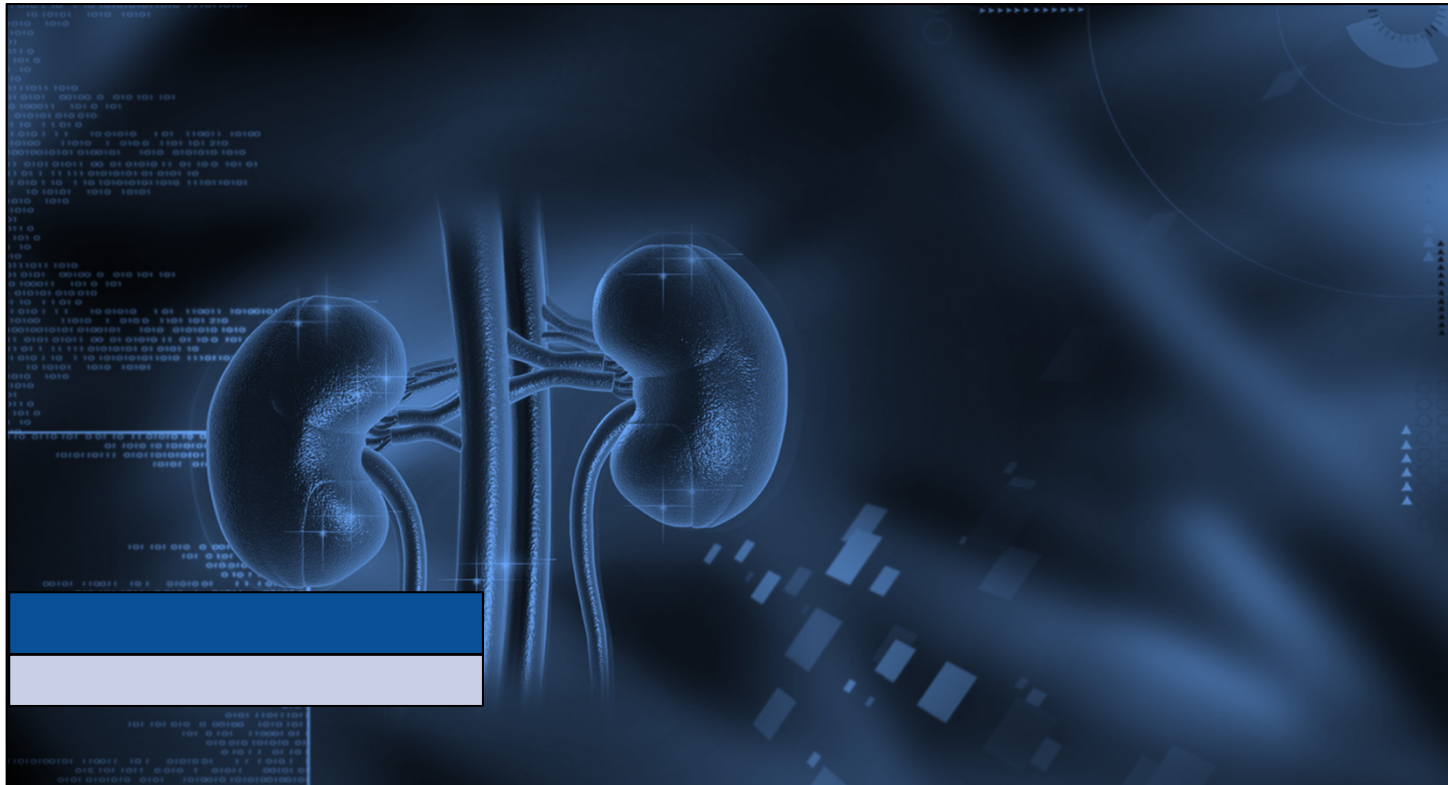




A Paradigm Shift in Contrast-Induced Acute Kidney Injury (CI-AKI) Prevention





RenalGuard®

Clinical Problem

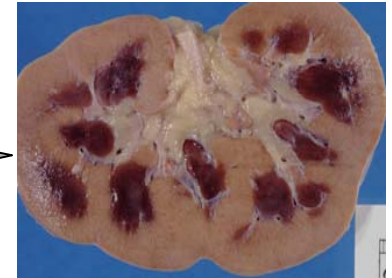
Contrast Media: Multiple Insults to Kidney



Contrast viscosity increases 50X in kidney. Impedes filtration, delivery of O₂, & contrast excretion

