Medical Notes Powerhouse

The Complete High-Yield Notes for NEET SS & INI SS-ET

Oncology & Haematology

02 VOLUME
of 10 · Volume II · CH 73–123

51	6	10
CHAPTERS	SECTIONS	VOLUME SET

SECTIONS IN THIS VOLUME

- Oncology — Principles
- Solid Tumours
- Haematopoiesis
- Anaemia & Red Cells
- Myeloid & Lymphoid Malignancies
- Transfusion & Haemostasis

Sources Harrison's Principles of Internal Medicine, 22nd Edition

DISCLAIMER

TERMS OF USE · INTELLECTUAL PROPERTY

Educational Use. All content provided herein — including notes, summaries, outlines and other instructional material — is intended strictly for the personal, non-commercial educational use of the registered subscriber. These materials are the intellectual property of **Sushruta Educations LLP** and are protected under applicable copyright and intellectual property laws.

Distribution. Unauthorised distribution, reproduction, sharing or dissemination of any part of this content in any format — physical or digital — is strictly prohibited. Any such action constitutes a violation of the terms of use and may result in legal consequences.

Sources. These materials are independently compiled summaries derived from a range of standard textbooks and academic resources. All rights and acknowledgements remain with the respective original authors and publishers. Copyrighted tables, charts and images commonly found in standard textbooks are deliberately excluded from this compilation to ensure full compliance with copyright regulations.

No Warranty. While diligent efforts have been made to ensure the accuracy, relevance and clarity of the content, Sushruta Educations LLP makes no representations or warranties of any kind, express or implied, about the completeness, accuracy, reliability, suitability or availability of the material for any purpose. Use of this content is at the user's own discretion and risk.

Not a Substitute. This compilation is not a substitute for original academic texts; users are strongly encouraged to refer to those sources for authoritative information. No infringement is intended, and any resemblance to copyrighted material is purely incidental and solely for educational context.

Sushruta Educations LLP

LEARNING · GUIDANCE · SURGERY

Table of Contents

Medical Notes Powerhouse · Volume II · 51 chapters · 6 sections

SECTION I
Oncology — Principles & Approach 8 chapters

73 **Approach to the Patient with Cancer** 1
Epidemiology, Screening, Staging

74 **Symptom Control in Cancer** 5
Practical Management

75 **Prevention & Early Detection** 9
Risk Factors, Screening Programs

76 **Cancer Genetics** 13
Oncogenes, Tumor Suppressors, Familial

77 **Cancer Cell Biology** 18
Hallmarks, Pathways, Targeted Therapy

78 **Principles of Cancer Treatment** 24
Local + Systemic Modalities

79 **Infections in Cancer Patients** 31
Risk Stratification, Management

80 **Oncologic Emergencies** 35
Structural, Metabolic, Treatment-Related

SECTION II
Solid Tumours 20 chapters

81 **Cancer of the Skin** 40
Melanoma, BCC, SCC, Merkel Cell

82 **Head & Neck Cancer** 45
Squamous Cell Cancers + Salivary

83 **Neoplasms of the Lung** 49
NSCLC + SCLC — Diagnosis & Treatment

84 **Breast Cancer** 54
Molecular Subtypes, Targeted Therapy

85 **Upper GI Cancers** 59
Esophagus, Stomach, GIST, MALT

86 **Colorectal Cancer** 63
Adenoma-Carcinoma Sequence, Targeted Rx

87 **Liver & Biliary Tumors** 67
HCC, Cholangiocarcinoma, Gallbladder

88 **Pancreatic Cancer** 71
Ductal AdenoCa — Genomics & Therapy

89 **GI Neuroendocrine Tumors** 75
Carcinoid, Pancreatic NETs

90 **Renal Cell Carcinoma** 80
VHL Pathway, ICI Combos, Targeted Rx

91 **Cancer of Bladder & Urinary Tract** 84
Urothelial Carcinoma

92 **Benign & Malignant Prostate Disease** 88
BPH, Prostatitis, PCa

93 **Testicular Cancer** 93
Germ Cell Tumors — Curable Malignancy

94 **Gynecologic Malignancies** 97
Cervical, Endometrial, Ovarian

95 **Primary & Metastatic CNS Tumors** 101
Gliomas, Meningiomas

96 **Sarcomas & Bone Metastases** 106
Soft Tissue Sarcoma, Bone Mets

97 **Carcinoma of Unknown Primary** 110
CUP — Workup, Favorable Subsets

98 **Paraneoplastic Syndromes** 113
Endocrinologic & Hematologic

99 **Paraneoplastic Neuro & AI Encephalitis** 117
Antibody-Mediated

100 **Cancer Survivorship** 122
Long-Term Impact of Cancer & Treatment

SECTION III
Haematopoiesis & Stem Cells 1 chapters

101 **Hematopoietic Stem Cells** 125
Biology, Niche, Mobilization

SECTION IV
Anaemia & Red Cell Disorders 6 chapters

102 **Iron Deficiency & Hypoproductive Anemias** 128
IDA, ACD, Sideroblastic

103 **Disorders of Hemoglobin** 132
Sickle Cell, Thalassemias

104 **Megaloblastic Anemias** 136
B12 & Folate Deficiency

105 **Hemolytic Anemias** 140
Intrinsic & Extrinsic Red Cell Defects

106 **Anemia Due to Acute Blood Loss** 145
Hemorrhagic Anemia

107 **Bone Marrow Failure Syndromes** 148
Aplastic Anemia & MDS

SECTION V
Myeloid & Lymphoid Malignancies

10 chapters

108 **PV & Other Myeloproliferative Neoplasms** 152
Ph– MPNs

109 **Acute Myeloid Leukemia** 156
Biology, Risk, Induction + Consolidation

110 **Chronic Myeloid Leukemia** 160
BCR::ABL1, TKIs, TFR

111 **Acute Lymphoid Leukemia** 164
ALL — Biology, Subtypes, Treatment

112 **Chronic Lymphocytic Leukemia** 168
CLL — IGHV, FISH, BTKi

113 **Non-Hodgkin's Lymphoma** 173
B + T/NK Subtypes, R-CHOP

114 **Hodgkin's Lymphoma** 178
RS cell, ABVD, BV-AVD, Checkpoint

115 **Less Common Lymphoid & Myeloid Malignancies** 182
HCL, MF, ET

116 **Plasma Cell Disorders** 187
MM, MGUS, Waldenström, POEMS

117 **Amyloidosis** 192
AL, ATTR, AA — Gene silencers + Stabilisers

SECTION VI
Transfusion, Transplant & Haemostasis

6 chapters

118 **Transfusion Therapy & Biology** 196
Components, ABO/Rh, Reactions

119 **Hematopoietic Cell Transplantation** 200
Auto + Allo HSCT, CAR-T

120 **Disorders of Platelets & Vessel Wall** 205
ITP, HIT, TTP, vWD

121 **Coagulation Disorders** 210
Hemophilia, DIC, Vit K, Liver

122 **Arterial & Venous Thrombosis** 214
VTE, Inherited + Acquired

123 **Antiplatelet, Anticoagulant & Fibrinolytic Drugs** 218
DOACs, Heparin

End of Table of Contents

SECTION I

Oncology — Principles & Approach

Cancer epidemiology, genetics, biology, treatment and emergencies

IN THIS SECTION — 8 CHAPTERS

73 **Approach to the Patient with Cancer**
Epidemiology, Screening, Staging

74 **Symptom Control in Cancer**
Practical Management

75 **Prevention & Early Detection**
Risk Factors, Screening Programs

76 **Cancer Genetics**
Oncogenes, Tumor Suppressors, Familial

77 **Cancer Cell Biology**
Hallmarks, Pathways, Targeted Therapy

78 **Principles of Cancer Treatment**
Local + Systemic Modalities

79 **Infections in Cancer Patients**
Risk Stratification, Management

80 **Oncologic Emergencies**
Structural, Metabolic, Treatment-Related

CH 73 · Approach to the Patient with Cancer — Epidemiology, ...

