Improving the detection and management of prostate cancer

KATE STEWART

Despite recent advances in the treatment of prostate cancer, the death rate in the UK is continuing to rise. This article examines how improvements in screening and management could have an impact on survival rates in the future.

If the current trend continues, by 2026 the number of men dying from prostate cancer in the UK will soar by a third from 10,900 to 14,500 per year unless urgent action is taken, Prostate Cancer UK has warned. Many of these deaths are blamed on the current problems and complexities surrounding prostate cancer diagnosis.

The most recent NICE guideline (QS91) divides prostate cancer into three stages, depending on whether and how far it has spread from the prostate to other parts of the body:

- Localised prostate cancer – where the cancer is only in the prostate and has not spread anywhere else in the body
- Locally advanced prostate cancer – where prostate cancer has spread from the prostate to the surrounding tissues and
- Metastatic prostate cancer – where it has spread further from the prostate; to the lymph nodes, the bones or other parts of the body.

The detection and treatment of prostate cancer is less straightforward. There is no national screening test for prostate cancer, but the prostate-specific antigen (PSA) blood test can be offered on the NHS to any man over 50 years old who requests it and may also be offered to other higher risk groups, including men with a family history of prostate cancer and African-Caribbean men. However, the test does not diagnose cancer; a raised PSA level may suggest there is a problem with the prostate, but not necessarily cancer and further investigations are needed, including scans and biopsies, to eventually confirm whether prostate cancer is present or not.

In addition, many men with prostate cancer never have symptoms. Early, localised prostate cancer does not usually cause any symptoms, although some men might have some urinary problems. These can be mild and develop over many years and can also be a sign of a benign prostate problem rather than prostate cancer.

Ten-year plan
Prostate Cancer UK estimates that the number of deaths from prostate cancer could be cut in half if key areas such as diagnosis and treatment could be better managed over the next 10 years and the charity has launched a 10-year plan to achieve this.

Prostate Cancer UK’s chief executive Angela Culhane says: “The urgent objective is to shift the science and change prostate cancer from a killer into something a man can live with – taming it so that it becomes a disease our sons and grandsons will not be afraid of.
“Right now prostate cancer kills a man every hour in the UK and that figure is set to rise. One in three men diagnosed with the disease currently dies from it, putting survival rates for our men behind most of Europe. It’s scandalous and we can’t let it continue."

To achieve its ambition, the charity is now targeting three key areas: diagnosis, treatment and prevention. As its first priority, Prostate Cancer UK recently announced plans to commit £2 million to crack the problems that surround diagnosis. It has assembled an international group of leading scientists to develop a new risk screening tool, which can be used as a first-line detector to establish underlying risk of aggressive prostate cancer.

Prostate Cancer UK hopes the tool will revolutionise diagnosis so that no man’s cancer is missed before it is too late, as well as ensuring men will not have to endure invasive and sometimes painful biopsies unnecessarily. It is expected to be in the hands of all GPs in the UK within the next five years.

Ms Culhane continues: “With the right resources, we are confident that we can move the science forward to halve the number of men who die from prostate cancer within a decade.”

Prostate Cancer UK’s director of research, Dr Iain Frame, adds: “The strategy is quite clear; it encompasses risk, diagnosis and prognosis. So we are taking the population, seeing who is most at risk, and being able to give a more accurate diagnosis and prognosis as to whether the cancer is aggressive or not and how that cancer will respond to specific types of treatment.”

He notes: “The major risk factors are still age, ethnicity and family history, but we are also looking at how obesity may also increase your risk. We then need to see improved treatments and make the most of what we’ve got, like the STAMPEDE trial, which has shown how we can use [chemotherapy drug] docetaxel to better effect. There is also the chance to look at how existing drugs can be repurposed. There is a very exciting development at the Institute of Cancer Research in London, who are looking at an ovarian cancer drug called olaparib and what effect it has on prostate cancer.

