





Permanent effects of tobacco exposure on urologic cancers

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Urology Research Center

Tehran, Iran, Nov.2015.

Plan

Urologic cancers

Bladder cancer

Prostate cancer

Kidney cancer

Testicular cancer

Tobacco effects

Gene involvement

Bladder cancer

Epidemiology

- ❖ *World's ninth most common tumor*
 - Men: seventh most common cancer*
 - Women: seventeenth most common cancer*
 - Iran: fifth most common cancer in male*
- ❖ *382,700 new cases diagnosed in 2012*
- ❖ *Four times as common in men as in women*
- ❖ *Worldwide age standardized incidence rate*
 - Men: 10.1/100,000*
 - Women: 2.5/100,000*
- ❖ *Iran age standardized incidence rate:*
 - Men: 12.59/100,000*
 - Women: 3.28/100,000*

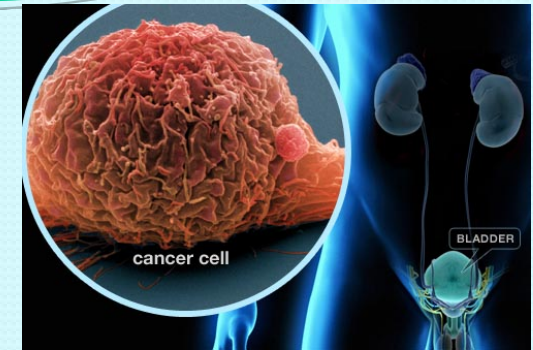


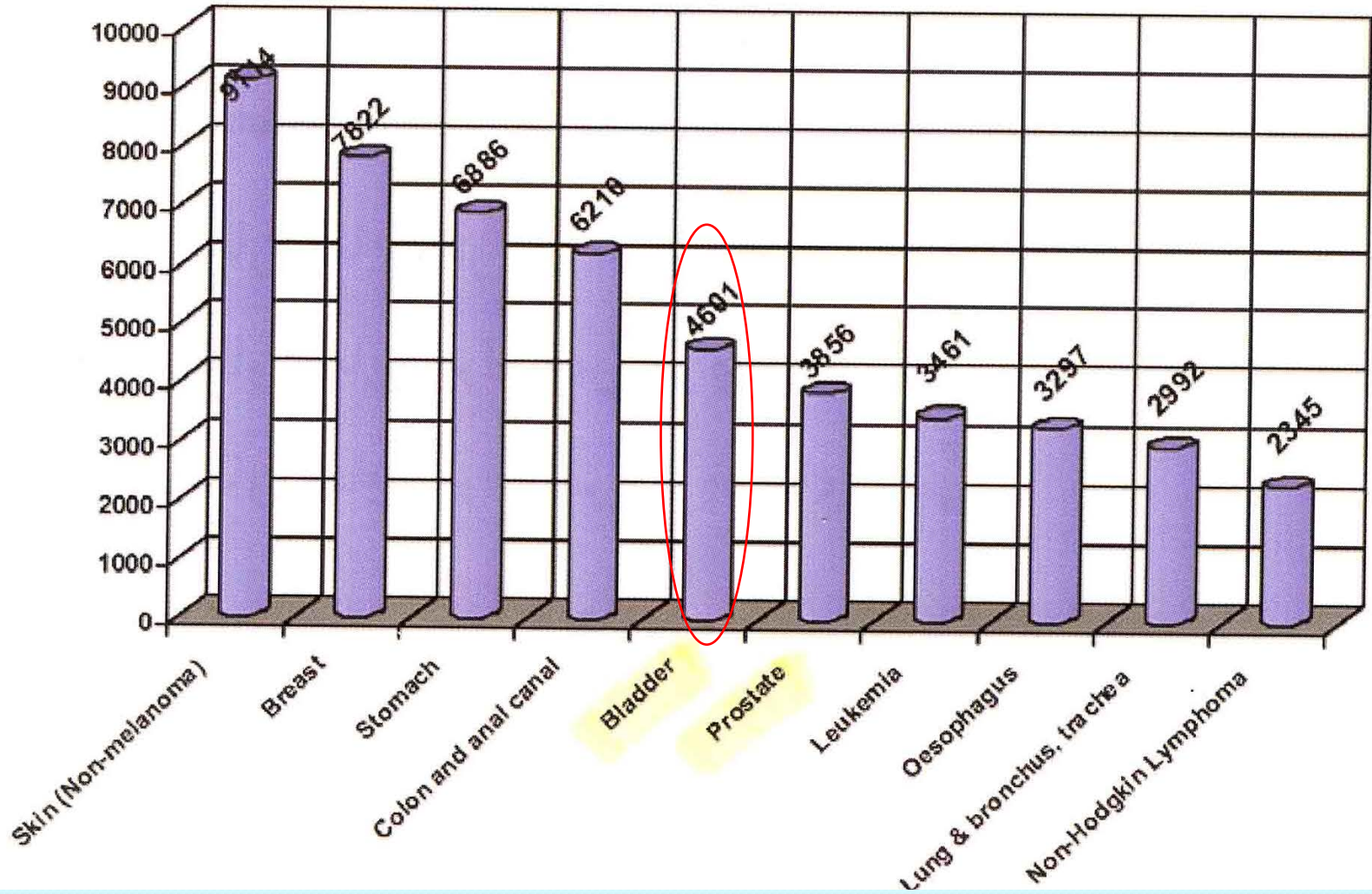
Table of Age specific rates and ASR of recorded malignancies based on ICD-10 classification in IRAN (1388) in Female population

| Topography Based on ICD 10 | Age specific rates in Age Groups | | | | | | | | | | | | | | | | | | N | Crude Rate | ASR (+/-se) | | |
|--|----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------------|-------------|------|---------|
| | 00-04 | 05-09 | 10-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ | | | | | Unknown |
| C58 Malignant neoplasm of placenta | 0.00 | 0.00 | 0.00 | 0.09 | 0.16 | 0.14 | 0.07 | 0.08 | 0.05 | 0.06 | 0.10 | 0.00 | 0.00 | 0.00 | 0.19 | 0.00 | 0.00 | 0.00 | 0.00 | 25 | 0.07 | 0.06 | 0.01 |
| Malignant neoplasms of urinary tract | 1.06 | 0.45 | 0.03 | 0.11 | 0.29 | 0.67 | 1.23 | 1.42 | 3.06 | 5.25 | 13.73 | 15.67 | 19.70 | 24.22 | 32.05 | 48.25 | 61.35 | 34.64 | 0.00 | 1360 | 3.96 | 5.35 | 0.15 |
| C64 Malignant neoplasm of kidney, except renal pelvis | 0.99 | 0.41 | 0.00 | 0.11 | 0.09 | 0.31 | 0.78 | 0.63 | 2.01 | 2.56 | 6.03 | 7.21 | 6.84 | 7.02 | 6.99 | 10.34 | 6.25 | 3.76 | 0.00 | 488 | 1.42 | 1.93 | 0.09 |
| C65 Malignant neoplasm of renal pelvis | 0.04 | 0.00 | 0.00 | 0.00 | 0.00 | 0.03 | 0.04 | 0.04 | 0.00 | 0.06 | 0.20 | 0.10 | 0.41 | 0.18 | 0.39 | 0.94 | 1.70 | 0.00 | 0.00 | 20 | 0.06 | 0.08 | 0.02 |
| C66 Malignant neoplasm of ureter | 0.00 | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.20 | 0.00 | 0.00 | 0.35 | 0.78 | 0.31 | 0.00 | 0.00 | 0.00 | 10 | 0.03 | 0.04 | 0.01 |
| C67 Malignant neoplasm of bladder | 0.04 | 0.04 | 0.03 | 0.00 | 0.18 | 0.34 | 0.41 | 0.75 | 1.06 | 2.62 | 7.21 | 8.25 | 12.18 | 16.68 | 23.89 | 36.35 | 53.39 | 30.87 | 0.00 | 637 | 2.44 | 3.28 | 0.12 |
| C68 Malignant neoplasm of other and unspecified urinary organs | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.10 | 0.10 | 0.27 | 0.00 | 0.00 | 0.31 | 0.00 | 0.00 | 0.00 | 5 | 0.01 | 0.02 | 0.01 |

