resonance imaging of the spine if they develop any spinal related symptoms, as the risk of spinal cord compression is high.

Treatment complications

- For men treated with radical radiotherapy, offer follow-up with flexible sigmoidoscopy every five years as an alternative to faecal occult blood testing in the bowel screening programme.
- Healthcare professionals should ensure that men with troublesome urinary symptoms after treatment have access to specialist continence services.
- Offer early and ongoing access to specialist erectile dysfunction services to men and their partners.

Follow-up

- For men who have had stable PSA levels for at least two years after radical treatment and no significant treatment complications, offer follow-up outside hospital (for example, in primary care) by secure electronic communications, unless taking part in a clinical trial that requires formal, clinic based follow-up. Offer direct access to the urological cancer multidisciplinary team.
- For men with localised prostate cancer who have chosen a watchful waiting regimen with no curative intent (whereby hormonal therapy is withheld until there is significant disease progres-

sion), arrange follow-up in primary care in accordance with locally agreed protocols. Measure the men's PSA levels at least once a year.

Overcoming barriers

Many of these recommendations have cost implications. A costing tool developed by NICE is available now, and an implementation pack will be available shortly. Most of the recommendations can be implemented by the multidisciplinary urological cancer teams under the supervision of the cancer networks.

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Commentary: controversies in NICE guidance on prostate cancer

Timothy J Wilt

Minneapolis VA Center for Chronic Disease Outcomes Research,
1 Veterans Drive (111-O),
Minneapolis, MN 55417
Tim.wilt@med.va.gov

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The NICE guidelines on prostate cancer provide comprehensive advice on best practice for diagnosis and treatment of prostate cancer. They are based on systematic reviews of the evidence, incorporate multidisciplinary opinions, and try to balance the values of healthcare providers and patients for various outcomes while emphasising a patient centred approach. Their conclusions are generally consistent with other reviews and guidelines evaluating similar evidence.¹⁻⁵ If followed, these recommendations will likely improve prostate cancer outcomes while reducing unnecessary, ineffective, harmful, and costly care.

Paucity of randomised controlled trials

Although NICE's recommendations are generally appropriate, any guidelines on prostate cancer are going to be hampered by the lack of high quality information available. The paucity of randomised trials limits the quality of data used for informed decision making, particularly regarding detection and treatment of localised disease. Even where randomised trials have

shown benefits, the absolute magnitude of benefit is generally small, requires many years to accrue, and must be weighed against accompanying harms and costs. Few studies enrolled men with disease that had been detected as a result of measuring the level of prostate specific antigen (PSA) or were adequately powered to assess survival outcomes. Individual patients and providers may place different values on a particular outcome or have clinical and tumour characteristics that have not been adequately assessed by the trials providing the evidence used for drafting guidelines. Thus, it is difficult to mandate rigid adherence to these recommendations or to create national practice standards.

Limitations that may reduce uptake by clinicians

The full NICE guideline is wide ranging and can serve as a single source of information on prostate cancer. However, an individual clinician or patient will find that many sections are not pertinent to their situation. The broad scope makes the guideline more

cumbersome than targeted recommendations aimed at specific points in the diagnosis and treatment pathway. Recommendations are made without adequate documentation as to their confidence, strength of evidence, magnitude of harms and benefits or methods for successful implementation and evaluation. The reader is required to spend considerable additional effort to determine the evidence base for these recommendations or accept or reject them as written.

These limitations can reduce clinicians' acceptance and implementation.⁶ For example, some detection, treatment, and monitoring recommendations are very prescriptive despite lack of evidence supporting this level of detail. In contrast, recommendations not to routinely use combined androgen suppression or bisphosphonates for metastatic disease are brief and relatively underemphasised, though information supporting NICE recommendations exists from many large, high quality randomised studies. Clinicians are encouraged to counsel patients about the risks and benefits of prostate cancer screening as well as different treatment options. The full guideline notes that patients "should be adequately informed about the effects of prostate cancer and the treatment options on their sexual function, physical appearance, continence and other aspects of masculinity. Healthcare professionals should support men and their partners or carers to make treatment decisions taking into account the effects on quality of life as well as survival." Although links to additional information are included, quantitative outcome data due to these effects and user friendly information tools to guide providers and patients in decision making are not immediately available.

Basing treatment recommendations on patient and tumour characteristics

For men found to have localised prostate cancer, NICE recommends that providers counsel men about several options and make treatment recommendations based on patient and tumour characteristics. NICE guidelines list watchful waiting as an option for low and intermediate risk disease. This is a step forward given the data on the natural course of the disease and the findings from randomised treatment trials.¹⁷ Active surveillance is recommended for low risk disease and radical prostatectomy or radiation therapy for high risk disease. However, consensus for these recommendations is lacking, little evaluation has been done for any active surveillance protocol, and little evidence shows superiority of one treatment option over another on the basis of disease risk status.