Cancer epidemiology (US + global), patient eval, staging (TNM, Karnofsky, ECOG), response criteria (CR/PR/SD/PD, RECIST), tumor markers, supportive care. NEET SS / INI SS-ET — definitions, numbers, scales high yield.

Magnitude — US

- Source = SEER (NCI Surveillance, Epidemiology, End Results) — 13 sites, ~10% US population.
- **2024 US**: 2.001 M new invasive cases (1.029 M M, 927 k F); **611,720 deaths** (322.8 k M, 288.9 k F).
- **Cancer = 1 in 4 deaths** in US; 2nd leading cause overall.
- **#1 cause of death in <85 y/o** (overtook heart disease).
- Mortality ↓ since 1990–91; incidence steady since 2013.
- 6 of 10 commonest cancers ↑ in incidence by 1–3% recent years.
- **Black:White mortality 2×** for prostate, stomach, uterine corpus.

Table 73.1 — Top US cancers 2024 (incidence)

Rank	Male	%	Female	%
1	Prostate	29	Breast	32
2	Lung	11	Lung	12
3	Colorectal	8	Colorectal	7
4	Bladder	6	Endometrial	7
5	Melanoma	6	Melanoma	4

Table 73.2 — Top US cancer deaths 2024

Rank	Male	Female
1	Lung (20%)	Lung (21%)
2	Prostate (11%)	Breast (15%)
3	Colorectal (9%)	Pancreas (8%)
4	Pancreas (8%)	Colorectal (8%)
5	Liver (6%)	Endometrial (5%)

Risk by Age & Sex

- **Age = single biggest risk factor**. 58% of cases in >65 y/o.
- Incidence 3rd–5th power of age (varies by site).
- **Lifetime risk**: M 40.5%, F 38.9%.

Table 73.3 — Age-stratified cancer risk

Age range	Male	Female
0–49 y	1 in 29	1 in 19
50–59 y	1 in 15	1 in 17
60–69 y	1 in 6	1 in 10
≥70 y	1 in 3	1 in 4

Global — GLOBOCAN 2022 (IARC)

- **~20 M new cases, 9.7 M deaths** worldwide 2022.
- **Lung** = commonest cancer + commonest cancer death worldwide.
- **Breast** = 2nd commonest; 4th cause of death (after lung, stomach, liver).
- Geographic distribution: Asia 50% (pop 59%), Europe 26% (9.6%), N America 13%, S/C America 7%, Africa 6%, Oceania 1%.
- **More developed**: lung (2×), breast (3×), prostate (2.5×), colorectal (3×) ↑.
- **Less developed**: liver (2×), cervix (2×), esophagus (2–3×) ↑.
- Stomach: similar across, but ↑ ↑ in Asia.
- **Africa top 3**: cervix, breast, liver.

✦ MNEMONIC

SAOPULIC *9 modifiable risk factors (1/3 of cancers)*
- **S** — Smoking
- **A** — Alcohol
- **O** — Obesity
- **P** — Physical inactivity
- **U** — Unsafe sex (HPV, HBV)
- **L** — Low fruit/vegetable intake
- **I** — Indoor smoke (household fuels)
- **C** — Contaminated injections + air pollution

Together account for >1/3 of cancers globally.

Patient Evaluation

- **History**: duration → chronicity; PMH → comorbid effect on tx; **social** → carcinogen exposure (occupational, smoking, alcohol).
- **Family hx** → hereditary predisposition + sibling surveillance.
- **ROS** → early metastatic Sx or paraneoplastic syndrome.

Diagnosis

- **Tissue biopsy MANDATORY** — no noninvasive test alone is sufficient.
- **Exception**: HCC diagnosable by CT/MRI showing characteristic **arterial hyperenhancement + venous/delayed washout**.
- **FNA** acceptable only in rare settings (e.g., thyroid nodules).
- Need: histology, grade, invasiveness, molecular markers (e.g., **t(8;14)** = Burkitt), surface markers.
- Unknown primary → search by age/sex/site/histology/markers/family hx — rule out treatable causes first.
- Management = multidisciplinary (med onc, surg onc, rad onc, oncology nurse, pharm, SW, rehab).

Staging

- **Curability 1 / tumor burden**.
- **Clinical staging** = exam + imaging (XR, CT, MRI, isotopic, PET).
- **Pathologic staging** = + intraop palpation, LN/tissue resection, organ inspection + biopsy + histology.
- **Neoadjuvant** tx before definitive surgery → stage prefixed with **y**.
- **TNM** = standard (UICC + AJCC):
- Components:
  - **T1–4** — primary tumor size (higher = larger).
  - **N0/N1** — nodal involvement (some tumors more elaborate).
  - **M0/M1** — distant metastasis absence/presence.
  - Combined into stage **I–IV** (Roman numerals).

Table 73.4 — Other staging systems

Tumor	System
Colorectal	Dukes
Gynecologic	FIGO (Int'l Fed Gynecologists & Obstetricians)
Hodgkin lymphoma	Ann Arbor
Hematologic (leukemia, myeloma, lymphoma)	Other prognostic factors — not TNM

Performance Status

Karnofsky (0–100)

Table 73.5 — Karnofsky Performance Index

KPS	Function
100	Normal, no complaints, no disease evidence
90	Normal activity, minor Sx
80	Normal activity with effort
70	Self-care, no normal work
60	Occasional assistance
50	Considerable assistance + frequent care
40	Disabled, special care
30	Severely disabled, hospitalization
20	Very sick, active support needed
10	Moribund
0	Dead

ECOG (0–5)

Table 73.6 — ECOG Performance Scale

Grade	Description
0	Fully active, no restriction
1	Restricted strenuous, ambulatory + light work
2	Ambulatory, self-care, no work, >50% waking hours up
3	Limited self-care, in bed/chair >50% waking
4	Completely disabled, totally bedridden
5	Dead

- **Poor prognosis**: KPS <70 OR ECOG ≥3 (unless reversible).
- Older + low PS → ↑ stress with tx.
- Geriatric assessment tools advocated for elderly.

♥ NEET SS HIGHLIGHTS

- ♥ **TNM** = UICC + AJCC; T1–4, N0–1, M0–1 → stage I–IV.
- ♥ **Neoadjuvant tx** → staging prefix **y**.
- ♥ **Karnofsky <70 or ECOG ≥3** = poor prognosis.
- ♥ **Dukes** = colorectal; **FIGO** = gyn; **Ann Arbor** = HL.
- ♥ **HCC** = only solid tumor diagnosable without biopsy (CT/MRI pattern).
- ♥ **Burkitt** = t(8;14); **Ki67/PCNA** = proliferation marker.

Treatment Planning

- Curative vs palliative — based on extent + prognosis + pt wishes.
- **Neoadjuvant** chemo ± RT → improves outcome in locally advanced breast, H&N;, lung.
- Tx sequencing (chemo, RT, surgery) — coordinate among onc team.
- Follow standard protocol OR enroll in ongoing clinical research.
- **Ad hoc modifications compromise outcome**.
- Resource: NCI PDQ (Physician Data Query) — standard protocols + research studies.
- Even when not curable — hand-holding, regular exams, time = vital.

