

# Gynecopathology I.

Pathology of the vulva, vagina and uterus

Petr Škapa

Department of Pathology and Molecular Medicine  
Charles University, Second Faculty of Medicine, University Hospital Motol



# Tumors of the lower female genital tract

(vulva, vagina, uterine cervix)

# Lower Anogenital Tract

(Vulva, Vagina, Uterine Cervix, Anus, Penis)

squamous epithelium  
glandular epithelium

Human  
PapillomaVirus  
(HPV)

vulva  
vagina  
uterine cervix  
anus  
penis

other factors  
(p53 mutations)

vulva  
penis

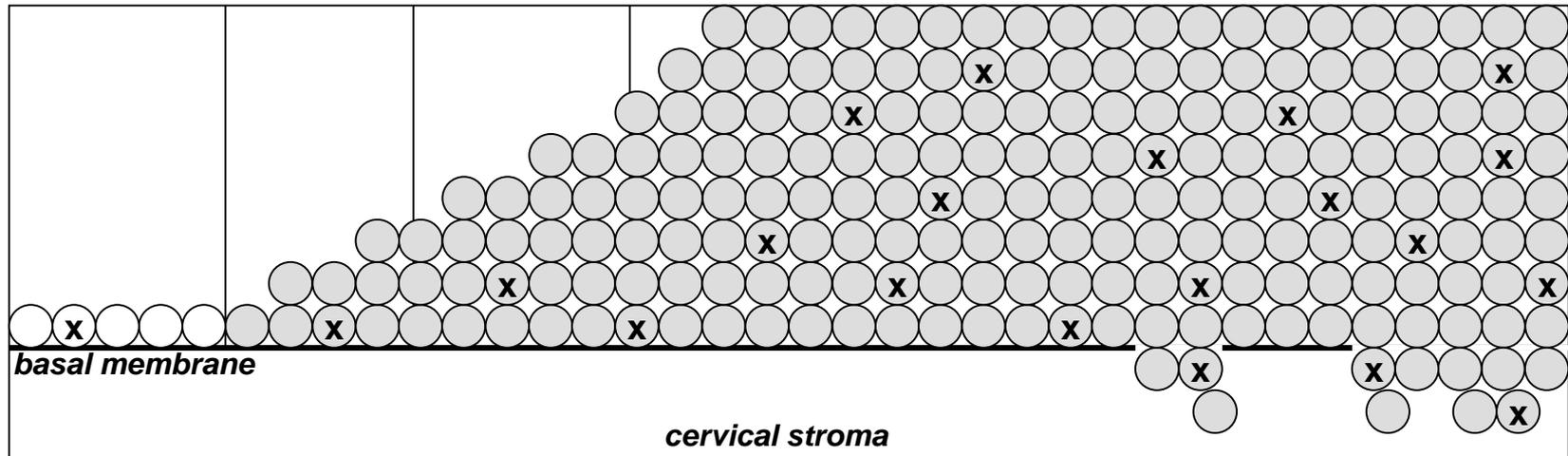
dysplastic (precancerous) lesions  
concept of „*Intraepithelial Neoplasia*“  
**CIN** (cervical) **VIN** (vulvar) **VaIN** (vaginal)  
**AIS** (adenocarcinoma in situ)  
**AIN** (anal) **PeIN** (penile)

**Squamous Cell Carcinoma (SCC)**  
Adenocarcinoma (ADC)

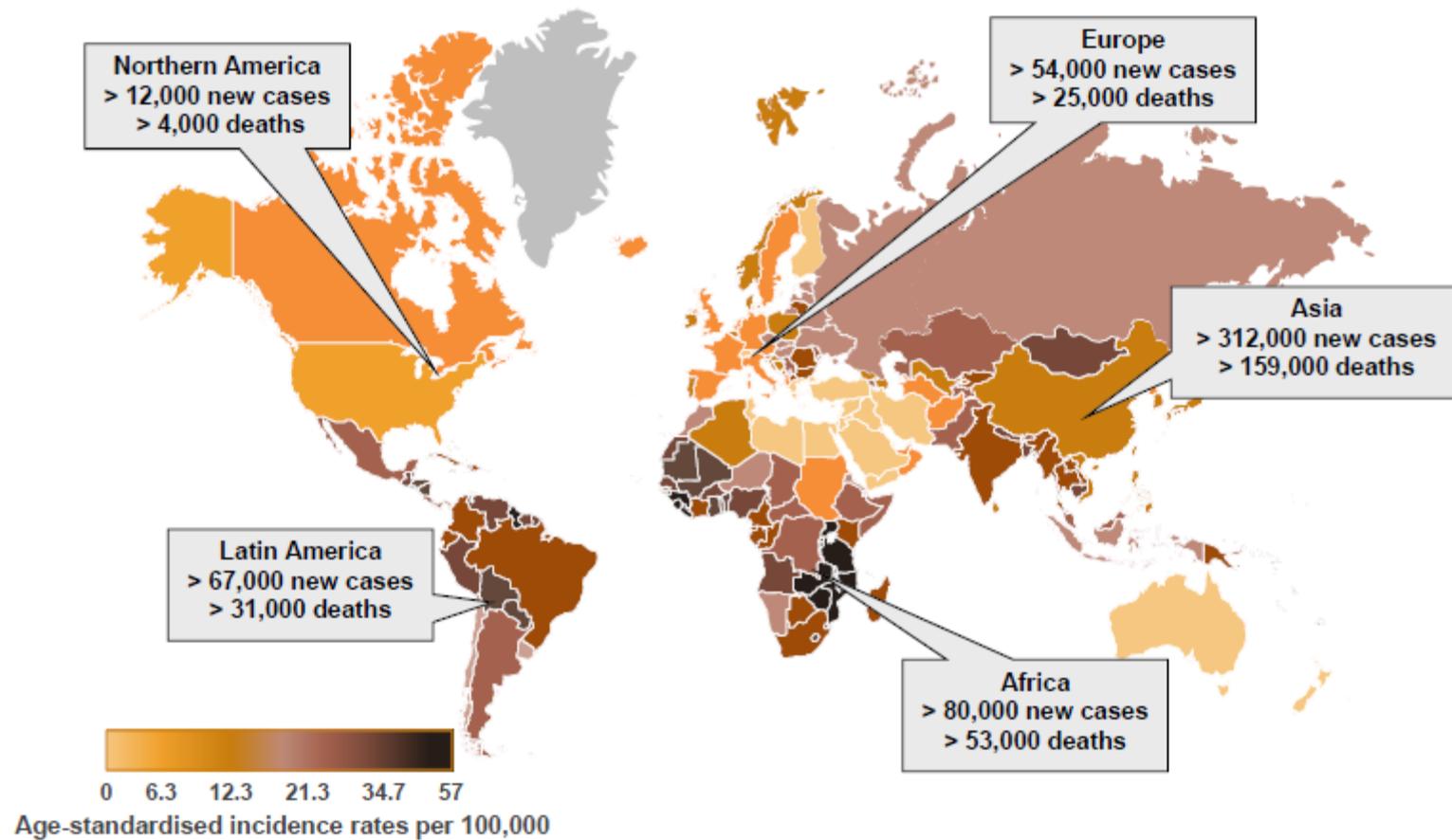
**Multicentric Lower Genital Tract Squamous Neoplasia**

