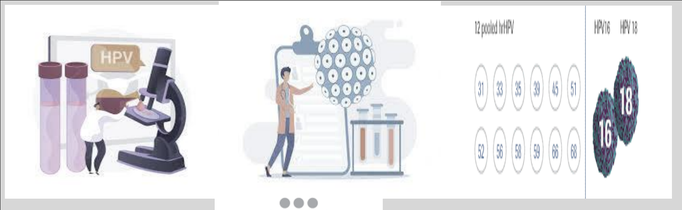

Economic Consequences of the Implementation of HPV Screening in Bulgaria

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OBJECTIVES

- The aim of the current study is to assess the economic consequences and cost-effectiveness of HPV screening programme in Bulgaria

BACKGROUND

- Cervical cancer ranks as the 4th leading cause of female cancer in Bulgaria and the 2th most common female cancer in women in Bulgaria [1]
- Relatively high share of patients at an advanced stage (1/3 of diagnosed cases) in the country have an impact on adverse mortality rates [1]
- The link between cervical cancer and Human Papillomavirus (HPV) has become clear over the past few decades — today we know that persistent infection with specific types of HPV account for nearly all cases of cervical cancer [2]
- High-risk HPV genotypes cause more than 99% of cervical cancer. 14 high-risk genotypes have been found in a large proportion of cases [3], [4]
- Two high-risk HPV genotypes, HPV 16 and HPV 18, are associated with 70% of all cervical cancers [5]
- Availability of opportunistic cervical screening, based on PAP Cytology (suboptimal test) and lack of organized population HPV primary screening for cervical cancer prevention could be one of the main reasons for late diagnosis
- There is a global call for action for Cervical Cancer elimination as a public health problem – WHO Strategy 90-70-90 [6]

METHODS

- We performed combined cost-effectiveness (CEA) and cost-benefit (CBA) analysis to evaluate the net benefit of HPV screening program among women aged 35-45 in Bulgaria for 3-year period (2023-2025)

Cost-effectiveness

- The current practice of PAP testing was used as main comparator
- ICER was presented separately for only direct costs and for direct + indirect costs

Cost-benefit analysis

- Net present value and benefit/cost ratio were calculated for HPV screening alternative

Method	Costs	Results
Cost-effectiveness analysis (CEA)	Direct costs – HPV genotype screening, CINTech triage testing, PAP test, colposcopy and physician visits presented as the average for the 3-y period Indirect costs – productivity loss due to premature death	LYG due to early screening and early access to therapy
Cost-benefit analysis (CBA)	Direct costs – HPV genotype screening, CINTech triage testing, colposcopy	Benefits measured as the LYG due to early screening and reduced mortality based on the Human capital approach

The costs were presented in local currency with fixed euro rate 1 BGN = 1.95583 euro

RESULTS

- The results show that with the current practice of PAP testing in Bulgaria almost 40% of the women remain under diagnosed [7]
- HPV is known to cause at least 99 percent of cervical cancer worldwide. Early detection is important for women at higher risk of developing cervical cancer as HPV infections are more likely to lead to cervical cancer if left untreated over time [8]
- Use of the CINtec® PLUS Cytology test for triage of positive HPV test enables efficient patient management by sending only women to colposcopy who can benefit most from it

