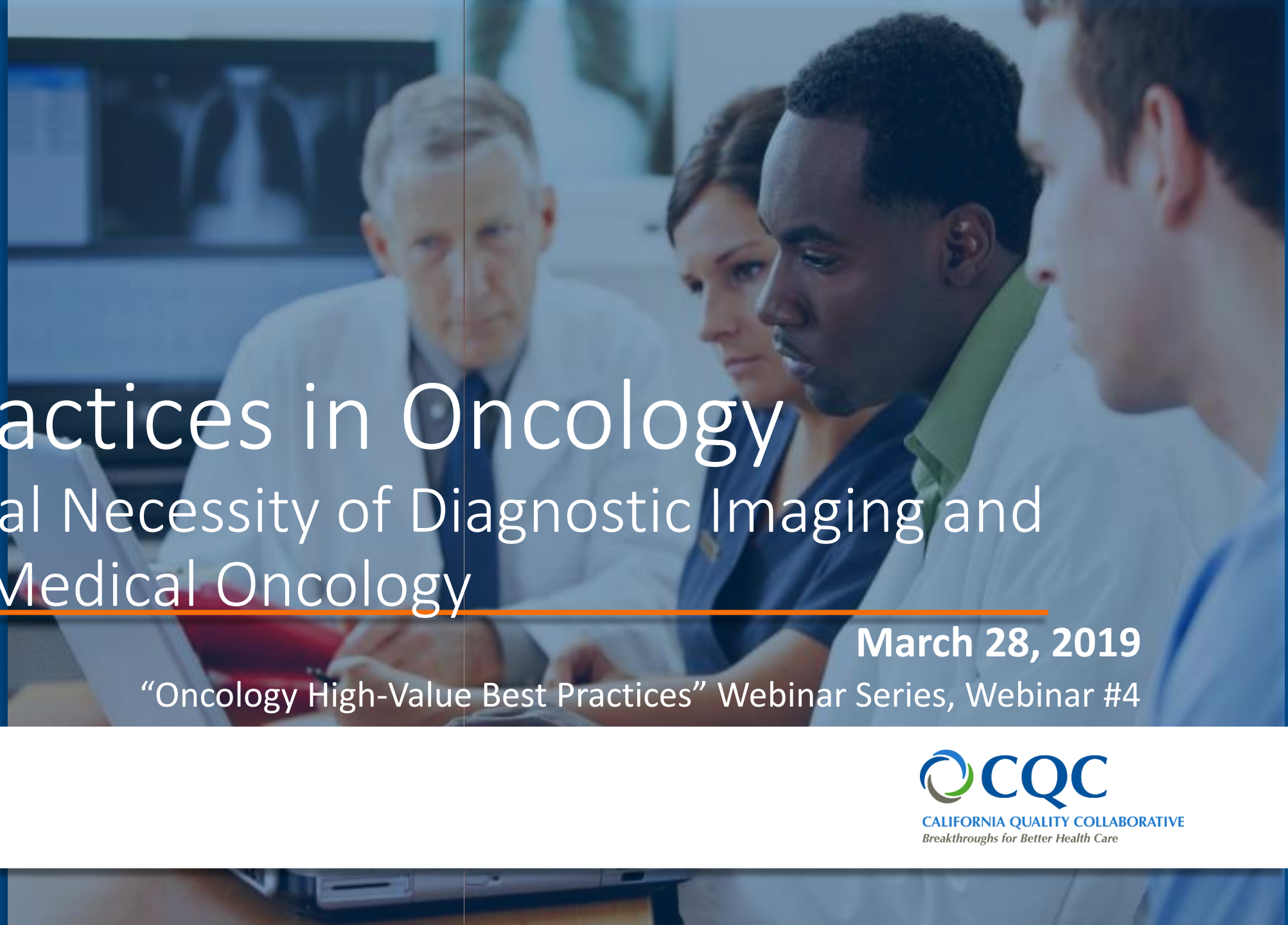


Best Practices in Oncology

The Medical Necessity of Diagnostic Imaging and Testing in Medical Oncology

March 28, 2019

"Oncology High-Value Best Practices" Webinar Series, Webinar #4

CQC
CALIFORNIA QUALITY COLLABORATIVE
Breakthroughs for Better Health Care

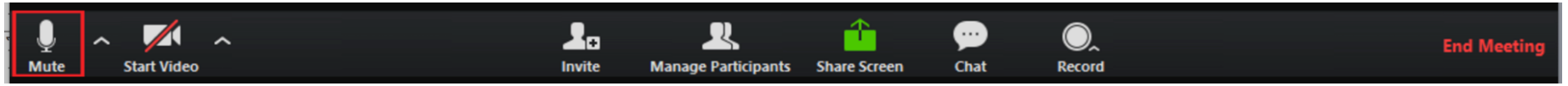
Tech Tips – Zoom Meetings

Attendees are automatically MUTED upon entry

Refrain from using the hold button

Use the chat box, raise your hand, or *unmute yourself and jump in* if you have questions or would like to participate

Direct messages to Jose if you have any technical issues



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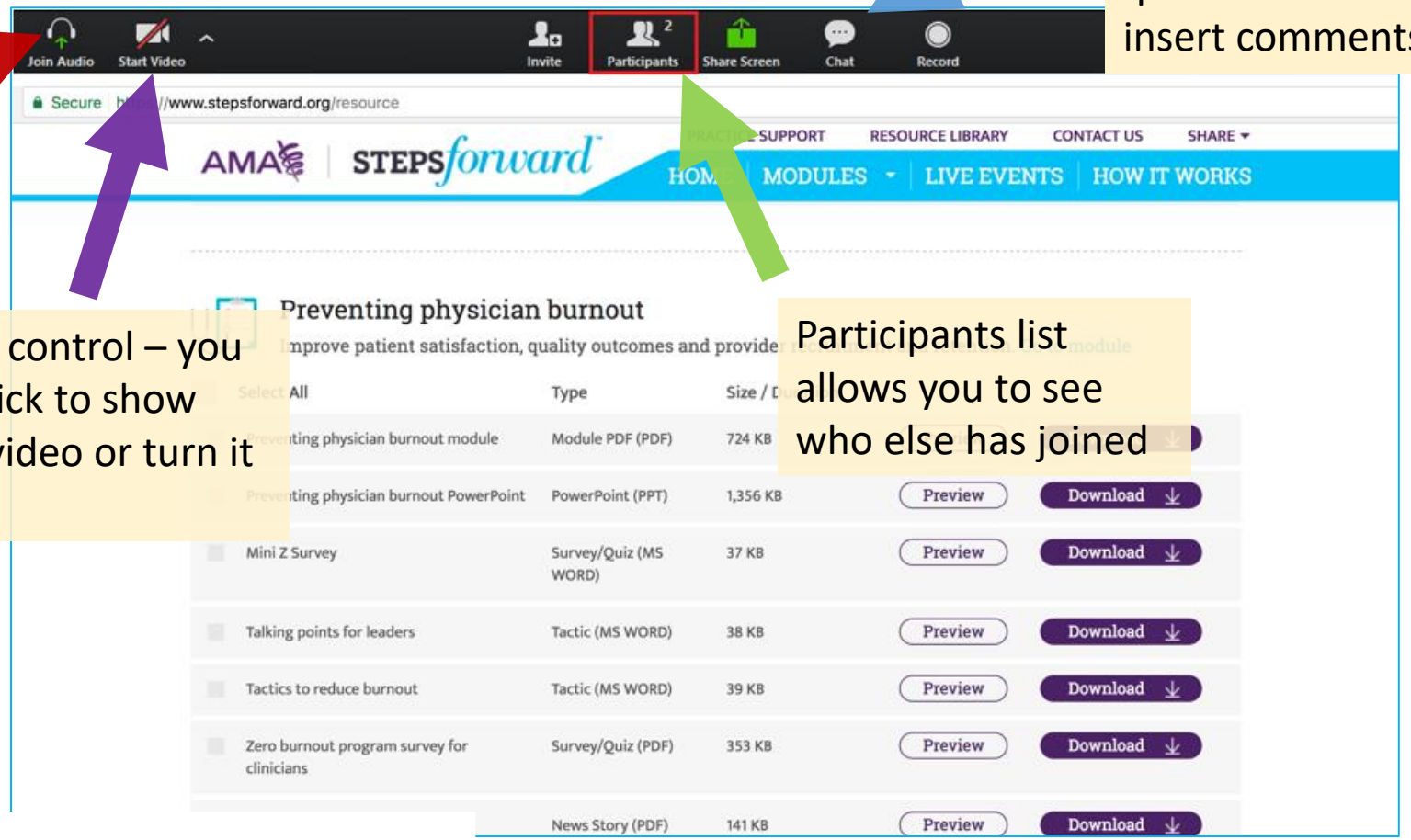
Zoom Tips & Tricks

Chat box so you can ask questions and insert comments

Click here to join audio



Video control – you can click to show your video or turn it off

Participants list allows you to see who else has joined

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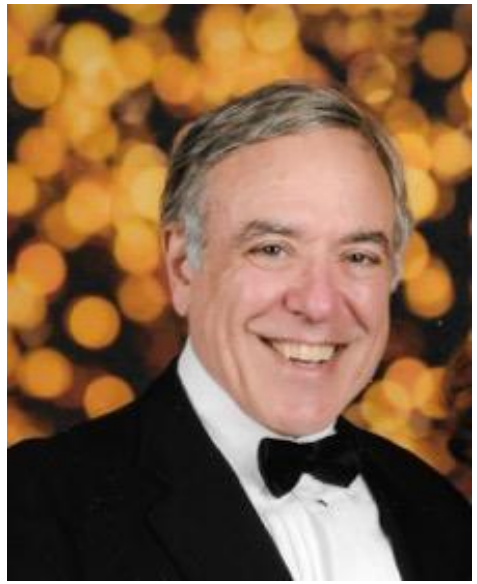
Today's Speakers

- Bart Wald, MD
- Medical Director, California Quality Collaborative



- Eric Chevlen, MD

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Who is the California Quality Collaborative (CQC)?

CQC is a health care improvement organization dedicated to advancing the quality and efficiency of the health care delivery system in California. CQC creates scalable, measurable improvement in the care delivery system important to patients, purchasers, providers, and health plans.

- Started in 2007
- Multi-stakeholder governance
  - Core funding from health plans sharing a delivery system
  - Administered by the Pacific Business Group on Health
- **Purpose:** Identify and spread best practices across outpatient delivery system in California
  - Trains 2,000 individuals from 250 organizations each year

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PBGH PACIFIC BUSINESS GROUP ON HEALTH
UnitedHealthcare

Oncology Series
Webinar Dates

- **Benefits & Limitations of Oncology Guidelines** (Anthony Ciarolla, MD)
- **Personalized Medicine** (Mark Pegram, MD)
- **Palliative Care** (Kavitha Ramchandran, MD)
- **The Medical Necessity of Diagnostic Imaging and Testing in Medical Oncology** (Eric Chevlen MD)

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“Is this test really necessary, doctor?”

UNDERSTANDING MEDICAL NECESSITY OF DIAGNOSTIC IMAGING AND LABORATORY TESTING IN MEDICAL ONCOLOGY

Eric Chevlen, MD

Lecture Outline

- Principles of medical necessity
- Types of testing
- Principles of screening tests (Bayes' theorem)
- Treatment-guiding tests
- Prognostic tests
- Surveillance tests
- Conclusions

Definition of medically necessary

Services that a medical practitioner, exercising prudent clinical judgment, would provide to a patient to prevent, diagnose, or treat an illness…in accordance with generally accepted standards of medical practice, clinically appropriate for the patient, not primarily for the patient's convenience, and not more costly than similar services likely to yield results which are at least as good.

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Benefit of health plan medical necessity policies

- Evidence-based
- Reduces variation in decision by one reviewer
- Reduces variation in decision between reviewers
- Part of contract between health plan and member

Types of tests

Test type	Definition	Example
Screening	No signs or symptoms of disease	Mammography
Diagnostic	Signs or symptoms, but no confirmed diagnosis	Chest X-ray for coughing smoker
Staging	Confirmed diagnosis, extent of disease unknown	PET scan for clinical stage I lung cancer
Treatment-guiding	Diagnosis and extent of disease known, ideal treatment not known	HER2 assay in breast cancer
Surveillance	Completed treatment, no signs or symptoms	CT scan after treatment of small cell lung cancer
Prognostic	Disease and stage known, likely outcome unknown	Genetic assay of untreated prostate cancer

Tacit assumptions of screening

- Some diseases can be detected before they cause symptoms
- Early detection improves health outcomes.
- Examples:
  - Hypertension
  - Hypercholesterolemia
  - Hypothyroidism in newborns
- Counter-examples:
  - Shingles (cannot be detected before symptomatic)
  - Alzheimer's disease (early detection not shown to improve health outcomes)

Screening for cancer

- Three patterns of cancer:
  - Early and rapid dissemination to metastatic sites
    - Ovarian cancer
    - Plasmacytoma / myeloma
  - Slow local progression without early metastasis
    - Well-differentiated prostate cancer in the elderly
  - Early asymptomatic period, during which disease is detectable and curable, followed by incurable metastases
    - Breast cancer
    - Cervical cancer

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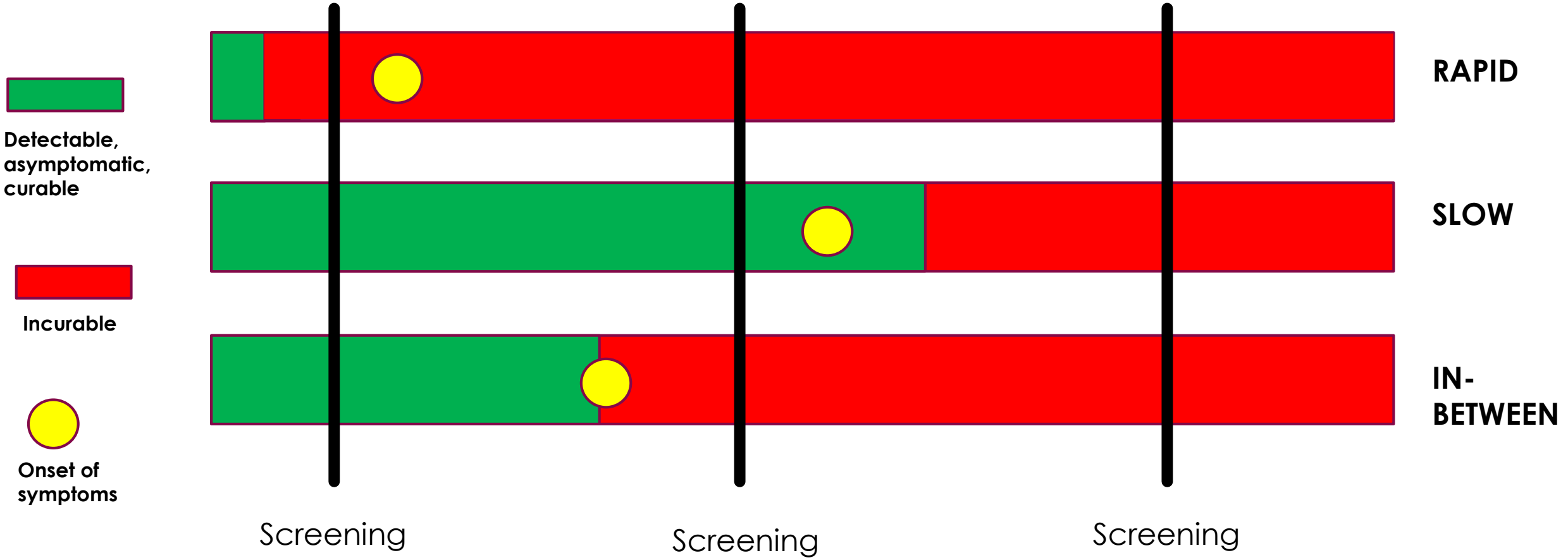
Three patterns of cancer



False positives and false negatives

SENSITIVITY

Sensitivity: if the disease is present, the test is positive.
Sensitivity = inverse of false negative rate.
High sensitivity = low false negative rate.

100 % Sensitivity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	POS	POS	POS	POS	POS	POS	NEG	NEG	NEG	NEG

X = disease present

67% Sensitivity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	POS	POS	POS	POS	NEG	NEG	NEG	NEG	NEG	NEG

O = disease absent

Also 100 % Sensitivity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	POS	POS	POS	POS	POS	POS	POS	POS	POS	POS

SPECIFICITY

Specificity: If the disease is absent, the test is negative.
Specificity = inverse of false positive rate.
High specificity = low false positive rate..

100 % Specificity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	POS	POS	POS	POS	POS	POS	NEG	NEG	NEG	NEG

X = disease present

75% Specificity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	POS	POS	POS	POS	POS	POS	NEG	NEG	NEG	POS

O = disease absent

Also 100 % Specificity	Disease status	X	X	X	X	X	X	O	O	O	O
	Test result	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG	NEG

Sensitivity/selectivity vs predictive value

In assessing sensitivity and selectivity, we KNOW whether the condition is present, and we ASK whether the test result corresponds with that known condition.

In assessing predictive value of a test, we KNOW the test result, and ASK whether the presence of the condition corresponds with that known test result.

	WE KNOW	WE ASK
Sensitivity/selectivity	Presence of condition	Test results
Predictive value	Test results	Presence of condition

Predictive value

- Positive predictive value: if the test result is positive, the patient has the condition.
- Negative predictive value: if the test result is negative, the patient does not have the condition.
- Predictive values depend on:
  - Test sensitivity
  - Test specificity
  - Prevalence of condition in tested population

Calculating predictive value

- **Positive predictive value =**

$$\frac{true\ positives}{true\ positives + false\ positives}$$

- **Negative predictive value =**

$$\frac{true\ negatives}{true\ negatives + false\ negatives}$$

Importance of prevalence in testing -1

Test 1000 people
Assume prevalence of condition in tested population = 10%
Assume test sensitivity of 90%
Assume test specificity of 90%

Test result	Condition present	Condition absent	Total
Positive	90 (true positive)	90 (false positive)	180 positives
Negative	10 (false negative)	810 (true negative)	820 negatives
Total	100	900	1000

Positive predictive value = true positives/true + false positives.
Positive predictive value = 90/180 = 50%
Negative predictive value = true negatives/true + false negatives.
Negative predictive value = 810/820 = 98%

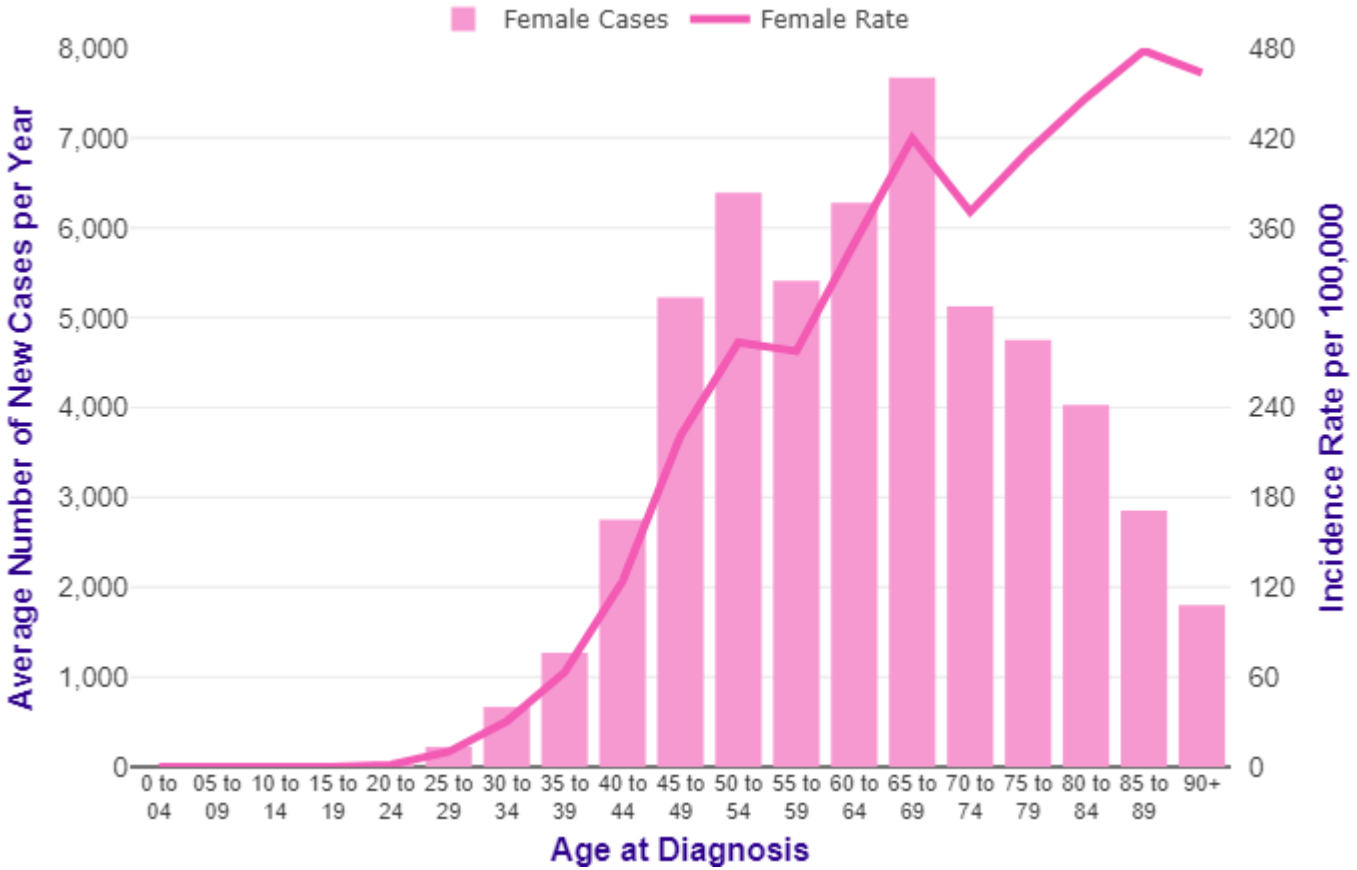
Importance of prevalence in testing - 2

Test 1000 people
Assume prevalence of condition in tested population = 5%
Assume sensitivity of 90%
Assume specificity of 90%

Test result	Condition present	Condition absent	Total
Positive	45 (true positive)	95 (false positive)	140 positives
Negative	5 (false negative)	855 (true negative)	860 negatives
Total	50	950	1000

Positive predictive value = true positives/true + false positives.
Positive predictive value = 45/140 = 32%
Negative predictive value = true negatives/true + false negatives.
Negative predictive value = 855/860 = 99.4%

Screening for breast cancer



www.cancerresearch.uk.org

Challenges of screening:

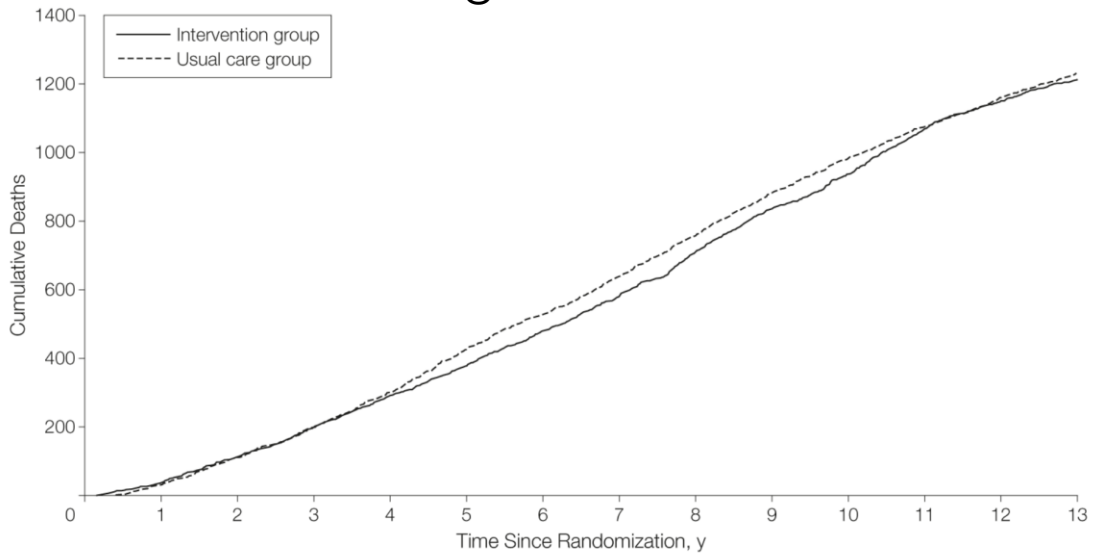
Prevalence in young women is low.
Radiation causes cancer.
Old women have competing causes of death.
Relative risk (RR) reduction of ~ 15%.
Absolute mortality risk reduction ~ 40 per 100,000.

JAMA, vol. 314(15), p.1615., 2015.

Screening standard risk subjects for lung cancer by CXR does not improve lung cancer death rate.

- **155,000 prospectively randomized**
- **Standard risk subjects**
- **Screening by chest radiograph annually x 4 years**

Lung cancer death rate



Intervention group													
Cumulative deaths	36	113	196	292	378	480	582	711	838	937	1070	1150	1213
Cumulative person-years	77 268	154 053	230 270	305 833	380 691	454 773	527 937	600 004	670 274	735 098	789 540	832 441	864 227
Usual care group													
Cumulative deaths	30	111	198	301	426	527	639	761	884	987	1076	1162	1230
Cumulative person-years	77 286	154 116	230 348	305 902	380 725	454 719	527 804	599 790	669 955	734 523	788 854	831 678	863 330

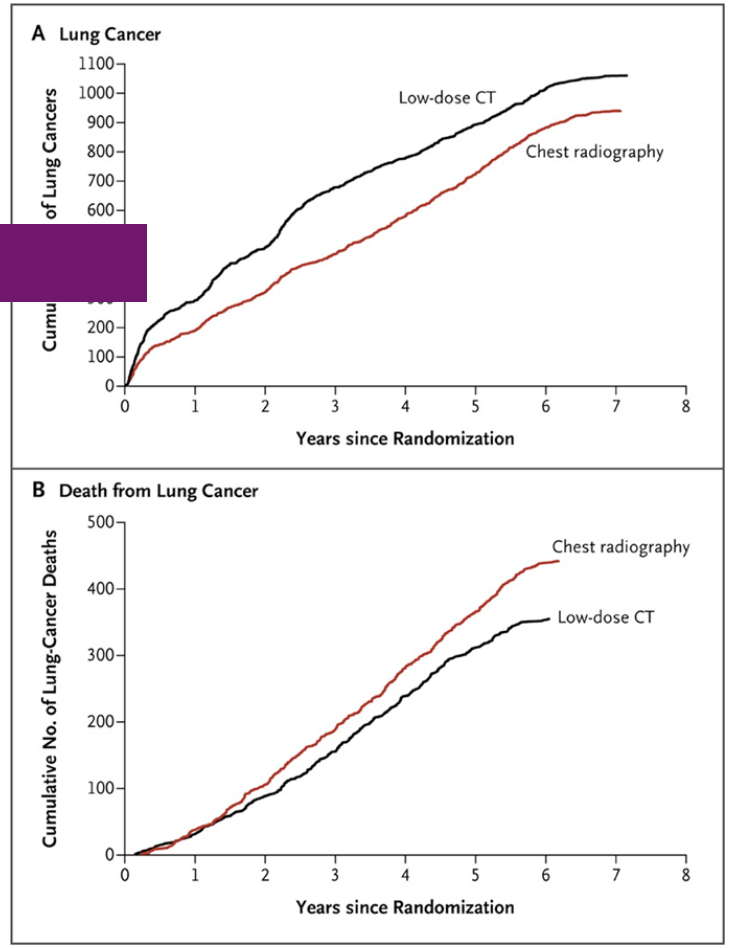
The Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Trial JAMA. 2011;306(17):1865-1873.

Screening high-risk population for lung cancer by low dose CT is beneficial

Higher prevalence

More sensitive

- **53,000 subjects randomized to CT or CXR yearly x 3 years**
- **Age 55 to 74 years**
- **History of cigarette smoking of at least 30 pack-years, and, if former smokers, had quit within the previous 15 years.**



Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011 Aug 4;365(5):395-409.

Staging of cancer with PET

If prevalence of metastatic disease at diagnosis is low, false positives far exceed true positives.

Example: early stage breast cancer

If metastatic disease is known from other studies, finding more metastases via PET does not improve outcome.

Example: stage IV colon cancer.

For many cancers, re-assessment via PET is no better than re-assessment via CT scan.

Risk prediction vs. risk reduction

Predicting increased risk does not improve outcome if no risk-reducing intervention is available.

Example: Decision-DX for uveal melanoma.

Predicting increased risk does not improve outcome if it dictates no change in therapy.

Example: Factor V Leiden in patient with recurrent deep vein thromboses.

Surveillance imaging may not improve outcome: Hodgkin lymphoma in first remission

	Number of patients	Number relapsing	Relapsing at 2 years or more	Relapse rate	5-year overall survival	Diagnostic images per detected relapse
Routine clinical follow-up + routine imaging	305	28 (9%)	4	13%	94%	47.5
Routine clinical follow-up + imaging only in case of relapse suspicion.	63	8 (13%)	2	9%	94%	4.7

Br J Haematol. 2014 Mar;164(5):694-700.

Molecular (genomic) profiling of cancer

Examples: FoundationOne, Guardian, Colaris
Tests for mutations of scores to hundreds of genes
A few tested genes may predict response to therapy, e.g. EGFR in lung cancer.
Specific predictive tests are available outside of a panel.
No evidence that therapy chosen on basis of test panel improves outcomes…

…yet.

Conclusions

Not all good ideas are proven ideas.

Evidence-based medicine requires…

…evidence!

Unnecessary testing is always expensive, and often harmful.