Il Progetto SCOPE: programma europeo per lo screening della insufficienza renale cronica nell'anziano

Andrea Corsonello

IRCCS-INRCA

Cosenza

SCREENING

Screening for kidney disease —a lost opportunity

Bruce A. Molitoris

The ACP has published 'weak' guidelines for screening patients for kidney disease based on limited or no data, which could harm patients with undiagnosed or progressive kidney disease. As kidney experts weren't involved in the development of these guidelines, what should all health professionals know about screening for kidney disease?

Molitoris, B. A. *Nat. Rev. Nephrol.* **10**, 6–8 (2014); published online 3 December 2013; doi:10.1038/nrneph.2013.258

Box 1 | ACP recommendations[1]

Recommendation 1: ACP recommends against screening for chronic kidney disease in asymptomatic adults without risk factors for chronic kidney disease.
(Grade: weak recommendation, low-quality evidence)

Recommendation 2: ACP recommends against testing for proteinuria in adults with or without diabetes who are currently taking an ACE inhibitor or an ARB.
(Grade: weak recommendation, low-quality evidence)

Recommendation 3: ACP recommends that clinicians select pharmacologic therapy that includes either an ACE inhibitor (moderate-quality evidence) or ARB (high-quality evidence) in patients with hypertension and stage 1 to 3 chronic kidney disease.
(Grade: strong recommendation)

Recommendation 4: ACP recommends that clinicians choose statin therapy to manage elevated low-density lipoprotein in patients with stage 1 to 3 chronic kidney disease.
(Grade: strong recommendation, moderate-quality evidence)

Abbreviations: ACE, angiotensin-converting enzyme; ACP, American College of Physicians; ARB, angiotensin II–receptor blocker. Reproduced with permission from the American College of Physicians © Qaseem, A. *et al. Ann. Intern. Med.* http://dx.doi.org/10.7326/0003-4819-159-12-201312170-00726.

Early detection and early intervention can slow the progression of kidney disease and reduce the likelihood of kidney failure. We should be committed to supporting all approaches that will change kidney disease from a silent disease too often discovered in its late stages to one that is identified when modifications can affect the progression of the disease. By the time patients have stage 3 CKD, they have lost more than 50% of their total kidney function and at stage 3b they are at a point where progression to ESRD is all-too likely. The entire medical community must act sooner and enlist patients' help in minimizing the comorbidities and progression that too often remain undetected until very late in the disease process.

