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Optimal cancer screening regimes in gastrointestinal evolution using mathematical modelling

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Mathematical modelling of the stochastic evolutionary process of carcinogenesis can be used to derive and to optimize the timing of clinical screens so that the probability is maximal that an individual is screened within a certain "window of opportunity" for intervention when early cancer development may be observed. By using data from epidemiological studies with long-term patient follow-up, empirical approaches aid in screening design and may inform cost-effectiveness analyses to compare proposed screening and intervention strategies. However, mechanistic modelling that incorporates a greater level of biological understanding and detail for how and when normal tissues progress to cancer can be used for a more refined screening design than typically implemented in population screening studies. With examples in inflammation-driven premalignant disease of the gastrointestinal tract, I will introduce calibrated multistage clonal expansion models of carcinogenesis, derive probability equations used for optimal screening times and risk estimation, and present results for screening strategies using inferred parameters from US cancer incidence data. These results 1) provide a robust statistical framework for quantifying when it is optimal to screen and begin surveillance for premalignant changes, and 2) are shown to be cost-effective in Barrett's esophagus patients, particularly with increasingly sensitive and minimally invasive sampling procedures used in clinical practice.

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