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Cost-Effectiveness of LGI-Flag in Austria: A Model-Based Evaluation

Evelyn Walter[a], Christian Datz[b], Atilla Kaya[c] ,Hans G. Mustafa[d]

a IPF Institute for Pharmaeconomic Research, Vienna, Austria
b General Hospital Oberndorf, Salzburg, Austria
c Roche Diagnostics GmbH, Vienna, Austria
d Laboratory for Medical, Chemical and Microbiological DiagnosticsGmbH, Salzburg, Austria

Objectives

Colorectal cancer (CRC) remains a leading cause of cancer-related morbidity and mortality. In Austria, CRC is the third most common cancer in men and the second in women, with approximately 4,500 new cases annually. Late-stage diagnoses contribute to significant economic burden. Early detection is critical for improving outcomes and reducing costs. LGI-Flag, an AI-based risk stratification tool using routine blood test data, may enhance early CRC detection and screening adherence. However, its cost-effectiveness in the Austrian healthcare context has not yet been thoroughly assessed.

Methods

A decision-analytic cohort simulation model was developed to assess CRC progression (UICC stages I–IV) over a lifetime horizon, based on Austrian epidemiological data. The model incorporated real-world screening adherence and compared six strategies starting at age 45: (1) annual LGI-Flag, (2) LGI-Flag after negative FIT, (3) LGI-Flag after negative Hemoccult, (4) annual FIT + LGI-Flag, (5) annual Hemoccult + LGI-Flag, and (6) no screening.

Outcomes included life-years (LYs), quality-adjusted life-years (QALYs), and positive test results. Probabilities and utilities were drawn from published literature; costs were based on Austrian data.

Results were expressed as incremental cost-effectiveness ratios (ICERs) from a societal perspective, with sensitivity analyses conducted to address uncertainty.

Table 1: Overview of methods applied

Methods	
Type of study	**Cost-utility analysis (CUA) and Budget-impact analysis (BIA)**
Type of the model	**State transition Markov cohort model**
Perspective	Austrian **societal perspective** (direct and indirect costs)
Time horizon	**Lifetime,** with a cycle length of 1 years
Discount rate	3% for costs & 3% for outcomes
Population	**Eligible patients:** Adults aged 45 walk into the model
Intervention	**Different screening strategies:** annual LGI-Flag, LGI-Flag after negative FIT, LGI-Flag after negative Hemoccult, annual FIT + LGI-Flag, annual Hemoccult + LGI-Flag
Comparator	No screening
Costs	**Direct costs:** Costs of screening, costs due to (advanced) adenomas, colonoscopy-related complication costs, costs of staging, inpatient CRC costs, costs of medication (UICC IV), follow-up costs and end of life costs **Indirect costs:** work absenteeism and presentism costs
Outcomes	Life years (LYs) saved; quality-adjusted life years (QALYs) saved
Results	Incremental cost-utility ratio (ICUR) & incremental cost-effectiveness ratio (ICER)
Timing	**2024**

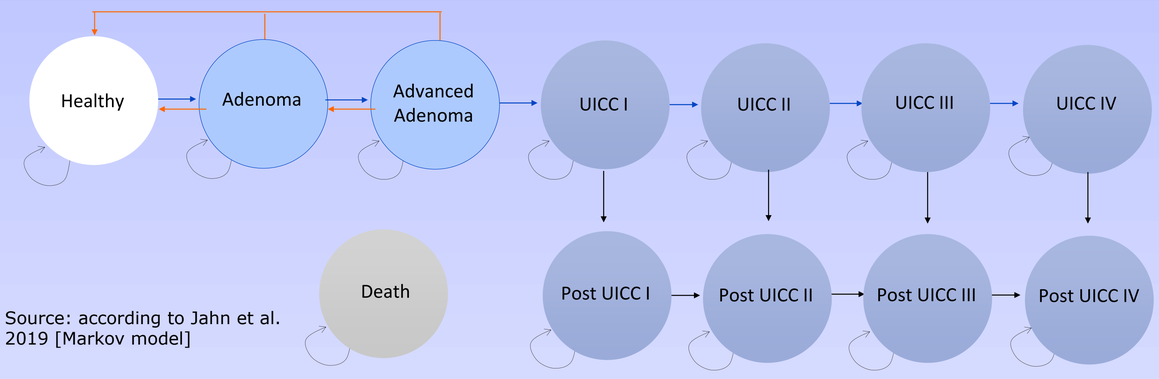
Model Structure

A state-transition (Markov) cohort model was developed to simulate the natural history, screening, and surveillance of colorectal cancer (CRC). Each circle represents a distinct health state, and arrows indicate possible annual transitions between these states.

