How to organize a population-based screening program? Can we extrapolate the Turkish experience to the rest of MEMAGO countries?

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What is population screening?

- Population screening refers to a test that is offered to all individuals in a target group, usually defined by age, as part of an organised program.

- Screening involves simple tests to look for particular changes, or early signs of a disease, before a disease has developed or in its early stages before any symptoms develop.

- No screening test is 100% accurate and the body changes over time, which is why it is important to be screened at regular intervals. If you are worried that you might have a symptom or sign of the disease, you should see your doctor, even if you have recently had a screening test

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Objectives of Cervical Cancer Screening

- Prevent morbidity and mortality from cervical cancer
- Optimal detection of CIN3 lesions
- Reduce the number of patients referred to Colposcopy
- Reduce unnecessary interventions
- Cost efficiency

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WHO Principles of Early Disease Detection-1

In 1968, Wilson and Jungner developed the WHO principles of screening.

- **Condition**
  - The condition should be an important health problem.
  - There should be a recognisable latent or early symptomatic stage.
  - The natural history of the condition, including development from latent to declared disease, should be adequately understood.
- **Test**
  - There should be a suitable test or examination.
  - The test should be acceptable to the population.
- **Treatment**
  - There should be an accepted treatment for patients with recognised disease.

WHO Principles of Early Disease Detection-2

- **Screening Program**
  - There should be an agreed policy on whom to treat as patients.
  - Facilities for diagnosis and treatment should be available.
  - The cost of case-findings (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
  - Case-findings should be a continuing process and not a ‘once and for all’ project.

Prevention and Control of Cervical Cancer

- Awareness (Education etc.)
- Socio-economic development
- Circumcision
- HPV Vaccination
- Population-based screening programmes
- Non-population-based screening programmes
- Early Diagnosis and Treatment

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Recommendations of WHO

You need to screen:

- Breast cancer
- Cervical cancer
- Colorectal cancer

in your country:

For Cervical Cancer:

- Don’t need to screen under 25 years of age
- Don’t need to screen over 65 years of age
- Never practice annual screening

Develop your national screening strategies !

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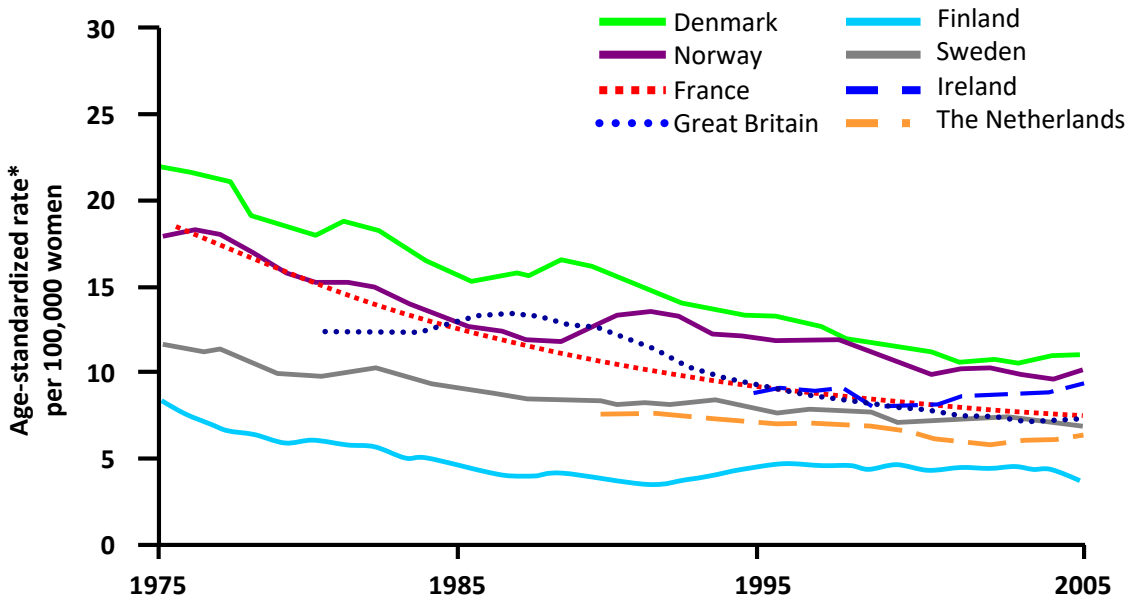
Widespread use of cytology-based screening has reduced cervical cancer incidence in Europe



Ferlay J, *et al.* GLOBOCAN 2008. Available at: http://globocan.iarc.fr/factsheets/cancers/cervix.asp (accessed April 2011). IARC CancerBase. Lyon; 2010. * standardised using the World reference population

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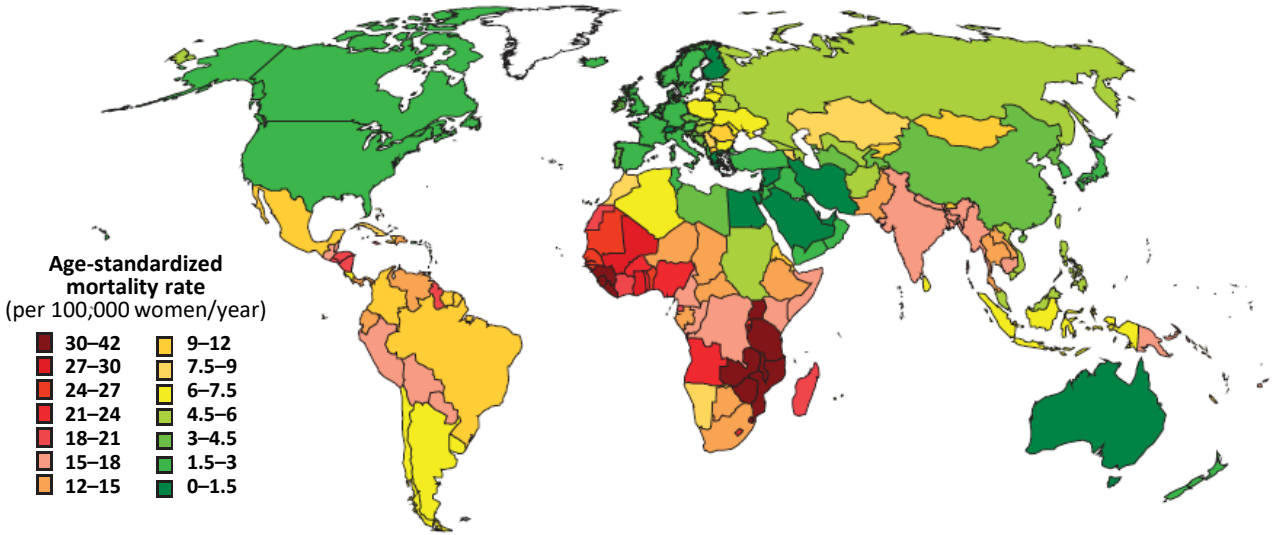
In spite of screening, women are still dying of cervical cancer



An estimated 530,000 cases and 275,000 deaths from cervical cancer in 2008

Arbyn M, *et al. Ann. Oncol.* 2011 Apr 6

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Successful Cervical Cancer Prevention Programs:

- The screening test is just one of the key components in an effective cervical cancer prevention program.
- There are multiple system elements that need to be optimized for the early diagnosis of cervical cancer.
  - Education
  - Coverage
  - Treatment
  - Follow-up

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Why is primary HPV testing replacing the Pap test?

