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HPV-based screening: How to formulate guidelines in low incidence countries?

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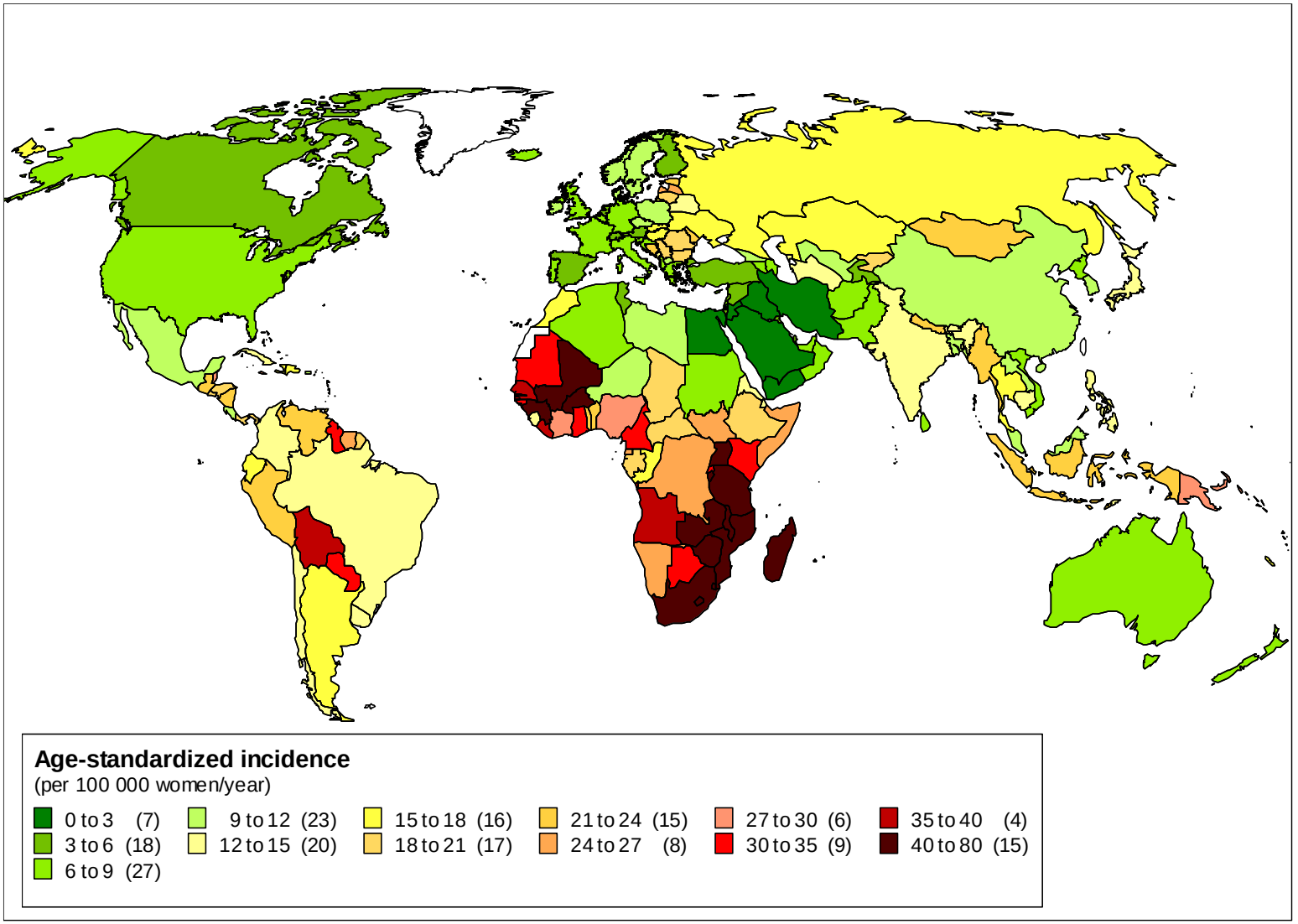
Contents

- **Which parts of the world have low incidence of cervical cancer (CC)?**
- **Policies/guidelines for cervical cancer prevention in low incidence countries**