The model starts with a hypothetical cohort of healthy individuals who may develop adenomas, which can either be detected and removed through screening or progress to advanced adenomas and subsequently to CRC. CRC is represented by four stages corresponding to the UICC I–IV classification.

Individuals with detected adenomas or cancers are moved to post-diagnosis (or "post-treatment") health states, reflecting outcomes after detection and therapy. All health states include the possibility of transition to death, either due to CRC or from other causes based on age- and sex-specific mortality rates for Austria.

Figure 1: Markov-Model design



Source: according to Jahn et al. 2019 [Markov model]

Screening and Surveillance

- The model captures the impact of regular screening and post-polypectomy surveillance:
  - Annual screening applies to healthy individuals according to the evaluated strategy.
  - 3-yearly surveillance follows the detection and removal of an advanced adenoma.
  - 5-yearly surveillance applies after detection of a non-advanced adenoma or a negative surveillance colonoscopy.
  - Screening can detect lesions at any stage (adenoma, advanced adenoma, or CRC). Upon detection, individuals transition to the appropriate post-treatment states, with screening intervals adjusted accordingly.
  - Adherence to screening and surveillance was incorporated based on literature estimates (Benamouzig et al., 2021).

Transition and Dynamics

- **Blue arrows** represent disease progression.
- **Orange arrows** indicate detection by screening.
- **Black arrows** represent transitions to post-UICC states, reflecting individuals who have been diagnosed and treated for CRC according to their UICC stage. These transitions capture movement from active disease to post-treatment follow-up phases.

Transitions between health states occur annually, allowing the model to estimate lifetime costs, life-years, and quality-adjusted life-years (QALYs) under different screening strategies.

Clinical Data

- Natural history parameters and hazard ratios were adopted from Jahn et al. (2019), an Austrian modeling analysis calibrated to national epidemiological data.
- In Jahn et al., parameter estimation was based on:
  - Epidemiological data (cancer incidence and stage distribution) from Statistics Austria and published literature as calibration targets.
  - Hierarchical model calibration using optimization algorithms (Nelder–Mead and Basin-Hopping).
  - Final parameter adjustment to match the observed stage distribution.
- All-cause mortality was derived from age-specific life tables from Statistics Austria (2019), with extrapolation beyond age 100 using an exponential distribution. CRC-specific mortality (post-diagnosis) originated from Statistics Austria (2017–2019) and was adjusted for detection mode (screening vs. symptomatic).

Input data for diagnostic accuracy

- Sensitivity and specificity were adjusted according to the testing strategy.
  - In "after" strategies, LGI-Flag was applied only among FIT- or Hemoccult-negative individuals,
  - whereas in "plus" strategies, both tests were conducted in parallel.

Table 2: Sensitivity and Specificity

Accuracy	LGI-Flag[1]	LGI-Flag after negative FIT[1,2]	LGI-Flag after negative Hemoccult[1,2]	FIT + LGI-Flag[1,2]	Hemoccult + LGI-Flag[1,2]
Sensitivity Adenoma	3.8%	7.9%	9.8%	7.9%	9.8%
Sensitivity Advanced Adenoma	42.8%	38.7%	27.2%	44.3%	44.2%
Sensitivity CRC	81.8%	88.0%	74.5%	88.0%	83.1%
Specificity	88.0%	93.3%	90.9%	93.3%	90.9%

Source: own calculation

1 Putri et al. 2024; 2 Jahn et al. 2019

Direct costs

The cost assessment relied on attributing costs to various health states.

