Cancer screening and Palliative care

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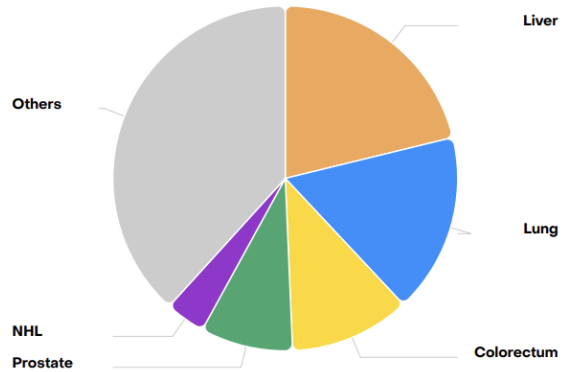
Outline

- Common cancers in Thailand
- Cancer screening
  - Lung cancer
  - Colorectal cancer
  - Breast cancer
  - Cervical cancer
- Pain management in cancer patients

Common cancers in Thailand

Top 5 most frequent cancers**

Males

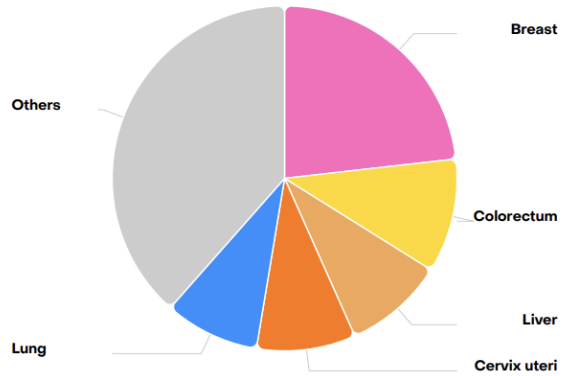


Total: 90 333

Rank	Cancer site	Number of cases	Percent
1st	Liver	19 139	21.2%
2nd	Lung	15 200	16.8%
3rd	Colorectum	10 216	11.3%
4th	Prostate	7 830	8.7%
5th	NHL	3 388	3.8%
-	Others	34 560	38.3%

Number of new cases in 2022, males, all ages

Females

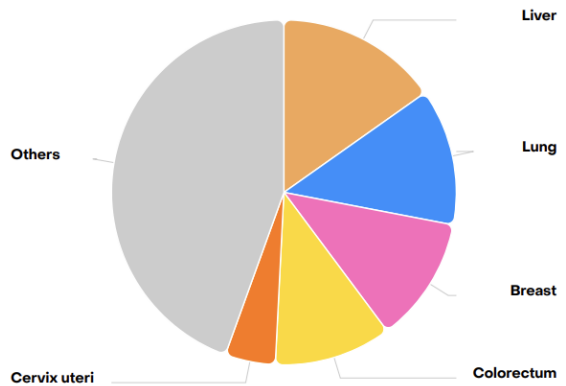


Total: 93 208

Rank	Cancer site	Number of cases	Percent
1st	Breast	21 628	23.2%
2nd	Colorectum	9 957	10.7%
3rd	Liver	8 797	9.4%
4th	Cervix uteri	8 662	9.3%
5th	Lung	8 294	8.9%
-	Others	35 870	38.5%

Number of new cases in 2022, females, all ages

Both sexes

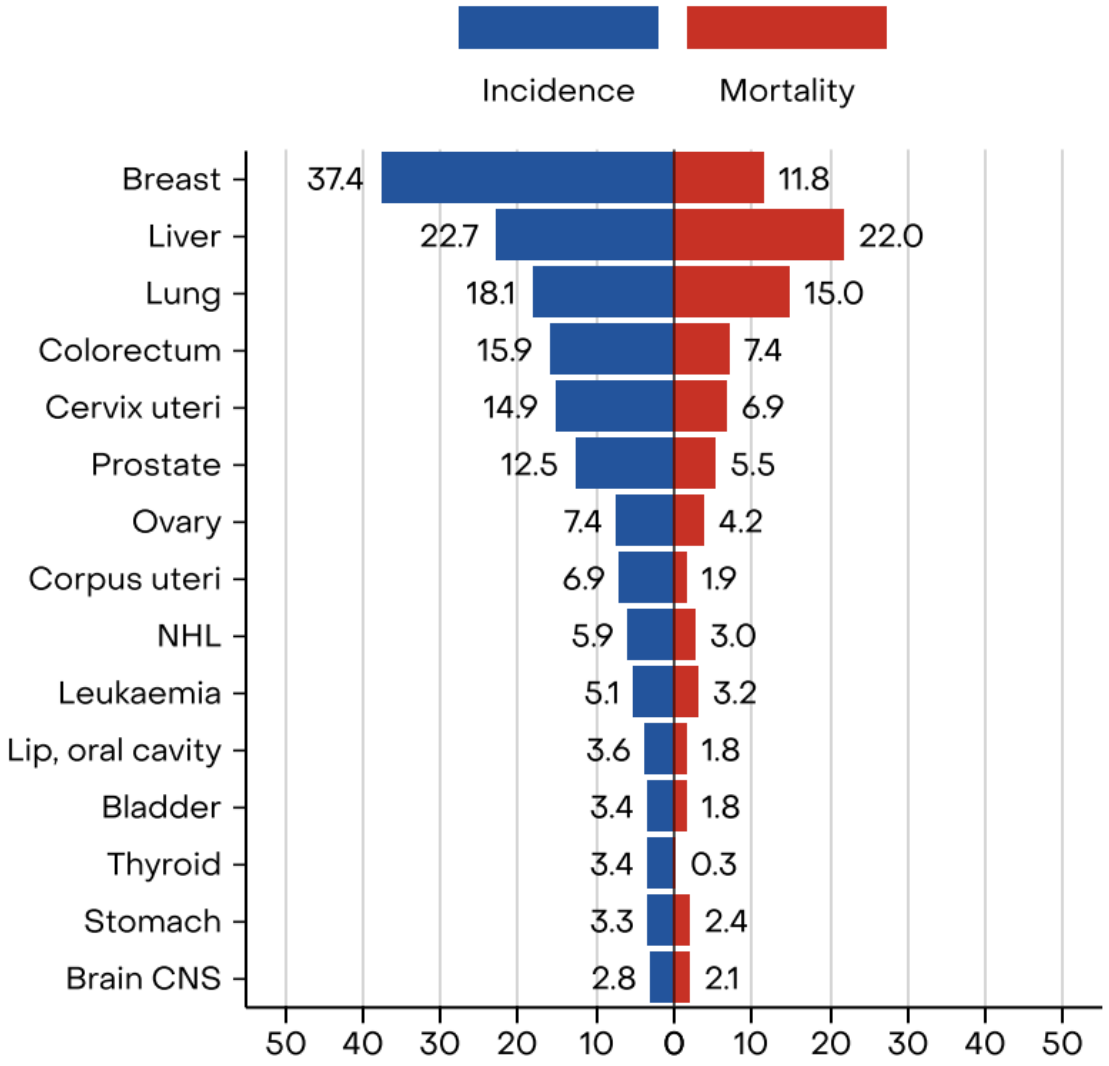


Total: 183 541

Rank	Cancer site	Number of cases	Percent
1st	Liver	27 936	15.2%
2nd	Lung	23 494	12.8%
3rd	Breast	21 628	11.8%
4th	Colorectum	20 173	11.0%
5th	Cervix uteri	8 662	4.7%
-	Others	81 648	44.5%

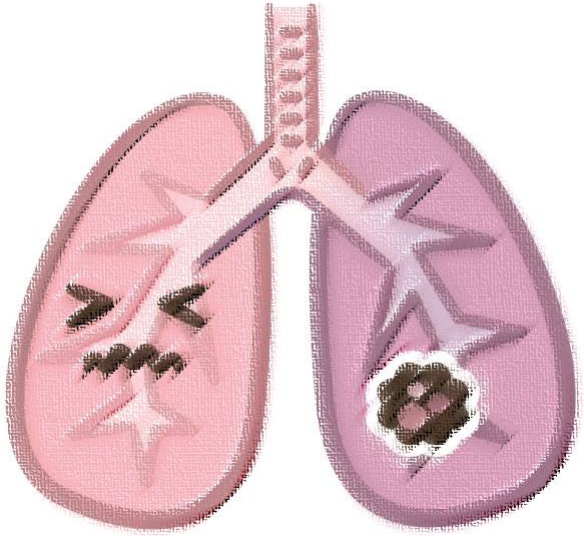
Number of new cases in 2022, both sexes, all ages

Globocan 2022



ASR (World) incidence and mortality rates, top 15 cancers**

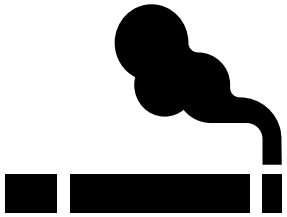
Globocan 2022



Lung cancer

Non-small cell lung cancer (NSCLC)

Lung Cancer: Risk factors

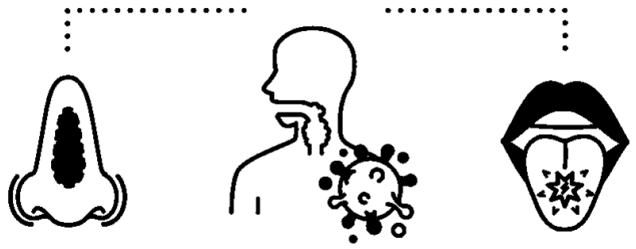


Smoking

Radon exposure

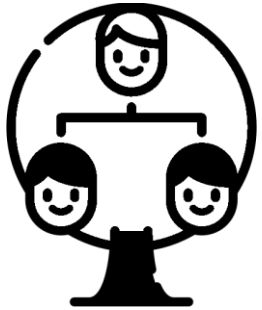
Arsenic, Asbestos, Beryllium, Cadmium, Chromium, Coal smoke, Diesel fumes, Nickel, Silica, Soot and Uranium

Occupational exposure



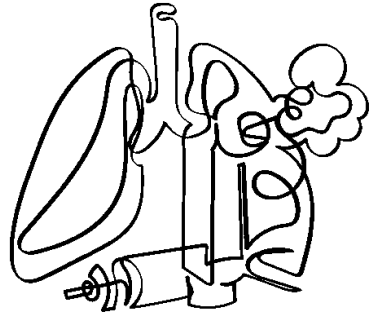
Cancer history

Smoking-related,
survivors of lymphomas



Family history

Lung cancer in first
degree relatives



History of lung disease

COPD or pulmonary fibrosis

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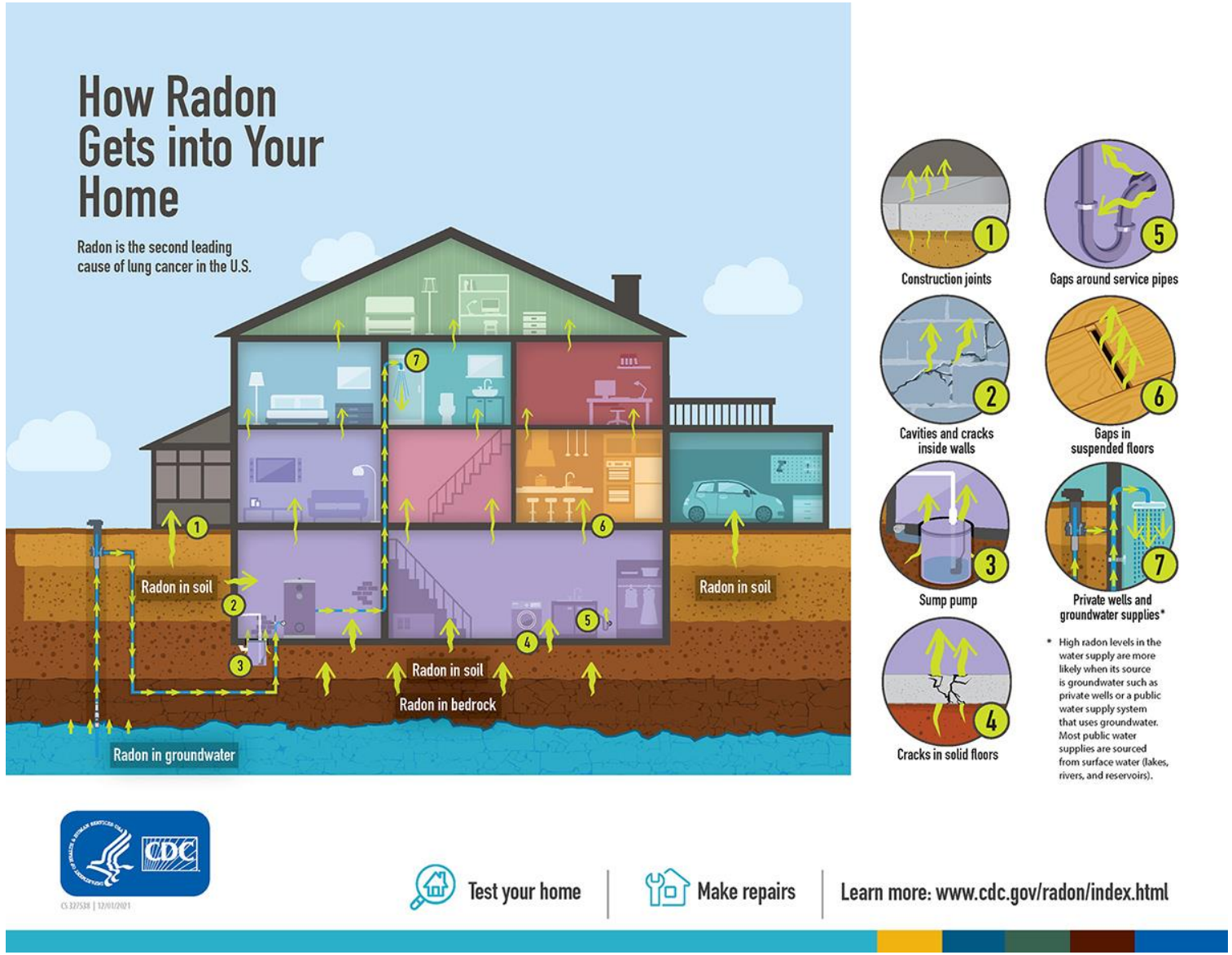
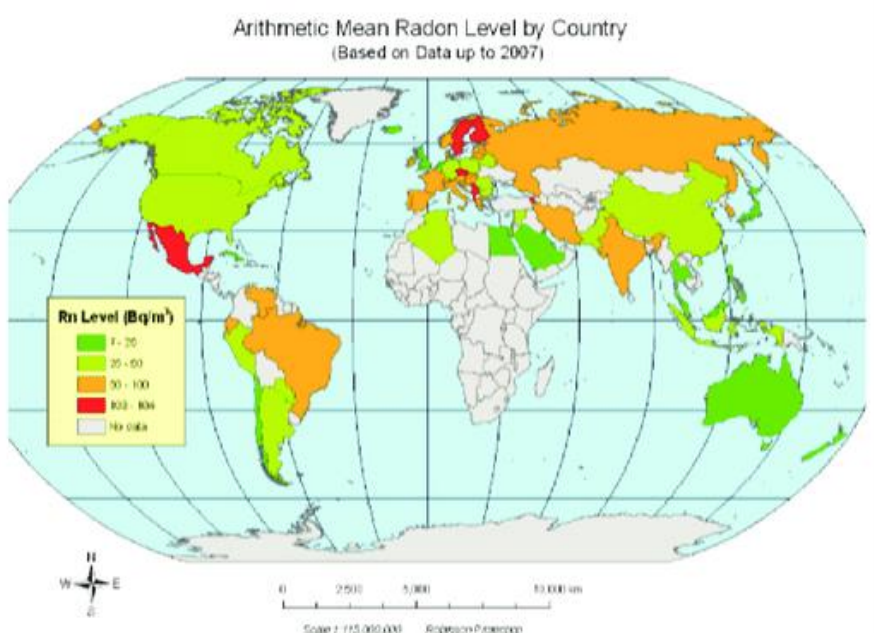




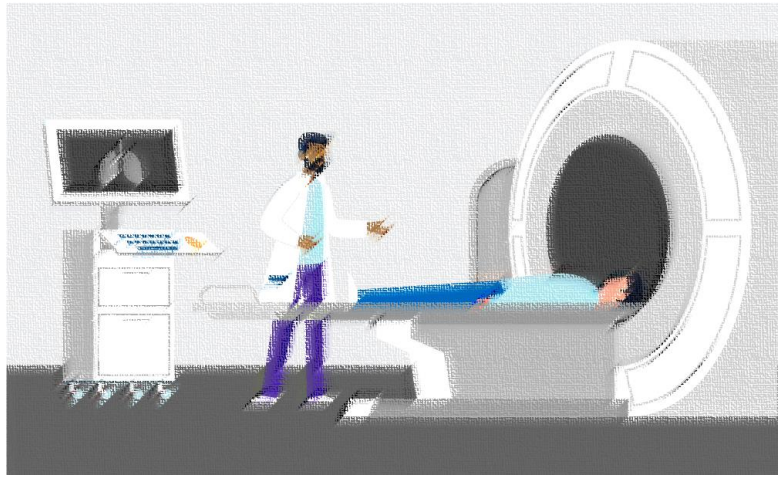
M, Al & Isaifan, Rima. *Journal of Environmental and Toxicological Studies*. 2018