Current burden of cervical cancer

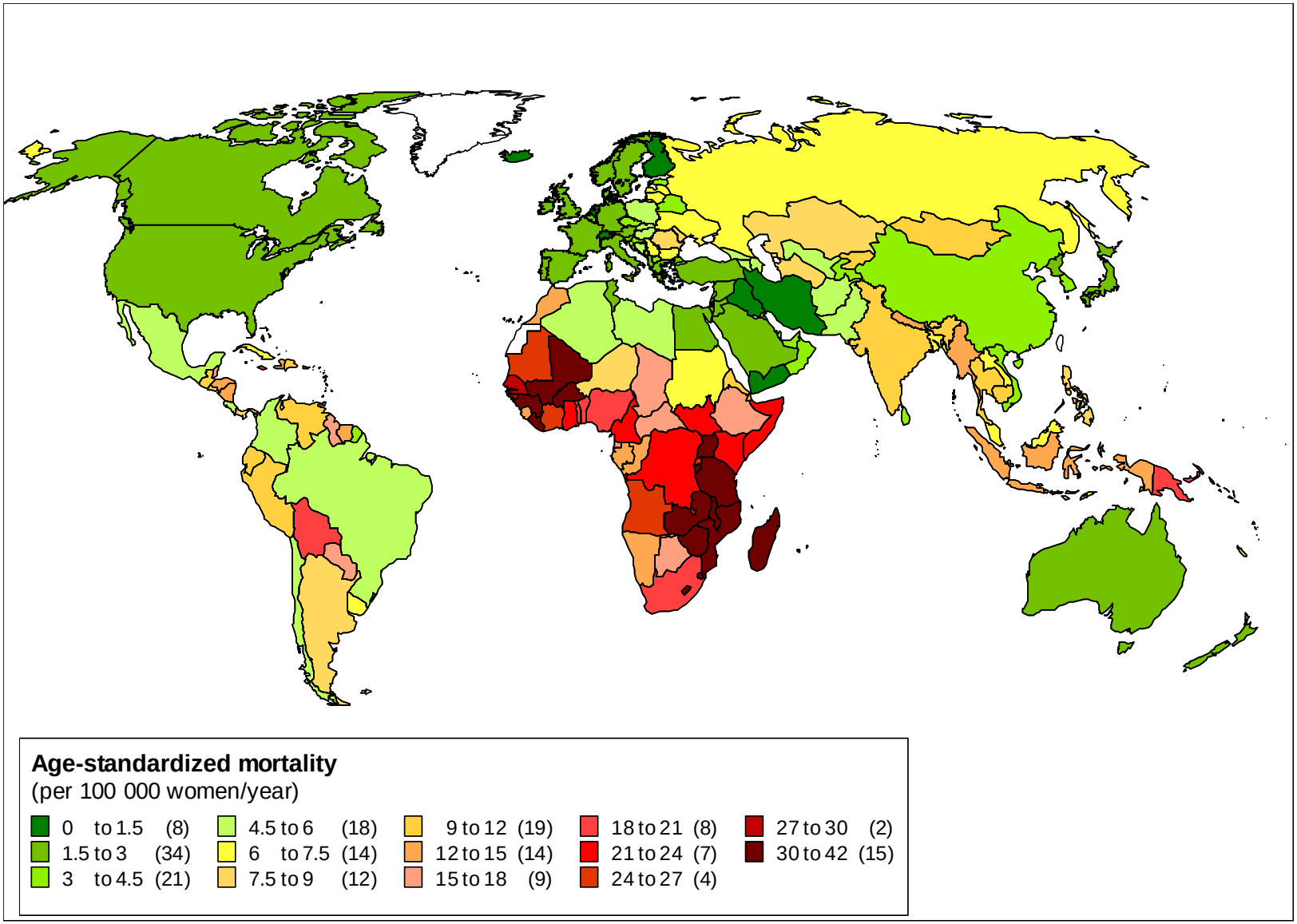
Arbyn M, Weiderpass E, et al, 2019 (submitted)

Cervical cancer incidence (2018)