Table of Age specific rates and ASR of recorded malignancies based on ICD-10 classification in IRAN (1388) in Male population

| Topography Based on ICD 10 | Age specific rates in Age Groups | | | | | | | | | | | | | | | | | | N | Crude Rate | ASR (+/-se) | | |
|--|----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|--------|--------|------|------------|-------------|-------|---------|
| | 00-04 | 05-09 | 10-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ | | | | | Unknown |
| C65 Malignant neoplasm of renal pelvis | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.06 | 0.07 | 0.22 | 0.31 | 0.53 | 0.59 | 0.62 | 1.47 | 1.52 | 0.72 | 0.00 | 1.97 | 0.00 | 60 | 0.15 | 0.21 | 0.03 |
| C66 Malignant neoplasm of ureter | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.49 | 1.23 | 1.32 | 0.30 | 0.48 | 2.48 | 0.00 | 0.00 | 33 | 0.08 | 0.13 | 0.02 |
| C67 Malignant neoplasm of bladder | 0.03 | 0.06 | 0.03 | 0.08 | 0.32 | 0.59 | 1.25 | 2.29 | 4.87 | 10.07 | 22.53 | 42.54 | 52.21 | 70.39 | 84.04 | 123.04 | 182.38 | 107.08 | 0.00 | 376 | 9.57 | 12.59 | 0.21 |
| C68 Malignant neoplasm of other and unspecified urinary organs | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.02 | 0.03 | 0.11 | 0.04 | 0.20 | 0.20 | 0.10 | 0.74 | 1.91 | 3.20 | 3.84 | 6.94 | 0.00 | 0.00 | 84 | 0.21 | 0.26 | 0.03 |

نمودار ۱: نمودار ده سرطان شایع در کل کشور بر اساس مجموع زنان و مردان در سال ۱۳۸۸



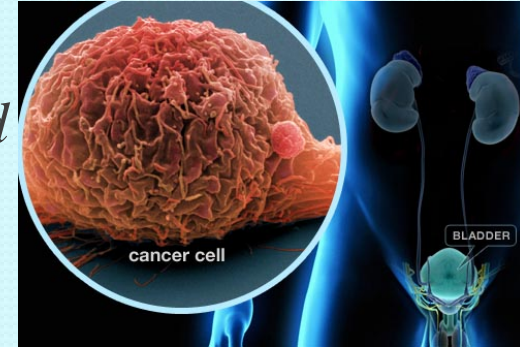
10 most common malignancies in IRAN,(1388)

| | | |
|----------------------------|-------|-------|
| 1 Skin (Non-melanoma) | 9114 | 12.3% |
| 2 Breast | 7822 | 10.6% |
| 3 Stomach | 6886 | 9.3% |
| 4 Colon and anal canal | 6210 | 8.4% |
| 5 Bladder | 4601 | 6.2% |
| 6 Prostate | 3856 | 5.2% |
| 7 Leukemia | 3461 | 4.7% |
| 8 Oesophagus | 3297 | 4.5% |
| 9 Lung & bronchus, trachea | 2992 | 4.0% |
| 10 Non-Hodgkin Lymphoma | 2345 | 3.2% |
| Others | 23483 | 31.7% |
| Total | 74067 | |

Bladder cancer

Epidemiology

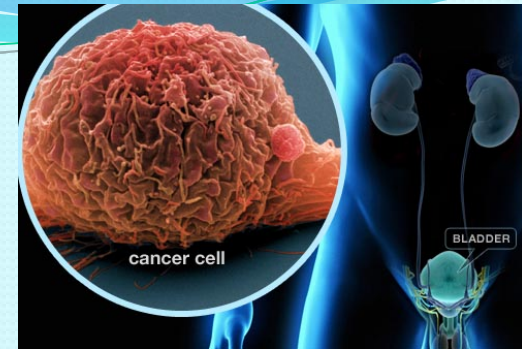
- ❖ *About 80% of patients are between the ages of 50 and 80 years*
- ❖ *Three to four times higher in developed countries*
- ❖ *Age-standardized incidence rate*
 - World: 5.3/100,000*
 - More developed: 9.5/100,000*
 - Less developed: 3.3/100,000*
- ❖ *The highest incidence: Northern America and Europe*
- ❖ *Lowest incidence: Asia, Latin America*
- ❖ *Mortality is strongly related to age*
 - Males: 4/100,000*
 - Females: 1.1/100,000*



Bladder cancer

Risk factor

- *Age*
- *Environmental factors: tobacco use, infectious diseases.*
- *Occupational carcinogens*
- *Radiation*
- *Family history of cancer (Genetic susceptibility)*
- *Alcohol*
- *Chemicals and other substance*



Prostate cancer

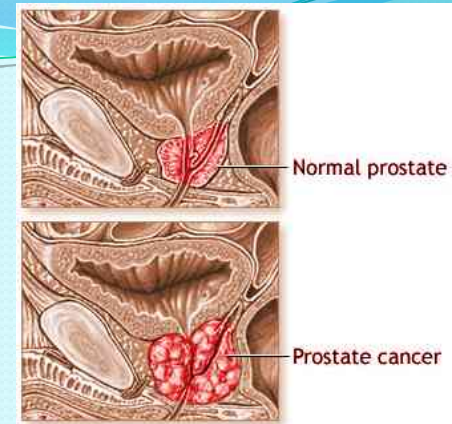
Epidemiology

- ❖ *Second most common cancer of GU*
- ❖ *Iran: third most common cancer in male*
- ❖ *Fifth most common cause of cancer death*
- ❖ *1.11 million new cases diagnosed in 2012*
- ❖ *Rarely diagnosed in men <50*
- ❖ *Highest incidence: Oceania and Northern America*
- ❖ *Lowest incidence: Asia and Africa*
- ❖ *Age-Standardized incidence rate*

World: 31.1/ 100,000

More Developed: 69.5/100,000

Less Developed: 14.5 / 100,000



Prostate cancer

Epidemiology

❖ Iran:

