

## Executive Summary

### Cost-effectiveness of conventional cytology and HPV DNA testing for cervical cancer screening in South Korea

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### □ Introduction

National Cervical Screening Programme in Korea recommends that a biannual cervical pap smear test interval is appropriate for women over 30 years. Conventional cytology is relatively simple and cheap method of cervical cancer screening and eventually has reduced the cervical cancer incidence and mortality. However, several studies in abroad have shown the relatively high false negative rate and reported that HPV testing is more sensitive than cytology. The recent updated guidelines from Korean Society of Gynecology Oncology and Korean Society of Pathologists in 2012 recommends that annual pap smear test in the age group 20~29 years and biannual

screening of pap smear and HPV test in the age group 30~70 years.

Although the most accurate or cost-effective cervical cancer screening methods is different in each country, there is a paucity of evaluative research in Korea. Therefore this study aims to suggest the evidence for guidelines of cervical cancer screening by comparing accuracy of cervical cancer test methods and performing cost-effectiveness analysis.

## □ Accuracy of cervical cancer screening methods

### I. Systematic Review of Korean literature

To ascertain the accuracy of cervical cancer screening methods in Korea, we performed a systematic review and meta-analysis among asymptomatic women for cervical cancer screening. We extracted sensitivity and specificity for the detection of cervical intraepithelial neoplasia 1 (CIN 1) or worse and the reference standard was colposcopy and histology. Study quality was determined by using the Quality Assessment of Diagnostic Accuracy (QUADAS-II) by independent reviewers. Summary ROC curve and bivariate random effects model were applied to synthesize diagnostic test accuracy. The rating of risk of bias among 33 studies were as follows. Most of studies were categorized into unclear in the selection criteria. In addition, the risk of bias in application was also high. Therefore, the caution should be exercised in the interpretation of results. Bivariate random effects meta analysis estimated the sensitivity and specificity for pap smear and HPV test as follows. The sensitivity and specificity was 0.84 and 0.78 respectively, in pap smear for detecting ASCUS or worse. In HPV test, the sensitivity and specificity was 0.77 and 0.79, respectively. According to HPV test methods, the sensitivity and specificity was 0.76, and 0.76 in HC II which was higher than that of HC I.

### II. Overview of systematic review in abroad

Overview of SR was conducted based on systematic reviews and meta-analysis of studies on the diagnostic accuracy of cervical screening methods. As a whole, the sensitivity of pap smear detecting ASCUS or worse was ranged 0.38~0.88, which was relatively low compared to pooled accuracy of studies in Korea. As most foreign

studies defined the disease endpoint CIN2+, sensitivity could be lower compared to Korean studies whose endpoint CIN1+. On the contrary, the diagnostic accuracy of HPV test was higher than that of Korean studies. The sensitivity was and specificity of HC II was generally higher than that of other screening methods.

## □ Economic evaluation of cervical cancer screening strategy

### I. Methods

We assessed the cost-effectiveness of incorporate human papillomavirus (HPV) DNA testing into existing cervical cancer screening programme in South Korea. The model compared two management of screening methods: (1) Pap smear, (2) Triage with HPV DNA testing (HPV DNA screening test after atypical or abnormal pap results at routine cervical cancer screening). To compared current screening policy with new strategy: (1) screening interval (1 year, 2 year, 3 year, 5 year), (2) screening start age (20 year-old, 30 year-old) (3) screening period (life-time, till 79 year-old). We considered these kind of strategies combination.

We conducted cost-utility analysis applying QALYs to which takes into account life span expansion and the quality of life according to screening method, screening interval, screening start age.

With the societal perspective, patient time costs, caregiver costs, and transportation costs were all considered as well as medical costs. Markov model was used with one year cycle and life time analysis period.

Sensitivity analysis was conducted to reflect the uncertainty of variables. Sensitivity analysis was carried for discount rate, cervical cancer transition rate, screening efficacy.

### II. Result

Cost-effectiveness analysis of selected cervical cancer screening strategies with various screening interval, start age, screening period of each screening method. In order to assess the cost-effectiveness, the orders are based in effectiveness.

As a result, pap smear test with 5 year interval was most inexpensive strategy,

pap smear test with 1 year interval was most effectiveness strategy.

In the South Korea, most of the interventions with an ICUR below KRW 30,000,000won/QALY are recommended routinely. Below on threshold 30,000,000won/QALY, pap smear test with 1 year interval (aged 30 to life-time) was most cost-effectiveness strategy.

Sensitivity analysis showed that discount rate, cervical cancer probability did not affect the result significantly. However, accuracy of cervical cancer screening led a change on whether to be cost-effectiveness.

## □ Conclusions

To estimated the accuracy of cervical cancer screening methods in Korea, we performed a meta-analysis among asymptomatic women for cervical cancer screening. The estimated sensitivity and specificity for pap smear was 0.84 and 0.78, respectively, and the variability among studies using pap smear was relatively low compared with that of HPV test. In contrast, the diagnostic accuracy of HPV was higher than that of pap smear from studies performed in abroad. However, there was possibility of selection bias of domestic studies as most of them were targeted high risk population and were performed secondary or tertiary hospitals. Cost-effectiveness analysis of selected cervical cancer screening strategies revealed that pap smear test with 1 year interval (aged 30 to life-time) was the most cost-effectiveness strategy with an ICUR below KRW 30,000,000won/QALY. It means that the period of age in cervical cancer screening should be setted as 30~life-time in terms of cost-effectiveness. However, we should consider that sensitivity analysis changed the most cost-effective strategy after applying for diagnostic accuracy. For the estimation of representative diagnostic accuracy and economic evaluation of cervical screening methods, it is strongly warranted that there should be more studies in various medical institutions targeting among asymptomatic women for cervical cancer screening.

Cervical screening, Pap smear, HPV test, Economic evaluation