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Cost-Effectiveness Evaluation of Combined Cervical Cancer Screening with CINtec PLUS in the Czech Republic

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Introduction

Cervical screening using cytology and/or HPV testing plays a crucial role in detecting cervical diseases associated with HPV infection. However, identification of women with high-grade cervical intraepithelial neoplasia remains challenging due to its low prevalence. Although cytological Pap testing has significantly contributed to reducing morbidity and mortality from HPV-related diseases, its sensitivity is limited, requiring frequent repeat testing. HPV testing provides higher sensitivity but lower specificity, particularly in ambiguous cytological results [1]. CINtec PLUS, an immunocytochemical test detecting co-expression of p16 and Ki-67, improves the triage of HPV-positive women and enables more accurate identification of high-grade lesions [2].

The aim is to evaluate the **cost-effectiveness of cervical cancer screening** under **different settings and combinations of cytology, HPV testing, and CINtec PLUS**, compared with **the current national screening program in the Czech Republic**.

Methods

- A Markov multistate model (Fig 1; A) was developed to simulate the natural history of HPV infection and cervical disease progression. The model was solved using Monte Carlo microsimulation, allowing for random individual-level transitions between health states in annual cycles.
- The main scenario simulated 10,000 women aged 30 years, followed over a 40-year time horizon (up to age 70). The current screening configuration (strategy A) and other possible screening program settings are presented in Table 1, while the CINtec PLUS algorithm is illustrated in Figure 1 (B).
- Input parameters, including transition probabilities, test performance, costs, and utilities (QALY), were derived from Czech national data, published literature, and expert estimates.
- All costs (from the payer's perspective) and QALYs were discounted at 3% per year.

Table 1: Evaluated variants of the main cervical cancer screening scenario

ID	Diagnostic strategy	Description
A	Cytology + HPV testing	Current program: annual cytology + HPV test at ages 35, 45, 55.
B	Cytology + HPV testing (both 5-year interval)	Cytology and HPV test every 5 years + CINtec Plus
C	HPV testing only (5-year interval)	HPV test every 5 years without cytology + CINtec Plus
D	Cytology (2-year interval) + HPV testing (5-year interval)	Cytology every 2 years + HPV testing every 5 years + CINtec Plus

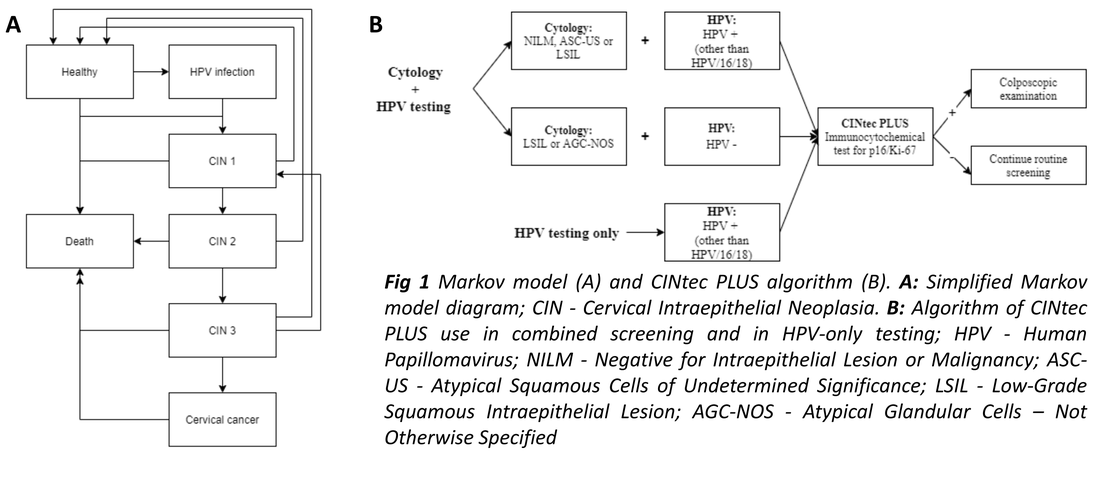

Fig 1 *Markov model (A) and CINtec PLUS algorithm (B).* ***A:*** *Simplified Markov model diagram; CIN - Cervical Intraepithelial Neoplasia.* ***B:*** *Algorithm of CINtec PLUS use in combined screening and in HPV-only testing; HPV - Human Papillomavirus; NILM - Negative for Intraepithelial Lesion or Malignancy; ASC-US - Atypical Squamous Cells of Undetermined Significance; LSIL - Low-Grade Squamous Intraepithelial Lesion; AGC-NOS - Atypical Glandular Cells – Not Otherwise Specified*

Results

- In the primary comparison, the impact of an **extended screening interval** (cytology every five years) in combination with HPV testing was evaluated (*Table 2*, strategy B).
- Strategy B achieves better outcomes in terms of CIN 2 prevalence compared to the current screening setting, while it shows slightly worse results for the prevalence of CIN 3 and carcinoma.