Response Assessment

- Periodic physical + repeat imaging tests that were initially abnormal.
- If imaging normal → repeat **biopsy** of previously involved tissue confirms CR pathologically.
- **New symptoms during tx = assume reversible until proven otherwise** (don't blame tumor).
- E.g., jaundice → cholecystitis possible; obstruction → adhesions possible; CNS Sx → drug effect.

Table 73.7 — Response criteria

Term	WHO (bidim.)	RECIST (unidim.)
CR	Disappearance of all disease + biopsy-proven	Same
PR	>50% ↓ sum products of perp diameters	≥30% ↓ sum longest diameters
PD	>25% ↑ sum products OR new lesion	≥20% ↑ sum longest OR new lesion
SD	Neither PR nor PD	Neither PR nor PD

- **Unmeasurable**: bone lesions, lymphangitic lung, diffuse pulmonary infiltrates.
- **MRD (minimal residual disease)**: flow cytometry/genetic detects 1 in 10,000 cells.
- MRD-negative → more durable remission; emerging interventions for MRD+ extend survival.

Tumor Markers

- **NOT diagnostic by themselves** — only for response monitoring once dx established.
- Rising/falling level tracks tumor burden.

Table 73.8 — Tumor markers (high yield)

Marker	Cancer	Also ↑ in
hCG	Gestational trophoblastic, gonadal GCT	Pregnancy
Calcitonin	Medullary thyroid Ca	—
Catecholamines	Pheochromocytoma	—
AFP	HCC, gonadal GCT	Cirrhosis, hepatitis
CEA	Colon, panc, lung, breast, ovary adenoCa	Pancreatitis, hepatitis, IBD, smoking
PAP (prostatic acid phos)	Prostate Ca	Prostatitis, BPH
NSE	SCLC, neuroblastoma	—
LDH	Lymphoma, Ewing sarcoma	Hepatitis, hemolysis
PSA	Prostate Ca	Prostatitis, BPH
Monoclonal Ig	Myeloma	Infection, MGUS
CA-125	Ovarian, some lymphomas	Menses, peritonitis, pregnancy
CA 19-9	Colon, pancreas, breast	Pancreatitis, UC
CD30	HL, ALCL	—
CD25	Hairy cell leukemia, ATLL	HLH

CLINICAL PEARLS

- Tumor marker **cannot diagnose** — only monitor.
- **AFP** = HCC + gonadal GCT (yolk sac); cirrhosis can elevate.
- **hCG** = trophoblastic + non-seminomatous GCT (pure seminoma rarely).
- **CA-125** can ↑ during menses → false +ve in screening.
- **CEA** ↑ in smokers — baseline higher than non-smokers.

Depression in Cancer

- **Incidence ~25%** — higher with debility.
- **Criteria**: dysphoria OR anhedonia ≥ 2 weeks + ≥3 of: appetite, sleep, psychomotor, fatigue, guilt/worthlessness, concentration, suicidal ideation.
- **1st line**: SSRI — fluoxetine 10–20, sertraline 50–150, paroxetine 10–20 mg/d.
- **2nd**: TCA — amitriptyline 50–100, desipramine 75–150 mg/d.
- Trial 4–6 wks for response; continue ≥6 mo after remission.
- Add psychosocial: support groups, psychotherapy, guided imagery.

Long-term Follow-up

- **5-year DFS ≈ cure** for most cancers.
- Typical schedule: q1 mo × 6–12 mo → q2 mo × 1y → q3 mo × 1y → q4 mo → q6 mo → annually.
- Studies (breast, melanoma, lung, colon, lymphoma): **asymptomatic relapses NOT cured more readily** than symptomatic.
- Trend → **less frequent** visits, focus on history + PE.
- Watch for: 2° malignancy, late tx complications (cardiac, pulm, endocrine, fertility).

Supportive Care & End-of-Life

- Credo: "**cure sometimes, extend life often, comfort always**".
- Top causes of cancer death: **infection→circulatory failure, respiratory failure, hepatic, renal failure**.
- **70% develop dyspnea preterminally**.
- Modern guide: "**primum succerrere**" (first hasten to help) > "primum non nocere".
- Hospice/home preferred by many over hospital.
- Advance directives elicited early — review periodically.
- Burnout in oncologists: fatigue, disengagement, ↓ self-fulfillment.

Kübler-Ross stages of adjustment

- **Denial → Isolation → Anger → Bargaining → Depression → Acceptance → Hope.**
- Not all patients go through all stages, or in this order.
- **Damocles syndrome** = ever-present fear of relapse in survivors.

MNEMONIC

DABDA *Kübler-Ross dying stages*
D — Denial
A — Anger
B — Bargaining
D — Depression
A — Acceptance
Isolation + Hope often added. Order/sequence variable.

✎ MCQ CORNER

Q1. 55 y/o man with rectal mass, biopsy = adenoCa. CEA = 25 (high). Best use of CEA here?
A. Diagnose colorectal cancer
B. Stage the tumor
✓ **C. Monitor response + recurrence**
D. Determine resectability
► *Tumor markers are NEVER diagnostic. CEA is used post-dx for monitoring response + recurrence.*

Q2. Patient on neoadjuvant chemo for breast Ca; post-op staging shown as **ypT2N1M0**. The 'y' means:
A. Yes — definitive surgery done
✓ **B. Staging after neoadjuvant therapy**
C. Young age <40
D. Yttrium-labeled imaging
► *Prefix 'y' = stage assessed after neoadjuvant tx. Stage prior to tx written without prefix.*

Q3. Cirrhotic patient, AFP 800; MRI = arterial hyperenhancement + venous washout in 4 cm liver mass. Next step?
A. Mandatory biopsy before treatment
✓ **B. Diagnose HCC and proceed**
C. PET-CT to confirm
D. Repeat AFP in 3 months
► ***HCC is the ONE exception** to mandatory biopsy. Classic dynamic CT/MRI pattern in cirrhotic = diagnostic.*

Q4. Patient with NSCLC: CT shows 30% reduction in sum of longest diameters of target lesions. RECIST response = ?
A. CR
✓ **B. PR**
C. SD
D. PD
► *RECIST PR = ≥30% ↓ sum of longest diameters. CR = total disappearance. PD = ≥20% ↑ or new lesion.*

Q5. Patient with metastatic pancreatic cancer, fully ambulatory but unable to work, up >50% of day. ECOG grade?
A. 1
✓ **B. 2**
C. 3
D. 4
► *ECOG 2 = ambulatory + self-care + no work + >50% waking up. 3 = bed/chair >50%. 4 = bedridden.*

Q6. Commonest cancer + commonest cause of cancer death worldwide (GLOBOCAN 2022)?
A. Breast
✓ **B. Lung**
C. Colorectal
D. Stomach
► *Lung = #1 worldwide for incidence + mortality. Breast = #2 incidence but #4 mortality (after lung, stomach, liver).*

◷ LAST MINUTE REVISION

► **SEER** = US cancer registry; **GLOBOCAN** = WHO/IARC global.
► US 2024: **2 M cases, 612 k deaths**; 1 in 4 deaths.
► **M incidence top 3**: prostate, lung, colorectal.
► **F incidence top 3**: breast, lung, colorectal.
► **Mortality #1 M&F** = lung.
► **Global #1 incidence + mortality** = lung.
► **HCC** = only cancer diagnosable without biopsy.
► **Burkitt** = t(8;14).
► Neoadjuvant tx → stage prefix '**y**'.
► **TNM** = UICC + AJCC.
► **Dukes** = CRC; **FIGO** = gyn; **Ann Arbor** = HL.
► **KPS <70** OR **ECOG ≥3** = poor prognosis.
► **RECIST PR** = ≥30% ↓; **PD** = ≥20% ↑ OR new lesion.
► **AFP** = HCC + GCT; **CA-125** = ovary; **CA 19-9** = pancreas; **CEA** = colon.
► **hCG** = trophoblastic + non-seminomatous GCT.
► **NSE** = SCLC + neuroblastoma.
► Depression in 25% — SSRI 1st line.
► **MRD** sensitivity = 1 in 10,000.
► **9 modifiable risks** = 1/3 of global cancers.
► Top deaths: **infection > resp > hepatic > renal failure**; 70% develop preterminal dyspnea.