Renal function in older CKD patients

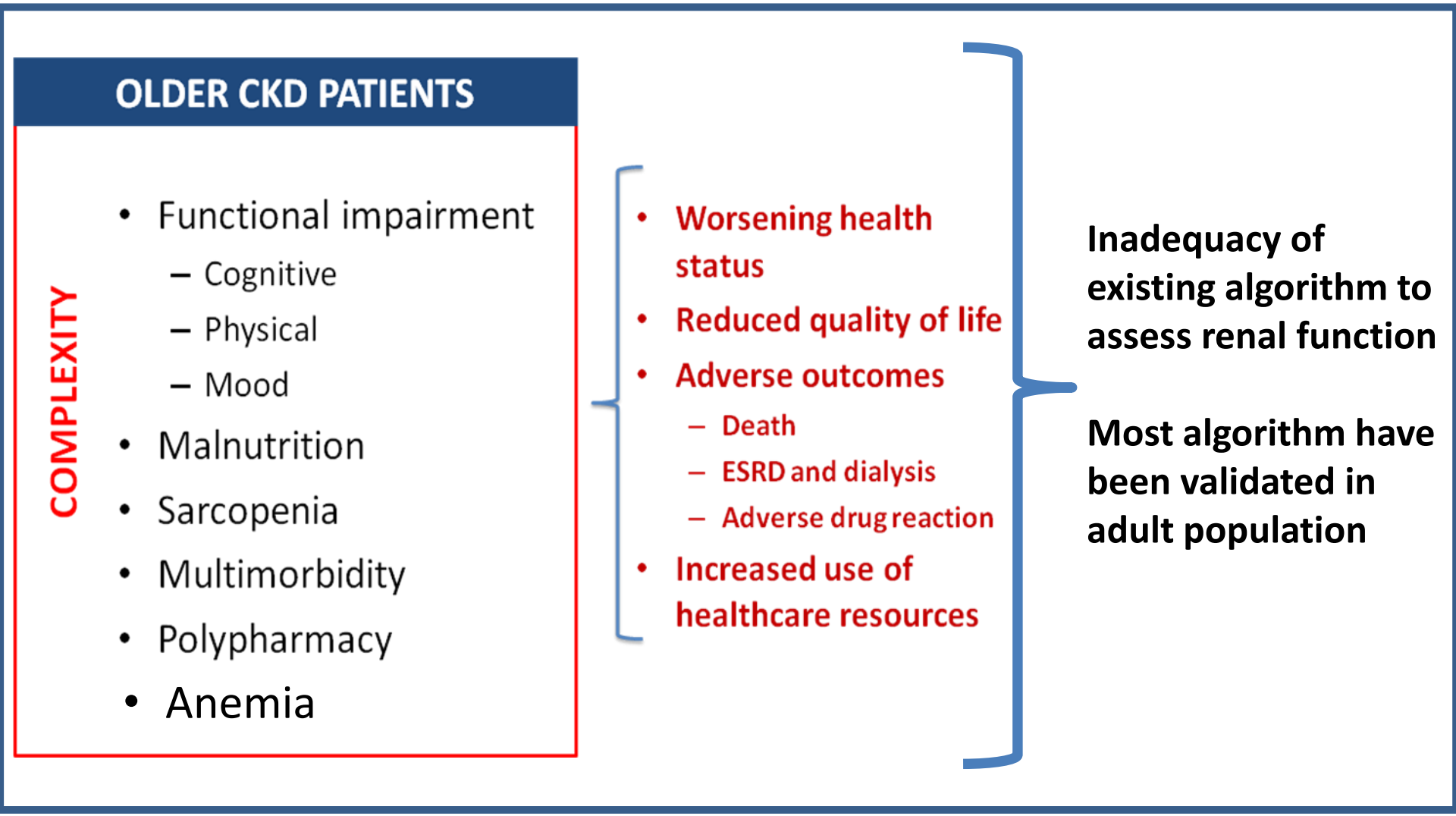
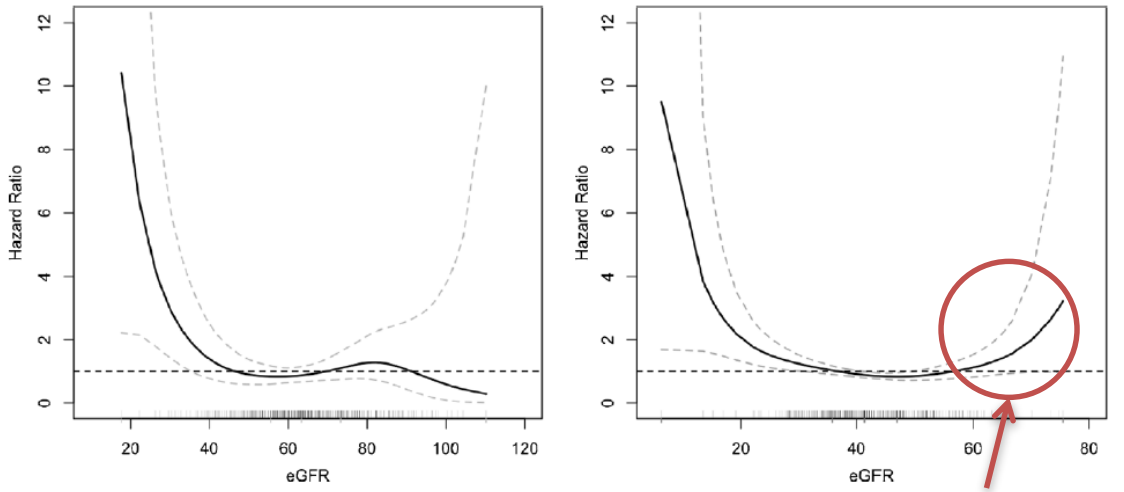


Figure 1.4b: Age and gender-adjusted spline of the relationship between eGFR and all-cause mortality in a cohort of older (A) and oldest-old (B) patients [26]



Lowest handgrip strength

Sarcopenia

↓ Serum creatinine

↓ Accuracy of eGFR

↓ Accuracy in:

- Diagnosis and management
- Prognostic stratification
- Drug dosing
- Cost-effectiveness

Novel application of existing biomarkers

Innovative biomarkers

↑ Accuracy in:

The SCOPE Consortium

SCOPE

Screening for CKD among Older People across Europe

SCOPE mission

Evaluating a 2-year screening program for CKD in the older patients to comprehend to which extent available screening methods may identify older people at risk of worsening kidney function

The SCOPE cohort

n = 2,450 in 7 Countries

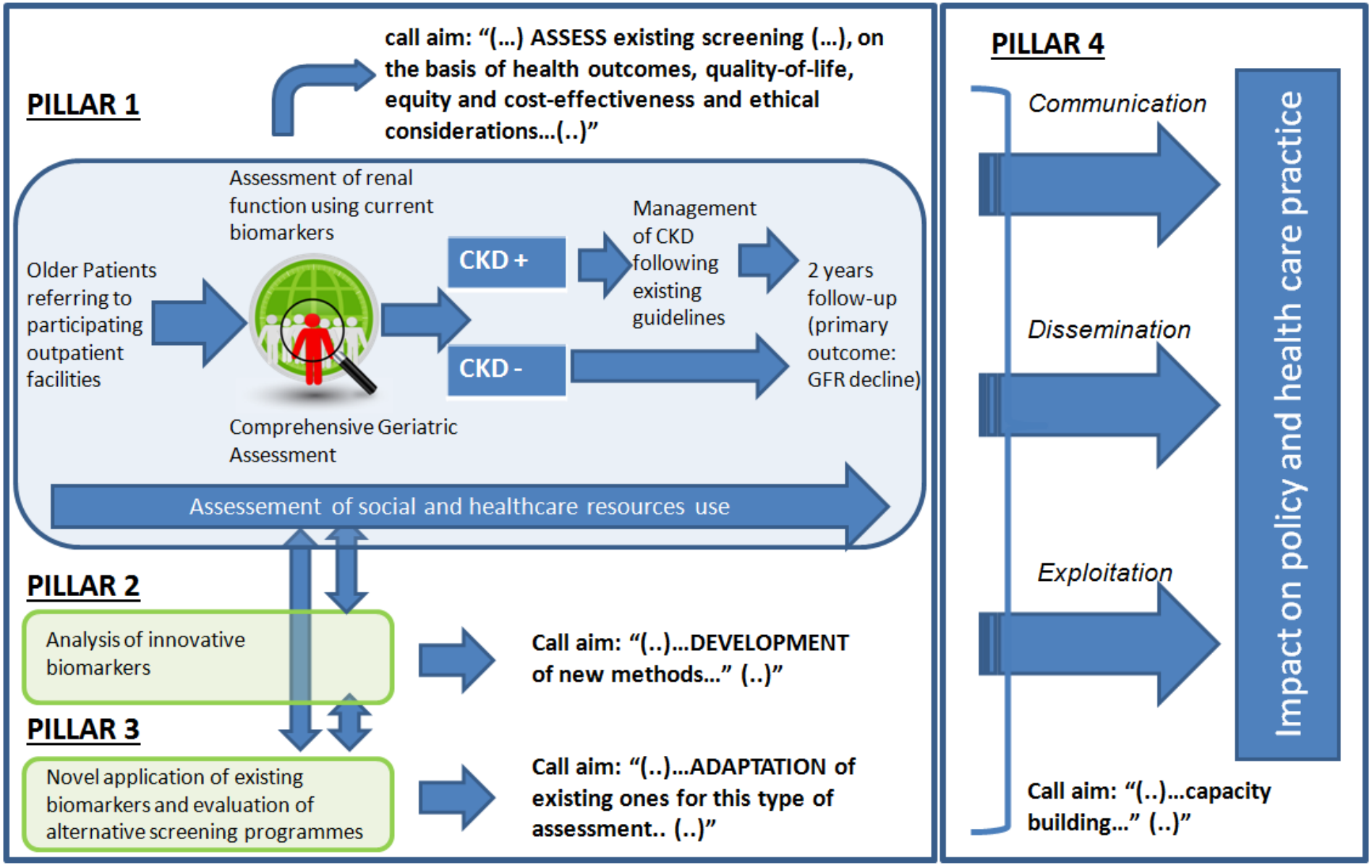
Primary End-points

- Rate of eGFR decline
- Incidence of ESRD

Secondary End-points

Effects of CKD screening programs on conventional and geriatric outcomes

SCOPE pillars and aims overview



Novel application of existing biomarkers

GFR Estimation: From Physiology to Public Health

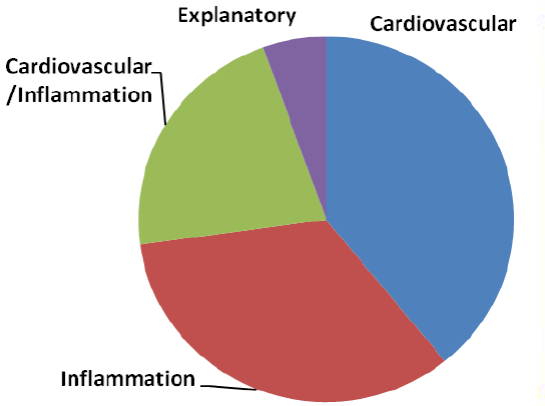
Box 1. Filtration Markers

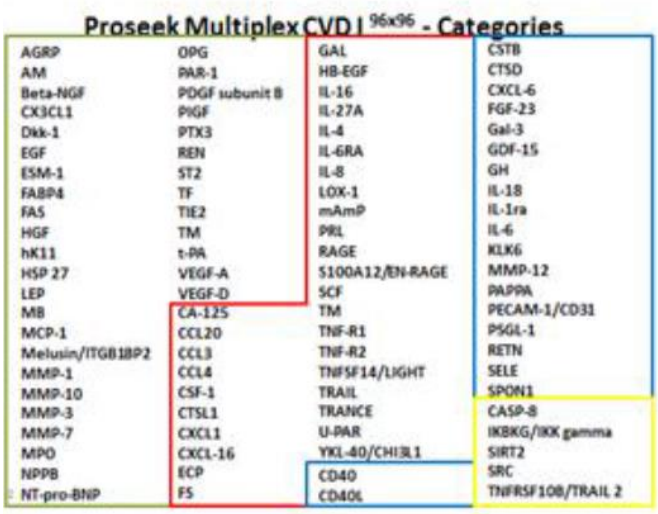
- Substances that are filtered by glomeruli that can be used to measure or estimate the GFR
- Ideal properties
  - ◇ Inert
  - ◇ Freely filtered
    - ▪ Molecular weight $< 20{,}000$ Da
    - ▪ Not protein bound
  - ◇ Not reabsorbed or secreted by the tubule