• Prostate cancer is the most common cancer in men in the UK
• Over 44,000 men are given a diagnosis of prostate cancer every year in the UK – more than 120 men every day
• Every hour one man dies from prostate cancer in the UK – more than 10,500 men every year
• One in eight men in the UK will get prostate cancer in their lifetime
• Over 330,000 men in the UK are living with and after prostate cancer
• The average age for men to receive a diagnosis of prostate cancer is between 70 and 74 years
• A man whose father or brother has been given a diagnosis of prostate cancer is two and a half times more likely to get prostate cancer than a man who has no affected relatives
• The risk of prostate cancer may be higher in a man whose mother or sister has had breast cancer, particularly if it was linked to faults in the BRCA1 or BRCA2 genes
• African Caribbean men are more likely to get prostate cancer than other men; in the UK, about one in four African Caribbean men will get prostate cancer at some point in their lives

Box. Prostate cancer facts and figures (provided by Prostate Cancer UK)

“As science develops and genetic testing comes down in price, we will be able to add new developments to our risk assessment tool so we don’t need to reinvent the wheel as progress is made. In the next 10 years, I would ideally like to see that when a man walks into a GP surgery, he has a blood test and the GP can say: you are at risk of prostate cancer, it’s an aggressive cancer but it will respond best to these treatments. We need to take out the guesswork to make it better for everybody.”

Therapeutic advances
Malcolm Mason, professor of clinical oncology at Cardiff University, says: “Over the last 5–10 years we have suddenly seen a plethora of new drugs appearing for prostate cancer, which have been largely tested in men with advanced disease. We also have some newer hormonal agents like abiraterone and enzalutamide, both of which have now become successfully established as part of the armamentarium.

“But in addition to that, we’ve seen several other drugs that have undoubtedly been shown to prolong survival in men with very advanced disease, which used to be called hormone refractory but is now called castrate-refractory disease. One of those is chemotherapy [docetaxel], which has been found to prolong survival. This was a huge surprise and really changed the whole approach to treating men with advanced prostate cancer. Prior to that, it was thought that chemotherapy did not have a place or might have a role in relieving bone pain,” he adds.

“It’s also possible that immunological therapy may have a place in the future, following on from [the immunotherapy vaccine] sipuleucel-T – which has not been taken further in Europe – but this sort of immunological therapy is one to watch. We also have another drug, which was also a bit of a surprise, and that is radium-223 – radioactive radium that gets taken up by bone. It’s an alpha emitter and that means it has a very short pathway and doesn’t cause much toxicity, and it does seem to prolong survival for a few months in patients with very advanced disease. It is expensive but I’m sure, in time, the costs will fall in line as we have seen others do.”

For example, in March NICE announced that abiraterone will now be available at a lower price and recommended as an option for men with prostate cancer at an earlier stage, without them needing to be treated with chemotherapy first.

Professor Mason continues: “There is also another chemotherapy called cabazitaxel, which seemed to show survival benefits in patients who are resistant to docetaxel and who are a notoriously difficult group of patients to treat. So all of a sudden, we have all these drugs to treat patients with very advanced disease, which is incredible, but it has also given us quite a lot of uncertainty because we..."
don’t quite know what combination to use them in, how to select the patients and what order to use them in.

“The excitement for us, as oncologists, is seeing that life can be prolonged at all in this group of patients, but we have to remember it is only for a few months. There are other things on the horizon, a class of drug called PARP inhibitors, which act particularly by targeting DNA repair pathways. Very recently there has been a study that suggests that for patients who have particular gene mutations in their tumour – such as the BRCA2 gene – agents like PARP inhibitors might be beneficial, but this needs more study,” Professor Mason notes.

“In terms of treatment, I should highlight the results of Cancer Research UK’s very large STAMPEDE trial, which used a very innovative clinical trial design. The trial looked at a range of treatments and giving them to prostate cancer patients much earlier on in their disease history when they start their first hormone treatment – not when the disease is very advanced and the hormone therapy is no longer working.