Lung cancer screening

- Modalities:
  - Sputum cytology
  - CXR

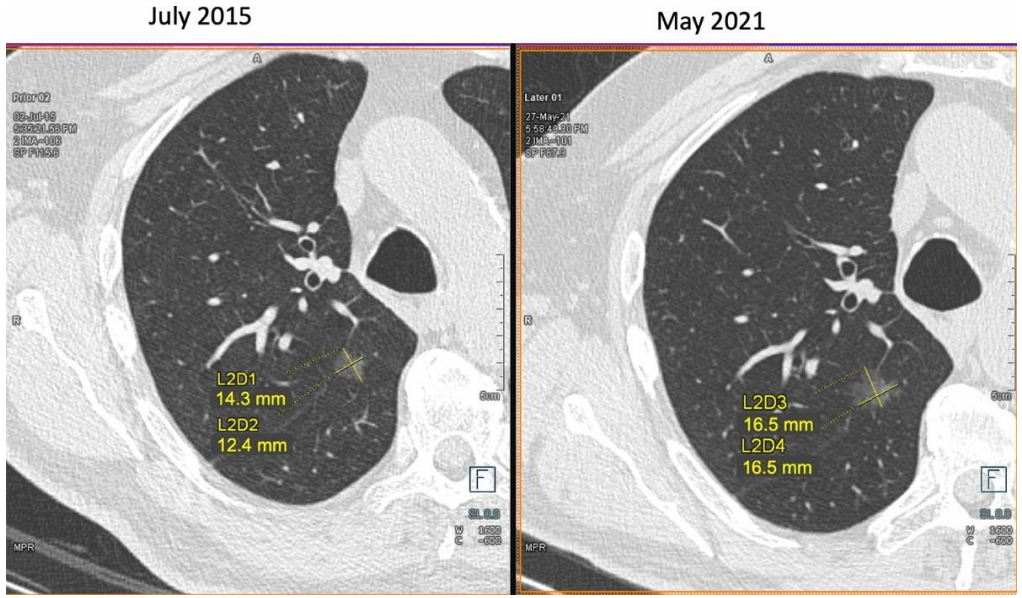
  } **No benefit in reduction of cancer mortality**

  - Low dose CT scan (LDCT)



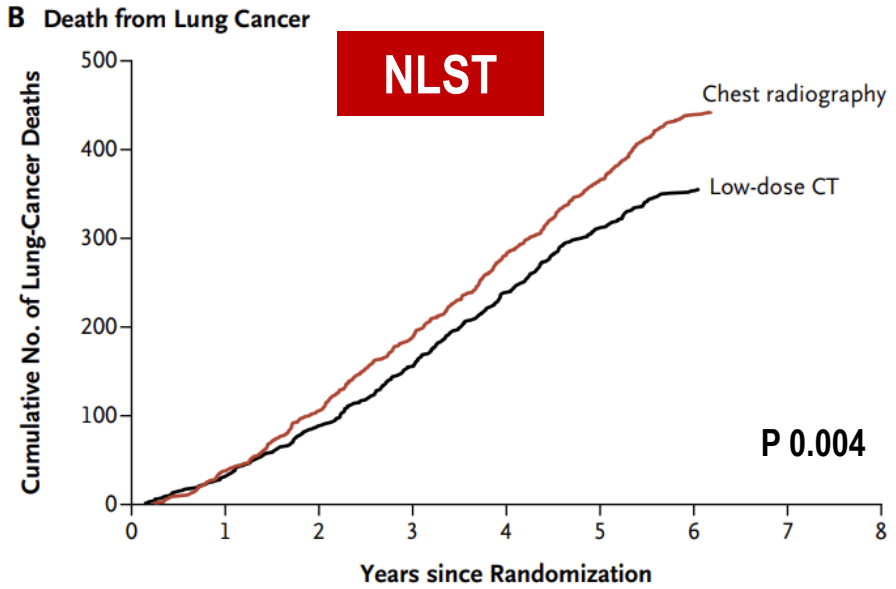
Low dose CT (LDCT)

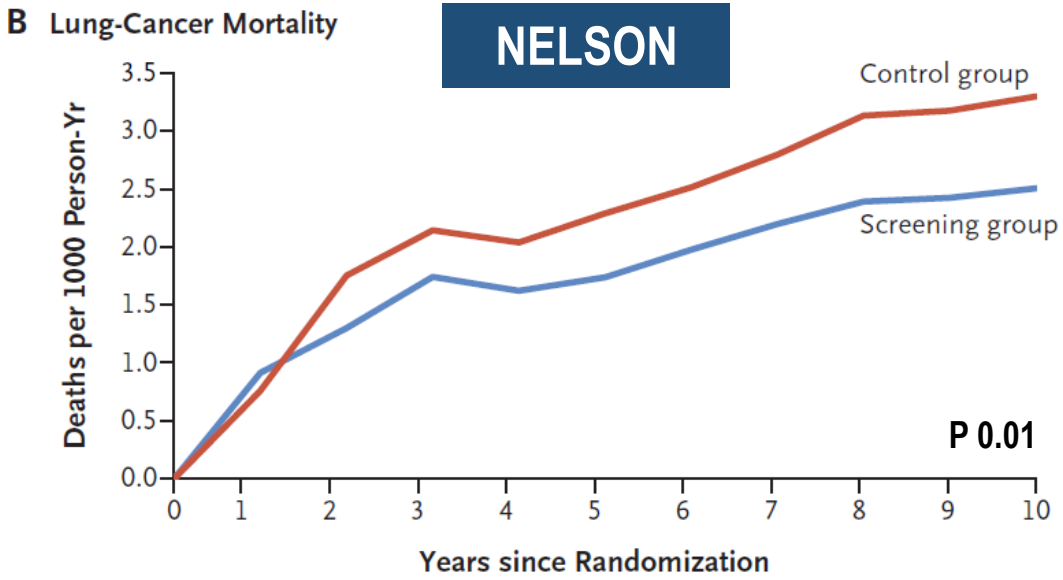
- Non-contrast CT scan
- Lower radiation exposure when compare with conventional CT scan
- Detect non-calcified lung nodules: size and type
  - Solid
  - Subsolid
    - Part-solid
  - Nonsolid or ground-glass opacities

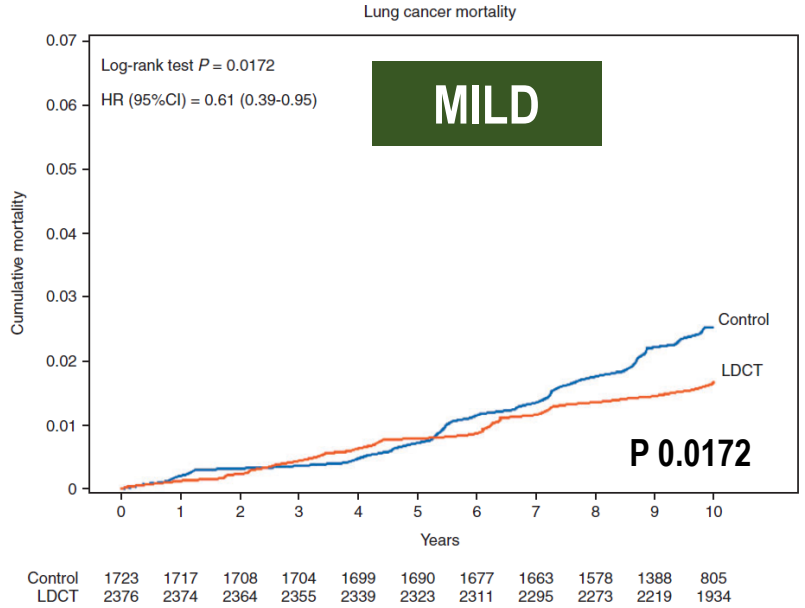


	National lung cancer screening trial (NLST[1])	NELSON[2]	MILD[3]
Country	USA, N = 53,454	Netherlands/Belgium, N = 13,195 (male)	Italy, N = 4,099
Eligibility	**Age 55-74 yrs** **≥30 pack-year smoking** **Quit ≤ 15 yrs**	**Age 50-74 yrs** **≥15 pack-year smoking** **Quit ≤ 10 yrs**	**Age 49-75 yrs** **≥20 pack-year smoking** **Quit ≤ 10 yrs**
Intervention and comparison	LDCT vs CXR	LDCT vs usual care	LDCT vs usual care
Screening Follow up	3 yrs annually 6.5 yrs	Baseline, year 1st , 3rd , and 5.5th 11 yrs	6 yrs annually (50%) or biennially 10 yrs
Stage at detection (%) • Stage I-II • Stage IV	 **65.0** vs 41.9 14.7 vs **30.4**	 **48.8** vs 23.4 26.7 vs **45.7**	 **54.1** vs 30.0 29.6 vs **53.3**
Lung cancer mortality **Death from any cause**	**20% decreased** **6.7% decreased**	**24% decreased** at 10 yrs HR 0.76 (0.62-0.94) HR 1.01 (0.92-1.11)	**39% decreased** at 10 yrs HR 0.61 (0.39-0.95) 20% decreased HR 0.80 (0.62-1.03)
		50-54 yrs (25%) HR 0.85 (0.48-1.5)	49-54 yrs (35%) Not analyzed

1.National Lung Screening Trial Research Team. *N Engl J Med*. 2011 Aug 4;365(5):395-409. 2. de Koning HJ, et al. *N Engl J Med*. 2020 Feb 6;382(6):503-513. 3.Pastorino U, et al. Ann Oncol. 2019 Jul 1;30(7):1162-1169.







1.National Lung Screening Trial Research Team. *N Engl J Med*. 2011 Aug 4;365(5):395-409. 2. de Koning HJ, et al. *N Engl J Med*. 2020 Feb 6;382(6):503-513. 3.Pastorino U, et al. Ann Oncol. 2019 Jul 1;30(7):1162-1169.

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Lung Cancer Screening

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RISK ASSESSMENT[a,b,c] | **RISK STATUS** | **SCREENING**

Smoker-related cancers

- **Cigarette smoking history[d]**
- **Radon exposure[e]**
- **Occupational exposure[f]** (Arsenic, Asbestos, Beryllium, Cadmium, Chromium, Coal smoke, Diesel fumes, Nickel, Silica, Soot and Uranium)
- **Cancer history[g]**
- **Family history of lung cancer in first-degree relatives**
- **Disease history (chronic obstructive pulmonary disease [COPD] or pulmonary fibrosis)**
- **Cigarette smoking exposure[h] (second-hand smoke)**
- **Risk calculator to enhance determination of risk status[i,j]**

Patients not eligible for lung cancer screening:

- **Symptoms of lung cancer (see NCCN Guidelines for Non-Small Cell Lung Cancer)**
- **Previous lung cancer (see Surveillance in the NCCN Guidelines for Non-Small Cell Lung Cancer)**
- **Functional status and/or comorbidity that would prohibit curative intent treatment[k] (see Principles of Surgery in the NCCN Guidelines for Non-Small Cell Lung Cancer and Principles of Radiation Therapy in the NCCN Guidelines for Non-Small Cell Lung Cancer)**

Randomized trial evidence support screening up to 77 years

High risk[i,l,m]
- **Age ≥50 y (category 1) and**
- **≥20 pack-year history of smoking cigarettes (category 1) or ≥20 year history of smoking cigarettes[1] (category 2B)**

→ **In candidates for screening, shared patient/provider decision-making is recommended, including a discussion of benefits/risks[c,j]**

→ **Low-dose CT (LDCT)[n] (category 1)**

→ **Screening Findings (LCS-2)**

Low risk
- **Age <50 y and/or**
- **<20 pack-year history of smoking cigarettes or <20 year history of smoking cigarettes[1] (category 2B)**

→ **Lung cancer screening not recommended**

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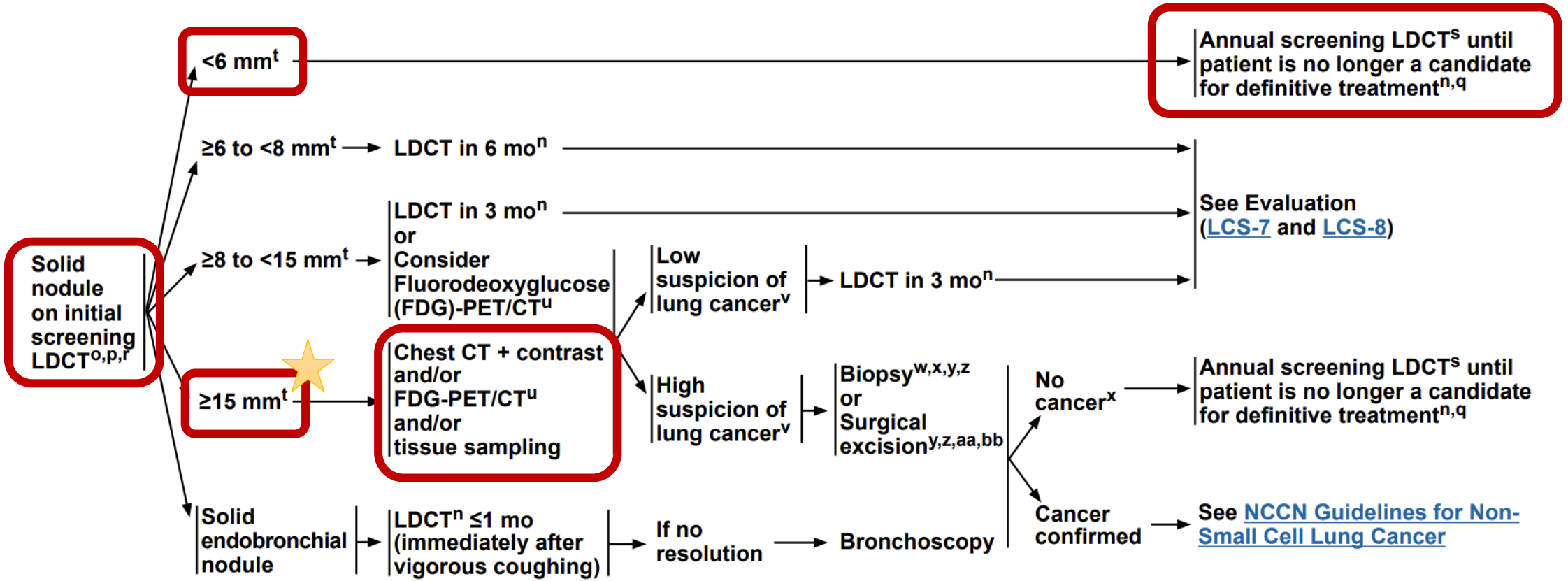
EVALUATION OF SCREENING FINDINGS

FOLLOW-UP OF SCREENING FINDINGS



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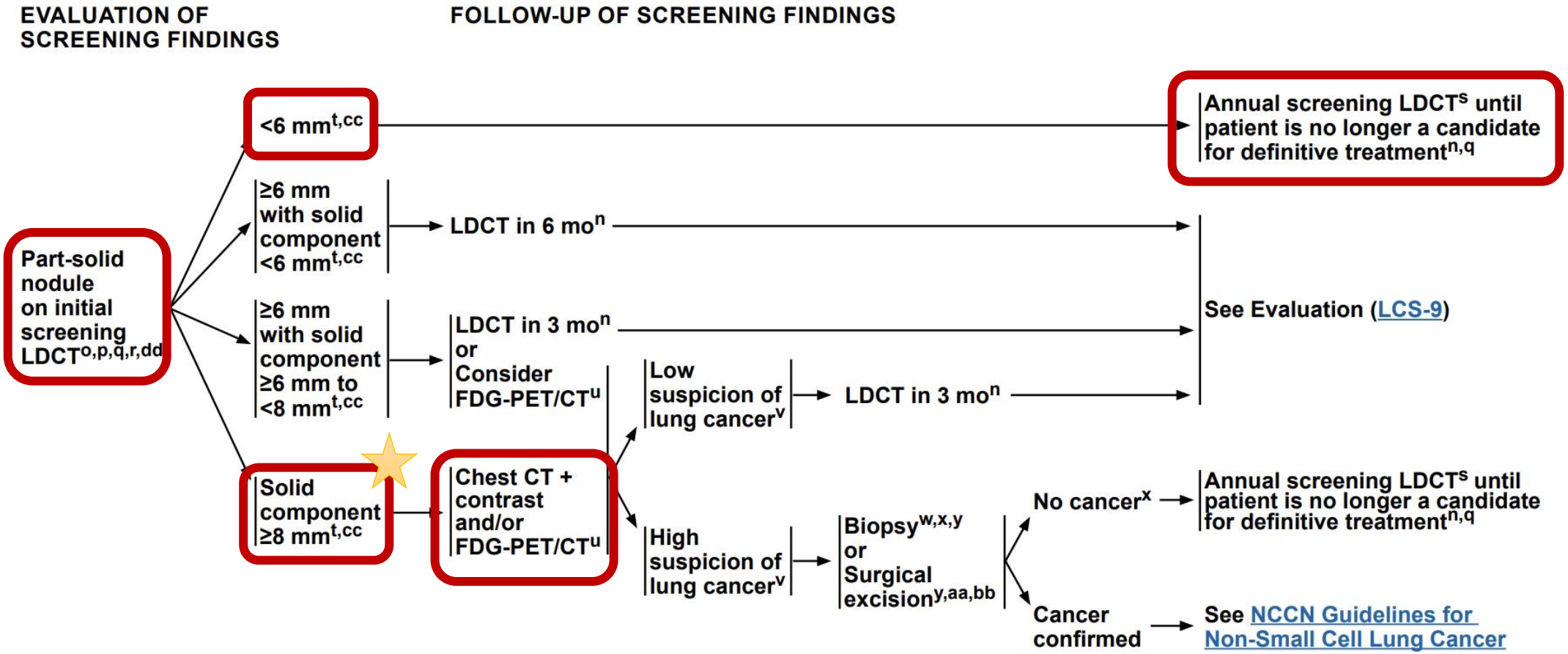

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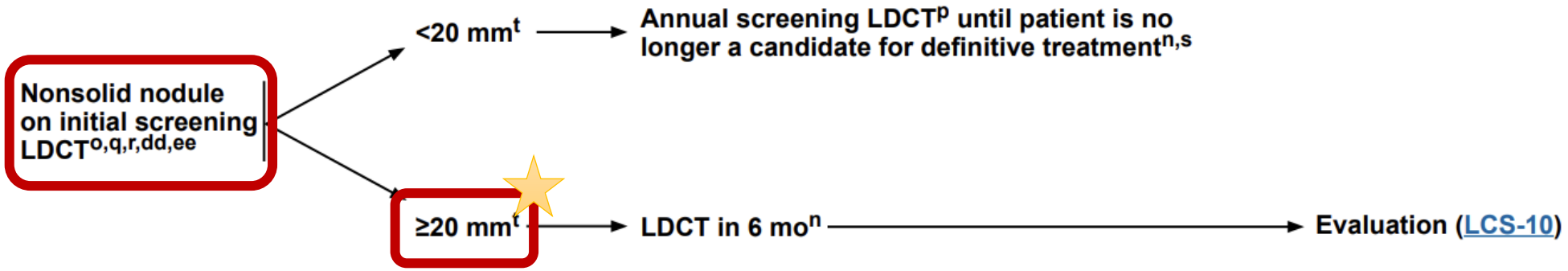


