Update from the ReIMAGINE Prostate Cancer Screening Study NCT04063566: inviting men for prostate cancer screening using MRI.

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Word count: 748

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Keywords: Prostate cancer, prostate cancer screening, MRI

Ethics: ReIMAGINE Prostate Cancer Screening has regulatory approval from the Regional Ethics Committee London – Stanmore (reference 19/LO/1129).

Funding: ReIMAGINE Screening is funded by The Medical Research Council, U.K. (MRC), grant number MR/R014043/1 and Cancer Research U.K. (CRUK).

Disclosures:

Caroline M Moore receives funding from Prostate Cancer UK, Movember, the Medical Research Council, Cancer Research UK and the NIHR. She receives fees for HIFU proctoring from SonaCare . She has received speaker fees from Astellas, and Jannsen. She carries out research into photodyanamic therapy supported by Spectracure.

Mark Emberton serves as a consultant/educator/trainer to Sonacare Inc., Exact Imaging, Angiodynamics Inc and Profound Medical. Acknowledgements - Mark Emberton receives research support from the United Kingdom's National Institute of Health Research (NIHR) UCLH/UCL Biomedical Research Centre.

Shonit Punwani receives research support from the United Kingdom's National Institute of Health Research (NIHR) UCLH/UCL Biomedical Research Centre.

Francesco Giganti is funded by the UCL Graduate Research Scholarship and the Brahm PhD scholarship in memory of Chris Adams.

Ton Coolen receives funding from Cancer Research UK and is Director of Saddle Point Science Ltd.

ReIMAGINE Prostate Cancer Screening will evaluate the feasibility of magnetic resonance imaging (MRI) as a potential screening investigation for prostate cancer, a leading cause of cancer specific death in the UK. [1] The disease is often asymptomatic in its early stages and presents a significant diagnostic challenge. We remain heavily reliant upon opportunistic prostate specific antigen (PSA) blood testing and clinical examination to inform referral to secondary care and are yet to establish an effective prostate cancer screening strategy in the UK.

PSA levels are not a reliable indicator of prostate cancer and may lead to over-detection of clinically unimportant disease and miss clinically significant cancer. [2, 3] Several large population-based screening studies have failed to show a reliable impact of PSA-informed screening on overall prostate cancer specific mortality but the European Randomised Screening study (ERSPC) suggests a significant benefit to screening in the longer term as the numbers needed to screen to avert one death fall over time. [4-7] Multiparametric MRI (mpMRI) is now established as the cornerstone of localised prostate cancer diagnosis in the UK. [8] mpMRI detects almost all clinically important cancers and is associated with a high negative predictive value (NPV). A significant proportion of men with a raised PSA can safely avoid biopsy following a triage MRI. [9] We explore whether we can apply the precision of diagnostic MRI to the screening setting.

The ReIMAGINE Prostate Cancer Screening study is a UK ethics approved (19/LO/1129) single centre prospective feasibility study inviting men aged 50 – 75, with no history of prostate cancer diagnosis, to undergo prostate cancer screening using PSA and MRI. The study is funded by the Medical Research Council, UK (MRC) and Cancer Research UK (CRUK).

The primary end points of the study include the acceptance rate of an invitation for a screening prostate MRI, the prevalence of MRI-defined suspicious lesions in men accepting a screening invitation and the presence of cancer for those men having biopsy as a result of their MRI findings. Secondary outcomes include the proportion of men ineligible due to prior prostate cancer diagnoses and the number of participants who screen negative on PSA density and/or MRI.

The study was designed in collaboration with General Practitioners (GPs) and members of the public who have been affected by, or have experience of, prostate cancer. Potential participants were identified via partner GP practices acting as participant identification centres (PICs) and were invited at random, in batches of 50 – 100 men, to enrol to the study until 300 participants were recruited.

Following informed written consent, each participant received a PSA blood test and a 3 Tesla research MRI consisting of axial T2-weighted, diffusion-weighted and research specific T2 exploratory acquisitions with a total scan time of less than 20 minutes. Exploratory research sequences (multiecho-T2W) were used to derive Luminal Water Fraction (LWF) maps. [10] Clinical sequences (biparametric T2-weighted axial turbo spin echo and diffusion-weighted imaging using a high b value of 2000 s/mm^2) were used to determine screen status.

A “screen-positive” result is conferred by either a clinically significant lesion on biparametric MRI (reported by two independent radiologists blinded to clinical data including PSA) or a

PSA density ≥ 0.12ng/ml (using MRI-derived prostate volume). A third, blinded radiologist is used when the first two reporters disagree on the presence of a clinically significant lesion. Exploratory sequences will be analysed retrospectively. All “screen-positive” participants will be encouraged to undergo further, standard of care, investigations. Resultant clinical data will be collected in line with the study protocol. The study design is outlined in Figure 1.

