cancer network and multidisciplinary teams*). Ideally, all radical cystectomies undertaken in each network should be carried out by a single team.

Teams providing this form of surgery should carry out a cumulative total of at least 50 radical operations (cystectomies or radical prostatectomies) for bladder or prostate cancer per year. This level of work-load is currently unusual in the UK and a transition period is likely to be required for re-organisation of services before the criterion of 50 operations can be met. In the meantime, surgeons who currently carry out fewer than five cystectomies per year should refer patients to designated surgeons who will become more specialised in this type of surgery.

Surgical outcomes should be carefully audited and centres should aim to achieve 30-day mortality rates of 3.5% or less. Suitable patients should be offered bladder reconstruction or an alternative form of urinary diversion; facilities for reconstruction should be available wherever cystectomy is carried out.

[61] Details available by email: bs06@ctu.mrc.ac.uk

Adjuvant and neo-adjuvant chemotherapy

It is not yet clear whether adjuvant or neo-adjuvant chemotherapy is beneficial for patients with bladder cancer. Patients at high risk of progression, such as those with tumour in lymph nodes, should be encouraged to participate in trials of these forms of treatment. Chemotherapy should be initiated only by an oncologist member of the specialist MDT treating the patient.

Radical radiotherapy

Radical radiotherapy is appropriate for patients who are not sufficiently fit for surgery or who wish to avoid cystectomy. Patients who have had radiotherapy but would be sufficiently fit to undergo surgery should be followed up systematically and regularly so that salvage cystectomy can be offered if the tumour recurs. Neo-adjuvant radiotherapy – that is, lower dose radiotherapy given shortly before radical cystectomy – is not recommended outside the context of a formal clinical trial.

Metastatic disease

A trial of palliative chemotherapy should be considered for patients with metastatic disease; chemotherapy can relieve symptoms in patients who respond.

Short courses of radiotherapy should be available both for palliation of symptoms of advanced disease in the pelvis and for problems such as bone pain which may be caused by metastatic cancer. Services for management of bone metastases are discussed in the context of prostate cancer (see Topic 5, *Prostate cancer*).

B. Anticipated benefits

When these recommendations are implemented, patients with bladder cancer will be more likely to receive effective treatment – particularly cystectomy and bladder reconstruction when appropriate. This will improve both survival time and quality of life among patients with invasive tumours.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Superficial cancer

Intravesical therapy

There is strong evidence from a series of meta-analyses of randomised controlled trials (RCTs) that intravesical therapy (bladder irrigation given after trans-urethral resection) delays recurrence of superficial bladder cancer. Intravesical chemotherapy reduces the risk of local recurrence by around 50% for one to two years after initial treatment, and the proportion of patients who remain disease-free at eight years is increased by 8%.(A)

Intravesical treatment with BCG also reduces tumour recurrence, and may be more effective than intravesical mitomycin C (the chemotherapeutic agent used most frequently) for higher-risk patients.(A) There is currently no evidence to show that intravesical treatment improves long-term survival and no significant differences have been found between agents in effects on disease progression or survival.(A)

The most common side-effect of intravesical treatment with chemotherapeutic agents or BCG is local inflammation in the bladder or urethra, leading to problems with urination such as frequency and urgency, haematuria and pain. Systemic adverse effects such as 'flu-like symptoms and fever are particularly associated with BCG and can be serious.(A)

Results from an MRC RCT suggest that post-operative treatment with glycine, which is not toxic, can also produce sustained benefits, reducing recurrence rates at five years by 6% (from 62% to 56%, p=0.05).(A) There have been no randomised trials comparing glycine with other agents.

Follow-up of patients treated for superficial bladder tumours

Follow-up may involve cystoscopy and/or ultrasound imaging of the bladder. There is no reliable evidence to show what the most appropriate follow-up strategy might be. Small-scale observational studies have reported that most recurrences occur within two years of initial treatment.(B)

An RCT comparing two follow-up schedules for patients treated for superficial bladder cancer found no difference in clinical outcomes.(A) A cost-effectiveness study reported that frequent cystoscopy produced no clinically meaningful advantage over less frequent follow-up, and that significant financial savings could be made by reducing follow-up. It was estimated that each cystoscopy led to one additional day of life.

Muscle-invasive disease

Surgery (radical cystectomy)

Surgeons with a special interest in uro-oncology working in NHS hospitals have reported peri-operative mortality rates of under 2% after cystectomy. Recent audit data from Newcastle show a post-operative death-rate of just 1.3% in a series of 300 consecutive patients who underwent cystectomy between 1999 and 2001.(B)

These results compare favourably with those reported by international centres of excellence, but they are unlikely to be representative of outcomes in most NHS hospitals. Fewer than 5% of hospitals which undertake cystectomy do as many in a year as Newcastle. Few surgeons, therefore, are able to develop the level of skill required to achieve such a low mortality rate in the context of current service arrangements. Although there is no clear evidence of a volume effect in outcomes after radical cystectomy, there is for radical prostatectomy (see Topic 5, *Prostate cancer*, and Topic 1, *The urological cancer network and multidisciplinary teams*), and for many other types of radical surgery for cancer.

In a US series which included over 1,000 patients with muscle-invasive bladder cancer who underwent radical cystectomy with iliac lymphadenectomy, the peri-operative death-rate was 3% and the overall survival rate was 66% at five years.(B) Whilst these results are impressive, it is likely that the patients were carefully selected.

Studies from the UK and elsewhere have demonstrated that there is no relationship between patients' age and mortality or morbidity associated with cystectomy. Co-morbidity and tumour grade, rather than age, are the important predictors of outcome.(B)

Radiotherapy

Radical radiotherapy can lead to long-term survival in patients with invasive bladder cancer.(B) There is currently no clear evidence to show whether radiotherapy is more or less effective than surgery for preventing disease progression and death from bladder cancer when either treatment modality could be used. There is evidence suggesting differences in outcome between these modalities, but some studies favour surgery whilst others do not. This could reflect wide variability between centres in techniques, skilled staff, and equipment.

A retrospective study of patients treated in Yorkshire between 1993 and 1996 found that, despite a 30-day death rate of 3%, three-month mortality rates were lower after radiotherapy (n=302) than after surgery (n=96), at 1.4% versus 8.3%, respectively. Five-year survival rates were similar, at 37.4% in the radiotherapy group (with or without salvage cystectomy), versus 36.5% after initial surgery. Another UK study (n=120) reported an overall median survival time of five years after radical radiotherapy.(B)

In patients whose disease has advanced beyond the bladder itself, surgery may not be an option. Radiotherapy has the advantage of leaving the bladder intact but can cause other adverse effects; one study of morbidity after radical radiotherapy found that 8% of patients had proctitis and 4% had cystitis a year later. The consequences of surgery may be more distressing for some patients, however; a study published in 1989 reported that all male patients who had undergone cystectomy were impotent, compared with 36% of those who had had radiotherapy; in addition, patients treated by surgery were more likely to complain of fatigue six months after treatment.(B)

A meta-analysis of three RCTs comparing pre-operative radiotherapy plus radical surgery with radical radiotherapy followed by salvage cystectomy for recurrence, suggests that patients whose primary treatment is surgery are almost twice as likely to become long-term survivors as patients treated by radical radiotherapy.(A) Mean five-year survival rates were 36% among patients treated by pre-operative radiotherapy and radical cystectomy and 20% in the radical radiotherapy/salvage cystectomy group. Another meta-analysis, of four RCTs, found that pre-operative radiotherapy followed by surgery does not improve survival, compared with surgery alone.(A)

The studies in these meta-analyses involved less sophisticated treatment techniques than are available today, and it is possible that the findings would be different now. A well-designed RCT comparing modern surgery with modern radiotherapy (with or without neo-adjuvant chemotherapy) is badly needed.