Lung cancer screening

	NCCN 2025	USPSTF 2021	ACS 2023
Age (yrs)	≥50	50-80	50-80
Population	Group1 (CAT 1): - Age ≥50 - Current/former smoker With ≥1 additional risk factors	- Current smoker Or - Quit in past 15 yrs	- Current smoker Or - Previously smoker
Smoking (pack-year)	≥20	≥20	≥20
LDCT	Q1yr	Q1yr	Q1yr
Stop	77 yrs	- Stop smoking for 15 yrs - Limit life expectancy - Limit ability to have lung surgery - >80 yrs	>80 yrs

Incidence of lung cancer diagnosed by sex according to smoking status

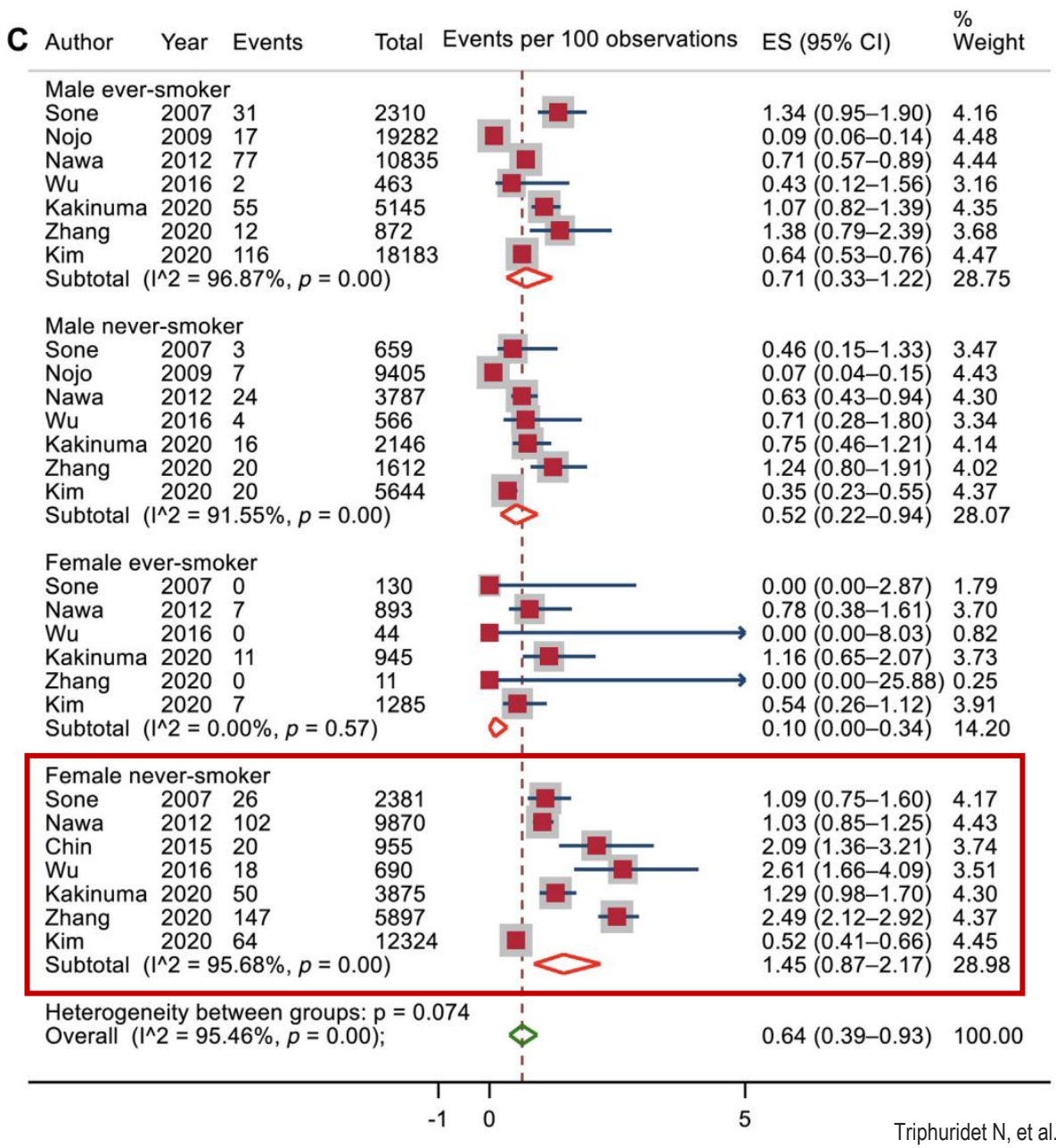
ORIGINAL ARTICLE

IASLC

Low-Dose Computed Tomography (LDCT) Lung Cancer Screening in Asian Female Never-Smokers Is as Efficacious in Detecting Lung Cancer as in Asian Male Ever-Smokers: A Systematic Review and Meta-Analysis

Natthaya Triphuridet, MD, PhD,[a] Shannon S. Zhang, MD,[b] Misako Nagasaka, MD, PhD,[b,c,d] Yanfei Gao, MSc,[e] Joseph J. Zhao, M.B.B.S.,[f] Nicholas L. Syn, M.B.B.S.,[f] Takaomi Hanaoka, MD,[g] Sai-Hong Ignatius Ou, MD, PhD,[b,c,*] Elaine Shum, MD[b]

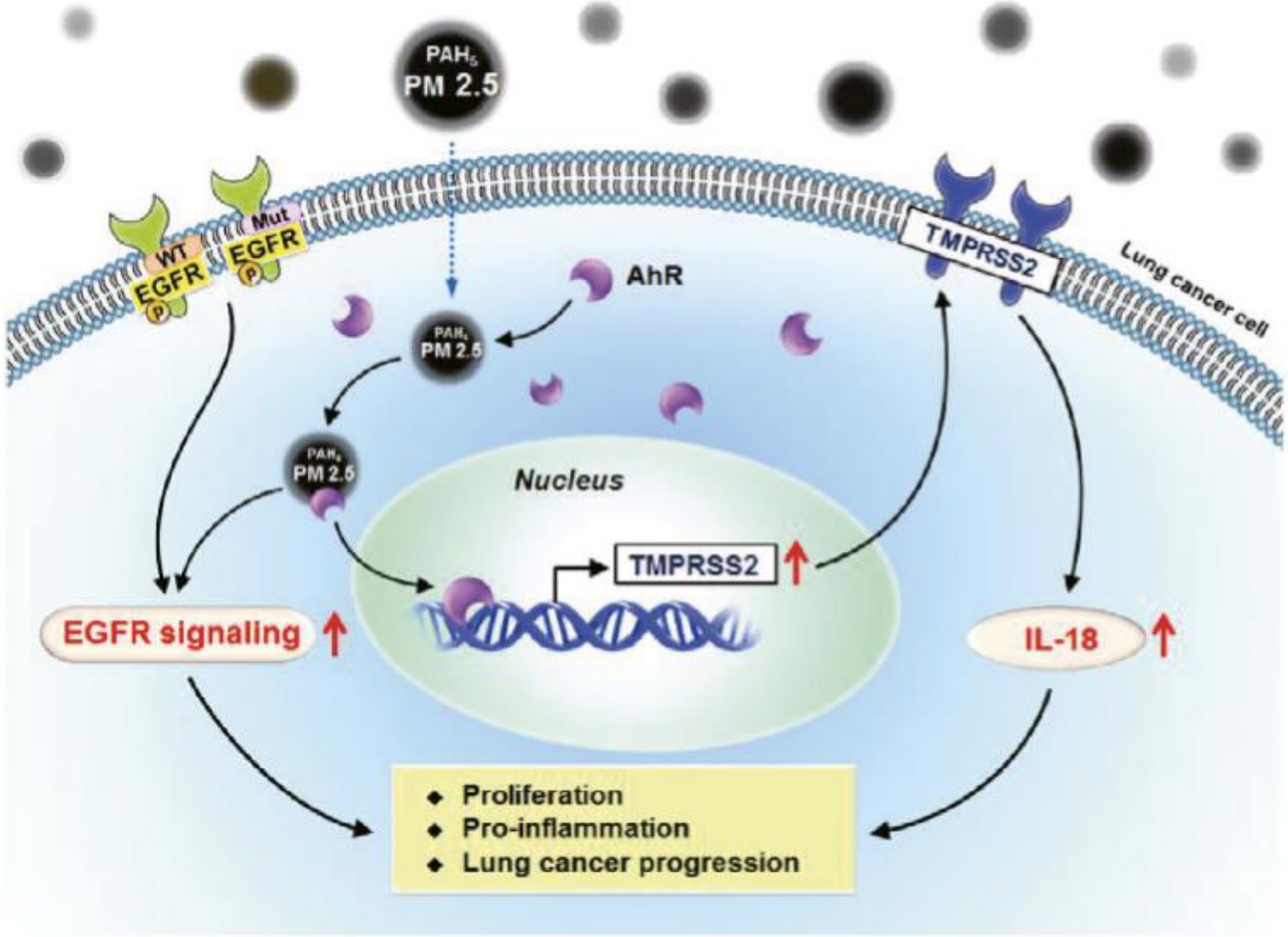
14 LDCT lung cancer screening studies:
Japan, China, Korea, Taiwan



Incidence of lung cancer diagnosed by LDCT:

- **Female never-smoker: 1.45%**
- Male ever-smoker: 0.71%
- Male never-smoker: 0.52%
- Female ever-smoker: 0.10%

Triphuridet N, et al. *J Thorac Oncol*. 2023 Jun;18(6):698-717.



PM2.5 promotes lung cancer progression through activation of AhR-TMPRSS2-IL18 pathway

Short-term exposure to PM2.5 for 24 h activated the EGFR pathway in lung cancer cells (EGFR wild-type and mutant), while long-term exposure of lung cancer cells to PM2.5 for 90 days persistently promoted EGFR activation, cell proliferation, anchorage-independent growth, and tumor growth in a xenograft mouse model in EGFR-driven H1975 cancer cells.

Wang TH, et al. *EMBO Mol Med*. 2023 Jun 7;15(6):e17014.

โครงการพัฒนาระบบคัดกรองมะเร็งปอดด้วย Low dose CT นำร่อง โดย เขตสุขภาพที่ 1

เกณฑ์การคัดเลือก ต้อง ครบทั้ง **3** ข้อ

1. คนไทย อายุ **55-75** ปี

2. อาศัยในเขตสุขภาพที่ **1** อย่างน้อย **20** ปี

3. มีความเสี่ยงอย่างน้อย **1** ข้อ ได้แก่

- สูบบุหรี่ ผู้ชาย **40 Pack-year** ผู้หญิง **20 Pack-year**
- มีประวัติครอบครัวเป็นมะเร็งปอด (ตั้งแต่ **third degree relatives**)
- มีโรค ปอดอุดกั้นเรื้อรัง ที่สูบบุหรี่ **20 Pack-year** ขึ้นไป

ทุกคนที่เข้าเกณฑ์จะได้รับ

- การทำ **CXR PA upright**

ส่งอ่านโดย **AI** ใช้ **platform** ที่มี **AI** ตัวเดียวกันทั้งเขต

- การทำ **Low dose CT** ภายใน **1** เดือนหลังจาก **CXR**

อ่านผลโดยรังสีแพทย์ โดย **report** ผลเป็น **LUNG-RADS 2022**

Further Management:

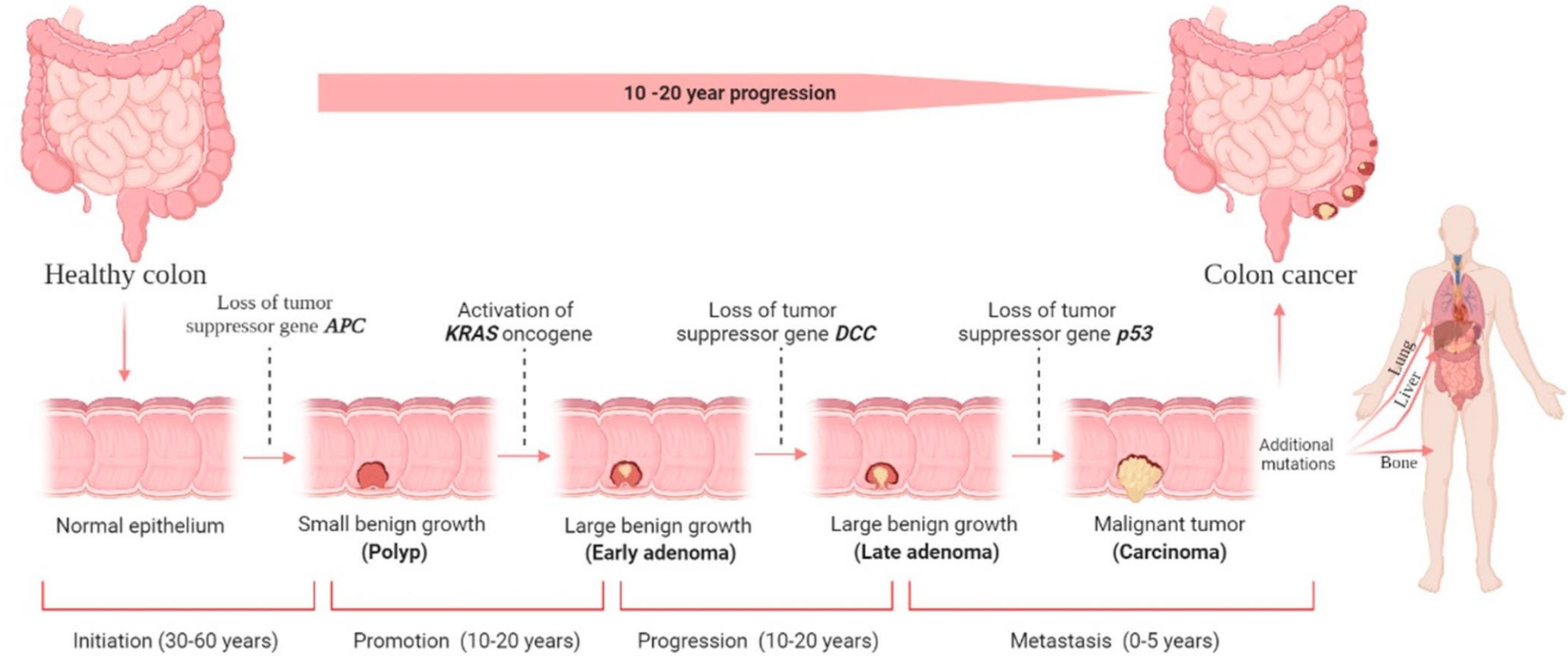
LUNG RADS Category 3 ขึ้นไป ==> ส่งพบอายุรแพทย์โรคทรวงอก แต่ละจังหวัด มี **consultant** เป็นอาจารย์ **Chest med CMU**

เป้าหมาย 3,200 ราย

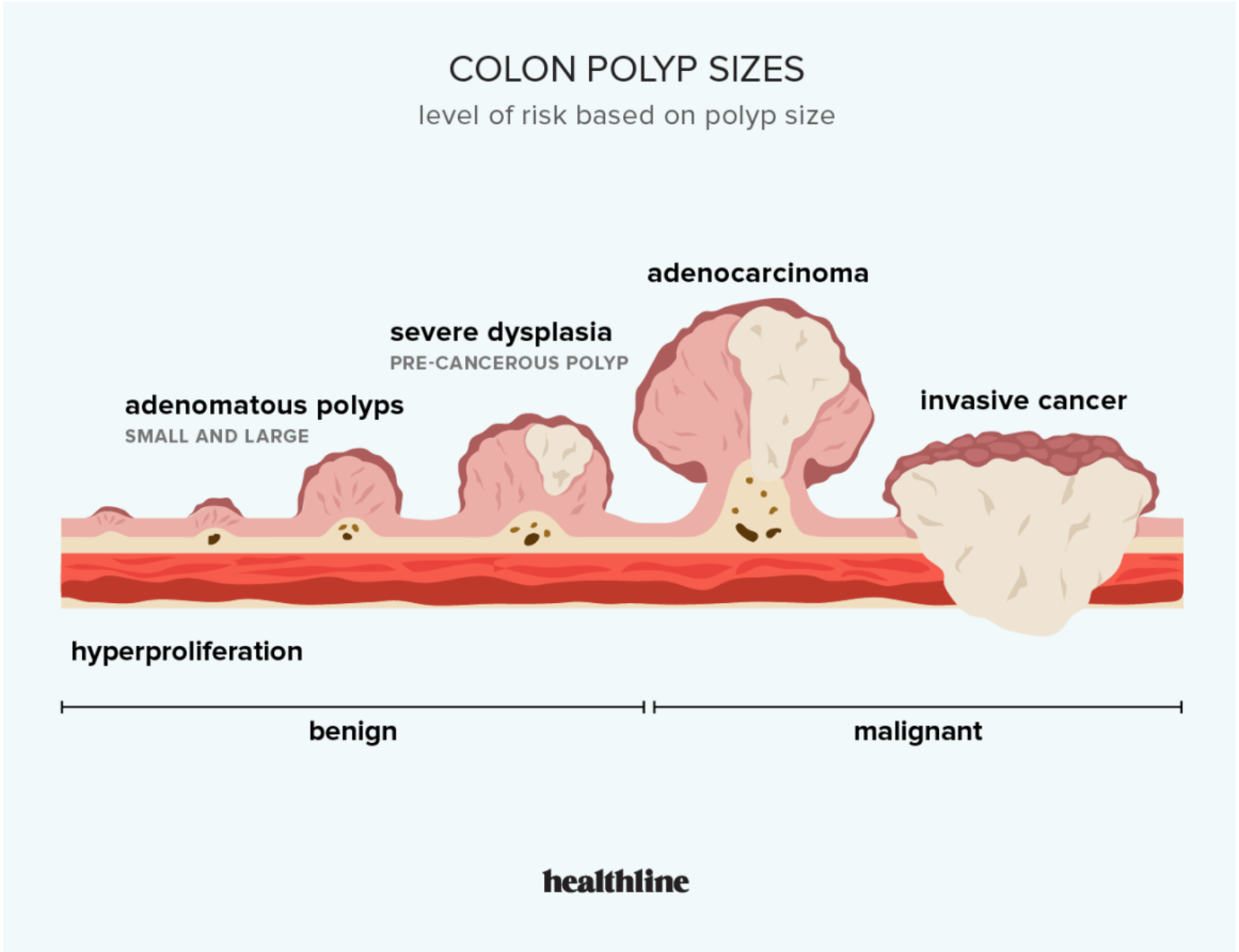
Suthira. The 8th Clinico-Radiologic-Pathologic Correlation conference

