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HOW CAN THE LONG-TERM BENEFITS AND HARMS BE TRANSPARENTLY QUANTIFIED AND CONTRASTED FOR INFORMED DECISION – MAKING? – COLORECTAL CANCER SCREENING FOR PERSONS AT FAMILIAL RISK (FARKOR)

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Introduction

In Germany, colorectal cancer (CRC) screening is recommended as of age 50. Individuals with familial CRC risk may benefit from early detection and treatment. Our aim was to systematically evaluate and compare the long-term benefit-harm balance of different screening strategies (colonoscopy or immunologic fecal blood testing [iFOBT]) for individuals younger than age 50 with identified familial colorectal cancer risk in Germany.

Methods

Study design

Model type / Time horizon: Markov state-transition model (Figure 1) with a cohort simulation / lifetime.
Population: German individuals (age 25 - 50 years) identified with familial CRC risk based on a simple questionnaire on CRC history in family members.
Strategies: Different screening strategies that differ by screening test (colonoscopy or iFOBT), screening age at start and end, screening interval, follow-up algorithms.
Current screening: choice of a) iFOBT annual age 50-54, biennial age 55+, b) 10-yearly colonoscopy, age 50 (men)/55 (women).
Outcomes: cancer cases and deaths, life years gained [LYG], potential harms associated with additional colonoscopies, colonoscopy-related severe complications (SC), incremental harm-benefit ratios (IHBR), compared to the next non-dominated strategy.
Perspective: target population.

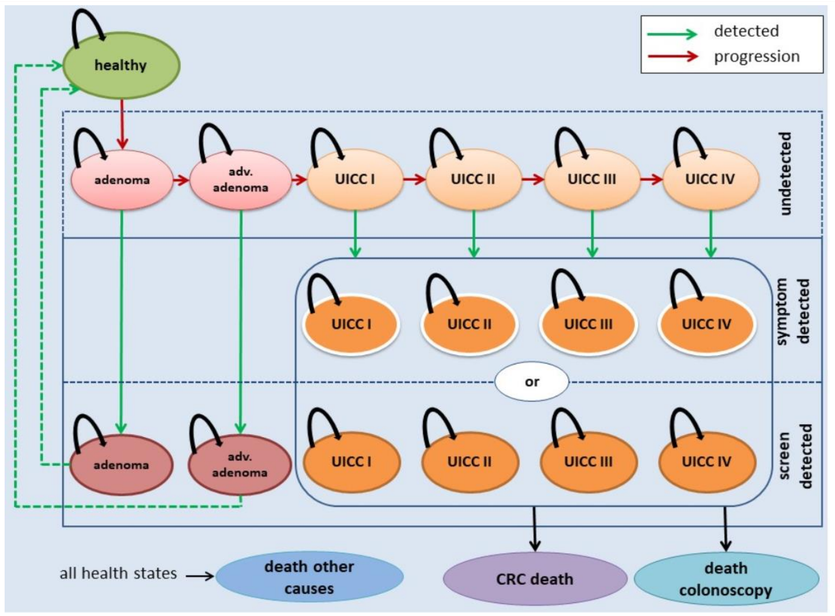

Figure 1. Schematic representation of the natural history model of colorectal cancer.
green arrows - detected, red arrows – progression, UICC - classification of the Union for International Cancer Control, CRC - colorectal carcinoma. adv. - advanced.

Data

Clinical & epidemiological data: German literature including guidelines and original German data. Data from German cancer registries and the German Statistical Office (DESTATIS).
Transition probabilities: international literature, calibration.
Test characteristics: international trial data, meta-analyses.

Calibration / Validation

Hierarchical calibration of transition probabilities to fit specific epidemiologic data observed in an unscreened German population (FARKOR study, literature data). Internal and external model validation using published observed data.

Sensitivity analysis

Deterministic one- and multi-way sensitivity analyses on test characteristics and adherence to screening.

Results

Base-case analyses

Clinical effectiveness

In the base-case analysis with full compliance with screening and follow-up, both benefits and harms increased with lower age for screening start and shorter intervals. When screening started before age 50, 32-36 CRC-related deaths per 1,000 screenees were avoided with colonoscopy and 29-34 with iFOBT, compared to 29-31 (colonoscopy) and 28-30 (iFOBT) CRC-related deaths avoided per 1,000 screenees when starting at age 50, respectively.

Benefit-harm trade-offs

The benefit-harm trade-offs of the different screening strategies with iFOBT screening or with colonoscopy screening are visualized for different harm outcomes in Figure 2.

Sensitivity analysis

In two-way sensitivity analyses for iFOBT screening the IHBRs increased with a simultaneous increase of test sensitivity and decrease of test specificity by absolute 5% each but not with a simultaneous decrease of test sensitivity and increase of test specificity by absolute 5% each compared to the base case. In two-way sensitivity analyses for colonoscopy screening a simultaneous de- and increase of these test performance parameters led to a slight increase (absolute 5% increase of test sensitivity and absolute 5% decrease of test specificity) or decrease (absolute 5% decrease of test sensitivity and absolute 5% increase test specificity) in life-years gained but did not affect the harms.