◉ UPDATES

◉ **Cancer Statistics 2024 (Siegel et al, CA Cancer J Clin)** — current SEER reference.
◉ **GLOBOCAN 2022 (Bray et al)** — 36 cancers, 185 countries.
◉ **2020 ASCO Antiemetics update (Hesketh)** — current chemo N/V guideline.
◉ **MRD** testing now standard in CML, MM, ALL, AML — intervention extends survival.

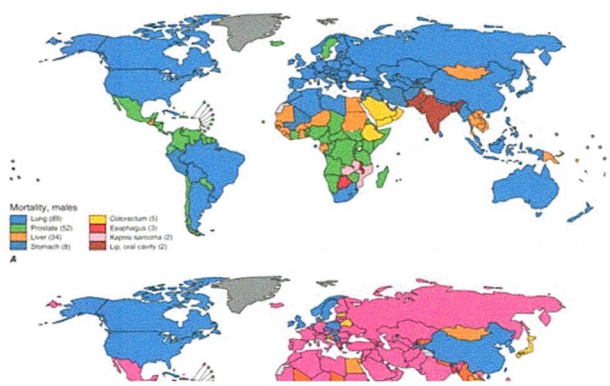


Fig 73.5 — Global maps showing commonest cause of cancer mortality by country, M (top) + F (bottom) (GLOBOCAN 2022).

CH 74 · Symptom Control in Cancer — Practical Management

Cancer symptom assessment via PROs; pain (nociceptive, visceral, neuropathic, incident), CIPN, mucositis, N/V, cachexia, constipation, dyspnea, hot flashes. Olanzapine emerging as multi-symptom drug. NEET SS — drugs + doses high yield.

PRO-Based Assessment

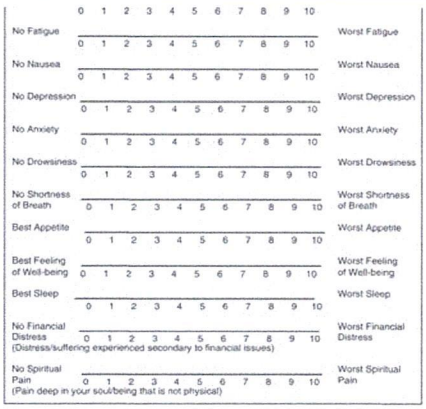


Fig 74.1 — Edmonton Symptom Assessment System–Revised (ESAS-R): 0–10 numerical scales for 12 symptoms incl. spirituality + financial distress.

- **Basch et al (MSKCC, 2017)** — weekly PRO monitoring vs usual care in metastatic solid tumors.
- **Median OS 31.2 vs 26 mo** (p=0.03); QoL ↑; absolute 6/100 ↑ OS at 5 y.
- Lung Ca PRO trial: **OS 22.5 vs 13.5 mo.**
- Homsi: median symptoms volunteered = **1**; checklist captured = **10.**
- **ESAS-R (Edmonton)** = free scale, paper or tablet, ~117 sec to complete.
- Latest ESAS includes **spirituality + financial distress**; available in many languages.
- Don't jump to 0–10 numeric scale — classify symptom subtype first → directed Rx.

Fatigue

- **#1 commonest symptom — 70–80% prevalence.**
- Causes: cancer itself, **hypercalcemia, anemia, hypothyroidism**, chemo, immunotherapy.
- **Checkpoint inhibitors (pembro, nivo, ipi)**: 5–22% hypothyroidism, 1–2% hypophysitis.
- Hypothyroidism usually at 6–8 wks but may appear months after stopping IO.
- Workup: TSH, Hb, Ca^{2+}, electrolytes, Cr, screen depression/demoralization.

Treatment

- Correct anemia, hypothyroidism, hypercalcemia.
- **Structured exercise** (45 min walk/d) — preventive + therapeutic; resume prior routine.
- **Methylphenidate** 5 mg at 7 + 11 a.m. × 48 h trial.
- Modafinil; **bupropion SR** — 6/7 systematic-review studies positive.
- **Dexamethasone 8 mg AM** — end-of-life option; monitor hyperglycemia.

Pain — Types

Table 74.1 — Cancer pain types

Type	Cause	Quality	Example
Nociceptive	Pressure on nerves	Deep, dull, aching, constant	Pancreatic Ca (boring, epigastric)
Visceral	Hollow viscus distention	Cramping, bloating, intermittent	Intestinal obstruction, renal colic
Neuropathic	Nerve damage (Ca or tx)	Sharp, shooting, burning, allodynia/hyperalgesia	**CIPN** — stocking-glove
Incident	Path fracture, bone mets	Minimal at rest, excruciating w/ movement	Bone-on-bone

- **80% of cancer pts** get pain at some point — most feared symptom.
- Ask 0–10 best/worst/average + acceptable target; prior tx, NOACs use.

Nociceptive — WHO ladder modified

- **Acetaminophen → NSAIDs → opioids**; always pair opioid w/ **bowel regimen.**
- Adding APAP to high-dose opioids = **no additional effect** (recent data).
- Steroids ↓ pain by 0.84/10 at 1 wk (Cochrane), also help fatigue/N/wellbeing.

Visceral

- Among hardest to treat.
- NSAIDs OR neuropathic agents (gabapentin, pregabalin) + opioids.
- **Octreotide** + opioids reduces visceral hyperalgesia — useful in malignant bowel obstruction.

Neuropathic

- NNT = 3–7 (some 10) for any single drug → trial 3–4 wks each.
- **Opioids DO help neuropathic pain** — equal to gabapentin/nortriptyline; combo even better.
- Drugs: gabapentin, pregabalin, **duloxetine**, nortriptyline, amitriptyline, CBZ, lamotrigine.
- Relief in 4–8 d if effective — trials don't need to exceed 2–3 wk.

CIPN (Chemo-Induced Peripheral Neuropathy)

- **40–70% on modern regimens**; dose-limiting.
- **Worst offenders:**
  - **Taxanes** (paclitaxel, docetaxel)
  - **Platinums** (cisplatin, oxaliplatin)
  - Epothilones, eribulin
  - Vinca alkaloids
  - **Bortezomib**, lenalidomide
- **Prevention**: NO established agent. **Cryotherapy/compression** of extremities for paclitaxel = promising.
- **ASCO**: if substantial CIPN during tx → consider dose reduction/stop offending drug.
- **Established CIPN: duloxetine** — only proven Rx (small effect, 0.6–1.0/10).