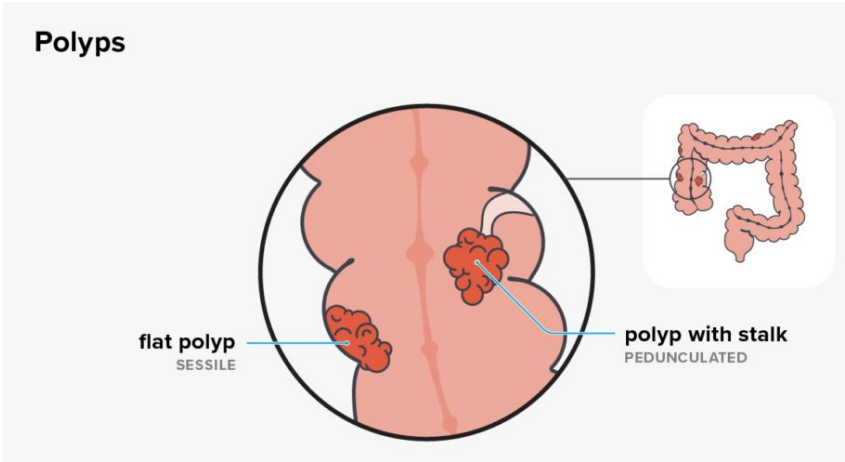
Colorectal cancer

Multistep carcinogenesis in CRC



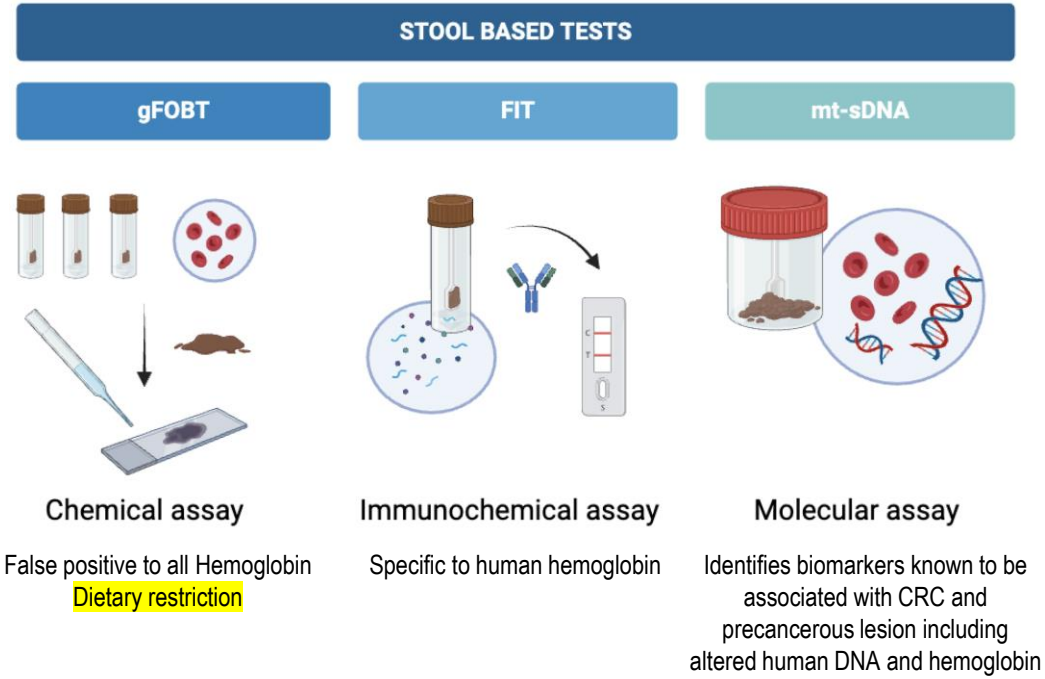
Hossain MS, et al. *Cancers (Basel)*. 2022 Mar 29;14(7):1732.


COLON POLYP SIZES
level of risk based on polyp size
adenocarcinoma
severe dysplasia
PRE-CANCEROUS POLYP
adenomatous polyps
SMALL AND LARGE
invasive cancer
hyperproliferation
benign
malignant
healthline


Polyps
flat polyp
SESSILE
polyp with stalk
PEDUNCULATED

CRC screening

- Modalities:
  - Stool-based
    - Guaiac fecal occult blood test (gFOBT)
    - Fecal immunohistochemical test (FIT)
    - Multitargeted stool DNA (mt-sDNA)
  - Colonoscopy
  - Flexible sigmoidoscopy
  - CT Colonography



SCREENING MODALITY AND SCHEDULE

Screening Test*	Recommended Testing Interval**	Sensitivity[5]		Specificity[5]	
		Colon Cancer		Colon Cancer	
Colonoscopy	Every 10 years	94.7%[4]	89%–95% (≥10 mm adenomas) 75%–93% (≥6 mm adenomas)	—	89% (≥10 mm adenomas) 94% (≥6 mm adenomas)
Flexible sigmoidoscopy***	Every 5–10 years	58%–75%[6]	72%–86%[6]	—	92%[7]
CT colonography	Every 5 years	86%–100%	89% (≥10 mm adenomas) 86% (≥6 mm adenomas)	—	94% (≥10 mm adenomas) 88% (≥6 mm adenomas)
High-sensitivity guaiac-based test	Annually	50%–75%	7%–21% (advanced neoplasia) 6%–17% (advanced adenoma)	96%–98%	96%–99% (advanced neoplasia) 96%–99% (advanced adenoma)
Quantitative FIT (using OC-Sensor)	Annually	74%	25% (advanced neoplasia) 23% (advanced adenoma)	94%	96% (advanced neoplasia) 96% (advanced adenoma)
Quantitative FIT (using OC-Light)	Annually	81%	27% (advanced neoplasia) 28% (advanced adenoma)	93%	95% (advanced neoplasia) 94% (advanced adenoma)
mt-sDNA test****	Every 3 years	93%	47% (advanced neoplasia) 43% (advanced adenoma)	85%	89% (advanced neoplasia) 89% (advanced adenoma)

* A blood test that detects circulating methylated SEPT9 DNA has been FDA-approved for CRC screening for those who refuse other screening modalities. Based on current data, the panel concludes that the interval for repeating testing is unknown/unclear. The panel will continue to review this strategy and monitor data as they emerge.
** Frequency based upon normal (negative) results.
*** Data for the sensitivity and specificity of flexible sigmoidoscopy are for the entire colon and are based on the completion of colonoscopy for those found to have a distal colon lesion on flexible sigmoidoscopy.
**** Optimal FIT thresholds will vary across screening programs, taking into consideration available colonoscopy resources to investigate abnormal results, including false-positive tests.

[4] Pickhardt PJ, Hasan C, Halligan S, Marmo R. Colorectal cancer: CT colonography and colonoscopy for detection--systematic review and meta-analysis. Radiology 2011:259:393-405.
[5] Lin JS, Perdue LA, Henrikson NB, et al. Screening for colorectal cancer: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA 2021;325:1978-1998.
[6] Whitlock EP, Lin JS, Liles E, et al. Screening for colorectal cancer: A targeted, updated systematic review for the U.S. Preventive services task force. Ann Intern Med 2008;149:638-658.
[7] Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, et al. Evaluating test strategies for colorectal cancer screening: A decision analysis for the U.S. Preventive Services Task Force. Ann Intern Med 2008;149:659-669.

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Colorectal Cancer Screening

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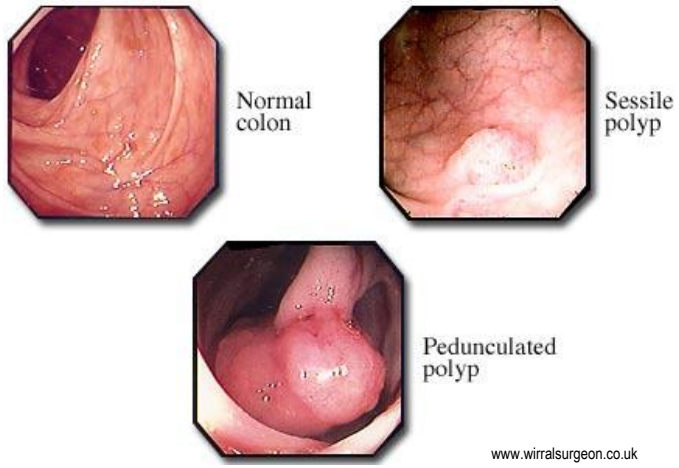
RISK ASSESSMENT FOR COLORECTAL CANCER

Average risk

Who might have life expectancy of ≥ 10 yrs

- **Age 45–75 years[a,b]**
- **No personal history of adenoma or sessile serrated polyp/sessile serrated lesion (SSP/SSL)[c] or CRC**
- **No personal history of inflammatory bowel disease (IBD)**
- **No personal history of high-risk CRC genetic syndromes (list of syndromes on CSCR-2)**
- **No personal history of cystic fibrosis**
- **No personal history of childhood cancer**
- **Negative family history for confirmed advanced adenoma (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology) or an advanced SSP/SSL[c,d] (≥1 cm, any dysplasia) in first-degree relatives[e]**
- **Negative family history for CRC[f]**

→ **Average-Risk Screening and Evaluation (CSCR-3)**



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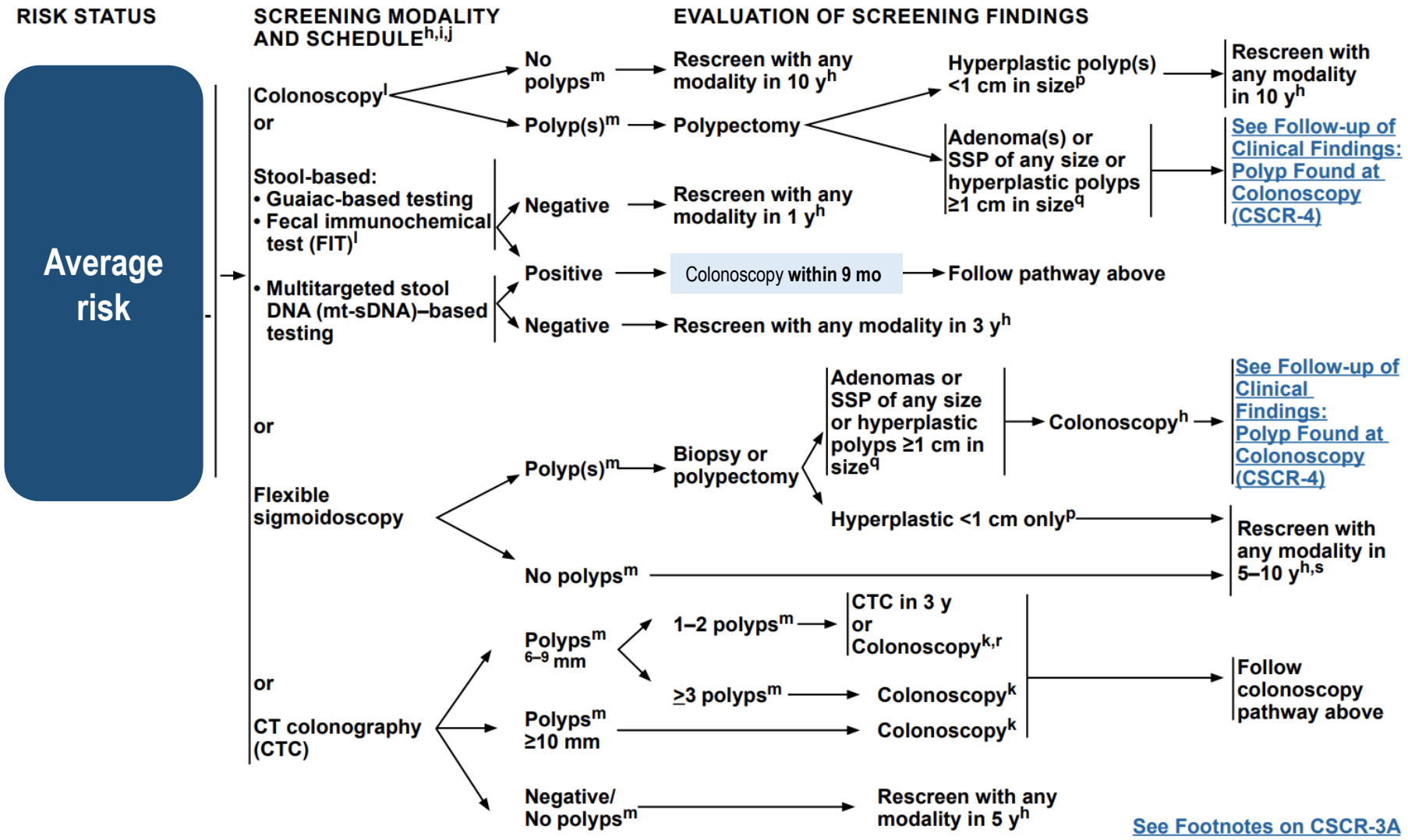

See Footnotes on CSCR-3A

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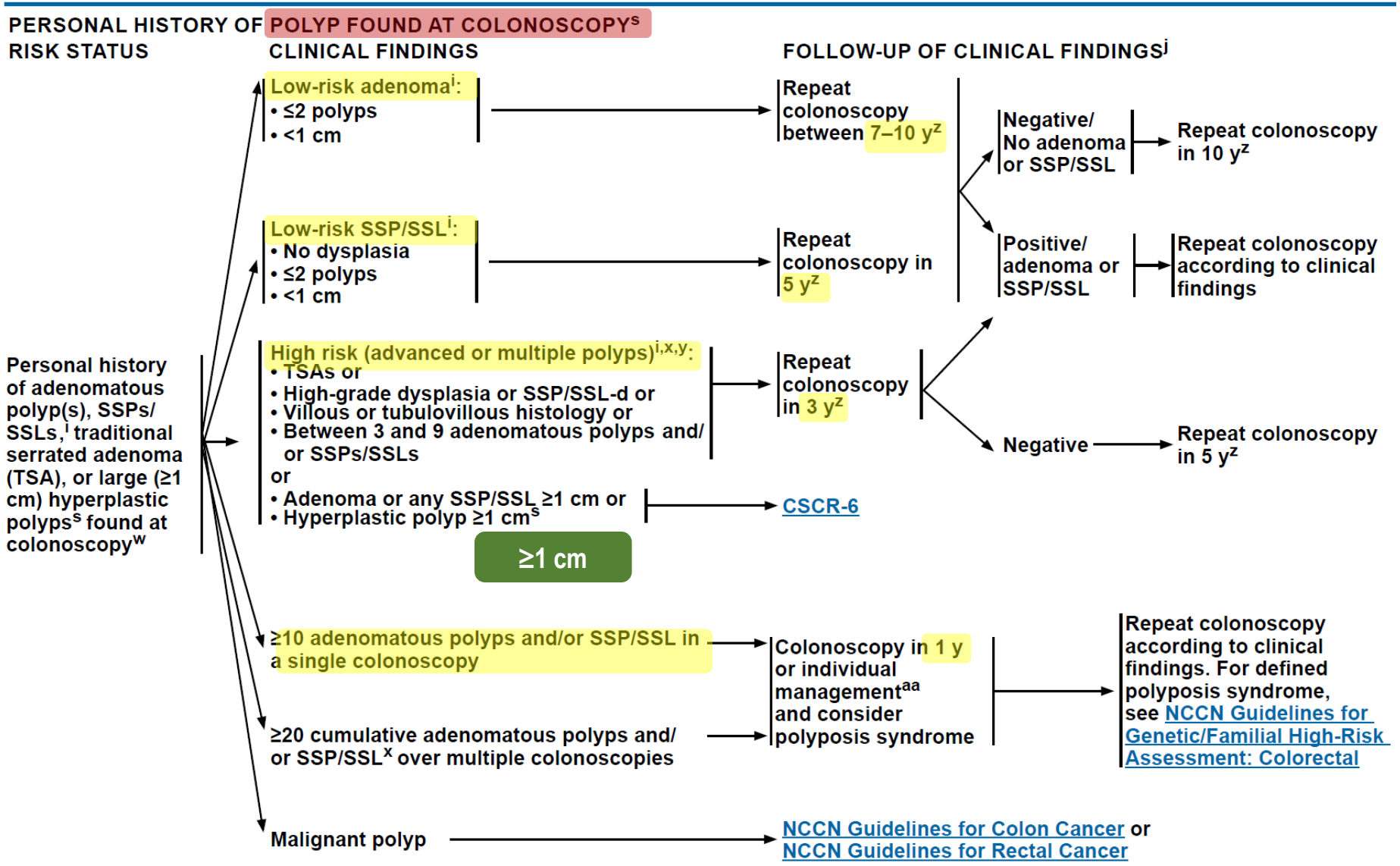
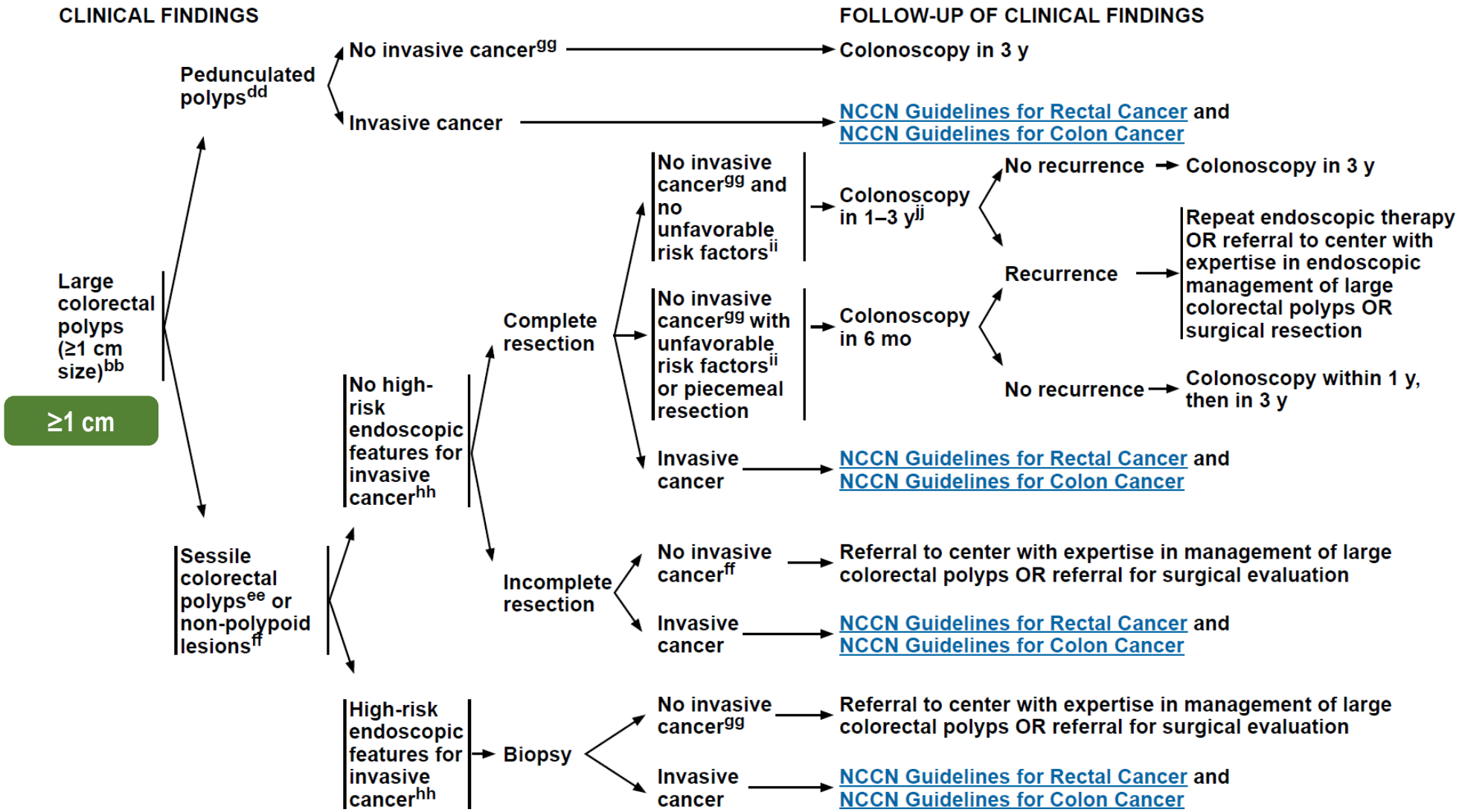


