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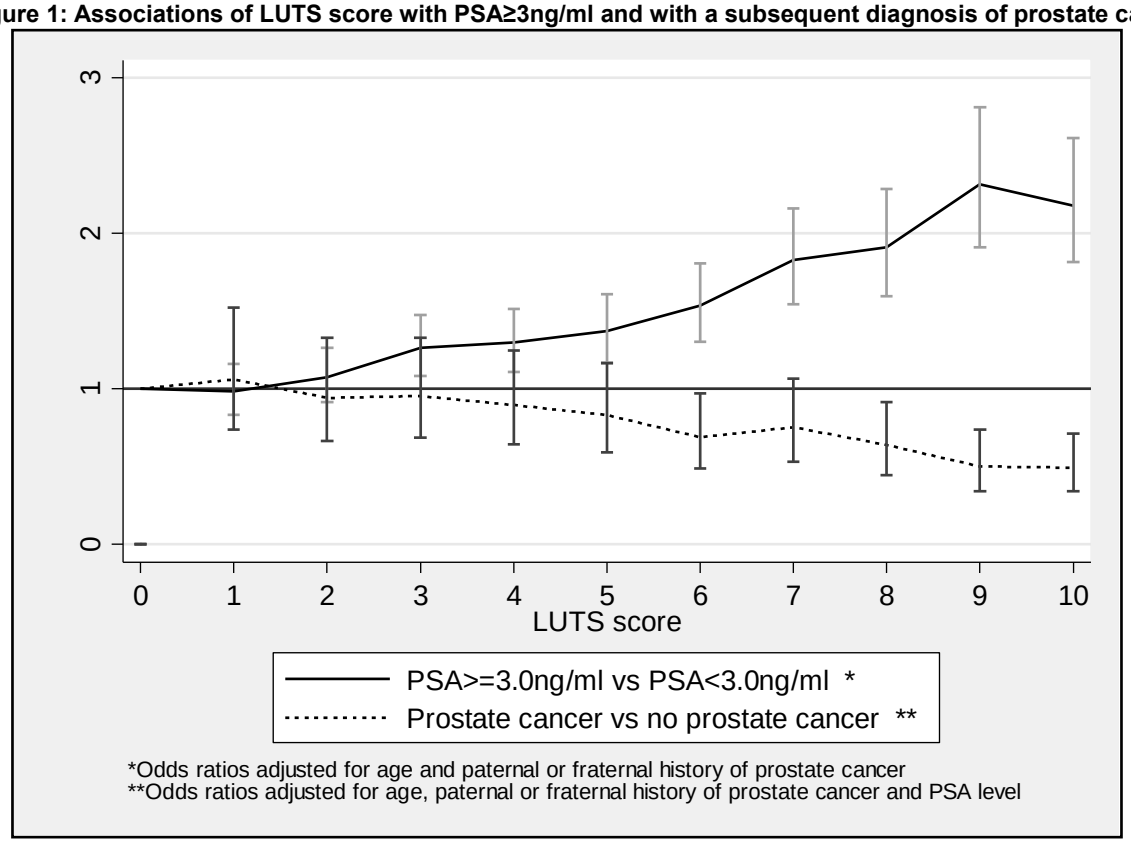
ASSOCIATIONS OF LOWER URINARY TRACT SYMPTOMS WITH PROSTATE-SPECIFIC ANTIGEN LEVELS AND SCREEN-DETECTED LOCALIZED AND ADVANCED PROSTATE CANCER: A CASE-CONTROL STUDY NESTED WITHIN THE UK POPULATION-BASED PROTECT (PROSTATE TESTING FOR CANCER AND TREATMENT) STUDY

Hypothesis / aims of study
To determine relationships between lower urinary tract symptoms, prostate-specific antigen levels and screen-detected localized and advanced prostate cancer in a population-based cohort.

Study design, materials and methods
Case-control study nested within the ProtecT (Prostate testing for cancer and Treatment) study. Men aged 50-69 years were invited for prostate-specific antigen (PSA) testing and those with PSA ≥ 3.0ng/ml were invited for biopsy. We determined whether lower urinary tract symptoms (LUTS) were associated with PSA ≥ 3.0ng/ml and prostate cancer using logistic regression models adjusted for age, family history of prostate cancer and PSA level as appropriate. Urinary symptoms were analysed individually and as an ordinal symptom score (range 0-10) derived from the overall number and severity of symptoms. Odds ratios for the association between each symptom and localised or advanced cancer were compared using Wald tests for heterogeneity, estimated from multinomial logistic regression models.

Results
65,871 men had a PSA test: 7,251 had PSA ≥ 3.0ng/ml including 2,467 subsequently diagnosed with prostate cancer (2,119 localised, 348 advanced). LUTS were positively associated with PSA ≥ 3.0ng/ml: odds ratios were 1.18 (95% CI 1.01-1.38), 1.69 (1.32-2.16), and 1.60 (1.33-1.93) for daytime urination frequency (hourly *vs* less frequent), urgency and hesitancy (most/all the time *vs* never), respectively. LUTS among men with PSA ≥ 3ng/ml were negatively associated with prostate cancer: odds ratios were 0.44 (0.22-0.83), 0.74 (0.63-0.87), and 0.83 (0.73-0.94) for nocturia (4+ *vs* 0), leakage and hesitancy (occasionally/sometimes *vs* never), respectively. Odds of PSA ≥ 3ng/ml increased, and odds of prostate cancer decreased, in a linear relationship with the overall number and severity of symptoms as measured by the LUTS score (**Figure 1**). Associations of LUTS with prostate cancer did not differ between localised or advanced disease.

Figure 1: Associations of LUTS score with PSA≥3ng/ml and with a subsequent diagnosis of prostate cancer



Interpretation of results
Our findings show clearly the negative relationship between LUTS and prostate cancer among men who have raised PSA levels. Raised PSA levels are positively associated with LUTS. Hence, men with raised PSA levels and the presence of LUTS are more likely to be diagnosed with benign disease than prostate cancer.

Concluding message

These findings are likely to be of some utility in developing nomograms for predicting biopsy outcome among men who have had a positive PSA test, thus potentially informing men of their risk of prostate cancer and perhaps avoiding 'unnecessary' biopsies. Men who have a raised PSA level in the absence of LUTS should be counselled that this is associated with a higher risk of prostate cancer than if they had symptoms.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Trent Multicentre Research Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**