  - ◇ Not metabolized by the kidney
  - ◇ Easy to measure
- Exogenous filtration markers, for clearance measurements (urinary or plasma)
  - ◇ Inulin (5,200 Da)
  - ◇ Iothalamate (usually with ^{125}I) (640 Da)
  - ◇ Iohexol (821 Da)
  - ◇ ^{51}Cr-EDTA (372 Da)
  - ◇ ^{99m}Tc-DTPA (938 Da)
- Endogenous filtration markers, for GFR estimation
  - ◇ Metabolites (if excreted in urine, may also be used for clearance measurements)
    - ▪ Urea (60 Da)
    - ▪ Creatinine (113 Da)
  - ◇ Low-molecular-weight serum proteins
    - ▪ Cystatin C (13,300 Da)
    - ▪ B2M (11,700 Da)
    - ▪ BTP (23,000-29,000 Da)

Am J Kidney Dis. 2014;63(5):820-834

Innovative biomarkers

The *omics era*: Metabolomic and proteomics profiling in ULSAM and PIVUS study





The SCOPE cohort (n=2,450)

*SCOPE **aims** at evaluating a 2-year screening program for CKD in the older patients (75+), in seven European Countries, in an attempt to investigate whether and to which extent currently available screening methods may identify older people at risk of worsening kidney function*