- A significant false-negative rate for Pap vs HPV tests
  - (30% vs 2-3%) required more frequent screening to minimise failure to detect disease
- Women who test HPV -ve are at very low risk of HSIL and cancer for at least 5 years
- Compared with cytology, HPV testing provides 60–70% greater protection against invasive cervical cancers; significantly reduced incidence of adenocarcinomas
- Opportunity for self collection in under-screened populations

Renshaw AA et al. Cancer Cytopathology 2001;93:106-10, Guglielmo Ronco et al. Lancet 2014;383:524-32

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Why use partial genotyping?

- Partial genotyping allows for separate detection of HPV 16 and 18; other oncogenic HPV types will be reported as a pooled result
- HPV 16 and 18 are associated with cervical abnormalities that are less likely to regress and more likely to progress to high-grade cervical abnormalities, compared with other oncogenic HPV genotypes
- Improves risk stratification/assessment in the screening program

Castle PE et al. Obstet Gynecol 2009;113:18-25; Kjaer SK, et al. J Natl Cancer Inst 2010;102:1478-88; Schiffman M, et al. Cancer Epidemiol Biomarkers Prev 2011;20:1398-409

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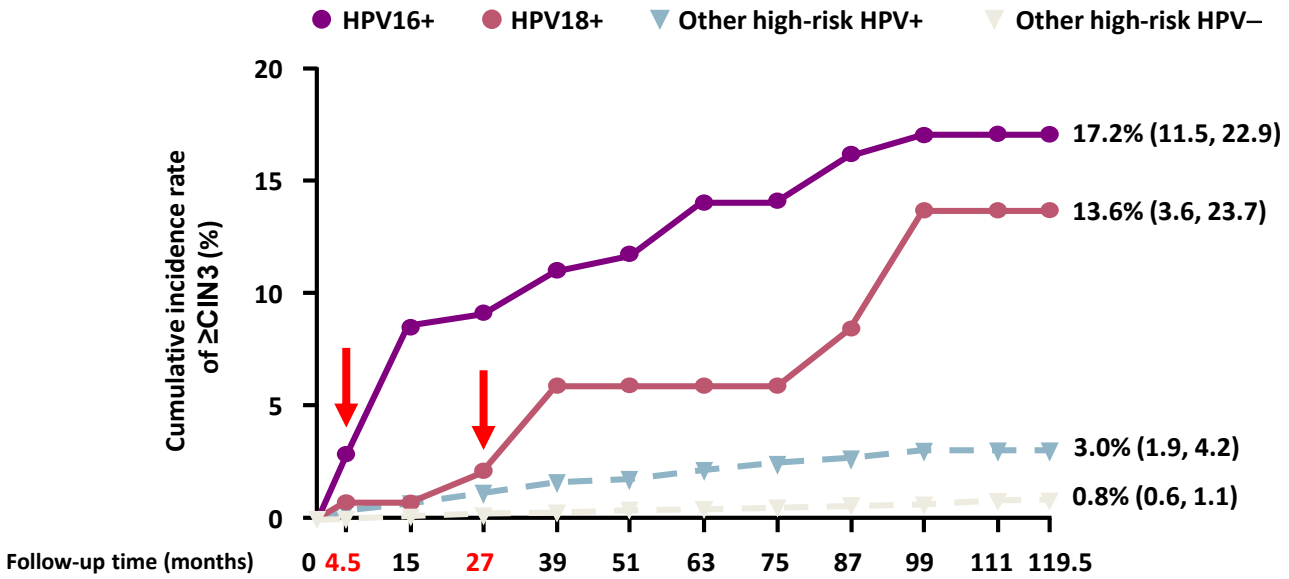
Women with HPV16 and HPV18 infections at baseline are more likely to develop CIN3+



HPV16/18 genotyping identifies more cervical disease earlier, improving outcomes

Khan MJ, et al. J Natl Cancer Inst 2005; 97:1072–1079.

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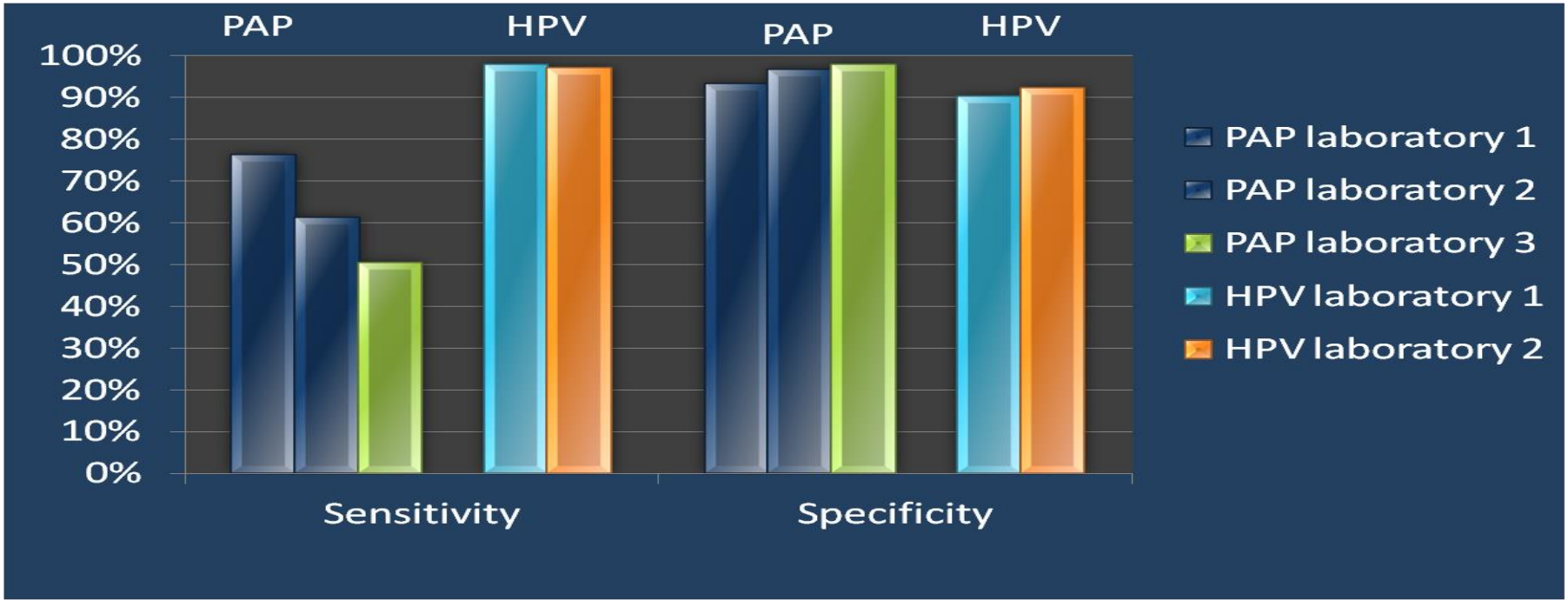
Efficacy of Laboratory Performance: Cytology vs HPV Testing (CCCaST Study)



