Health-Economic Evaluation of Early Screening for Individuals Younger than Age 50 with Familial Colorectal Cancer Risk Based on a Decision Analysis within the FARKOR Study

Gaby Sroczynski (1); Lára R. Hallsson (1); Nikolai Mühlberger (1); Beate Jahn (1,2); Sabine Hoffmann (3); Raphael Rehms (3); Doris Lindörfer (3); Alexander Crispin (3); Ulrich Mansmann (3); Uwe Siebert (1,2,4,5)

(1) Institute of Public Health, Medical Decision Making and Health Technology Assessment, Department of Public Health, Health Services Research and Health Technology Assessment, UMIT - University for Health Sciences, Medical Informatics and Technology, Hall i. T., Austria; (2) ONCOTYROL - Center for Personalized Cancer Medicine, Division of Health Technology Assessment and Bioinformatics, Innsbruck, Austria; (3) Institute for Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians University, Munich, Germany; (4) Harvard T.H. Chan School of Public Health, Center for Health Decision Science, Department of Health Policy and Management, Boston, MA, USA; (5) Harvard Medical School, Institute for Technology Assessment and Department of Radiology, Massachusetts General Hospital, Boston, MA, USA

Objectives

FARKOR is a prospective population-based intervention study in Bavaria, Germany offering colonoscopy or immunologic fecal blood testing (iFOBT) for individuals at age 25-50 identified with familial colorectal cancer (CRC). We systematically evaluated the benefit-harm and cost-effectiveness ratios of different screening strategies in German individuals younger than age 50 with familial CRC risk.

Methods

Study Design

Model type: Markov state-transition cohort model (Figure 1).
Time horizon: lifelong.
Population: German individuals (age 25 - 50 years) identified with familial CRC risk based on a simple questionnaire on CRC history in family members.
Strategies: Choice of Colonoscopy or iFOBT screening starting / ending at different age, various screening intervals. Current screening: iFOBT annual age 50-54/biennial age 55+ or 10-yearly colonoscopy at age 50 (men)/55 (women). Colonoscopy and iFOBT screening were analysed separately, because individuals have the choice to decide.
Outcomes: Reduction in cancer cases and deaths, life years gained [LYG], severe complications (SC) from colonoscopy, incremental harm-benefit ratios (IHBR), and incremental cost-effectiveness ratios (ICER; in Euro/LYG), compared to the next non-dominated strategy.
Perspective: German statutory health insurance.
Discount rate: Annual 3% for cost and effects.

Table 1. Excerpt of relevant model input parameters

	Test characteristics		Source
	Colonoscopy	*iFOBT*	
Sensitivity adenomas (w/m), %	75.0	10.7/15.7	Heisser et al. 2020, Launois et al. 2014
Sensitivity adv. Adenomas, %	95.0	26.3/31.3	
Sensitivity CRC, %	95.0	75.6/80.6	
Specificity, %	100	96.2/91.2	
Procedures	**Aggregated Costs (€2020)**		**Source**
Risk assessment	60.00		FARKOR Pilot study
iFOBT screening	19.50		
Colonoscopy after positive iFOBT	248.40		
Colonoscopy screening	268.10		
Polypectomy (colonoscopy screening)	66.60		
Polypectomy (iFOBT screening)	63.80		
Bleeding after colonoscopy	2,139		Severin et al. 2015
Perforation after colonoscopy	6,336		
CRC therapy UICC stage I-IV	25,050 - 44,564		
Death after colonoscopy	15,327		Haug et al.2014
End-of-life cost	76,797		

iFOBT: immunologic fecal blood testing ; CRC: Colorectal cancer, adv.: advanced; w: women; m: men

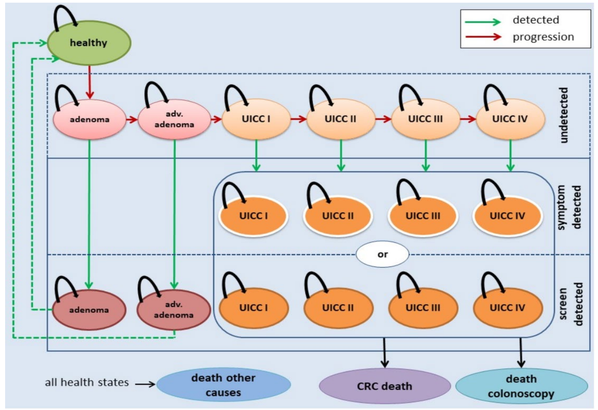

Figure 1. Schematic representation of the natural history model of colorectal cancer. green arrows - detected, red arrows – progression, UICC - classification of the Union for International Cancer Control, CRC - colorectal carcinoma. adv. - advanced.

Data

Clinical & epidemiological data: German literature including guidelines and from original German data from the FARKOR study. Data from German cancer registries and the German Statistical Office (DESTATIS).
Transition probabilities: international literature, calibration.
Test characteristics: international trial data, meta-analyses (Table 1).
Cost data: direct medical inpatient and outpatient cost (year 2020) based on German reimbursement system (ambulatory fees in FARKOR study) and Diagnosis-Related-Groups as well as published aggregated costs from German literature (Table 1).
Calibration of disease progression and detection without screening to observed epidemiologic data (German Cancer Registry).
Validation to observed data from cancer registries and published studies.