Primary Study End-points

→ rate of eGFR decline

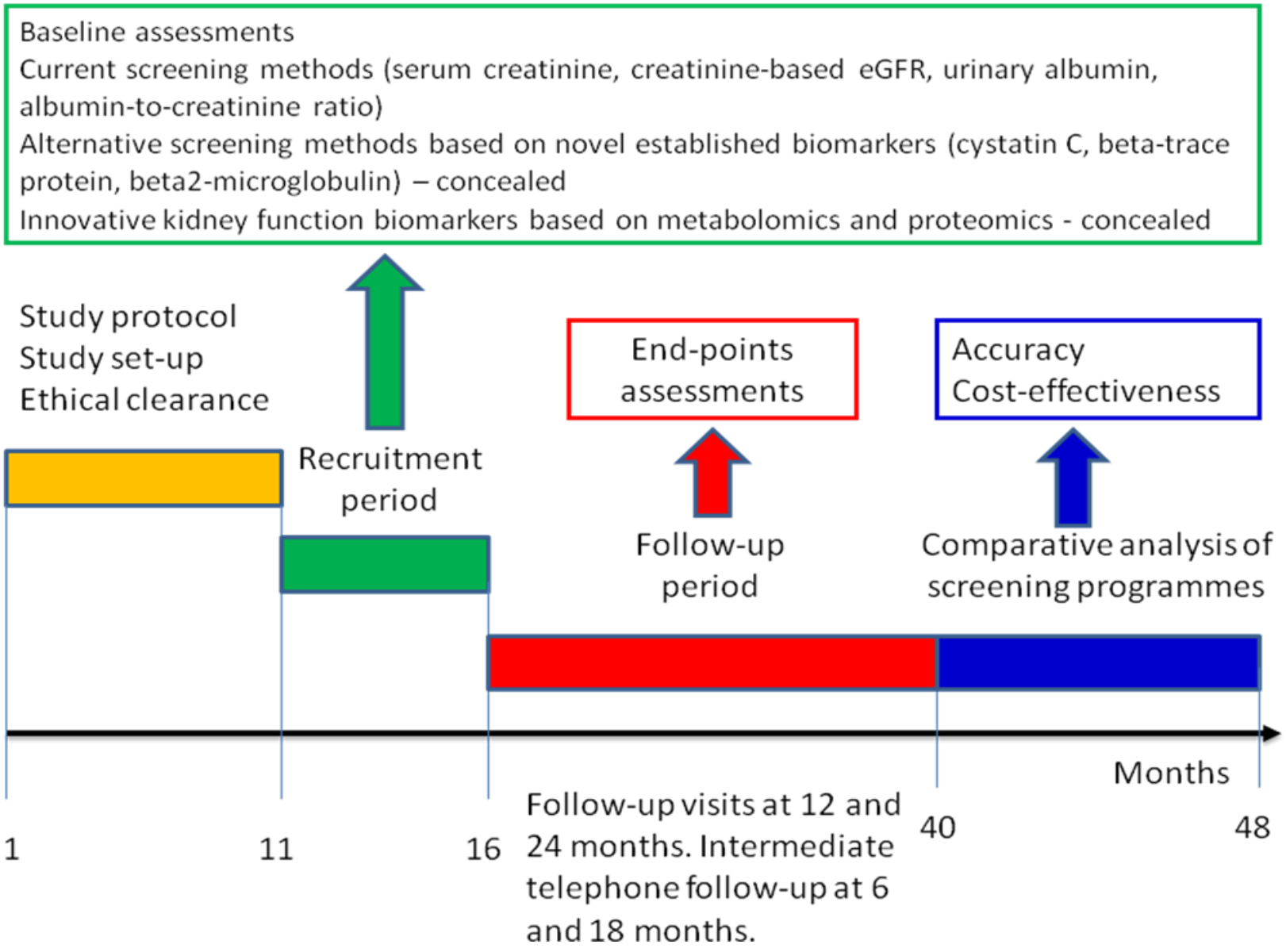
→ incidence of ESRD

Secondary Study End-points

→ effects of CKD screening programs on conventional and geriatric outcome measures

- *rate of CKD complications (anemia, hyperphosphatemia, acidosis, hypoalbuminemia, hyperparathyroidism, hyperkaliemia);*
- *rate of major comorbidities (e.g. hypertension and CV diseases);*
- *overall and CV mortality;*
- *adverse drug reactions (ADRs);*
- *self-reported disability and objectively measured physical performance decline;*
- *cognitive impairment;*
- *depression;*
- *malnutrition/undernutrition;*
- *health-related quality of life;*
- *healthcare resource consumption, including the estimation of caregiver burden*

The SCOPE cohort (n=2,450)