Mayrand MH, Unpublished Data

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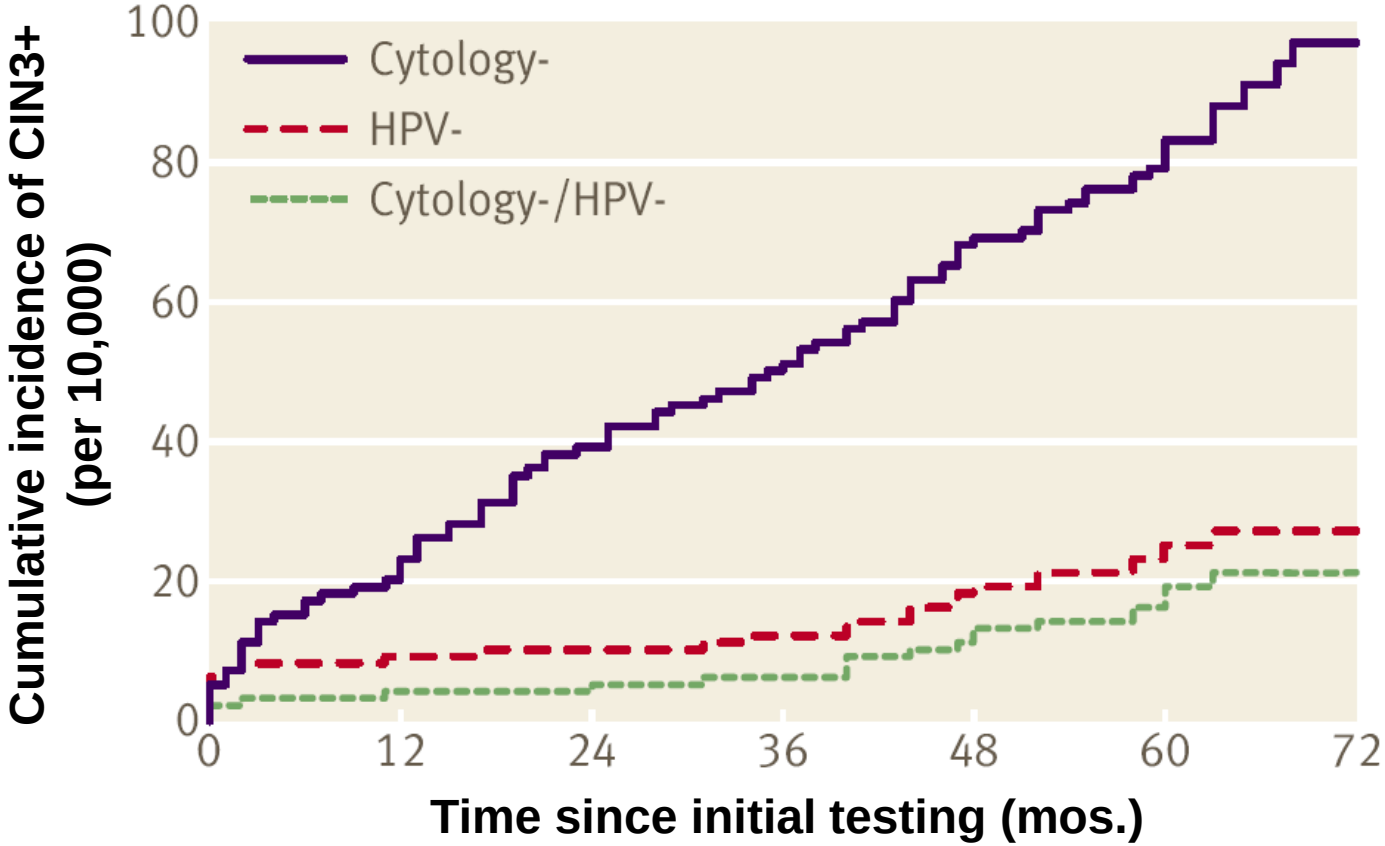
Cumulative incidence of CIN3+ according to baseline test results in European sites (excluding Denmark and Tubingen)



Dillner, J. et al. BMJ 2008;337:a1754

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Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Evidence Regarding Human Papillomavirus Testing in Secondary Prevention of Cervical Cancer

Marc Arbyn[a,b,*], Guglielmo Ronco[c], Ahti Anttila[d], Chris J.L.M. Meijer[e], Mario Poljak[f], Gina Ogilvie[g], George Koliopoulos[h], Pontus Naucler[i], Rengaswamy Sankaranarayanan[j], Julian Peto[k]

- Strong evidence that HPV-based screening using validated HPV assays is more effective than cytology-based screening among women age 30 years or older
- Interval can be extended safely to 5-7 years.
- Implementation will require a well-organized and monitored system
- HPV screening more cost-effective than cytology
- Reduced specificity requires appropriate triage to compensate for the loss in specificity(typing HPV 16/18, p16, Ki67)
- Not in women <30 years.

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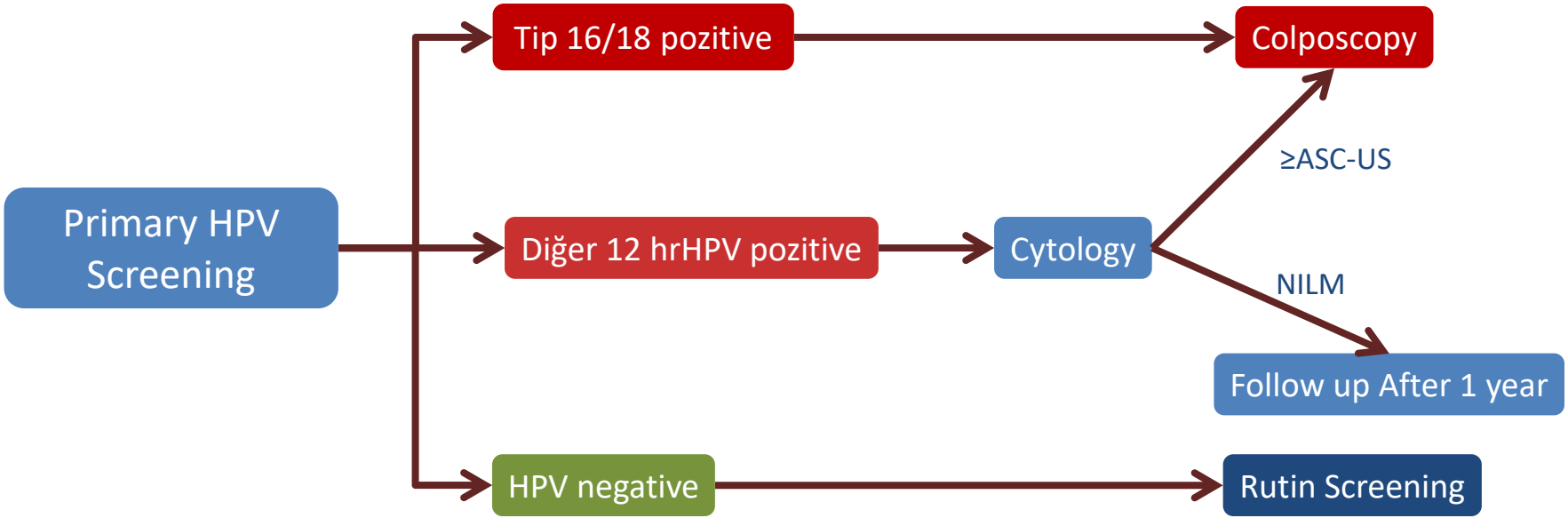
Primary HPV Screening



NILM: Negative for Intraepithelial Lesion or Malignancy

Huh WK, Gynecol Oncol 2015

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Screening project in Şanlıurfa Cervical Early Detection Project

- 2005-2007
- 538.000 Euro
- 10.000 women screened

Advisors

İnternational	Domestic
• Marc Arbyn	• Ali Ayhan
• R. Sankar	• Kunter Yüce
• Eduardo Franco	• Faruk Köse
• Xavier Bosch	• Fırat Ortaç
• Ulrich Petry	• Macit Arvas
• Albert Singer	• Ali Haberal
• Christine Bergeron	• Gökhan Tulunay

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Şanlıurfa Study(2005)

