

GARY NEILL



PROSTATE CANCER

# 4 BIG QUESTIONS

*Despite advances in detection and therapy, much about this common malignancy remains unknown. Here are some of the most important unresolved issues.*

BY RICHARD HODSON

QUESTION

WHY IT MATTERS

WHAT WE KNOW

NEXT STEPS

1

**What causes prostate cancer?**

Worldwide, prostate cancer is the second most common cancer in men, after lung cancer. Identifying a preventable cause of this disease could reduce the number of cases.

Risk increases with age, and inherited factors are estimated to be responsible for 5–9% of cancers. Risk is five times higher in men with *BRCA2* mutations. Despite extensive research, the disease has not been clearly linked to any preventable risk factors.

Taking into account the differing rates of prostate-specific antigen (PSA) testing in populations could help to firm up links. Arsenic and cadmium compounds, anabolic steroids and ionizing radiation may be causes; carrots and soya may reduce the risk.

2

**Is PSA testing an effective method of screening?**

Measuring levels of PSA in the blood is often used to detect prostate cancer. Without a reliable test, in some cases, the first symptoms of the cancer are signs that it has spread to the bones, where it is much less treatable.

Rates of diagnosis spiked in the 1990s in the United States, partly because of the use of PSA screening for men without symptoms. But it is likely that many men were unnecessarily treated for cancers that would never have caused harm.

The PSA test could be a useful procedure if it is applied using evidence-based guidelines (page S123). Combining the screen with other analyses, such as testing for genetic markers, could reduce the number of unnecessary treatments.

3

**Is it safe to leave prostate cancer alone?**

The most common treatments for localized disease — removal of the prostate and radiotherapy — have side effects, such as incontinence and sexual dysfunction. Men with less-aggressive tumours might be better off avoiding these procedures.

Half of US men with low-risk prostate cancer between 2010 and 2013 had their prostates removed, whereas 40% opted to watch and wait. Some studies have suggested that low-risk patients can be safely monitored for more than a decade.

The challenge facing active surveillance is knowing which men have slow-growing tumours that can be left, and which are more aggressive. New methods for telling aggressive and indolent cancer cells apart are being investigated.

4

**Can advanced prostate cancer be treated?**

Once prostate cancer has spread to the lymph nodes and bones, the outlook is poor. Five-year survival rates for metastatic cancer are one-third of those for localized disease; advanced prostate cancer is considered incurable.

Therapies for advanced prostate cancer have emerged only in the past decade. The go-to treatment is chemical castration: drugs are used to suppress male hormones. This can prolong life by two or three years before tumours become resistant.

Drugs designed to treat castration-resistant tumours are also facing a resistance problem — 20–40% of patients do not respond to these therapies, and their efficacy is eventually lost in all men (see page S128).

Richard Hodson is supplements editor for Nature.