# Classification of **anogenital** squamous precancerous lesions

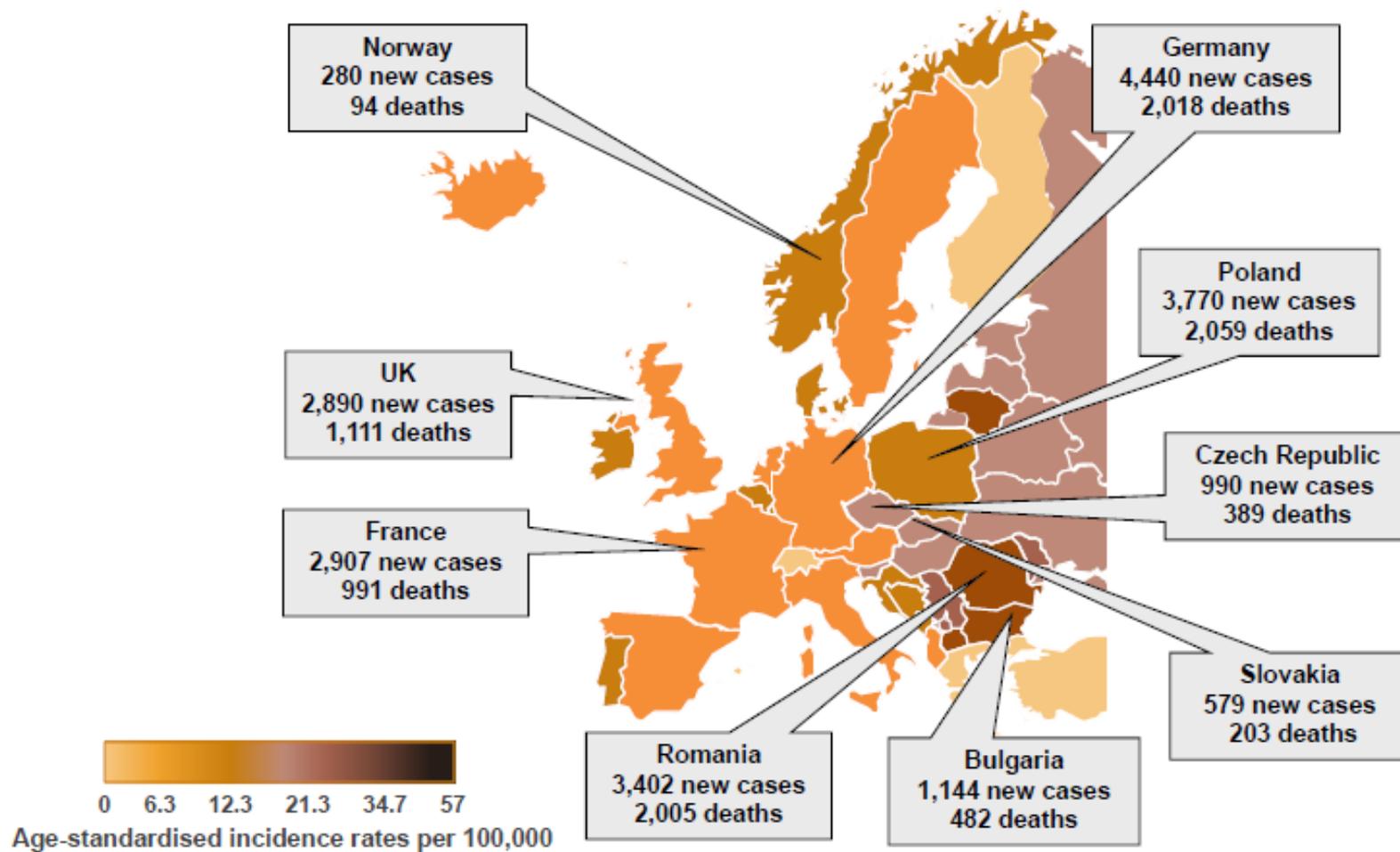
Normal squamous epithelium	Dysplasia			Carcinoma		
	<i>mild</i>	<i>moderate</i>	<i>severe</i>	<i>in situ</i>	<i>microinvasive</i>	<i>invasive</i>
	Intraepithelial Neoplasia					
	<i>-IN1</i>	<i>-IN2</i>	<i>-IN3</i>			
	Squamous Intraepithelial Lesion					
HPV	<i>LSIL</i>	<i>HSIL</i>				



