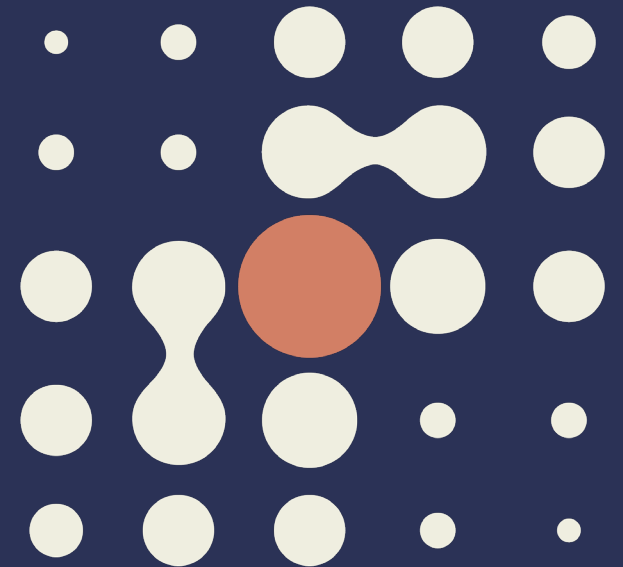


# The *IARC Handbooks of Cancer Prevention* Vol. 18 – Cervical Cancer Screening

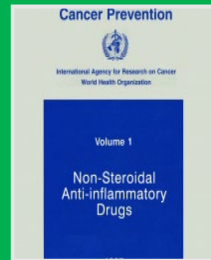
Béatrice Lauby-Secretan, PhD  
*on behalf of the IARC Working Group  
and the IARC Handbooks team*

International Agency  
for Research on Cancer



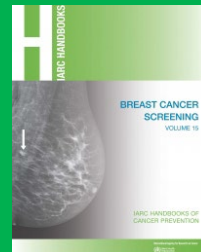
# The IARC Handbooks

Comprehensive review & consensus evaluation of the effectiveness of interventions to reduce the risk of cancer or mortality from cancer.



