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Economic Analysis of Liquid-based Cytology for Cervical Cancer Prevention in Women in Austria

Evelyn Walter^a, Franz Meyer^a, Mattäus Traunfellner^a

^aIPF Institute for Pharmaeconomic Research, Vienna, Austria

Objectives

Since the introduction of cytological examinations in the 1950s, the Pap-smear has significantly reduced the mortality rate of cervical cancer (CxCa). Austria is among the European countries with an opportunistic screening program, where annual Pap-smears are reimbursed for women aged 18 and over. Liquid-based cytology (LBC), available since the mid-1990s, has numerous advantages. The Austrian Society for Clinical Pathology and Molecular Pathology and the Austrian Society for Cytology advocate for LBC despite its higher costs. This economic analysis assesses the cost-effectiveness and budget-impact of LBC compared to conventional Pap-smears in Austria.

Resource Use and Costs

- All direct cost components are based on 2024 values.
- Outpatient costs were calculated as the population-weighted average across the nine tariff catalogs of the Austrian health insurance fund.
- Inpatient service costs were determined using the respective DRG flat rates.
- The costs associated with cervical carcinoma were calculated based on tumor stage cost data from an Austrian HTA report (Fuchs et al., 2019) and the official statistics (Statistik Austria). The average therapy CxCA cost (FIGO stages I to IV) is 36,844.18 €.

Methods

The analysis focuses on the adherent Austrian screening population, utilizing a decision tree and a Markov model to depict the screening pathway and long-term outcomes, including CIN health states, CxCa (FIGO stages), mortality, and quality-adjusted life years (QALYs). Resource utilization and direct costs (in 2024 euros) were sourced from published data from the Austrian payer's perspective.

Screening population

Figure 1: Derivation of the target population



1 Statistik Austria, Population forecast 2 Prütz et al. 2013 3 Fuchs et al. 2019

The economic evaluation is based on the 1-year adherent target population, this includes 1,146,344 adherent women per year.

The age distribution is shown in the figure below, with the highest adherence rates observed in the 20-29 age group (43.2%) and the 30-39 age group (42.2%).³

Figure 2: Adherent women according age



Modeling approach

Figure 3a: Decision tree



Figure 3b: Markov-Model design

Utilities

- The CIN- and CxCa-stage-dependent utility values were taken from an economic analysis for Austria on HPV vaccination by Boiron et al. (2016).
- The utility for a CIN 1 is 0.91, for a CIN 2 and CIN 3 0.87.
- CxCa corresponds to a utility of 0.70.

Results

Cost-effectiveness results

Performing cervical-screening with LBC instead of Pap-cytology is expected to increase costs by 99 € per woman over lifetime. However, it is associated with a higher detection rate (relative benefit: 1.076) and improved quality of life (+1/3 month in perfect health). Women screened with LBC have a reduced risk of an undetected CIN, which reduce the relative risk (RR) of e.g. CIN3/CIS over lifetime (RR: 0.808). The ICUR or the additional cost per QALY gained exhibits 3,558 € and can be considered highly cost-effective.

Table 2: Cost-effectiveness results

Cost components	LBC	Pap-cytology	Difference		
Pap 0 (Consultation, cytology and repeat cytology costs)	1.37 €	3.01 €	-1.63 €		
Pap I (Consultation and cytology costs)	8.85€	8.49 €	0.36 €		
Pap II (Consultation, cytology and clarification test costs)	1,185.40 €	1,136.83€	48.56 €		
Pap III (Consultation, cytology, colposcopy and CIN clarification costs)	34.71 €	32.99 €	1.72 €		
Pap III-V (Consultation, cytology, colposcopy, biopsy and CIN clarify. costs)	477.30 €	453.75 €	23.55€		
Repeat tests in the same year (6-12 months)	327.08 €	308.15€	18.94 €		
Costs CxCa	134.60 €	127.31 €	7.29 €		
Total costs	2,169.32 €	2,070.53 €	98.79 €		
Total QALYs	28.50	28.47	0.03		
ICUR per QALY gained	3,558.02 €				

ICOR: Inremental cost effectiveness ratio; QALY: quality-adjusted-life-yea Source: own calculations

Sensitivity Analysis

A one-way sensitivity-analysis (OWSA) and a probabilistic sensitivity-analysis (PSA) were performed to



Source: own developed [decision tree]; Sroczynski et al., 2020 [Markov model]