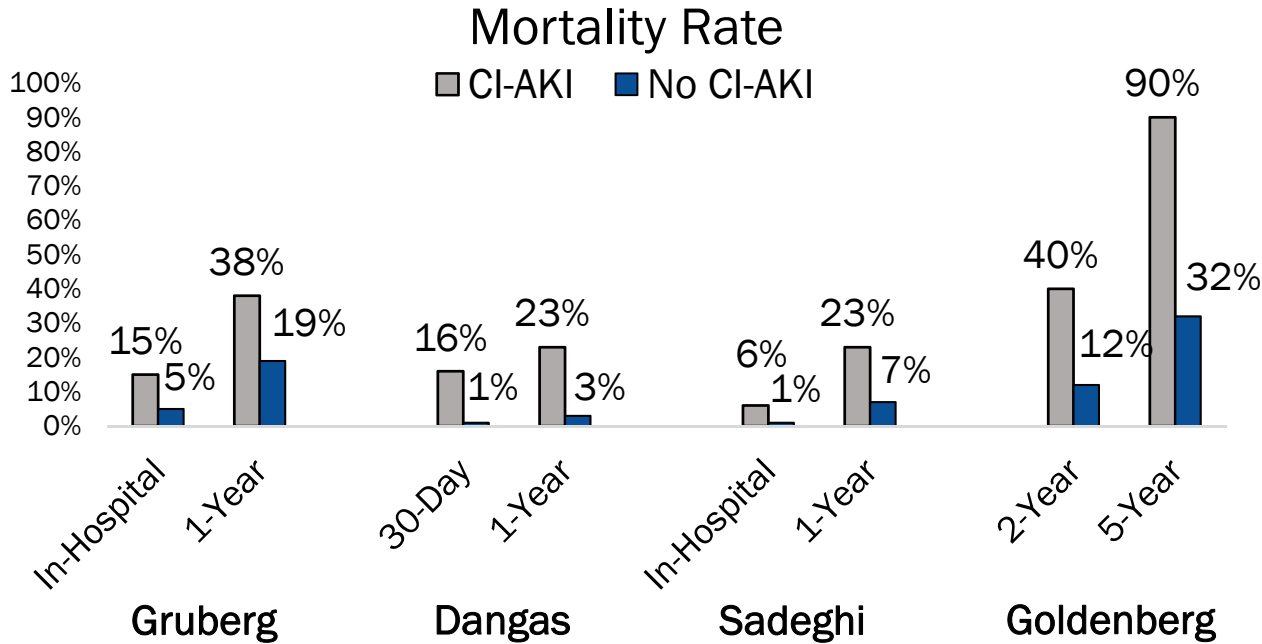
Toxic to nephrons

Combination impedes kidney function and kills nephrons



Takes up to 5 days to flush contrast unaided





30K

Estimated CI-AKI 1-year mortality in US/EU

13x

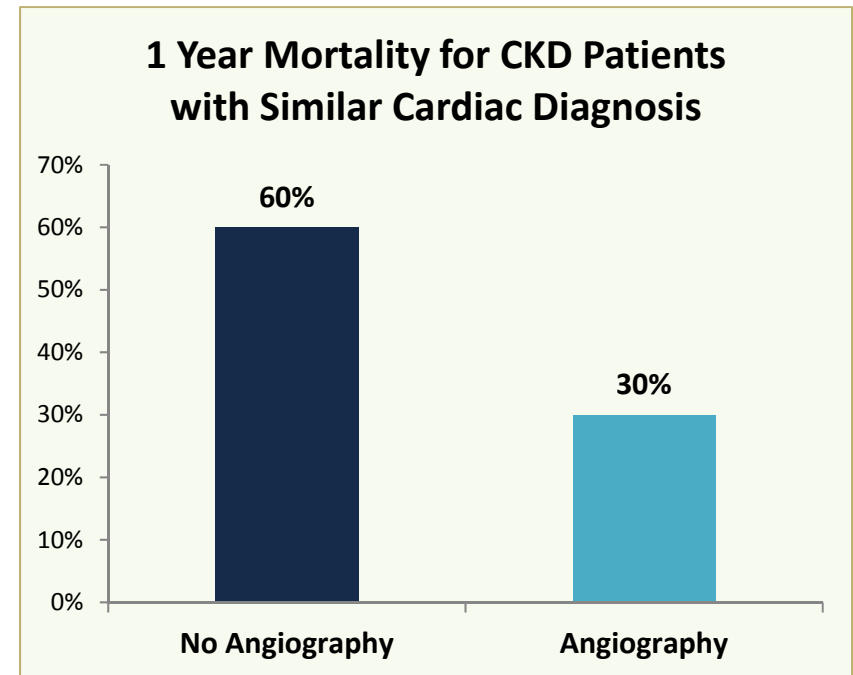
Increased 30-day mortality risk due to CI-AKI

15x

Increased major adverse cardiac event rate due to CI-AKI

- CI-AKI drastically increases the risk of:
 - Serious cardiac and renal diseases
 - Kidney transplant
 - Worse outcomes from cardiac and renal diseases
 - Mortality
 - Acute and chronic dialysis
- CI-AKI causes immediate and irreversible loss of nephrons, leading to long-term decline in kidney function

- In a review of matched group of Medicare patients with cardiac diagnosis, 25% of patients with chronic kidney disease (CKD) received catheterization, compared to 47% of patients with similar cardiac diagnosis without CKD
- This “Renalism”, resulted in one year mortality for CKD patients who did not receive angiography of 60%, compared to 30% mortality for patients who did receive angiography
- In many cases, patient is still better off receiving catheterization than not
- Often, CKD patients have worsened cardiac disease due to their renal dysfunction



Need a solution that allows patients with poor renal function and cardiac disease to safely undergo procedures using contrast



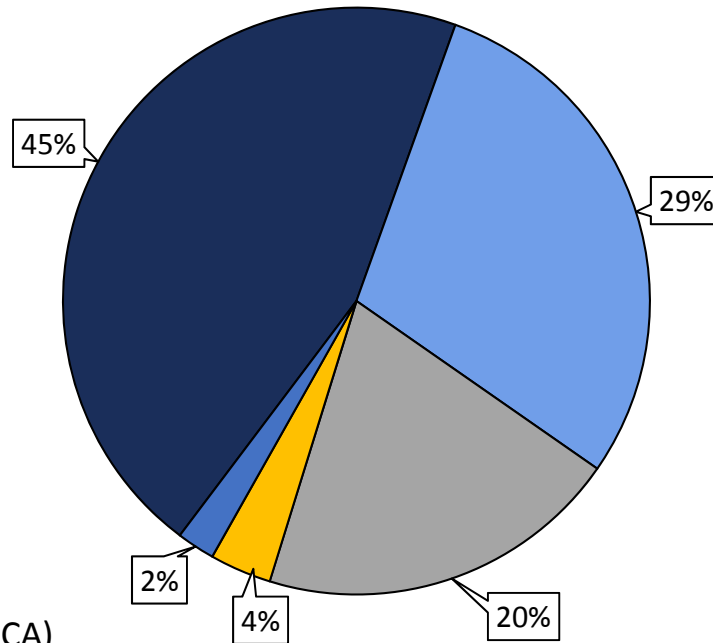
RenalGuard®

Economic Cost

Economic
Cost

€4.3B In Direct CI-AKI Cath Lab Costs (€ 2.1B US/ € 2.2B EU)

Mix by Procedure



- Coronary Angiogram (CA)
- Percutaneous Coronary Intervention (PCI)
- Peripheral Vascular Intervention (PVI)
- Transcatheter Aortic Valve Replacement (TAVR)
- Endovascular Aneurysm Repair (EVAR)

\$10K

Average per-patient cost
resulting from CI-AKI

3.75

Additional hospital days due to
CI-AKI

1.6MM

Hospital days in US and EU
resulting from CI-AKI

CI-AKI Chronic Dialysis Cost

€ 3.8B



19K

Cases of acute dialysis in EU/US related to CI-AKI (75% lead to chronic dialysis)

€89K

Average annual cost of chronic dialysis

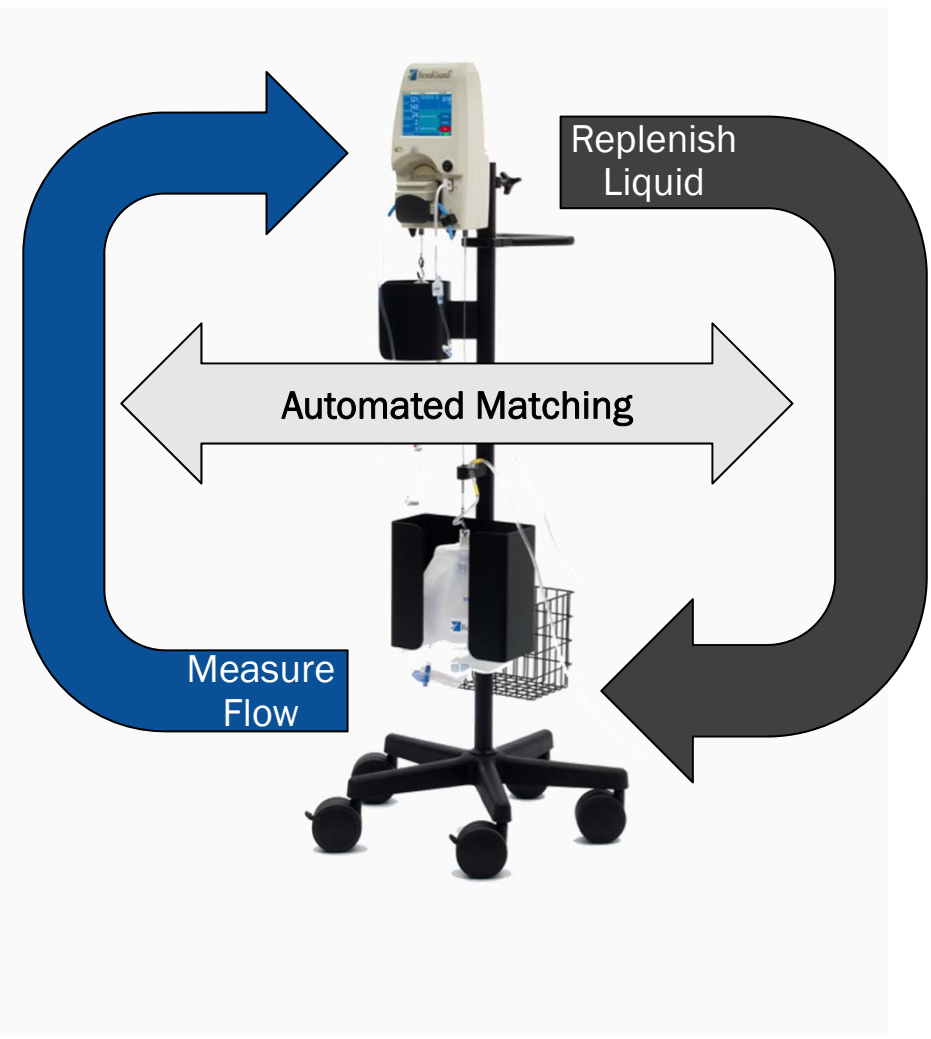
3

Years spent on average on chronic dialysis

CI-AKI results in additional indirect costs incurred from:

