Evidence-Based Laboratory Performance Measures

Chronic Kidney Disease

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Cooperative Agreement

- National Center for Preparedness, Detection and Control of Infectious Diseases (NCPDCID) and Kaiser Permanente Center for Health Research (KPNW and KPSE)
- Colleagues at KP
  - Eric Johnson, PhD
  - Micah Thorp, DO MPH
  - Suma Vupputuri, PhD
  - Jessica Weinstein, MD
  - Douglas Roblin, PhD
  - Evelyn Whitlock, MD
  - Adrianne Feldstein, MD

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CDC Sponsored Investigation

- NCPDCID funded 3 groups to create evidence based performance measures in laboratory medicine
  - Our work focuses on Chronic Kidney Disease (CKD)
    - Pre-dialysis CKD
  - Phase I
  - Phase II

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Classification and Prevalence by Stage of Disease Estimated glomerular filtration rate (eGFR)

In ml/min/1.72m^2 = 186.3*(sCr)-1.154 * Age-0.203 * (0.742 if female) * (1.21 if African-American)

	Definition	US Prevalence
Stage 1	eGFR normal (>90) + kidney damage	3.6 million (1.8%)
Stage 2	eGFR 60-90 + kidney damage	6.5 million (3.2%)
Stage 3	eGFR 30-59	15.5 million (7.7%)
Stage 4	eGFR 15-29	0.7 million (0.35%)

From: Coresh, et al. JAMA 2007

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Changing Prevalence of CKD in Adults

- Estimates from NHANES data:
  - 10.0% (95% CI, 9.2%-10.9%) in 1988-1994
  - 13.1% (95% CI, 12.0%-14.1%) in 1999-2004

  - 26.3 million total (2000 census estimate)

From: Coresh, et al. JAMA 2007

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Clinical Outcomes in CKD

- Five year follow-up in those with eGFR<60
  - 1.6 progressions to renal replacement/100 person-years
  - 11.4 deaths/100 person-years
    - *Johnson, et al. AJKD 2008*
- USRDS data on death rates for Medicare
  - 17 to 22 deaths/100 person years for CKD
  - 5 deaths/100 person years for non-CKD

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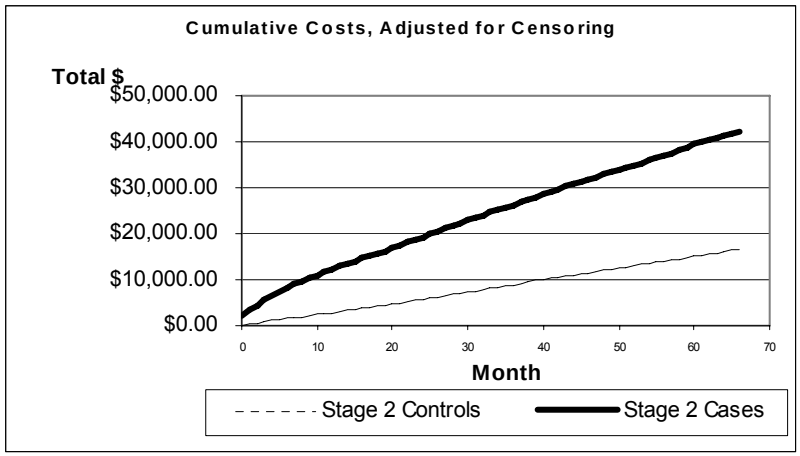
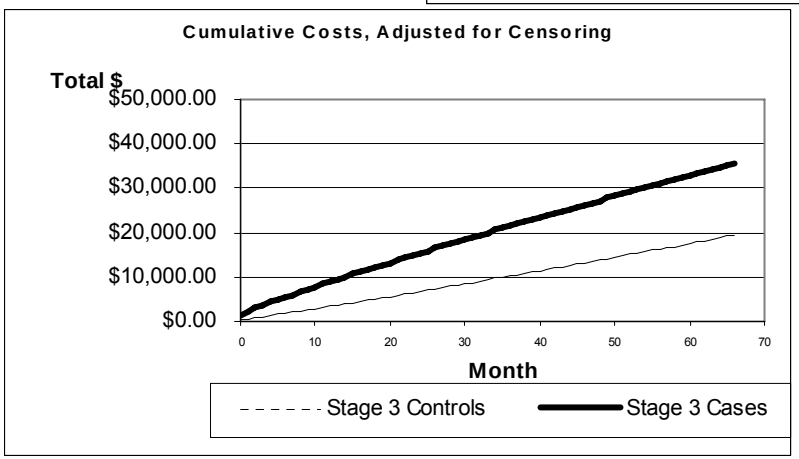
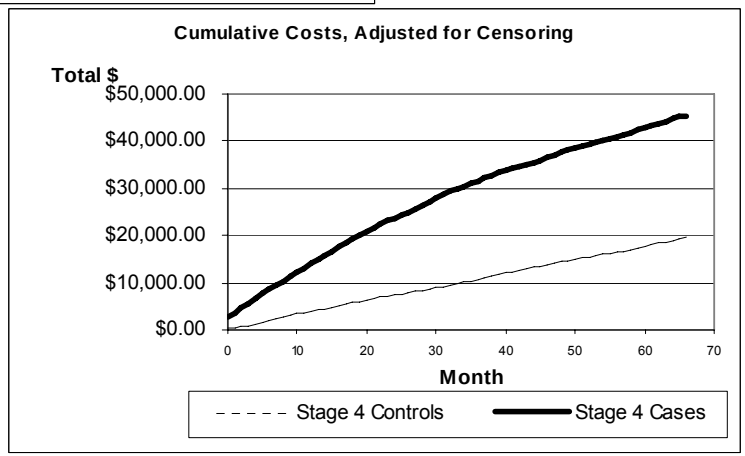
Cost of Care by CKD Stage, Compared to Patients without CKD