Anormallikler	N (%)
ASC-US	144 (1.60)
ASC-H	6 (0.06)
AGC	5 (0.05)
LGSIL	7 (0.07)
HGSIL	2 (0.02)
Invasive Cancer	1 (0.01)

Total Cytology: 9,079

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KETEM Study(2011)

- 17 Centers
- 3500 Normal populations

- **Hpv Prevalence: % 2.9**

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Estimating Prevalence of Genital Warts in Turkey: Survey among KETEM-affiliated Gynecologists across Turkey

Nejat Ozgul*, Murat Tuncer, Melike Abacioglu, Murat Gultekin

Asian Pac J Cancer Prev. 2011;12(9):2397-400

- N=4,013,084 >30 yaş
- Prevalence: 154 / 100.000(26-326)
- Number: 21.684
- Recurrence rate: %15-%37

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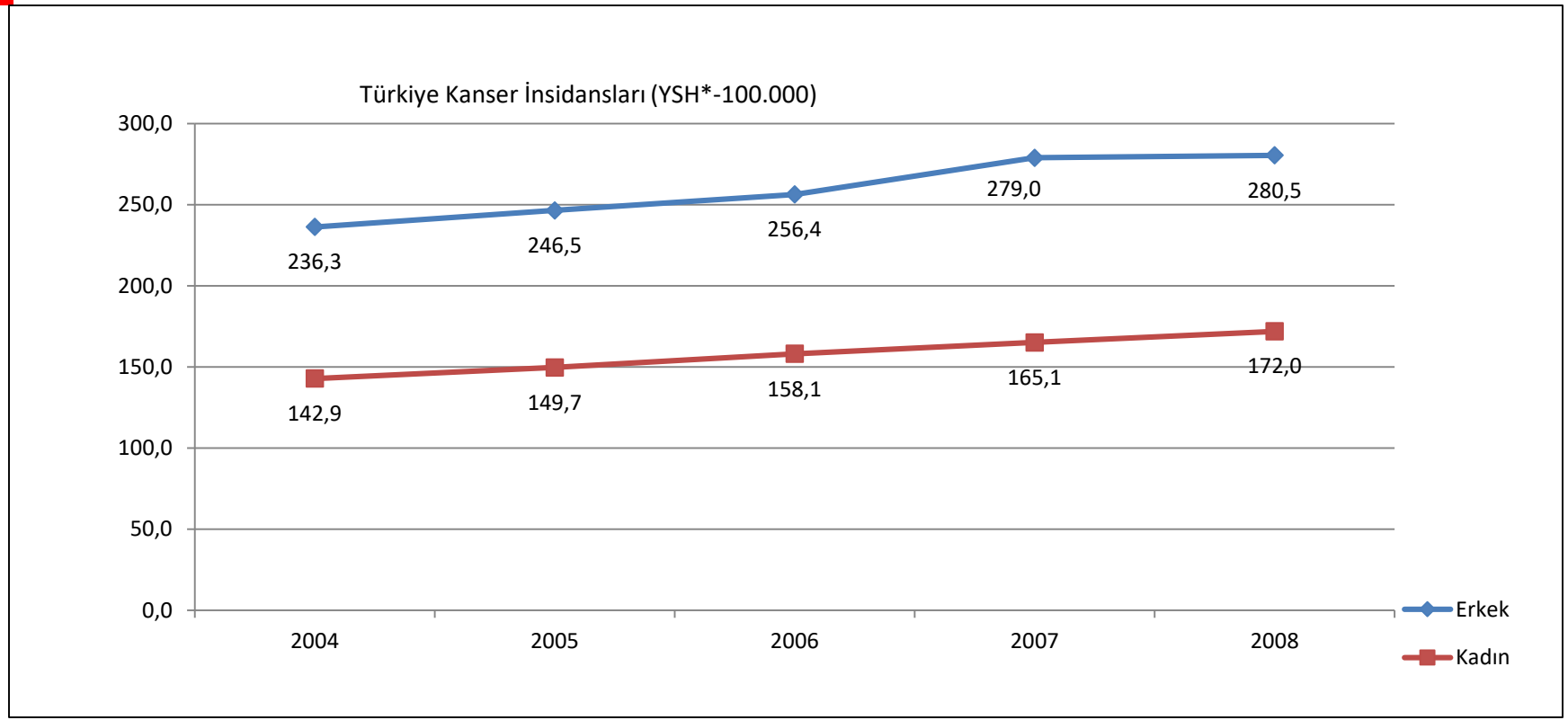
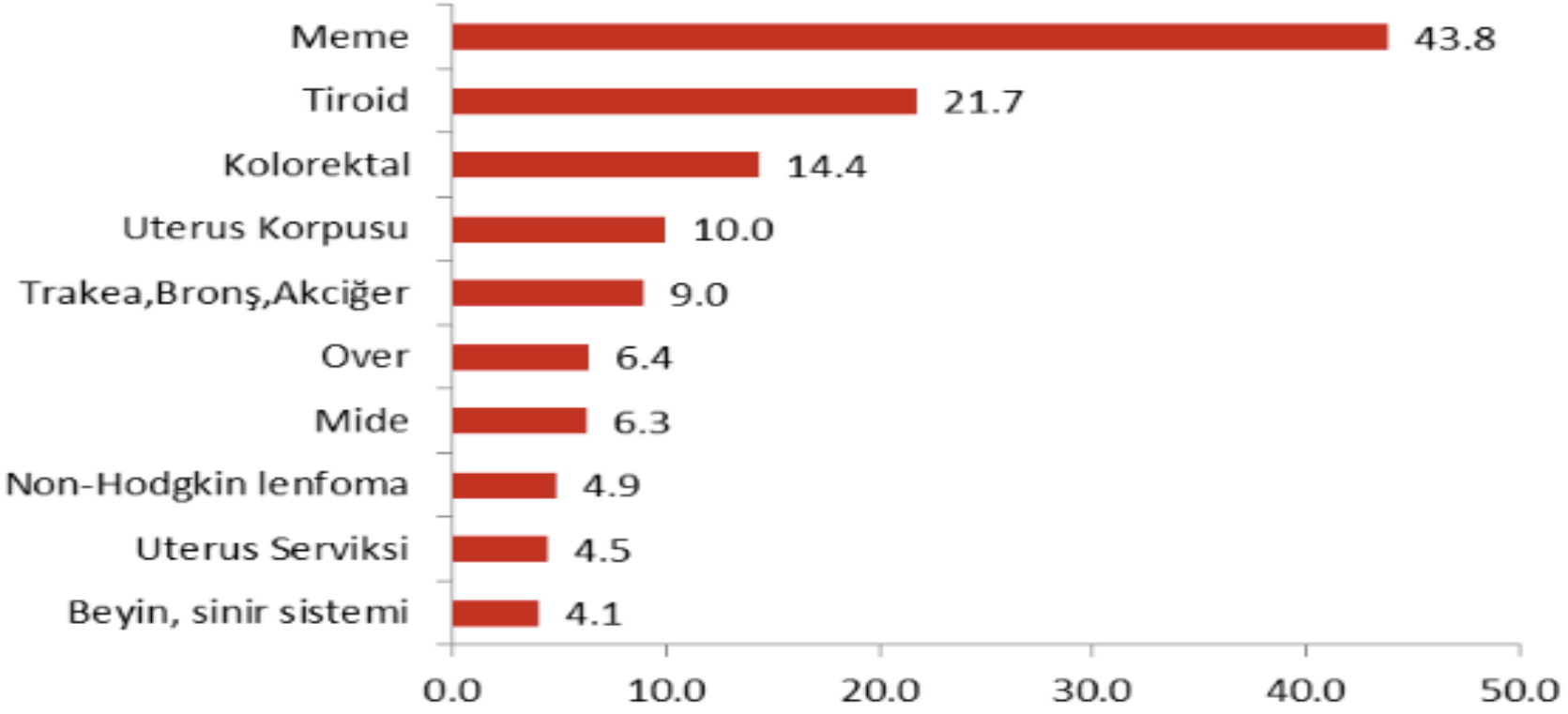
Increase of Cancer Data Quality