Age standardized incidence rates: 12.59/100,000

Total number of known cases (2008): 3856

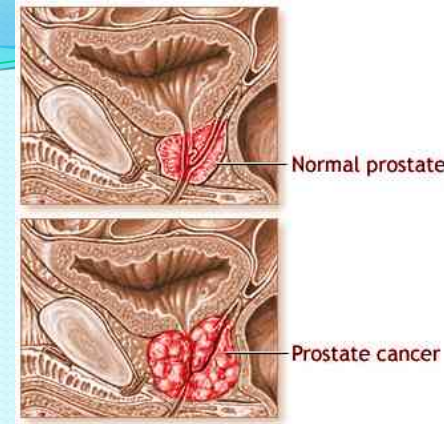
Highest relative risk: fars

❖ *The second most common cause of cancer death in UK men, after lung cancer*

❖ *Worldwide, more than 307,000 men were estimated to have died from prostate cancer in 2012*

27,244 men in the United States

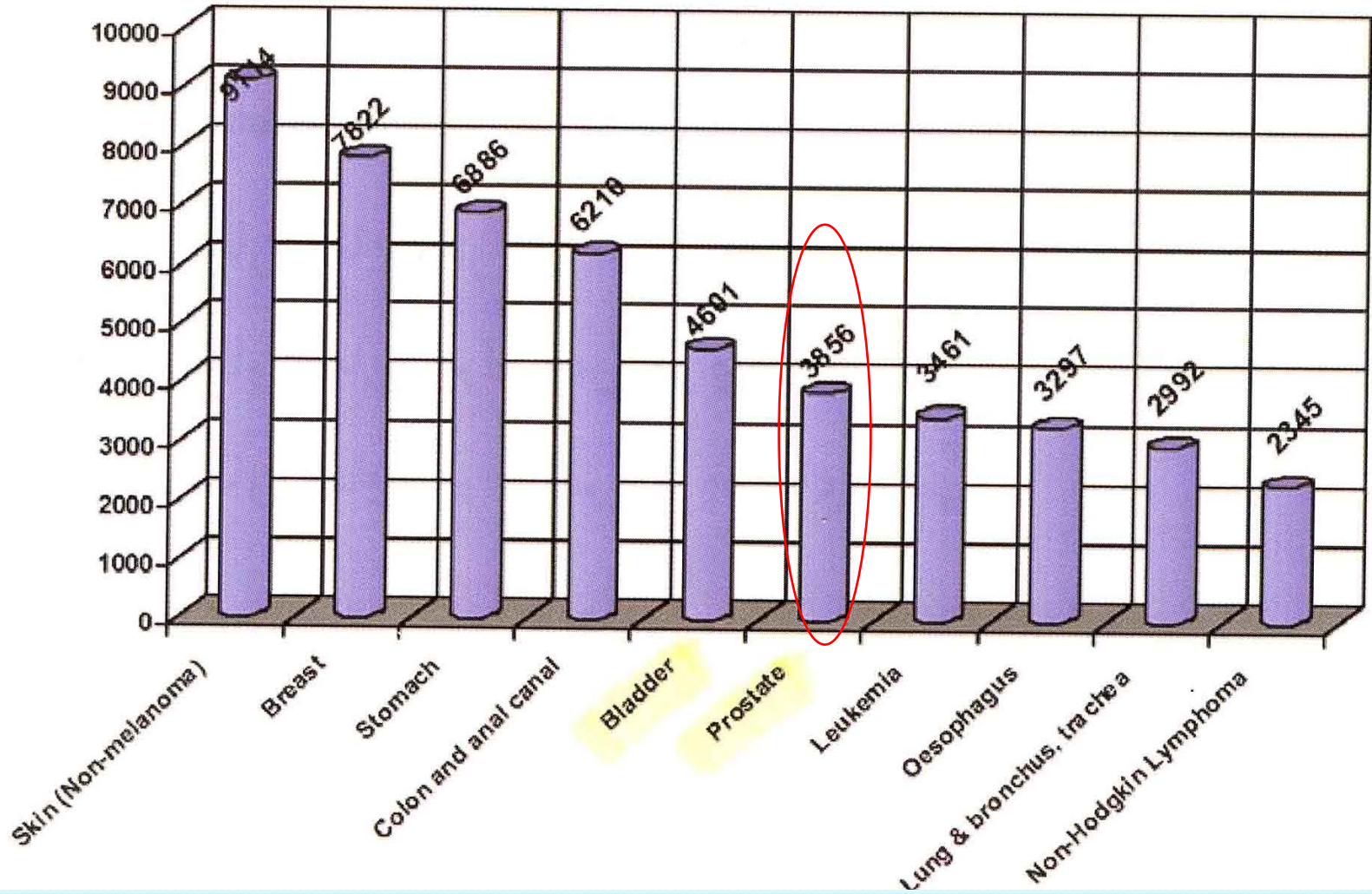
❖ *In the 1970s, a quarter of men diagnosed with prostate cancer survived their disease beyond ten years, now it's more than 8 in 10*



10 most common malignancies in IRAN,(1388)

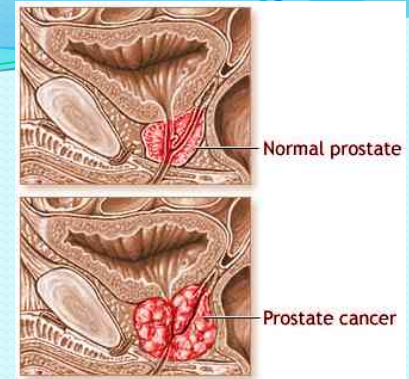
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Prostate cancer

Risk factor



- *Environmental factors: **tobacco** use, diet.*
- *Radiation*
- *Family history of cancer (Genetic susceptibility)*
- *Alcohol*
- *Obesity*

Kidney cancer

Epidemiology

❖ *13th most common malignancy*

Men: seventh most common cancer

Women: tenth most common cancer

❖ *338,000 new cases diagnosed in 2012*

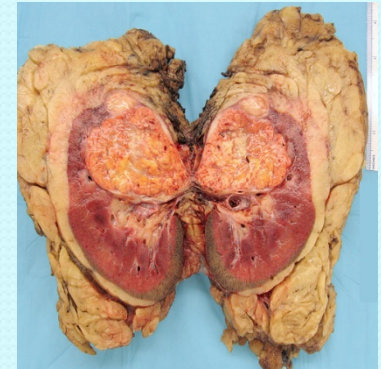
❖ *Renal cell carcinoma is the most predominant form*

