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PROSTATE CANCER

What is the real IMPACT of *BRCA1/BRCA2* mutation?

European Urology has published the first year's screening results of the IMPACT study—a trial set up to evaluate targeted prostate cancer screening in men with *BRCA1*/*BRCA2* mutations, who have a 1.8–8.6-fold increased risk of developing this cancer.

2,481 men aged 40–69 years (791 *BRCA1* carriers, 531 *BRCA1* controls, 731 *BRCA2* carriers, and 428 *BRCA2* controls) from 62 centres in 20 countries were enrolled in the study. In total, 199 men (8%) presented with PSA levels of >3.0 ng/ml, 162 biopsies were performed, and 59 prostate cancers were diagnosed—18 in *BRCA1* carriers (2.3%), 10 in *BRCA1* controls (1.9%), 24 in *BRCA2* carriers (3.3%), and seven in *BRCA2* controls (1.6%).

Although differences between the detection rates for carriers and controls were not deemed to be statistically significant, they suggest a trend towards improved detection in men with *BRCA1*/*BRCA2* mutations, and the authors predict that these differences will increase over the next few years of follow-up assessment. "We will continue to follow up this cohort for a further 5 years and expect to offer clinical recommendations for the management of men with *BRCA1/2* mutations," says Rosalind Eeles, who led the study.

A similar trend was observed in the positive predictive value (PPV) of biopsy using a PSA threshold of 3.0 ng/ml, which was 48% versus 33.3% in *BRCA2* carriers and controls, respectively, and 37.5% versus 23.3% in *BRCA1* carriers and controls, respectively. Again, differences were not statistically significant, but the authors note that a PPV of 48% is about twofold greater than the PPVs reported in population-screening studies such as the ERSPC, possibly owing to the fact that the IMPACT study involved younger men.

BRCA2 carriers are thought to present at a younger age with more aggressive disease, and Bancroft *et al*. reported a significant difference in the rates of intermediate-risk and high-risk disease between *BRCA2* carriers and controls (71% versus 43%). Conversely, men with the *BRCA1* mutation were less likely to be diagnosed with intermediate-risk or high-risk disease than controls (61% versus 80%), highlighting the complexity of the situation. Although some data suggest that *BRCA1* carriers are more likely to present with aggressive disease, an association is far from clear.

The authors suggest lowering the PSA threshold in *BRCA2* carriers to increase the detection of early-stage cancers, although they stress that the results of their study cannot be generalized to all ethnic groups, as 95% of the men were white. "Future research will be directed at using targeted screening for other genetically high-risk cohorts; for example, we have recently started to recruit men with mismatch repair gene mutations following reports that prostate cancer incidence is higher in these men," explains Eeles.

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Original article Bancroft, E. K. *et al*. Targeted prostate cancer screening in BRCA1 and BRCA2 mutation carriers: results from the initial screening round of the IMPACT study. *Eur Urol*. doi:10.1016/j.eururo.2014.01.003