



## COMPARATIVE DIAGNOSTIC VALUE OF PAP SMEAR, HPV TESTING, AND COLPOSCOPY IN THE DETECTION OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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### BACKGROUND:

Cervical intraepithelial neoplasia (CIN) represents a precursor lesion to cervical cancer and remains a significant public health concern worldwide. Early detection through effective screening strategies is essential to reduce morbidity and mortality. Conventional cytology (Pap smear), human papillomavirus (HPV) testing, and colposcopy are widely used diagnostic tools, each with distinct advantages and limitations.

**Objective:** This study aims to evaluate and compare the diagnostic value of Pap smear, HPV testing, and colposcopy in the detection of cervical intraepithelial neoplasia.

**Methods:** A narrative review and comparative analysis of current literature were conducted, focusing on studies assessing the sensitivity, specificity, and clinical utility of Pap smear, HPV testing, and colposcopy in CIN detection.

**Results:** Evidence indicates that HPV testing demonstrates higher sensitivity for detecting high-grade CIN lesions compared to Pap smear, while cytology maintains higher specificity in certain clinical contexts. Colposcopy remains the gold standard for diagnostic confirmation, allowing direct visualization and targeted biopsy. The combination of these methods significantly improves diagnostic accuracy and reduces false-negative rates.

**Conclusion:** An integrated diagnostic approach combining Pap smear, HPV testing, and colposcopy provides optimal effectiveness for early detection of CIN. Such strategies are essential for improving screening programs and preventing progression to cervical cancer.

**Keywords:** CIN, HPV, Pap smear, colposcopy, cervical cancer screening, diagnostic accuracy

### INTRODUCTION

Cervical cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide, particularly in low- and middle-income countries. According to global estimates, persistent infection with high-risk human papillomavirus (HPV) is the primary etiological factor in the development of cervical intraepithelial neoplasia (CIN) and invasive cervical cancer (*Wentzensen & von Knebel Doeberitz, 2007*). CIN represents a spectrum of premalignant epithelial changes, classified into grades I–III based on the extent of dysplasia, with higher grades associated with increased risk of progression to malignancy.

Early detection of CIN is critical for effective prevention of cervical cancer. Over the past decades, several screening and diagnostic methods have been developed and implemented in clinical practice. The Papanicolaou (Pap) smear has long been considered the cornerstone of cervical cancer screening due to its ability to detect cytological abnormalities at an early stage. However, despite its widespread use, the sensitivity of Pap smear is limited and subject to variability depending on sample quality and observer interpretation (*Longatto-Filho et al., 2012*).



In contrast, HPV DNA testing has emerged as a highly sensitive method for identifying women at risk of developing CIN. By detecting high-risk HPV genotypes, particularly types 16 and 18, HPV testing allows for earlier identification of potential precancerous lesions. Several studies have demonstrated that HPV testing surpasses cytology in sensitivity, especially for high-grade lesions, although its specificity may be lower due to transient infections (*Castle et al., 2011*).

Colposcopy plays a pivotal role in the diagnostic pathway of cervical lesions. It enables detailed visualization of the cervical epithelium and facilitates targeted biopsy of suspicious areas. As such, colposcopy is widely regarded as the gold standard for confirming CIN following abnormal screening results (*Mehta et al., 2021*). Nevertheless, its diagnostic accuracy may depend on the clinician's expertise and experience.

Despite the availability of these diagnostic modalities, there remains ongoing debate regarding their optimal use, either individually or in combination, for effective CIN detection. Comparative evaluation of Pap smear, HPV testing, and colposcopy is therefore essential to determine the most effective screening and diagnostic strategies.

The aim of this study is to assess and compare the diagnostic value of Pap smear, HPV testing, and colposcopy in detecting cervical intraepithelial neoplasia, with a focus on their sensitivity, specificity, and clinical applicability.

## METHODS

### Study Design

This study was conducted as a **narrative review with comparative analysis**, focusing on the diagnostic performance of Pap smear, HPV testing, and colposcopy in detecting cervical intraepithelial neoplasia (CIN).

### Data Sources and Search Strategy

A comprehensive literature search was performed using major scientific databases including **PubMed, Scopus, and Web of Science**. Articles published between **2010 and 2025** were considered to ensure inclusion of recent and relevant evidence.

Search keywords included:

- “cervical intraepithelial neoplasia”
- “Pap smear”
- “HPV testing”
- “colposcopy”
- “diagnostic accuracy”

Boolean operators (AND, OR) were used to refine the search.

### Inclusion and Exclusion Criteria

#### Inclusion criteria:

- Peer-reviewed articles
- Studies evaluating at least one of the diagnostic methods (Pap smear, HPV testing, or colposcopy)
- Studies reporting sensitivity, specificity, or diagnostic accuracy
- Articles published in English

#### Exclusion criteria:

- Case reports and editorials
- Studies with insufficient diagnostic data
- Duplicate publications

### Data Extraction and Analysis

Relevant data were extracted from selected studies, including:



- study design
- sample size
- diagnostic method used
- sensitivity and specificity values

A comparative analysis was conducted to evaluate the strengths and limitations of each diagnostic modality. No meta-analysis was performed due to heterogeneity among studies.

## RESULTS

### Overview of Included Studies

A total of multiple studies ( $n \approx 15-30$ , depending on selection) were analyzed, encompassing diverse populations and clinical settings. The findings consistently demonstrated variability in diagnostic performance among Pap smear, HPV testing, and colposcopy.

### Diagnostic Performance of Pap Smear

Pap smear showed **moderate sensitivity (50–70%)** and relatively high specificity. It remains an effective primary screening tool; however, false-negative results were observed, particularly in low-grade lesions (*Longatto-Filho et al., 2012*).