❖ *Arising from proximal tubular epithelium*

❖ *Twice as common in men as in women*

❖ *Highest incidence: Northern America and Europe*

❖ *Lowest incidence: Africa and Asia*



Kidney cancer

Epidemiology

- ❖ *Age-Standardized incidence rate*

 - World: 4.4/ 100,000*

 - More Developed: 9.2/100,000*

 - Less Developed: 2.6 / 100,000*

- ❖ *Occurs most commonly in the fourth to sixth decades of life*

- ❖ *The 16th most common cause of cancer death*

 - Mortality rate: 40%*

- ❖ *Iran: age-Standardized incidence rate*

 - Men: 2.65/100,000*

 - Women: 1.93/100,000*

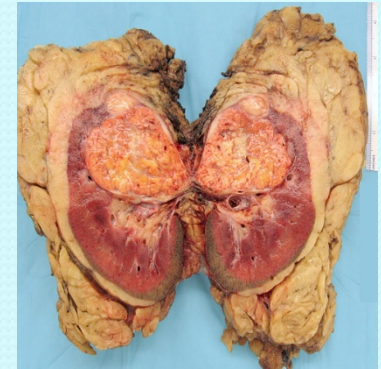


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| C58 Malignant neoplasm of placenta | 0.00 | 0.00 | 0.00 | 0.09 | 0.16 | 0.14 | 0.07 | 0.08 | 0.05 | 0.06 | 0.10 | 0.00 | 0.00 | 0.00 | 0.19 | 0.00 | 0.00 | 0.00 | 0.00 | 25 | 0.07 | 0.06 | 0.01 |
| Malignant neoplasms of urinary tract | 1.06 | 0.45 | 0.03 | 0.11 | 0.29 | 0.67 | 1.23 | 1.42 | 3.06 | 5.25 | 13.73 | 15.67 | 19.70 | 24.22 | 32.05 | 48.25 | 61.35 | 34.64 | 0.00 | 1360 | 3.06 | 5.35 | 0.15 |
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| C66 Malignant neoplasm of ureter | 0.00 | 0.00 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.20 | 0.00 | 0.00 | 0.35 | 0.78 | 0.31 | 0.00 | 0.00 | 0.00 | 10 | 0.03 | 0.04 | 0.01 |
| C67 Malignant neoplasm of bladder | 0.04 | 0.04 | 0.03 | 0.00 | 0.18 | 0.34 | 0.41 | 0.75 | 1.06 | 2.62 | 7.21 | 8.25 | 12.18 | 16.68 | 23.89 | 36.35 | 53.39 | 30.87 | 0.00 | 837 | 2.44 | 3.28 | 0.12 |
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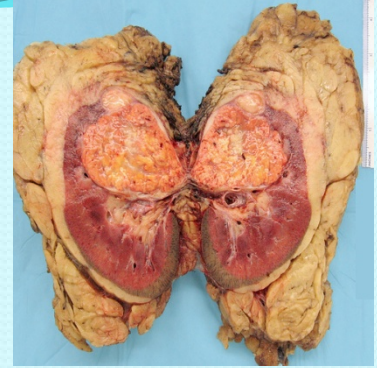
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| Malignant neoplasms of urinary tract | 1.11 | 0.39 | 0.11 | 0.08 | 0.44 | 0.81 | 1.90 | 3.41 | 7.54 | 14.19 | 30.17 | 52.63 | 67.63 | 86.71 | 99.87 | 139.59 | 207.16 | 114.97 | 0.00 | 4717 | 11.99 | 15.84 | 0.24 |
| C64 Malignant neoplasm of kidney, except renal pelvis | 1.07 | 0.32 | 0.08 | 0.00 | 0.12 | 0.20 | 0.55 | 0.94 | 2.41 | 3.61 | 6.92 | 8.90 | 12.84 | 11.61 | 10.81 | 11.51 | 15.36 | 5.91 | 0.00 | 176 | 1.97 | 2.65 | 0.10 |

Kidney cancer

Risk factor

- *Tobacco use.*
- *Radiation*
- *Family history of cancer (Genetic susceptibility)*
- *Obesity*
- *Occupational exposure to petroleum products, heavy metals, solvents, or asbestos*
- *HTN*
- *Von Hippel-Lindau syndrome*
- *Tuberous sclerosis*



Testicular cancer

Epidemiology

- ❖ *1% to 2% of cancers among men*
- ❖ *The most common malignancy among men aged 20 to 40 years*
- ❖ *99% of all Testicular Tumors are malignant.*
- ❖ *Highest rates: white Caucasian populations in industrialised countries, particularly in western and northern Europe and Australia/New Zealand*
- ❖ *Rare in non-Caucasian population*
- ❖ *Testicular cancer is five times more common in the developed regions than in the less developed regions*



Testicular cancer

Risk factor

- *Cryptorchidism*
- *Testis Atrophy (infection, trauma)*
- *Radiation*
- *Family history of cancer (Genetic susceptibility)*
- ***Tobacco use?***
- *Personal history of testicular cancer*



Risk Factor/ Cancer Type

| Cancer Type | Risk Factor |
|--------------------------|---|
| <i>Bladder</i> | <u><i>Tobacco smoking</i></u> <i>Occupation</i> <i>Certain infection</i> |
| <i>Prostate</i> | <i>Diet</i> <u><i>Tobacco smoking</i></u> <i>Certain prostate changes</i> <i>Race Africans Americans</i> |
| <i>Kidney</i> | <u><i>Tobacco smoking</i></u> <i>HTN</i> <i>Von-Hippel-Lindau syndrome (VHL)</i> |
| <i>Testicular cancer</i> | <i>Cryptorchidism</i> <i>Testis Atrophy</i> <u><i>Tobacco smoking</i></u> |



*Permanent
or
Transient
Effects?*

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Persistence of urothelial carcinoma of the bladder risk among former smokers: Results from a contemporary, prospective cohort study

Christopher J. Welty, M.D.^{a,*}, Jonathan L. Wright, M.D., M.S.^{a,b}, James M. Hotaling, M.D., M.S.^a, Parveen Bhatti, Ph.D.^b, Michael P. Porter, M.D., M.S.^{e,a}, and Emily White, Ph.D.^{c,d}

^aDepartment of Urology, University of Washington, Seattle, WA

^bProgram in Epidemiology, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA

^cCancer Prevention Program, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA

Results

- Study included 77,719 men and women
- **Current smoker** had an increased risk of bladder cancer compared with **never smokers** (HRs:3.81)
- **Former smoker** had an increased risk of bladder cancer compared with **never smokers** (HRs:2.0)
- The risk of bladder cancer in former smokers remains **elevated >32** years after quitting, **even** among those with **moderate smoking** histories
- Smoking has association with bladder cancer recurrence ($p=0.02$) while smoking cessation only **at ≥ 10 yr** mitigates the risk of disease recurrence

Results

Adjusted^a risk of urothelial carcinoma of the bladder by smoking status

| | Cases (<i>n</i>) | Noncases (<i>n</i>) | HR (95% CI) | <i>P</i> -value |
|----------------|--------------------|-----------------------|------------------|-----------------|
| Never smoked | 92 | 36,373 | 1.00 (referent) | |
| Former smoker | 228 | 33,648 | 2.00 (1.55–2.58) | <0.001 |
| Current smoker | 58 | 6,412 | 3.81 (2.71–5.35) | <0.001 |

^aAdjusted for age, race, gender, education, and family history of urothelial cancer.

Results

Adjusted^a risk of urothelial carcinoma of the bladder by pack-years and years since quitting among former smokers

| Smoking variables | Cases (n) | Noncases (n) | HR (95% CI) | P-value ^b |
|---|-----------|--------------|------------------|----------------------|
| Pack-years smoked^c | | | | |
| Never smoked | 92 | 36,281 | 1.00 (referent) | <0.001 |
| <7.5 | 46 | 11,640 | 1.46 (1.02–2.09) | |
| 7.5–<22.5 | 55 | 8,002 | 2.06 (1.46–2.90) | |
| 22.5–<37.5 | 53 | 7,668 | 1.91 (1.34–2.71) | |
| 37.5 and above | 72 | 6,069 | 2.77 (2.00–3.85) | |
| Years since quitting^d | | | | |
| Never smoked | 92 | 36,281 | 1.00 (referent) | <0.001 |
| 32 and above | 56 | 8,208 | 1.50 (1.07–2.11) | |
| 23.5–<32 | 59 | 8,267 | 2.16 (1.54–3.03) | |
| 14–<23.5 | 52 | 8,323 | 2.10 (1.42–2.86) | |
| <14 | 59 | 8,297 | 2.52 (1.79–3.53) | |

^a Adjusted for age, race, gender, education, and family history of urothelial cancer.