The Most Frequent 10 Cancers in Turkey(Women)
TCSB-2015



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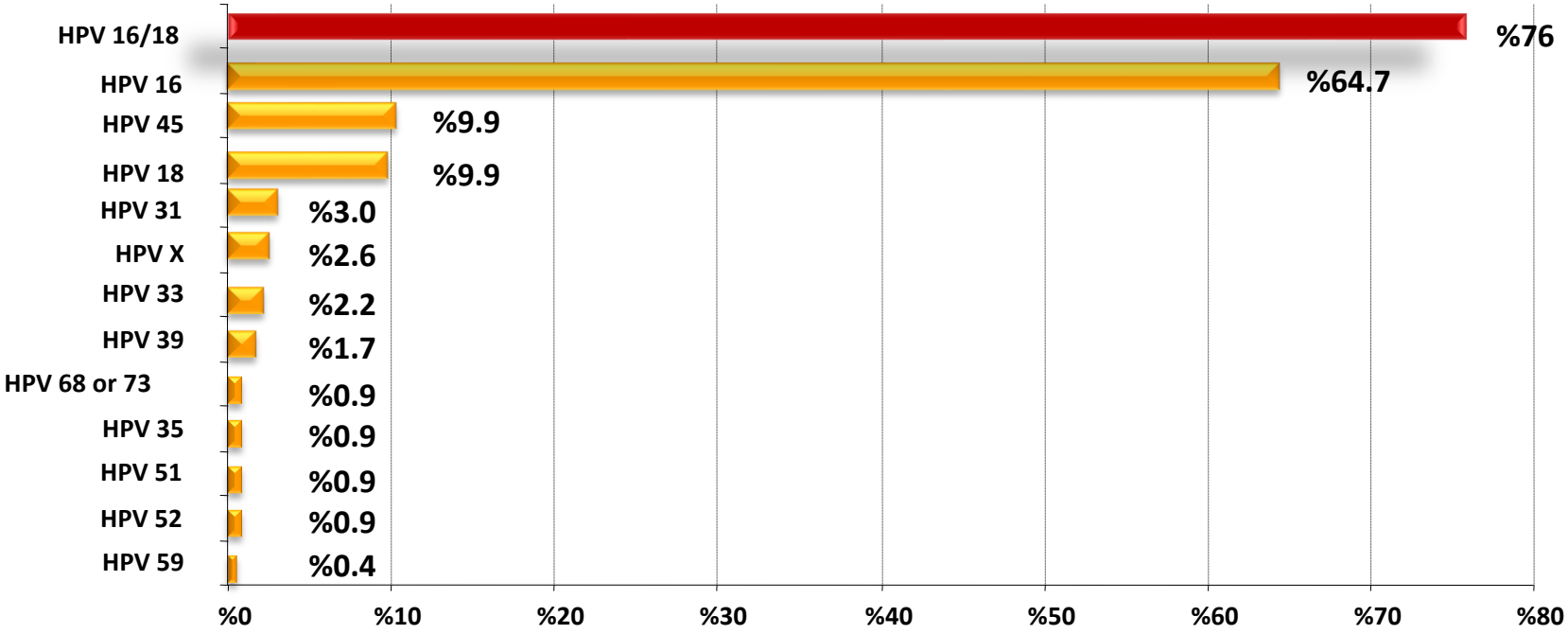
Distribution of HPV Types in Turkey

- HPV16 + HPV18 %75.4



Usubutun A, Int J Gynecol Pathol, 2009

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National Cancer Screening Standarts in Turkey

Breast

Woman self-examination
20 years old, every month

Doctor's breast examination
20 Years old 2 years
40 Years old, every year

Mammography

40-69 years old, 2 years interval

Cervix

Cervical Cytology

30-65 years old, 5 years interval

HPV Test

30-65 years old, 5 years interval

Colorectal

Stool Occult Blood Test
50-70 Years old, 2 years interval

Colonoscopy

10 yıears interval

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Medical Societies

- Turkish Society of Gynecologic Oncology
- Turkish Society for Colposcopy and Cervical Pathologies
- Turkish Cytopathology Society
- Turkish Pathology Society
- Turkish Microbiology Society

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Current Cervical Cancer Screening Programme in Turkey

- Screening Test: **HPV Testing**
- Target Age Group: **30-65 years**
- Screening Interval: **5 years**
- **Population based screening** through KETEMs (free of charge) + **Opportunistic screening**
- EU Quality guidelines are implemented by on site monitorization and evaluation
- KETEMs have consultant Ob&Gyn specialists in addition to other experts. If the smear result is abnormal, consultations, treatments after screening and follow ups of patients are free of charge without strict referral rules.

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KETEM

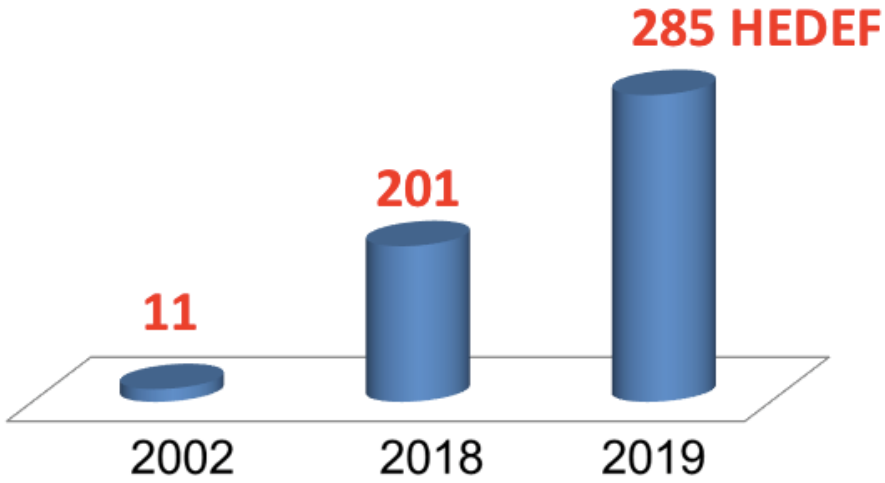
(Cancer Early Detection, Screening and Education Centers)

201 KETEM

- 175 sabit KETEM

(47 KETEM, SHM içinde)

- 26 Mobil KETEM



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High-Risk HPV Testing

High-Risk HPV testing
(13 High-Risk types HPV 16/18/31/33/35/39/45/51/52/56/58/59/68)
Reflex cytology and genotyping
for the (+) ones.
Results are taken within 7 days after the samples arrival to the laboratory.
1 Million Screening in 1 Year