- Chronic Dialysis
- Renalism¹
- Major Adverse Cardiac Events
- Palliative Care
- Worse outcomes from Adverse Cardiac and Renal Events
- Opportunity costs to providers from over-utilization
- PR costs due to decline in brand/reputation
- Malpractice costs (litigation)
- Opportunity costs to society from CI-AKI and related hospitalizations

- RenalGuard matches fluid in- and out-flows through automated saline infusion
 - Achieves previously infeasible urine rates shown to protect kidneys
 - Eliminates danger of over- or under-hydration
 - Infuses saline after diuretic administration and urination
- Requires minimal nurse intervention
- No interference with cath operation
- RenalGuard results in:
 - Lower concentration of contrast
 - Faster elimination of contrast
 - Decrease in kidney oxygen demand
 - Increase in kidney oxygen supply

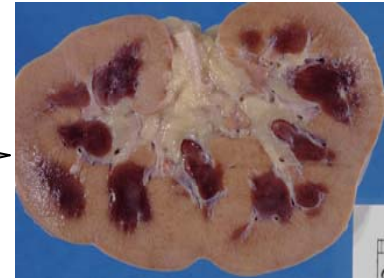




✓ Contrast viscosity increases 50X in kidney. impedes filtration, delivery of O₂, & contrast excretion

✓ Toxic to nephrons

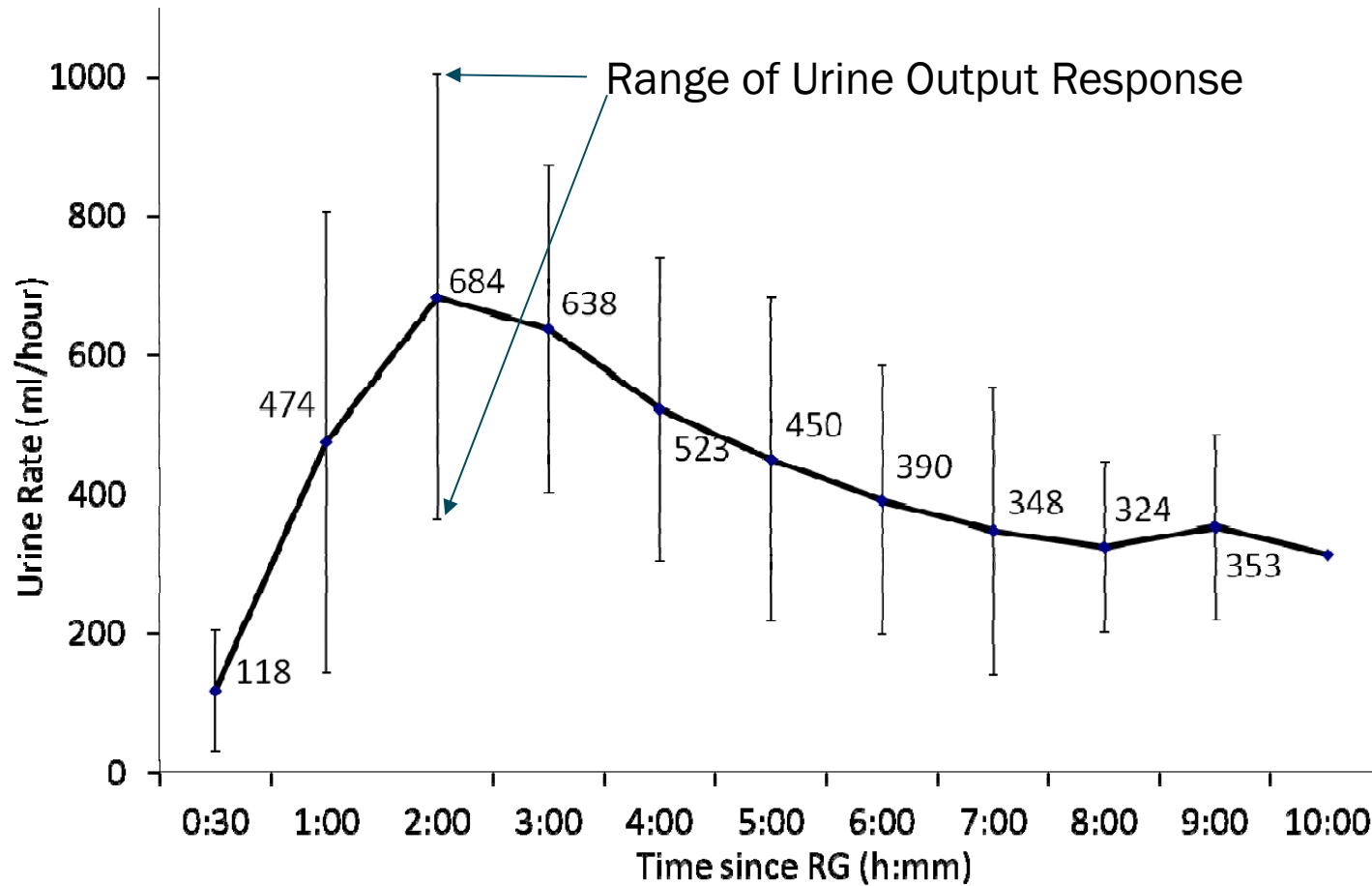
✓ Combination impedes kidney function and kills nephrons