Association of Cigarette Smoking and Smoking Cessation with Biochemical Recurrence of Prostate Cancer in Patients Treated with Radical Prostatectomy.

Rieken M¹, Shariat SF², Kluth LA³, Faikovic H⁴, Rink M⁵, Karakiewicz PI⁶, Seitz C⁴, Briganti A⁷, Rouprêt M⁸, Loidl W⁹, Trinh QD¹⁰, Bachmann A¹¹, Pourmand G¹².

⊕ Author information

Abstract

BACKGROUND: Cigarette smoking seems to be associated with prostate cancer (PCa) incidence and mortality.

OBJECTIVE: To elucidate the association between pretreatment smoking status, cumulative smoking exposure, and time since smoking cessation and the risk of biochemical recurrence (BCR) of PCa in patients treated with radical prostatectomy (RP).

DESIGN, SETTING, AND PARTICIPANTS: Retrospective analysis of 6538 patients with pathologically node-negative PCa treated with RP between 2000 and 2011. Clinicopathologic and smoking variables, including smoking status, number of cigarettes per day (CPD), duration in years, and time since smoking cessation were collected.

INTERVENTION: RP without neoadjuvant therapy.

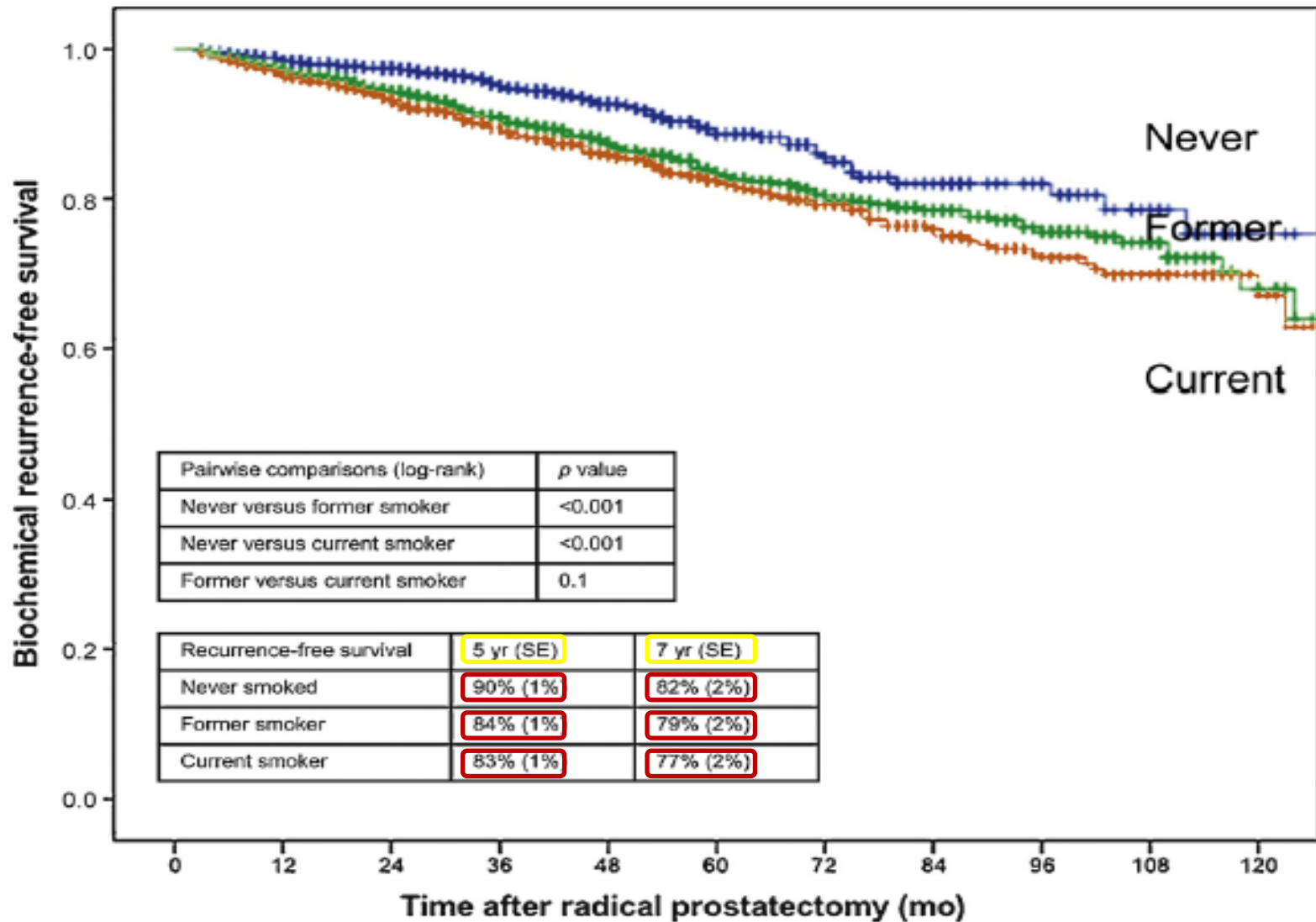
OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Univariable and multivariable Cox regression analyses assessed the association between smoking and risk of PCa BCR.

RESULTS AND LIMITATIONS: Of 6538 patients, 2238 (34%), 2086 (32%), and 2214 (34%) were never, former, and current smokers, respectively. Median follow-up for patients not experiencing BCR was 28 mo (interquartile range 14-42). RP Gleason score ($p=0.3$), extracapsular extension ($p=0.2$), seminal vesicle invasion ($p=0.8$), and positive surgical margins ($p=0.9$) were comparable among the three groups. In multivariable Cox regression analysis, former smokers (hazard ratio [HR] 1.63, 95% confidence interval [CI] 1.30-2.04; $p<0.001$) and current smokers (HR 1.80, 95% CI 1.45-2.24; $p<0.001$) had a higher risk of PCa BCR compared with non-smokers. Smoking cessation for ≥ 10 yr mitigated the risk of BCR in multivariable analyses (HR 0.96, 95% CI 0.68-1.37; $p=0.84$). In multivariable analysis, no significant association between cumulative smoking exposure and risk of BCR could be detected. Limitations of the study include the retrospective design and potential recall bias regarding smoking history.