MANAGEMENT OF LARGE COLORECTAL POLYPS[cc]



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RISK ASSESSMENT FOR COLORECTAL CANCER

Average risk:
- Age 45–75 years[a,b]
- No personal history of adenoma or sessile serrated polyp/sessile serrated lesion (SSP/SSL)[c] or CRC
- No personal history of inflammatory bowel disease (IBD)
- No personal history of high-risk CRC genetic syndromes (list of syndromes on CSCR-2)
- No personal history of cystic fibrosis
- No personal history of childhood cancer
- Negative family history for confirmed advanced adenoma (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology) or an advanced SSP/SSL[c,d] (≥1 cm, any dysplasia) in first-degree relatives[e]
- Negative family history for CRC[f]

→ Average-Risk Screening and Evaluation (CSCR-3)

Increased risk

Increased risk:
- Personal history
  - Adenoma or SSP/SSL[c] → Follow-up of Clinical Findings: Polyp Found at Colonoscopy (CSCR-4)
  - CRC → Diagnosis of Colorectal Cancer (CSCR-7)
  - IBD (ulcerative colitis, Crohn's colitis) → Increased Risk Screening Based on Personal History of Inflammatory Bowel Disease (CSCR-8)
  - Cystic fibrosis → Increased Risk Based on Personal History of Cystic Fibrosis (CSCR-11)
- Positive family history → Increased Risk Based on Positive Family History (CSCR-12)
- Personal history of childhood, adolescent, and young adult cancer (including individuals who meet criteria for therapy-associated polyposis) → Increased Risk Based on Personal History of Childhood, Adolescent, and Young Adult Cancer (CSCR-13)

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INCREASED RISK BASED ON POSITIVE FAMILY HISTORY
(Not meeting criteria for consideration of a hereditary cancer syndrome or appropriate testing for a hereditary cancer syndrome non-diagnostic or not done)[yy]

FamHx

FAMILY HISTORY CRITERIA	SCREENING[bbb]	
≥1 first-degree relative with CRC at any age	Colonoscopy beginning at age 40 y or 10 y before earliest diagnosis of CRC	Repeat every 5 y[zz,bbb,ccc,ddd] or if positive, repeat per colonoscopy findings
Second- and third-degree relatives with CRC at any age	Colonoscopy beginning at age 45 y[zz]	Repeat every 10 y or if positive, repeat per colonoscopy findings
First-degree relative with confirmed advanced adenoma(s) (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology, TSA), or advanced SSPs (≥1 cm, any dysplasia) at any age [aaa,eee,fff]	Colonoscopy beginning at age 40 y or at age of onset of adenoma in relative, whichever is first	Repeat every 5–10 y[bbb,ccc] or if positive, repeat per colonoscopy findings

Routine screening

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INCREASED RISK BASED ON PERSONAL HISTORY OF INFLAMMATORY BOWEL DISEASE

IBD

RISK STATUS	INITIATION OF SURVEILLANCE	SURVEILLANCE MODALITY AND SCHEDULE	EVALUATION OF SURVEILLANCE FINDINGS
Personal history of • Ulcerative colitis[nn] • Crohn's colitis[nn]	8 y after onset of symptoms[nn] (8 yrs)	**Colonoscopy** • Colonoscopy ▸ High-definition white light endoscopy (HD-WLE)[oo,pp] ◊ Targeted biopsies of any mucosal abnormality ◊ Random 4-quadrant biopsies every 10 cm with ≥32 total samples OR • Chromoendoscopy (dye spray or high-definition virtual)[oo] ▸ Targeted biopsies of any mucosal abnormality ◊ Consider 2 biopsies in every bowel segment (placed in separate specimen jars to document microscopic disease activity and extent of disease involvement) ▸ Non-targeted (random) biopsies as described above should be considered in addition to chromoendoscopy in patients with a history of dysplasia or primary sclerosing cholangitis (PSC)[qq]	Invisible dysplasia Non-resectable polypoid lesion or mass → CSCR-9 Resectable lesion No dysplasia Colon stricture → CSCR-10

Invisible dysplasia → Reviewed by GI pathologist

- Dysplasia confirmed →
  - Assess with chromoendoscopy if not already performed or refer to endoscopist with expertise in chromoendoscopy[uu]
  - Consider referral to a surgeon with expertise in IBD[vv]
- No dysplasia → CSCR-10

Non-resectable polypoid lesion or mass

- Refer to endoscopist with expertise in advanced resection techniques
- Consider referral to a surgeon with expertise in IBD[vv]

Resectable lesion[rr,ss]
- Sessile or pedunculated
- Nonpolypoid (flat lesion)

Complete endoscopic resection[ss,tt]

- Lower risk
  - ▸ Hyperplastic or normal mucosa
  - ▸ No endoscopic/histologic active inflammation
  - ▸ <1 cm low-grade dysplasia
  - → Colonoscopy follow-up in 1–3 y[1]
- Higher risk:
  - ▸ PSC
  - ▸ ≥1 cm low-grade dysplasia
  - ▸ Active inflammation
  - ▸ Family history of CRC <50 y
  - ▸ Any high-grade dysplasia
  - → Colonoscopy follow-up in 1 y
  - In dysplastic lesions with low-grade dysplasia ≥2 cm, high-grade dysplasia, or piecemeal resection, colonoscopy follow-up within 3–6 mo

Incomplete endoscopic resection

- Refer to endoscopist with expertise in advanced resection techniques
- Consider referral to a surgeon with expertise in IBD[vv]

No dysplasia

- Low risk:
  - ▸ No endoscopic/histologic active inflammation
  - → Colonoscopy follow-up in 2–5 y[yy]
- High risk:
  - ▸ PSC
  - ▸ Active inflammation
  - ▸ Family history of CRC <50 y
  - → Colonoscopy follow-up in 1 y

Colon stricture[ww,xx]

Traversable stricture

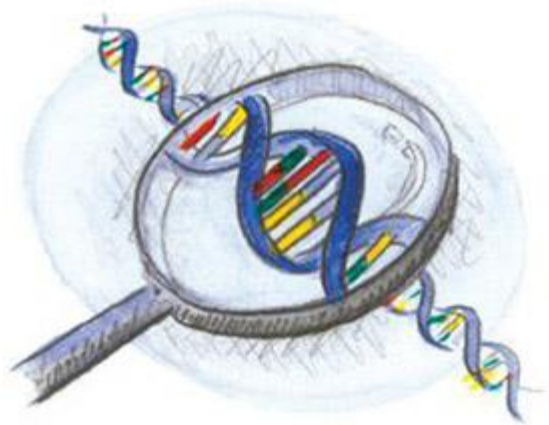
- Obtain extensive targeted biopsies from the stricture
- Consider assessment with chromoendoscopy if not already performed
- Referral to center with expertise in IBD
- Colonoscopy follow-up in 1 y if surgery not performed

Non-traversable stricture

Consider referral to an IBD or therapeutic endoscopy expert with expertise in large/complex polyp resection and/or a surgeon with expertise in IBD for resection at a center with expertise in management of IBD-associated colonic strictures[vv]

Hereditary CRC syndrome

- **Lynch syndrome** (HNPCC)
- Polyposis syndromes
  - **Familial Adenomatous Polyposis (FAP)**
  - *MUTYH*-associated syndrome
  - Peutz-Jeghers syndrome
  - Juvenile polyposis syndrome
  - Serrated polyposis syndrome (Rare)
- Cowden syndrome/ PTEN hamartoma tumor syndrome
- Li-Fraumeni syndrome



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Lynch syndrome

Table 2. LS surveillance recommendations

Site	Technique	Age (years)	Interval (years)
Colorectum	Colonoscopy	• *MLH1/MSH2*: 25[a,b] • *MSH6/PMS2*: 35	1–2
Uterus	TV US Endometrial biopsy	30–35	1
Ovaries	CA 125 + TV US	30–35	1
Stomach	UGI endoscopy[c] Consider testing *Helicobacter pylori*	30–35	1–3
Other LS-associated cancers	None[d]		

[a]Or 5 years before the earliest CRC, if diagnosis <25 years.
[b]Consider later age for *MSH6* carriers.
[c]Consider in high-incidence countries or family history of gastric cancer.
[d]Consider pancreatic/urinary tract cancer surveillance if family history.
CA 125, cancer antigen 125; CRC, colorectal cancer; LS, Lynch syndrome; TV, transvaginal; UGI, upper gastrointestinal; US, ultrasound.

FAP

Table 3. Classical FAP surveillance guidelines

Site	Technique	Age (years)	Interval (years)
Colorectal	Sigmoidoscopy and colonoscopy (if adenomas)[a]	12–15	1–2
Duodenum	Gastroduodenal endoscopy (front and side view)	25–30	1–5[b]
Thyroid	Cervical US or cervical palpation	25–30	1
Liver	Abdominal US Serum alpha foetoprotein	0.5[c]	1
Desmoids	CT/MRI[d]		

[a]If adenomas are found at sigmoidoscopy, carry out annual colonoscopies until colectomy.
[b]Periodicity according to the Spigelman stage.
[c]Until age 7 years.
[d]If family history or symptoms. Periodicity is not well-established.
CT, computed tomography; FAP, familial adenomatous polyposis; MRI, magnetic resonance imaging; US, ultrasound.

Stjepanovic N, et al. *Ann Oncol*. 2019 Oct 1;30(10):1558-1571.

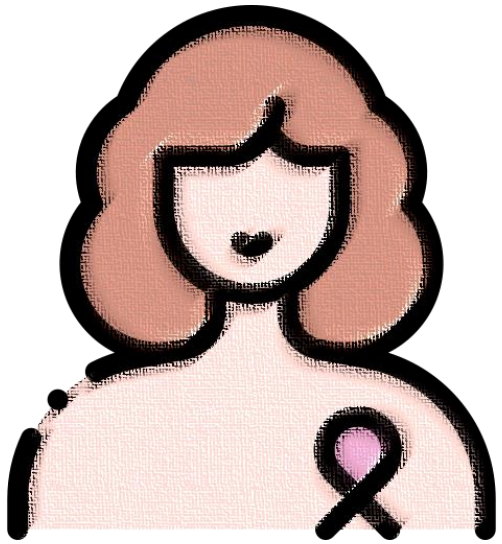
CRC screening

USPSTF 2021

Adults aged 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years.	A
Adults aged 45 to 49 years	The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years.	B
Adults aged 76 to 85 years	The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences.	C

	NCCN 2024	USPSTF 2021	ACS 2024
Age (yrs)	**45-75**	**45-75**	**45-75**
High-sensitivity gFOBT Or FIT	Q1yr	Q1yr	Q1yr
(mt)-sDNA-FIT	Q3yr	Q1-3yr	Q3yr
Colonoscopy	Q10yr	Q10yr	Q10yr
CT colonography	Q5yr	Q5yr	Q5yr
Flexible sigmoidoscopy	Q5-10yr	Q5yr	Q5yr

In case of negative or no polyps



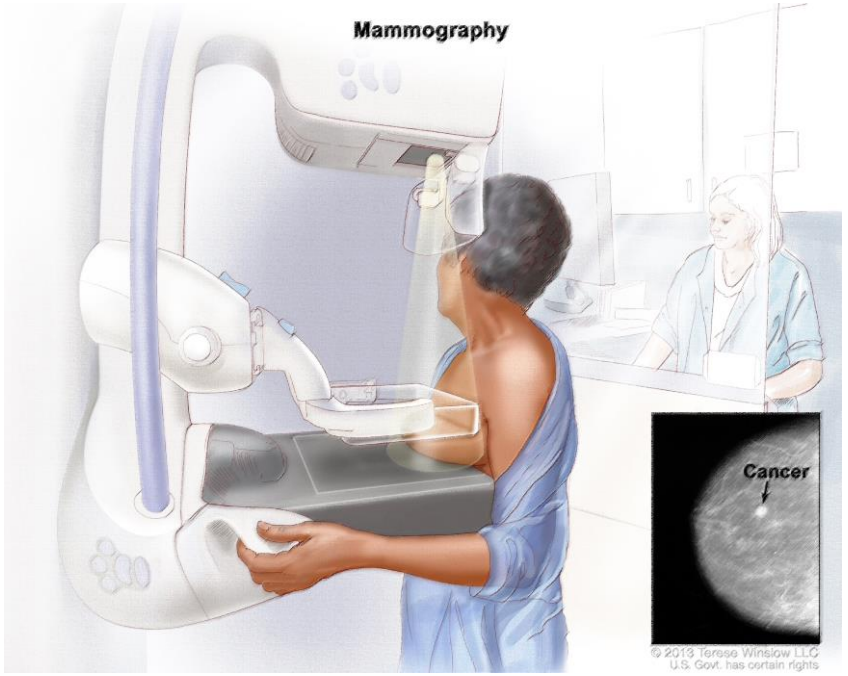
Breast cancer

Risk factors

- Female
- Ageing
- Family history of breast cancer at a young age
- Hormonal factors:
  - Early menarche <12 yrs
  - late menopause >55 yrs
  - Nulliparity or older age at 1st live childbirth >30 yrs
  - Postmenopausal hormonal replacement
- Previous exposure to therapeutic chest wall irradiation
- Benign proliferative breast disease
- Increased mammographic breast density
- Genetic mutation such as *BRCA1/2* genes
- Lifestyles: Obesity, alcohol consumption

Breast cancer screening

- Modalities:
  - Clinical encounters
    - Breast awareness
    - Breast cancer risk assessment
    - Breast self examination (BSE)
    - Clinical breast examination (CBE)
  - Breast imaging:
    - Mammography
    - Ultrasonography of breast
    - Breast MRI

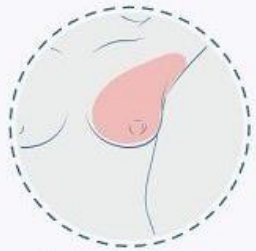


Breast Self Examination Steps

Check your breast once a month, 2-3 days after periods

PACE HOSPITALS

State-of-the-art Liver and Kidney Transplant Centre

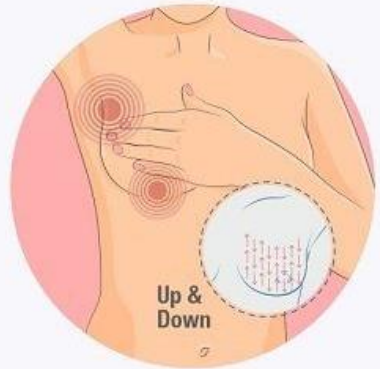


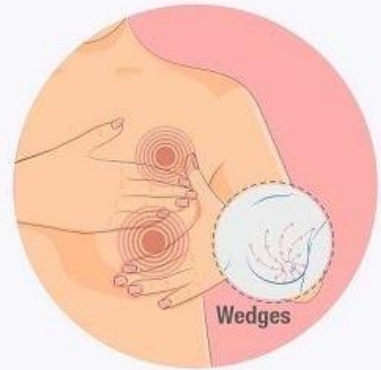
Stand in front of a mirror & look for any changes in..