Incident pain (bone mets)

- Minimal evidence — RT, opioids, bisphosphonates.
- Small trial: gabapentin 100–200 mg tid + opioid → 6/6 near-complete response.
- Scrambler therapy (cutaneous nerve stim), burst ketamine + morphine — case reports.

> ♥ **NEET SS HIGHLIGHTS**
>
> ♥ **Duloxetine** = only proven Rx for established CIPN.
> ♥ **Taxanes + platinums** = worst CIPN offenders.
> ♥ **Octreotide** for visceral pain in malignant bowel obstruction.
> ♥ **Olanzapine** = emerging multi-symptom drug (N/V, anorexia).
> ♥ Opioids DO help neuropathic pain (contrary to teaching).
> ♥ Add APAP to high-dose opioids = no benefit.

Mucositis

Oral

- 30–40% with targeted agents (**regorafenib, sorafenib, erdafitinib, palbociclib, everolimus**).
- Worst (historical): **5-FU**; commonest current: **doxorubicin**.
- Cause: TKI interference w/ EGFR / VEGFR; mTOR (everolimus) → endothelial inflammation.
- Timing: 7–10 d post-tx.
- DDx: thrush, aphthous stomatitis, herpes.
- **Treatment**:
  - **Bolus 5-FU → oral cryotherapy (ice chips during infusion) ↓ incidence/severity by ~50%.**
  - Glucocorticoid rinses — improvement w/ palbociclib/everolimus.
  - **Viscous lidocaine 2%** for pain.
  - Topical high-potency steroids for ulceration; short systemic steroid course if severe.

GI

- 50–80% chemo pts have some diarrhea.
- Whole GI can be denuded — can't reabsorb 25 L/d intestinal fluid → high-output diarrhea.
- **Loperamide up to 24 mg/d** = 1st line.
- **Octreotide up to 300 mg/d** = refractory.
- Glucocorticoids commonly added.

Chemo-Induced N/V

- Highly emetogenic: **cisplatin, doxorubicin**; minimal: 5-FU.
- Treatment timeline (historic build):
- Four-drug antiemetic cocktail (for highly emetogenic chemo):
  - **1970s: Dexamethasone.**
  - **1990s: 5-HT3 RA** (ondansetron, palonosetron) — controls first 24 h.
  - **2000s: NK1 RA** (aprepitant, fosaprepitant) — delayed N/V (after 24h); added, NOT replacing 5-HT3.
  - **2010s: Olanzapine** — most effective; ↓ need for others.
- Decreasing dex dose/duration may ↓ long-term dex toxicity.

Non-Chemo N/V

- Up to 40–70% of cancer pts.
- Causes: RT, bowel obstruction, other meds, electrolyte abnormalities, post-anesthesia, brain mets.
- Standard agents (modestly effective): diphenhydramine, metoclopramide, prochlorperazine, haloperidol, ondansetron, dronabinol.
- **Olanzapine 2.5–5 mg/d** (2020/2023 RCTs) — dramatic effect: **9/10 → 2/10 nausea** in advanced cancer.

Anorexia / Cachexia

- **Cachexia → up to 20% of cancer deaths**; anorexia ~10–50% of pts.
- Cachexia = weight + skeletal muscle + adipose loss + metabolic imbalance + ↓ intake.
- **Cannot be reversed by replacing calories alone.**
- Defn: **5–10% pre-cancer weight loss** ± fatigue, anorexia, ↑ CRP, BMI <20, sarcopenia on CT.
- **Treatment (ASCO):**
  - Dietary counseling — modest benefit.
  - **Enteral tubes + IV nutrition NOT recommended routinely.**
  - **Olanzapine 2.5 mg HS = 1st line** — 60% gained ≥5% weight vs 9% placebo.
  - Megestrol acetate, corticosteroids → ↑ appetite but SE + no survival benefit.
  - **Mirtazapine ineffective** in large RCT — don't use.
  - **Ponsegromab** (anti-GDF-15 mAb) — phase 2 ↑ appetite + weight; not FDA-approved.

> ❦ **CLINICAL PEARLS**
>
> ❦ **Olanzapine** emerging as multi-symptom drug: chemo N/V, non-chemo N/V, anorexia, sleep.
> ❦ Mirtazapine is widely prescribed for cachexia but proven ineffective.
> ❦ **Ponsegromab** (GDF-15 inhibitor) is the novel cachexia agent — watch the literature.
> ❦ **Bolus 5-FU** + ice chips = classic test answer for mucositis prevention.

Constipation

- 20–90% of cancer pts.
- Causes: **opioids**, APAP, ondansetron, vandetanib, thalidomide, lenalidomide, diuretics, antidementia, dehydration, low fiber, hypercalcemia, **hypothyroidism (incl. IO-induced 20%)**.
- Ask last BM — >3 d ago = likely constipated; stool scales not recommended.
- **Treatment ladder:**
  - **Senna** 1–2 tabs/d up to 8 — 1st line; pair w/ every opioid Rx.
  - **PEG** added next.
  - Lactulose / sorbitol — palatability issues.
  - Magnesium oxide (1 oz of 300 mL bottle hourly until BM).
  - **Peripheral opioid antagonists (methylnaltrexone, alvimopan)** for refractory opioid constipation — reverse periph SE without losing analgesia.

Dyspnea

- 10–70% of cancer pts; worse at end of life.
- **Poor prognostic sign** in advanced Ca — survival days–weeks–months.
- Triggers serious illness conversation + advance directives.
- Causes: cancer, RT, chemo, **checkpoint inhibitor pneumonitis** (~9.5%, mean onset 52 d, may appear months after stopping).
- **ASCO**: systematic dyspnea assessment every inpatient/outpatient visit.

- Workup: r/o reversible — hypoxia, PE, pneumonia, effusion, COPD/asthma, bronchospasm.
- **Treatment:**
  - Treat cancer if feasible.
  - **Low-dose opioids** = mainstay for air hunger.
  - Low-dose BZD for anxiety component.
  - **Fan blowing cool air on face** — comforting; evidence-based.
  - High-dose steroids for lymphangitic carcinomatosis, COPD, asthma exacerbation.
  - **O_2 for SpO_2 ≤90%** on RA.
  - HFNO = bridge therapy; complicates hospice.
  - Refer to palliative care + truthful prognosis discussion.

Hot Flashes

- **2/3 of postmenopausal breast Ca** women on endocrine tx; ~50% night sweats.
- **3/4 of prostate Ca** men on ADT/orchiectomy.
- May persist **decades** (not 'few years' as previously thought).
- Cause: rapid ↓ in estrogen/testosterone.

Women

- **SSRIs/SNRIs: citalopram 20 mg/d** (preferred), venlafaxine, paroxetine, sertraline, fluoxetine.
- **Gabapentin** — also helps anxiety in breast Ca survivors.
- **Oxybutynin** — IR or SR; cheap; caution mental status changes in elderly.
- **Megestrol acetate 20–40 mg/d** — refractory.
- Medroxyprogesterone acetate 400–500 mg IM × 1 — months of relief.
- **Fezolinetant** (2023) — NK3 receptor antagonist, nonhormonal; equivalent to other Rx; works regardless of tamoxifen.

Men

- Venlafaxine: pilot+; **RCT negative**.
- **Gabapentin 900 mg/d** works — RCT proven.
- Progesterone analogues — effective.
- **Oxybutynin** — RCT positive.