✓ Takes up to 5 days to flush contrast unaided



RenalGuard and Urine Rate Output

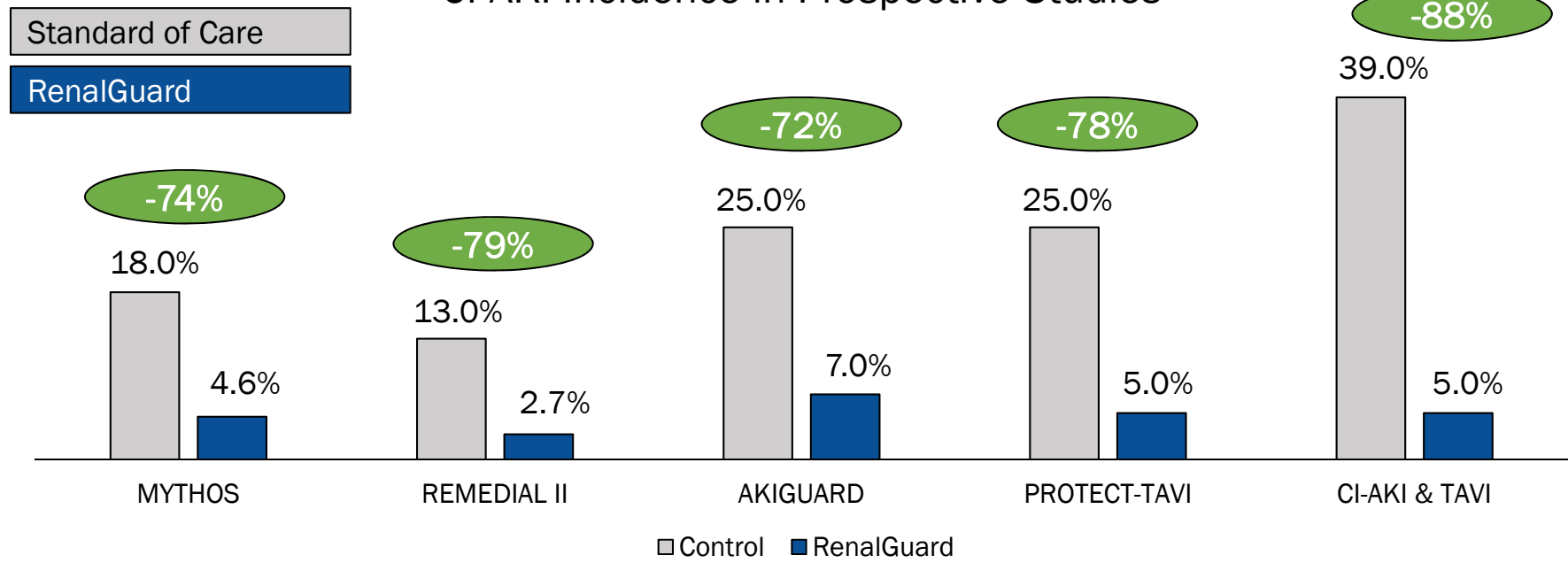




RenalGuard®

Clinical Studies

CI-AKI Incidence in Prospective Studies



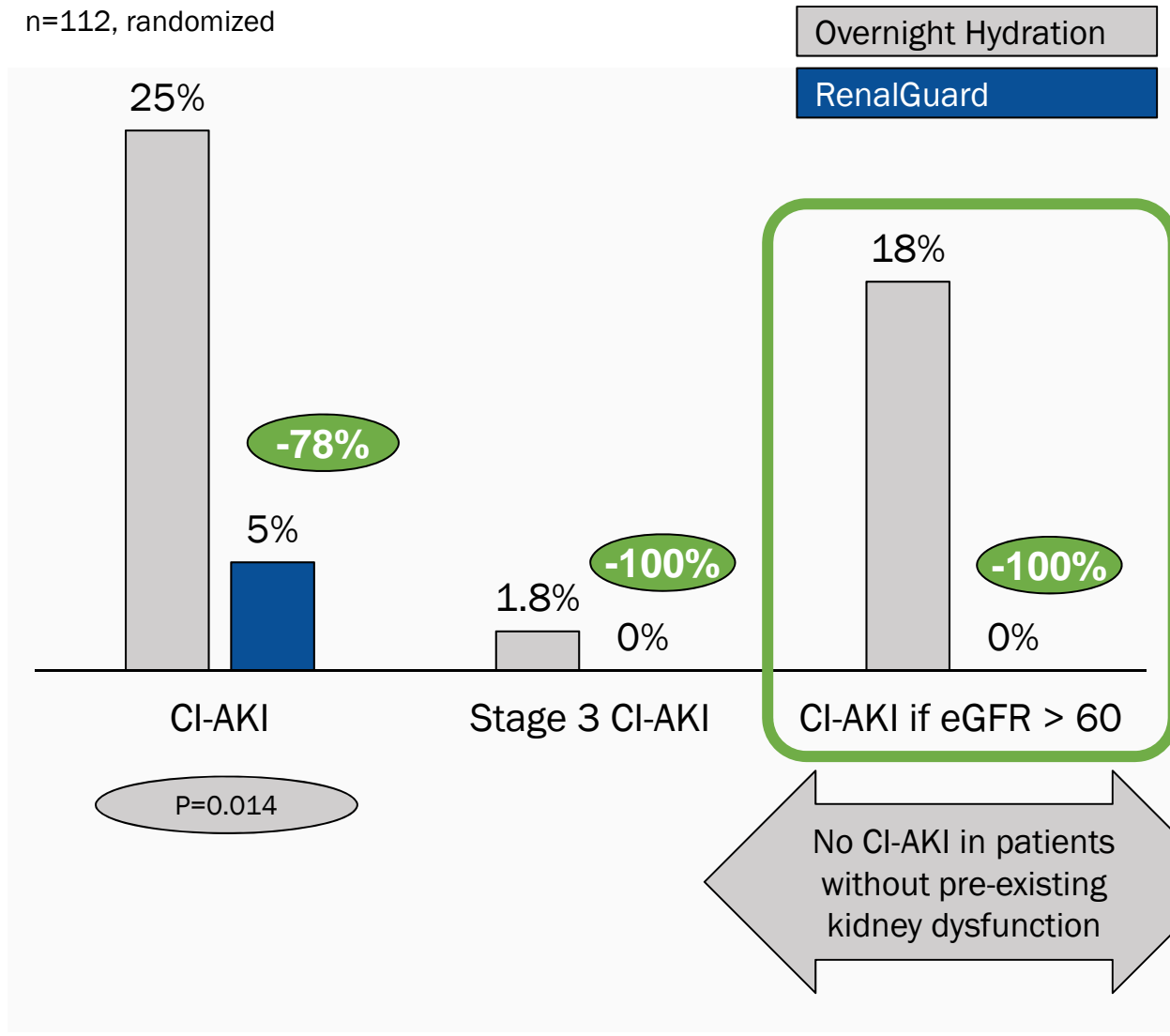
77%

Weighted Average Decrease of CI-AKI using RenalGuard in Prospective Studies

Marenzi. MYTHOS *JACC Cardiovasc Interv.* 2012.
 Briguori. REMEDIAL II *Circulation* 2011.
 Usmiani. AKIGUARD. *J Cardiovasc Med* 2015.

Barbanti PROTECT-TAVI *JACC: Cardiovascular Interventions* 2015.
 Visconti *EuroIntervention.* 2016.

n=112, randomized



- CI-AKI strong predictor of 1-year mortality (One study: 47.9% vs. 15.7%)
- TAVI Patients without AKI actually see GFR increase
- PROTECT-TAVI results project 27% reduction in 1-year mortality

“Our experience with RenalGuard has been very positive...
RenalGuard has become the Standard of Care for at-risk patients at our center.”

Professor Shmuel Banai, MD - KOL

Director of Interventional Cardiology, Tel Aviv Sourasky Medical Center
Associate Professor of Cardiology, Hebrew University of Jerusalem
Author of 150 peer-reviewed publications

How integrated is RenalGuard into your cath lab?

“All of the nurses in the CCU, ICU, cath lab, and the ward know how to set up the system and connect it to the patient.
It’s a routine treatment now.”

Professor Antonio Bartorelli, MD – KOL, INVESTOR

Associate Professor of Cardiology, University of Milan
Head Coordinator of Invasive Cardiology, Monzino Cardiology Center
Fellow of European Society of Cardiology
Fellow of American College of Cardiology
Author of 135 peer-reviewed publications

What did it take to get RenalGuard integrated?