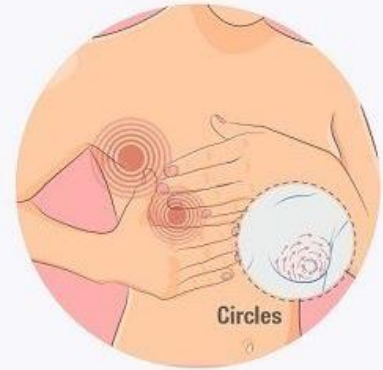
the look, feel or size of the breast, breast swelling

dimpling or puckering of the skin

change in the look or feel of the nipple or discharge from nipple







Examine Breast & Armpit with Raised Arms.
Use Fingerpads with Massage Oil or Shower Gel

Hyderabad, Telangana, India 040 4848 6868 pacehospital.com

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Breast Cancer Screening and Diagnosis

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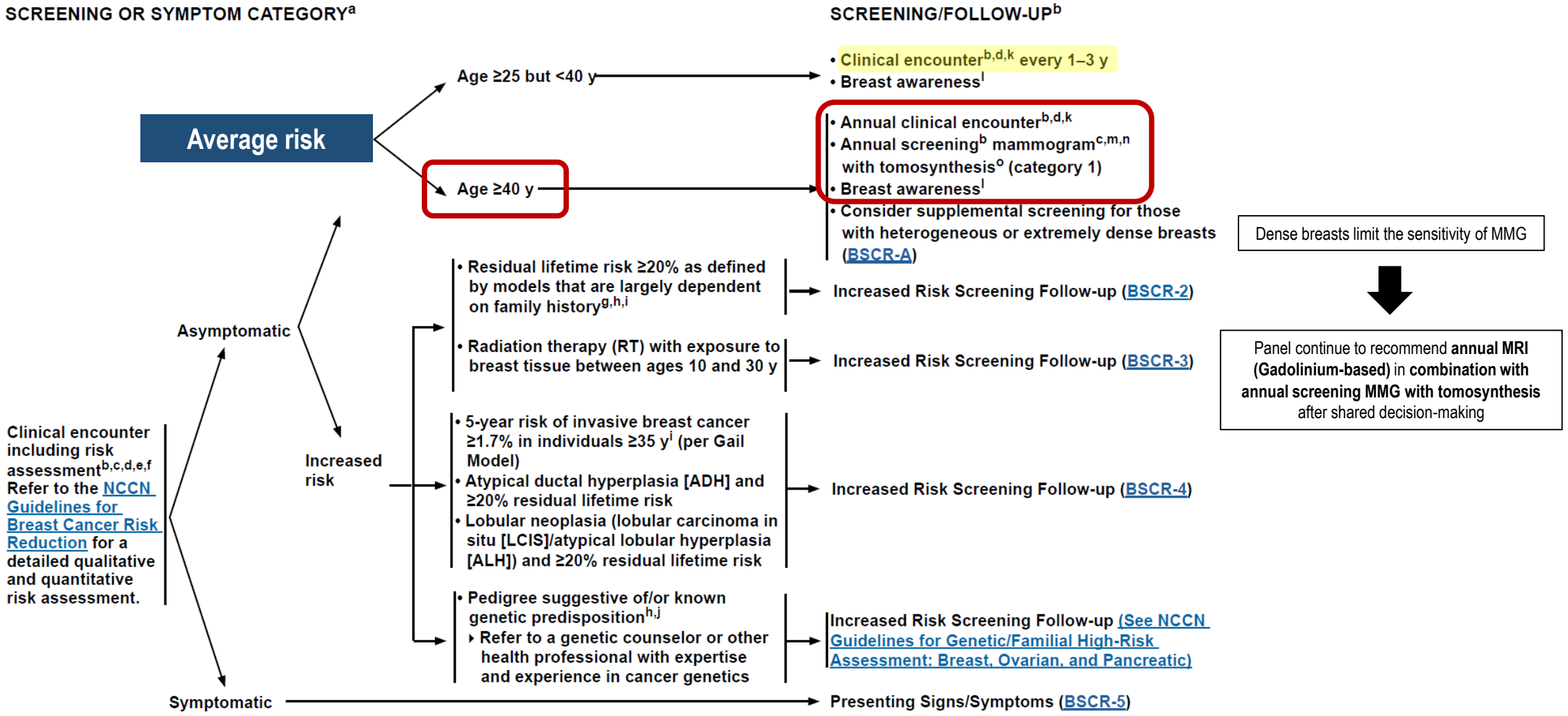

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Breast Cancer Screening and Diagnosis

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SCREENING OR SYMPTOM CATEGORY[a]	SCREENING/FOLLOW-UP

Increased risk
 	
Residual lifetime risk ≥20% as defined by models that are largely dependent on family history[g,h,i]
	• Clinical encounter[b,d,k] every 6–12 mo
	  ▸ To begin when identified as being at increased risk
	  ▸ Consider referral to a genetic counselor or other health professional with expertise and experience in cancer genetics, if not already done
	  ▸ Consider referral to a breast specialist as appropriate
	• Annual screening[b] mammogram[c,m] with tomosynthesis[o]
	  ▸ To begin 10 years prior to when the youngest family member was diagnosed with breast cancer, or after risk assessment if determined to be at high risk, not prior to age 30 y,[p] or begin at age 40 y (whichever comes first)
	• Annual breast MRI[q,r] with and without contrast
	  ▸ Consider contrast-enhanced mammography (CEM)[b] or molecular breast imaging (MBI)[b] for those who qualify for but cannot undergo MRI. Whole breast ultrasound[b] may be done if contrast-enhanced imaging or functional imaging is not available/accessible
	  ▸ To begin 10 years prior to when the youngest family member was diagnosed with breast cancer, not prior to age 25 y,[s] or after risk assessment if determined to be at high risk, or begin at age 40 y (whichever comes first)
	• Consider risk reduction strategies (see NCCN Guidelines for Breast Cancer Risk Reduction)
	• Breast awareness[l]

[a] For individuals with a prior history of breast cancer, please refer to the NCCN Guidelines for Breast Cancer - Surveillance Section.
[b] Breast Screening Considerations (BSCR-A).
[c] Medicare and insurers allow the individual direct access to scheduling for screening mammography.
[d] At minimum, medical and family history should be reviewed and clinical encounter should encompass ongoing risk assessment (by age 25), risk reduction counseling, and preferably a CBE even in individuals who are asymptomatic when feasible.
[g] Individuals with a residual lifetime risk of 15%–20% may be considered for supplemental screening on an individual basis, depending on risk factors.
[h] Risk models that are largely dependent on family history (eg, BRCAPRO, Tyrer-Cuzick, BOADICEA/CanRisk). See NCCN Guidelines for Breast Cancer Risk Reduction. Ongoing validation studies using the PRS polygenic risk score are underway, including those with diverse populations. At the present time, PRS would best be utilized in the setting of a clinical trial. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
[i] See Comparison of Predictive Models for Risk Assessment (NCCN Guidelines for Breast Cancer Risk Reduction).
[k] Rationale for recommending clinical encounter is to maximize earliest detection of breast cancers and assure ongoing risk assessment, particularly in regions where mammographic screening may not be accessible. Randomized trials comparing incremental CBE versus mammographic screening have not been performed.
[l] Individuals should be familiar with their breasts and promptly report changes to their health care provider. See Symptomatic During Clinical Encounter, Presenting Signs and Symptoms (BSCR-5).
[m] Mammographic Evaluation (BSCR-18).
[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.
[p] Consider mammogram beginning at age 25 years on a case by case basis depending on family history.
[q] High-quality breast MRI requires a dedicated breast coil, access to biopsy under MRI guidance, experienced radiologists in breast MRI, and regional availability. MRI should be correlated with other breast imaging modalities.
[r] Many experts recommend alternating the mammogram and breast MRI with and without contrast every 6 months. While there is limited data to support this approach, the presumption is that this may lead to earlier identification of cancer.
[s] Except in rare circumstances of a family history of very early-onset breast cancers before age 30 years.

SCREENING OR SYMPTOM CATEGORY[a] **SCREENING/FOLLOW-UP**

Increased risk

RT with exposure to breast tissue between ages 10 and 30 y[t]

RT

Current age <25 y →

- Annual clinical encounter[b,d,k]
  - Begin 8 y after RT
- Breast awareness[l]

Current age ≥25 y →

- Clinical encounter[b,d,k] every 6–12 mo
  - Begin 8 y after RT
- Annual screening[b] mammogram[c,m] with tomosynthesis[o]
  - Begin 8 y after RT but not prior to age 25 y
- Annual breast MRI[q,r] with and without contrast
  - Consider CEM[b] or MBI[b] for those who qualify for but cannot undergo MRI. Whole breast ultrasound[b] may be done if contrast-enhanced imaging or functional imaging is not available/accessible
  - Begin 8 y after RT but not prior to age 25 y
- Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
- Breast awareness[l]

[a] For individuals with a prior history of breast cancer, please refer to the NCCN Guidelines for Breast Cancer - Surveillance Section.
[b] Breast Screening Considerations (BSCR-A).
[c] Medicare and insurers allow the individual direct access to scheduling for screening mammography.
[d] At minimum, medical and family history should be reviewed and clinical encounter should encompass ongoing risk assessment (by age 25), risk reduction counseling, and preferably a CBE even in individuals who are asymptomatic when feasible.
[k] Rationale for recommending clinical encounter is to maximize earliest detection of breast cancers and assure ongoing risk assessment, particularly in regions where mammographic screening may not be accessible. Randomized trials comparing incremental CBE versus mammographic screening have not been performed.
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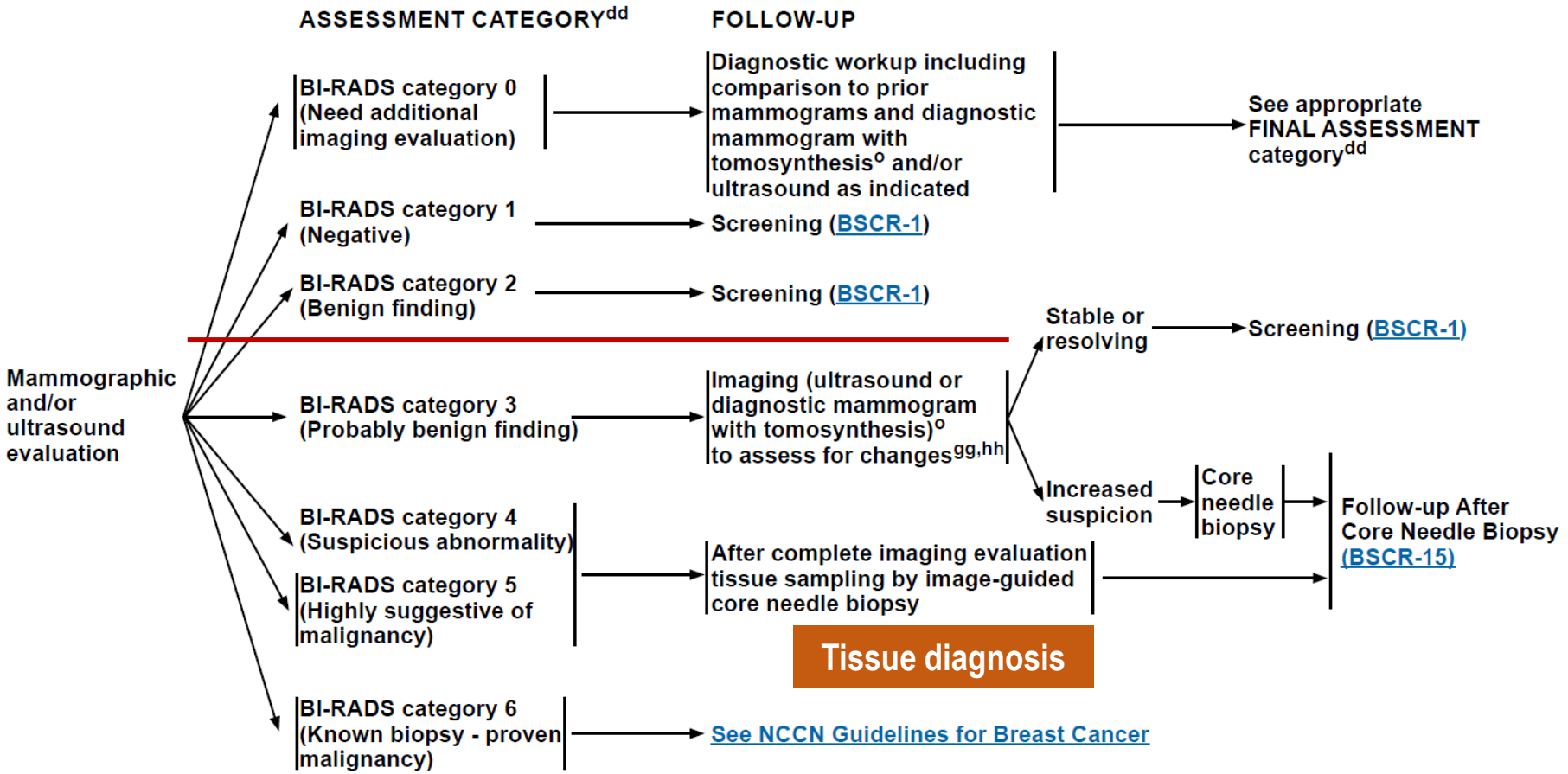
[m] Mammographic Evaluation (BSCR-18).
[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.
[q] High-quality breast MRI requires a dedicated breast coil, access to biopsy under MRI guidance, experienced radiologists in breast MRI, and regional availability. MRI should be correlated with other breast imaging modalities.
[r] Many experts recommend alternating the mammogram and breast MRI with and without contrast every 6 months. While there is limited data to support this approach, the presumption is that this may lead to earlier identification of cancer.
[t] Consider screening on a case by case basis for those who received RT with exposure to breast tissue outside of this age range. While screening mammography would not be done under the age of 25, breast MRI may be considered.

NCCN Guidelines Version 2.2024
Breast Cancer Screening and Diagnosis



[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.
[dd] Assessment Category Definitions (BSCR-C).
[gg] Imaging modality would depend on original imaging. Probably benign findings are typically monitored at 6, 12, and 24 months.
[hh] If a return visit is uncertain or there is strong patient preference, may include biopsy.

Breast cancer screening

Age (yrs)	NCCN 2024		Stop
≥25 - <40 yrs	Clinical encounters	Q1-3yr	-
≥40 yrs	Clinical encounters Mammogram	Q1yr	Consider severe comorbid conditions limiting life expectancy (eg, ≤10 years)
	ACS 2023		**Stop**
40-44 yrs	Mammogram (option)	Q1yr	As long as women is in good health + life expectancy ≥10 yrs
45-54 yrs	Mammogram	Q1yr	
≥55 yrs	Mammogram	Q1-2yrs	
	USPSTF 2024		**Stop**
40-74 yrs	Mammogram	Q2yr	≥75 yrs

Add **MRI breast** typically start at **30 yrs**: (ACS 2023)
- Lifetime risk of BC 20-25% (NCCN 2024 risk≥20%)
- Known ***BRCA1 or BRCA2 mutation***
- Have first-degree relative (**FDR**) **with *BRCA1 or BRCA2 mutation*** (no had genetic testing themselves)
- **RT at chest before 30 yrs** (NCCN 2024 current age ≥25 yrs)
- Have or have FDR with Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome

USPSTF 2024: **Insufficient evidence** to assess the balance of benefits and harms of additional **screening MRI or US in women with dense breasts** following an otherwise **negative screening MMG**

Breast cancer screening

Age (yrs)	NCI 2017		Stop
20-39 yrs	SBE CBE	Q1mo Q3yrs	≥70 yrs (case by case)
40-69 yrs	Regular SBE CBE Mammogram (add US if dense breasts)	- Q1yr Q1-2yrs	

NCCN Guidelines Version 2.2025
Hereditary Cancer Testing Criteria

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST CANCER SUSCEPTIBILITY GENES

(Genes such as *BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11,* and *TP53*. See GENE-A)[a,f,g,h,i]

Testing is clinically indicated in the following scenarios:

- See General Testing Criteria on CRIT-1.
- Personal history of breast cancer with specific features:
  - ≤50 y
  - Any age:
    - ◊ Treatment indications
      - – To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting[j,k] (NCCN Guidelines for Breast Cancer)
      - – To aid in adjuvant treatment decisions with olaparib for high-risk,[l] HER2-negative breast cancer[j]
    - ◊ Pathology/histology
      - – Triple-negative breast cancer
      - – Multiple primary breast cancers (synchronous or metachronous)[m]
      - – Lobular breast cancer with personal or family history of diffuse gastric cancer (NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric)
    - ◊ Male breast cancer
    - ◊ Ancestry: Ashkenazi Jewish
  - Any age (continued):
    - ◊ Family history[n]
      - – ≥1 close blood relative[o] with ANY:
        - ▪ breast cancer at age ≤50 y
        - ▪ male breast cancer
        - ▪ ovarian cancer
        - ▪ pancreatic cancer
        - ▪ prostate cancer with metastatic,[p] or high- or very-high-risk group (Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
      - – ≥3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer
- Family history criteria: unaffected; or affected but does not meet above criteria
  - Individual with a first- or second-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making).[q]
  - Individuals who have a probability >5% of a *BRCA1/2* P/LP variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk).[r]

Criteria met → GENE-1

If testing criteria not met, consider testing criteria for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

Cervical cancer

Updated 2 Aug 2024

NIH NATIONAL CANCER INSTITUTE

Cervical cancer

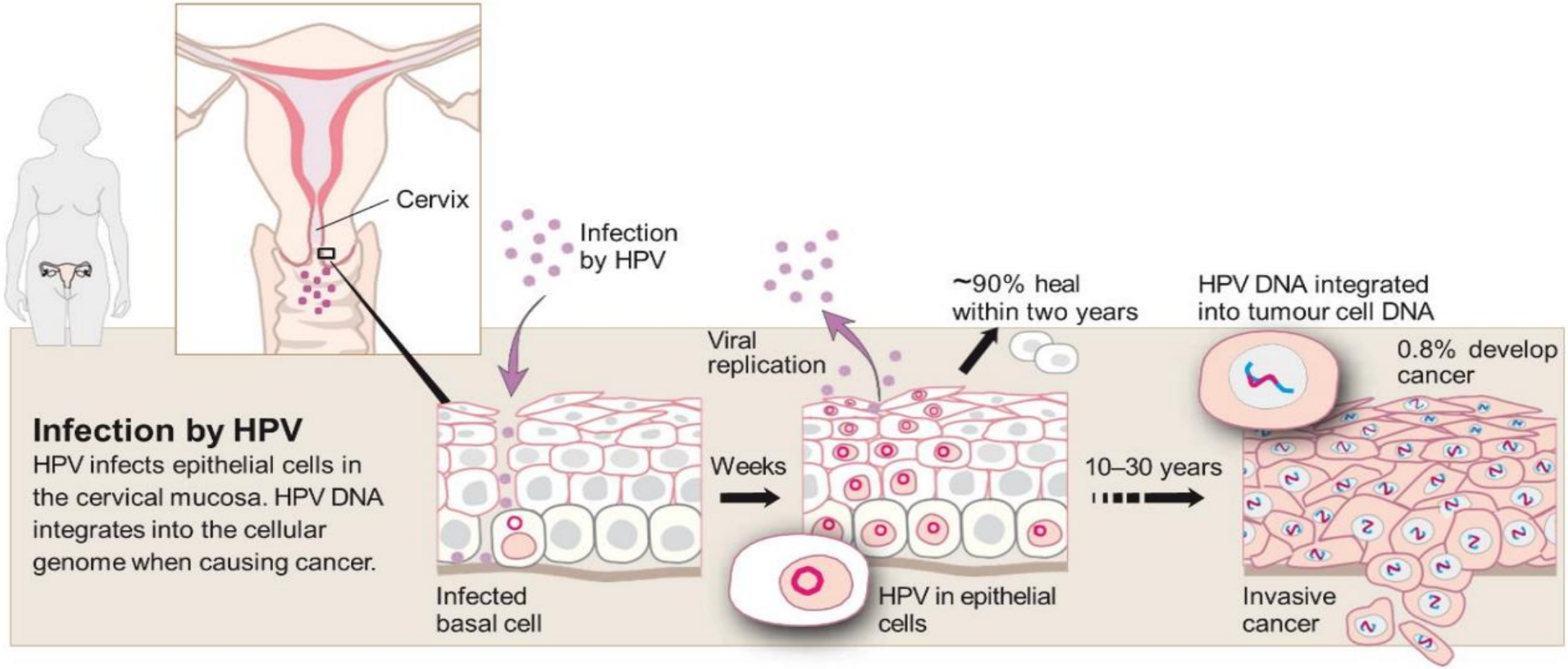
- Long-lasting (persistent) infection with high-risk types of human papillomavirus (HPV)
- **HPV 16** and **18** → cause 70% of cervical cancer worldwide
- Nearly all people who are sexually active will become infected with HPV at some point in their lives
- Factors that increase risk that an HPV infection → will cause cancer
  - Immunocompromised
  - Smoker or 2nd hand smoker
  - Reproductive factors: not well understood
    - Oral contraceptives
    - Multiparity
  - Obesity
    - Lower detection of precancer