- The decision tree outlines the process for opportunistic screening, which includes:
- Using LBC or conventional Pap smears as the primary testing method for women aged 18 and older, conducted on an annual basis.
- A follow-up diagnostic algorithm is applied to clarify positive results from initial cytological screenings using the Pap clarification test, colposcopy and/or biopsy.
- This approach aligns with Austrian guidelines on the diagnosis, treatment, and procedural management of cytological findings
- Table 1: Overview of methods applied

Methods				
Type of study	Cost-utility analysis (CUA) and Budget-impact analysis (BIA)			
Type of the model	Combined decision tree and semi-Markov cohort model			
Perspective	Austrian health care systems perspective (payers' perspective; direct costs)			
Time horizon Cycle length	CUA: Lifetime BIA: 5 years			
Discount rate	CUA: 3% for costs & 3% for outcomes BIA: no time adjustment			
Population	Eligible patients: Women who adhere annually			
Intervention	CUA: Liquid-based cytology (LBC) BIA: LBC's market share increases from 10% in the first year to 50% in the fifth year			
Comparator	Conventional Pap-smears			
Direct costs	Direct costs: Consultation, testing and histology costs incl. repeat cytologies, clarification tests, colposcopies, biopsies, conizations, curettages and hysterectomies for Pap0 to PapV, CIN1 to CIN3 and costs from CxCa according FIGO stages.			
Outcomes	Quality-adjusted life-years (QALYs) of the defined health-states were derived from the Austrian health economic analysis (Boiron et al. 2016)			
Results	CUA: Incremental cost utility ratio (ICUR) BIA: Budget impact due to the market shift			
Timing	2024			

- The transition probabilities of the Markov model are based on a benefit-harm analysis conducted by Sroczynski et al. (2020).
- The Markov simulation includes the following health conditions:
 - CIN 1 •
 - CIN 2
 - CIN 3 / CIS
 - Cervical cancer (CxCa)
 - Death from CxCa
 - Death other reasons

examine the robustness of the model.

Figure 4: Scatterplot, LBC versus Pap-cytoloy





Figure 5: OWSA tornado diagram, LBC versus Pap-cytology

- The Monte-Carlo PSA results of 500 second-order simulations plotting incremental cost versus incremental effects (Figure 4).
- The acceptability-curve revealed that in case of a WTP of 25,000 € the LBC was a highly cost-effective strategy in 99.8% of the simulations.

Source: own calculations

- The one-way-sensitivity-analysis (OWSA) allows to assess the impact of a certain input parameter on ICUR.
- The following input parameters have the greatest influence on results:
 - The utility of patients with CIN 3, CIN 2 and CIN 1 as well as
 - the discount rate have the greatest influence on the result.
 - This is followed by the costs for the Pap II.
 - The sensitivities only follow in sixth and seventh place.

Source: own calculations

Budget-impact results

The BIM shows the economic and clinical consequences due to a market shift towards

Input data for diagnostic accuracy

- The analysis incorporates sensitivity and specificity values derived from a Cochrane review and meta-analysis. (Table 2).
- The distribution of Pap-smear findings by age group, along with histological results (CIN I, CIN II, CIN III; CIS, and CaCx), is based on a retrospective study assessing the Pap-smear as an early detection method for cervical cancer in Tyrol (Geiger-Gritsch et al. 2016).

Table 2: Sensitivity and specificity

Cytology	CIN	Sensitivity	Specificity
Рар	CIN 1 ¹	0.471	
	CIN 2 ²	0.659	0.963
	CIN 3+ ²	0.703	0.967
LBC	CIN 1 ³	0.649	
	CIN 2 ²	0.755	0.919
	CIN 3+ ²	0.760	0.912

1 Fuchs et al. 2019 2 Koliopoulos et al. 2018 3 Wang et al. 2019



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: <u>e.walter@ipf-ac.at</u> Web: www.ipf-ac.at

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LBC.

Over a 5-year period, with an anticipated market growth from 10% to 50%, the budgetimpact is estimated to be an additional 1.6 million €. This leads to the detection of an additional 10 cases of CxCa and the prevention of 4 deaths.



Conclusion

The analysis demonstrates that LBC is a cost-effective screening-strategy compared to Pap cytology in Austria, as it improves CxCa detection rates and reduces related mortality.

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Additional literature with the author