Smith, et al, J Am Soc Neph 2006

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Phase I: Strategies for Development of Performance Measures

- Based on what a ‘good’ clinician would do
- Expert consensus
- Clinical practice guidelines

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KDOQI Guideline	Subject	Clinical Performance Measures?
1	Stages of Chronic Kidney Disease	
2	Evaluation and Treatment	Yes[a]
3	Individuals at Increased Risk for Chronic Kidney Disease	Yes[a]
4	Estimation of GFR	Yes[a]
5	Assessment of Proteinuria	Yes[a]
6	Markers of Kidney Damage Other than Proteinuria	
7	High Blood Pressure	Yes[b]
8	Anemia	Yes[a]
9	Malnutrition	Yes[a]
10	Bone Disease and Disorders of Calcium and Phosphorus Metabolism	Yes[a]
11	Neuropathy	
12	Functioning and Well-Being	Yes[a]
13	Loss of Kidney Function	Yes[b,c]
14	Diabetic Complications	Yes[b]
15	Cardiovascular Disease	Yes[a,b,c]

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Key Questions for iPTH Testing

- Good evidence that patients with CKD have elevated levels of iPTH
- But no clear evidence that treatment of iPTH (e.g. with phosphate binders) leads to changes in either 'final' or intermediate outcomes

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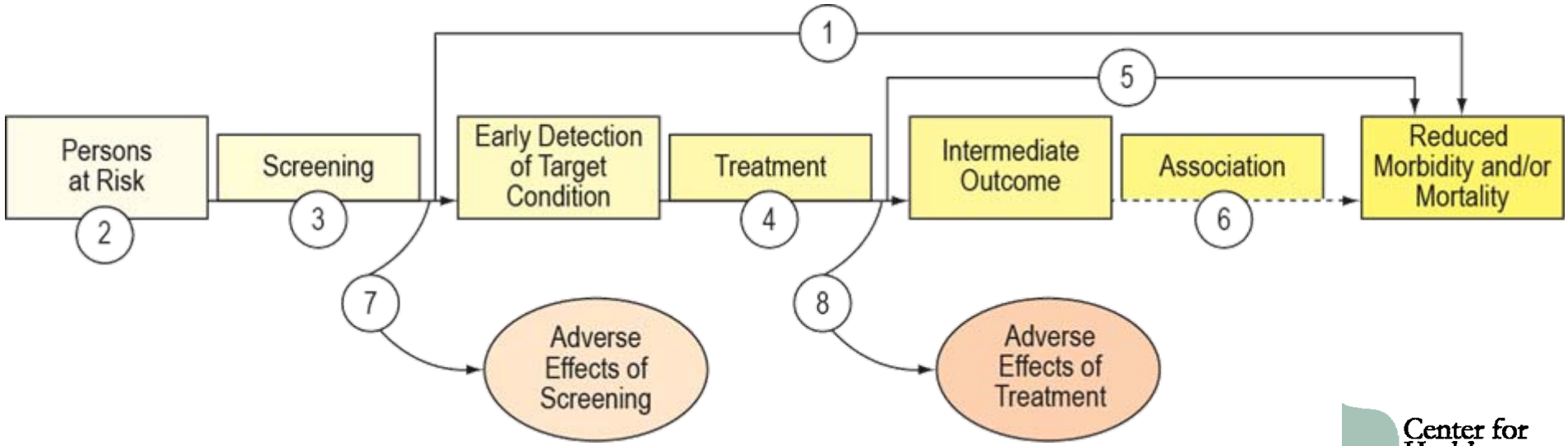
US Preventive Services Task Force (USPSTF) Framework for Screening

- Key questions identified in terms of framework
- Systematic review of evidence is key to framework's usefulness
- We have adapted the framework in our performance measure development



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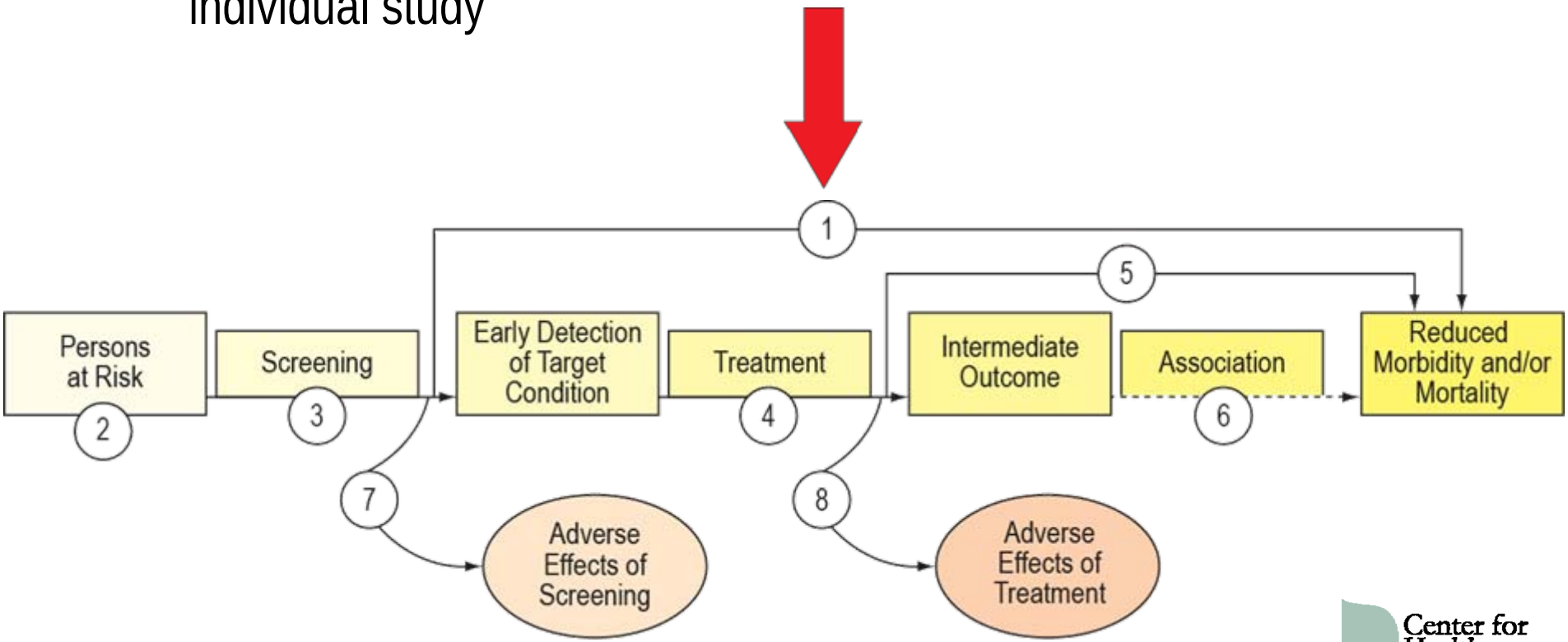
Key Question 1:

Direct evidence that testing for protein reduces morbidity and/or mortality?

Overarching question, rarely answered by an individual study



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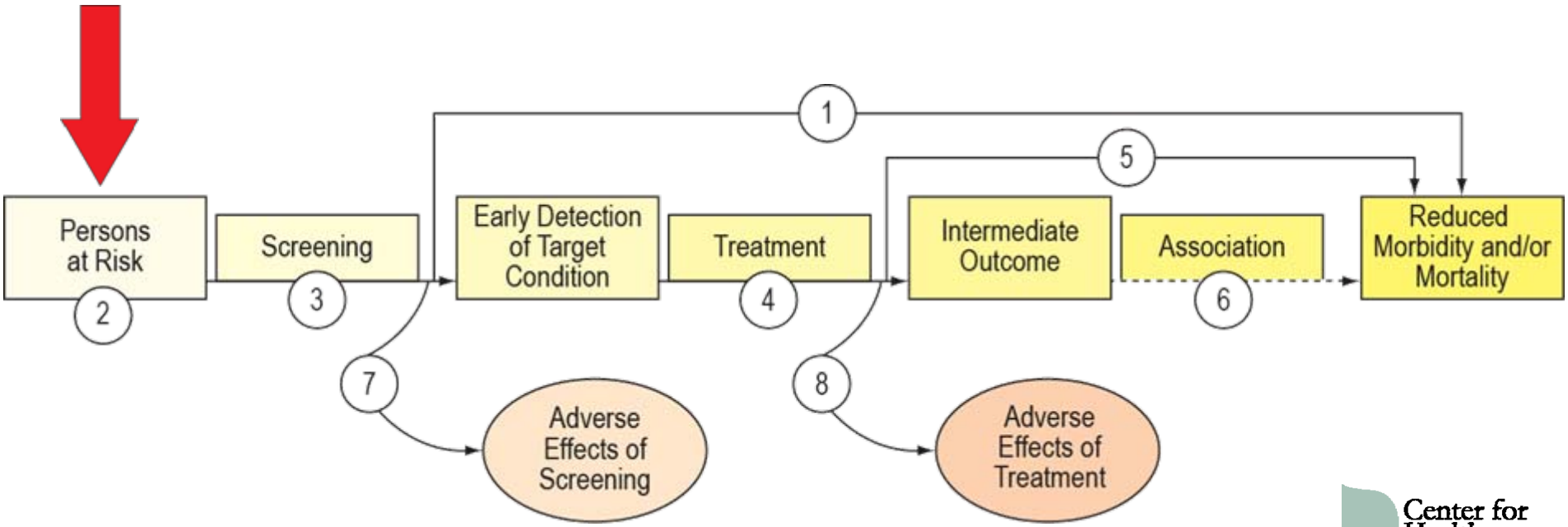
Key Question 2:

Can a high risk group be identified reliably?

Yes, CKD patients with eGFR <60



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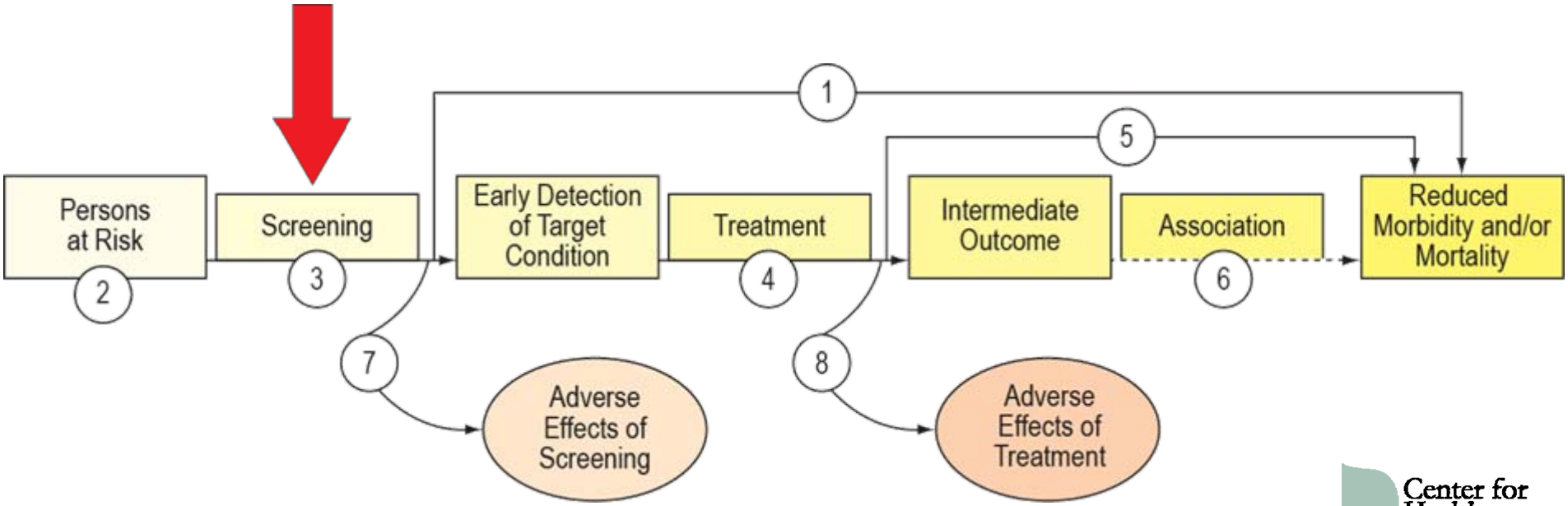
Key Question 3:

What are the test properties?



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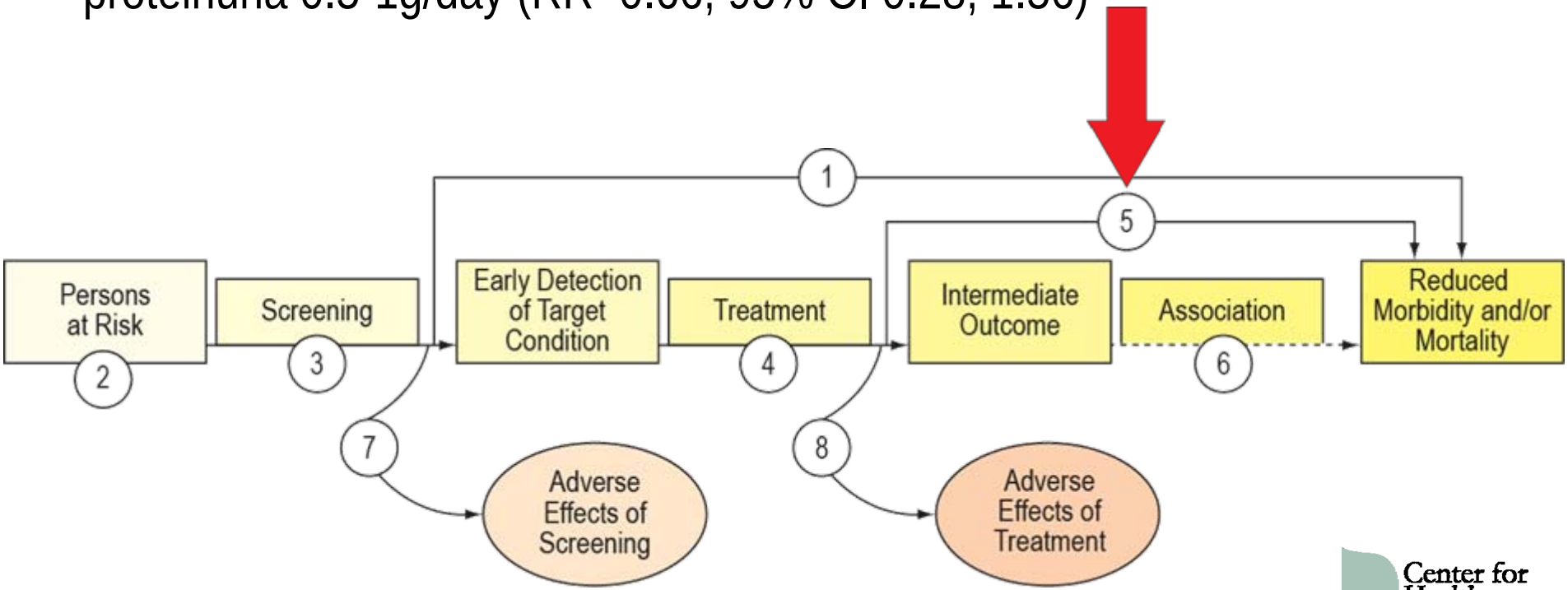
Key Question 5:

Does treatment improve 'final' outcomes?

Yes, by using RAS agents the risk of end-stage renal disease (ESRD) was lowered for patients with proteinuria 0.5-1g/day (RR=0.66, 95% CI 0.28, 1.56)



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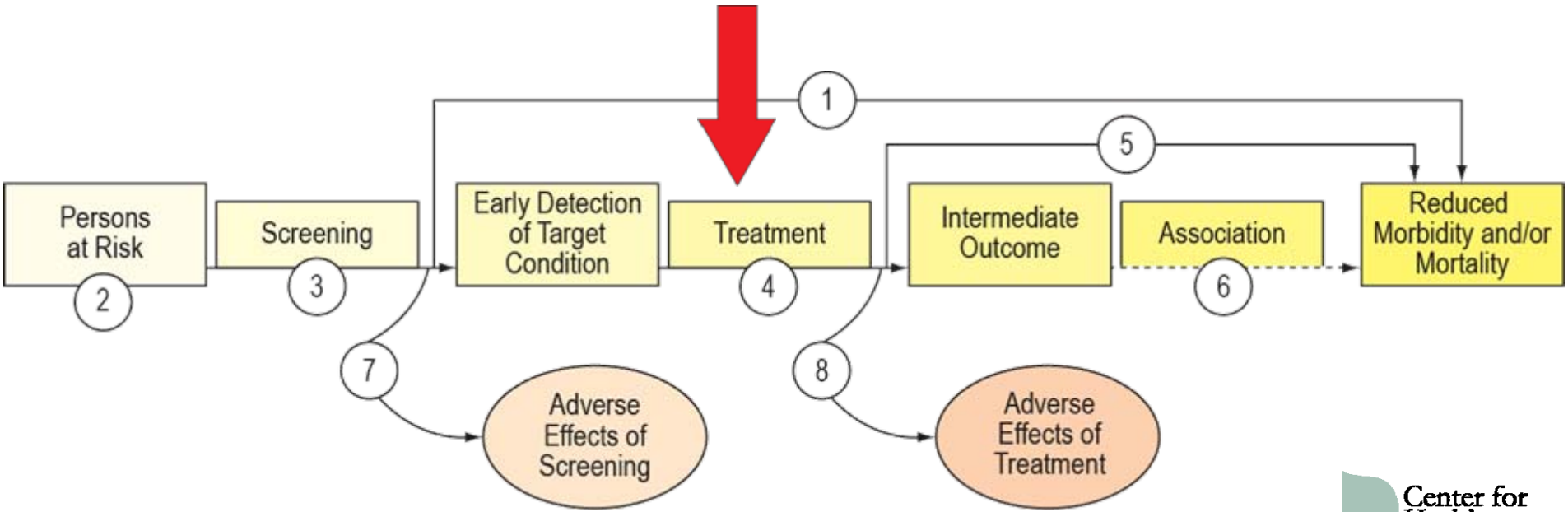
Key Question 4:

Does treatment of patients with proteinuria reduce intermediate outcomes (e.g. protein load, eGFR)?

Yes, by using renin-angiotensin system (RAS) agents.



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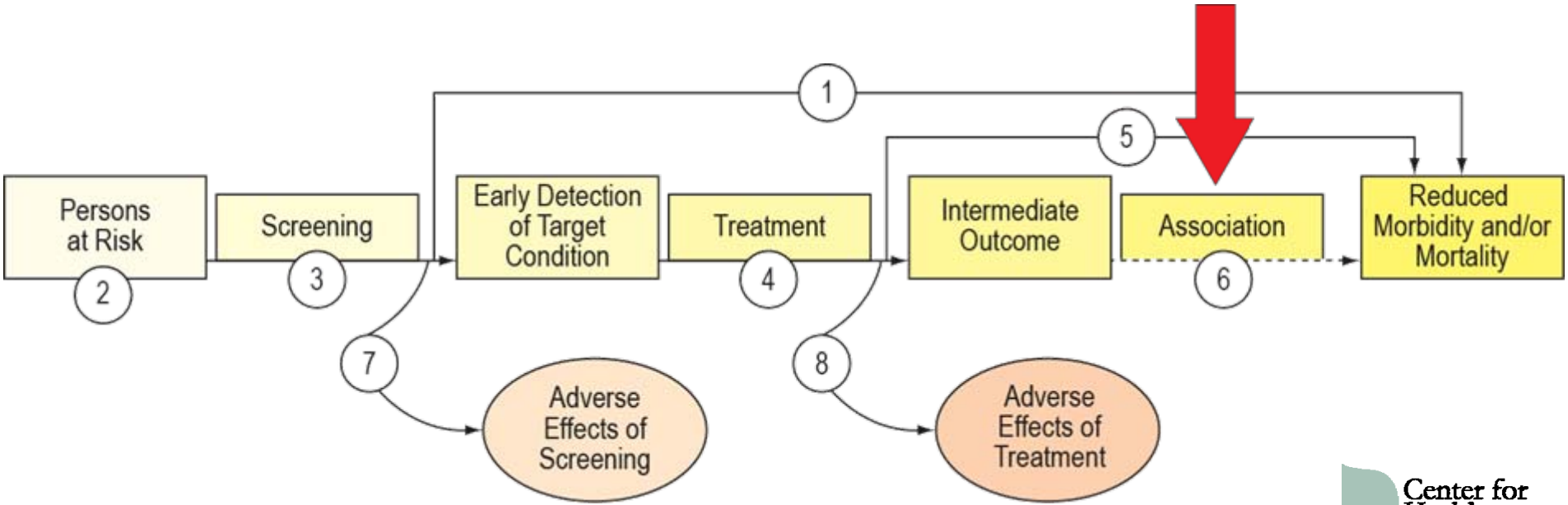
Key Question 6:

Is the intermediate outcome reliably associated with reduced morbidity/mortality?



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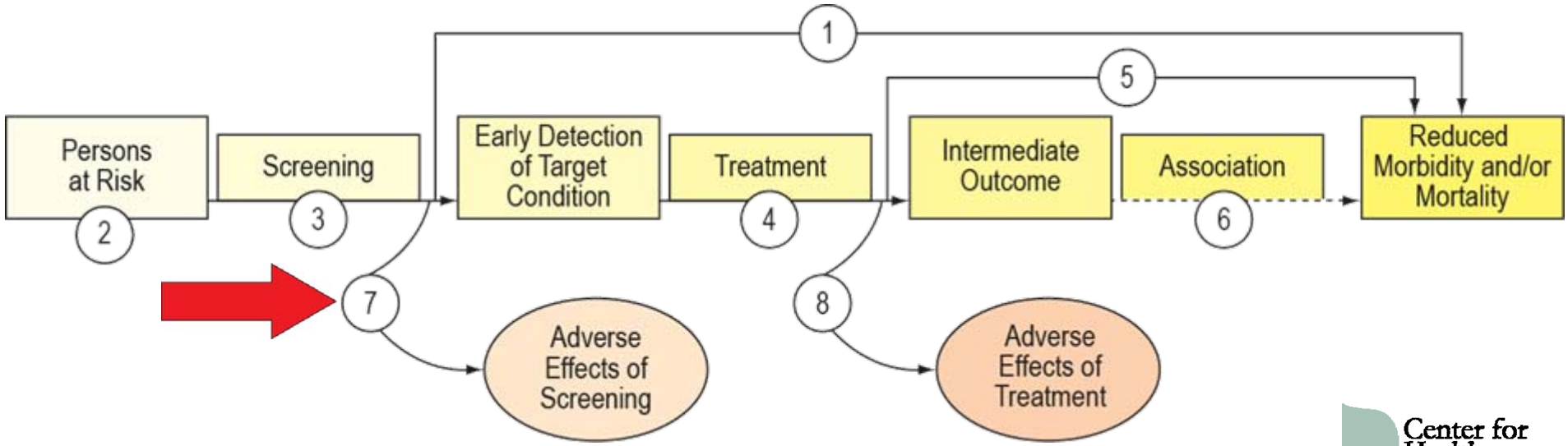
Key Question 7:

Are there adverse effects of screening?