Classification of HPV Types Based on Cervical Cancer Risk

High risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82
Probable high risk	25, 53, 56
Low risk	6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81

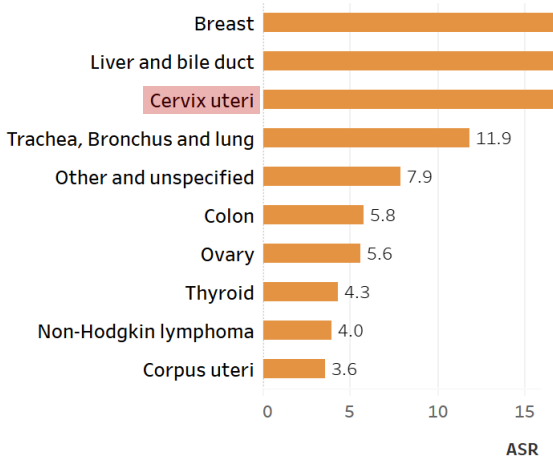
Muñoz N, et al. *N Engl J Med*. 2003;348(6):518-527.

Pathogenesis



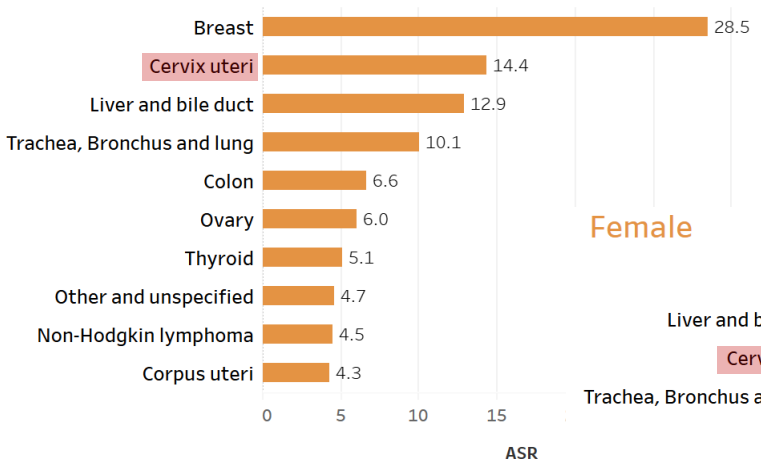
NCI 2005

Female



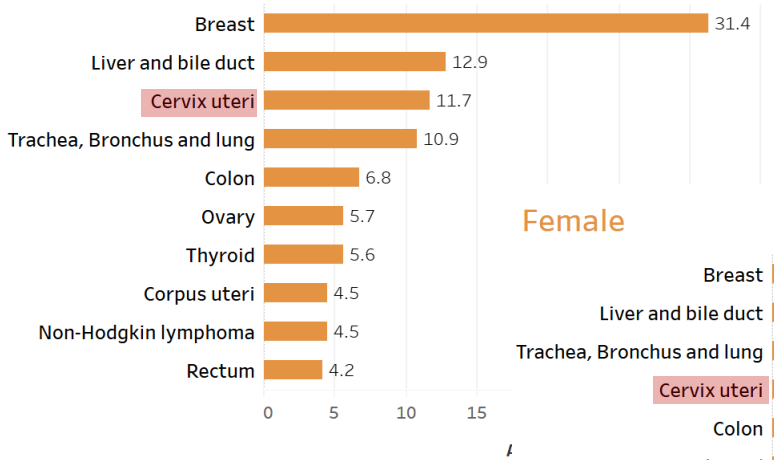
NCI 2011

Female



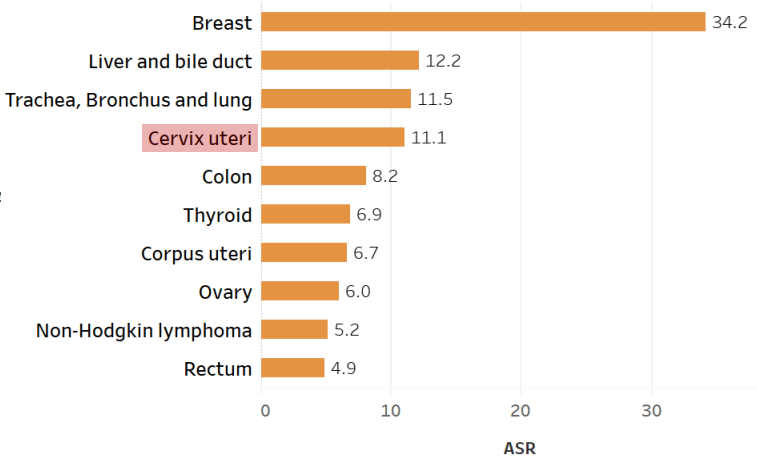
NCI 2014

Female



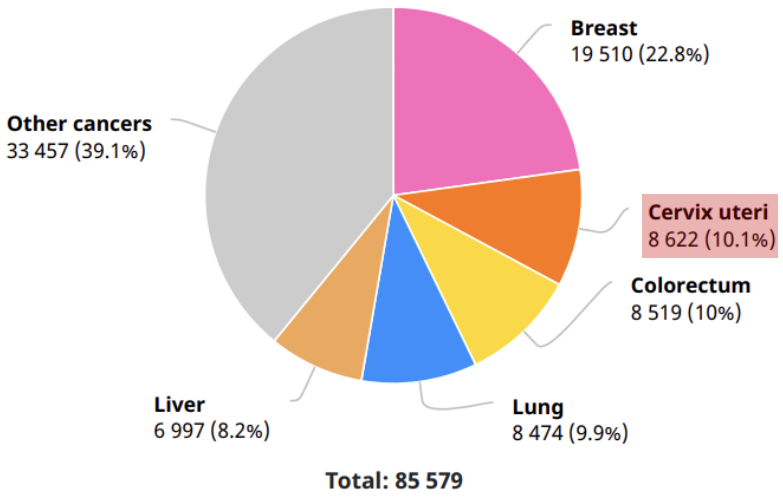
NCI 2017

Female



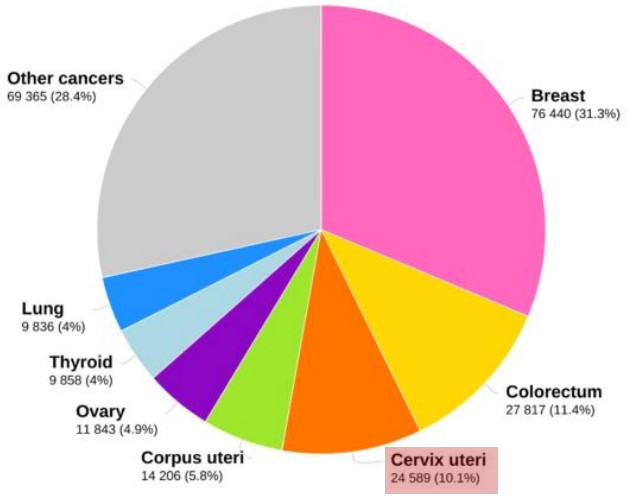
Globocan 2018

Females



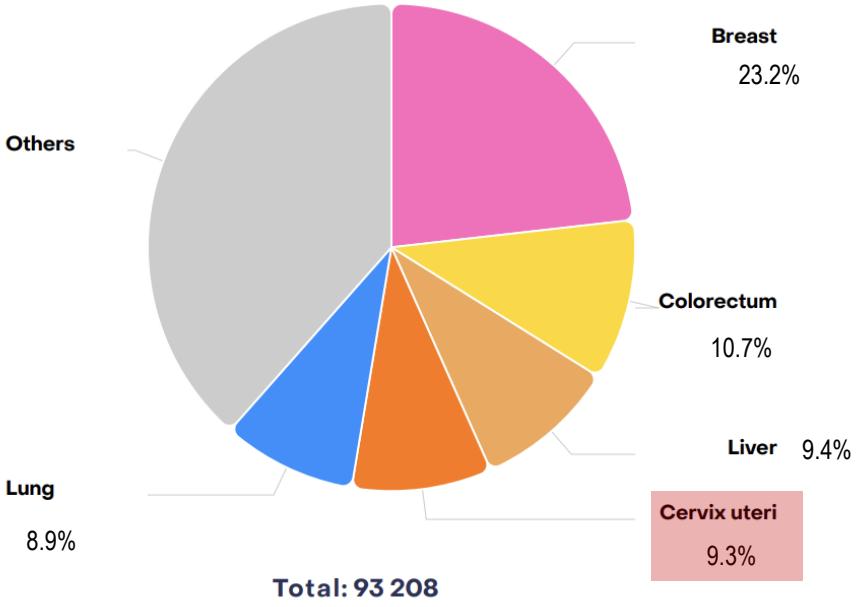
Total: 85 579

Globocan 2020



Total : 243 954

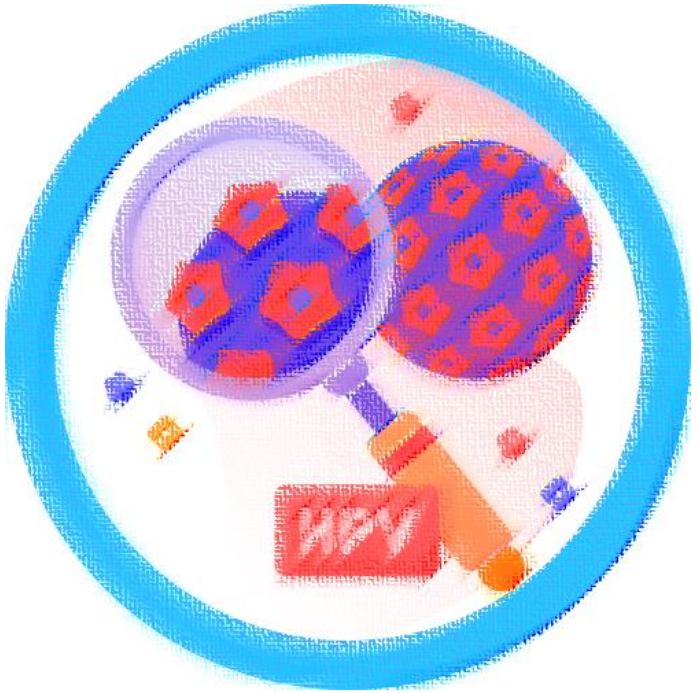
Globocan 2022



Total: 93 208

Cervical cancer screening

- Modalities:
  - PAP smear
  - HPV DNA test
    - Cobas HPV: 16 and 18
    - Onclarity HPV: 16, 18, 45, 31, 51, 52, 33+58, 35+39+68, and 56+59+66
  - Cotest: PAP smear and HPV DNA test



Cervical cancer screening

	ACS 2020		Stop
25-65 yrs	PAP (acceptable) High risk HPV test (preferred) Cotesting	Q3yrs Q5yrs Q5yrs	>65 yrs with no history of CIN grade2 or more severe diagnosis within past 25 yrs + adequate negative prior screening in the 10-yr period
HPV vaccinated	Follow age-specific screening recommendation		
After hysterectomy	Individuals without a cervix and without history of CIN2 or more aggressive diagnosis in past 25 yrs or cervical cancer ever should not be screened		

	USPSTF 2018		Stop
21-29 yrs	PAP	Q3yrs	>65 yrs with adequate prior screening and are not otherwise at high risk for cervical cancer (e.g. high grade precancerous lesions, immunocompromised host)
30-65 yrs	PAP High risk HPV test Cotesting	Q3yrs Q5yrs Q5yrs	

1.US Preventive Services Task Force. *JAMA*. 2018 Aug 21;320(7):674-686. 2. Fontham ETH, et al. *CA Cancer J Clin*. 2020 Sep;70(5):321-346.

Cervical cancer screening
NCI of Thailand 2018

	การตรวจเซลล์วิทยา * (Pap smear หรือ liquid-based cytology)	การตรวจทางเซลล์วิทยา + HPV DNA testing
อายุที่เริ่มตรวจ	30 ปี (อาจเริ่มตรวจได้ตั้งแต่ 25 ปี ตามความเหมาะสม)	30 ปี (อาจเริ่มตรวจได้ตั้งแต่ 25 ปี ตามความเหมาะสม)
ความถี่	ทุก 2-3 ปี	ทุก 3-5 ปี
อายุที่หยุดตรวจ	> 65 ปี ถ้าผลตรวจไม่พบความผิดปกติติดต่อกัน 3 ครั้ง	> 65 ปี ถ้าผลตรวจไม่พบความผิดปกติติดต่อกัน 3 ครั้ง
สตรีที่ตัดมดลูกพร้อมกับปากมดลูกออกแล้วและไม่มีประวัติเป็น CIN หรือมะเร็งปากมดลูก ไม่จำเป็นต้องตรวจคัดกรอง		
* ในพื้นที่ที่การดำเนินการตรวจคัดกรองทางเซลล์วิทยาไม่สามารถเชื่อมโยงกับการรักษาได้อย่างมีประสิทธิผล และ/หรือมีความครอบคลุมต่ำกว่าเป้าหมาย การตรวจคัดกรองโดยวิธี VIA และรักษาโดยวิธีจี้เย็น (อาจทำโดยพยาบาลวิชาชีพที่ผ่านการฝึกอบรมและนิเทศงาน) เป็นอีกทางเลือกหนึ่งของการตรวจคัดกรองมะเร็งปากมดลูก โดยทำในสตรีช่วงอายุ 30-45 ปี ตรวจทุก 5 ปี ถ้าอายุ > 45 ปี ให้ตรวจคัดกรองด้วยการตรวจทางเซลล์วิทยา		

Case study

Case study

- A **52-year-old** Thai healthy single female without underlying medical conditions
- History of **smoking 20 pack-year**
- **Family history of her father diagnosed with colon cancer at age of 60**
- She came to your hospital for consultation due to concerns about cancer
- Upon performing an initial physical examination, no abnormalities were found

What is your recommendation?

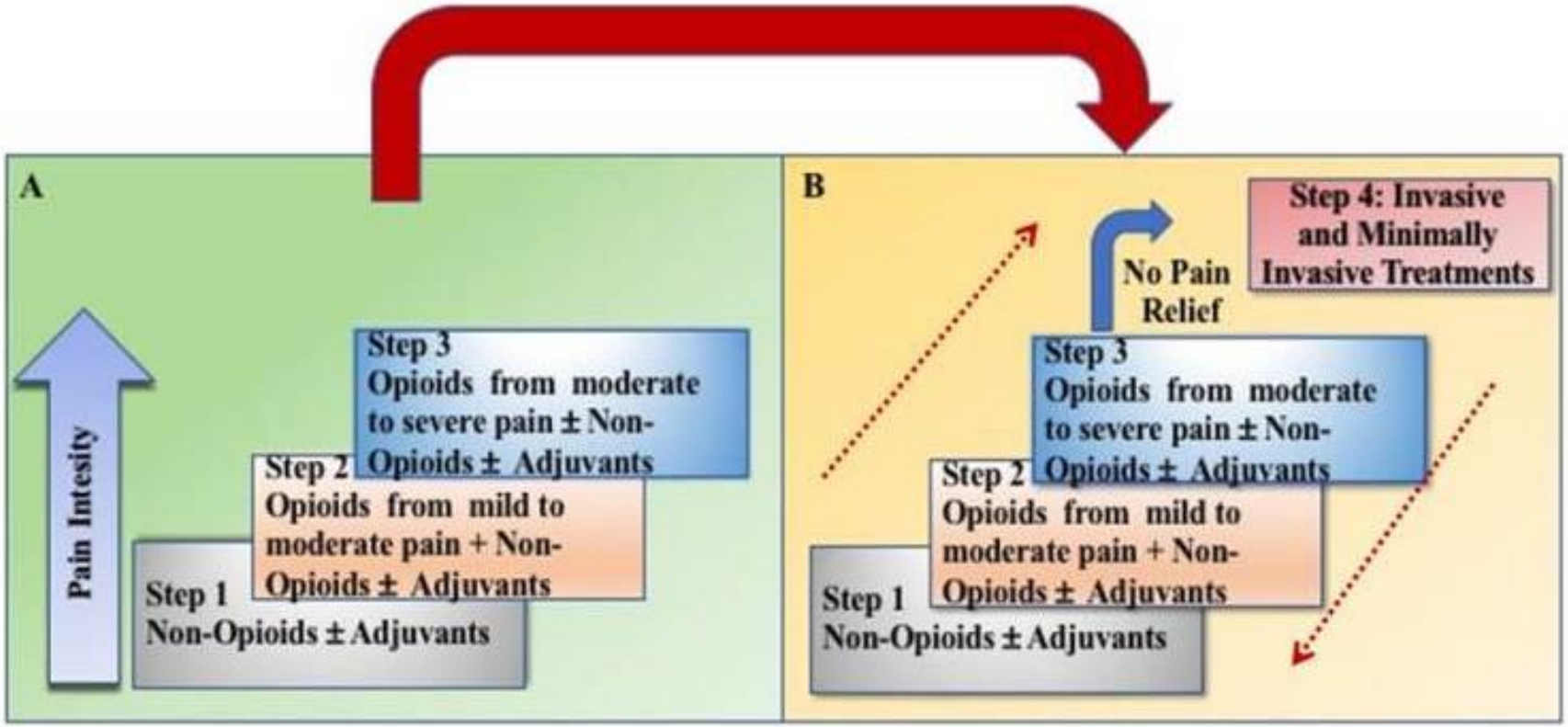
Case study

- A **42-year-old** Thai healthy single female, non-smoker
- She was diagnosed with **FAP and underwent a proctocolectomy at age of 25**
- **She completed her HPV vaccination at age of 20**
- She has no family of breast cancer
- She came to your hospital for a consultation about cancer screening
- Upon performing an initial physical examination, no abnormalities were found

What is your recommendation?