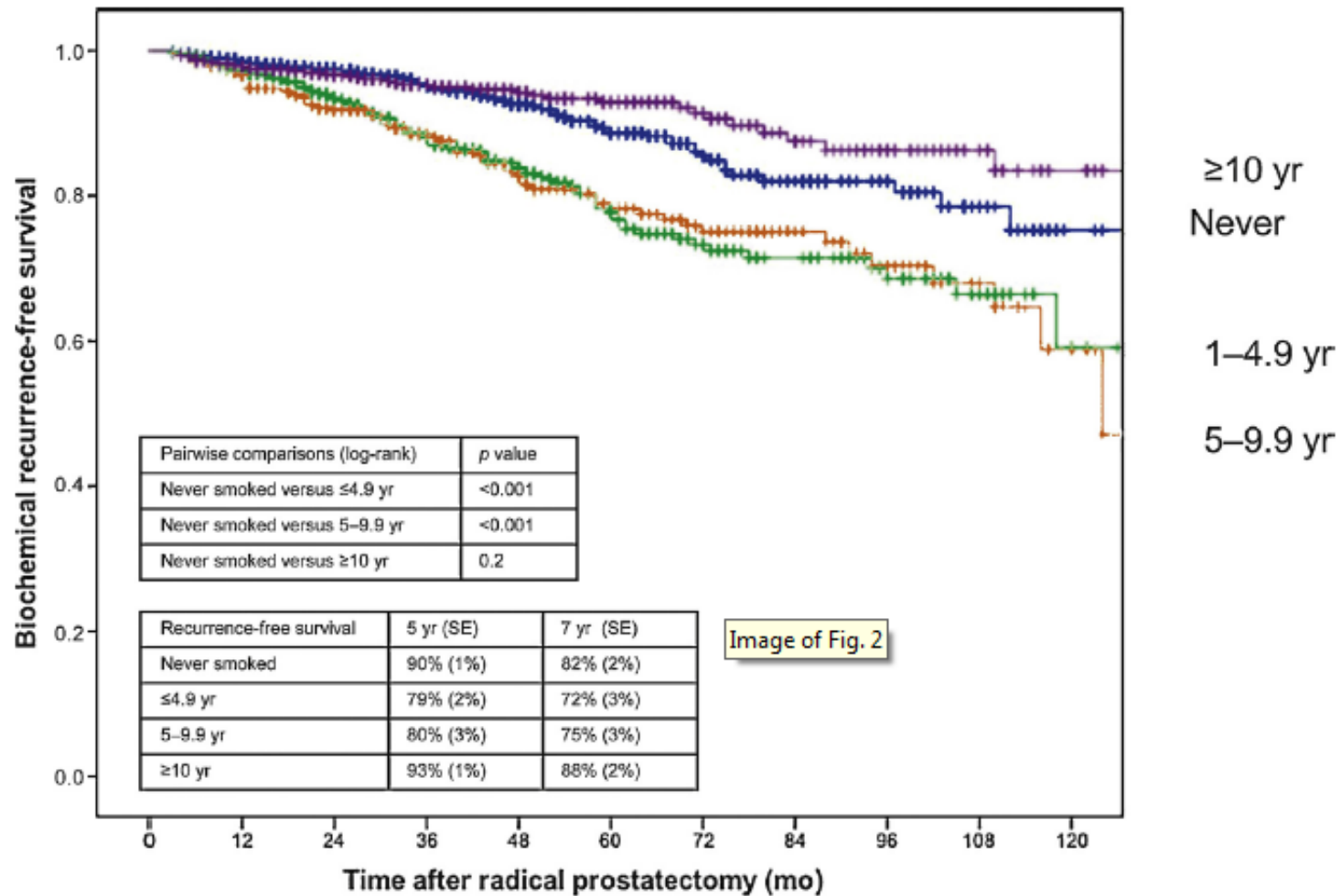
Results

- *Current* smoking is associated with a higher risk of biochemical recurrence of prostate cancer (**HR 1.80**; $p < 0.001$)
- *Former* smoking is associated with a higher risk of prostate cancer recurrence (**HR 1.63**,; $p < 0.001$)
- *Cessation* of smoking only after 10 years mitigates the rate of recurrence (**HR 0.96**)

Smoking status and biochemical recurrence of prostate cancer



Smoking cessation and biochemical recurrence of prostate cancer



RESEARCH ARTICLE

The impact of smoking on survival in renal cell carcinoma: a systematic review and meta-analysis

Yunze Xu · Yicheng Qi · Jin Zhang · Yongning Lu ·
Jiajia Song · Baijun Dong · Wen Kong · Wei Xue ·
Yiran Huang

Received: 9 January 2014 / Accepted: 18 March 2014 / Published online: 4 April 2014

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Abstract Epidemiological evidence suggests that cigarette smoking is the best-established risk factor for renal cell cancer (RCC). However, the effect of smoking on survival of RCC patients remains debated. We therefore conducted a meta-analysis to investigate the impact of smoking status on overall mortality (OM), disease-specific mortality (DSM), overall sur-

smoking was significantly associated with poorer OS (HR 1.45; 95 % CI 1.00–2.09) and poorer CSS (HR 1.01; 95 % CI 1.00–1.02), compared with never smokers. Current smoking was associated with poorer PFS (HR 2.94, 95 % CI 1.89–4.58). This review provides preliminary evidence that current smoking in a patient with RCC is associated with poorer

Results

- *Relative risk of renal cell cancer for **current smokers**: 1.29 (higher than non smokers).*
- *Relative risk of renal cell cancer for **former smokers**: 1.14 (higher than non smokers).*
- *Ever smoking is significantly associated with poorer overall survival (HR 1.45).*
- *Ever smoking is significantly associated with poorer cancer-specific survival (HR 1.01).*



ORIGINAL PAPER

Smoking cessation in long-term survivors of germ cell tumour

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Christoph Jost · Arthur Gerl

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Abstract

Purpose Long-term survivors of germ cell tumours (GCT) are at increased risk of cardiovascular morbidity. We investigated the use of tobacco in patients after therapy for GCT.

Methods Four hundred and seventy-four patients

stage, whether they had received chemotherapy or not, and irrespective of the number of chemotherapy courses applied.

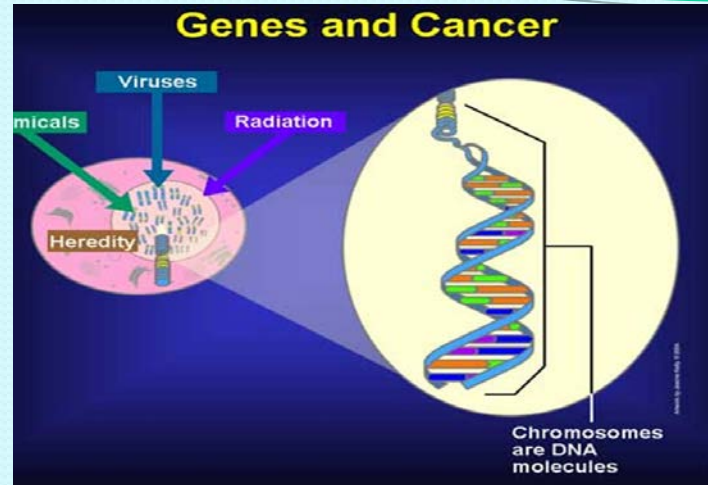
Conclusion Most patients changed their habit of tobacco smoking after diagnosis and treatment of GCT but only a minority of patients are sustained quitters. Patients

Testicular cancer

- *Contribution of tobacco to the development of testis cancer is **still under debate***
- *A study from Canada identified an increased risk of testicular germ cell tumors in men with a **greater than 12** pack-year history (OR 1.96)*
- *An increased risk of testicular germ cell tumors for those smoking for more than **21 years** (OR 3.18).*
- *Cessation of smoking had no effect on preventing the development of testicular germ cell tumors*

*Moderate risk reduction
after smoking cessation
points to
both reversible
and
permanent changes
induced by smoking*