- Costs associated with each health state were determined based on the utilization of resources linked to that state.
- This resource usage, encompassing the type and frequency of medical goods and services provided to the patient, along with their monetary value, was employed to compute the total direct costs within the Austrian context. Cost data were obtained from tariff catalogues and published literature and, where necessary, adjusted to 2024 values for inflation.

Indirect Costs

Indirect costs captured productivity losses arising from absenteeism and reduced work performance (presenteeism).

- **Absenteeism:** Estimated from workdays lost due to CRC and related complications using ICD-10 diagnoses.
- **Presenteeism:** Derived from literature data (Malaguarnera et al., 2013); no presenteeism was considered for complications.
- **Valuation**: Indirect costs were valued using gross salaries including employer contributions.

Utilities

Utilities reflected health-related quality of life by age and disease state.

- **Baseline utilities:** Age-specific utility values were applied according to Marten et al. (2021).
- **Disease-related disutilities:** Utility decrements for CRC and post-CRC health states were derived from published literature.
- **Procedure-related disutilities:** Temporary disutilities associated with colonoscopy-related complications were included based on literature sources.

Results

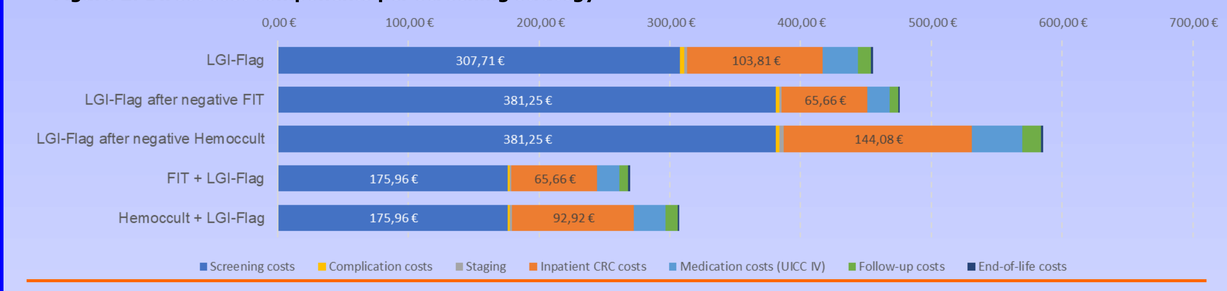
Cost-effectiveness results

The LGI-Flag-based screening yields a total cost of 1,504.97 € per person screened (625.02 € direct, 879,95 € indirect), while no screening costs 3,234.03 €. LGI-Flag provides an incremental gain of 0.10 QALYs and is dominant over no screening. Costs for alternative strategies range from 1,195.59 € to 1,630.53 €. Strategies that include LGI-Flag remain the most cost-effective. Detection rates are highest when LGI-Flag follows a negative FIT or is combined with FIT.

Table 3: Cost-effectiveness results

Costs	LGI-Flag	LGI-Flag after negative FIT	LGI-Flag after negative Hemoccult[1]	FIT + LGI-Flag[1]	Hemoccult + LGI-Flag[1,]	No screening
Direct costs	625.02 €	610.73 €	720.24 €	342.17 €	380.16 €	1,694.72 €
Indirect costs	879.95 €	853.44 €	910.29 €	853.42 €	873.21 €	1.539.31 €
Total costs	**1,504.97 €**	**1,464.16 €**	**1,630.53 €**	**1,195.59 €**	**1,253.37 €**	**3,234.03 €**
Outcomes						
QALYs	21.1785	21.1825	21.1756	21.1833	21.1809	21.0747
LYs	22.5929	22.5931	22.5929	22.5931	22.5930	22.5726
Positive Test results	1.2841	1.5525	1.5493	1.5525	1.5514	0
CRC Lifetime prevalence	4.75%	4.57%	4.89%	4.57%	4.68%	13.61%
ICUR	**Dominant [vs. No screening -974.58 € - 1,352.56 €]**					

