Aalto-yliopisto
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Optimising Colorectal Cancer Screening with Decision Programming

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Background

- Colorectal cancer (CRC) is the second most common malignancy in both women and men with 3600 new cases and 1400 disease-specific deaths in Finland in 2019
- CRC cancer screening reduces CRC incidence and mortality
  - Programme pilot began in 2019 and screening became nationwide in 2022 in Finland
  - The screening is conducted every 2 years for 65-74 year-old men and women, and will be later expanded to 56-74 year-olds during the next 10 years

FIT testing

- CRC screening is implemented with the feacal immunochemical test (FIT), which measures the hemoglobin level (blood) in the stool sample
- Patients with positive test will be directed to further examinations (colonoscopy)
- Heinävaara et al. (2022) used a simulation model to determine the threshold values for the hemoglobin levels for both genders
  - The optimal strategy was **25 µg/g for men** and **10 µg/g for women**, no optimisation for different age groups
- Based on these results, the threshold value was set to **25 µg/g** for both genders due to the cost-effectiveness

Objective and methods

- The aim of this study was to optimise the threshold value for feacal immunochemical testing used in CRC screening in Finland for different age-groups and both genders
- The Decision Programming framework was constructed to optimise the problem
  - The decision programming framework combines stochastic programming and decision analysis
  - Influence diagram can be formulated into a mixed integer linear programming (MILP) problem
- Model was implemented using Julia language and DecisionProgramming.jl package

Optimisation model

- The aim is to optimise FIT threshold for both genders and different age-groups
  - Discrete variable, possible levels 10, 25, 40, 55, 70 µg/g
- The incidence of CRC depends on gender and age
- Sensitivity of FIT test depends on gender and threshold
  - Sensitivity = the probability that the test result is positive for a patient with the disease

Men, FIT sensitivity

	10	25	40	55	70
Normal	0.04	0.01	0.01	0.01	0.01
Benign	0.27	0.26	0.24	0.18	0.14
Premalignant	0.6	0.55	0.5	0.35	0.21
Malignant	0.9	0.8	0.75	0.7	0.65

Women, FIT sensitivity

	10	25	40	55	70
Normal	0.03	0.02	0.01	0.01	0.01
Benign	0.09	0.09	0.08	0.06	0.03
Premalignant	0.4	0.35	0.25	0.2	0.15
Malignant	0.57	0.5	0.35	0.25	0.19

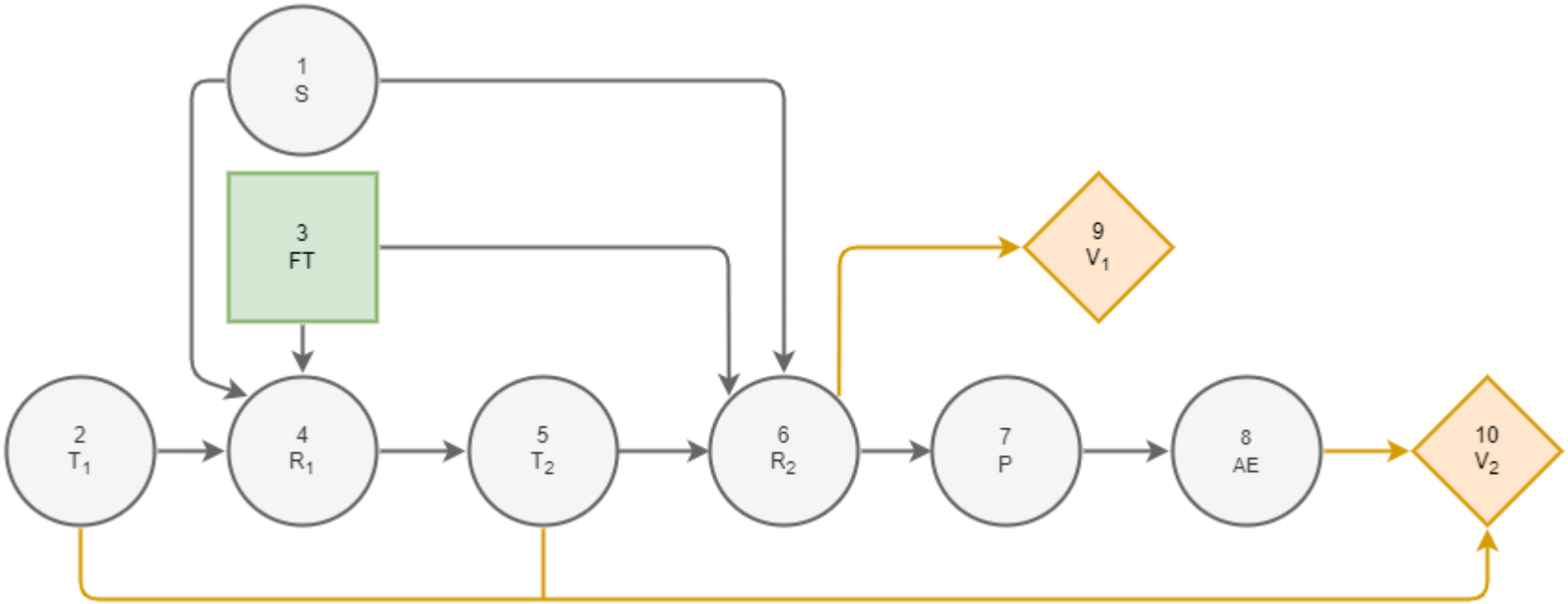
Objective

- The objective is the maximisation of net monetary benefit

$$NMB = \underbrace{health\ outcomes \cdot \mathrm{WTP}}_{\text{health benefits}} - costs$$

  where WTP describes the willingness-to-pay threshold
- Health outcomes of finding a tumor are difficult to evaluate
  - Usually presented as QALYs (quality adjusted life years) or LYGs (life years gained)
- WTP for CRC screening is not determined in Finland
  - In Sweden 2400€/LYG, in France 4000€/LYG
- Since the values are not readily available and their evaluation is beyond the scope of this thesis, the health benefits are approximated