Chemotherapy

The effectiveness of chemotherapy is uncertain. Meta-analysis of individual patient data from four RCTs shows no significant survival benefit from neo-adjuvant or concurrent chemotherapy in combination with radical surgery or radiotherapy for locally advanced bladder cancer.(A) A more recent European study of neo-adjuvant cisplatin methotrexate vinblastine (CMV) chemotherapy also shows no significant benefit.(A) By contrast, a recent North American study of methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) followed by cystectomy has reported significantly higher survival rates in the chemotherapy arm, with estimated median survival times of 6.2 years in the MVAC arm, compared with 3.8 years after cystectomy only: a hazard ratio 0.74 (95% CI: 0.55 to 0.99, p=0.027).(A) The research evidence on adjuvant chemotherapy is also inconclusive. Randomised trials are in progress and should be supported.

Advanced disease

Radiotherapy

Radiotherapy can provide effective palliation for symptoms of locally advanced or metastatic bladder cancer. Two-thirds of symptoms were reported to be alleviated for a median period of nine months after

treatment with 35Gy in 10 fractions or 21Gy in three fractions. These two radiotherapy schedules were equally effective.(A)

Chemotherapy

Advanced bladder cancer can respond to chemotherapy but chemotherapy has not been compared with best supportive care in a randomised trial. The combination of cisplatin and gemcitabine is relatively well tolerated and appears to be as effective as the more toxic regimen, MVAC;(A) however, no randomised trial has reported response rates over 65% with any drug or combination, and median survival times are generally less than one year.(A)

Treatment in the NHS

Treatment in the NHS is currently fragmented and it appears that the level of expertise for effective management of invasive cancers is not available for the majority of patients. Few urologists treating patients with invasive bladder cancer work with oncologists.(B) Furthermore, the surgical management of bladder cancer does not appear to be adequate. Figures derived from hospital episode statistics (HES) and British Association of Urological Surgeons (BAUS) data suggest that fewer than half of the patients who might benefit from cystectomy actually receive this operation (see Appendix 1, *Economic implications of the guidance*).

A study of the management of muscle-invasive bladder cancer in the South West Region in 1989 and 1993 revealed that 46% of patients received no definitive treatment for their tumours. Just 12% of patients with T2 tumours and 19% with T3 tumours underwent cystectomy; the treatment most frequently used was radiotherapy (radical or palliative). Significantly more patients with T2 tumours received no definitive treatment than patients with T3 tumours, which suggests that many with T2 tumours, in particular, had sub-optimal treatment. There were no differences in co-morbidity between patients who received different types of treatment or no treatment at all, but their ages were significantly different: median ages of those who had primary cystectomy, radical radiotherapy and no definitive treatment were 64 years, 69 years, and 76 years, respectively.(B)

D. Measurement

Structure

- Network-wide protocols for treatment and monitoring of patients with bladder cancer; these protocols should specify intervals for follow-up cystoscopy after different stages and grades of disease.

- Access to an MDT which includes surgeons with specialist expertise in cystectomy and bladder reconstruction.

- Systems for provision of rapid access to short courses of palliative radiotherapy.

Process

- Evidence that patients are informed and involved in decision-making about treatment, unless they refuse opportunities for such involvement or they suffer from such severe cognitive impairment that they are unable to understand treatment options.

- Evidence that patients with muscle-invasive or recurrent cancer are given even-handed advice by the MDT on radical treatment options.

- Evidence that each surgeon responsible for cystectomy does a large enough number of these operations each year for meaningful audit of individual outcomes.

- Evidence that the total annual number of cystectomies plus radical prostatectomies carried out for cancer by any team offering cystectomy is at least 50.

- Markers of quality of radical surgery, including the proportion of excised specimens with clear margins and blood transfusion requirements.

- Proportion of patients who receive each form of treatment, stratified by tumour stage and grade, age and co-morbidity.

- Time between diagnosis and initial treatment.

Outcome

- Audit data demonstrating peri-operative mortality rates of <4% after cystectomy.

- Major surgical complication rates within three months of operation.

- Five-year survival rates for all patients, with information on cancer grade and stage, co-morbidity, age and other features of case-mix.

- Audit of short-term and long-term adverse effects of treatment.

E. Resource implications

The estimated costs of centralisation of radical cystectomy are combined with prostatectomy (see Topic 1, *The urological cancer network and multidisciplinary teams*).

Kidney cancer

The information below is primarily concerned with renal cell cancer. Patients with less common forms of kidney cancer should be referred to specialist urological cancer teams for treatment.

A. Recommendations

All patients who are sufficiently fit to undergo surgery should be offered radical nephrectomy (except those with small tumours – see below); this should be considered even when there is metastatic disease. Usually, nephrectomy is a relatively straightforward procedure which can be safely carried out by the local urological cancer team. Although surgery is normally the only treatment necessary for localised tumours, oncologists should be involved in discussions about the management of all patients.

Probably 80% of patients with kidney cancer can be managed by local cancer teams, but adequate assessment using appropriate imaging-computed tomography (CT) or magnetic resonance imaging (MRI) – is essential to identify those who should be referred for specialist treatment at cancer centres. (See Topic 2, *Diagnosis and assessment.)*

Patients who should be managed by specialist urological cancer teams at cancer centres include the following:

- Those whose tumours have, or may have, invaded the renal vein or vena cava, or which may involve the heart;
- Those with limited metastatic disease which might be amenable to resection;
- Those who have bilateral disease or who will require dialysis;
- Patients with von Hippel-Lindau disease or hereditary papillary tumours.

Patients with small tumours for whom nephron-sparing surgery may be possible, should be discussed with a surgeon from a specialist urological multidisciplinary team (MDT). Referral to the centre is likely to be appropriate for these patients.

Treatment with immunotherapeutic agents (normally interferon alpha) should be available for patients with metastatic kidney cancer. Such therapy should be given by specialist oncologists with experience of its use, preferably in the context of a well-designed clinical trial. Patients should be encouraged to participate in open discussions with members of the MDT about the balance of potential harm and benefit associated with different therapeutic options.

When a patient has not undergone surgical resection, the nature of the tumour should be confirmed by biopsy before anti-cancer therapy is offered.

B. Anticipated benefits

Surgery is usually curative in early disease, and may be curative even when there is limited metastatic disease. Nephrectomy may also improve outcomes in more widespread metastatic disease. Immunotherapy can increase survival time in metastatic disease and offers the hope of complete remission for a small minority (around 5%) of patients.

C. Evidence

Note: The reliability and quality of evidence supporting the recommendations is graded A, B and C, where A is the strongest evidence. The grading taxonomy is explained in Appendix 2.

