IARC HANDBOOKS OF CANCER PREVENTION

- Collana di monografie sulla prevenzione dei tumori
- Diversi metodi di prevenzione primaria: es. Non-steroidal Anti-inflammatory Drugs, Sunscreens, Weight Control and Physical Activity, Fruit and vegetables
- Un volume pubblicato sullo screening del cancro della mammella (No 7) e uno sullo screening del cancro cervicale (in stampa)

The evaluations of the IARC Working Groups are scientific, qualitative judgements about the evidence for preventive efficacy and safety provided by the available data.

This initiative aims at providing the scientific basis for national and international decisions on the implementation of cancer preventive strategies and for assessing the associated benefits and risks.

1. Cervix cancer and screening

1.1 Cervix cancer incidence and mortality worldwide

1.2 Cervix cancer characteristics (1.2.1 Biology and pathology 1.2.2 Diagnosis and treatment)

1.3 Etiology

1.4 Principles of screening

1.5 Natural history of precursors of cervical cancer

2 Screening tests

2.1 Cytology

2.2 Visual inspection methods

2.3 Colposcopy

2.4 HPV DNA testing

2.5 Other emerging techniques

2.6 Combination of different modalities

3. Use of cervical cancer screening
3.1 Delivery and uptake of screening
3.2 Behavioural considerations in screening participation

4. Efficacy of screening

5 Effectiveness of population-based screening
5.1 Incidence and mortality trends in different countries worldwide in relation to screening
5.3 Issues in implementation of screening
5.4 Hazards of screening
5.5 Effectiveness of screening in populations
5.6 Cost effectiveness

- EVALUATION valuta l’efficacia (efficacy) usando gli stessi livelli di evidenza delle monografie sui cancerogeni (sufficient, limited, insufficent).

- RESEARCH RECOMMENDATIONS
- PUBLIC HEALTH RECOMMENDATIONS (riunite)

Evaluation

In reaching its evaluation, the Working Group distinguished evidence of two types.

The strongest evidence derives from historical or prospective data on efficacy, currently available only for cervix cancer from observational studies or time trends in populations.
("has reduced incidence and mortality rates")

However, evidence based upon surrogate markers of reduction in cancer incidence was utilized when derived from a comparison with comparable data following screening with a test shown to reduce cancer incidence by the first type of evidence.
("can reduce incidence and mortality rates")

There is *sufficient evidence* that screening by conventional cytology has reduced cervical cancer incidence and mortality rates.

There is *sufficient evidence* that screening by liquid-based cytology can reduce cervical cancer incidence and mortality rates.

There is *sufficient evidence* that screening by automated cytology can reduce cervical cancer incidence and mortality rates.

There is *sufficient evidence* that testing for human papillomavirus infection as the primary screening modality can reduce cervical cancer incidence and mortality rates.

There is *sufficient evidence* that screening for cervical cancer precursors every 3–5 years between the ages of 35 and 64 years by conventional cytology in a high-quality programme reduces the incidence of invasive cervical cancer by 80% or more among the women screened.

In women aged 25–34 years, the impact of screening at three-year intervals or less may be less.

There is no evidence that screening annually in either age group results in much greater efficacy.

Efficacy of conventional cytology has been demonstrated only for squamous cell carcinoma

Other forms of cytology screening using a validated system at the same ages and frequency can be expected to be as effective as conventional cytology.

There is *sufficient evidence*, based on surrogate markers, that the efficacy of HPV testing, using a validated system, as the primary screening modality can be expected to be at least as good as that of conventional cytology.

Screening in well organized programmes is more cost-effective, with less harm due to overscreening and overtreatment, than opportunistic screening.

Data for analysing cost-effectiveness must be gathered locally and any conclusions drawn must be appropriate to the context.

Investing in obtaining high rates of population coverage is critically important in achieving a cost-effective intervention.

Recommendations for public health implementation and further research

A. Introduction

Much of the evidence to be generated on the long-term effectiveness of modified or new screening modalities, in terms of reduction in the incidence of invasive disease, will come from an evaluation of the results of organized population-based programmes.

Modifications of screening modalities in existing screening programmes therefore need to be introduced in a way that will facilitate rigorous evaluation of long-term effectiveness. This is best achieved by incorporating randomization.

B. General

B2. Once an organized system is in place, opportunistic (or unscheduled) screening should be discouraged.

B5. The adoption of a new screening modality in a population-based screening programme should be matched to the local cost environment, expertise and facilities. These include the capacity both for the primary screening test and for management of screen-detected lesions. Any such implementation should be based on population-based studies.

B6. All screening will have associated negative effects. These include psychosocial, biological and economic effects of the screening episode. Research is needed to minimize the impact of each of these components.

In particular for cervical screening, research is needed into the possible negative effects of overtreatment of screen-detected lesions.

In all comprehensive assessments and comparisons, full account needs to be taken of the potential harmful consequences of screening.

C. Conventional cytology

C1. There is minimal benefit and substantial harm in screening below age 25. Organized programmes should not include women aged less than 25 years in their target populations.

C2. Women who have always tested negative in an organized screening programme should cease screening once they attain the age of 65, as there is little benefit of screening to women over the age of 65 who have had at least two negative tests in the last 10 years. Research is needed to determine whether screening can cease earlier.

C3. For women over age 50, a five-year screening interval is considered appropriate. For women aged 25–49, a three-year rather than a five-year interval might be considered in countries with the necessary resources. Annual screening is not recommended at any age.

D. New developments in cytological screening

The implementation of liquid-based cytology and automation-assisted screening in organized screening programmes needs to be based on cost and local feasibility.

It is imperative that the introduction of each a new modality is accompanied by long-term evaluation of impact on invasive cancer and continuing quality assurance and monitoring.

The age and screening interval for conventional cytology should also apply here.

New modifications to these modalities are frequently proposed. Each such modification needs rigorous evaluation in short-term ..relative sensitivity and specificity for histologically diagnosed CIN 3 compared to the current standard, as well as economic and logistic

E. HPV testing

If a country, on reviewing the available evidence, decides to introduce HPV testing as a primary screening modality, it will need to consider local circumstances, including the acceptability of the test.

Introduction would be facilitated by the availability of low-cost public-domain HPV tests.

Implementation should be preceded by demonstration projects. Large-scale implementation needs to be designed so as to allow rigorous long-term evaluation.

E. HPV testing

E1. It is likely that the same reduction in incidence of invasive disease could be achieved with a longer interscreening interval using HPV testing as a screening test than the intervals recommended above for cytological screening.

It is anticipated that evidence supporting a longer interval may emerge from properly designed public health screening programmes in which HPV has been incorporated.

E2. The optimal ages for starting and stopping HPV screening require further research

E3. The management of women who are HPV-positive but negative on cytology is of vital importance to avoid overtreatment, particularly in younger women, in whom transient infections are common.

Research is required to identify secondary biomarkers, whether cellular or viral, which are accurate predictors of either persistence of viral infection and/or progression of cervical lesions

E5. Efficient implementation of HPV-screening requires research into HPV as a viral infection as well as a screening test. (i) ..transmission and susceptibility..; (ii) .. age-specific rates of infection, reinfection, duration...older women..; (iii) .. behavioural and psychosocial impact; (iv) the natural history of HPV infection in males...

E6 Health professionals and the population at large must be educated...

E7 HPV testing systems need to be standardized and specification requirements for test performance need to be defined.

E8 New commercial testing systems need rigorous evaluation and validation before being adopted by the public health system.