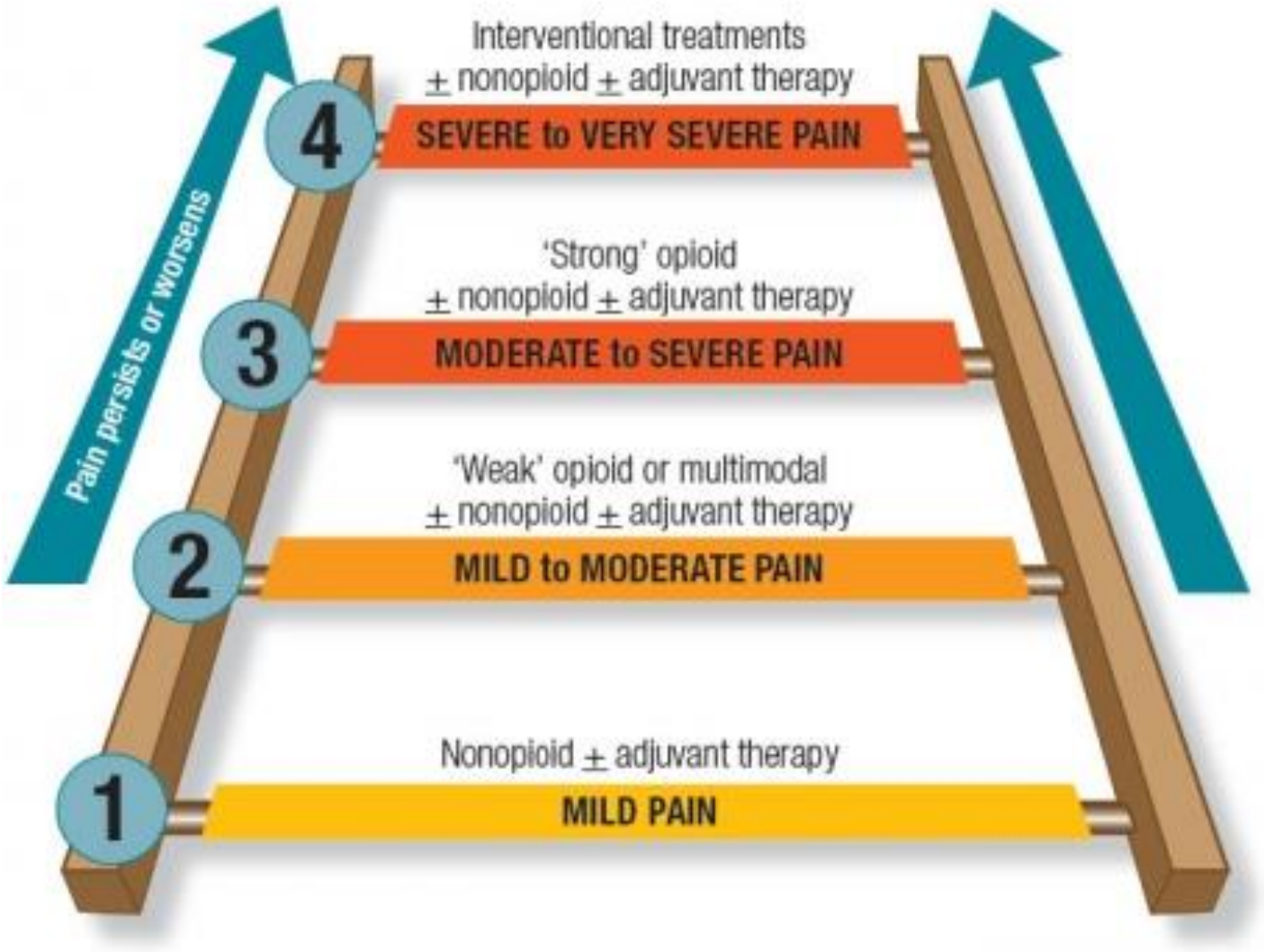
Pain management

In cancer patients



Transition from the original WHO three-step analgesic ladder (**A**) to the revised WHO fourth-step form (**B**). The additional step 4 is an "interventional" step and includes invasive and minimally invasive techniques. This updated WHO ladder provides a bidirectional approach.

Anekar AA, Hendrix JM, Cascella M. WHO Analgesic Ladder. [Updated 2023 Apr 23].



Nerve block, Neurolytic block

Morphine, Kapanol, Oxycodone, Hydromorphone, Fentanyl

Codeine, Tramadol

Multimodal (Opioids + non-opioids)
→ Lower cumulative dose of opioid
→ Similar efficacy with opioid monotherapy
→ Reduce opioid S/E

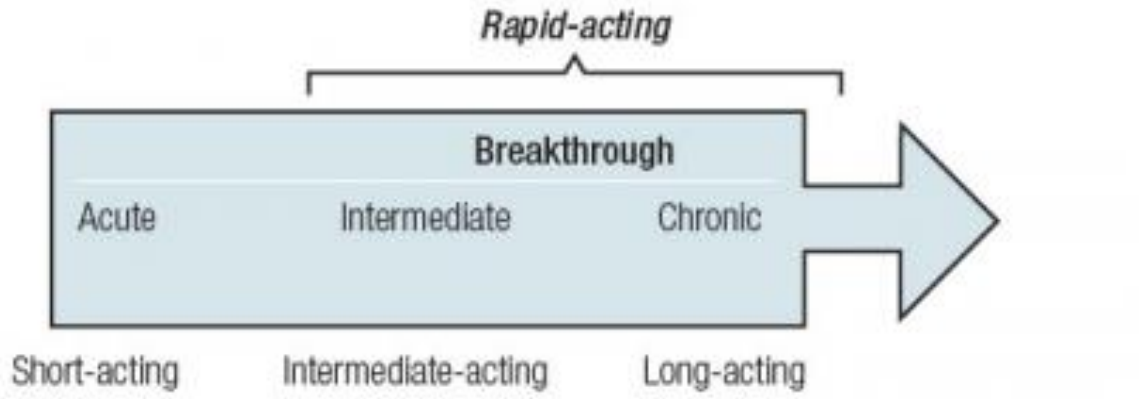
ASA, acetaminophen, NSAIDs

Adjuvant therapy
Bone metastasis: bisphosphonate, denosumab
Antipsychotic, Antidepressant, Anxiolytics, Anticonvulsants, corticosteroids

Pergolizzi J, Raffa R. The WHO Pain Ladder: Do We Need Another Step?. Pract Pain Manag. 2014;14(1).

Table 2. List of FDA-Approved Fixed-Dose Combination Products

- Codeine combined with acetaminophen or aspirin
- Dihydrocodeine combined with acetaminophen or aspirin
- Hydrocodone plus acetaminophen or aspirin or ibuprofen
- Oxycodone combined with acetaminophen or aspirin or ibuprofen
- Pentazocine combined with acetaminophen
- Tramadol plus acetaminophen



Pergolizzi J, Raffa R. The WHO Pain Ladder: Do We Need Another Step?. Pract Pain Manag. 2014;14(1).

Clinical significance

- **Oral dosing** of drugs whenever possible
- **Around-the-clock** rather than on-demand
- Prescribed according to **pain intensity**
  - As evaluated by a scale of pain severity
- Individualized therapy (including dosing)
- Proper **adherence**

Anekar AA, Hendrix JM, Cascella M. WHO Analgesic Ladder. [Updated 2023 Apr 23].

WHO ladder step I

Non-opioids

- Paracetamol: <4g/day
- NSAIDs: may benefit in bone pain
- ASA

**Ceiling effect: hepatic/renal impairment, GI side effect

**Frailty

WHO ladder step II

Weak opioids

- **Codeine**
  - Max dose: **360 mg/day**
  - Ceiling effect: 300 mg/day

- **Tramadol**
  - Max dose: **400 mg/day**
  - Renal insufficiency (CrCl < 30 ml/min)
    - Q12hrs
    - Dose < 200 mg/day

WHO ladder step III

Strong opioids

Short-acting opioids

- **Morphine IR** (10mg)
  - Starting dose: 5-10 mg
  - Onset 10-30 mins
  - Q4-6hrs
- **Morphine syrup** (2mg/ml)
  - Onset 15-60 mins
  - Q4-6hrs

Immediate-release

- **Morphine injection** (10mg/ml) → not recommend IM (painful, variable absorption)
  - Onset 5-10 mins
  - Q2-4hrs

WHO ladder step III

Strong opioids

Long-acting opioids

- **MST** (10,30 mg)
  - Starting dose: 10-15 mg
  - Onset 3-4 hrs
  - Q8-12hrs

Do not crush or break!!!

- **Hydromorphone**
  - Starting dose: 3 mg
  - Onset 3-4 hrs
  - Q8-12hrs

Do not crush or break!!!

- **Kapanol** (20, 50 mg)
  - Onset 3-4 hrs
  - Q12-24hrs

NG feed is acceptable

Extended-release

- **Oxycodone**
  - Starting dose: 2.5-5 mg
  - Onset 3-4 hrs
  - Q8-12hrs

Extended-release

Do not crush or break!!!

- **Fentanyl patch** (12.5, 25, 50 mcg)
  - Onset 12-24 hrs
  - Q72hrs

Pain stable

Calculating Morphine Milligram Equivalents (MMEs)

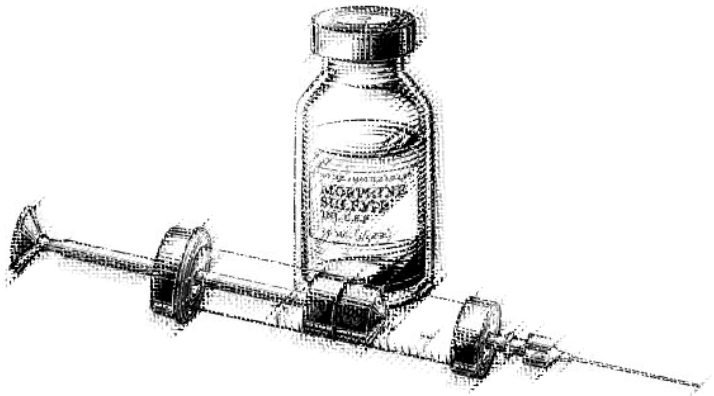
OPIOID PRODUCTS	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1 – 20 mg/day	4
21- 40 mg/day	8
41-60 mg/day	10
61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
*mme = based on morphine milligram equivalency	mcg = microgram
Adapted from "Calculating Total Daily Dose of Opioids For Safer Dosage." Available at: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. Accessed September 9, 2020.	

Convert to Morphine (x conversion factor)

From Morphine to other (÷ conversion factor)

Morphine

- Oral bioavailability 30% (15-50%)
- Metabolized by glucuronyl transferases
  - **Enterohepatic recirculation**
  - **Renal clearance**
- 1/3 Albumin bound



CrCl	Morphine dosage (% of normal)
> 50 ml/min	100%
20-50 ml/min	75%
10-20 ml/min	50%
< 10 ml/min	25%

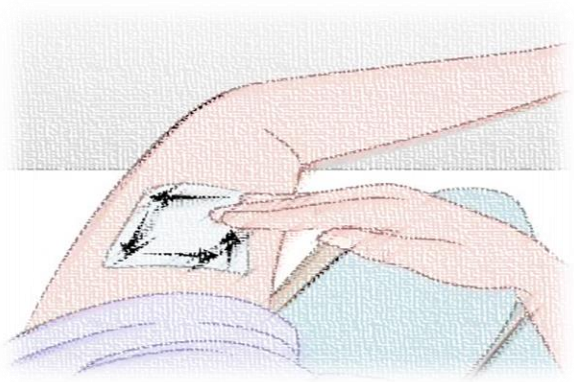
Liver disease	Renal disease
Morphine T1/2 is prolonged with • Altered clotting times • Presence of ascites • History of encephalopathy	Reduced clearance of glucuronide metabolite • Delayed opioid and neurotoxicity
Clinical importance	
• Relatively spared T1/2 • **Start lower than usual doses** • **Maintain intervals** • Avoid sustained release in advanced cirrhosis	• **Dose reduction** • **Extend intervals** • Avoid sustained release • HD (not PD) remove glucuronide metabolites

Hydromorphone

- Moderate bioavailability (50-60%)
- Cross CNS similar to Morphine
- Glucuronidated to Hydromorphone-3-glucuronide (H3G)
  - **Neurotoxin**
  - **Renal clearance**
- Low albumin bound (<40%)

Liver disease	Renal disease
Albumin levels have little influence on unbound drug • Relative sparing of glucuronidation	Reduced clearance of glucuronide metabolite • Increased potential for neurotoxicity
Clinical importance	
• Increased bioavailability > MO • Relatively spared T1/2 • **Start lower than normal doses** • **Maintain intervals**	• **Better tolerated** > MO in renal failure • **Neurotoxicity** • Subject to dialysis

Fentanyl



- Low oral bioavailability
- High 1st pass clearance
- Lipophilic with rapid CNS penetration
- Metabolized by **CYP3A4**
  - **No active metabolites**
  - Steady state clearance limited by **CYP3A4**
  - **Minimally excreted by kidney**
- Albumin bound

Liver disease	Renal disease
• Reduced albumin • Reduced CYP3A4 • Reduced hepatic blood flow	• Uremia inhibit CYP3A4 • Reduced albumin in nephrotic syndrome • Larger volume of distribution?
Clinical importance	
• **Do not use patch** in advanced liver disease • Low doses, watch for delayed toxicity	• **Do not start** with patch • Transdermal absorption may be altered • Dialysis dose not remove fentanyl

- Fentanyl patch dosing based on oral morphine dose:

Oral 24-hour morphine (mg/day)	Fentanyl Sandoz Dose (micrograms/hour)
< 60	12.5*
60-134	25
135- 224	50
225- 314	75
315- 404	100
405- 494	125
495- 584	150
585- 674	175
675- 764	200
765- 854	225
855- 944	250
945- 1034	275
1035- 1124	300

Opioids side effects

- GI
  - Nausea/Vomiting
  - Dry mouth
  - Ileus
  - Constipation
- GU
  - Urinary retention
- Respiratory
  - Respiratory depression
- Skin
  - Pruritus
- Nervous system
  - Somnolence
  - Confusion
  - Abnormal dreams
  - Hallucination
  - Myoclonus

Opioid-induced neurotoxicity

- Prevention:
  - Hydration
  - **Start low, go slow** in elderly, frail, CKD, liver disease
- Opioids antagonist
  - Naloxone starting dose 0.4 mg iv/sc q 2-5 mins

  Use if
  - RR < 8/mins
  - Pinpoint pupil
  - Decreased consciousness with difficulty arousing

Calculating Morphine Milligram Equivalents (MMEs)

OPIOID PRODUCTS	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1 – 20 mg/day	4
21- 40 mg/day	8
41-60 mg/day	10
61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
*mme = based on morphine milligram equivalency	mcg = microgram
Adapted from "Calculating Total Daily Dose of Opioids For Safer Dosage." Available at: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. Accessed September 9, 2020.	

Morphine iv → po (3:1)

Convert to Morphine (x conversion factor)
From Morphine to other (÷ conversion factor)

Opioid (mg/day)	Convert to oral morphine (x conversion factor)	Oral morphine in 24 hrs	Convert to oxycodone (÷ conversion factor)
IV Morphine 20 mg	x 3	60 mg	÷ 1.5 = 40 mg
Fentanyl TTS 50 mcg/hr	x 2.4	120 mg	÷ 1.5 = 80 mg

ตารางที่ 2 ระดับการตอบสนองของความปวดแบบต่างๆ ที่พบได้ในผู้ป่วยมะเร็งต่อยาแก้ปวดกลุ่มต่างๆ

	Nociceptive pain*	NCP**	CIBP**	TIH**	Vis/MBO**
Opioids	ดีมาก	ปานกลาง	ดีมาก	ดี	ดีมาก สำหรับอาการปวดตลอดเวลา ปานกลาง สำหรับอาการปวดบิดเป็นพักๆ
NSAIDs/Coxibs	ดีมาก	ไม่ดี	ดีมาก	ดี	ไม่แนะนำ
Antidepressants TCAs และ SNRIs	น้อย	ดีมาก	ปานกลาง	ไม่แนะนำ	ไม่แนะนำ
Gabapentinoids	น้อย	ดีมาก	ดี	ไม่แนะนำ	ดี สำหรับ visceral hyperalgesia
Carbamazepine	ไม่ดี	ดี สำหรับ paroxysmal sharp shooting pain	น้อย	น้อย ยกเว้นใช้เป็นยากันชัก	ไม่ดี
Bisphosphonates	ไม่ดี	ไม่ดี	ดี เมื่อให้ยาในระยะยาว	ไม่ดี	ไม่ดี
Corticosteroids	ไม่แนะนำ	ดีมาก สำหรับ nerve/spinal cord compression	ปานกลาง	ดีมาก	ดี สำหรับ liver capsule distension

NCP = neuropathic cancer pain
CIBP = Cancer-induced bone pain → Opioids, NSAIDs, Gabapentinoids, bisphosphonate
TIH = Tumor-induced headache
Vis/MBP = Visceral pain/ Malignant bowel obstruction


รับสมัครตั้งแต่วันนี้
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แพทย์ประจำบ้านต่อยอด
อายุรศาสตร์มะเร็งวิทยา
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Good luck with your examination