Surgery

There have been no randomised studies comparing partial nephrectomy with radical nephrectomy, but evidence from observational studies suggests that some patients survive for many years after partial nephrectomy without evidence of recurrent cancer.(B)

Radical nephrectomy is often curative in early stage kidney cancer; non-randomised studies report relapse rates of 20-30%.(B) It also has a palliative role, reducing symptoms, thereby presumably improving quality of life. In some patients, surgical resection of a solitary metastasis after radical nephrectomy can lead to long-term disease control.(B) Radical nephrectomy, carried out prior to treatment with interferon, may improve survival even in metastatic kidney cancer; however, few patients in this situation are sufficiently fit to undergo major surgery.

Systemic therapy

Kidney cancer rarely responds to chemotherapy and few patients benefit from it. Adjuvant immunological therapies such as interferon alpha have also been found to be ineffective in early disease.

In patients with advanced or metastatic disease, however, interferon alpha can increase survival time despite adverse effects – most often a 'flu-like syndrome – in the majority of patients.(A) The strongest evidence for the effectiveness of interferon comes from two randomised trials. One compared interferon with medroxyprogesterone acetate in 335 patients and found that those in the interferon group lived 2.5 months (median) longer ($p=0.017$).(A) The second trial, which randomised 160 patients to vinblastine alone or in combination with interferon-alpha, reported median survival times of 38 weeks with vinblastine alone, compared with 68 weeks with both agents together ($p=0.049$).(A)

Around 5% of patients experience complete, and sometimes long-lasting, responses to treatment with interferon alpha or interleukin-2.(A) However, spontaneous remission is known to occur occasionally in untreated patients.(B)

A triple regime which includes interleukin 2, fluorouracil (5-FU) and interferon has been linked with the highest reported response rates both in non-randomised studies and in a randomised controlled trial in which it was compared with tamoxifen.(A) In the latter study, median survival in the triple-therapy group was 42 months, compared with 14 months in the tamoxifen group ($p<0.04$). However, toxicity problems increase when additional agents are given in combination with interferon, and other studies have failed to confirm that improved response rates are associated with enhanced survival.(A)

Research into a variety of forms of treatment, particularly combination therapies based on biological agents, is continuing.

D. Measurement

Structure

- Systems to ensure that appropriate patients are promptly referred to the specialist MDT.
- Availability of immunotherapy for patients with metastatic disease.

Process

- Evidence that patients are fully informed and involved in decision-making about treatment.

Outcome

- One and five-year survival rates for all patients, with information on cancer grade and stage, co-morbidity, age and other features of case-mix.

- Audit of short-term and long-term adverse effects of treatment.

E. Resource implications

No resource implications specific to the recommendations in this topic have been identified.

Appendix 1

Economic implications of the guidance

The cost implications of the urological cancer guidance can be divided into five main categories, listed below. Three are general categories of relevance to all urological cancers, while the last two are site-specific.

- Multidisciplinary teams (MDTs)
- Centralisation
- Specialist nurses
- Prostate cancer (incidence and other costs)
- Bladder cancer (diagnostic testing and treatment)

The increase in costs for the diagnosis and treatment of patients with kidney, testicular and penile cancers is likely to be small.

Multidisciplinary teams

Multidisciplinary team working is intended to ensure that patients benefit from the expertise of a range of specialists for their diagnosis and treatment, and that care is given according to recognised guidelines. For some cancers MDTs are well established in most Trusts, but for urological cancers even the concept of MDTs is not well-accepted in all Trusts.

While most centres hold regular MDT meetings, many have insufficient time to review all patients. At units the problems are more severe, with lack of administrative support being a particular problem. Both units and centres struggle to get a full team together, with the lack of availability of radiologists, pathologists and oncologists a special problem, exacerbated at units where they may only have visiting clinicians for a session every two weeks. The cost of ensuring that all MDTs have a co-ordinator, and of additional staff time for MDT meetings is estimated to be an additional £6.4 million per year.

Centralisation

The guidance recommends some centralisation of services, in particular requiring that MDTs which undertake radical prostatectomy and cystectomy should perform a combined total of at least 50 operations per year. Ideally there should be only one team per network, covering a population of at least one million people, undertaking this type of surgery. Analysis of the data shows that this is a radical change from current practice.

A1

To estimate the effect of greater specialisation of services for radical prostatectomy and cystectomy, an analysis was undertaken of the current (1999/2000) number of operations by hospital, network and region, and an estimate made of the proportion of work that will have to move from units to centres in each network in order to fulfil the requirements of the guidance. Different configurations are possible, so maximum and minimum scenarios were developed to cover the likely range. The central cost estimate is £4.4 million per year, with a range of £3.8 to £5.0 million.

The impact on Trusts taking on the work may be significant. Typically the number of prostatectomies and cystectomies they will undertake will more than double (from around 35 per year) as a result of the guidance, but increasing incidence of prostate cancer and more aggressive treatment of bladder cancer may also considerably increase the demand for these operations. This may mean that they have to increase their capacity by a factor of four or five, with knock-on effects on demand for theatre capacity and special care nursing.

Specialist nurses

The guidance emphasises the need for improved information and support for urological cancer patients, and the central role that nurse specialists should play in delivering more patient-centred care.

The current provision of nurse specialists is patchy. There are several specialist nurses who are providing the levels of support indicated in the guidance. However, some are stretched very thinly, being solely responsible for several hundred cancer patients. Audit data from the North West Region suggests that many urological cancer patients do not receive counselling from a specialist nurse, and that consequently they may lack significant information about their treatment. The recent Commission for Health Improvement and Audit Commission (CHI/AC) report[1] indicates that at the time of the survey (winter 2000/2001) only around 50% of Trusts providing a urological cancer

[1] Commission for Health Improvement, The Audit Commission. *NHS Cancer Care in England and Wales*. London; 2001. Report No: 1.

service had a nurse specialist. The situation is changing rapidly with nurses being appointed, so for the cost estimate it is assumed that it is only 30% of Trusts that still require a specialist nurse. For the 70% of Trusts that are assumed to already have at least one nurse it will be assumed that on average they need 30% more nursing resource, on the basis that around 30% of specialist urological cancer nurses reported severe time constraints on the service that they could provide.[1]

On the basis of these assumptions, around 80 more nurse specialists will be required, at an annual cost of £2.68 million. If it is assumed that these additional nurses will need to complete a post-registration diploma in oncology nursing (ENB 237) the training cost is £0.32 million.

Prostate cancer

Incidence

The greatest increase in the costs of caring for urological cancer patients over the next few years is likely to arise from the increasing incidence in prostate cancer, rather than in implementing the guidance. This probable increase in incidence is expected as a consequence of many more men being screened for prostate cancer with the prostate specific antigen (PSA) test. Many urologists believe that it is not just plausible, but probable, that incidence rates in the UK will rise to American levels. Whether incidence will really more than double, and how fast incidence will increase, is very difficult to predict. Currently there is very little hard evidence of an increase in incidence, but the latest national figures are for 1998. The 1998 figures do show an increase of 12.6% over 1997, which may signal the start of an upward trend, but could be owing to statistical variation.[2,3,4] However, there is evidence that PSA testing increased during the late 1990s, and is likely to have increased further. Urologists report seeing many more patients with possible prostate cancer, and expect to see even more in the future.

