# Colposcopy and cervical intraepithelial neoplasia

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## Abstract

Cervical cancer is both preventable and curable. It has a long natural history with a prolonged pre-cancerous phase that is easily detectable and treatable. Exfoliative cytology has been the mainstay for screening of cervical intra-epithelial neoplasia (CIN). Assessment of women presenting with abnormal cervical cytology and the selection of those requiring treatment relied mainly on colposcopic impressions of the cervical transformation zone and the histological appraisal of directed punch biopsies. The need to maximise clinical resources, achieve quicker and more effective management of patients, limit postoperative complications and preserve reproductive function has led to the popularity of local excisional methods for cervical premalignancy. Although the cure rates for all local ablative and excisional methods are more than 90% after one treatment, the excisional methods provide a more reliable histopathological diagnosis and the patient can be treated at the initial visit. The recognition that persistent infection with oncogenic human papillomavirus (HPV) causes cervical cancer has led to the development of new HPV tests/biomarkers and prophylactic vaccines against HPV. The HPV DNA test that targets the viral DNA has been introduced as a test of cure after CIN treatment and as a triage tool in women presenting with borderline or low-grade findings at cytology. HPV DNA test will be introduced in primary screening in the future. The national HPV immunisation programme was initiated in the NHS in September 2008. The vaccines are safe, well tolerated and highly efficacious in HPV naive women.

**Keywords** cervical cancer; CIN; colposcopy; human papillomavirus

## Introduction

Cervical cancer is largely preventable through treatment of screen-detected cervical lesions. Despite this, cervical cancer remains the most common female malignancy in virtually all developing countries and the seventh most common in women worldwide. Globally in 2012, an estimate of 528,000 women develops cervical cancer and almost 266,000 die from this disease every year. Of all cervical cancers, 83% occur in the less developed world (Figures 1 and 2).

The trends in the incidence of cervical cancer in different countries relate largely to the availability, quality and coverage of screening programmes, as well as exposure to human papillomavirus (HPV) and other risk factors, which reflect sexual habits, cultural and socioeconomic influences. Organised screening programmes in countries like the UK, have led to a dramatic decrease in the incidence and mortality from cervical cancer, especially when viewed with statistics for the other major cancers. During the 10-year period from 1993 to 2002, the overall age-standardised incidence of cancer increased by 3% in women, whereas the corresponding data for cervical cancer showed a decrease of approximately 30%.

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## Classification of cervical intraepithelial neoplasia

### Squamous lesions

In the UK, cervical cytology was previously classified into mild, moderate and severe dyskaryosis, with borderline nuclear abnormalities used for changes that fall short of dyskaryosis. The previous terminology for cytology results used by the British Society of Clinical Cytology (BSCC) in 2001 was replaced by a new version introduced by the British Association for Cytopathology (BAC) and the NHSCSP in 2013 (Table 1).

The Bethesda system that is used widely outside the UK, was introduced in the United States in 1988 and was modified in 2001 (see Table 1). This classifies abnormalities into atypical squamous cells of undetermined significance (ASCUS); atypical squamous cells cannot exclude HSIL (ASC-H); low-grade squamous intraepithelial lesions, LSIL (encompassing HPV and CIN1); high grade SIL, HSIL (encompassing CIN 2 and CIN 3) and squamous cell carcinoma. The cervical intraepithelial neoplasia (CIN) classification introduced by Richart in 1967 for histogenetic classification of cervical precancerous lesions has generally replaced the World Health Organization (WHO) classification and reflects the depth of epithelial involvement (Figure 3).

### Glandular lesions

Although the natural history and biology of glandular lesions is less clear, attempts have been made to mirror the range of cellular changes of the squamous into the glandular mucosa (Cervical Glandular Intraepithelial Neoplasia — cGIN). The BAC/NHSCSP 2013 classification system divides the glandular lesions in two groups, borderline changes and glandular neoplasia. The Bethesda 2001 system classifies glandular cytological abnormalities into four subcategories: atypical glandular cells (AGC); AGC, favour neoplastic; endocervical adenocarcinoma *in situ* (AIS) and adenocarcinoma (Table 2).

## Risk factors

Several risk factors for cervical precancer and cancer have been investigated in the past. There is now a strong and consistent body of evidence demonstrating that HPV infection is a necessary (although not a sufficient) cause of cervical cancer. It is also now recognised that it is the persistence of HPV infection that is related to the development of CIN and subsequently cervical cancer rather than the exposure to the virus itself. Most HPV infections do not progress to CIN or cancer and, therefore, 'cervical cancer is considered a rare complication of very common infection'.