“The nurses train each other to operate the system. **They love it - it’s very simple to operate, much easier than bringing patients in for overnight hydration, and they love seeing its impact on reducing adverse events for patients.**”

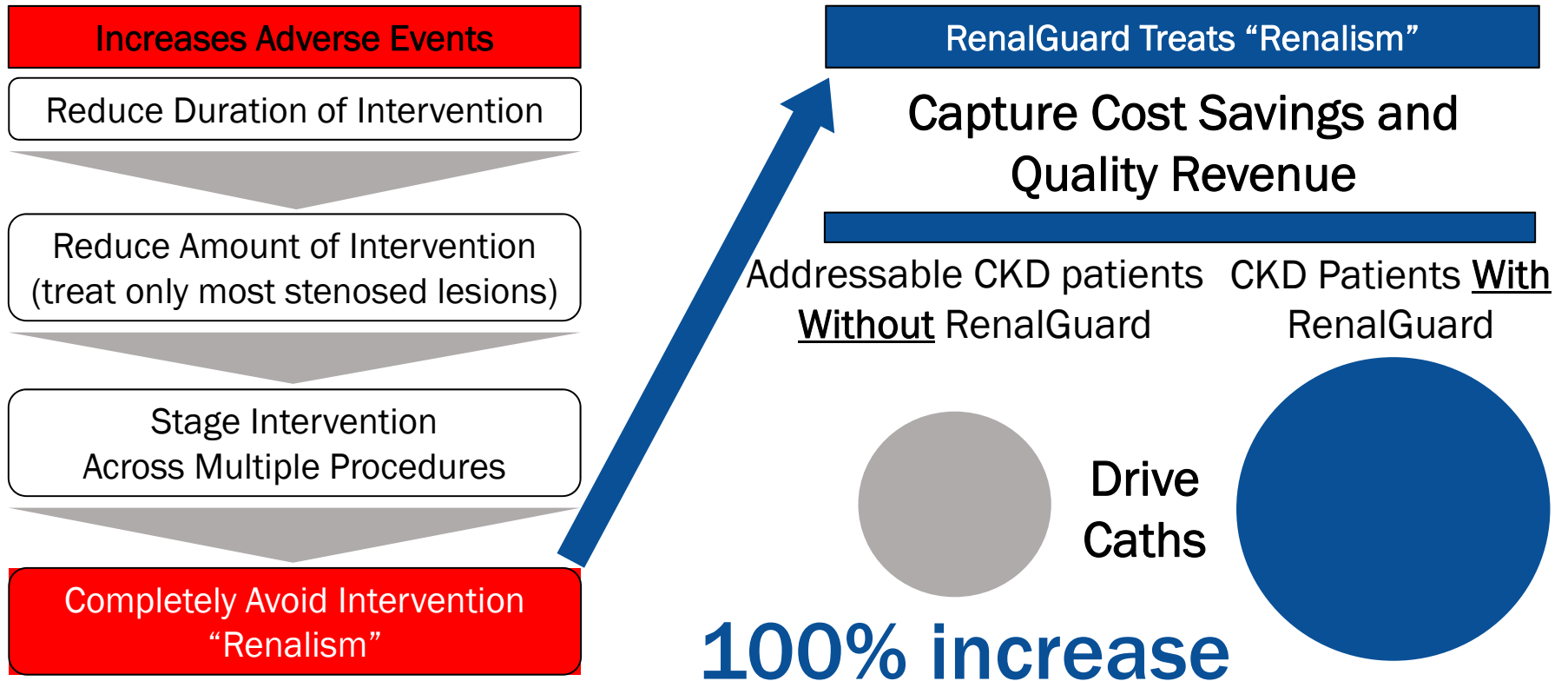
Professor Vaikom Mahadevan, MD – KOL

Associate Professor of Medicine, University of California, San Francisco
Ex-Director of Adult Congenital Heart Disease (ACHD) and Transcatheter Aortic Valve Replacement (TAVR) Program, Manchester Royal Infirmary
Founder, Ex-Director of ACHD Interventional Program, NW England
Author of 56 peer-reviewed publications

“RenalGuard has **performed very nicely** in a difficult patient population.”

Procedure Avoidance to Prevent CI-AKI Leads to Poor Outcomes

- Without effective CI-AKI prevention solutions, clinicians often reduce CM exposure by purposefully avoiding normal cath procedure when treating high-risk patients
- Cath avoidance dramatically increases Major Cardiac Events, Mortality, and other adverse outcomes relative to normal cath procedure



2014 European Society of Cardiology Guidelines: RenalGuard Results Amend EU Standard of Care

Recommendations	Dose
Patients with moderate-to-severe Chronic Kidney Disease	
<p>Furosemide with matched hydration may be considered over standard hydration in patients at very high risk for CI-AKI or in cases where prophylactic hydration before the procedure cannot be accomplished.</p>	<p>Initial intravenous bolus of normal saline over 30 min followed by an i.v. Bolus of furosemide. Hydration infusion rate has to be adjusted to replace the patient's urine output. When the rate of urine output is >300 mL/h, patients undergo the coronary procedure.</p> <p>Matched fluid replacement maintained during the procedure and for 4 hours post-treatment.</p>