Given this uncertainty, three different scenarios were devised. The highest increase assumes that there has been a steady increase from 1998 to 2001, but that incidence will then rise more steeply to reach American levels by 2004. This would give an incidence of 45,000 for England and Wales, compared to approximately 20,500 in 1998. The low scenario is based on a continuing steady increase from 1998 to

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2 Quinn M, Babb P, Brock A, et al. *Cancer trends in England and Wales 1950-1999.* London: Stationery Office, 2001.

3 Office for National Statistics. *New cases of cancer diagnosed in England, 1998.* ONS, 2002. Available from: http://www.statistics.gov.uk

4 Welsh Cancer Intelligence and Surveillance Unit. Personal Communication. 2002.

2004, with the central scenario based on mid-point estimates for 2001 and 2004. These scenarios give a range of additional costs of £15.4 to £43.8 million per year, with a central estimate of £28.2 million.

Other costs

The guidance will result in more patients having magnetic resonance imaging (MRI) prior to radical treatment - not currently routine practice for all patients. This is likely to cost an additional £0.4 million per year. This cost should be more than offset by the reduction in bone scans. Scans are rarely useful for patients with a PSA level of less than 10ng/ml and Gleason score less than 8, but audit data suggests that a third of patients with localised cancer having a scan fall into this category. The potential annual cost saving is £0.5 million.

The guidance encourages the use of conformal radiotherapy where possible. Conformal radiotherapy requires more consultant oncologist, radiographer and medical physicist time than conventional external beam radiotherapy. Assuming that machines are provided, the ongoing additional cost of providing all patients with conformal radiotherapy is modest, at £0.2 million per year. This total annual cost assumes cost savings resulting from the phasing out of the use of the low melting point alloy method of providing conformal radiotherapy, which is more laborious, and therefore more expensive, than conformal radiotherapy with multileaf collimators.

Bladder cancer

Audit and HES data show that patients are being more actively treated for bladder cancer than a few years ago, but that there is still a need for further improvement. Increased treatment costs will be incurred as a result of the guidance. Additional intravesical chemotherapy for superficial cancers will cost £2.0 million, and an additional 850 cystectomies a year may be required, at a cost of £3.9 million.

Cost Summary

(All costs in millions of pounds per year)

Multidisciplinary teams		
MDT co-ordinator for all units and additional consultant sessions	£3.56	
Additional costs of staff time at units and centres	£2.84	
Subtotal		**£6.40**
Centralisation – central		**£4.39**
Low scenario	£3.79	
High scenario	£4.98	
Patient-centred care (specialist nurses)		**£2.68**
Prostate cancer		
Potential increase in prostate cancer incidence		**£28.19**
Low scenario	£15.40	
High scenario	£43.84	
MRI prior to radical treatment		**£0.37**
Low scenario	£0.23	
High scenario	£0.40	
Conformal radiotherapy for radical treatment		**£0.16**
Low scenario	£0.10	
High scenario	£0.17	
Bone scans		**-£0.53**
Low scenario	-£0.34	
High scenario	-£0.58	
Bladder cancer		
Diagnosis	£0.28	
Treatment	£5.93	
Subtotal		**£6.21**
Total		**£47.87**
Range		**£34.47 - £64.10**

Appendix 2

How this guidance manual was produced

A2

The Manuals in this series are intended to guide health organisations (strategic health authorities, primary care Trusts, cancer networks, and Trusts), their managers and lead clinicians in improving the effectiveness and efficiency of services for patients with cancer. The information and recommendations in the Manual are based on systematic reviews of the best available evidence on diagnosis, treatment and service delivery. This evidence is assessed by experts and the recommendations are the product of extensive discussion with leading clinical specialists. The production process is described briefly below; more detail is available in earlier guidance Manuals in the series.

The production process begins with a two-day residential event where proposals for improving services for patients with cancer of a specific site are generated. A large group of relevant health care professionals, people with personal experience of the particular type of cancer being considered, health care commissioners and academics from around the country, meet to put forward structured proposals based on their experience and knowledge of the research literature. All proposals share a common structure and are intended to improve outcomes for patients. These proposals are then sent to referees, including clinicians, academics, representatives of health authorities, the Department of Health, patient organisations, and relevant charities, many of whom make detailed comments and suggestions. Systematic reviews of the research literature, designed to evaluate the proposals, are then carried out or commissioned by the NHS Centre for Reviews and Dissemination (CRD) at the University of York.

This process culminates in the production of two large sources of information, one with a practical or operational focus, and the other containing detailed research evidence on effectiveness. The guidance draws on both these sources, with added input from commissioners, patients, and experts in the particular fields. The writing of the guidance manual is overseen by an editorial group chaired by Professor Bob Haward, accountable to the National Cancer Guidance Steering Group. The writing is undertaken by Dr Arabella Melville, in conjunction with CRD.

Complementary research, designed to quantify the potential cost of major changes in services, is carried out by the School of Health and Related Research at the University of Sheffield. This work involves literature searching, interviews with clinicians and managers, and analyses of costs.

Evidence grading

The reliability and quality of evidence which supports the recommendations in the guidance manual is graded throughout the document. The grades are as follows:

A. Evidence derived from randomised controlled trials or systematic reviews of randomised trials.

B. Evidence from non-randomised controlled trials or observational studies.

C. Professional consensus.

The quality of research evidence forms a continuum and there is overlap between these categories. Most of the published research on cancer focuses on clinical evaluations of treatment; little direct research has been carried out on the organisation and delivery of services, issues on which randomised controlled trials (categorised here as the highest quality evidence) may not be feasible. Research designs which might be regarded as of relatively poor quality for evaluating a clinical intervention may therefore be the most reliable available for assessing the organisational issues.

The systematic reviews used to inform the Manual are summarised in the document *Improving Outcomes in Urological Cancers: The Research Evidence*. This document includes details of all the studies to which the Manual refers. It is available on the CD-rom provided with this Manual, and can be purchased in printed format as a CRD report (email: crdpub@york.ac.uk, tel: 01904-433648).

Appendix 3

People and organisations involved in production of the guidance

3.1 National Cancer Guidance Steering Group

3.2 Participants in the proposal generating event

3.3 People/organisations invited to comment on original proposals

3.4 Researchers carrying out literature and economic reviews

3.5 Members of focus groups

Guidance synthesis and writing

Ms A Eastwood	Senior Research Fellow, NHS Centre for Reviews and Dissemination, University of York
Mr A Flynn	Research Fellow NHS Centre for Reviews and Dissemination, University of York
Professor J Kleijnen	Director, NHS Centre for Reviews and Dissemination, University of York
Dr D Lister-Sharp	Research Fellow, NHS Centre for Reviews and Dissemination, University of York
Dr A Melville	Independent Consultant

assisted by members of the National Cancer Guidance Steering Group, together with:

Mr N Clarke, Consultant Urologist, Hope Hospital, Salford
Dr S Harland, Consultant Medical Oncologist, Middlesex Hospital, London
Dr P Harnden, Consultant Urological Pathologist, St James's University Hospital, Leeds
Professor A Horwich, Professor of Clinical Oncology, Royal Marsden Hospital, Sutton
Professor J Husband, Professor of Diagnostic Radiology, Royal Marsden Hospital, Sutton
Professor M Mason, Professor of Clinical Oncology, Velindre Hospital, Cardiff
Professor D E Neal, Professor of Surgery, University of Newcastle Medical School, Newcastle upon Tyne

