

Cervical cancer

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Description of condition and intervention

Cervical cancer is 4th most common cancer among the women. Estimates indicate that 5,70,000 women were diagnosed with cervical cancer, and about 3,11,000 women died due to this condition in the year 2018. It represented 7.5% of all cancer deaths in that year.

Moreover, more than 85% of these deaths occurred in low- and middle-income countries (LMICs). A global strategy for eliminating cervical cancer was adopted by World health Assembly (WHA) in 2020. It recommended a comprehensive approach for the prevention and control of cervical cancer. As per this, 90% of girls should be fully vaccinated with HPV vaccine by age 15 years, 70% of women screened with a high-performance test by 35 years of age and again by 45 years of age, and 90% of women identified with cervical disease receive treatment (90% of women with precancer treated, and 90% of women with invasive cancer managed) (WHO 2020). The intervention should be multidisciplinary which includes components like community education, social mobilization, vaccination, screening, treatment, and palliative care. Screening followed by immediate treatment of pre-cancerous lesions if diagnosed. Secondary treatment (women as needed) includes treatment of invasive cancer at any age which includes surgery, radiotherapy, chemotherapy, palliative care (WHO 2021).

There are 3 different types of screening tests recommended by WHO: HPV DNA testing for high-risk HPV types, Visual inspection with Acetic Acid (VIA), conventional (Pap) test and liquid-based cytology (LBC). For treatment of pre-cancer lesions, cryotherapy or thermal ablation and Loop Electrosurgical Excision Procedure (LEEP) is recommended. In the case of

advanced lesions, women are referred for to an appropriate facility for further evaluation, diagnosis, and treatment (WHO 2021).

Interventions included in this evidence brief for assessment of effects and costs are:

Human Papilloma virus (HPV) immunization

Treatment of cervical precancerous lesions: Confirmatory diagnostics of cervical precancerous lesions

Treatment of cervical precancerous lesions: Cryotherapy or LEEP

Treatment of cervical cancer: Confirmatory diagnostics of cervical cancer and staging

Treatment of early-stage cervical cancer: Stage I & Stage II

Palliative care for late-stage cervical cancer: Stage III & Stage IV

International guidelines

Organization	Indications/recommendations	Applicability in LIC & Lower MIC settings
World Health Organization 2014	Comprehensive cervical cancer control: A guide to essential practice – 2nd edition	

Intervention attributes

Type of interventions

Cervical cancer confirmatory diagnostics is a type of diagnostic intervention. HPV vaccination is a preventive intervention. The rest of the interventions are considered as curative category.

Delivery platform

HPV vaccination may be delivered at community level. The interventions involving treatment of cervical cancer including treatment of precancerous lesions with cryotherapy may be delivered at first-level hospital and referral. Treatment of early-stage cervical cancer and

palliative care for late-stage cervical cancer may be delivered at referral and specialty hospital.

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency. Treatment outcomes not highly affected by some days of delay.

Population in need of interventions

Table 1: Population in need of interventions

Intervention	Treated population		Affected population		Disease state addressed
	Treated age	Treated fraction	Affected age	Affected fraction	
1. Human Papilloma virus (HPV) immunization	10 to 14 years; female; all	0.2 (adjusted for 5-year cohort)	15 to 99 years	1	Cervical cancer

(DCP4 ID: CANC02-01,02,03,04,05)

Cluster: Cancer

2. Treatment of cervical precancerous lesions: Confirmatory diagnostics of cervical precancerous lesions	20 to 69 years; female; incidence based	0.0314*	No effects		Cervical cancer
3. Treatment of cervical precancerous lesions: Cryotherapy or LEEP	20 to 69 years; female; incidence based	0.0314*	20 to 69 years of those with the condition	0.65 for mortality outcome	Cervical cancer
4. Treatment of early-stage cervical cancer: Confirmatory diagnostics of cervical cancer and staging	20 to 69 years; female; incidence based	0.236	20 to 69 years of those with the condition	0.65 for mortality outcome	Cervical cancer
5. Treatment of early-stage cervical cancer: Stage I & Stage II	20 to 69 years; female; incidence based	0.236	20 to 69 years of those with the condition	0.095	Cervical cancer
6. Palliative care for late-stage cervical cancer: Stage III & Stage IV	20 to 69 years; female; all	1	Only costs considered for this intervention		Cervical cancer

*15.7% (95% CI: 11.3%-20.1%) were found to be positive for precancerous cervical lesion (Merera D, Jima GH 2021)

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Affected population: In the event of no active screening programs distribution of cervical cancer in the population is assumed to be like breast cancer distribution rates: Stage 1 (9.4%), Stage 2 (14.2%), Stage 3 (58%) and Stage 4 (18.4%). The proportion of yearly deaths expected from stage 1 and 2 as a proportion of all cervical cancer deaths were modelled with the help of simplified Markov trace and stagewise distribution of the disease. Time dependency in the affected fraction was estimated using the geometric mean as a yearly estimate. Based on these calculations, mean affected fraction over time came out to be 9.5%. Source: NCD Countdown appendix

Disease state addressed

The included interventions target cervical cancer.