Indirect evidence on this topic suggests clinically unimportant changes



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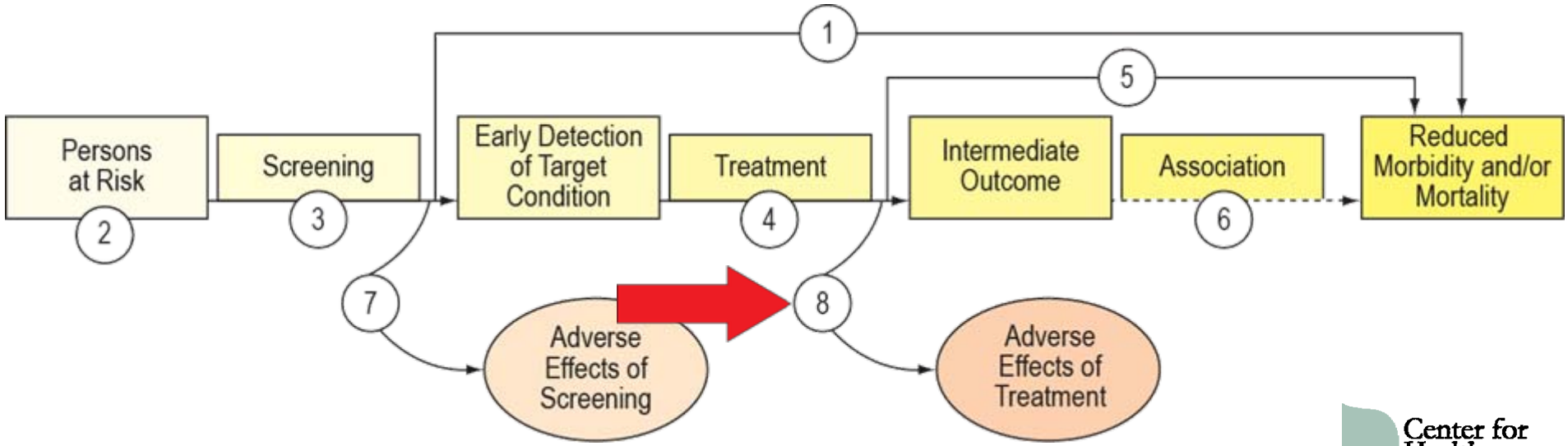
Key Question 8:

Does treatment with RAS agents result in adverse effects?

- Yes, hyperkalemia and cough
- <2% of patients treated with ACE inhibitors developed hyperkalaemia >6 mmol/l and serum potassium levels increased by an average of 0.4 to 0.6 mmol/l. Increased K monitoring recommended.
- Patients with troublesome cough can be switched to ARB



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Phase II: Draft Proteinuria Performance Measure

- Numerator
- Denominator
- Operationalize the measures in our health plans (KPNW and KPSE)
  - Current state of play with regard to performance
  - Subgroups with higher or lower performance
    - Age, comorbidities, etc.

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Update on the Methods of the U.S. Preventive Services Task Force: Estimating Certainty and Magnitude of Net Benefit

Annals of Internal Medicine (2007)

"Using outcomes tables, the USPSTF estimates the magnitude of benefits and the magnitude of harms, and synthesizes them into an estimate of net benefit."

Known CKD patients at Kaiser Permanente Northwest	10,000
True (unknown) prevalence of macroalbuminuria at KPNW	1,000
Observed prevalence of macroalbuminuria at KPNW	?
True positive finding	?
False positive finding	?
Patients treated with an ACE-inhibitor	?
Patients who develop harms from ACE-inhibitor	?
Patients whose end-stage disease prevented by ACE-inhibitor	?
Net ESRD cases prevented or caused by ACE-inhibitor (1-year)	?