# **Carcinoma of the Uterine Cervix**

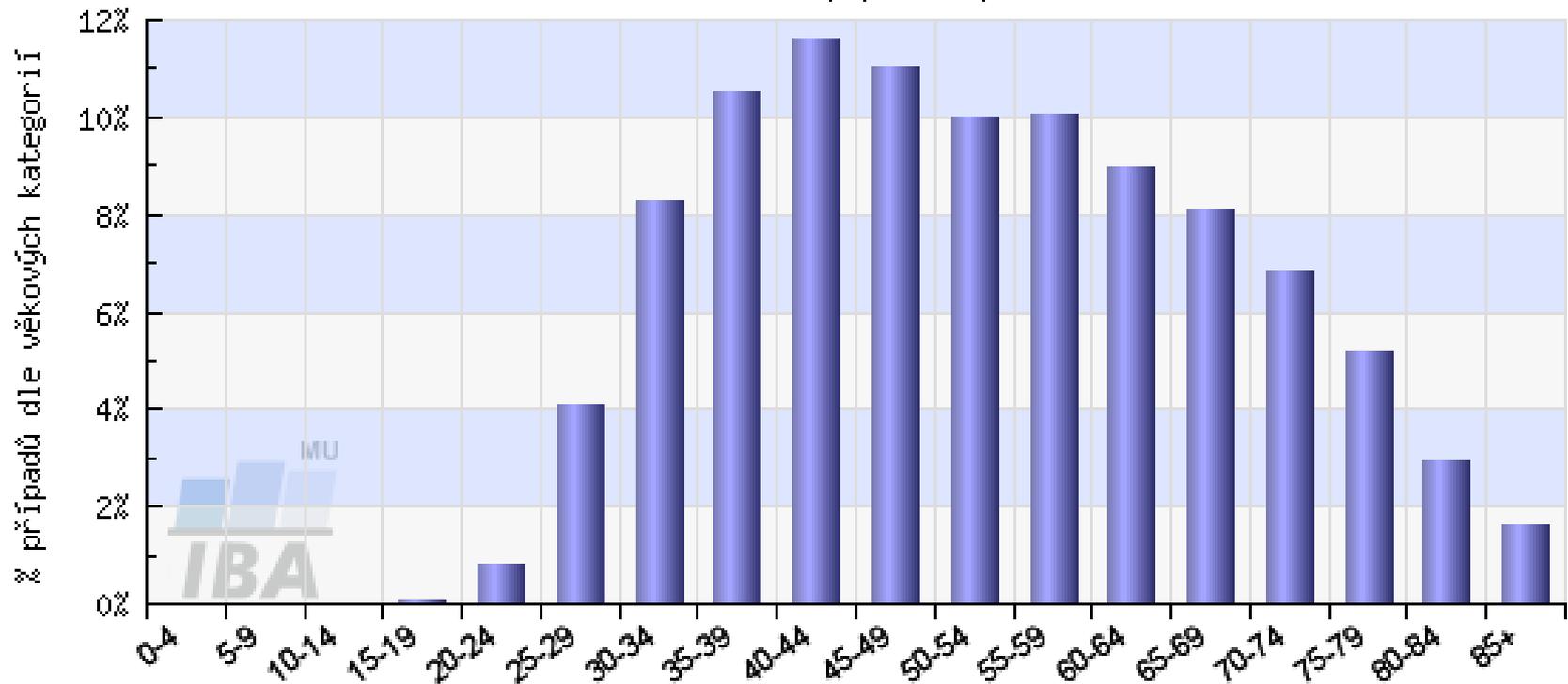


Ferlay J, et al. GLOBOCAN 2008 Cancer Incidence and Mortality Worldwide. IARC CancerBase; Lyon, 2010.



# Age distribution

**C53 - ZN hrdla děložního - cervicis uteri - Incidence, ženy**  
věková struktura populace pacientů



Analyzovaná data: N=37175

<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

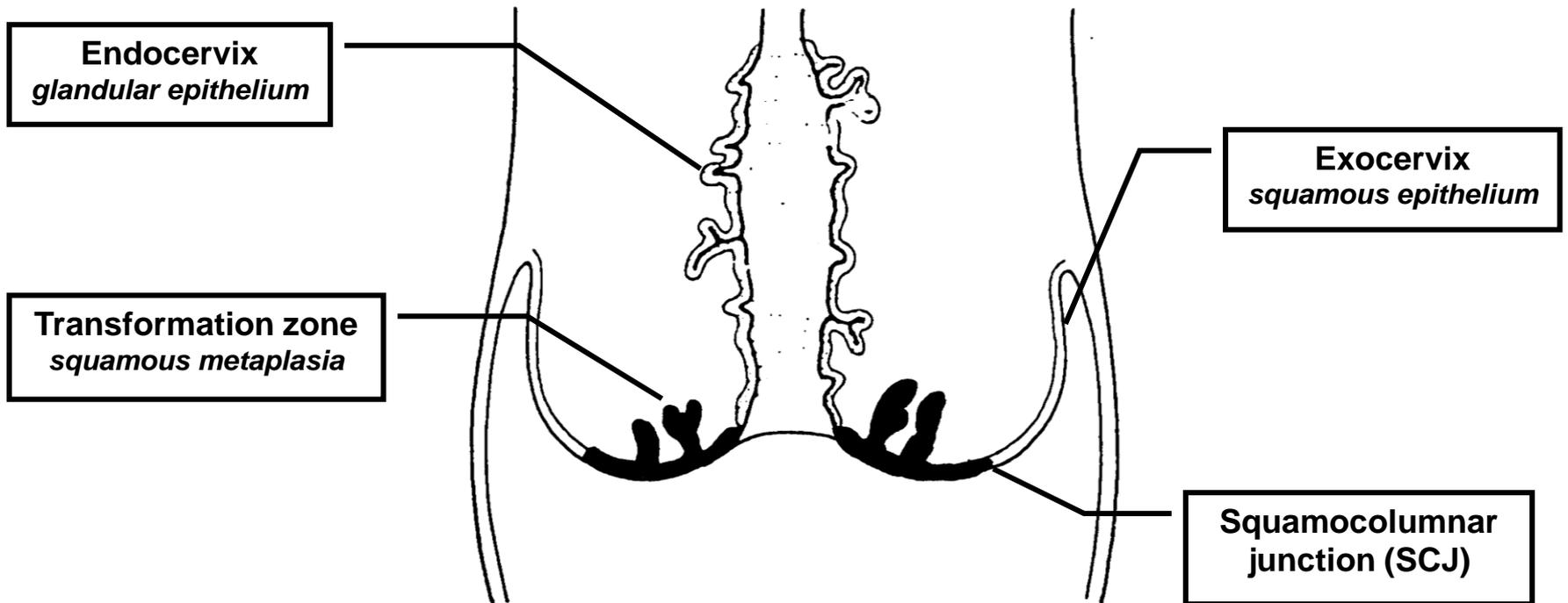
# Risk factors

- **HPV infection**
- **cigarette smoking**  
(immunosuppressive and carcinogenic effect)
- **immunosuppression**
- early age at first intercourse
- risk sexual partner
- multiple sexual partners
- other STDs (Chlamydia)
- individual susceptibility
- hormonal contraception  
**is not** a risk factor

*Correlation does not imply causation!*

# Uterine cervix

(morphology of the transformation zone)



# Precancerous lesions of the uterine cervix

(diagnostical methods)

## 1) morphological methods

- **cytology** (PAP smear) - screening
- **biopsy** (punch biopsy, cone excision – therapeutic effect)
- **colposcopy** (clinical method)

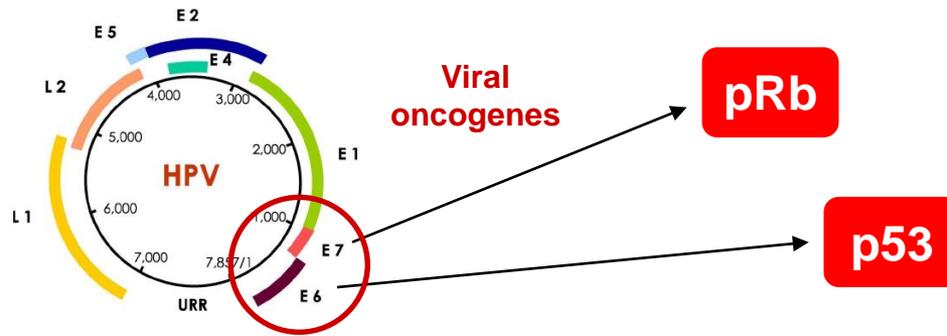
## 2) HPV testation (latent HPV infection)

- **hybridisation methods** – used in daily practice
- amplification methods (PCR) – epidemiological studies

## 3) serological methods (anamnestical antibodies – epidemiological studies)

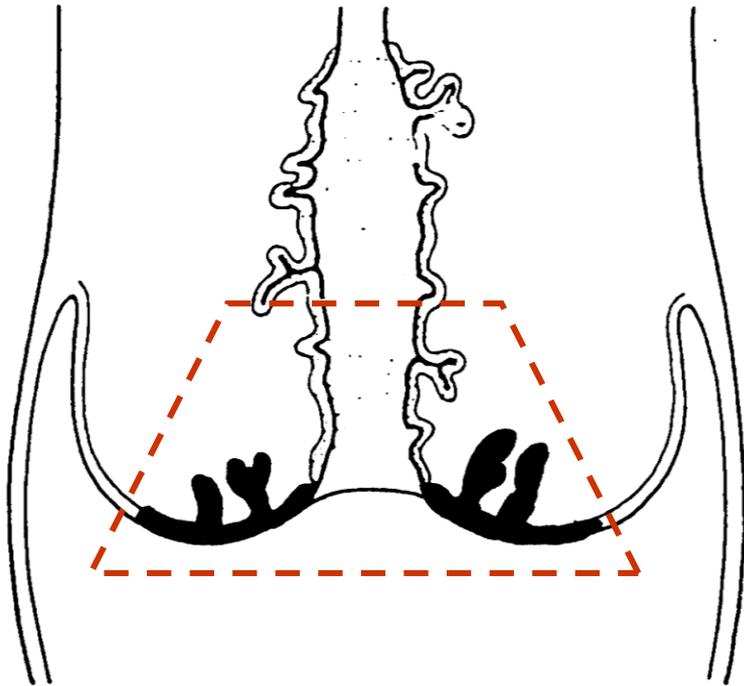
## 4) immunohistochemistry – possible, not used

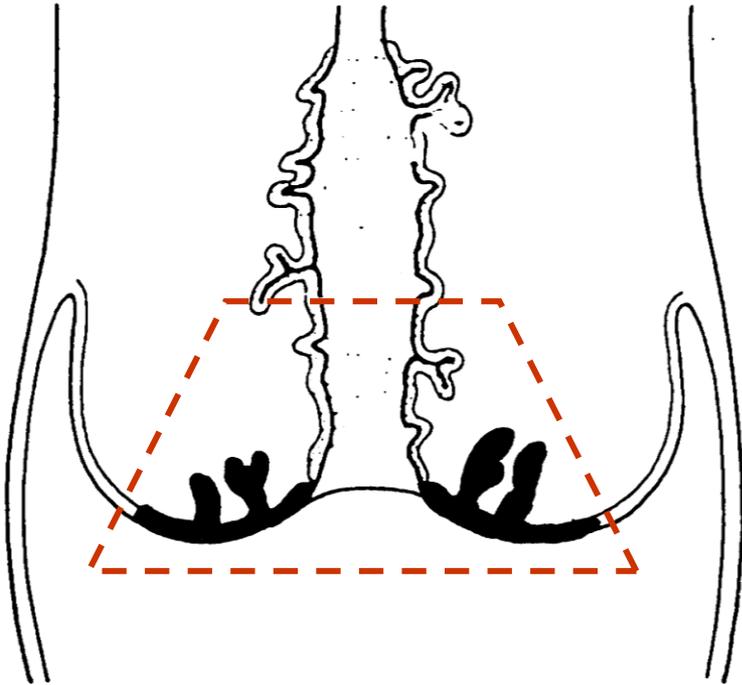
## 5) electron microscopy – possible, not used



# Conisation of the Uterine Cervix

(LEEP – Loop Electrosurgical Excision Procedure)





**3 surgical margins of the specimen:**

Endocervical

Exocervical

Lateral (radial, stromal)

# Carcinoma of the uterine cervix

- exophytic or endophytic growth, superficial ulceration
- destruction of uterine cervix, infiltration of parametria, uterine body, vaginal fornixes, wall of rectum and urinary bladder
- stenosis of ureter(s) – *hydronephrosis*
- necrosis, gangrene – *vesicovaginal and rectovaginal fistula*
- metastatic spread to the regional lymph nodes (pelvic LN)
- distant metastases in advanced stage
- TNM staging
- surgical treatment: *conservative* or *radical abdominal hysterectomy with bilateral adnexectomy and pelvic lymphadenectomy*

# Tumors of the Vagina

# Tumors of the Vagina

## 1) Squamous cell carcinoma

- the etiology and sequence of dysplastic changes is similar to the uterine cervix – **Vaginal Intraepithelial Neoplasia (HSIL)** (*ValN 1, 2, 3*)

## 2) Clear cell carcinoma

- precursor lesion: **vaginal adenosis** (glandular epithelium in vaginal squamous epithelium)
- vaginal adenosis develops as a sporadic congenital anomaly or affects daughters of women treated with **diethylstilbestrol (DES)** during the pregnancy – synthetic estrogen formerly used for the substitution of hormonal placentary dysfunction (for preservation of pregnancy)

## 3) Embryonal rhabdomyosarcoma (sarcoma botryoides)

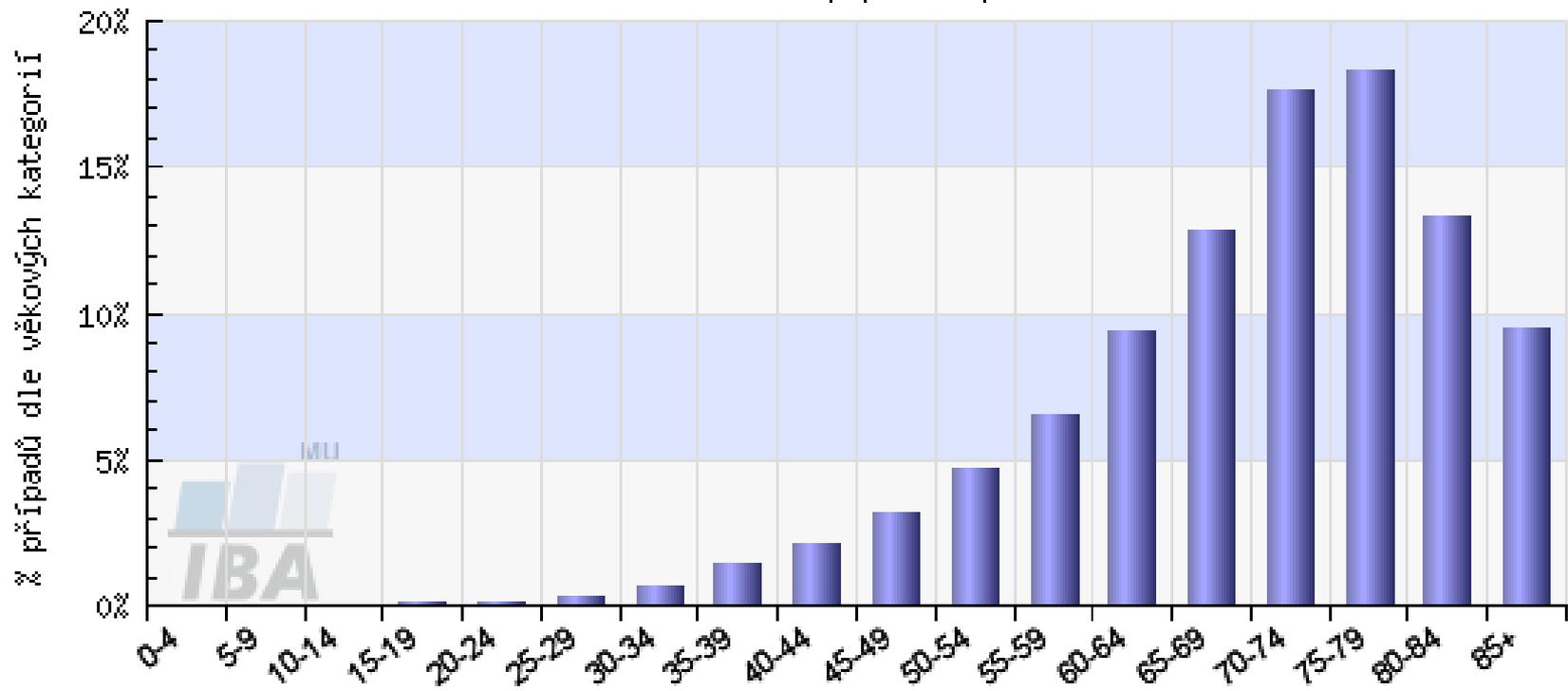
- disease of infancy and childhood (up to 5 years of age)

## 4) Melanoma

# **Squamous Cell Carcinoma of the Vulva**

# Age distribution

**C51 - ZN vulvy - Incidence, ženy**  
věková struktura populace pacientů

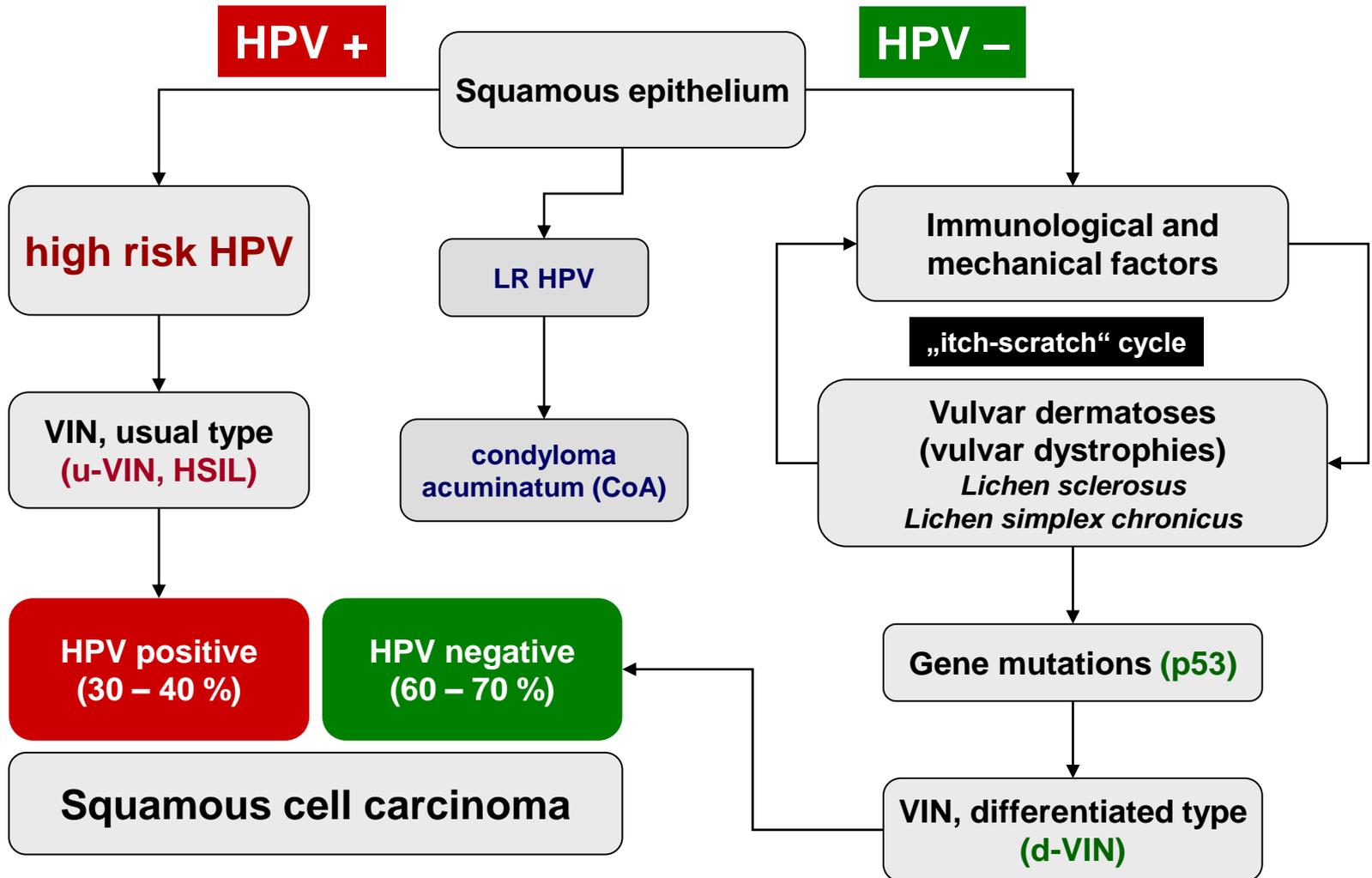


Analyzovaná data: N=5792

<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

# Etiopathogenesis



# VIN – clinicopathologic features

	<b>VIN, usual type (u-VIN, HSIL)</b>	<b>VIN, differentiated type (d-VIN)</b>
<b>Frequency</b>	> 80 %	< 20 %
<b>Age predilection</b>	premenopausal women	postmenopausal women
<b>Main etiological factor</b>	high risk HPV	gene mutations (p53)
<b>Other etiological factors</b>	cigarette smoking immunosuppression	vulvar dermatoses (LS, LSC)
<b>Multicentric lower genital tract squamous neoplasia (CIN, VaIN, AIN)</b>	frequent	infrequent
<b>History of condylomata acuminata and STDs</b>	frequent	infrequent
<b>Multifocality</b>	frequent	infrequent
<b>Invasive potential</b>	low	high
<b>Immunohistochemical marker</b>	p16 <sup>INK4a</sup>	p53
<b>Associated SCC</b>	Basaloid Warty	Well differentiated keratinizing

# Rare Tumors of the Vulva

- **extramammary Paget's disease**
  - perimenopausal and postmenopausal women
  - eczematous and erythematous lesions, pruritus

= intraepithelial spread of adenocarcinoma

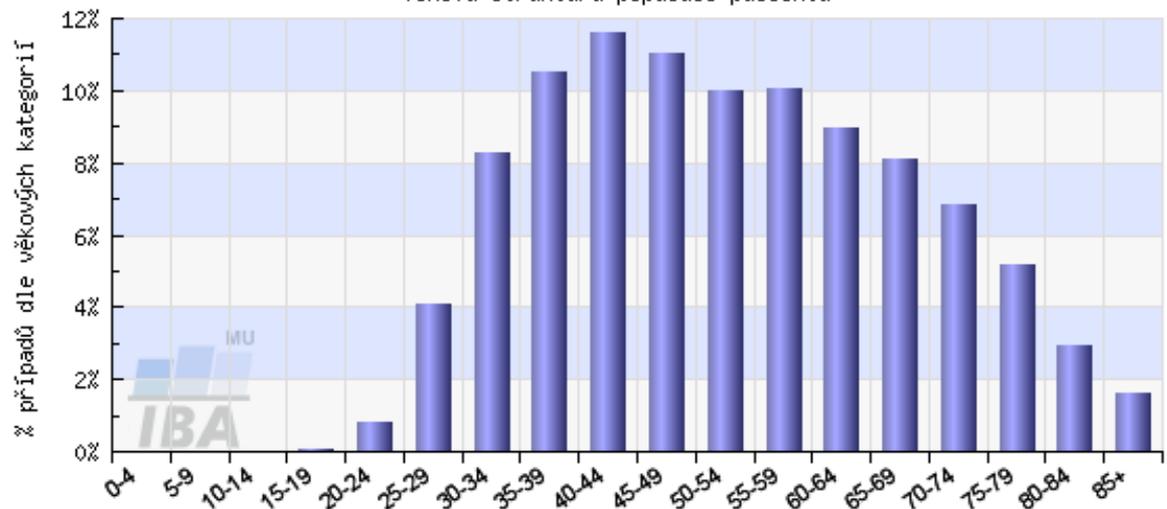
  1. from apocrine anogenital glands
  2. from adenocarcinoma of internal organs  
(*uterine cervix, colon, urinary bladder*)
  3. development *de novo* in the epidermis
  - *tumor cells = Paget's cells*
- **melanoma**