People/organisations invited to comment on drafts of the guidance

National Cancer Guidance Steering Group
Focus groups
Various professional organisations
Department of Health
NICE Stakeholders

Economic reviews

School of Health and Related Research, University of Sheffield

Project support

The Northern and Yorkshire Cancer Registry and Information Service

Appendix 3.1

Membership of the National Cancer Guidance Steering Group

Chairman

Professor R A Haward	Professor of Cancer Studies, University of Leeds

Vice Chairman

Professor M Richards	Sainsbury Professor of Palliative Medicine, St Thomas' Hospital, London and National Cancer Director

Members

Dr J Barrett	Consultant in Clinical Oncology and Clinical Director, Four Counties Cancer Network
Mrs G Batt	Section Head, Cancer Policy Team, Department of Health, Wellington House
Mr A Brennan	Director of Operational Research, School of Health and Related Research, University of Sheffield
Ms A Eastwood	Senior Research Fellow, NHS Centre for Reviews & Dissemination, York
Dr J Hanson	Cancer Services Project Co-ordinator, Welsh Office
Dr G Harding	GP and Medical Director, St John's Hospice, Doncaster
Professor J Kleijnen	Director, NHS Centre for Reviews & Dissemination, York
Professor P Littlejohns	Clinical Director, National Institute for Clinical Excellence
Professor R E Mansel	Chairman, Division of Surgery, University of Wales College of Medicine, Cardiff
Dame G Oliver	Director of Service Development, Macmillan Cancer Relief
Mrs V Saunders	Manager, Northern and Yorkshire Cancer Registry and Information Service
Dr J Verne	Consultant in Public Health Medicine, Department of Health South and West Regional Office

Appendix 3.2

Participants in the urological cancers proposal generating event

Mr M Aitchison	Consultant Urologist, Gartnavel General Hospital, Glasgow
Dr I D Ansell	Consultant Histopathologist, Nottingham City Hospital
Mr R C Beard	Consultant Urologist, Worthing Hospital
Dr A Benghiat	Cancer Lead Clinician, Leicester Royal Infirmary
Ms J Booker	Macmillan Urology Nurse Specialist, Christie Hospital, Manchester
Dr D Bottomley	Consultant in Clinical Oncology, Cookridge Hospital, Leeds
Mr S Brewster	Consultant Urologist, Churchill Hospital, Oxford
Mrs M Bullen	Director of Cancer Nursing, Maidstone Hospital, Kent
Mr M Carr	Patient
Ms E Cheesman	Senior Information Nurse, CancerBACUP
Mr T Christmas	Consultant Urologist, Charing Cross Hospital, London
Dr P Clark	Consultant in Medical Oncology, Clatterbridge Centre for Oncology
Dr R Clements	Consultant Radiologist, Royal Gwent Hospital, Newport
Dr S Closs	Consultant in Palliative Medicine, Morriston Hospital, Swansea
Dr D Cochlin	Consultant Radiologist, University Hospital of Wales, Cardiff
Dr D Dearnaley	Consultant in Clinical Oncology, The Royal Marsden Hospital, Sutton
Ms J Farrell	Urology Nurse Specialist, Rotherham District General Hospital
Mr D Fawcett	Consultant Urologist, Battle Hospital, Reading
Mr R Firth	Patient
Mr M V P Fordham	Consultant Urologist, Royal Liverpool University Hospital

Mr T Gittings	Patient
Dr J Graham	Consultant in Clinical Oncology, Bristol Oncology Centre
Dr K Grigor	Consultant Pathologist, Western General Hospital, Edinburgh
Ms C Grose	Urology Nurse Practitioner, Stepping Hill Hospital, Stockport
Dr J Halpin	Consultant/Senior Lecturer in Public Health Medicine, East & North Hertfordshire Health Authority
Dr P Harnden	Consultant Urological Pathologist, St James's University Hospital, Leeds
Ms S Hunton	Director, Bradford Cancer Support Centre
Dr N James	Consultant in Clinical Oncology, Queen Elizabeth Hospital, Birmingham
Dr M Jefferson	Consultant in Palliative Medicine, University of Wales College of Medicine, Cardiff
Dr J Joffe	Consultant in Medical Oncology, Huddersfield Royal Infirmary
Mr M Khan	Patient
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Ms S Lynch	Radiotherapy Section Manager, Clatterbridge Centre for Oncology
Dr A Marks	Consultant in Palliative Medicine, Dellwood Community Hospital, Reading
Professor M Mason	Professor of Clinical Oncology, Velindre Hospital, Cardiff
Dr G Mead	Consultant in Medical Oncology, Royal South Hants Hospital, Southampton
Dr J Melia	Project Co-ordinator, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton
Mr L Moffat	Consultant Urologist, Aberdeen Royal Infirmary
Dr L N S Murthy	Consultant Radiologist, Freeman Hospital, Newcastle upon Tyne
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Dr P Norris	GP, Kingston upon Thames
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Dr E A Scott	Director of Public Health, Leeds Health Authority
Professor P Selby	Professor of Cancer Medicine, St James's University Hospital, Leeds
Mr C Sloane	Patient
Dr N Summerton	Clinical Senior Lecturer in Primary Care Medicine, University of Hull
Dr G Tanner	GP, Bridgwater
Dr J Thomas	Director of Public Health, Sunderland Health Authority
Mr S Vesey	Consultant Urologist, Southport and Formby District General Hospital
Mrs S Weatherall	Patient
Dr J Wilkinson	Director, Northern & Yorkshire Public Health Observatory
Dr C Wolfe	Reader in Public Health Medicine, Guy's, King's and St Thomas' School of Medicine, London

Facilitated by:

Dr J Barrett	Consultant in Clinical Oncology and Clinical Director, Four Counties Cancer Network
Professor R A Haward	Professor of Cancer Studies, University of Leeds
Professor J Kleijnen	Director, NHS Centre for Reviews and Dissemination
Professor M A Richards	Sainsbury Professor of Palliative Medicine, St Thomas' Hospital, London and National Cancer Director

Appendix 3.3

Referees of the urological cancers proposals

The guidance was subject to the NICE consultation process (see website www.nice.org.uk for details)

The individuals listed below were also invited by the Developer to act as referees (347) of whom 37% responded.