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RESULTS

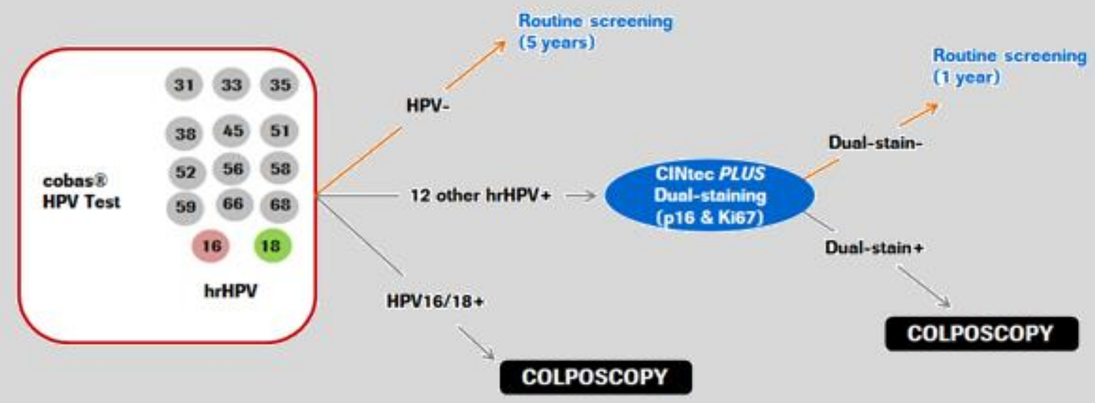

Fig.1 Primary HPV test with triage by the CINtec® PLUS Cytology

HPV primary screening with triage by the CINtec® PLUS Cytology test uses an algorithm that leverages the high sensitivity of HPV DNA, the built-in risk stratification of HPV genotypes 16 and 18, and triage with the high specificity for CIN2, CIN3 and cervical cancer [9]– figure 1.

Cost-effectiveness analysis

HPV testing with triage is expected to lead 1467 life years gained (LYG) compared to current practice of PAP testing and to almost 3 times decrease in the life years lost (LYL) – table 1.

Table 1. Input data for CEA

Current practice - PAP testing	
Input data	**Value**
Years life lost due to premature death(2020 data) cervical cancer mortality/yearly	503
avg age of diagnosis	39
average age of mortality	59
life years lost	15.9
LYL total	7998
Indirect costs	
LYL	7998
GDP/capita [BGN]	17172
Indirect costs [Human capital approach]	137336504

HPV testing	
Input data	**Value**
Years life lost due to premature death(2020 data) cervical cancer mortality/yearly	331
avg age of diagnosis	39
average age of mortality	66
life years lost	8.53
LYL total	2823
LYG	1467
Indirect costs	
LYL	2823
GDP/capita [BGN]	17172
Indirect costs [Human capital approach]	48480132

CEA shows that HPV screening is dominant over the current practice of PAP testing with ICER -461 euro/LYG when considering only direct costs and-31421 euro/LYG for both direct and indirect costs. The LYG earned with the HPV testing account for 1461 for the observed cohort of women – table 2.

Table 2. ICER of HPV screening compared to current PAP testing

Alternatives	Cost	LYG	ΔC	ΔLYG	ICER	ICER/euro
Direct + indirect costs						
PAP screening	148705251					
HPV screening	58526484		-90178766	1467	-61455.6	**-31421.7**
Direct costs only						
PAP screening	11368746					
HPV screening	10046353		-1322393	1467	-901.192	**-460.8**

Cost-benefit analysis

	2023	2024	2025	AVG/y
Cost				
cost of HPV screening	9195517.5	8645018.571	8126078.91	
Cost of colposcopy	499359.0411	491573.6445	484977.896	
Cost of CINTech triage testing	954919.125	897751.9286	843862.041	
Total cost	**10649796**	**10034344**	**9454919**	**10046353**
Benefits				
LYG due to early screening and reduced mortality	**25197880**	**25197880**	**25197880**	**25197880**

The CBA analysis shows that the benefit/cost ratio of HPV screening is 2.51 and the net present benefit accounts for 7 746 853 euro thus making the program beneficial for the healthcare system in Bulgaria.

CONCLUSION

Primary hrHPV testing provides important scientific and clinical advance in cervical cancer screening since it offers better reassurance of low cancer risk compared to cytology-only screening conducted at the same interval. Primary HPV screening can be considered as dominant alternative to current cytology-based cervical cancer screening approaches including cytology alone and contesting and providing better benefit for the healthcare system and the society in Bulgaria.