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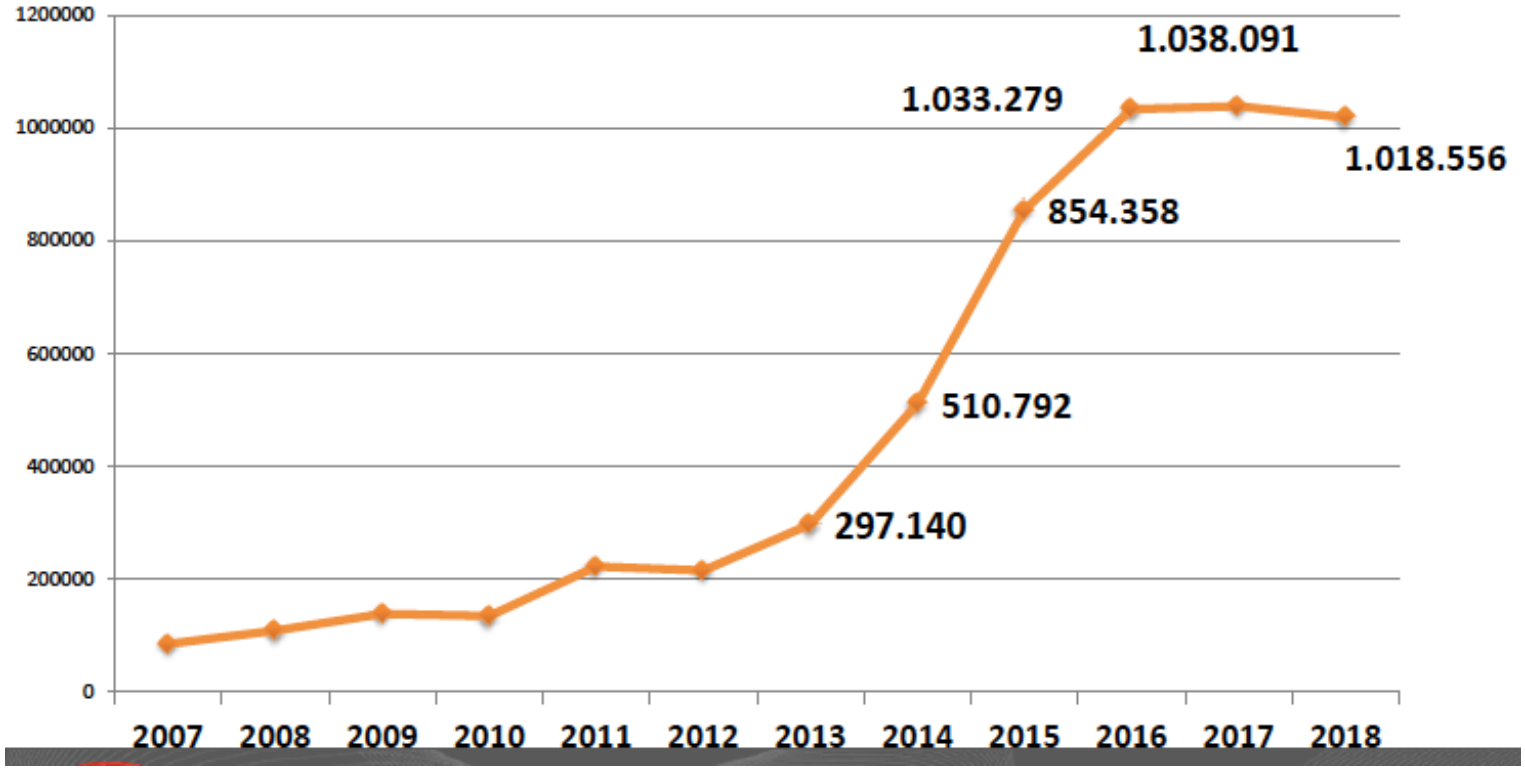
Population Based Screening Numbers



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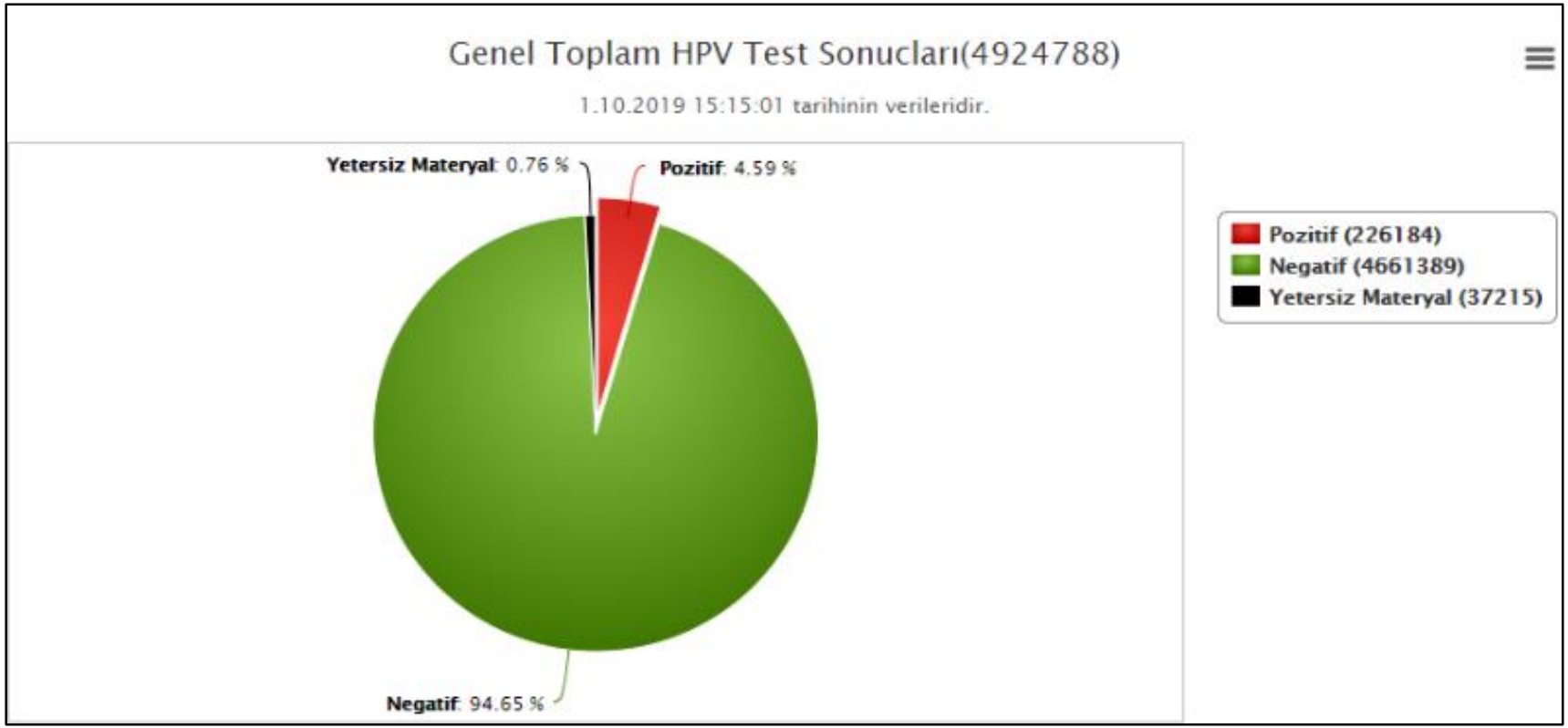
HPV Test Results- 02.10.2019