A3

Mr P Abel	Consultant Urologist, Hammersmith Hospital, London
Dr S Adam	Director of Health Services, Department of Health
Mr M Aitchison	Consultant Urologist, Gartnavel General Hospital, Glasgow
Professor Sir G Alberti	President, Royal College of Physicians
Professor F E Alexander	Professor of Epidemiology, University of Edinburgh
Mr J Anderson	Consultant Urological Surgeon, Royal Hallamshire Hospital, Sheffield
Mr R W Anderson	Economic Adviser, Department of Health
Dr I D Ansell	Consultant Histopathologist, Nottingham City Hospital
Mr I Appleyard	Consultant Urologist, Airedale General Hospital, Keighley
Professor P Armstrong	Professor of Radiology, St Bartholomew's Hospital, London
Dr D V Ash	Consultant in Clinical Oncology, Cookridge Hospital, Leeds
Professor Sir W Asscher	Chairman, United Kingdom Co-ordinating Committee on Cancer Research
Dr S Atkinson	Director of Public Health, Department of Health, London Regional Office
Mr M J Bailey	Consultant Urologist, St George's Hospital, London
Dr S I Baithun	Consultant Histopathologist, The Royal London Hospital
Dr M Baker	GP, Lincoln
Professor M R Baker	Cancer Lead, Yorkshire Cancer Network
Mr C J M Beacock	Consultant Urologist, Royal Shrewsbury Hospital

Mr R C Beard	Consultant Urologist, Worthing Hospital
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Mr M Bishop	Consultant Urologist, Nottingham City Hospital
Mr D T Blachford	Patient
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Mr P Bollina	Consultant Urologist, Western General Hospital, Edinburgh
Dr D Bottomley	Consultant in Clinical Oncology, Cookridge Hospital, Leeds
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Dr S A Bridgman	Consultant in Public Health Medicine, North Staffordshire Health Authority
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Ms J Brodie	Head of Cancer Support Service, CancerBACUP
Dr R Buchanan	Dean, Faculty of Clinical Oncology, Royal College of Radiologists
Mrs M Bullen	Director of Cancer Nursing, Maidstone Hospital, Kent
Ms K Burden	Research Nurse, Royal Berkshire Hospital, Reading
Dr H Burton	Consultant in Public Health Medicine, Cambridgeshire Health Authority
Mrs V Cameron	Secretary, Royal College of Psychiatrists
Mr D Campbell	Chief Executive, Liverpool Central Primary Care Trust
Professor L Cardozo	Professor of Urogynaecology, King's College Hospital, London
Dr B M Carey	Consultant Radiologist, Cookridge Hospital, Leeds
Mr M Carr	Patient
Ms L Cassapi	Conformal Therapy Research Radiographer, Clatterbridge Centre for Oncology
Mr D Chadwick	Consultant Urologist, South Cleveland Hospital, Middlesbrough
Mrs C Chard	Head of Hospital Business, ASTA Medica Ltd
Mr S Chiverton	Consultant Urologist, St Mary's Hospital, Portsmouth
Dr N Clarke	Head of Outcomes and Effectiveness, Department of Health

Mr N W Clarke	Consultant Urologist, Hope Hospital, Salford
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Mr G Das	Consultant Urologist, Mayday University Hospital, Surrey
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Mr A R De Bolla	Consultant Urological Surgeon, Wrexham Maelor Hospital
Dr G P Deutsch	Consultant in Clinical Oncology, Royal Sussex County Hospital, Brighton
Ms R Devlin	Practice Development Nurse, Derriford Hospital, Plymouth
Mr A Doble	Consultant Urologist, Addenbrooke's Hospital, Cambridge

Dr D Dodds	Consultant in Medical Oncology, Western Infirmary, Glasgow
Ms S Dolan	Critical Care Nurse Specialist, The Royal Marsden Hospital, Surrey
Professor L Donaldson	Chief Medical Officer, Department of Health
Dr R Donnelly	Medical Director, Janssen-Cilag Ltd
Dr C du Boulay	Director, Professional Standards Unit, Royal College of Pathologists
Mrs C Duddle	Macmillan Palliative Care Nurse Specialist, Fazakerley Hospital, Liverpool
Dr R Dunlop	Medical Director, St Christopher's Hospice, London
Ms J Eaton	Professional Affairs Officer, British Dietetic Association
Miss C Edwards	Assistant Director of Commissioning, North Derbyshire Health Authority
Dr J E Ellershaw	Medical Director, Liverpool Marie Curie Centre
Dr C Evans	Consultant Radiologist, University Hospital of Wales, Cardiff
Ms S Faithful	Lecturer in Cancer Care, Centre for Cancer and Palliative Care Studies, The Royal Marsden Hospital, London
Dr M Fallon	Consultant in Palliative Medicine, Western Infirmary, Glasgow
Ms J Farrell	Urology Nurse Specialist, Rotherham District General Hospital
Professor A Faulkner	Professor of Communication in Health Care, Great Barrow, Cheshire
Mr D P Fawcett	Consultant Urologist, Battle Hospital, Reading
Ms J Fenelon	Member of the National Cancer Implementation Group
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Professor I Finlay	Medical Director, Holme Tower Marie Curie Centre, Penarth
Dr C Fisher	Consultant Histopathologist, The Royal Marsden Hospital, London
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Appendix 3.4

Researchers carrying out literature reviews and complementary work

A3

Overall co-ordinators

Ms A Eastwood Mr A Flynn Professor J Kleijnen and Dr D Lister-Sharp	NHS Centre for Reviews and Dissemination, University of York

i) Literature reviews

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Contributed reviews which were used to inform guidance on all topics.

Professor I Higginson and Dr J Potter	Department of Palliative Care and Policy, King's College School of Medicine and Dentistry, London

Contributed reviews which were used to inform guidance on topics 3 and 4.

Mr A Flynn and Ms R Lewis	NHS Centre for Reviews and Dissemination, University of York

Contributed reviews which were used to inform guidance on topics 1 and 2.

Ms K Misso and Mrs B Coles	NHS Centre for Reviews and Dissemination, Velindre NHS Trust, undertook the literature searches for the review work.

ii) Patient views of urological cancer services

Ms R Miles and Ms C Smith	National Cancer Alliance, Oxford

iii) Economic reviews

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Appendix 3.5

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Appendix 4

Glossary of terms

Adjuvant treatment
Treatment given in addition to the main treatment, usually *radiotherapy* or *chemotherapy* given after surgery.

Aetiology
The origins or causes of disease.

Agonists
Drugs that trigger an action from a cell or another drug.

Alpha-fetoprotein (AFP)
A protein which may be found in the blood of men who have testicular cancer, used as a biochemical tumour marker.

Analgesia
Pain relief. In oral analgesia, drugs are given by mouth, whilst parenteral analgesia is given by injection. Titration of analgesia means gradually increasing the dose and/or using more powerful drugs until the pain is controlled.

Androgens
A family of hormones that promote the development and maintenance of male sex characteristics.

Antagonists
Drugs that oppose the action of another drug or natural body chemical.

Anti-androgens
Drugs that act by binding to the hormone receptors of cancer cells, thereby blocking the hormone from reaching, and stimulating, the cancer.

Aorta
The large artery originating from the left ventricle of the heart. Its branches carry blood to all parts of the body.

Assay
An analysis done to determine the presence of a substance and the amount of that substance.

Audit
A method by which those involved in providing services assess the quality of care. Results of a process or intervention are assessed, compared with a pre-existing standard, changed where necessary, and then reassessed.

Bacille Calmette-Guerin (BCG)
An anti-cancer drug that activates the immune system. Filling the bladder with a solution of BCG is a form of *biological therapy* for superficial bladder cancer. BCG is also the vaccine used to prevent tuberculosis.

Benign prostatic hyperplasia (BPH)
A non-cancerous condition in which an overgrowth of *prostate* tissue pushes against the *urethra* and the bladder, restricting or blocking the normal flow of urine. Also known as benign prostatic hypertrophy. This condition is increasingly common in older men.