“For the last 70 years, patients with very advanced, metastatic disease have only had the option of hormone therapy and nothing else, so what STAMPEDE has done is really establish that the new standard treatment for patients who are fit enough should be hormone therapy plus docetaxel as it seems to be more potent at prolonging survival when given earlier.

“So this has been a real change and a challenge because it has undoubtedly changed the landscape of how we should treat this disease and put particular pressures on the NHS as to how these patients are managed, how we get them into the oncology clinics rather than the urology clinics and how we manage the logistics and the resources that are needed to treat them.”

Identifying the right treatment
Professor Mason, Cancer Research UK’s prostate cancer expert, says: “The UK has really been leading the way in some of these pivotal studies and another development has been the treatment of patients with nonmetastatic but locally advanced prostate cancer.

Changes to look for include:
- Needing to urinate more often than usual, including at night
- Difficulty starting to urinate
- Straining or taking a long time to finish urinating
- A weak flow when urinating
- A feeling of incomplete bladder emptying
- Needing to rush to the toilet – sometimes leaking before getting there
- Dribbling urine after finishing

Less common symptoms include:
- Pain when urinating
- Pain when ejaculating
- Blood in the urine or semen (can be caused by other health problems)
- Erectile dysfunction (this is not a common symptom of a prostate problem and is more often linked to other health conditions such as diabetes or heart problems)

Table 1. Signs and symptoms of prostate cancer

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“Being able to give people different treatments at different stages of the disease is great, but we need to give each prostate cancer patient a personalised plan of care to get the best survival for each individual and limit side-effects.

“There is a lot of useful work being done around diagnosis. The PSA test is useful, but it can be raised in conditions that are not cancer and can lead to a lot of worried well as well as men having biopsies, which are very invasive and uncomfortable. Different diagnostic tests are coming, but this will take time.

“We are also looking at survivorship and making sure that those men who survive prostate cancer have the best and healthiest quality of life possible. The acute treatment is good, but there is a large group of men with prostate cancer who fall outside acute care but still need to be looked after.

“On the agenda is sexual dysfunction. We know that if men have intervention at the earliest possible point for erectile dysfunction, the chance of us solving the problem is much greater. But so many men post-treatment for prostate cancer don’t mention it soon enough and it is then harder to treat and, in some cases, too late to protect their sexual function. So we need to encourage men to mention it as soon as possible and the best way to do this is to upskill GPs and

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community staff as well as the patients so they are more knowledgeable to flag up erectile dysfunction earlier. This will also give health professionals the confidence and skill to discuss all the different treatment options and have, often difficult, conversations.”

Access to specialist nurses for prostate cancer patients does not currently seem to be a problem, Ms Morris says. But she warns: “We need to recognise that there is a growing number of men affected by prostate cancer so will there be enough specialist nurses to cope and target those hard-to-reach groups who can be at risk of prostate cancer?

“It’s hard for doctors and nurses working in the community to be experts in everything, especially when they work in such busy settings, but we need to give them the skills so they can be confident, knowledgeable and competent to deal with these patients, counsel them where necessary and give them access to a specialist pathway if they need it,” she adds.

**Increasing GP awareness**

Letchworth GP and professor of general practice at the University of Hertfordshire, Mike Kirby, says: “We are making fantastic progress in managing this disease. Twenty years ago, if you were diagnosed with metastatic prostate cancer you were given 18 months to live – but in the last 10 years, lots of very good treatments have arrived.”

Professor Kirby understands why the PSA test has received much criticism and agrees it is not ready to be used as a screening tool but that it has made “a real difference” and has meant men with prostate cancer are presenting a lot earlier, he explains.

“Any man over 50 years is entitled to have a PSA test on the NHS and in my view it’s worth knowing your PSA number if you don’t want to die of prostate cancer. There is, of course, a balance to be struck between doing harm to those who have not got the disease [a man with a false positive PSA result] and making sure we spot those with aggressive prostate cancer as quickly as possible.