Figure 2: Direct cost components per screening strategy



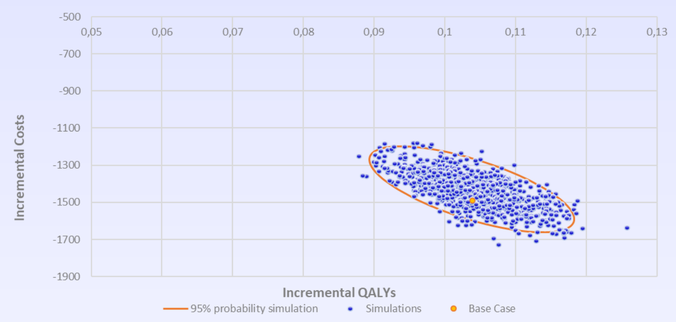
Icremental results

- Across all comparisons, strategies including LGI-Flag were dominant compared with no screening. Incremental cost-utility ratios (ICURs) versus no screening ranged from –974.58 € (*LGI-Flag after Hemoccult*) to –1,352.56 € (*FIT + LGI-Flag*). When comparing LGI-Flag alone against other screening alternatives, ICURs ranged from -10,344.87 € (*LGI-Flag after negative FIT*) to -56,268.25 € (*FIT + LGI-Flag*).
- LGI-Flag remained the dominant strategy when considering only direct costs from the payer's perspective.
- Results refer to an average screened individual within the hypothetical cohort of 1,000 individuals rather than a detected case. Therefore, incremental costs and QALYs are smaller than they would be when comparing detected CRC cases with non-CRC individuals.

Sensitivity Analysis

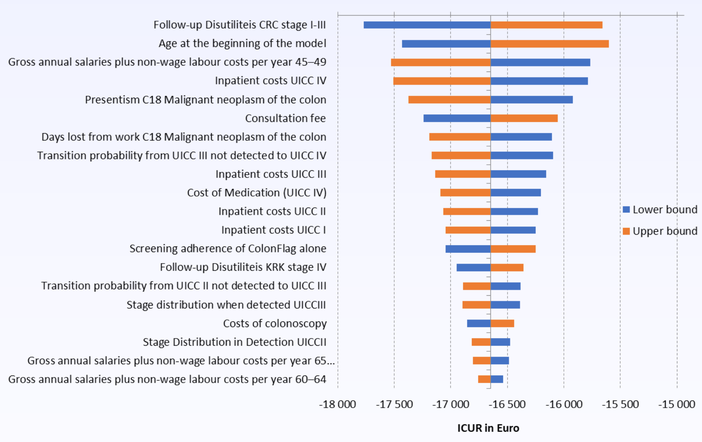
Probabilistic sensitivity analysis (PSA) and deterministic one-way sensitivity analysis (OWSA) were carried out to examine the robustness of the model.

Figure 3: Scatterplot, LGI-Flag versus No screening



- The Monte Carlo PSA, based on 1,000 second-order simulations, plotted incremental costs against incremental effects (Figure 3)
- All simulations fall within the lower-right quadrant, indicating dominance of the LGI-Flag strategy.
- The average probabilistic incremental cost was –1,430.01 €, with incremental QALYs of 0.104, resulting in an incremental cost-utility ratio (ICUR) of –13,773.80 €, confirming dominance.

Figure 4: OWSA tornado diagram, LGI-Flag versus No screening



- The OWSA assessed the impact of individual input parameters on the ICUR.
- When comparing LGI-Flag with No Screening, the five parameters with the greatest influence were:
  - Follow-up disutilities for CRC stages I–III
  - Age at model entry
  - Gross annual salary including non-wage labor costs (age group 45–49 years)
  - Inpatient costs for UICC IV
  - Day of presenteeism for ICD-10 C18 (malignant neoplasm of the colon)
- The other comparator strategies that combine LGI-Flag with additional tests showed similarly dominant results.

Source: own calculations

Conclusion

LGI-Flag is a cost-effective and dominant screening strategy for CRC in Austria. Its integration—especially following negative FIT or in combination with FIT—offers potential to improve early detection while reducing long-term healthcare and societal costs.

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Additional literature with the author

CONTACT:
Dr. Evelyn Walter
IPF Institute for Pharmaeconomic Research
Wolfengasse 4/7
1010 Vienna, Austria
Phone: +43-1-5132007-13
Fax: +43-1-5132007-15
Email: e.walter@ipf-ac.at
Web: www.ipf-ac.at

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