Beta-human chorionic gonadotrophin (βhCG)
A hormone which may be found in the blood of men who have testicular cancer, used as a biochemical tumour marker.

Bilateral disease
Cancer that occurs in both paired organs, such as both kidneys or *testicles*.

Biological treatment
Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen the side-effects that may be caused by some cancer treatments. Also known as *immunotherapy*.

Biopsy
Removal of a sample of tissue or cells from the body to assist in diagnosis of a disease.

Bisphosphonates
A type of cytotoxic drug used to treat bone metastases.

Bladder reconstruction
A surgical procedure to form a storage place for urine following a *cystectomy*. Usually, a piece of bowel is removed and is formed into a balloon-shaped sac, which is stitched to the *ureters* and the top of the *urethra*. This allows urine to be passed in the usual way.

Brachytherapy
Radiotherapy delivered within an organ such as the prostate.

Carcinoma in situ (CIS)
Cancer that involves only the cells in which it began and that has not spread to neighbouring tissues.

Case series studies
A series of case reports involving patients who were given similar treatment. Reports of case series usually contain information about individual patients including demographic information, information on diagnosis, treatment, response to treatment and follow-up.

Chemotherapy
The use of drugs that kill cancer cells, or prevent or slow their growth.

Cisplatin methotrexate vinblastine (CMV)
A type of *chemotherapy* using a combination of cisplatin methotrexate and vinblastine.

Clinical oncologist
A doctor who specialises in the treatment of cancer patients, particularly through the use of *radiotherapy*, but may also use *chemotherapy*.

Cognitive and behavioural interventions
Types of therapy, often delivered by psychologists, usually based on talking and practising specific types of voluntary activity. This group of interventions can include, for example, relaxation training, counselling, and psychological approaches to pain control.

Cohort studies
Research studies in which groups of patients with a particular condition or specific characteristic are compared with matched groups who do not have it.

Combination chemotherapy
The use of more than one drug to kill cancer cells.

Computed tomography (CT)
An x-ray imaging technique. In spiral CT the x-ray machine scans the body in a spiral path. Also known as helical CT.

Congenital abnormalities
Abnormalities that are present at birth.

Contralateral
Referring to the opposite side of the body.

Cryopreservation
Preservation by freezing.

Cystectomy
Surgery to remove all or part of the bladder.

Cystitis
Inflammation of the bladder.

Cystoscope
A thin, lighted instrument used to look inside the bladder and remove tissue samples or small tumours.

Cystoscopy
Examination of the bladder and *urethra* using a *cystoscope.*

Digital rectal examination (DRE)
An examination in which a doctor inserts a lubricated, gloved finger into the rectum to feel for abnormalities.

Epidemiology
The study of populations in order to determine the frequency and distribution of disease and measure risks.

Field
In *radiotherapy*, the area selected for treatment, on which the *radiotherapy* beam is focused.

Fraction
Radiotherapy is usually given over an extended period. The dose delivered each day is known as a fraction.

Genital
Referring to the external sex or reproductive organs

Germ cells
The reproductive cells of the body. In men, the testicular cell that divides to produce the immature sperm cells; in women the ovarian cell that divides to form the egg.

Germ cell tumours
Tumours that begin in the *germ cells*. 95% of all testicular cancers are germ cell tumours. Germ cell tumours in men are classified as either *seminomas* or *non-seminomas*.

Gleason scoring
A system of grading prostate cancer cells to determine the best treatment and to predict how well a person is likely to do. A low Gleason score means the cancer cells are very similar to normal prostate cells, a high Gleason score means the cancer cells are very different from normal.

Grade
The degree of malignancy of a tumour, usually judged by it histological features.

Great vessel involvement
Involvement of one of the five major blood vessels above the aortic arch.

Gynaecomastia
Enlargement of the breasts in men.

Haematuria
The presence of blood in the urine. Macroscopic haematuria is visible to the naked eye, whilst microscopic haematuria is only visible with the aid of a microscope.

Histology
Examination of the microscopic structure of tissue.

Hormone treatment
Treatment of cancer by removing, blocking or adding hormones.

Human papillomavirus (HPV)
A virus that causes warts and is often associated with some types of cancer.

Hypertension
Abnormally high blood pressure.

Immunotherapy
See *biological treatment.*

Impotence
Inability to have an erection adequate for sexual intercourse.

Incontinence
Inability to control the flow of urine from the bladder (urinary) or the escape of stool from the rectum (faecal).

Insulin-like growth factor (IGF)
Growth factors are chemicals that have a variety of roles in the stimulation of new cell growth and cell maintenance. IGF induces cell proliferation and is thought to be involved in the abnormal regulation of growth seen in cancer when produced in excessive amounts.

Intravenous urography
Radiological examination of the urinary tract, or any part of it, after the introduction of a contrast medium into a vein.

Intravesical treatment
Treatment within the bladder. Intravesical *chemotherapy* is given directly into the bladder through a catheter.

Lactate dehydrogenase (LDH)
An enzyme which may be found in the blood of men who have testicular cancer, used as a biochemical tumour marker.

Laparascopic surgery
Surgery performed using a laparascope; a special type of endoscope inserted through a small incision in the abdominal wall.

Libido
Sexual drive.

Luteinising hormone-releasing hormone (LHRH)
A hormone that controls the production of sex hormones in men and women.

LHRH analogues
Drugs that inhibit the secretion of *androgens* from the testes.

Lymph node dissection
See *lymphadenectomy.*

Lymph nodes
Small organs which act as filters in the lymphatic system. Lymph nodes close to the primary tumour are often the first sites to which cancer spreads.

Lymphadenectomy
A surgical procedure in which *lymph nodes* are removed and examined to see whether they contain cancer. Also known as lymph node dissection.

Lymphoedema
A condition in which excess fluid collects in tissues and causes swelling. It may occur in the legs after lymph vessels or *lymph nodes* in the groin are removed or treated with radiation.

Magnetic resonance imaging (MRI)
A non-invasive method of imaging which allows the form and metabolism of tissues and organs to be visualised (also known as nuclear magnetic resonance).

Maximum androgen blockade
The combined use of *LHRH analogues* and *anti-androgen* treatment.

Median
The middle value of an ordered set of measurements.

Mediastinum
The space in the chest between the lungs.

Medical oncologist
A doctor who specialises in the treatment of cancer by *chemotherapy*, and for some tumours *immunotherapy*.

Meta-analysis
A form of statistical analysis used to synthesise results from a collection of individual studies.

Metastases/metastatic disease
Spread of cancer away from the primary site.

Modal
The most commonly occurring value of a set of measurements.

Neo-adjuvant treatment
Treatment given before the main treatment; usually *chemotherapy* or *radiotherapy* given before surgery.

Nephrectomy
Surgery to remove all or part of a kidney. Radical nephrectomy removes the entire kidney, nearby lymph nodes and other surrounding tissue. Partial nephrectomy (also known as nephron-sparing surgery) removes only the tumour and part of the kidney surrounding it.

Nephron-sparing surgery
See *nephrectomy*.

Non-seminoma
A type of testicular cancer that begins in the *germ cells* (cells that give rise to sperm). Non-seminomas are identified by the type of cell in which they begin and include *teratomas*.