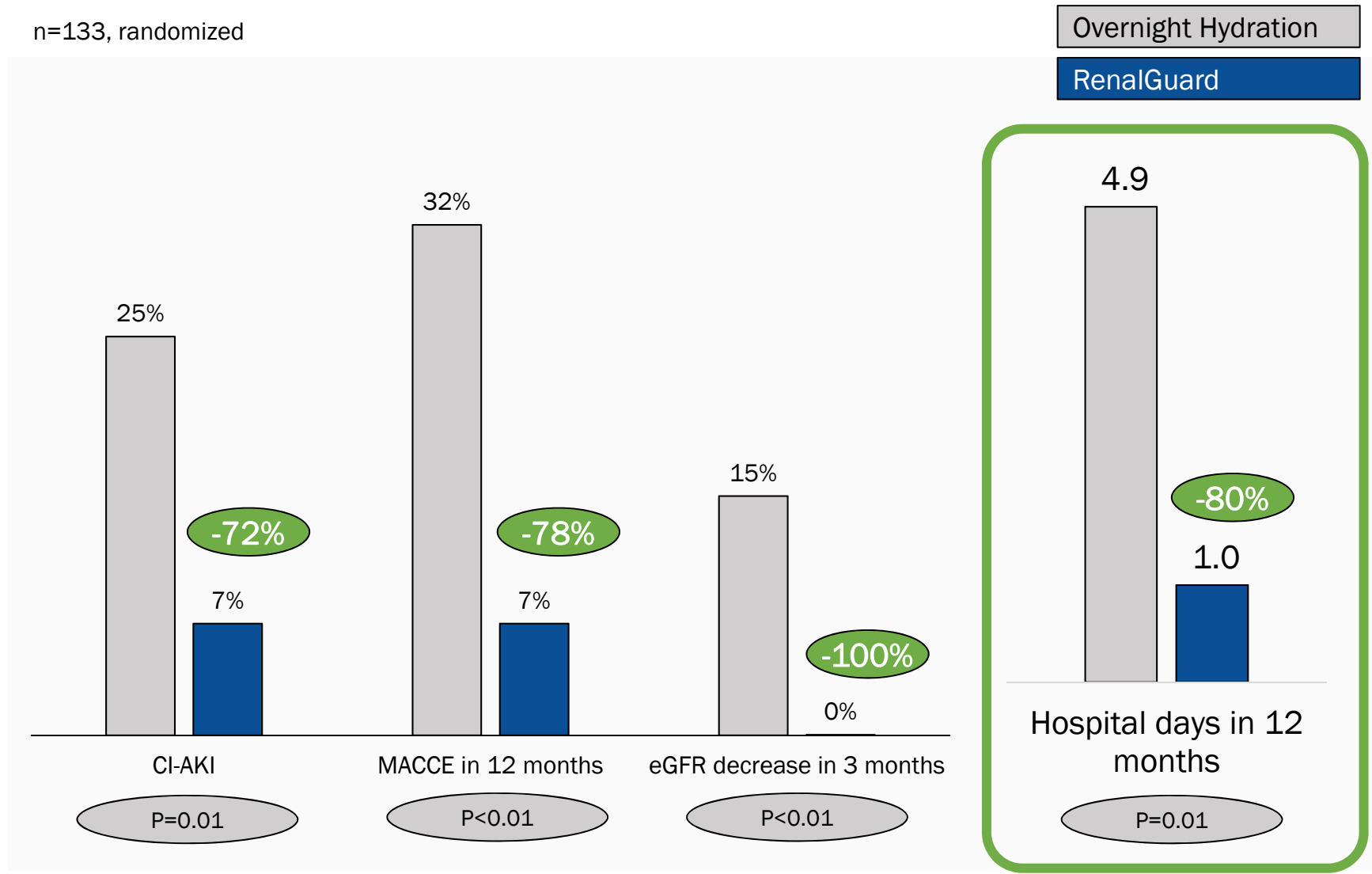


RenalGuard®

Cost Savings

AKIGUARD Indicates RenalGuard Cost Savings Extend beyond CI-AKI

n=133, randomized



Cost Savings

AKIGUARD Indicates RenalGuard Cost Savings Extend beyond CI-AKI

Approximate Cost Savings

RenalGuard Cost



3.9

Reduction in hospital days
out to 12 months

€1800

Approx. daily hospital cost

1300%

ROI

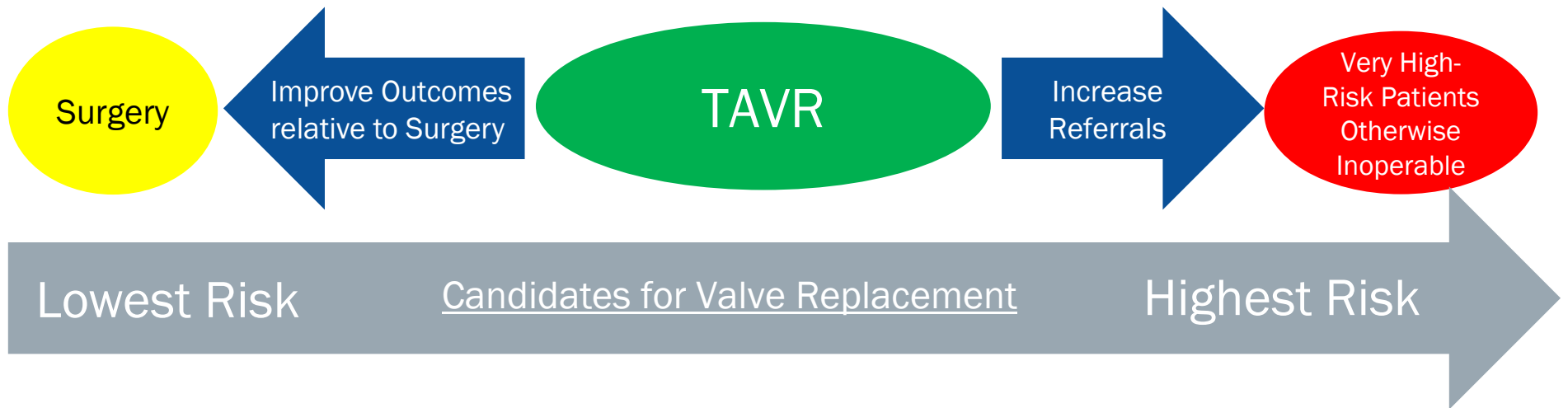
Benefits to Cath Lab and Hospital

- **Increase Overall Cath Volume:** Allow high-risk CKD patients who would otherwise not receive cath due to concerns about renal damage, **expanding high-risk market by up to 100%**
- **Increase per-patient revenue:** Many payers reimburse at a higher rate for patients at high risk for CI-AKI
- **Increase utilization of high-risk procedures:** Enables more CKD patients to be treated with advanced procedures, such as TAVI, CTO, and complex PCI.
- **Competitive Advantage and Differentiation:** Allows hospitals to become centers of excellence for treatment of CKD patients, increasing the lab's overall referral base.
- **Cost Savings, Quality Revenue:** Reduced adverse events reduces costs and improves quality and clinical reputation.

Benefits to Integrated Care Networks

- **Improved cardiac care:** RenalGuard allows patients with advanced CKD to receive optimal cardiac care while reducing risk of AKI.
- **Reduced adverse events and re-admission:** Results of AKIGUARD suggest significant potential for reduction in costly adverse events and re-admission
- **Reduce progression to end stage renal disease (ESRD):** Improved cardiac care should improve renal function and prevent deterioration of high-risk patients under management into dialysis
- **Higher quality, lower costs:** Reduction in dialysis population under management allows more competitive pricing of new high-risk patients, potentially providing a competitive advantage relative to other integrated care networks

RenalGuard expands market for complex procedures, such as TAVR:



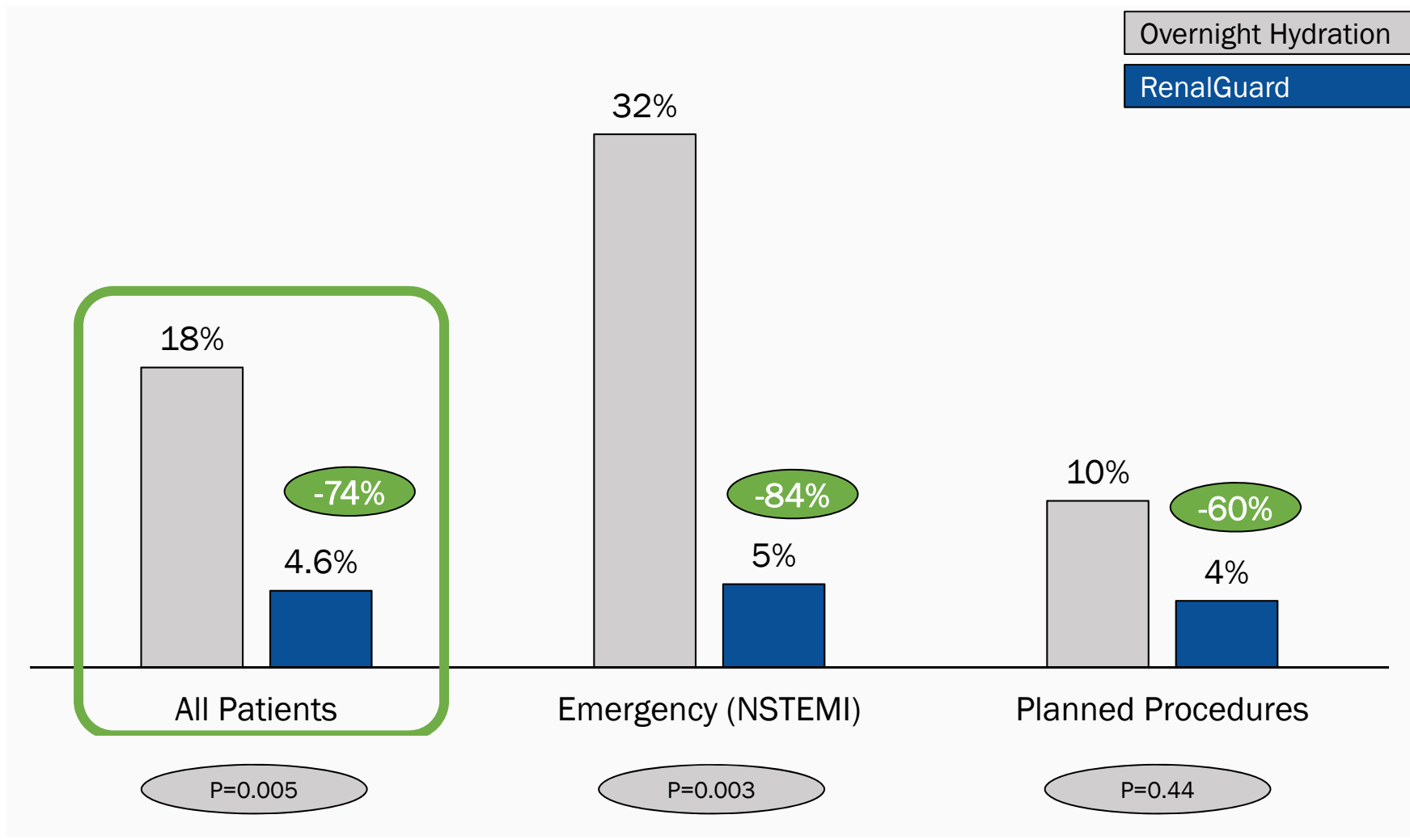
- CIN remains a real and growing problem in modern cath lab
- Evidence continues to mount that RenalGuard can reduce the incidence of CIN and the adverse events associated with the condition
- Preventing CIN improves patient outcomes, reduces cath lab costs, improves hospital quality metrics, and can increase catheterization lab utilization and revenue.



Expanded Clinical Results

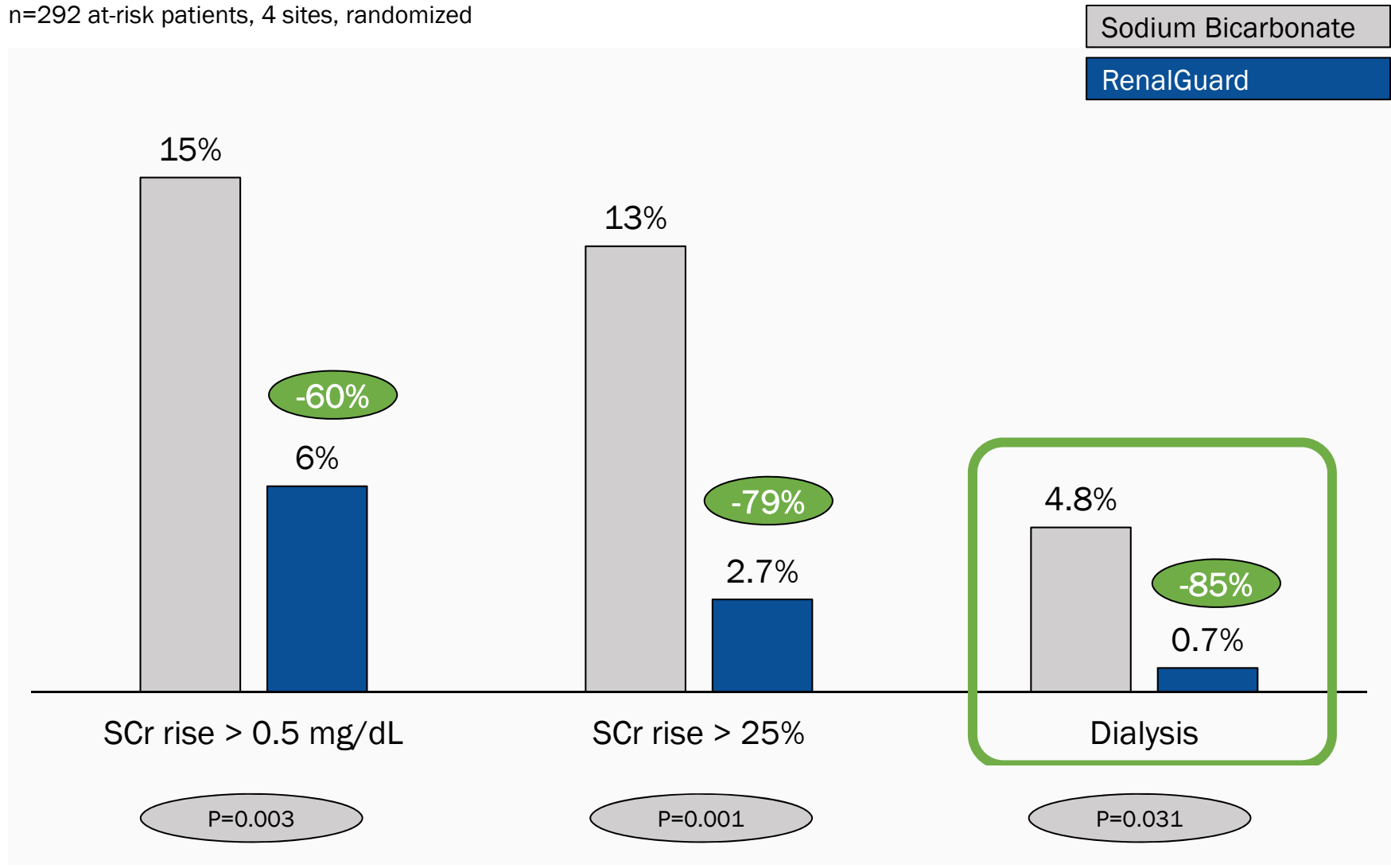
MYTHOS Trial: RenalGuard vs. Overnight Hydration