“I got interested in this disease because I had a patient who came through my door whose cancer was already so advanced there was nothing I could do. We may not have a screening test yet, but we should be ready for case finding people who are at more risk of prostate cancer: those with a family history of prostate cancer and African-Caribbean men. And we should also make sure that we counsel and support those men who would like to have a PSA test.

“The NHS-run Prostate Cancer Risk Management Programme has just completed advice sheets for patients and GPs on prostate cancer and they will be available very soon to help advise us. Dealing with prostate cancer in general practice is a challenge. It’s a busy place; we get four new guidelines a week and most GPs, female or male, do not list men’s health as their specialist interest.

“Most GPs only have a handful of patients with prostate cancer on their list and there is low awareness of the scale of

**Table 2. Treatments for prostate cancer (see http://prostatecanceruk.org/prostate-information for more detailed information)**

<table>
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<td><strong>Active surveillance</strong></td>
<td>Monitoring slow-growing prostate cancer rather than treating straight away in order to avoid unnecessary treatment or delay treatment</td>
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<tr>
<td><strong>Watchful waiting</strong></td>
<td>Monitoring prostate cancer that is not causing symptoms or problems over the long term and avoiding treatment unless there are symptoms</td>
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<tr>
<td><strong>Surgery: radical prostatectomy</strong></td>
<td>Removal of the prostate and the cancer contained within it: may be performed using laparoscopy, robot-assisted surgery or open surgery</td>
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<tr>
<td><strong>Surgery: orchidectomy</strong></td>
<td>Removal of the testicles or the parts that make testosterone; used less often than other hormone therapy (see below)</td>
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<tr>
<td><strong>External beam radiotherapy</strong></td>
<td>Uses high-energy X-ray beams to treat prostate cancer</td>
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<tr>
<td><strong>Permanent seed brachytherapy (low dose-rate brachytherapy)</strong></td>
<td>Involves implanting tiny radioactive seeds in the prostate gland to destroy the cancer cells</td>
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<tr>
<td><strong>Hormone therapy</strong></td>
<td>Controls prostate cancer cell growth by reducing levels of testosterone or blocking its action. Includes luteinising hormone-releasing hormone (LHRH) agonists, gonadotrophin-releasing hormone (GnRH) antagonists and antiandrogens (including the newer treatments abiraterone and enzalutamide)</td>
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<tr>
<td><strong>Temporary brachytherapy (high dose-rate brachytherapy)</strong></td>
<td>Involves inserting a source of high dose-rate radiation into the prostate gland for a few minutes to destroy the cancer cells</td>
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<tr>
<td><strong>High-intensity focused ultrasound (HIFU)</strong></td>
<td>Uses high-frequency ultrasound energy to heat and destroy cancer cells in the prostate</td>
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<tr>
<td><strong>Cryotherapy</strong></td>
<td>Uses freezing and thawing to kill cancer cells in the prostate gland</td>
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<tr>
<td><strong>Chemotherapy</strong></td>
<td>Uses anticancer drugs to kill prostate cancer cells, wherever they are in the body. Includes docetaxel and cabazitaxel</td>
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the problem. There is also the problem of symptoms. Many men with prostate cancer don’t have any symptoms and when they do, the cancer has already spread.

“I would encourage all GPs to offer a PSA test to anyone who requests it and where possible encourage all men to be as healthy as they can be – eat healthily, exercise regularly and ‘know your numbers’ in all the areas you can, so that if your body shows signs of change that can be picked up.

“Public health has a lot to answer for and needs to focus on men’s health because men are notoriously bad at presenting early with any kind of health problem. I want us all to do our best to make sure that we don’t have men walking through our doors with an ‘it’s too late’ diagnosis,” Professor Kirby adds.

Prostate Cancer UK senior specialist nurse, Ali Rooke, agrees with Professor Kirby that GPs have a very difficult job because they are not specialists in the prostate or prostate cancer. She explains: “The PSA test is not the best, but it’s the best we’ve got and yet 76 per cent of men who have a raised PSA level do not go on to be diagnosed with prostate cancer.