Nasal Vestibulitis

- **>70% on taxanes; >80% on bevacizumab**; >75% on paclitaxel/nab-paclitaxel/bevacizumab.
- Sx: pain, bleeding, scabbing, crusting, dryness.
- Cause: chemo damages nasal epithelium → drying + cracking + 2° infection.
- Heals in 7–10 d but infection risk.
- **Rx: rose geranium in sesame oil** nasal spray > saline (compounded; recipe — Mayo).

✦ MNEMONIC

FOPCANE *Olanzapine-responsive symptoms*

F — Fatigue / sleep
O — Oncology N/V (chemo + non-chemo)
P — Poor appetite (anorexia/cachexia)
C — Cachexia (weight gain in ≥60%)
A — Anxiety / agitation
N — Nausea — refractory advanced cancer
E — Emesis breakthrough on standard cocktail

2.5–5 mg HS — broad symptomatic relief in advanced Ca.

✎ MCQ CORNER

Q1. 65 y/o w/ breast Ca on paclitaxel, develops painful stocking-glove neuropathy after cycle 6. Best Rx for established CIPN?
A. Gabapentin
✓ **B. Duloxetine**
C. Amitriptyline
D. Lidocaine patch
► *Duloxetine = only drug with RCT evidence for established CIPN (modest effect 0.6–1.0/10). Others tried but not proven.*

Q2. Patient receiving bolus 5-FU. Best evidence-based prophylaxis for oral mucositis?
A. Chlorhexidine mouthwash
✓ **B. Oral cryotherapy (ice chips during infusion)**
C. Prophylactic acyclovir
D. Sucralfate slurry
► *Oral cryotherapy during bolus 5-FU infusion ↓ mucositis incidence/severity by ~50%. Classic test answer.*

Q3. Advanced pancreatic Ca, no chemo × 4 wk, persistent nausea 9/10. Most effective single agent?
A. Ondansetron
B. Metoclopramide
✓ **C. Olanzapine 5 mg/d**
D. Dronabinol
► *RCT (2020): olanzapine 5 mg/d in advanced cancer ↓ nausea 9/10 → 2/10 next day. Non-chemo N/V responds best to olanzapine.*

Q4. Postmenopausal breast Ca on tamoxifen, severe hot flashes. Preferred 1st-line?
A. HRT estrogen patch
✓ **B. Citalopram 20 mg**
C. Paroxetine 20 mg
D. Clonidine
► *Paroxetine inhibits CYP2D6 → ↓ tamoxifen activation. Citalopram preferred — equivalent efficacy, no CYP2D6 interaction. Avoid HRT in breast Ca.*

Q5. Patient on chronic opioids develops refractory constipation despite senna + PEG. Next step?
A. Stop opioids
B. Lactulose 30 mL bid
✓ **C. Methylnaltrexone SC**
D. Bisacodyl daily
► *Peripheral opioid antagonists (methylnaltrexone, alvimopan) reverse opioid constipation without crossing BBB → preserve analgesia. For refractory opioid-induced constipation.*

Q6. Anorexia + 8% weight loss in non-small cell lung Ca. ASCO 1st-line drug?
A. Mirtazapine 15 mg HS
B. Megestrol acetate 800 mg/d
✓ **C. Olanzapine 2.5 mg HS**
D. Dronabinol
► *RCT: olanzapine 2.5 mg HS → 60% gained ≥5% weight vs 9% placebo. Mirtazapine ineffective. Megestrol works but no survival benefit + SE.*

◷ LAST MINUTE REVISION

► **Basch PRO trial**: weekly PRO monitoring → OS 31.2 vs 26 mo.
► **ESAS-R** = Edmonton scale; includes spirituality + financial distress.
► **Fatigue** = #1 sx, 80%; r/o hypothyroid (esp ICI), Ca^{2+}, anemia.
► **Bupropion** ↓ cancer fatigue; methylphenidate, modafinil, dexamethasone.
► **4 pain types**: nociceptive, visceral, neuropathic, incident.
► **Duloxetine** = only proven Rx for established CIPN.
► CIPN worst: **taxanes, platinums, bortezomib, vinca, eribulin**.
► **Octreotide** for visceral pain in malignant bowel obstruction.
► Opioids DO help neuropathic pain — combo > monotherapy.
► **Bolus 5-FU + ice chips** ↓ mucositis ~50%.
► Loperamide 24 mg/d → octreotide 300 mg/d for refractory diarrhea.
► **4-drug antiemetic cocktail**: dex + 5-HT3 RA + NK1 RA + olanzapine.
► **Olanzapine 2.5 mg HS** = 1st line cancer anorexia/cachexia.
► **Mirtazapine ineffective** for cachexia.
► **Ponsegromab** = anti-GDF-15 mAb (cachexia, investigational).
► **Senna → PEG → methylnaltrexone** for opioid constipation.
► **Dyspnea** in advanced Ca → low-dose opioids + BZD + fan.
► Hot flashes: **citalopram** 20 mg (preferred over paroxetine in BRCA on tamoxifen).
► **Fezolinetant** = NK3 RA (2023) — nonhormonal hot flash agent.
► Nasal vestibulitis (taxanes, beva): **rose geranium in sesame oil**.

◉ UPDATES

◉ **2017 Basch trial (JAMA)** — PRO monitoring → ↑ OS.
◉ **2020 Loprinzi (ASCO CIPN update)** — duloxetine confirmed; cryocompression promising.
◉ **2020 Navari (JAMA Oncol)** — olanzapine 5 mg/d for non-chemo nausea.
◉ **2023 ASCO Cachexia update** — olanzapine 2.5 mg HS preferred.
◉ **2023 Fezolinetant** (NK3 RA) approved — nonhormonal hot flash Rx.
◉ **2024 Groarke (NEJM)** — ponsegromab (GDF-15 mAb) for cachexia, phase 2 positive.

CH 75 · Prevention & Early Detection of Cancer — Risk Factor...

Carcinogens, lifestyle interventions, chemoprevention (tamoxifen, raloxifene, aromatase Is, 5-α-reductase Is), vaccines (HPV, HBV), screening (Pap, mammo, colonoscopy, LDCT), USPSTF + ACS guidelines. NEET SS — screening ages high yield.

Smoking

- Smokers' lifetime risk of premature death from tobacco-related disease = **1 in 3**.
- Smoking shortens life by **~10 yr on average**.
- Tobacco-related cancers: **lung, larynx, oropharynx, esophagus, kidney, bladder, colon, pancreas, stomach, cervix**.
- Quitting → **30–50% ↓ 10-y lung Ca mortality** vs continued smoking.
- **Light/low-tar = NOT safer** (deeper inhalation compensates).
- >80% of adult smokers began <18 yo.
- E-cigarette use ↑ rapidly; net health effects poorly studied.
- Cigars: 1–2/d **doubles** oral/esophageal Ca; 3–4/d → 8× oral, 4× esoph.
- **Smokeless tobacco** → dental caries, gingivitis, leukoplakia, oral Ca.
- Cessation aids: **nicotine replacement, bupropion, varenicline**.

Other Modifiable Lifestyle

Physical activity

- ↓ Risk of **colon + breast Ca**; mechanisms multifactorial.
- Studies prone to recall bias + reverse causality.

Diet

- Fat intake: associated but **not proven causal** for breast, colon, prostate, endometrial Ca.
- **WHI** (n=100,000): low-fat diet did NOT ↓ invasive breast or colorectal Ca over 8 y.
- Fiber + fruit/veg: no proven protective effect (Polyp Prevention Trial, professional cohorts).
- **Vitamin/mineral supplements** beyond balanced diet = no anticarcinogenic value.
- Red/processed meat: small effect on Ca, weak evidence overall.