# **Tumors of the Uterine Body**

## **Endometrial Carcinoma**

### C53 - ZN hrdla děložního - cervicis uteri - Incidence, ženy

věková struktura populace pacientů



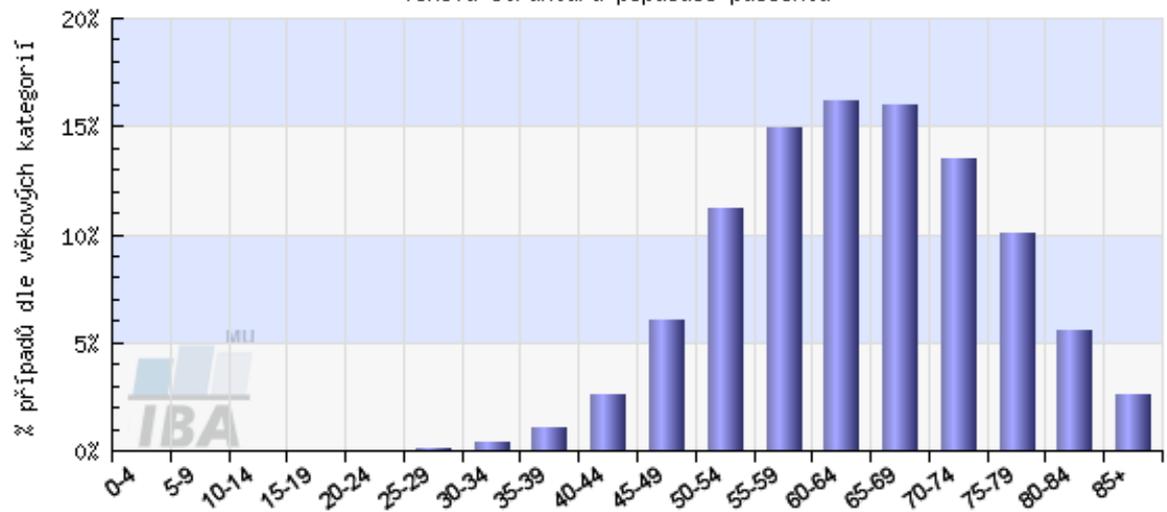
Analýzovaná data: N=37175

<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

### C54 - ZN těla děložního - Incidence, ženy

věková struktura populace pacientů

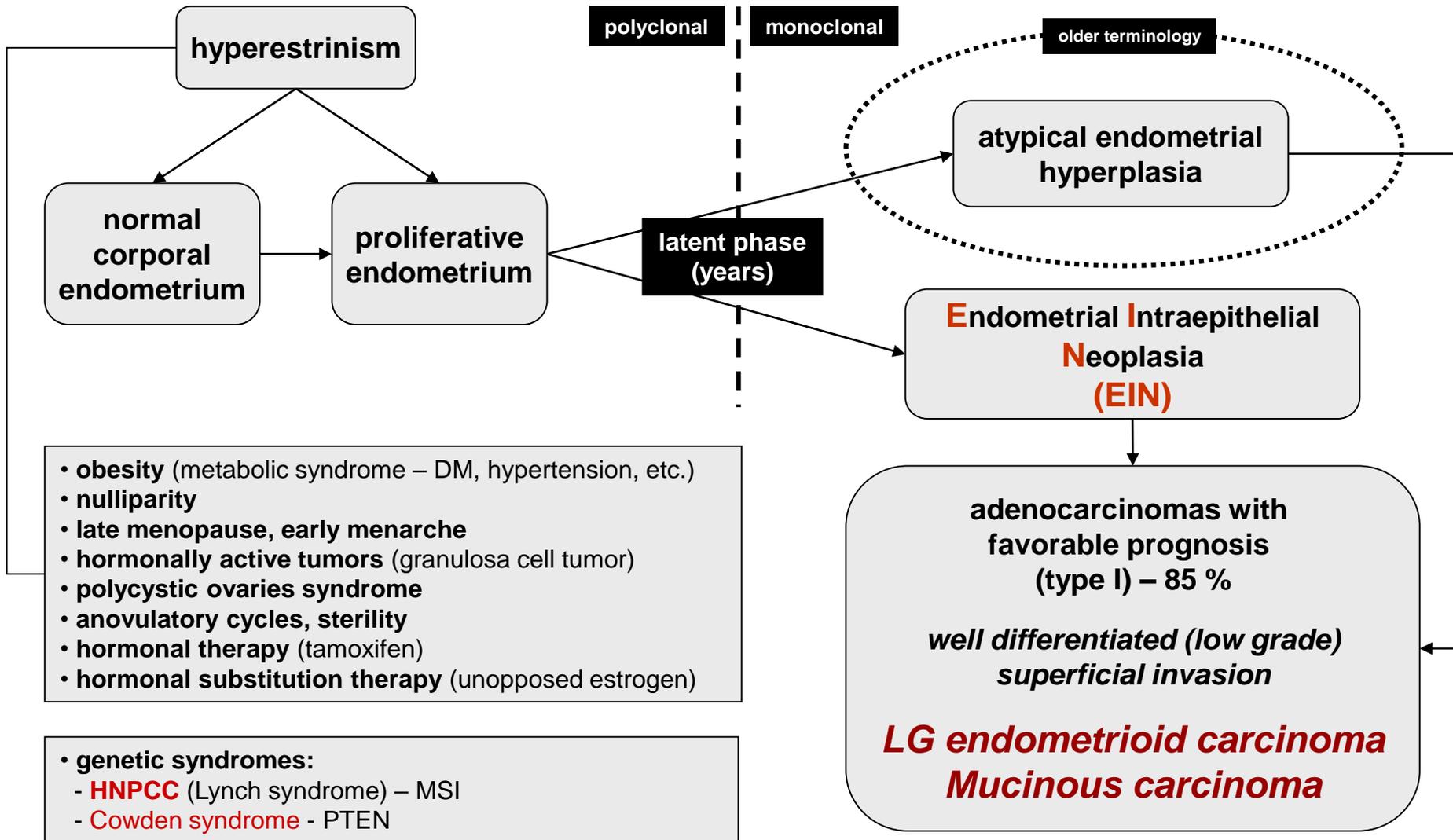


Analýzovaná data: N=51235

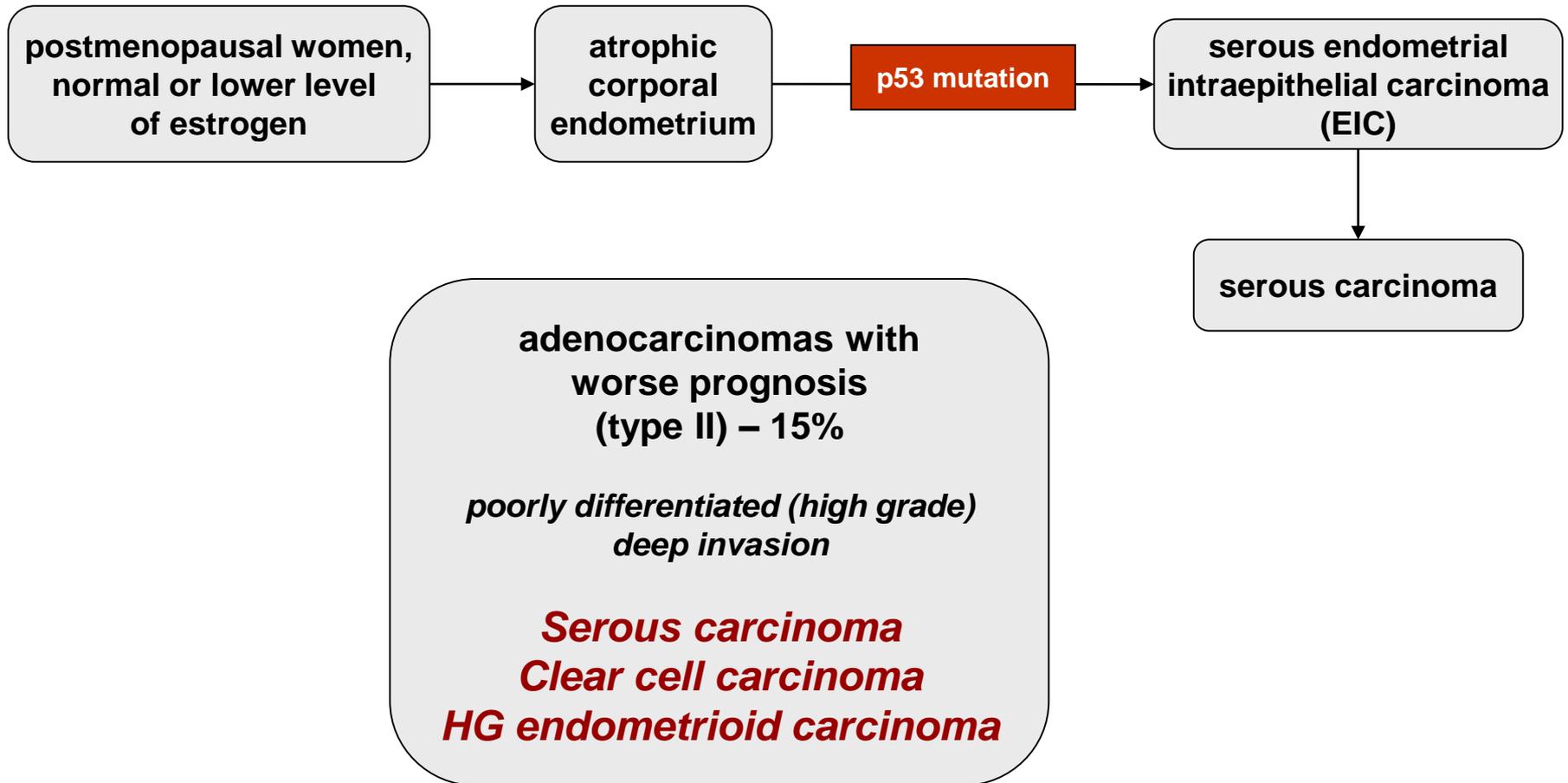
<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