Table 2: Cycle prevalence of high grade lesion and total prevalence of cervical cancer

ID	Strategy description	CIN 2 cycle prevalence [cases/100,000]	CIN 3 cycle prevalence [cases/100,000]	Total cervical cancer prevalence [cases/100,000]
A	Cyt. + HPV (35, 45, 55)	508	335	7,31
B	Cyt. + HPV (both 5 year)	472	394	8,28

Table 3: Cost and effectiveness outcomes of extended screening (B) compared with current screening.

ID		Costs [CZK]	Δ Costs [CZK]	Outcomes [QALYs]	Δ Outcomes [QALYs]	ICER [CZK/QALY]	Decision*
A	Cyt. + HPV (35, 45, 55)	27,089	---	20.4630	---	---	---
B	Cyt. + HPV (both 5 year)	12,040	-15,049	20.5179	0.0549	-274,117	**Dominant**

**Dominant – less costly and more effective strategy*

- The extended screening strategy combined with HPV testing is substantially **less costly** and provides, on average, greater benefits per patient in terms of QALYs (*Table 3*).
- From a cost-effectiveness perspective, **extended screening strategy combined with HPV testing** is therefore a **dominant strategy** compared to the current screening setting.

Alternative screening settings – epidemiological results

- *Table 4* presents the simulated epidemiological parameters of the other evaluated screening strategies with alternative settings of cytology screening frequency and HPV testing.

Table 4: Cycle prevalence of high grade lesion and total prevalence of cervical cancer – alternative settings

ID	Strategy description	CIN 2 cycle prevalence [cases/100,000]	CIN 3 cycle prevalence [cases/100,000]	Total cervical cancer prevalence [cases/100,000]
A	Cyt. + HPV (35, 45, 55)	508	335	7,31
B	Cyt. + HPV (both 5 year)	472	394	8,28
C	HPV (every 5 let)	459	440	5,78
D	Cyt. (2 year) + HPV (every 5 year)	455	289	5,03

- *Table 4* shows that other alternative screening configurations may achieve comparable or even better epidemiological outcomes.
- In particular, **strategies involving more frequent HPV testing** (every five years) **demonstrate favourable epidemiological results**, even when the interval between cytology examinations is extended (strategy C and D).

Alternative screening settings – cost-effectiveness results

- *Table 5* presents the cost-effectiveness results for these alternative strategies.
- All evaluated alternative screening strategies **were cost-effective**. In all cases, they **provided greater benefits** (QALYs).

Table 5: Cost and effectiveness outcomes of alternative settings compared with current screening.

ID	Strategy description	Costs [CZK]	Δ Costs [CZK]	Outcomes [QALYs]	Δ Outcomes [QALYs]	ICER [CZK/QALY]	Decision*
A	Cyt. + HPV (35, 45, 55)	27,089	---	20.4630	---	---	---
B	Cyt. + HPV (both 5 year)	12,040	-15,049	20.5179	0.0549	-274,117	Dominant
C	HPV (every 5 let)	6,706	-20,383	20.5139	0.0509	-400,452	Dominant
D	Cyt. (2 year) + HPV (every 5 year)	29,682	2,593	20.4996	0.0366	70,847	Effective

**Dominant – less costly and more effective strategy; Effective – more costly and more effective strategy with ICER < 1.2 mil. CZK per QALY*

- Strategies involving more frequent HPV testing (when not accompanied by a substantial extension of the interval between cytology examinations) were associated with higher costs compared to the current screening program (strategy D).
- However, these increased costs were offset by greater health benefits. The resulting ICER values were therefore well below the willingness-to-pay threshold of CZK 1.2 million per QALY.

CONCLUSIONS

- The results suggest that screening programs incorporating more frequent HPV testing and optimized intervals between examinations may represent an effective and cost-efficient strategy (B and C) for cervical cancer prevention in the Czech Republic.
- Extending the intervals between cytology examinations and increasing the frequency of HPV testing yield comparable epidemiological outcomes; however, compared with the current screening program, these represent cost-effective strategies.
- Further evaluation in real-world conditions is warranted to refine the balance between screening frequency, costs, and clinical outcomes.

References

1. NANDA, Kavita, Douglas C. MCCRORY, Evan R. MYERS, Lori A. BASTIAN, Vic HASSELBLAD, Jason D. HICKEY a David B. MATCHAR. Accuracy of the Papanicolaou Test in Screening for and Follow-up of Cervical Cytologic Abnormalities: A Systematic Review. Annals of Internal Medicine.
2. WRIGHT, Thomas C., Catherine M. BEHRENS, James RANGER-MOORE, Susanne REHM, Abha SHARMA, Mark H. STOLER a Ruediger RIDDER. Triaging HPV-positive women with p16/Ki-67 dual-stained cytology: Results from a sub-study nested into the ATHENA trial. Gynecologic Oncology.

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