Sensitivity Analyses

Deterministic one- and multi-way sensitivity analyses. Adherence rate, annual discount rate, the age of start and end of screening, accuracy and cost of screening tests were varied.

Results

Base-case analyses

Clinical effectiveness

In the base-case analysis with full compliance, both benefits and harms increased with lower age for screening start and shorter intervals. When screening started before age 50, 32.4-35.5 CRC-related deaths per 1,000 screenees were avoided with colonoscopy and 28.7-33.5 with iFOBT, compared to 28.7-31.4 (colonoscopy) and 28.0-30.2 (iFOBT) CRC-related deaths avoided per 1,000 screenees when screening started at age 50.

Benefit-harm ratios

The IHBRs measured in additional severe complications per additional LYG (SC/LYG) for iFOBT screening were 0.00054 (biennial, age 45-65), 0.0014 (biennial, age 35-65), 0.0024 (biennial, age 30-70) and 0.0135 (annual, age 35-54; biennial, age 55-65) compared to the next non-dominated strategy. Corresponding IHBRs for 10-yearly colonoscopy were 0.001 (age 55-65), 0.004 (age 45-65), 0.006 (age 35-65) and 0.012 (age 30-70) SC/LYG.

Cost effectiveness

Compared to standard care, biennial iFOBT age 35-75 was cost saving. The next more effective iFOBT strategies yielded ICERs of 2,630 (biennial, age 30-70), and 34,675 Euro/LYG (annual, age 30-54; biennial, age 55-75), respectively (Figure 2). Compared to standard care, 10-yearly colonoscopy age 45-65 was cost-saving. Moving to earlier start and later stop yielded ICERs of 2,962, 3,240 and 9,279 Euro/LYG for 10-yearly colonoscopy screening at age 40-70, 35-65, and 30-70, respectively (Figure 3).

Sensitivity analysis

ICER results for iFOBT were most sensitive to variations of discount rates, screening adherence, test sensitivity and specificity for advanced adenomas. The ICER increases to more than 50,000 Euro/LYG when the discount rate is increased to more than 4.5% or the specificity is reduced below 90% (Figure 4). For colonoscopy, influential parameters were the annual discount rate, the adherence to screening, and slightly the cost of colonoscopy screening. However, the ICER increases to more than 50,000 Euro/LYG only when the discount rate increased to more than 9%.

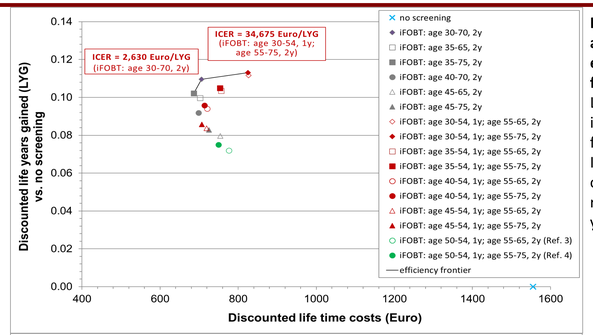

Figure 2. Base-case analysis: cost-effectiveness frontier for iFOBT screening. LYG: life year gained, iFOBT: immunologic fecal blood testing , ICER: incremental cost-effectiveness ratio (Euro/LYG), y: years.

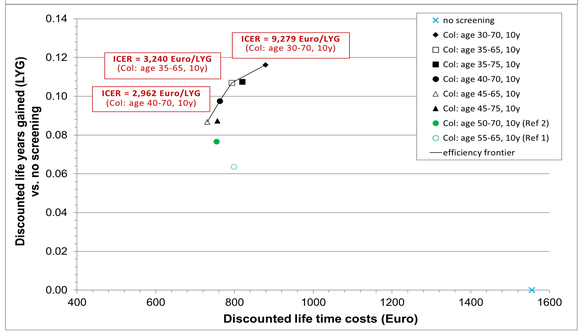

Figure 3. Base-case analysis: cost-effectiveness frontier for colonoscopy screening. LYG: life year gained, Col: colonoscopy, ICER: incremental cost-effectiveness ratio (Euro/LYG), y: years.

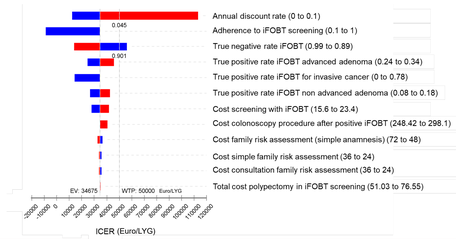

Figure 4. Tornado Diagram. Influence of relevant model parameters on ICER of iFOBT screening (annual age 30-54; biennial age 55-75) compared with biennial iFOBT screening.

Conclusions

Offering colonoscopy or iFOBT screening to individuals younger than 50 years with familial CRC risk may be beneficial and can be considered cost effective in the German health-care setting. Benefit-harm ratios suggest 10-yearly colonoscopy or alternatively biennial iFOBT from age 30 to 70 to be acceptable.

Funding: *This work was supported by Funded by GB-A Innovationsfonds Grant: 01NVF17026. The funding agreement ensured the authors' independence in designing the study, analyzing and interpreting the data, writing, and publishing the report.*

Contact: gaby.sroczynski@umit-tirol.at
www.umit-tirol.at