Influence diagram



FT	FIT threshold (10, 25, 40, 55, 70)		
S	bowel state (normal, benign, premalignant, malignant)		
		P	polypectomy i.e. biopsy of a tumor (yes, no)
T1	FIT test returned (yes, no)	**AE**	adverse effects i.e. bleed or perforation (yes, no)
R1	FIT result (+, -, NA)		
T2	colonoscopy (yes, no)	**V1**	health benefits of found tumors
R2	colonoscopy result (N, B, PM, M, NA)	**V2**	costs of examinations and complications

Costs and benefits

- Costs were obtained from the study by Heinävaara et al. (2022)

	FIT test	Colonoscopy	Adverse effects
Costs (€)	12.4	400	3280

- Primary treatment of CRC costs 22.200€ (Färkkilä et al. 2014)
  - Based on this value, the health benefits were approximated
  - The sensitivity of the model to these parameters was later assessed

	Normal	Benign	Premalignant	Malignant
Benefits (€)	0	800	11100	22200
LYGs **(WTP 2400€/LYG)**	0	0.33	4.63	9.25

Results

- The optimal thresholds were found for both genders in four age groups
- Optimal thresholds were similar to the thresholds in the study by Heinävaara et al. (2022)

Threshold µg/g	55-59	60-64	65-69	70-74
Men	25	25	25	10
Women	25	25	10	10

Sensitivity analysis: men

- The sensitivity analysis was conducted by changing the value of one health benefit parameter while keeping other parameters constant
- The new thresholds obtained by the analysis are presented below for each situation

55-59 y

change in parameter	benign	premalignant	malignant
-50%	25	25	25
0%	25	25	25
50%	25	25	25
100%	25	25	25

60-64 y

change in parameter	benign	premalignant	malignant
-50%	25	25	25
0%	25	25	25
50%	25	25	25
100%	25	25	25

65-69 y

change in parameter	benign	premalignant	malignant
-50%	25	25	25
0%	25	25	25
50%	25	**10**	25
100%	25	**10**	**10**

70-74 y

change in parameter	benign	premalignant	malignant
-50%	10	25	25
0%	10	10	10
50%	10	10	10
100%	10	10	10

Sensitivity analysis: women

55-59 y

change in parameter	benign	premalignant	malignant
-50%	25	25	25
0%	25	25	25
50%	25	25	25
100%	25	10	25

60-64 y

change in parameter	benign	premalignant	malignant
-50%	25	25	25
0%	25	25	25
50%	25	**10**	**10**
100%	25	**10**	**10**

65-69 y

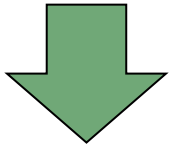
change in parameter	benign	premalignant	malignant
-50%	10	25	10
0%	10	10	10
50%	10	10	10
100%	10	10	10

70-74 y

change in parameter	benign	premalignant	malignant
-50%	10	10	10
0%	10	10	10
50%	10	10	10
100%	10	10	10

Updated results

Threshold µg/g	55-59	60-64	65-69	70-74
Men	25	25	25	10
Women	25	25	10	10



Threshold µg/g	55-59	60-64	65-69	70-74
Men	25	25	**10**	10
Women	25	**10**	10	10

- Based on the sensitivity analysis lowering the thresholds in men ages 65-69 and in women ages 60-64 would be beneficial

Total colonoscopies

Threshold µg/g	55-59	60-64	65-69	70-74
Men	2588	2900	3314 **+ 4026 = 7340**	7695
Women	3751	3886 **+ 1444 = 5330**	5550	5948

- Choosing the lower thresholds would increase the number of colonoscopies
  - In the current screening for ages 65-74 with 17.9% from 22507 to 26533 (cost increase of 1.6M€) per 2 years
  - In the future screening for ages 55-74 with 15.4% from 35632 to 41102 (cost increase of 2.2M€) per 2 years
- The availability of colonoscopies might be a limiting factor

Conclusions and future directions

- The Decision Programming framework was successfully applied to the problem and the model provided similar results to the study by Heinävaara et al. (2022)
- The model was limited by the evaluation of the health benefit parameters. However, based on the sensitivity analysis, the model was not highly sensitive for the selection of parameters for most of the age groups.
  - Based on the sensitivity analysis the thresholds for some age groups could be lowered, however, the availability of colonoscopies might limit this
- The model should be further improved:
  - Using more accurate evaluation of health benefits or multi-objective optimisation (maximising number of found tumors)
  - Adding a constraint for the number of colonoscopies performed
  - Using smaller intervals or/and continuous threshold

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