Energy balance

- **BMI ≥25** → modest ↑ risk (RR 1.0–2.0).
- Per 5 kg/m² ↑ BMI: linear ↑ in **uterine, gallbladder, kidney, cervix, thyroid Ca + leukemia**.
- Inverse: prostate + premenopausal breast Ca.

Sun avoidance

- Cumulative UV → **BCC, SCC** (nonmelanoma).
- Melanoma–UV link **weaker**; **70–80% melanomas arise de novo** (not from nevi).
- Sunscreens ↓ actinic keratosis (SCC precursor) but may NOT ↓ melanoma.

Carcinogens

Table 75.1 — Suspected carcinogens (high yield)

Carcinogen	Cancer
Alkylating agents	AML, bladder
Aromatic amines (dyes)	Bladder
Arsenic	Lung, skin
Asbestos	Lung, pleura (mesothelioma), peritoneum
Benzene	AML
DES (prenatal)	Vaginal clear cell
EBV	Burkitt, nasal T-cell lymphoma
Estrogen	Endometrial, liver, breast
Alcohol	Breast, liver, esophagus, H&N;
H. pylori	Gastric Ca, MALT lymphoma
HBV/HCV	HCC
HIV	NHL, Kaposi, SCC urogenital
HPV	Cervix, anus, oropharynx
HTLV-1	Adult T-cell leukemia/lymphoma
Immunosuppressants	NHL
Ionizing radiation	Breast, bladder, thyroid, bone, heme
Nickel dust	Lung, nasal sinuses
Phenacetin	Renal pelvis, bladder
Polycyclic hydrocarbons	Lung, scrotal SCC
Radon	Lung
Schistosomiasis	Bladder SCC
Vinyl chloride	Liver angiosarcoma
Sunlight UV	Skin Ca, melanoma

NEET SS HIGHLIGHTS

- **Aromatic amines** → bladder Ca (dyes).
- **Vinyl chloride** → hepatic angiosarcoma.
- **Arsenic** → skin + lung.
- **Asbestos** → mesothelioma.
- **Benzene** → AML.
- **Schistosoma** → bladder SCC.
- **HTLV-1** → ATLL.
- **DES** in utero → vaginal clear cell adenoCa.
- Phenacetin → renal pelvis + bladder.
- Scrotal SCC = chimney sweeps (Percival Pott, polycyclic hydrocarbons).

Chemoprevention

Concept

- Use of agents to **reverse, suppress, or prevent** carcinogenesis before invasive malignancy.
- Initiator vs promoter distinction indistinct; cigarette smoke = **complete carcinogen** (both).
- Promoters: **androgens → prostate**; **estrogen → breast, endometrium**.

Aerodigestive (lung)

- Cured H&N;/lung/esophagus SCC pts → **2nd primary risk ~5%/y**.
- Cessation doesn't markedly ↓ 2nd Ca risk in cured pts (does in never-Ca pts).
- **HPV-16** → oropharyngeal Ca (sexually acquired; HPV vaccine ↓ rates).
- **Isotretinoin**: regresses leukoplakia at toxic dose; doesn't prevent H&N; Ca at tolerable doses.
- **ATBC trial**: β-carotene ↑ lung Ca incidence + mortality in heavy smokers.
- **α-tocopherol (vit E)** → no lung Ca effect, but ↑ hemorrhagic stroke.
- **CARET trial** (smokers + asbestos): β-carotene → 6 vs 5/1000 lung Ca → **HARM**.
- Lesson: **RCT mandatory** before population-wide chemoprevention.

Colon

- **No agent with sufficient evidence** for general population.
- Aspirin/NSAID: insufficient evidence for incidence/mortality reduction; clear bleeding harms.
- **COX-2 inhibitors**: ↑ CV events → unsuitable for chemoprevention.
- **WHI estrogen+progestin** → 44% RRR for colorectal Ca but ↑ CV + breast Ca; NOT recommended as Rx.
- Statins: no protective effect on Ca overall.

Breast

- **Tamoxifen** (SERM): ↓ breast Ca **49%** in high-risk women (43.4 → 22/1000); ↓ fractures.
- Side effects: ↑ **endometrial Ca, stroke, PE, DVT**.
- **Raloxifene** (postmenopausal only): equivalent to tamoxifen for invasive Ca, **NO endometrial Ca risk**, fewer VTE; slightly less effective for invasive Ca.
- **Gail risk model**: ≥1.66% 5-y risk → eligible for chemoprevention.
- **Exemestane** (AI): 65% RRR (5.5 → 1.9/1000); SE = arthralgia, hot flashes, fatigue, insomnia.
- AIs vs SERMs head-to-head: not done.

Prostate

- **Finasteride (PCPT)**: 18.4% vs 24.4% prostate Ca incidence — but ↑ **Gleason ≥7 tumors (6.4% vs 5.1%)**.
- **Dutasteride (REDUCE)**: 23% RRR; ↑ Gleason 8–10 in years 3–4.
- High-grade ↑ = likely **detection bias** (↓ prostate vol → more sensitive PSA/DRE), but causal role can't be excluded.
- **Neither finasteride nor dutasteride FDA-approved for prevention.**
- **SELECT trial**: vit E ↑ prostate Ca trend (HR 1.17); selenium no effect.

Vaccines

- **HBV vaccine** → prevents hepatitis + HCC.
- **HPV nonavalent** (6, 11, 16, 18, 31, 33, 45, 52, 58): cervical, anal, oropharyngeal.
- HPV 6/11 → genital warts; rest → cancer.
- HPV 16+18 alone could prevent **>70% cervical Ca** globally.
- **US schedule**: 9–14 y → 2 doses; 15–26 y → 3 doses.
- Vaccine does NOT impact preexisting infections.
- Single-dose efficacy under study (RCT ongoing).

Surgical Prevention

- **FAP, UC** → prophylactic colectomy.
- Severe cervical dysplasia → laser, LEEP, conization.
- **BRCA1/2**: prophylactic bilateral mastectomy → ~90% ↓ in breast Ca incidence + 81–94% ↓ Ca deaths.
- **Prophylactic salpingo-oophorectomy**: ~36% RRR ovarian/peritoneal Ca; ~50% RRR breast Ca (best if <45–50 y).
- **High-grade serous 'ovarian' Ca** mostly arises in **fallopian fimbria** → ovary-sparing salpingectomy under study.
- BSO at hysterectomy in premenopausal women → ↑ CV disease + ↑ mortality trend.

Screening — Principles

- **Endpoint**: cause-specific mortality (NOT survival from dx).
- Sensitivity = a/(a+c) (true-pos rate).
- Specificity = d/(b+d).
- **PPV depends heavily on prevalence** — for rare Ca, poor specificity dramatically ↓ PPV.
- Screening best when: Ca common in population + effective Rx exists.

Screening biases

- **Lead-time bias**: ↑ time aware of disease without prolonging life.
- **Length-time bias**: detects slow indolent tumors preferentially; aggressive interval Ca missed.
- **Overdiagnosis**: extreme length bias — detects 'pseudo disease' that wouldn't clinical present.
- **Selection bias / healthy volunteer effect**: screened pts are healthier intrinsically.
- **Stage shift** without ↓ late-stage absolute incidence = overdiagnosis signal.