Enrolment is now complete. 309 participants were recruited between November 2019 and December 2020. 6 participants were withdrawn. Study MRI reporting allowed for non-diagnostic images on diffusion weighted imaging (DWI) as with usual practice e.g. rectal gas. However, owing to select incidents of non-diagnostic images on DWI due to machine failure, the study team aligned the individual participants’ management with standard of care, but replaced the data in the study by recruiting additional men over the original target of 300. In total, 303 participants received a study MRI. Study activity was stopped between March and August 2020 due to the COVID-19 pandemic. Data collection to inform primary outcomes is ongoing.

ReIMAGINE Screening is a single centre feasibility study assessing the feasibility of biparametric MRI as a screening tool for prostate cancer. Study outcomes will inform the design of a multi-centre UK screening study, and take us a step towards a more accurate, and less harmful, prostate cancer screening approach.

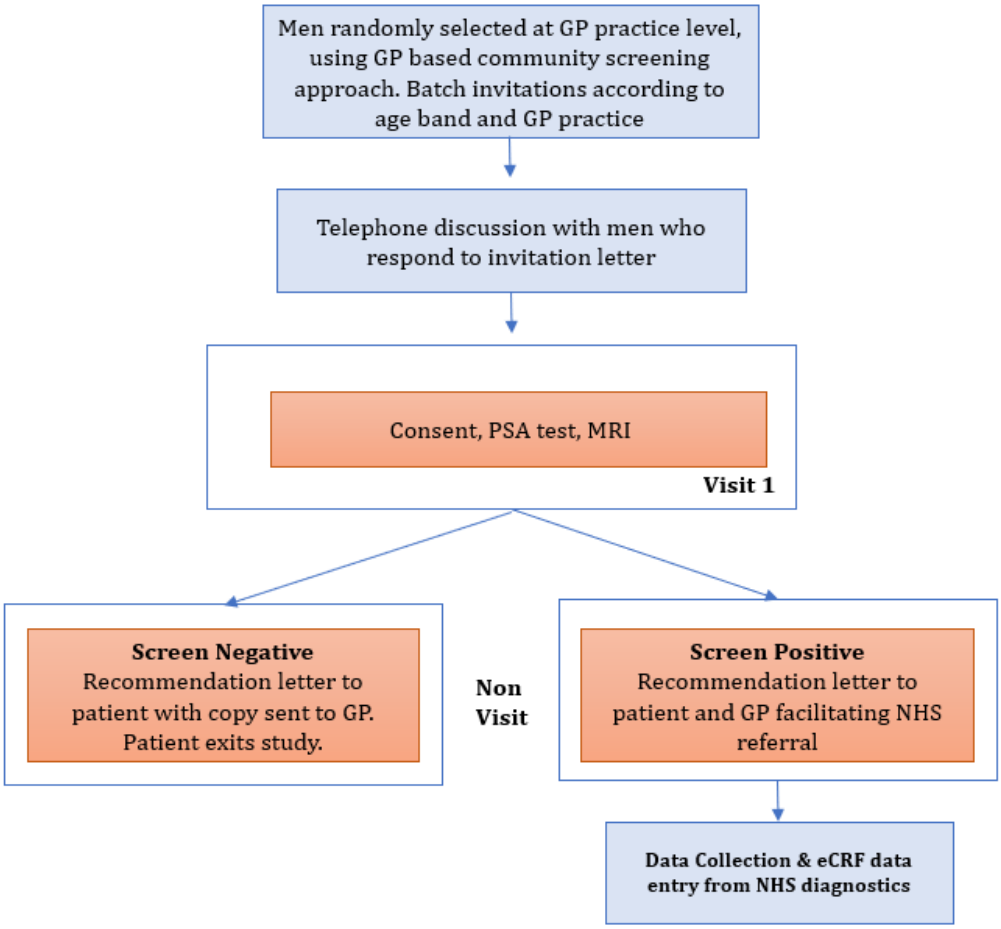

Figure 1: ReIMAGINE Prostate Cancer Screening Study design. ReIMAGINE Screening will recruit eligible men from partner General Practitioner (GP) surgeries. Each participant will receive a prostate specific antigen (PSA) blood test and a research MRI of the prostate consisting of biparametric clinical sequences (axial T2-weighted and diffusion-weighted acquisitions) and research specific sequences. Clinical sequences will be used to determine screen status within the study. A "screen-positive" result is conferred by a suspicious lesion on biparametric MRI or a PSA density of ≥ 0.12ng/ml using MRI-derived prostate volume. All "screen-positive" participants will be invited to undergo standard of care prostate cancer investigations.

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