The authors suggest that these data could help patients weigh treatment options, and support early adjuvant therapy (reduced relapse and recurrence rates, delayed hormonal therapy) as well as delayed radiotherapy once PSA becomes detectable (without exacerbating the risk of metastatic disease).

Original article Thompson IM Jr *et al.* (2006) Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial. *JAMA* **296:** 2329–2335

Combination therapy for men with lower urinary tract symptoms

Lower urinary tract symptoms and overactive bladder are commonly treated with antimuscarinic agents or α-receptor antagonists. Kaplan *et al.* investigated the efficacy and safety of the antimuscarinic tolterodine extended release (ER), the α_1-receptor antagonist tamsulosin, and a combination of both, in men with overactive bladder and benign prostatic hyperplasia.

In this 12-week, randomized, double-blind, placebo-controlled trial at 95 clinics in the US, patients received a single daily dose of tolterodine ER 4 mg ($n = 217$), tamsulosin 0.4 mg ($n = 215$), tolterodine ER plus tamsulosin ($n = 225$), or placebo ($n = 222$). The primary outcome measure was patient perception of benefit after 12 weeks of treatment. Other end points included bladder diary variables, International Prostate Symptom Scores (IPSS), safety, and tolerability.

With regard to efficacy, 80% of patients receiving tolterodine ER plus tamsulosin had perceived a benefit from their treatment, compared with 62% receiving placebo, 65% receiving tolterodine ER, and 71% receiving tamsulosin. Patients receiving tolterodine ER plus tamsulosin experienced significant reductions in urgency urinary incontinence, urgency episodes, and micturitions per 24 h compared with patients receiving placebo. They also had significant improvements in the IPSS ($P = 0.003$) compared with placebo patients. All three interventions were well tolerated.

The results of this study indicate that combined treatment with an antimuscarinic agent and an α_1-receptor antagonist for 12 weeks is beneficial for men with lower urinary tract symptoms, including overactive bladder, who might not respond to monotherapy with either agent.

Original article Kaplan SA *et al.* (2006) Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder. *JAMA* **296:** 2319–2328

Can increased PSA velocity detect early, life-threatening prostate cancer?

Serum PSA values >4.0 ng/ml are routinely used to select patients for prostate biopsy, although this approach misses some early-stage cancers. Some researchers advocate dropping the PSA threshold to 2.6 ng/ml, but this strategy might result in overdiagnosis and unnecessary intervention. Carter and colleagues suggest that the rate of increase in PSA level (PSA velocity) might detect life-threatening prostate cancer at a potentially curable stage—well before the 4.0 ng/ml threshold is reached.

The authors evaluated data from 980 participants in the Baltimore Longitudinal Study of Aging. They compared 856 men without a diagnosis of prostate cancer and 124 men diagnosed with prostate cancer (20 died of prostate cancer, 38 died of other causes; and 66 remained alive). PSA velocity was calculated from two or three successive PSA measurements for 788 men. Patients' PSA velocity 10–15 years before diagnosis predicted their prostate-cancer-specific survival 25 years later: 92% of men with an annual PSA velocity ≤0.35 ng/ml survived, whereas only 54% of men with a higher PSA velocity than this survived. The risk of prostate cancer death was nearly fivefold higher in men with an annual PSA velocity >0.35 ng/ml than in men whose PSA velocity was below this threshold, although most still had absolute PSA levels <4.0 ng/ml. The authors infer that even small rises in PSA could indicate the presence of life-threatening prostate cancer.

Carter and colleagues suggest that men with a low PSA velocity might be appropriate candidates for observation, whereas those with a high PSA velocity might benefit from early intervention.

Original article Carter HB *et al.* (2006) Detection of life-threatening prostate cancer with prostate-specific antigen velocity during a window of curability. *J Natl Cancer Inst* **98:** 1521–1527