Title:

Full BLOOD count TRends for colorectal cAnCer deteCtion (BLOODTRACC): development of dynamic prediction models for early detection of colorectal cancer using trends in blood tests from primary care.

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Objectives:

Colorectal cancer is common in the UK. Around 55% of patients are diagnosed late-stage, where likelihood of survival is low: five-year survival is 93% at Stage 1 versus 10% at stage 4. Early detection is crucial to save lives. The full blood count (FBC) is a common blood test in primary care. Patients with colorectal cancer have specific trends among their FBCs over time for many years before their diagnosis, not seen in patients without colorectal cancer. We developed the BLOODTRACC models, dynamic prediction models utilising patient-level trends in repeated FBC measurements for two-year risk of colorectal cancer.

Methods:

We performed a cohort study using patient data from the Clinical Practice Research Datalink, with colorectal cancers identified from the National Cancer Registration and Analysis Service. We developed a multivariate joint model of longitudinal and time-to-event data to derive two-year risk of diagnosis for males and females separately. Using all historical FBCs over five years prior to the current FBC (baseline), trends in haemoglobin, mean cell volume, and platelet measurements informed risk of diagnosis in two years (+/- 3 months). Model performance in the internal validation sample was assessed using Harrell's c-statistic for discrimination and calibration plots.

Results:

The joint models were developed using 250,716 males and 246,695 females, of whom 0.4% (n=865) and 0.3% (n=677) were diagnosed in two years (+/- 3 months) following their current FBC, respectively. Simultaneous decreases in haemoglobin and mean cell volume and increase in platelets from the average population trend (patients with no diagnosis) were associated with an increased risk of diagnosis in two years for both males and females. The c-statistic was 0.751 (95% CI: 0.739,

0.764) for males and 0.763 (95% CI: 0.753, 0.775) for females in the internal validation cohort. Calibration plots indicate the models are well calibrated.

Conclusions:

Our dynamic BLOODTRACC prediction models identify patients with undiagnosed colorectal cancer and perform well in bringing their diagnosis forward by two years. As relevant FBC trends are present before symptoms become apparent, blood test abnormality, and referral thresholds in national guidelines are reached (these results will be presented), the models can facilitate earlier detection. Future research will focus on comprehensive testing of the BLOODTRACC models in further primary care patients.