Begining of Screening- 01.08.2014



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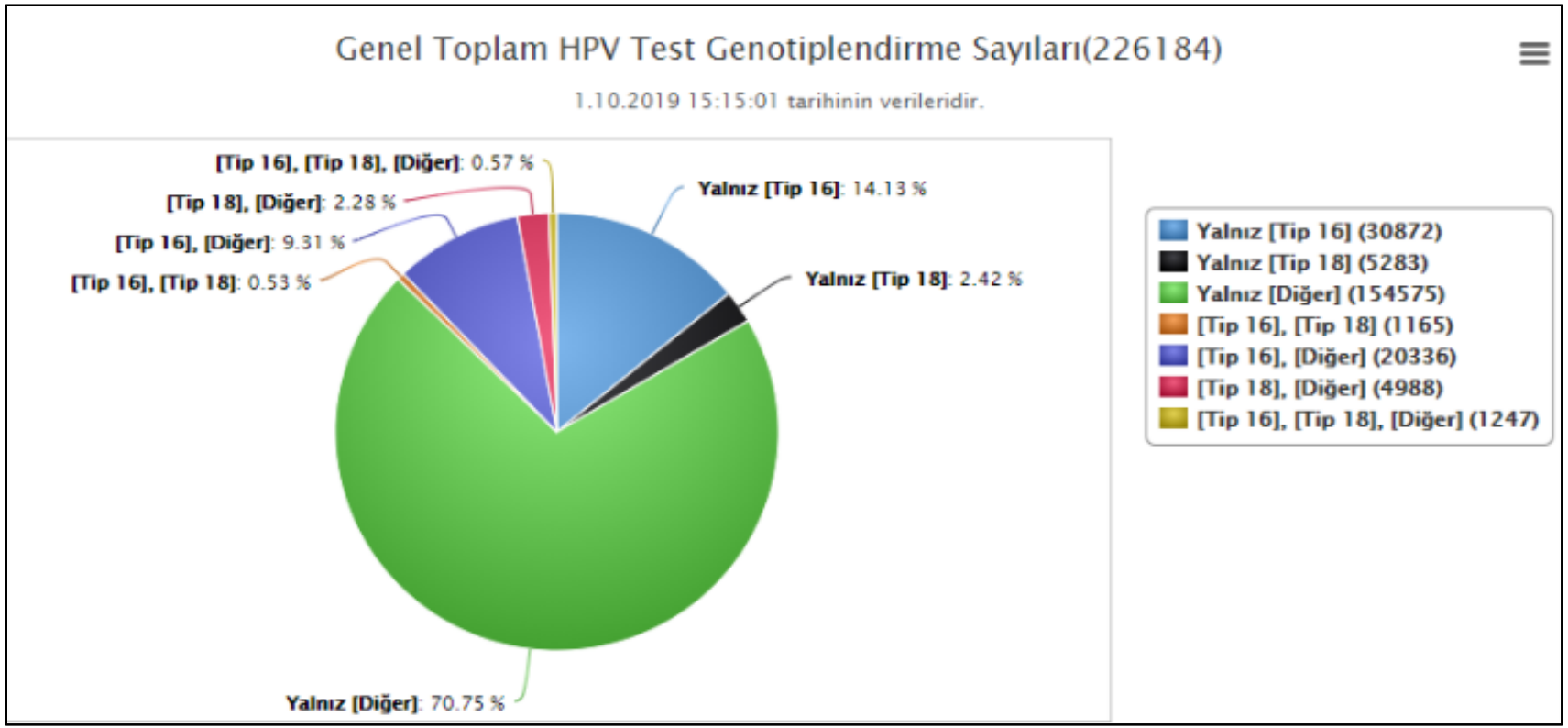
HPV Genotyping Results- 02.10.2019



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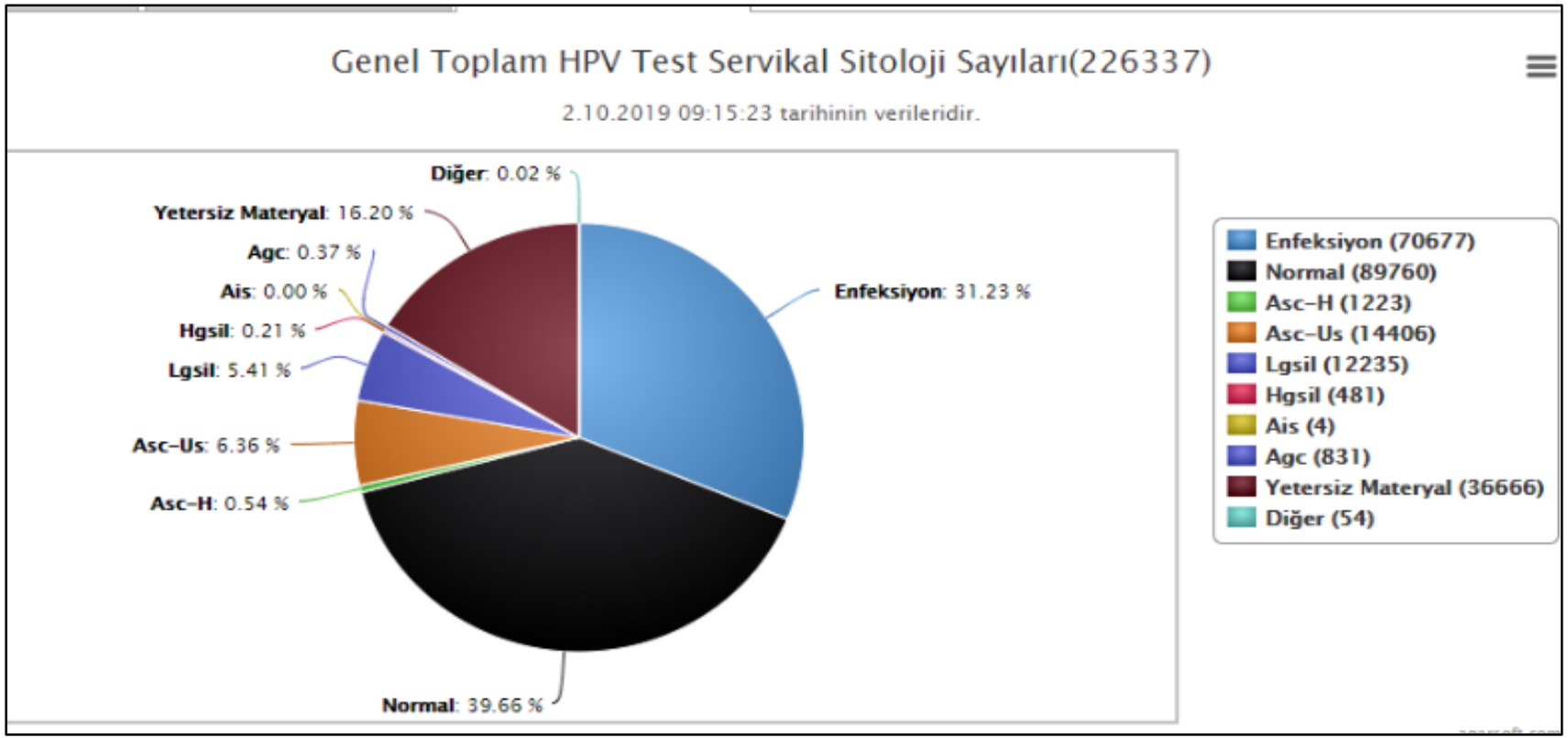
HPV(+), Cytology Results-02.10.2019