# Endometrial Carcinoma - Type I

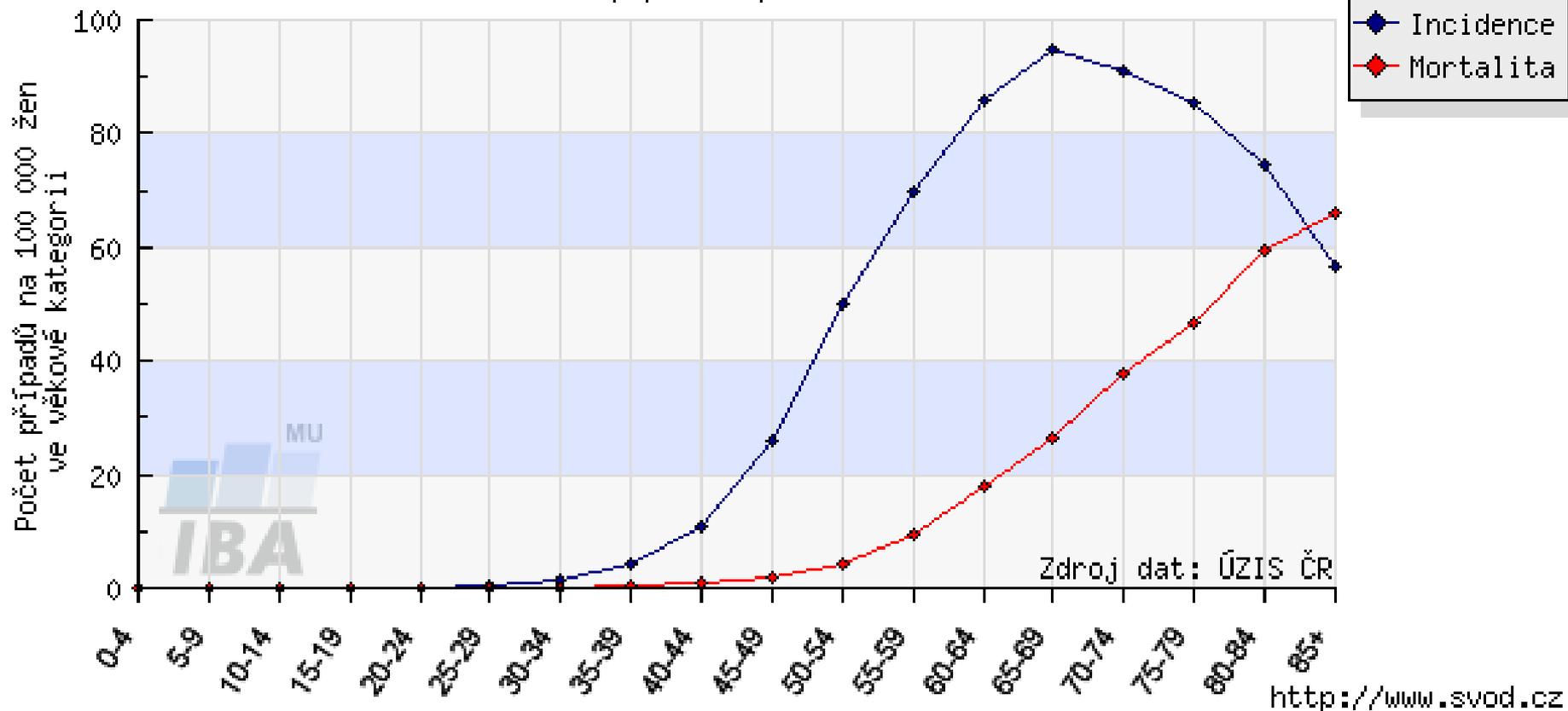


# Endometrial Carcinoma - Type II



## C54 - ZN těla děložního, ženy

věková struktura pacientů za období 1977 - 2012



Type I carcinomas

Type 2 carcinomas

# Endometrial Carcinoma

- typical clinical symptoms:
  - ***postmenopausal bleeding***
  - *irregular bleeding during the menstrual cycle*
- protective factors:
  - *hormonal contraception*
- macroscopically diffuse or intraluminal polypoid growth
- late hematogenous and lymphatic spread
- prognostic factors:
  - *depth of myometrial invasion*
  - *grade (1-3)*  
*(not applicable to serous and clear cell carcinomas – always grade 3)*
  - *focal squamous differentiation does not influence prognosis*

# **Tumors of the Uterine Body**

## **Smooth Muscle Tumors**

# Leiomyoma vs. Leiomyosarcoma

	Leiomyoma	Leiomyosarcoma
<b>Biological behavior</b>	benign	malignant
<b>Multiple nodules</b>	+++	-
<b>Size</b>	various	large
<b>Margins</b>	distinct	poorly defined
<b>„Acute“ regressive changes (necrosis, haemorrhage, edema)</b>	+	+++
<b>„Chronic“ regressive changes (fibrosis, hyalinization, calcification)</b>	+++	-
<b>Mitotic activity</b>	+/-	+++
<b>Postmenopausal growth</b>	+	+++

# Leiomyoma vs. Leiomyosarcoma

- Mitotic activity
- Cytologic atypia
- Coagulation type necrosis

Leiomyoma variants	Mitotically active leiomyoma
	(Highly) cellular leiomyoma
	Atypical (bizarre) leiomyoma

**Smooth muscle tumor of uncertain malignant potential  
(STUMP)**

# Leiomyoma

- **intramural**
- **submucosal** (event. pedunculated)
- **subserosal** (event. pedunculated)

# **Tumors of the Uterine Body**

## **Endometrial Stromal Tumors**

# Endometrial Stromal Tumors

- mesenchymal tumors resembling endometrial stroma

## ***Endometrial stromal nodule***

- benign, well circumscribed

## ***Endometrial stromal sarcoma, low grade***

- poorly defined margins (infiltrative growth), angioinvasion, mild cellular atypia and mitotic activity
- favorable prognosis, local recurrences

## ***Endometrial stromal sarcoma, high grade***

- cytologic atypia and mitotic activity

## ***Undifferentiated uterine sarcoma***

- highly malignant, poor prognosis

# **Tumors of the Uterine Body**

## **Mixed Epithelial and Mesenchymal Tumors**

# Carcinosarcoma

(Malignant Mixed Müllerian Tumor, MMMT)

- not a true mixed tumor, but a **metaplastic high grade carcinoma**
- **homologous tumors** – mesenchymal-like component resembling primary uterine sarcomas (leiomyosarcoma, high grade endometrial stromal sarcoma, undifferentiated uterine sarcoma)  
**heterologous tumors** – mesenchymal-like component resembling chondrosarcoma, rhabdomyosarcoma, liposarcoma or osteosarcoma
- postmenopausal age - bleeding
- poor prognosis

Petr Škapa, MD, PhD

Department of Pathology and Molecular Medicine  
Charles University, Second Faculty of Medicine, University Hospital Motol  
V Úvalu 84  
150 06 Prague 5

Tel.: 224 435 623

Email: [petr.skapa@lfmotol.cuni.cz](mailto:petr.skapa@lfmotol.cuni.cz)