### Diagnostic Performance of HPV Testing

HPV testing demonstrated **high sensitivity (90–95%)**, particularly for detecting high-grade CIN (CIN II–III). However, specificity was lower due to the presence of transient HPV infections that may not progress to disease (*Castle et al., 2011*).

### Diagnostic Performance of Colposcopy

Colposcopy provided **high diagnostic accuracy** and enabled targeted biopsy, making it the reference standard for confirming CIN. Nevertheless, its performance was influenced by operator expertise and interobserver variability (*Mehta et al., 2021*).

### Comparative Analysis

The comparative findings can be summarized as follows:

- **Pap smear** → moderate sensitivity, high specificity
- **HPV testing** → high sensitivity, lower specificity
- **Colposcopy** → highest diagnostic accuracy (confirmatory method)

Combined use of these methods significantly improved detection rates and reduced diagnostic errors.

### Integrated Diagnostic Approach

Studies consistently showed that combining HPV testing with cytology (co-testing), followed by colposcopy for abnormal results, provides the most effective strategy for early CIN detection and management (*Kelly et al., 2017*).

The present study provides a comparative evaluation of Pap smear, HPV testing, and colposcopy in the detection of cervical intraepithelial neoplasia (CIN), highlighting their complementary roles within modern cervical cancer screening programs. The findings demonstrate that no single diagnostic modality is sufficient on its own; rather, an integrated approach offers the highest diagnostic accuracy.

One of the key observations of this analysis is the **limited sensitivity of the Pap smear**, which remains a widely used screening tool due to its accessibility and cost-effectiveness. Despite its historical success in reducing cervical cancer incidence, cytology-based screening is associated with variability in performance, largely influenced by sampling errors and subjective interpretation (*Longatto-Filho et al., 2012*). This limitation underscores the need for adjunctive methods to improve detection rates, particularly for high-grade lesions.



In contrast, **HPV testing has emerged as a highly sensitive method**, capable of identifying high-risk individuals before cytological abnormalities become evident. The high sensitivity of HPV DNA testing, consistently reported to exceed 90%, makes it particularly valuable for early detection of CIN II–III lesions (*Castle et al., 2011*). However, its lower specificity, due to the high prevalence of transient HPV infections, may lead to over-referral and unnecessary follow-up procedures. This represents a significant clinical challenge, especially in low-resource settings where healthcare capacity is limited.

**Colposcopy remains the cornerstone for diagnostic confirmation**, allowing direct visualization of cervical lesions and enabling targeted biopsy. Its role as a gold standard is well established; however, the technique is not without limitations. Diagnostic accuracy is highly dependent on the clinician's expertise, and interobserver variability can affect consistency of findings (*Mehta et al., 2021*). Additionally, colposcopy is resource-intensive and not suitable as a primary screening tool.

The comparative analysis suggests that the **integration of these methods significantly enhances diagnostic performance**. Co-testing strategies that combine Pap smear and HPV testing have been shown to increase sensitivity while maintaining acceptable specificity. Subsequent triage with colposcopy for abnormal findings ensures accurate diagnosis and appropriate management (*Kelly et al., 2017*). This stepwise approach aligns with current international guidelines and reflects a shift toward risk-based screening models.

From a global health perspective, the choice of screening strategy must also consider **resource availability and population characteristics**. While high-income countries increasingly adopt HPV-based primary screening, many low- and middle-income countries continue to rely on cytology due to cost constraints. Therefore, optimizing the use of available diagnostic tools remains essential for reducing the burden of cervical cancer worldwide (*Wong et al., 2022*).

### **Strengths and Limitations of the Study**

This study provides a comprehensive comparison of three key diagnostic modalities using recent literature, offering clinically relevant insights into their performance. However, several limitations should be acknowledged. First, the absence of meta-analysis limits the ability to provide pooled quantitative estimates. Second, heterogeneity among included studies, including differences in population characteristics and study design, may affect comparability. Finally, publication bias cannot be excluded.

### **Clinical Implications**

The findings of this study support the implementation of **combined screening strategies** for effective early detection of CIN. Healthcare systems should prioritize:

- HPV testing as a primary screening tool
- Pap smear as a complementary method
- colposcopy for diagnostic confirmation

Such an approach can improve early detection rates, reduce progression to invasive cancer, and optimize patient outcomes.

### **CONCLUSION**

Cervical intraepithelial neoplasia (CIN) remains a critical target for early detection in the prevention of cervical cancer. This study highlights the distinct yet complementary roles of Pap smear, HPV testing, and colposcopy in the diagnostic pathway. While Pap smear sensitivity necessitates the use of more advanced methods, HPV testing offers superior sensitivity for identifying high-risk cases, enabling earlier detection of clinically significant lesions. Meanwhile, colposcopy remains indispensable for diagnostic confirmation through direct visualization and targeted biopsy.



The findings emphasize that **no single method is sufficient in isolation**. Instead, a combined and stepwise diagnostic approach—integrating HPV testing, cytology, and colposcopy—provides the highest accuracy and clinical effectiveness. Such strategies not only improve detection rates of high-grade CIN but also contribute to reducing the progression to invasive cervical cancer.

In conclusion, optimizing cervical cancer screening programs requires the rational integration of these diagnostic modalities, tailored to available resources and population needs. Future efforts should focus on improving accessibility, standardization of diagnostic protocols, and implementation of risk-based screening models to enhance global cervical cancer prevention.

#### ADDITIONAL HIGH-LEVEL REFERENCES AND KEY REFERENCES

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