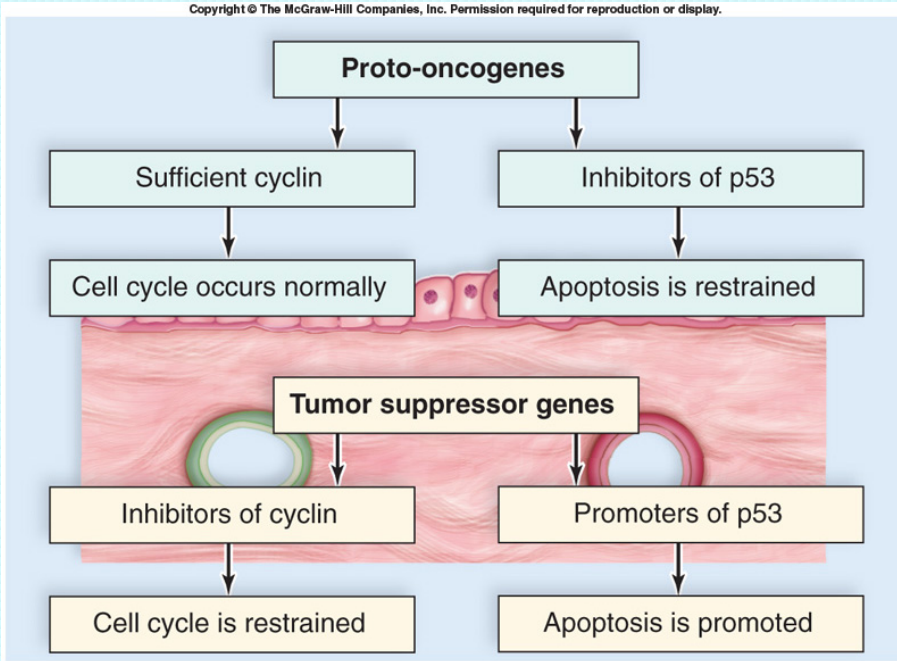
Cancer as a Genetic Disease



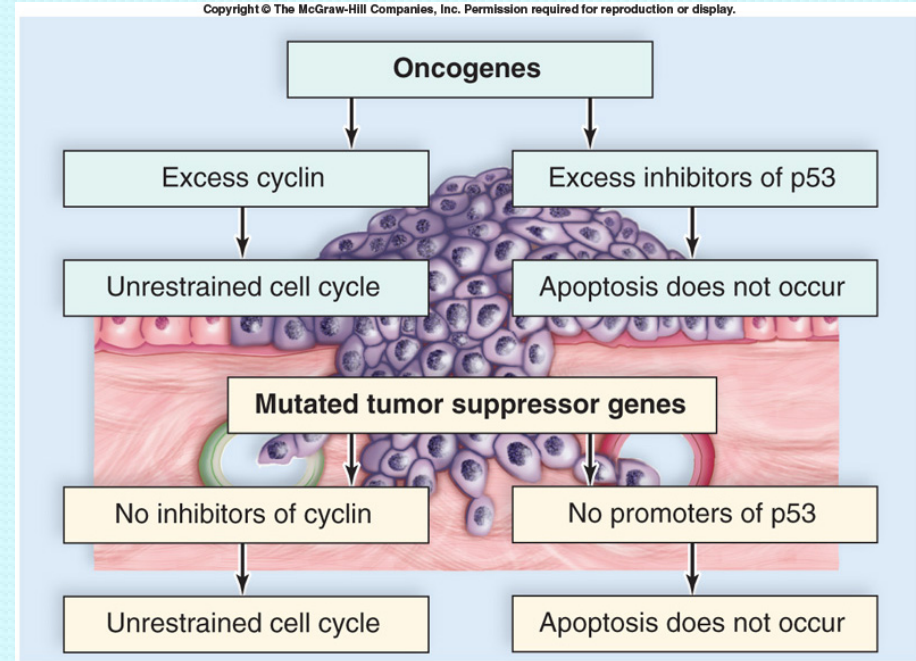
- *Proto-oncogenes products: promote the cell cycle and prevent cell death (apoptosis)*
- *Tumor-suppressor genes products: inhibit the cell cycle and promote apoptosis*
- *Mutations in the genes above can cause cancer*

Comparing genes in normal and cancer cells

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Mechanisms of Cancer Induction by Tobacco

- *Nicotine-derived nitrosamine ketone (NNK) and N-Nitrosonornicotine (NNN) are **two key tobacco-specific nitrosamines** which play an important role in carcinogenesis*
- *NNK and NNN induce **deleterious mutations** in oncogenes and tumor suppression genes*
- *Binding of NNK and NNN to the **nicotinic acetylcholine receptor** promotes tumor growth by enhancing and deregulating cell proliferation, survival, migration, and invasion*
- *These two unique aspects of NNK and NNN **synergistically** induce cancers in tobacco-exposed individuals*

Epigenetics changes and cancer

- *Definition:*

*Epigenetics is the study of inherited changes in gene expression caused by mechanisms other than changes in the **underlying DNA sequence**.*

- *These changes may remain through cell divisions for the remainder of the **cell's life** and may also last for multiple generations.*