Arbyn M, Weiderpass E, et al, 2019 (submitted)

Cervical cancer mortality (2018)



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Sub-continents with lowest CC incidence (ASIR<7.5 / 100,000)

1. **Western Asia: 4.1 / 100,000**
2. **Australia / N-Zealand: 6.0 / 100,000**
3. **North-America: 6.4 / 100,000**
4. **Western-Europe: 6.8 / 100,000**
5. **Northern Africa: : 7.2 / 100,000**

Current incidence is determined by

- **Back ground risk: low in subcontinents: 1 & 5**
- **Screening & treatment of precancer: established in subcontinents 2-4.**

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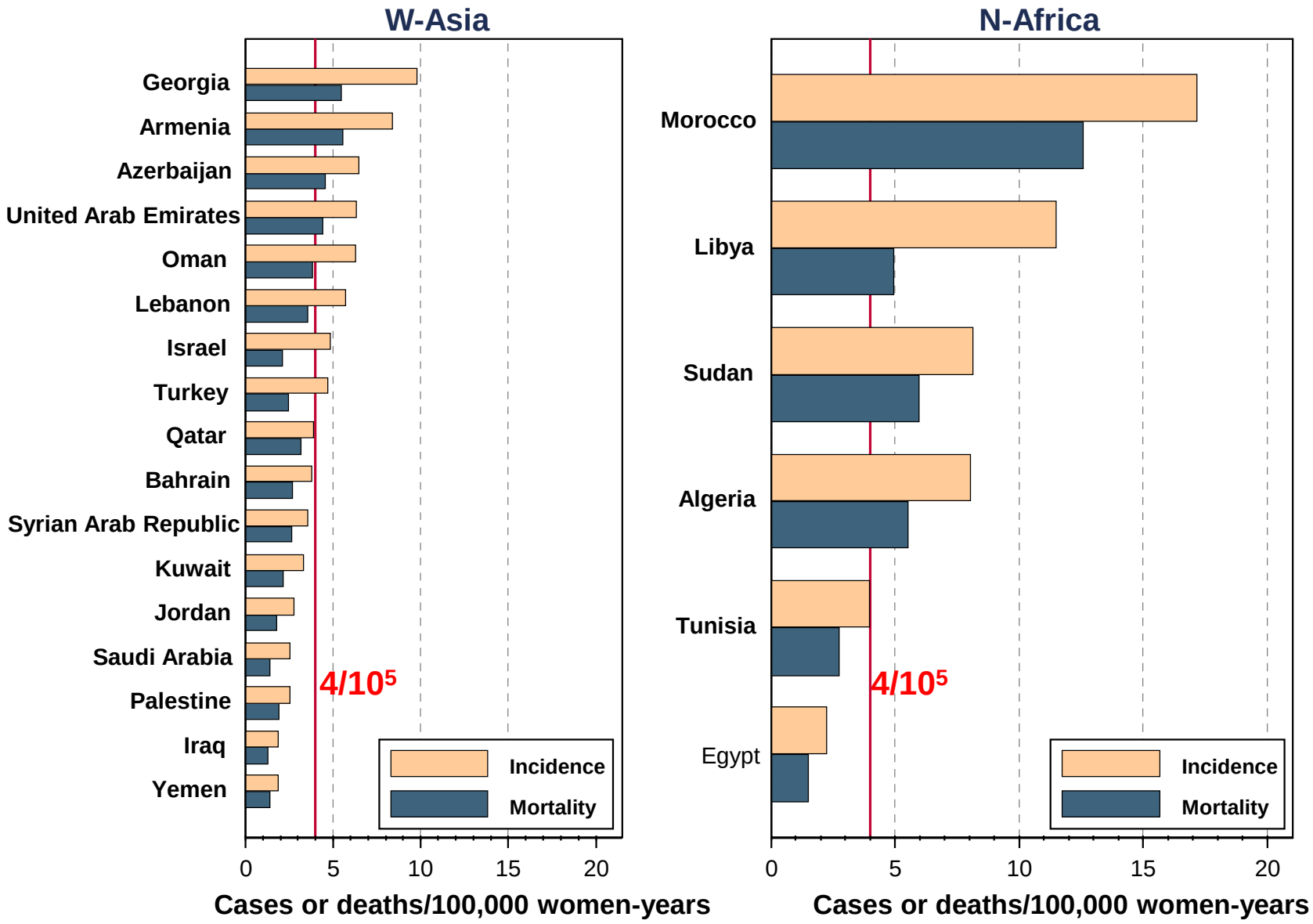
Sub-continents with lowest CC incidence due to low back ground risk (2018)