“Also many GPs do not always feel confident doing a digital rectal examination [DRE]. If you are not performing this examination all the time you might feel you are lacking in the skills to perform it properly and if you are not able to feel the whole gland, the test can also be unreliable.

“Practice nurses and GPs need to be more aware of the side-effects of prostate cancer treatment, which can include incontinence and erectile dysfunction, and can often get mistaken for something else.

“There is no prostate cancer treatment that does not have side-effects and we are working with GPs and nurses in the community to make sure that they have all the information they need. Many men and their families need support postacute treatment and during ongoing treatment, and education is crucial to beating the disease and the damage it can do to patients’ lives,” she adds.

Surgical advances
Ben Challacombe, consultant urologist at London’s Guy’s and St Thomas’ Hospital, says: “A lot of progress has been made in the last few years and we have started to redress the balance between prostate cancer and other cancers. We are now so much better at assessing whether a patient needs a biopsy because we can offer multiparametric MRI (MP-MRI) scans and we are far better at stratifying men who have prostate cancer into lower, middle and high-risk disease.

“We will be able to choose increasing numbers of men for active surveillance and more minimally invasive treatments like brachytherapy and potentially focal therapy. The worry in the past was overtreatment and overdiagnosis – now we are much better at working out whether there is any treatment needed at all.

“The MP-MRI scan tells us not only how cells in the prostate look but how they react, which gives us a better ability to determine between cancerous and non-cancerous cells. This is a standard that we offer all our patients at Guy’s, but not all patients in the UK will be offered this type of scan. There needs to be far greater availability of imaging prior to biopsy UK-wide. I have not done a biopsy or an operation in the last five years without the patient having had an MRI scan first. This allows the biopsy to be far more targeted and we no longer have to do blind biopsies.”

Mr Challacombe adds that the number of surgeons performing robotic prostatectomies like him is increasing. He predicts that over the next 10 years this procedure will take over with the number of laparoscopic and open prostatectomies dropping from “30 to 5 per cent”. “Robotic surgery can improve outcomes by enhancing surgical dexterity, providing 3D vision, a greater range of movement and motion scaling. This allows a more precise operation to be carried out,” he says.

“There are now 52 robots in the UK and the technique can’t get much better, but in the future we may be looking at taking out lymph nodes during the prostatectomy. The mandatory national audit of surgeons is also helpful because we know that volume in this area is king – so the more operations you perform, the better your nerve-sparing technique will be, giving your patients the best chance of avoiding incontinence and erectile dysfunction and the best chance of beating prostate cancer.”

Mr Challacombe calls on GPs to attend a dedicated masterclass on prostate cancer (run by Prostate Cancer UK). “Prostate cancer is the commonest cancer in men and yet many GPs are not well informed about it. Target those men in your practice who are at increased risk of the disease and talk to them about a PSA test because undoubtedly it will save lives.”

References
4. MRC Clinical Trials Unit. Adding radiotherapy to hormone therapy halves deaths from high-risk prostate cancer (PR07 trial). http://www.ctu.mrc.ac.uk/news/2015/PR07_longterm_results_18022015
6. Prostate Cancer UK. http://prostatecanceruk.org/prostate-information

Further information
If you have any patients with concerns about prostate cancer, advise them to contact Prostate Cancer UK’s specialist nurses in confidence on 0800 074 8383 or online via the Live Chat instant messaging service: http://prostatecanceruk.org. The specialist nurse phone service is free to landlines and open from 9am to 6pm, Monday to Friday, with late opening until 8pm on Wednesdays.

For more information on research into treatments for prostate cancer, see: http://www.cancerresearchuk.org/about-cancer/type/prostate-cancer/treatment/research/research-into-treatments-for-prostate-cancer

Declaration of interests
Kate Stewart is the former Prostate Cancer UK head of media and public affairs. She worked with the charity’s media team for 10 years and left in 2014.

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