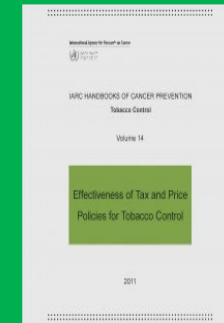
## Primary prevention

Chemo-prevention  
Personal actions



## Secondary prevention

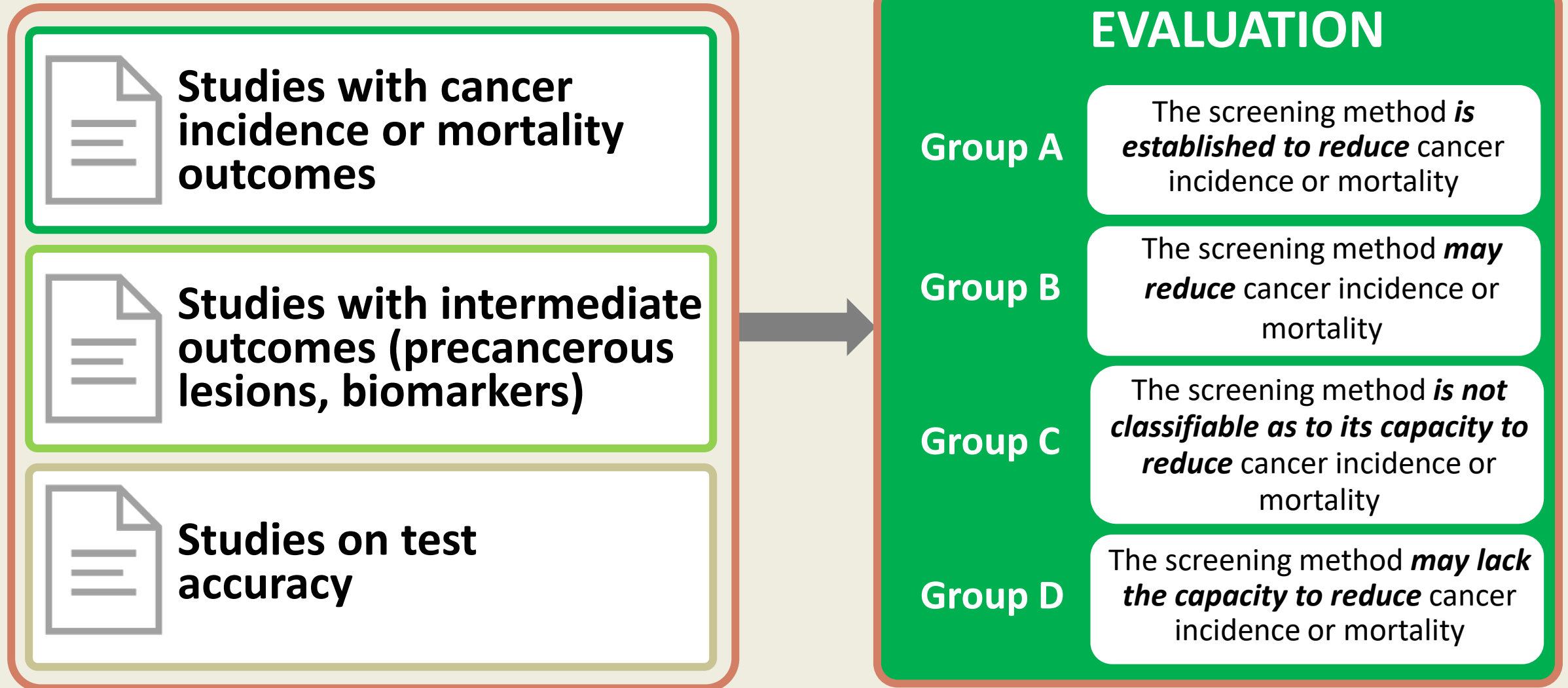
Screening  
Early diagnosis



## Policies and public interventions

Tax policies  
Bans

# Evaluation of secondary prevention interventions



# Content of Handbook Vol. 18

IARC Handbooks of Cancer Prevention News

*IARC Handbooks - Volume 18: Cervical cancer screening*

24 September 2019

We are pleased to announce the meeting for the *IARC Handbooks of Cancer Prevention Volume 18*, which will take place on 23-30 June 2020. For more information, please see [Upcoming Meetings](#).

- Cervical cancer burden & neoplasia
- Screening programmes & practices
- **Preventive and adverse effects of screening methods**
  - Conventional cytology
  - Liquid-based cytology
  - HPV nucleic acid tests
  - VIA
  - Romanovsky-Giemsa stain
  - **HPV DNA versus VIA**
  - **HPV DNA versus cytology**
  - HPV DNA versus co-testing
- Other topics
  - Emerging technologies
  - Screen-and-treat approach
  - Screening of HIV-positive women
  - Screening of women with a personal history of precancer
  - Screening of vaccinated population
  - Determinants of participation

for update of WHO  
Recommendations

# Cytological methods

Screening with **conventional cytology** is established to reduce the incidence of cervical cancer and the mortality from cervical cancer

	Body of evidence
Previous Handbook	7 cohort studies 20 case-control studies
Additional data	1 RCT 5 cohort studies 20 case-control studies Numerous ecological studies

Screening with **liquid-based cytology** is established to reduce the incidence of cervical cancer and the mortality from cervical cancer

	Body of evidence
LBC alone	1 RCT 2 observational studies
Comparison with conv'l cytology	8 RCTs Numerous observational studies

# Visual inspection with acetic acid (VIA)

Outcome	Body of evidence
Cancer incidence/mortality	3 cluster-randomized trials
Precancerous lesions	1 RCT

Screening with VIA **is established** to reduce the mortality from cervical cancer

Screening with VIA **may reduce** the incidence of cervical cancer

# HPV nucleic acid tests

Test/comparator	Body of evidence
HPV alone	1 RCT
Comparison of HPV test with cytology (conv'l or liquid-based)	1 pooled analysis of four RCTs 4 additional RCTs 10 cohort studies
Comparison of co-testing with cytology alone	1 pooled analysis of 7 cohort studies 6 additional cohort studies
	Numerous diagnostic test accuracy studies

