

IMPACT: Identification of Men with a genetic predisposition to Prostate Cancer: Targeted screening in BRCA1 and BRCA2 mutation carriers and controls.

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Background

Prostate cancer is now the largest cancer burden in Europe. There is controversy over the efficacy of population based screening programs and research studies in both Europe and the UK are underway to determine this. The current marker used in screening is prostate specific antigen (PSA). However this is known to be raised in other conditions therefore there is a need to identify better markers of the disease.

There is evidence for genetic disposition to prostate cancer. To date approximately 9% of patients are found to have a family history of the disease. This doubles if the proband aged 60 or less. Genetic variants that increase the risk of prostate cancer have been identified and more are likely to be found from large scale genome association studies.

The IMPACT study

IMPACT was set up to determine the value of targeted screening in a population known to be genetically predisposed to the disease (initially *BRCA1/2* mutation carriers).

An increased incidence of prostate cancer has been identified in *BRCA2* carriers, particularly in those with young onset disease. A poorer survival rate is present compared to that in non-carriers. Corresponding evidence in *BRCA1* carriers is less conclusive at present but will be determined following inclusion of these individuals in the IMPACT study.

The study aims to: establish an international targeted prostate cancer screening study in *BRCA1/2* mutation carriers; determine the incidence of raised PSA and abnormal biopsy as a result of screening in this group and whether this is different from screen-detected disease in controls; determine the specificity and sensitivity of PSA screening; and evaluate new markers of early prostate cancer in *BRCA1/2* mutation carriers.

The study is looking to recruit 850 *BRCA1* and *BRCA2* mutation carriers and 850 controls. For 5 years individuals have an annual PSA test and give serum, plasma and urine samples. Men with a raised serum PSA of > 3.0ng/ml are offered a prostate biopsy.

Controls are predictive test negative men from families with a *BRCA1/2* mutation because even though there will be access to data from 2 current population based screening groups these are not perfectly matched – in the European study screening is done every 4 years and in the UK study individuals are only offered a single screen.

Pilot data

Fifty-seven men have been recruited in the UK to date. Early data were presented on PSA and testosterone levels from the pilot cohort.

Future work

The UK pilot has recruited over 50% of its target (100 individuals). Recruitment is about to begin in both national and international centres including Cambridge, Australia and Spain. The pilot data will be analysed for publication and further funding sought to continue and extend the study. The next logical progression from IMPACT is IMPACT2 – targeted screening of individuals to identify low penetrance prostate cancer predisposition genes.