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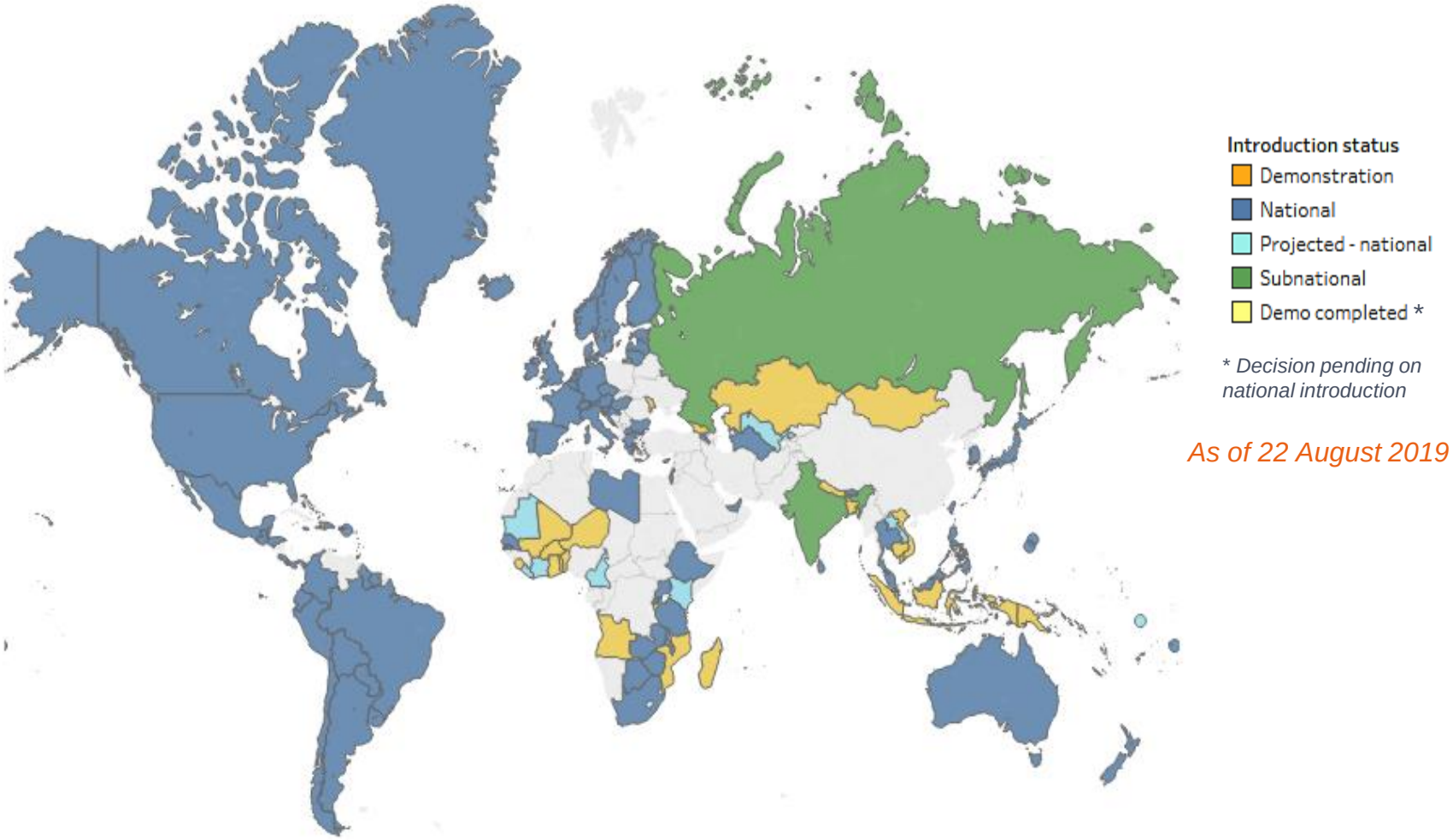
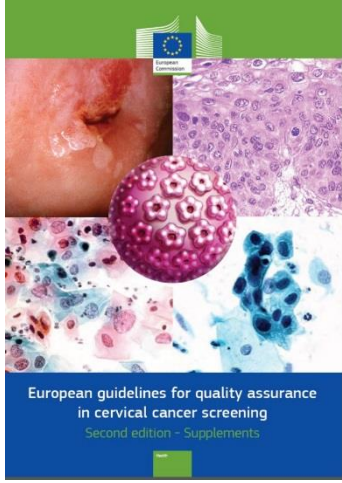
Global HPV Vaccine Introduction (2019)