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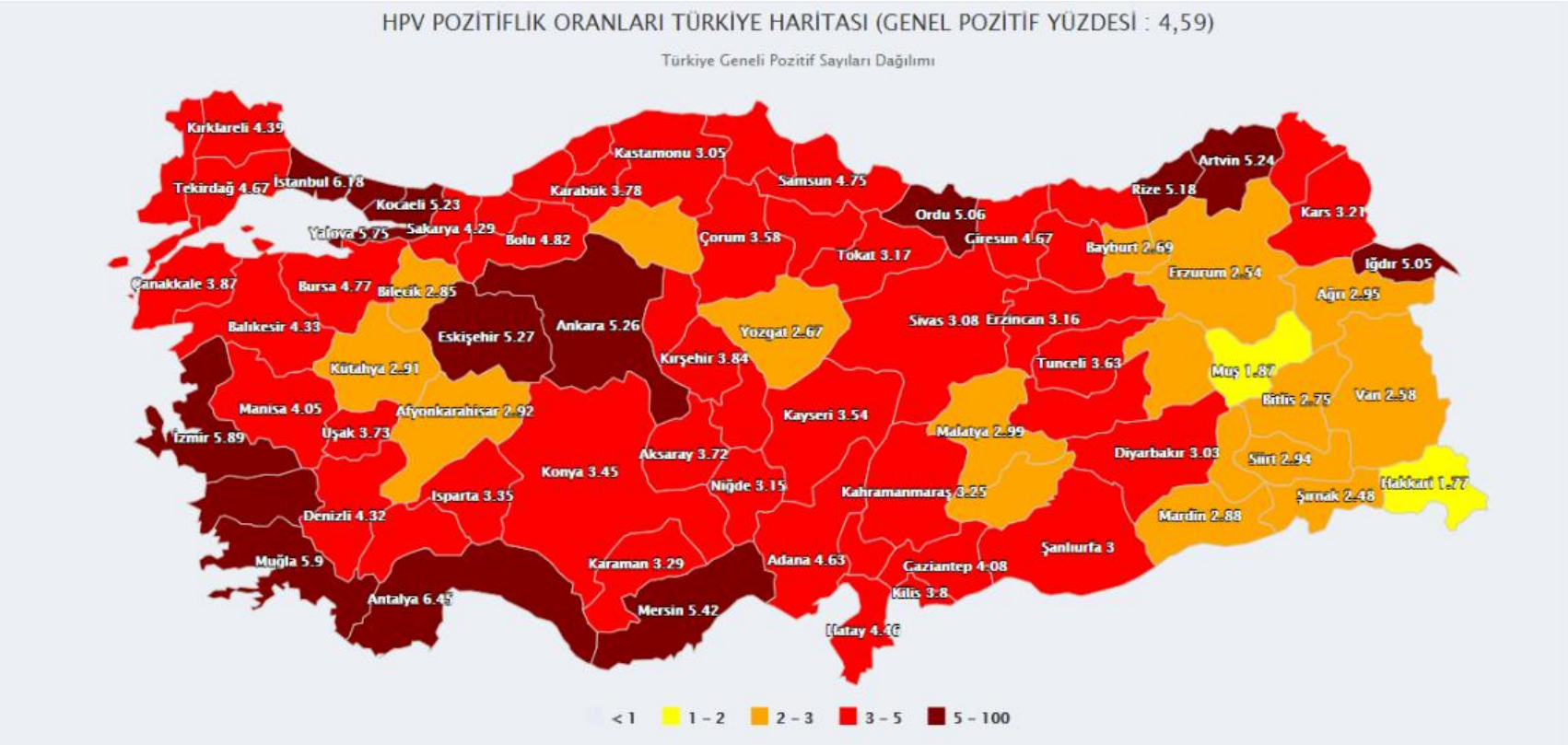
Map of Turkey- HPV Prevalence 02.10.2019



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Turkish Programme

- The only country with Population Based HPV DNA Screening in the world
- The only country with National Mega-HPV Laboratory in the world
- The only country with Mobile KETEMs and a national mamography report center

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Debates on HPV Screening

- Too much HPV positive cases without cytoabnormality
  - Overdiagnosis of regressive lesions
    1. It has to be done age appropriately
    2. Second Round Data

       POBASCAM, Swedescreen, ARTISTIC,NTCC
    3. Risk stratification to Avoid Unnecessary Colposcopies

       Reflex Cytology / HPV Genotyping / Moleculer Testings

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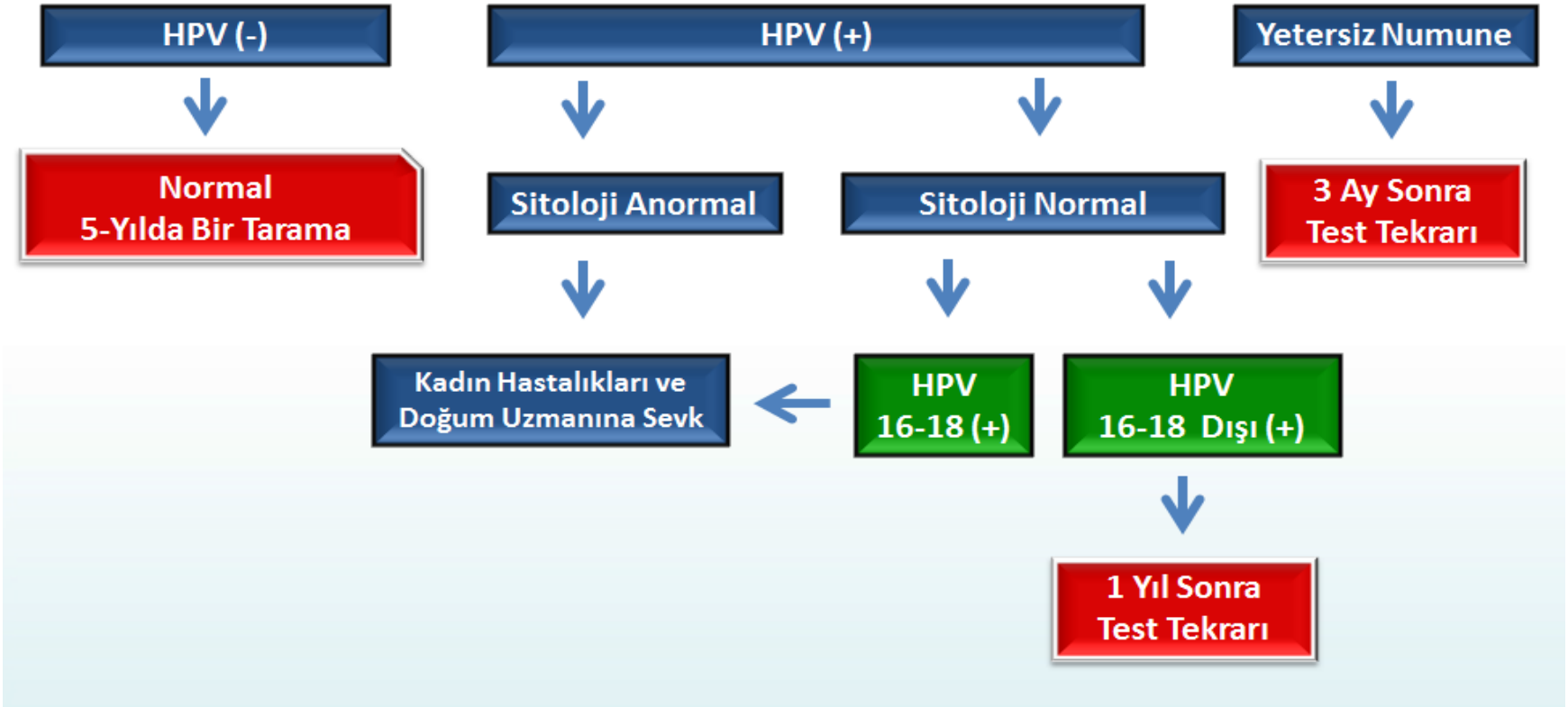
HPV Based Screening Programme-Turkey

“New screening Algorithm – Women between 30-64 years of age”



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Thank You for your attention!

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