The role of PSA testing in deciding when to perform biopsy

NICE's recommendations that the serum PSA level alone should not automatically lead to a prostate biopsy are sound. The aim of prostate biopsy is to detect prostate cancers that have the potential for causing harm and that can effectively be treated, rather than finding each and every cancer. No

randomised trial has shown that PSA testing reduces overall or disease specific mortality. No PSA value accurately rules in or out prostate cancer or high grade disease. Widespread PSA testing and referral for prostate biopsy of all men with values greater than an arbitrary threshold of 4 ng/ml has labelled many men "abnormal," increased the number having a biopsy, and resulted in detection of a large reservoir of clinically unimportant "pseudo-tumours."⁵

Incorporating a patient's age, race, family history of prostate cancer, digital rectal examination, and past biopsy results can predict the likelihood of a biopsy specimen proving to be positive for any cancer and high grade cancer.⁴ However, data are not available to determine the impact these indices have on patient anxiety or decision making, number of biopsies performed, and frequency of serendipitously detected pseudo-tumours⁵ versus tumours missed that would be clinically important but potentially effectively treated. Raising the PSA threshold for prostate biopsy (for example to >10 ng/ml) is more likely to reduce unnecessary diagnostic and treatment interventions, although missing clinically important but treatable disease may result.⁵

Emerging technologies

The use of emerging technologies such as cryotherapy, high intensity focus ultrasonography, photon beam radiation therapy, and robotic radical prostatectomy has increased in many countries. However, a comprehensive review found that no randomised trials had evaluated effectiveness. Few data exist on long term comparative effectiveness and harms.¹ NICE is wise to caution against early adoption of these unproved therapies.

Does the structure and process of health services affect patient outcomes?

The guideline did not fully discuss the evidence for any effects of the structural and process measures of care on outcomes. Surgeons and hospitals with high annual volumes of radical prostatectomy have better outcomes.¹ Additional structural and process measures to define quality of care have been proposed. Whether improved outcomes for prostate cancer will result is not yet known but needs evaluation.

Dissemination and implementation

The next steps for improving care for men with prostate cancer should focus on effective dissemination and implementation of the NICE guidelines as well as evaluation of subsequent practice patterns, healthcare costs, and patient centred outcomes. Development of effective and readily usable patient and provider tools are needed for targeting unique steps in the diagnosis and treatment pathway. NICE should create, use, and link understandable levels of strength of evidence, confidence in recommendation, and magnitude of risk and benefits with different options that incorporate

patient and tumour characteristics as well as preferences. In the few instances where evidence is very strong and confidence high, performance standards and practice incentives might be introduced. Unfortunately, for most situations related to detection and treatment of prostate cancer, more definitive recommendations will require completion of randomised trials.

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CHANGE PAGE

Don't add aspirin for associated stable vascular disease in a patient with atrial fibrillation receiving anticoagulation

Gregory Y H Lip

University Department of
Medicine, City Hospital,
Birmingham B18 7QH
g.y.h.lip@bham.ac.uk

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The clinical problem

Atrial fibrillation is the commonest cardiac arrhythmia, with increasing prevalence and incidence.¹ Adjusted dose oral anticoagulation (such as with warfarin) is the most effective treatment for stroke prevention in high risk patients with atrial fibrillation.²

However, common practice is to add aspirin (or other antiplatelet treatment) to warfarin in atrial fibrillation if there is associated chronic stable coronary or peripheral artery disease.² This is despite relatively little evidence that adding aspirin to warfarin reduces stroke or other vascular events in patients with atrial fibrillation.

I propose here that we should not add aspirin for associated stable vascular disease in a patient with atrial fibrillation receiving anticoagulation, given the lack of evidence for benefit and the potential for harm.

The evidence for change

Randomised clinical trials in patients with atrial fibrillation using combinations of anticoagulation and aspirin either compared fixed dose (or low intensity, international normalised ratio (INR) <1.5) anti-coagulation plus aspirin with adjusted dose warfarin² or compared adjusted dose anticoagulation (INR 2.0-3.0) plus aspirin with adjusted dose anticoagulation.

The first trial type found that fixed dose anti-coagulation plus aspirin was no better than adjusted dose warfarin.² In the second category, one trial was stopped early owing to poor recruitment but showed a substantially higher bleeding rate in the anti-coagulation plus aspirin arm than in the anti-coagulation alone arm.³ A retrospective analysis of the combined dataset of two large recent randomised

clinical trials⁴ of warfarin versus ximelagatran (an oral direct thrombin inhibitor) in moderate to high risk patients with atrial fibrillation compared aspirin users with non-users. This analysis found no additive effect of taking aspirin (with either of the anticoagulation treatments) in preventing stroke or reducing vascular events (including death or myocardial infarction).⁴ Specifically, the rate of myocardial infarction with aspirin and warfarin was not significantly different from that with warfarin alone (0.6% and 1.0% a year respectively). However, aspirin use resulted in a substantial higher bleeding risk compared with warfarin alone (major bleeding 3.9% and 2.3% a year respectively; $P < 0.01$).

Various cohort studies (either case series or registry analyses) in which aspirin was added among patients receiving anticoagulation treatment who were having percutaneous coronary intervention and stenting (only a proportion of patients had atrial fibrillation) also suggest an increase in bleeding risk by adding antiplatelet treatment to warfarin.⁵⁻⁸ In one registry analysis of 10 093 patients with atrial fibrillation, the use of antiplatelet treatment was associated with a threefold increase in intracranial haemorrhage (relative risk 3.0; 95% confidence interval 1.6 to 5.5).⁹

Barriers to change

The perception that aspirin plus warfarin is needed in patients with atrial fibrillation and vascular disease is based on the fact that antiplatelet treatment works on the platelet-rich thrombus ("white clot") associated with vascular disease, whereas warfarin is effective for the fibrin-rich thrombus ("red clot") associated with atrial fibrillation.

Change Page aims to alert clinicians to the immediate need for a change in practice to make it consistent with current evidence. The change must be implementable and must offer therapeutic or diagnostic advantage for a reasonably common clinical problem. Compelling and robust evidence must underpin the proposal for change.