Screening for Chronic Kidney Disease among Older People across Europe

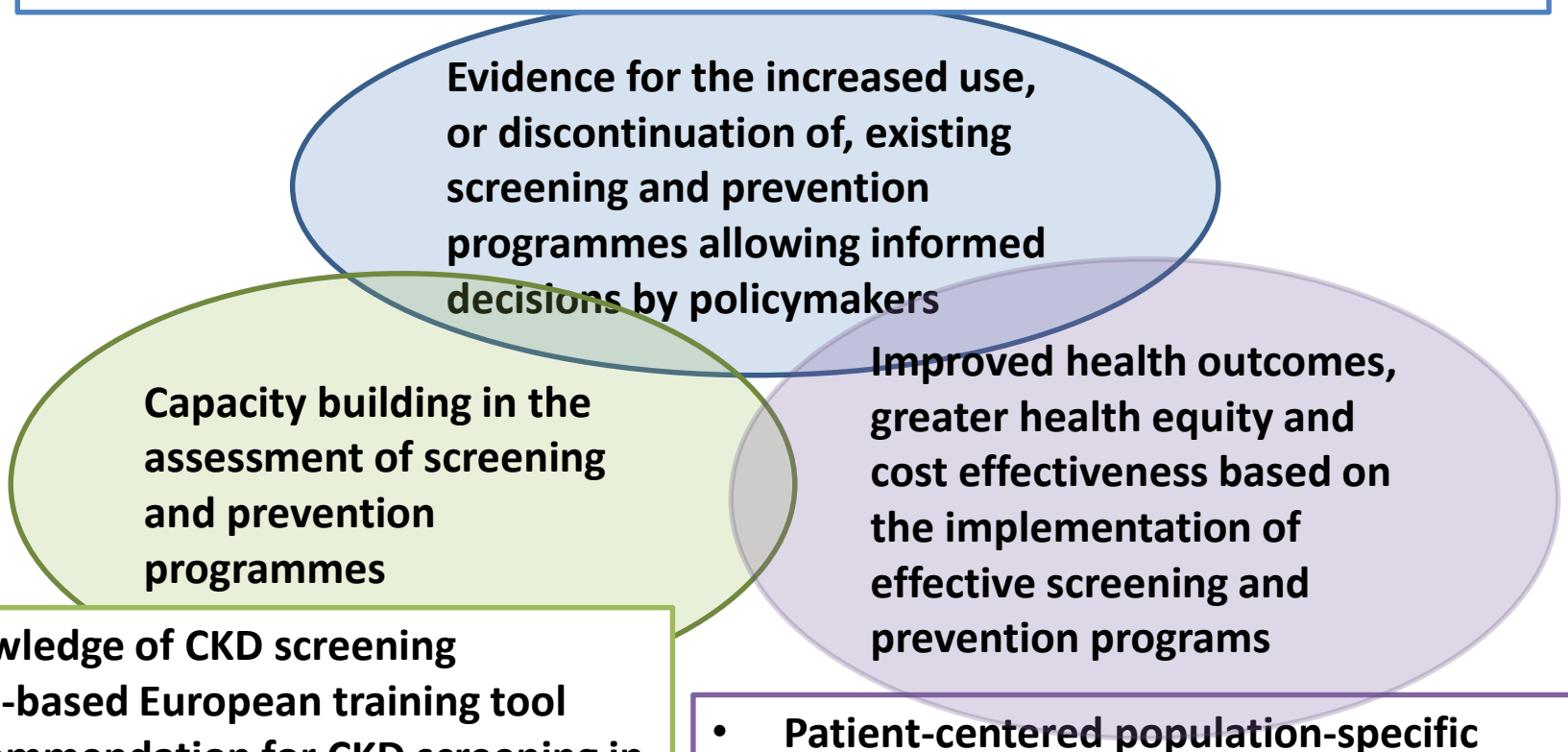
ProtocoL for GFR measurement USing iohexol (SCOPE+)

While the relationship between already known biomarkers (e.g. creatinine, cystatin C, beta-trace protein and beta2-microglobulin) and objectively measured kidney function is well established, such relationship still needs to be investigated in the case of novel biomarkers. In this respect, in order to open up the possibility to derive new equations based on these novel biomarkers, the correlation between novel biomarkers and measured glomerular filtration rate (mGFR) needs to be tested.

300 min. iohexol clearance will be measured in 400 patients enrolled in the SCOPE cohort study

Expected outcomes

Evidence for increased use, or discontinuation of, current screening methods
Evidence for the use of alternative and innovative biomarkers/equations
Evaluation of the disability potential of CKD
Better informed decisions by policymakers



- Knowledge of CKD screening
- Web-based European training tool
- Recommendation for CKD screening in older patients
- Functional dimensions (geriatric outcomes) of CKD

- Patient-centered population-specific outcomes
- Systematic use of CGA
- Real-world older people population