microRNA, gut microbiome and lifestyle related factors as indicators of different risk profiles for colorectal cancer and pre-invasive lesions

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Background
High false positives rates, leading to unnecessary colonoscopies, represent a limitation of FIT as primary screening test. Moreover, current screening protocols are based on age only, ignoring other risk factors.
This study aims to: identify miRNA signatures as biomarkers for Advanced Neoplasia (advanced adenoma/CRC , AN) risk among FIT+ subjects (as triage tests); investigate the association of microbiome profiles with the AN risk; explore modulation from lifestyle factors (diet and other lifestyle factors) of AN risk associated with biomarkers profiles and to identify risk patterns (miRNA profiles, lifestyle factors, haemoglobin levels at baseline) among FIT- subjects

Methods
miRNA profiles will be characterized by NGS in plasma/stool samples of AN patients, and healthy subjects recruited at colonoscopy. The identified miRNAs will be evaluated in a nested case-control study within a cohort of subjects undergoing screening with FIT+. miRNA expression profiles and microbiome composition will be compared between AN subjects and a matched sample of subjects with FIT+ test and negative colonoscopy. Information on lifestyle risk factors and plasma/stool samples will be collected at the time of enrolment. A sample of subjects with FIT- result will be followed up to compare risk patterns at baseline and at the second round among 3 ‘risk groups’ of subjects.

Expected Results
An overview of miRNA profiles in plasma/stool by NGS, with identification of dysregulated signatures in AN. A bio-bank useful to validate the selected biomarkers and future novel ones. miRNA signatures to be employed as a triage test among FIT+ subjects in a population-based screening setting. A risk pattern based on haemoglobin concentration, diet and lifestyle, miRNA expression profiles, microbiome composition.

Conclusion
The present study will help to identify biomarkers to complement the available screening tests, and to reduce unnecessary invasive and expensive procedures. Tailored screening programmes according to different CRC risk criteria may maximize the impact of screening.