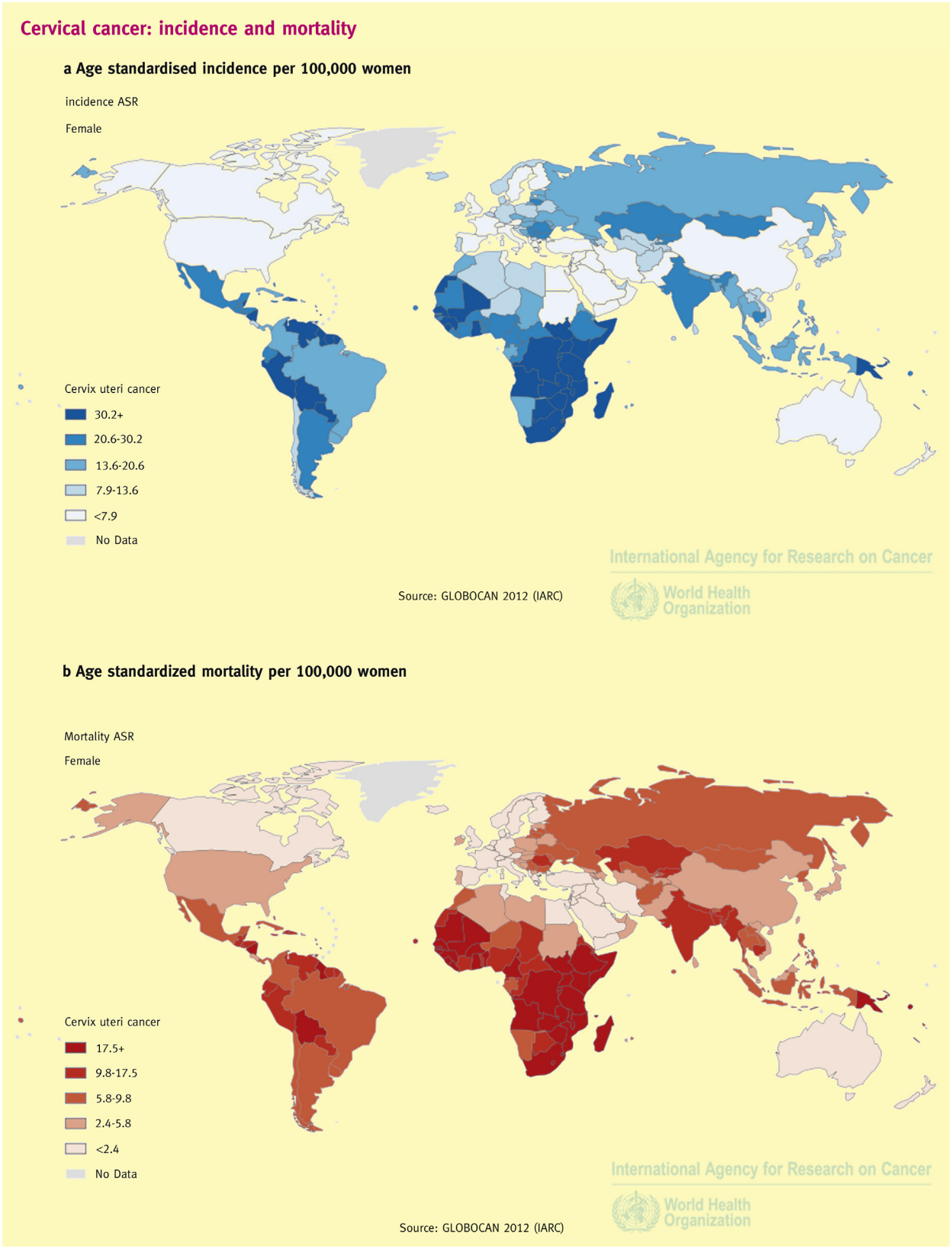


**Figure 1**

Out of more than 100 HPV genotypes, 20 have been identified as carcinogenic; types 16 and 18 are found most commonly in almost 70% of all malignant lesions. The common types are classified according to their oncogenic potential as follows:

- low risk: 6, 11, 41, 44
- intermediate risk: 31, 33, 35
- high risk: 16, 18, 45, 56.