Oncologist
A doctor who specialises in treating cancer.

Oncology
The study of the biology and physical and chemical features of cancers. Also the study of the causes and treatment of cancers.

Orchidectomy
Surgery to remove one (unilateral) or both *testicles*.

Osteoporosis
Loss of bony tissue resulting in bones that are brittle and liable to fracture.

Palliative
Anything which serves to alleviate symptoms due to the underlying cancer but is not expected to cure it. Hence palliative care, palliative *chemotherapy*.

Para-aortic region
The prefix 'para' means besides. The region besides the *aorta*.

Pathologist
A person who specialises in the diagnosis of disease through study of the microscopic structure of cells and tissues.

Peri-operative
Around the time of surgery. Usually the time from admission to hospital to discharge following surgery.

Plaques
Patches of skin which appear different from the surrounding skin and are usually raised.

Proctitis
Inflammation of the rectum.

Prophylaxis
An intervention used to prevent an unwanted outcome.

Prostatectomy
Surgery to remove part, or all of the *prostate gland*. Radical prostatectomy is the removal of the entire *prostate gland* and some of the surrounding tissue.

Prostate gland
A small gland found only in men which surrounds part of the *urethra*. The prostate produces semen and a protein called *prostate specific antigen (PSA)* which turns the semen into liquid. The gland is surrounded by a sheet of muscle and a fibrous capsule. The growth of prostate cells and the way the prostate gland works is dependent on the male hormone *testosterone*.

Prostate specific antigen (PSA)
A protein produced by the *prostate gland* which turns semen into liquid. Men with prostate cancer tend to have higher levels of PSA in their blood (although up to 30% of men with prostate cancer have normal PSA levels). However, PSA levels may also be increased by conditions other than cancer and levels tend to increase naturally with age.

Prosthesis
An artificial device used to replace a missing part of the body.

Protocol
A policy or strategy which defines appropriate action.

Psychological interventions
Interventions directed at altering mental processes which do not involve the use of drugs or any physical or invasive procedure. These include a large group of therapeutic approaches including counselling, cognitive therapy, and relaxation.

Psychosexual
Concerned with psychological influence on sexual behaviour.

Psychosocial
Concerned with psychological influence on social behaviour.

Quality of life
The individual's overall appraisal of his/her situation and subjective sense of well-being.

Radical treatment
Treatment given with curative, rather than *palliative* intent.

Radioisotope treatment
A type of *radiotherapy*. A radioisotope liquid is given, either by mouth or as an injection into a vein. As the radioisotope material breaks down it releases radiation within the body.

Radiologist
A doctor who specialises in creating and interpreting pictures of areas inside the body. The pictures are produced with x-rays, sound waves, or other types of energy.

Radiotherapy
The use of radiation, usually x-rays or gamma rays, to kill tumour cells. Conventional external beam radiotherapy also affects some normal tissue outside the target area. Conformal radiotherapy aims to reduce the amount of normal tissue that is irradiated by shaping the x-ray beam more precisely. The beam can be altered by placing metal blocks in its path or by using a device called a multi-leaf collimator. This consists of a number of layers of metal sheets which are attached to the radiotherapy machine; each layer can be adjusted to alter the shape and intensity of the beam.

Randomised controlled trial (RCT)
A type of experiment which is used to compare the effectiveness of different treatments. The crucial feature of this form of trial is that patients are assigned at random to groups which receive the interventions being assessed or control treatments. RCTs offer the most reliable (i.e. least biased) form of evidence on effectiveness.

Refactory disease
Disease that is resistant to treatment.

Renal
Having to do with the kidneys.

Resection
The surgical removal of all or part of an organ.

Retroperitonium
The area behind the peritoneum (the tissue that lines the abdominal wall and covers most of the organs in the abdomen).

Salvage treatment
Treatment that is given after the cancer has not responded to other treatments.

Scrotum
The external sac that contains the testicles.

Seminoma
A type of testicular cancer.

Sperm banking
Freezing sperm in liquid nitrogen for use in the future. This procedure can allow men to father children after loss of fertility.

Staging
The allocation of categories (stage I to IV) to tumours defined by internationally agreed criteria. Stage I tumours are localised, whilst stage II to IV refer to increasing degrees of spread through the body from the primary site. Staging helps determine treatment and indicates prognosis.

Stoma
A surgically created opening.

Teratoma
A type of testicular cancer that arises from *germ cells* at a very early stage in their development.

Testicle or testis (plural testes)
Egg shaped glands found inside the scrotum which produce sperm and male hormones.

Testosterone
A hormone that promotes the development and maintenance of male sex characteristics.

Transitional cell carcinoma
A type of cancer which develops in the lining of the bladder, *ureters* or renal pelvis.

Trans-rectal ultrasound (TRUS)
An *ultrasound* examination of the prostate using a probe inserted into the rectum.

Trans-urethral resection (TUR)
Surgery performed with a special instrument inserted through the urethra.

Trans-urethral resection of the prostate (TURP)
Surgery to remove tissue from the prostate using an instrument inserted through the urethra. Used to remove part of the tumour which is blocking the urethra.

Tumour markers
Substances sometimes found in increased amounts in the blood, other body fluids or tissues which suggests that a certain type of cancer may be in the body, e.g. *PSA*.

Ultrasound
High-frequency sound waves used to create images of structures and organs within the body.

Ureters
Tubes which carry urine from the kidneys to the bladder.

Ureterscopic biopsy
A *biopsy* taken from the upper urological tract using a ureterscope; an endoscopic instrument passed through the *urethra* into the bladder and *ureters*.

Urethra
The tube leading from the bladder through which urine leaves the body.

Urinary diversion
Alternative methods of removing urine from the body following a *cystectomy*. Most commonly, a small piece of bowel is removed, the *ureters* are stitched to one end and the other end is attached to a *stoma* in the abdomen. Urine is brought to the surface and collected in a stoma bag. Alternatively, a pouch can be formed in the abdomen using a piece of bowel which is used to store urine. Urine is removed from the body by passing a small catheter through the stoma about four or five times per day to drain the urine (self-catheterisation).

Urogenital system
The organs concerned in the production and excretion of urine, together with the organs of reproduction.

Urologist
A doctor who specialises in diseases of the urinary organs in females and urinary and sex organs in males.

Urology
A branch of medicine concerned with the diagnosis and treatment of diseases of the urinary organs in females and the *urogenital system* in males.

Uro-oncologist
A doctor who specialises in the treatment of cancers of the urinary organs in females and urinary and sex organs in males.

Vasectomy
Surgery to cut or tie off the two tubes that carry sperm out of the *testicles*.

Vena cava
Either of two large veins that return blood to the heart. The superior vena cava returns blood from the head, neck and upper limbs and the inferior vena cava returns blood from the lower part of the body.

von Hippel-Lindau syndrome
A rare inherited disorder in which blood vessels grow abnormally in the eyes, brain, spinal cord or other parts of the body. People with von Hippel-Lindau syndrome have a higher risk of developing kidney and other types of cancer.

Watchful waiting
A surveillance technique. Treatment is omitted in favour of regular check-ups to see whether the cancer is beginning to grow.

Wilms' tumour
A kidney cancer that occurs in young children usually younger than five years old.