Vaccine coverage will influence future incidence considerable. Too early to observe impact of vaccination on current incidence

Guidelines for EU



- **Screening with validated hrHPV test starting at age of 30, intervals of ≥ 5 y. Cytology from 25-30y.**
- **Triage of hrHPV+ women:**
  - **Reflex cytology**
  - **If reflex cyto -: cyto or hrHPV 6-12 months later**
- **Where cytology still exists: age 25-64, every 3y, with HPV triage of equivocal cyto**
- **After treatment of precancer: HPV or cotesting 6 & 18 months after T**

hrHPV assays validated for CC screening (Signal-amplification; PCRs)

- **Fully validated (multiple studies)**
  - **HC2 & GP5+/6+-EIA**
  - **Abbott RT hrHPV; Cobas 4800; BD Oncolarity; PapillocCheck; Anyplex II hr; Risk HPV assay**
- **Fully validated (1 study)**
  - **Xpert HPV; Linear Array (13hr types), Cobas 6800**
- **Partially validated**
  - **GP5+/6+ PCR-LMNX (reproducibility)**
  - **Cervista (inconsistency specificity)**
  - **RIATOL qPCR (E6/E7) (no inter-lab reproducibility)**
- **Validated after cut-off optimisation**
  - **EuroARRAY**

Arbyn, Clin Microbiol Infect 2015; HPV World 2018

Guidelines in USA

- **HPV every 3 years or cotesting every 5 years**
- **Risk based management guidelines using genotyping & cytology, updated in 2020**
- **HPV vaccination of females & males 9-26y (27-45y)**

Arbyn M, Weiderpass E, et al, 2019 (submitted)

Guidelines in Australia

- **HPV every 5 years women aged 25-69y**
- **Triage with HPV16/18 genotyping & cytology (at cutoff ASCH)**
- **Self kits for non-responders**
- **9-valent HPV vaccine HPV vaccination 2 doses for girls & boys 12-13y (at schools)**
- **Less screening (1-4x/lifetime) of vaccinated cohorts is considered (Velentzis, Gynecol Oncol 2019)**

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Guidelines in W-Asia & N-Africa

- **No existing international guidelines**
- **Policy proposed in the framework of the WHO call to eliminate CC.**
  - **Vaccination of ≥ 90% of girls before the age 15y**
  - **Screening of ≥ 70% with validated HPV tests, 2x over lifetime at age 35y & 45y**
  - **Treatment of ≥ 90% of women with precancer**
- **Only validated HPV assays for screening**
- **Recommended test for triage of hrHPV+: VIA, genotyping, (AVE?), … or screen & treat**

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Guidelines for HPV testing on self-samples

- **Evidence that HPV testing with a validated hrHPV DNA test is as sensitive & specific on self-samples compared to clinician-taken cervical samples (Arbyn, Lancet Oncol 2014; BMJ 2018)**
- **Offering self-sampling kits more effective than mailed invitations to reach underscreened populations (Arbyn, BMJ 2018)**
- **Direct offer by health professional very effective**
- **Piloting needed on best way to offer SS kits before general roll-out**

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