Screening with HPV nucleic acid (DNA or mRNA) tests **is established** to reduce the incidence of cervical cancer and the mortality from cervical cancer

# HPV DNA testing versus cytology

## Increased benefits

- Increased sensitivity in detecting CIN2+ in first round
- Reduced detection rates of CIN2+ in the subsequent rounds
- Greater reduction in cervical cancer incidence when using the same screening interval
- Lower 3–10-year risk of CIN3+ after a negative HPV DNA test than after negative cytology

## Increased harms

- Increase in positive tests
- Increase in colposcopy referrals
- Potential increase in psychological harms

- The increased benefits of HPV DNA testing outweigh the increased harms.
- Triage can greatly reduce colposcopy referral rates.
- HPV DNA testing allows for longer screening intervals compared with cytology.



# HPV DNA testing versus VIA

## Increased benefits

- Increased detection of high-grade cervical lesions (CIN2+ and/or CIN3+)
- Greater reduction in detection rates of CIN2+ at 6 and 36 months
- Greater reduction in stage II+ cervical cancer and cervical cancer mortality

## Increased harms

- Because of the high variability of VIA, respective harms could not be compared:
  - ↑ positive tests ?
  - ↑ colposcopy referrals ?

- The increased benefits of HPV DNA testing largely outweigh the increased harms.
- VIA has other substantial limitations, such as subjectivity, heterogeneity, and potential outcome misclassification.

# Co-testing versus HPV DNA testing

## Increased benefits

- Minimal increase in sensitivity for detecting CIN2+ and CIN3+
- Minimal difference in cumulative risks for CIN2+ and CIN3+ b/w co-test-negative women and HPV-negative women

## Increased harms

- Lower specificity for detecting CIN2+ and CIN3+
- Increase in referrals to colposcopy, and possibly treatment
- Decrease in positive predictive value in referred women (increased detection of regressive lesions)

- The benefits of co-testing do not outweigh the harms.
- The impact of the cytological component of co-testing is very limited.
- The impact on cancer incidence is unclear.

# Evaluations and comparison of methods

Screening method	Reduction in incidence	Reduction in mortality	Benefit outweigh harms?
Conventional cytology	A	A	Yes
Liquid-based cytology	A	A	Yes
HPV-nucleic acid tests	A	A	Yes
Visual inspection (VIA)	B	A	May
Romanovsky-Giemsa stain	C	C	No

Comparison of methods	Comparison of benefit to harm balance
HPV DNA test vs cytology (conv'l or liquid-based)	HPV DNA test > Cytology
HPV DNA test versus VIA	HPV DNA test >> VIA
HPV DNA test alone versus co-testing	HPV DNA test ~ Co-testing

# Additional considerations for screening with HPV tests

## Self-sampling (compared to clinician-collected sampling)

- Sensitivity and specificity for detecting CIN2+ or CIN3+:
  - Similar when using PCR-based HPV DNA tests
  - Lower when using signal amplification or HPV mRNA tests

## HPV mRNA test (compared with HPV DNA test)

- Similar cross-sectional sensitivity for detecting CIN3+
- Higher specificity for detecting CIN3+
- 3-year risk of CIN2+:
  - Lower than that of a negative **cytology** result
  - Equal to that of a negative **HPV DNA** result ?

## Triage after HPV positive result

- Genotyping for HPV16/18, cytology, p16/Ki67 dual stain, colposcopy, VIA, and combinations thereof

# Meeting participants

## Working Group Members:

- Silvina Arrossi
- Karima Benddahou
- Johannes Berkhof
- Julia Brotherton
- Karen Canfell
- Mike Chirenje
- Michael Chung
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- Vitaly Smelov
- Salvatore Vaccarella
- Patricia Villain

## Representative:

- Jae-Weon Kim





# Thank you!

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- The Center for Disease Control, USA
- Medical Research Council, UK



International Agency  
for Research on Cancer



[www.handbooks.iarc.fr](http://www.handbooks.iarc.fr)