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Future Directions and Strategies

- Newer thinking on testing and diagnosis involves simultaneous consideration of several characteristics vs. each singly
  - Narrow mandate with PTF Framework
  - Prognostic risk scores to predict final outcomes
  - Framingham Risk Score as example
  - Allow the use of several different lab measures or characteristics for patient identification

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Case Study of CKD patients

- Predicting the risk of dialysis and transplant among patients with CKD: a retrospective cohort study
- *American Journal of Kidney Diseases* October 2008

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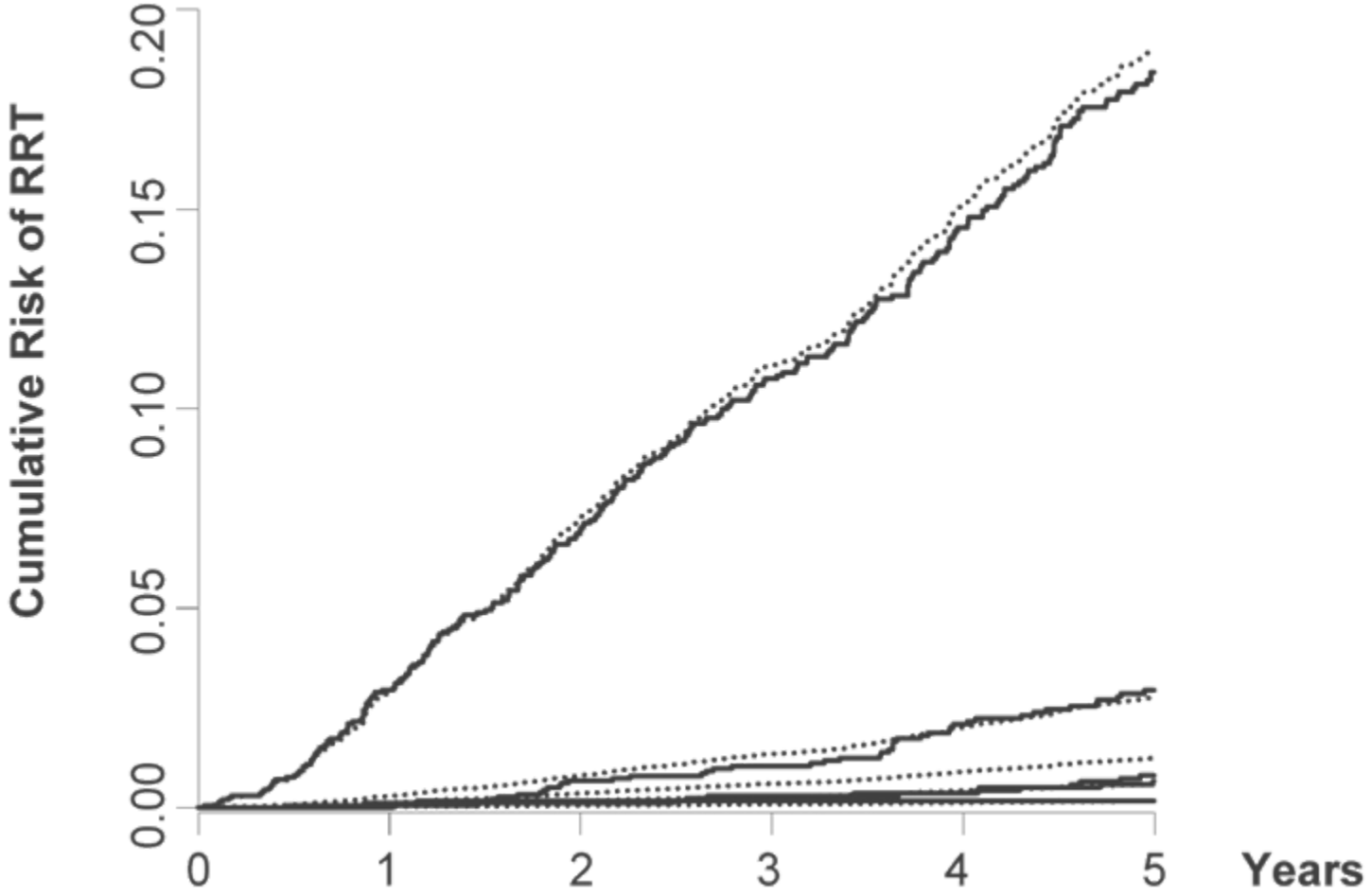
The 5-year risk of dialysis or transplant among patients with chronic kidney disease according to quintiles of predicted risk. The darker lines show the observed risk; the lighter lines show the predicted risk. The observed and predicted risks agree within 1%.



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Hypothetical patient with chronic kidney disease:

49 years old	58 points
Male	16 points
No diabetes	0 points
High blood pressure	58 points
eGFR = 34 mL/mi	44 points
No anemia	0 points
Total risk score	**176 points**
	≥ 20% risk

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Comparing strategies for identifying high-risk CKD patients

NKF <30 mL/min	Risk score: 10% or higher
46% sensitivity	60% sensitivity
94% specificity	95% specificity
98% predictive value -	99% predictive value -
20% predictive value +	27% predictive value +
0.73 c-statistic	0.89 c-statistic
+/- 4% calibration	+/- 1% calibration

Both strategies identified ~800 patients at KPNW

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