USPSTF grades

Table 75.2 — USPSTF recommendation grades

Grade	Meaning
A	Recommend — high certainty, substantial net benefit
B	Recommend — moderate certainty, moderate/substantial benefit
C	Selectively offer — small net benefit
D	Recommend AGAINST — harms outweigh
I	Insufficient evidence

Specific Screenings — USPSTF

Table 75.3 — USPSTF screening (high yield)

Cancer	Test	Age + interval
Breast	Mammography	40–74 y biennial (B); ≥75 y (I); ≤39 y not recommended
	Breast self-exam	D — don't recommend
	MRI	I (insufficient)
Cervical	Pap (cytology)	21–29 y q3y; 30–65 q3y OR co-test q5y (A); <21 (D); >65 + neg hx (D)
	HPV alone or co-test	30–65 y q5y; <30 (don't use)
Colorectal	FIT	Annual
	FOBT	Annual
	Fecal DNA (Cologuard)	q3y
	Sigmoidoscopy	q5y
	Colonoscopy	**q10y**
	CT colonography	q5y
	Start age	**45 y (B); 50–75 y (A); 76–85 (C)**
Lung	Low-dose CT	50–80 y, ≥20 pack-yr, current OR quit <15 y, annual (B)
Ovary	TVUS / CA-125	D — don't screen
Prostate	PSA	55–69 y individual decision (C); ≥70 (D)
	DRE	No specific reco
Skin	Skin exam	I — insufficient

CLINICAL PEARLS

- **FDA Sept 2016**: advised AGAINST ANY ovarian Ca screening test.
- **Breast self-exam**: large Chinese RCT (266k) — no mortality benefit, more biopsies of benign lesions.
- **BRCA carriers**: mammography less sensitive (younger pts, denser breasts); MRI > mammo in sensitivity.
- **Pap reduces cervical mortality** — no formal RCT in West; Indian visual inspection RCT showed mortality benefit.
- **CRC screening**: USPSTF lowered to 45 y in 2021 (B grade).
- **Sigmoidoscopy**: ↓ CRC incidence 18%, mortality 28%.
- **Colonoscopy**: detects ~25% more advanced lesions than FOBT+sig; perforation 4/10,000.
- **NLST** (LDCT): ~3 fewer lung Ca deaths per 1000 screened.
- **ERSPC** PSA: 570 to screen + 18 detected to avert 1 death — modest, debated benefit.

MNEMONIC

ABCDI *USPSTF screening grades*

A — Absolute go — high net benefit
B — Better than not — moderate
C — Conditional — small net benefit
D — Don't — harms outweigh
I — Indeterminate — insufficient evidence

Memorize cervical 21 y + colon 45 y + lung 50 y (LDCT) + breast 40–74 y.

✎ MCQ CORNER

Q1. 55 y/o postmenopausal woman, Gail 5-y risk 2.3%. Best chemoprevention if priority is avoiding endometrial Ca?
A. Tamoxifen
✓ **B. Raloxifene**
C. Aspirin
D. Estrogen-progestin
► *Raloxifene = equivalent to tamoxifen for breast Ca prevention but NO endometrial Ca risk (postmenopausal only).*

Q2. 55 y/o smoker, 30 pack-yr, current. Which agent ↑ his lung Ca risk in RCTs?
A. Selenium
B. Vitamin C
✓ **C. β-carotene**
D. Folate
► *ATBC + CARET trials: β-carotene ↑ lung Ca incidence + mortality in smokers. Classic test answer.*

Q3. USPSTF colorectal Ca screening — start age for average risk (2021 update)?
A. 40 y
✓ **B. 45 y**
C. 50 y
D. 55 y
► *USPSTF 2021 lowered start age to 45 y (B grade). 50–75 (A grade). 76–85 (C grade — selective).*

Q4. USPSTF lung Ca LDCT — eligibility?
✓ **A. 50–80 y, ≥20 pack-yr, current/quit <15 y**
B. 55–80 y, ≥30 pack-yr only current smokers
C. All adults >60 y
D. ≥40 y with any smoking history
► *USPSTF 2021: age 50–80, ≥20 pack-year, current OR quit within 15 years, annual LDCT (B grade).*

Q5. BRCA1 mutation carrier, 35 y. Best ovarian Ca prevention?
A. Annual TVUS + CA-125
✓ **B. Prophylactic bilateral salpingo-oophorectomy**
C. Oral contraceptives only
D. Annual MRI pelvis
► *Bilateral salpingo-oophorectomy = 36% RRR ovarian/peritoneal + 50% RRR breast Ca. TVUS+CA-125 ineffective. FDA advises against ANY ovarian screen.*

Q6. Postmenopausal woman, hysterectomy for fibroids 10 y ago, 65 y. Cervical screening?
A. Continue annual Pap
B. Pap every 3 y
C. HPV every 5 y
✓ **D. Discontinue screening**
► *USPSTF D: after total hysterectomy for noncancerous reasons → stop. Also stop if >65 y with adequate prior screening.*

Q7. Bias when screening detects slow-growing tumors that would never have caused symptoms?
A. Lead-time bias
✓ **B. Length-time bias / overdiagnosis**
C. Selection bias
D. Recall bias
► *Length-time bias = preferential detection of indolent tumors. Extreme form = overdiagnosis (pseudo disease).*

◷ LAST MINUTE REVISION

► Smoking shortens life ~10 y; 1 in 3 lifetime risk of dying from smoking-related disease.
► Quit smoking → 30–50% ↓ 10-y lung Ca mortality.
► **β-carotene HARMFUL** in smokers (ATBC, CARET).
► **Vinyl chloride** → hepatic angiosarcoma; **arsenic** → skin + lung; **aromatic amines** → bladder.
► **EBV** → Burkitt, nasopharyngeal Ca, NK/T lymphoma.
► **HPV nonavalent** → 6, 11, 16, 18, 31, 33, 45, 52, 58.
► HPV 16+18 → >70% cervical Ca.
► **Tamoxifen**: 49% ↓ breast Ca, ↑ endometrial Ca + VTE.
► **Raloxifene**: equivalent, NO endometrial Ca; postmeno only.
► **Exemestane**: 65% RRR breast Ca.
► **Gail score** ≥1.66% 5-y risk → chemoprevention.
► **Finasteride**: ↓ overall prostate Ca but ↑ Gleason ≥7 — NOT FDA-approved for prevention.
► **Pap**: 21 y start, q3y; 30+ HPV co-test q5y; stop >65 if neg hx.
► **CRC**: 45 y start (B); colonoscopy q10, FIT annual, sig q5.
► **LDCT lung**: 50–80 y, ≥20 pack-yr, current/quit <15 y.
► **Mammogram**: 40–74 biennial (B).
► **PSA**: 55–69 shared decision (C); ≥70 (D).
► **Ovarian Ca screening NOT recommended** in any group.
► BRCA → prophylactic mastectomy + BSO; oophorectomy <45–50 y best.
► Most high-grade serous 'ovarian' Ca arises in **fallopian tube fimbria**.
► Screening biases: **lead-time, length-time/overdiagnosis, selection**.

◉ UPDATES

◉ **USPSTF 2021**: CRC start age lowered to **45 y** (B grade).
◉ **USPSTF 2021**: LDCT lung lowered to 50 y + ≥20 pack-yr.
◉ **USPSTF 2024**: Mammography expanded to 40–74 y biennial (B).
◉ **HPV vaccine** — single-dose schedule under WHO consideration.
◉ **FDA 2016**: advised against any ovarian Ca screening test.