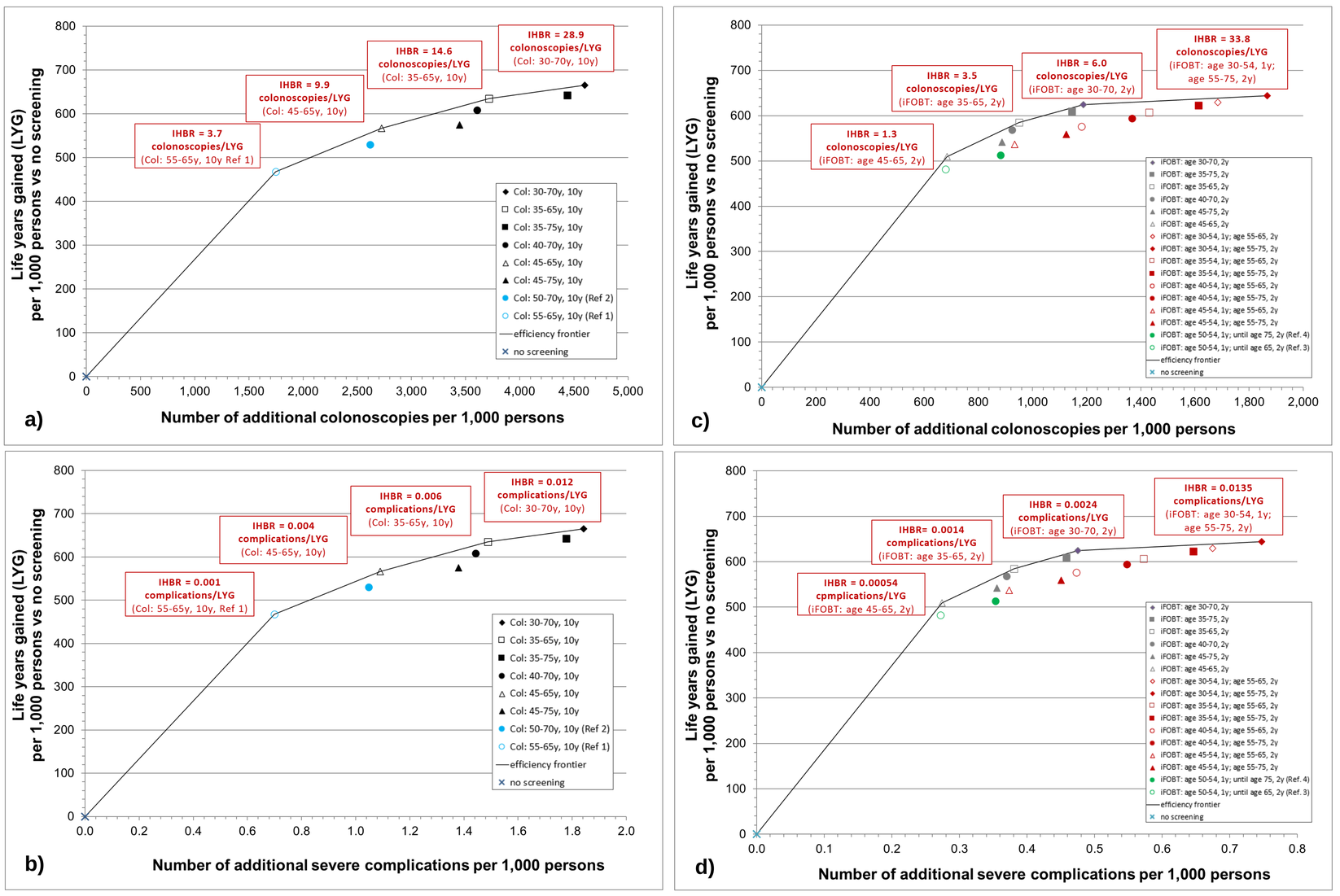

Figure 2. Base-case analysis: benefit-harm frontiers for iFOBT and colonoscopy screening.
Benefit-harm frontiers expressed as a) additional colonoscopies/LYG and b) additional severe complications/LYG for iFOBT screening as well as c) additional colonoscopies/LYG and d) additional severe complications/LYG for colonoscopy screening.

Col: colonoscopy, iFOBT: immunologic fecal blood testing , IHBR: incremental harm-benefit ratio, LYG: life years gained, y: years.

Conclusion

Based on our decision analyses, offering colonoscopy or iFOBT screening to individuals younger than 50 years with familial CRC risk in Germany may be beneficial. Depending on the acceptance for additional harms per additional unit of benefit, 10-yearly colonoscopy or alternatively biennial iFOBT from age 30 to 70 may be recommended for individuals with familial CRC risk. Future research is needed to acquire evidence-based information on the impact of screening results on quality of life.

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