Intervention effect and safety

Table 1: Effect and safety of treatment for cervical cancer

Effect of intervention		Certainty of evidence
Mortality (due to condition)	Reduction in mortality from the screening and treatment of precancerous lesions is based on a mathematical modelling study showing a reduction of lifetime risk of cervical cancer of 83% from 5 yearlyscreening57and a study in Thailand showing that compared with no screening, use of VIA could achieve 83% reduction in mortality.58Reduction in mortality from the treatment of cervical cancer is consistent with One Health Tool effect size estimates, dependent on stage at diagnosis:	See appendix
Early treatment		
Stage 1	77.5%	
Stage 2	68.4%	
Stage 3	65.0%	
Stage 4	75.0%	
Weighted effect size for stage 1 & stage 2 treatment leading to mortality reduction is estimated in countdown		

	appendix as 91% (Source: NCD Countdown appendix)	
Incidence HPV vaccination	Incidence reduction, assuming 95% vaccine efficacy (Jit, 2014) and the proportion of ICC associated with HPV16 and/or 18 (HPV16/18) was 73% (Li, 2011), the intervention efficacy for this intervention is approximately 69%.	

Model assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Interventions		
Cost calculation		
Treated population	Incidence of cervical cancer	Global Burden of Disease Study 2019
Gender	female	
Age	0-14 years	
Treated fraction Stage 1 Stage 2 Stage 3 Stage 4	0.094 0.142 0.58 0.184	
Effect calculation		
Affected population	Those with condition	
Affected gender	Female	
Affected fraction age	0 to 14 years	
Affected fraction Stage 1 Stage 2 Stage 3 Stage 4	0.094 0.142 0.58 0.184	
Comparison	No intervention	
Mortality Reduction (RRR) Early treatment of precancerous and early-stage cervical cancer	0.91	Sources listed in Table 2

Incidence HPV vaccination	0.69	Jit 2014 & Li 2011

Intervention cost

The cost for Human Papillomavirus (HPV) immunization is estimated at \$9.14, per girl fully immunised, in 2016 USD. The immunization cost is based on the cost of 2 doses of HPV vaccine each at the cost of \$4.5 per dose based on GAVI prices, in addition to the cost of 5 min nurse time (DCP3 volume 8).

The cost of screening for cervical cancer and precancerous lesions with visual inspection with acetic acid (VIA) is estimated at \$5.29, per woman screened, in 2012 USD.

The screening component is costed based on the weighted average cost per screening type of VIA or HPV (Campos, 2017). Assuming $\frac{1}{3}$ of sites using HPV screening and $\frac{2}{3}$ of sites using VIA (Coleman, 2016).

- LI: $\$1.60 \text{ (VIA)} * 0.67 + \$6.61 \text{ (HPV)} * 0.33 = \3.27
- LMI: $\$3.52 \text{ (VIA)} * 0.67 + \$8.52 \text{ (HPV)} * 0.33 = \5.19

Assuming the proportion of screened positives that require cryotherapy is 17.7% (Mvundura, 2014), the treatment unit cost is calculated as:

- o LI: $\$11.39 \text{ (Cryotherapy)} * 0.177 = \2.02 (2013 USD)

The cost of treatment of cervical precancerous lesions using Cryotherapy or Loop Electrosurgical Excision Procedure (LEEP) is estimated at \$35.14 per woman treated in 2012 USD (Mvundura, Mercy & Tsu, Vivien 2014).

For the cost of the treatment of Cervical cancer treatment: Stage I, assuming that all suspicious lesions are referred to a first-level hospital for treatment, the unit cost is calculated as the average procedure cost of colposcopy/biopsy plus the average procedure cost of LEEP (Campos, 2017). Assuming a false positive rate of 15% (Campos, 2017) we divide the cost of colposcopy/biopsy by (1-0.15) to ensure that 100% of true positives are detected:

- LI: $\$22.74/0.84 \text{ (Colposcopy/biopsy)} + \$47.72 \text{ (LEEP)} = \$74.79 \text{ (2013 USD)}$
- LMI: $\$49.87/0.84 \text{ (Colposcopy/biopsy)} + \$101.64 \text{ (LEEP)} = \$161.01 \text{ (2013 USD)}$

The cost for palliative care was estimated to be 64.36 USD per capita in 2016 in low-income countries (LIC) (source DCP 3 Volume 9).

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Cluster: Cancer

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Appendix

Literature Review for effectiveness & safety

This literature search is an example of Level 1 search for intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines).