What makes something clinically useful?

From ROC curves to clinical practice

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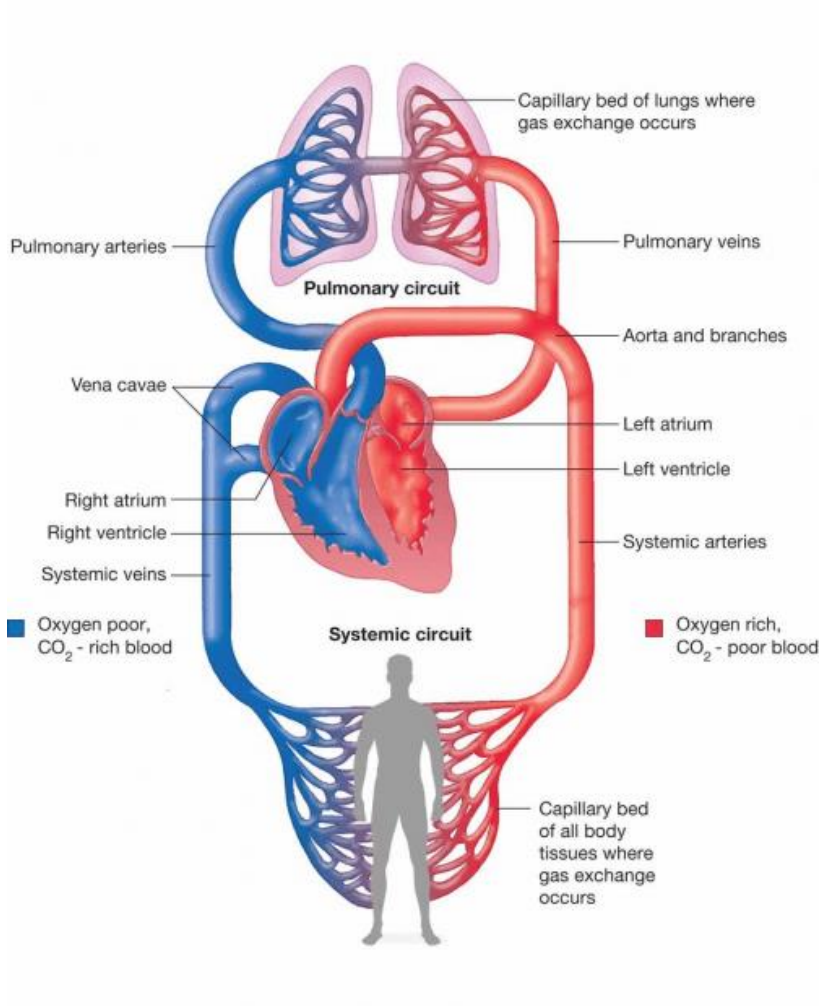
Pulmonary embolism



Pathophysiology

- A thrombus (blood clot) in the venous system
- This clot then travels to the pulmonary capillary bed

Symptoms

- Swollen leg
- Shortness of breath
- Cardiac arrest

Diagnosis

- Chest-CT with IV contrast

Treatment

- Anticoagulants

https://www.google.com/url?sa=i&url=https%3A%2F%2Fdifference.guru%2Fdifference-between-pulmonary-and-systemic-circulation%2F&psig=AOvVaw2iYd5kIdgTY4kl4zlE74vd&ust=1631619948960000&source=images&cd=vfe&ved=0CAsQjRxqFwoTCNiL14_w-_ICFQAAAAAdAAAAABAJ

Patient Alfred

Patient	• Male • 55 years old • Present at the emergency department with shortness of breath
Prior history	• Has atrial fibrillation (common heart rhythm abnormality) • Takes anticoagulation medication
Signs and symptoms	• Shortness of breath since this morning • Left leg hurts
Physical examination	• Breathing 22/min • Saturation of 97% • Swollen left leg

If a test does not change decisions, it is not useful.

Patient Dana

Patient	• Female • 55 years old • Present at the emergency department with shortness of breath
Prior history	• Had knee surgery 2 weeks ago • Takes no medication
Signs and symptoms	• Shortness of breath since three days • No other complaints
Physical examination	• Breathing 25/min • Saturation of 94% • Heart rate of 120/min

Making a biomarker for predicting pulmonary embolism

Biomarker A

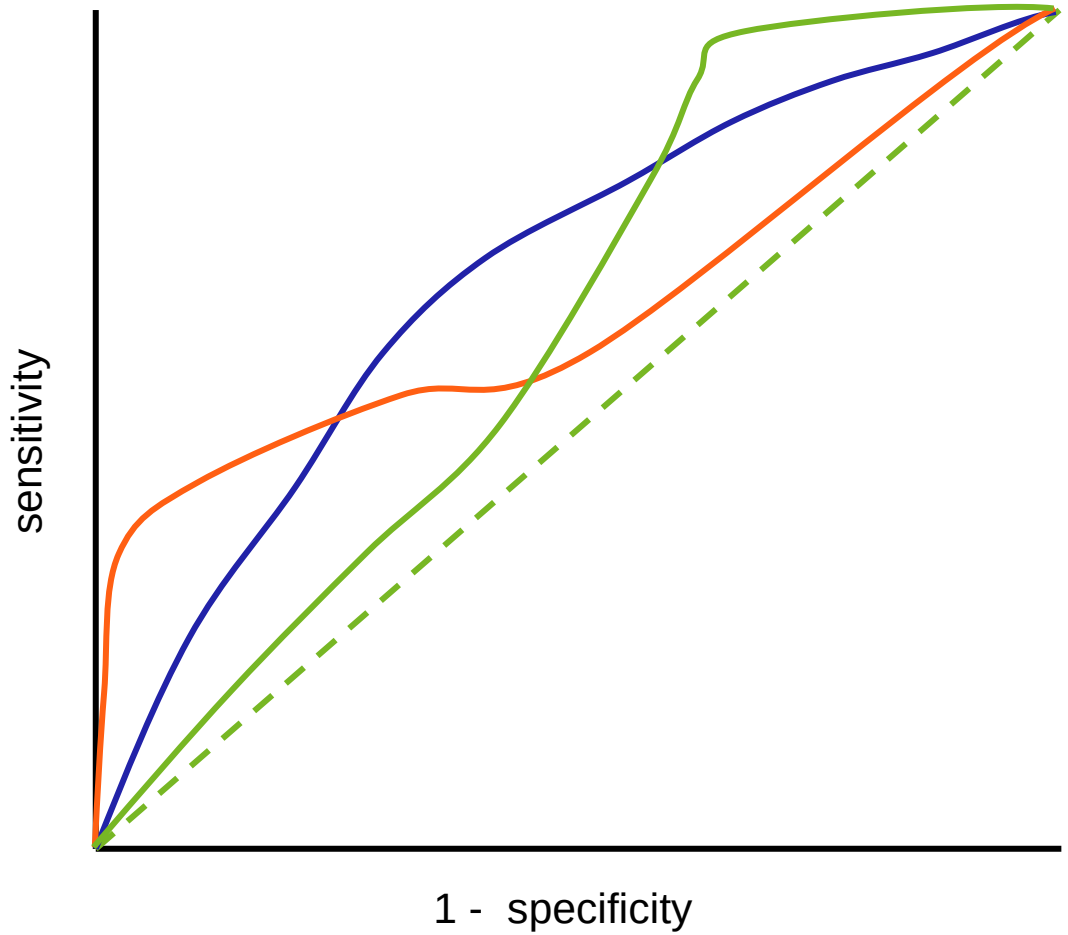
- AUC: 0.71

Biomarker B

- AUC: 0.65
- Highest specificity

Biomarker C

- AUC: 0.64
- Highest sensitivity



	Does not have the disease	Has the disease
Test is negative	True negative Cool	False negative **BAD**
Test is positive	False positive Okay	True positive Cool

In this case, we want **high sensitivity**

Making a biomarker for classifying abnormalities as cancer or not

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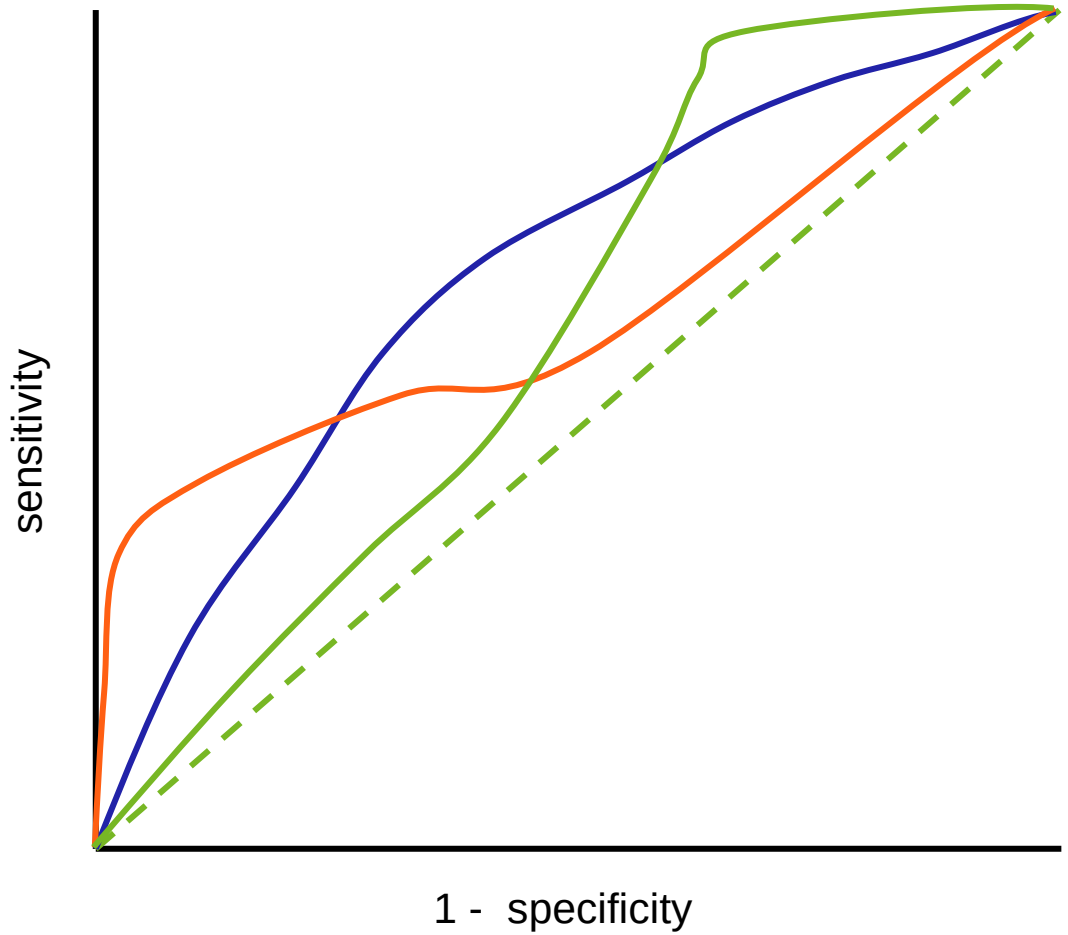
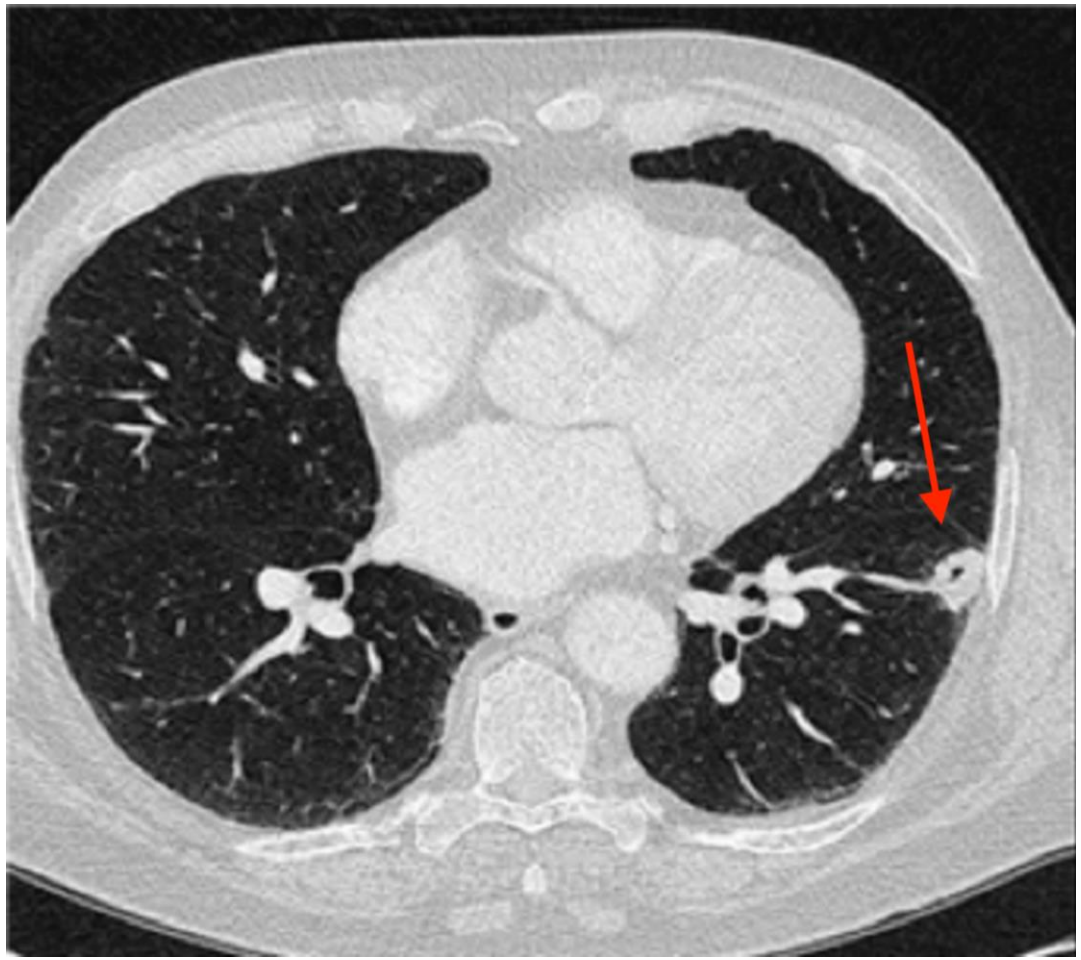


Chest-CT shows no pulmonary embolism, but something that might be cancer



Diagnosis

- Biopsy

Treatment

- Lung surgery
- Chemotherapy

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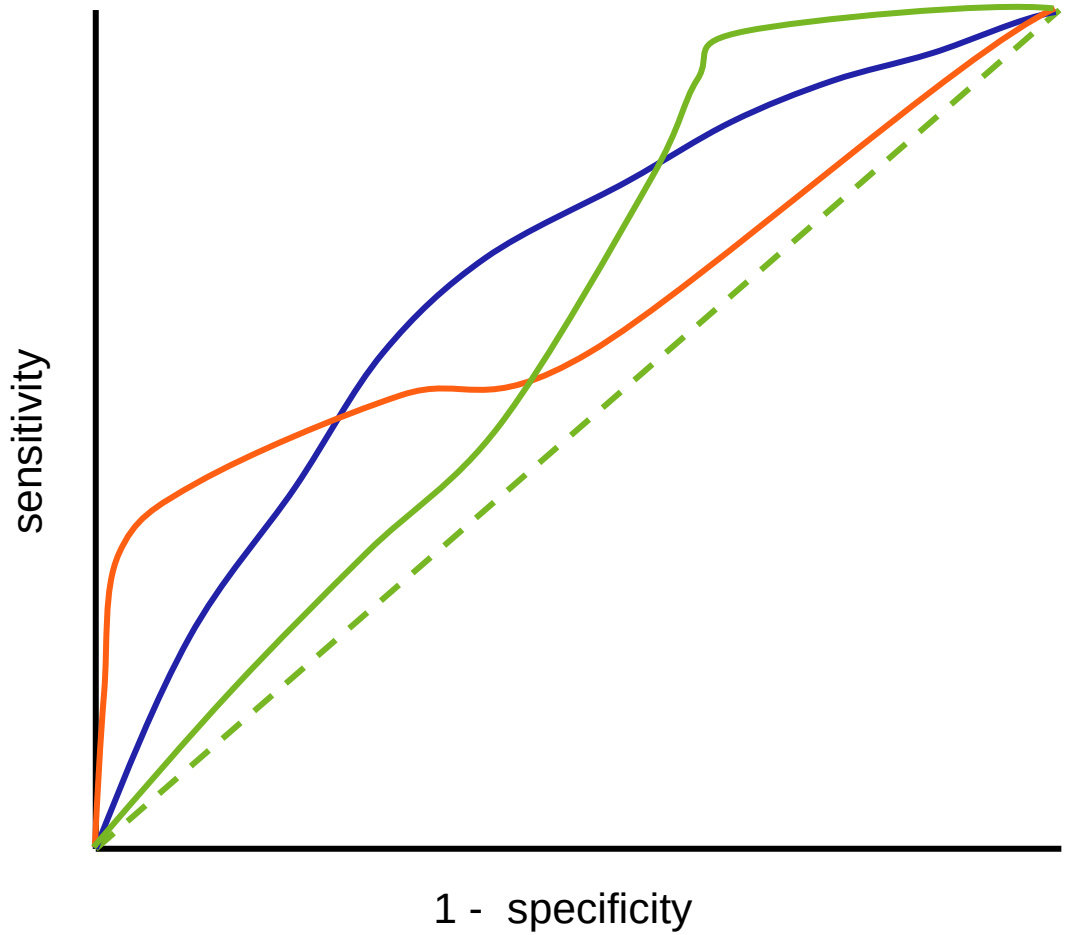

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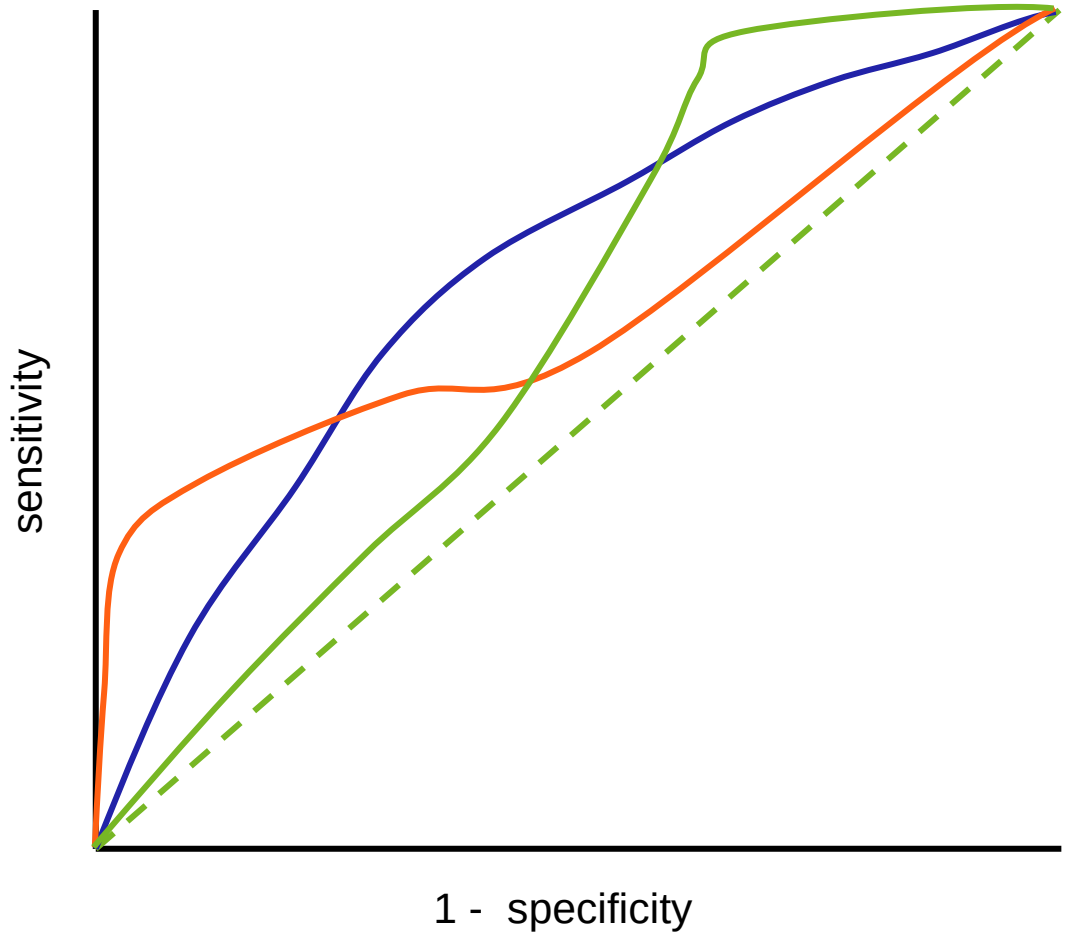
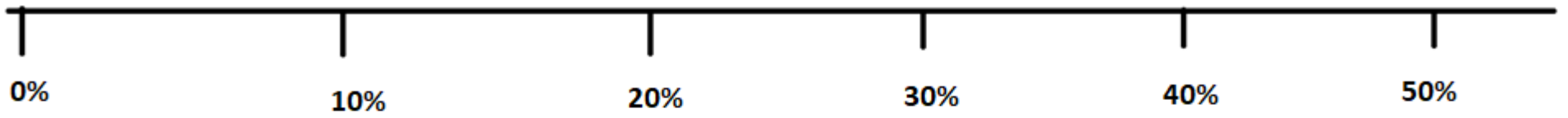


If a **false negative** is bad, **high sensitivity** is needed

If a **false positive** is bad, **high specificity** is needed

Pathology report and other test results comes back…

Diagnosis	• Cancer, but more advanced than initially thought • Only an experimental drug is a treatment option
Prognosis without treatment	• Median survival of 6 months
Prognosis with treatment	• 40% of patients respond and live several years • 60% of patients have no benefit
Side-effects	• Fatigue • Diarrhoea and/or vomiting • Joint pain



Probability threshold (p)

More worried about disease progression

More worried about side-effects

Making a biomarker for predicting response

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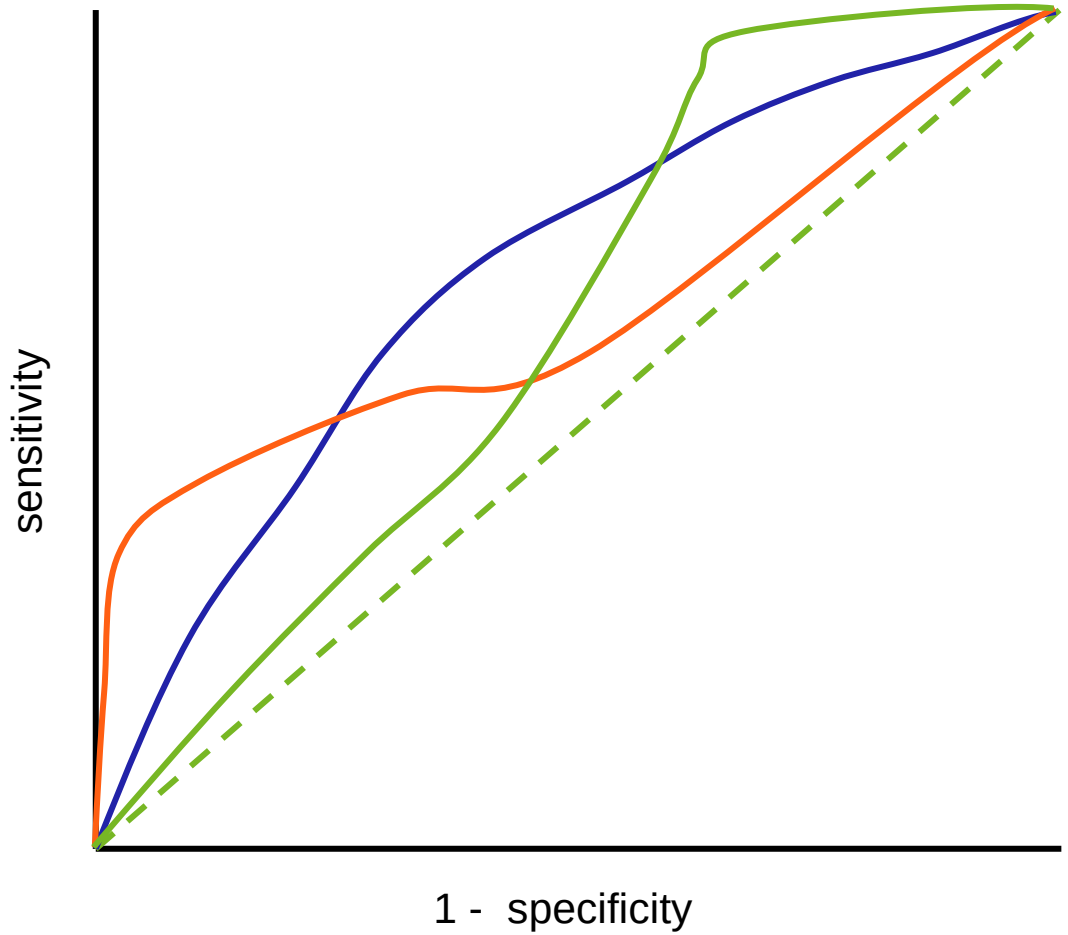
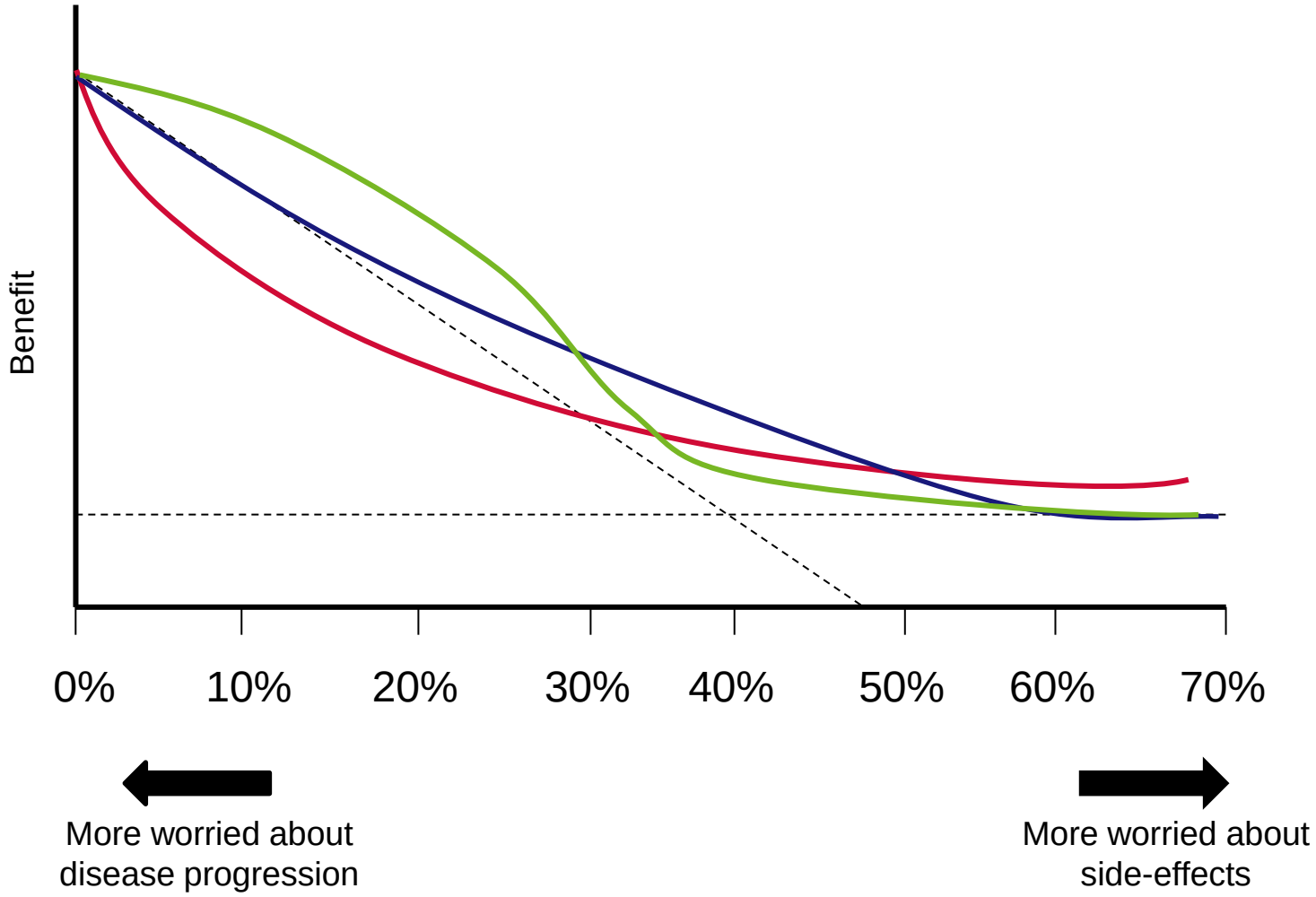


How useful a biomarker is depends greatly on the preference of the patient, and these may vary considerably.



Vickers, Andrew J., and Elena B. Elkin. "Decision curve analysis: a novel method for evaluating prediction models." *Medical Decision Making* 26.6 (2006): 565-574.

Summary

1. Explain how your model will **change decisions.**

2. **False negatives** are bad stuff? Optimize for **sensitivity**.

3. **False positives** are bad stuff? Optimize for **specificity**.

4. If patient **preferences differ** significantly, use a **decision curve.**