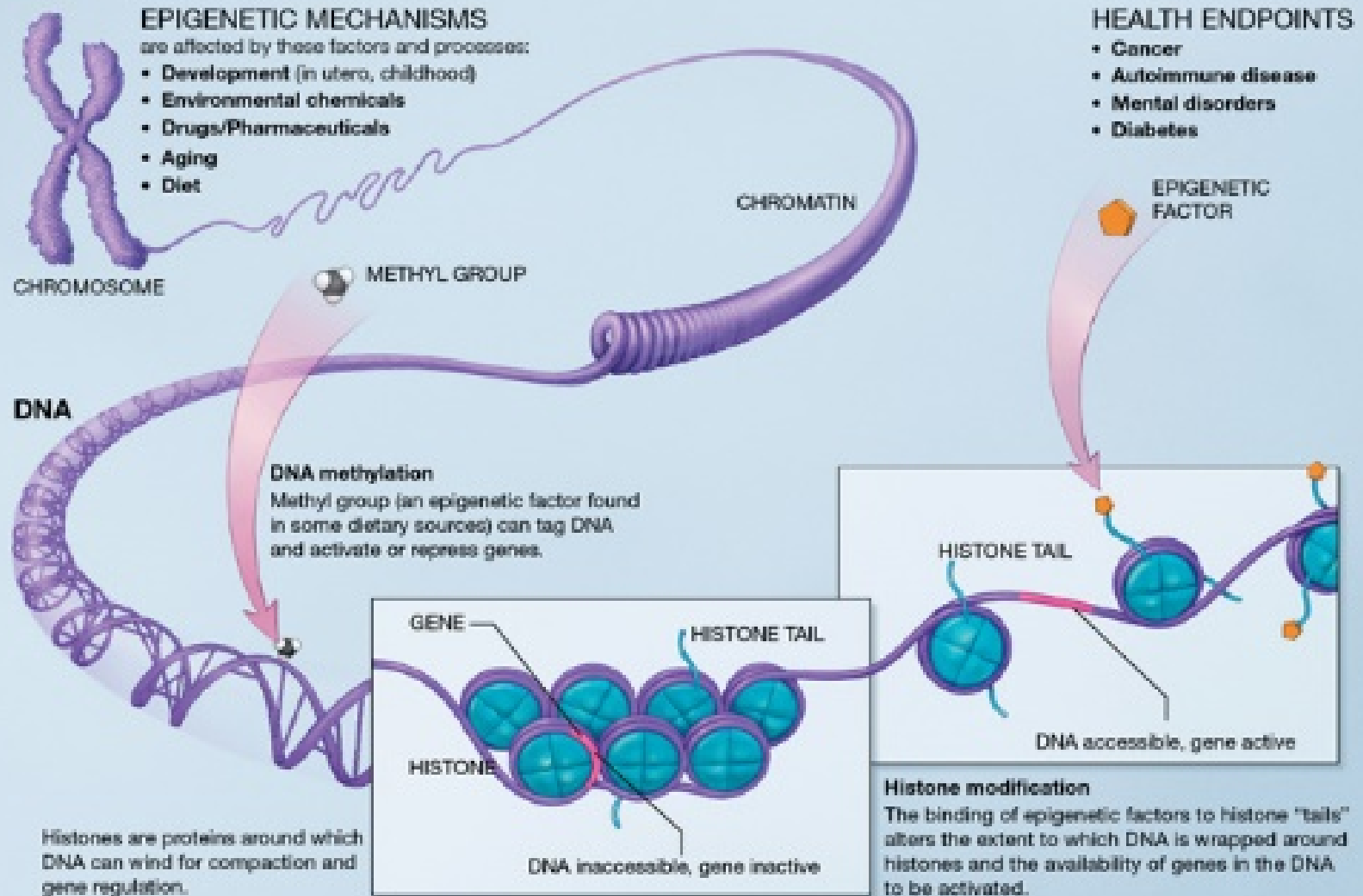
- *Epigenetic Modifications*

DNA Methylation

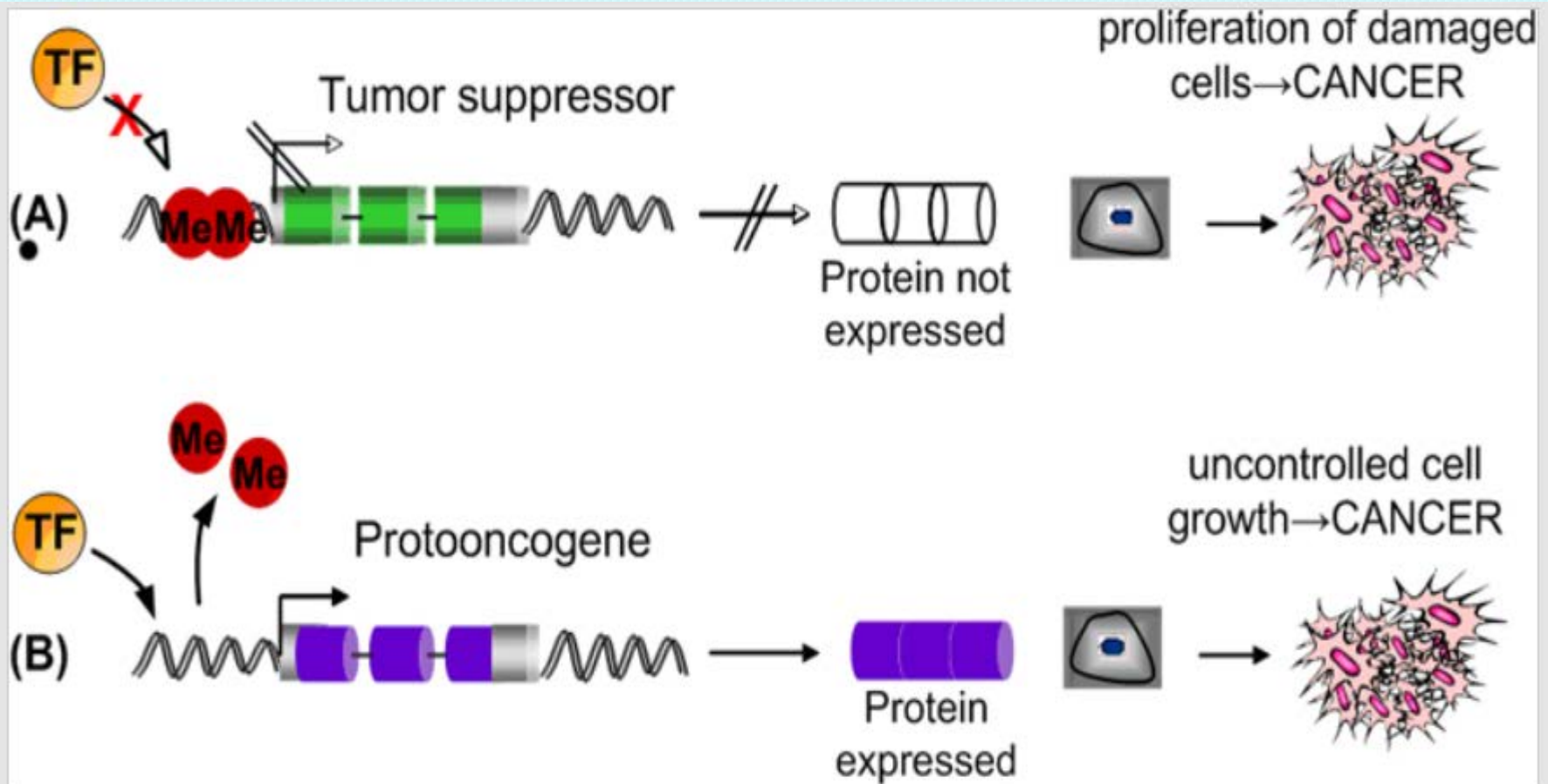
Histone Modification

Non-coding RNAs

Epigenetic mechanisms



Possible mechanisms by which epigenetic modification can lead to cancer



Dynamics of smoking-induced genome-wide methylation changes with time since smoking cessation.

Guida F¹, Sandanger TM², Castagné R¹, Campanella G¹, Polidoro S³, Palli D⁴, Krogh V⁵, Tumino R⁶, Sacerdote C³, Panico S⁷, Severi G⁸, Kyrtopoulos SA⁹, Georgiadis P⁹, Vermeulen RC¹⁰, Lund E², Vineis P¹¹, Chadeau-Hyam M¹².

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Epigenetics changes and cancer

- *Epigenome-wide association studies to evaluate dynamics of smoking-induced epigenetic changes after smoking cessation*
- *Two distinct classes of CpG sites were identified*
 - Sites whose methylation regress to levels typical of never smokers within decades after smoking cessation
 - Sites remaining methylated, even more than 35 years after smoking cessation
- *Conclusions*
 - Persistent epigenetic markers of smoking can be detected decades after cessation

Conclusions

- ❖ *The risk reduction after smoking cessation points to **both reversible and permanent changes** induced by smoking*
- ❖ *As a rich source of chemical carcinogens and reactive oxygen species, **tobacco** smoking can **directly or indirectly** damage DNA*
- ❖ *Damages include: genomic instability, p53 mutations, chromosomal deletion, changes in **DNA methylation** in the promoter regions of several genes as well as changes in telomerase activity*

Conclusions

- ❖ Some genes alteration happens in smokers are *rapidly reversible upon smoking cessation*
- ❖ while the remainders are either *slowly reversible or irreversible*
- ❖ These *irreversible gene events* might reflect a more permanent host-response to tobacco smoke and explain the higher risk of mortality or recurrence in former smokers

**NEVER START
SMOKING**



Thank you

wiseGEEK