Rate of CI-AKI, n=170, randomized

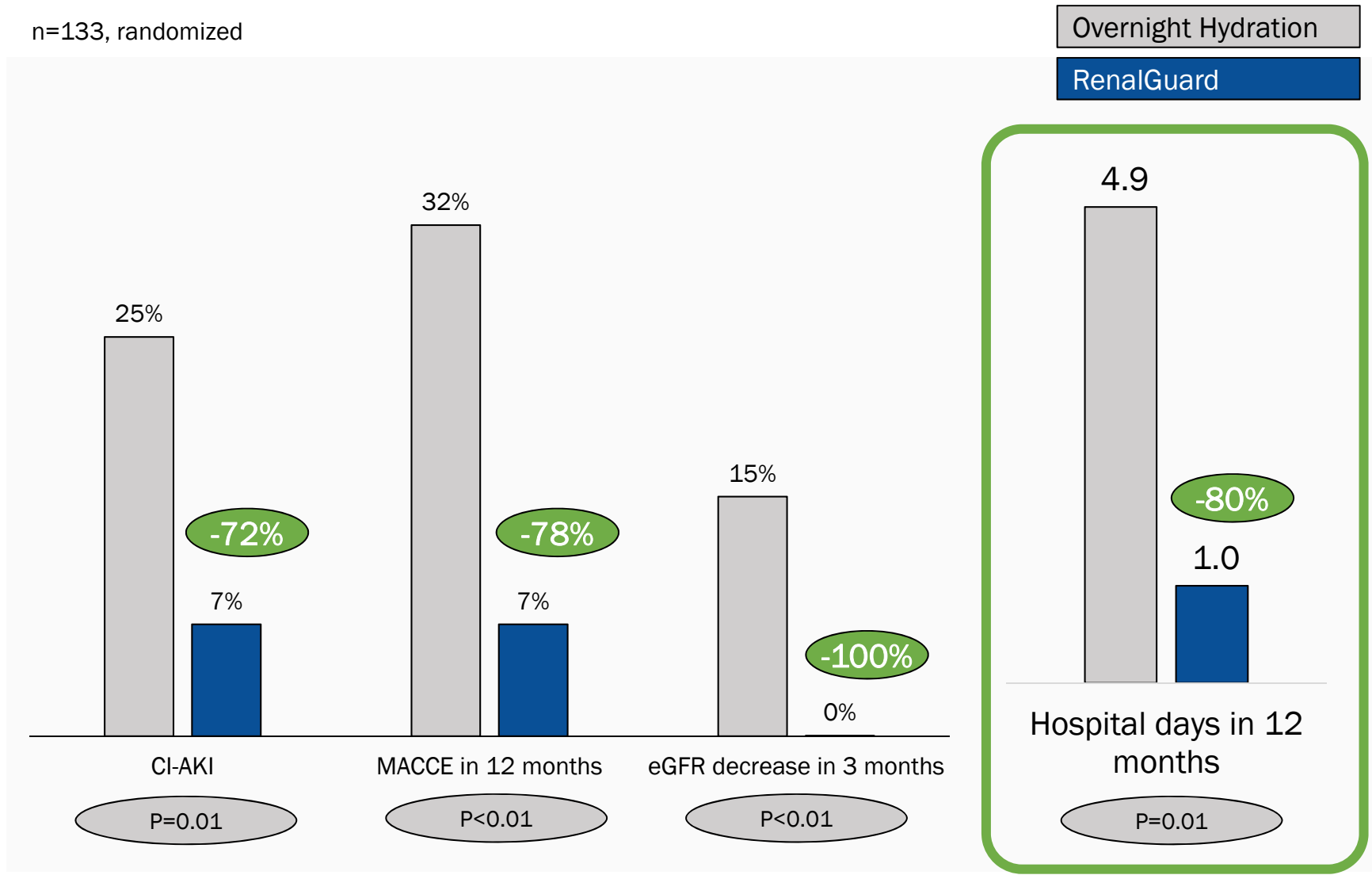


REMEDIAL II: RenalGuard vs. Sodium Bicarbonate

n=292 at-risk patients, 4 sites, randomized

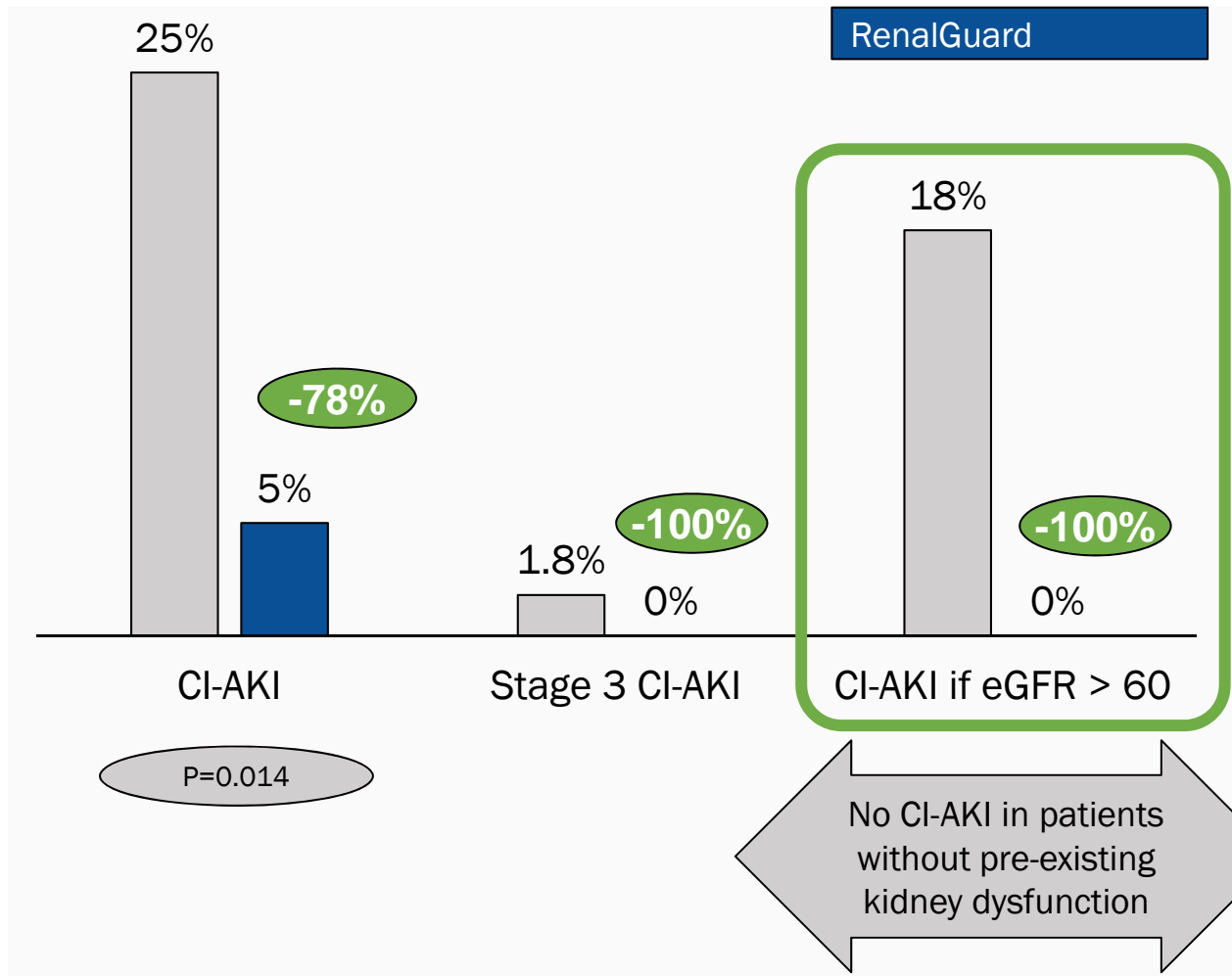


n=133, randomized



n=112, randomized

Overnight Hydration
RenalGuard



- TAVI new, growing (25% / year) procedure to replace aortic valves via catheter in patients too frail for surgery
- Up to 1/3 of TAVI patients develop CI-AKI
- CI-AKI strong predictor of 1-year mortality (47.9% vs. 15.7%)

n=48, not randomized¹

Sodium Bicarbonate/NAC

RenalGuard

- Significant reduction in incidence of CI-AKI
- Severe CI-AKI, strongest predictor of 1-year mortality, eliminated

