

# Nephrotoxicity of Contrast Imaging: Understanding the Actual Risk

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**AKDN**  
ALBERTA KIDNEY DISEASE NETWORK

# Objectives

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1. To describe the epidemiology of acute kidney injury following iodinated contrast exposure.
2. To identify the attributable risk of acute kidney injury associated with contrast exposure in contemporary practice.
3. To recognize how the risk of acute kidney injury should be balanced with the potential benefit of contrast procedures in patients with kidney disease.

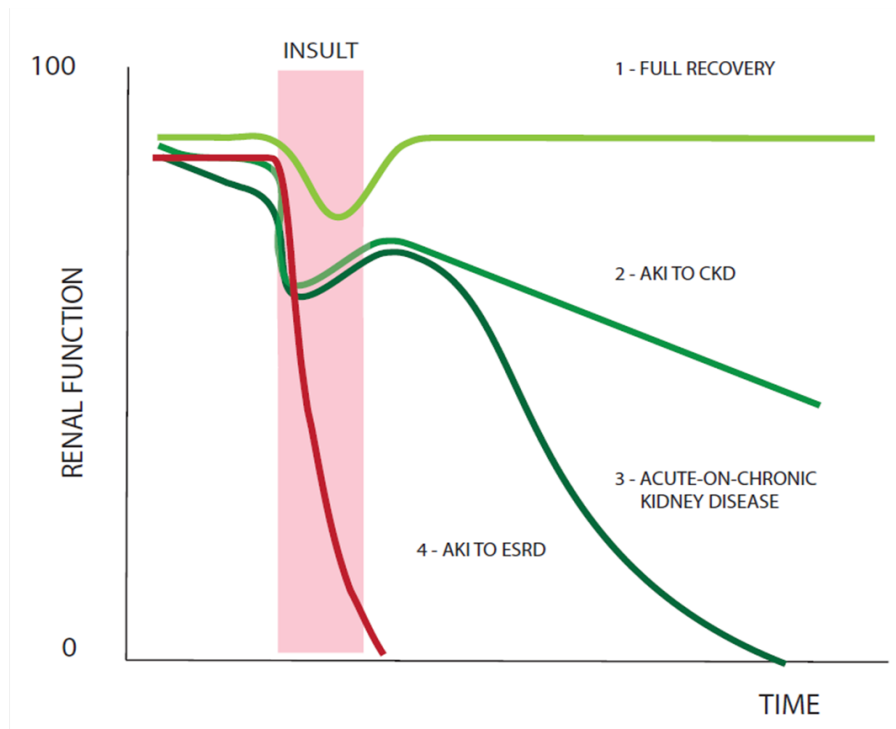
# Contrast-Induced Acute Kidney Injury (CI-AKI)

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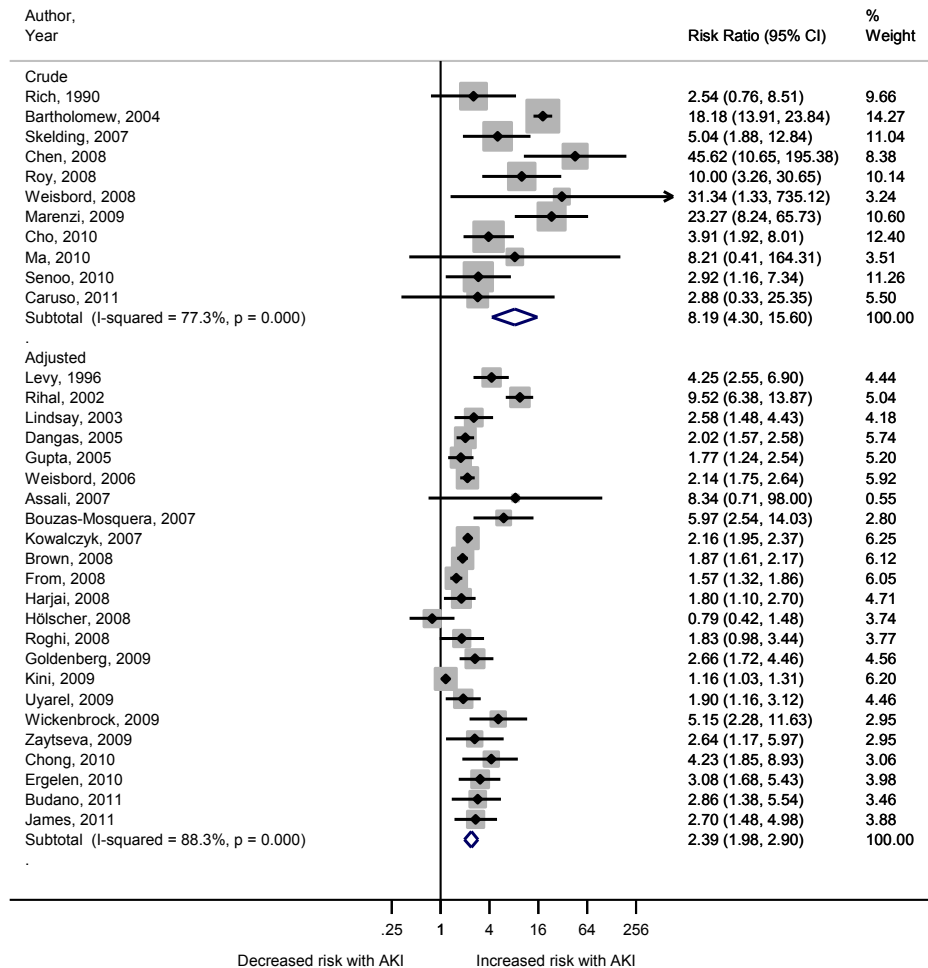
# Contrast-Induced Acute Kidney Injury (AKI)

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1. Increase in serum creatinine
2. 48-72 after exposure to contrast agent
2. Absence of alternative causes for AKI

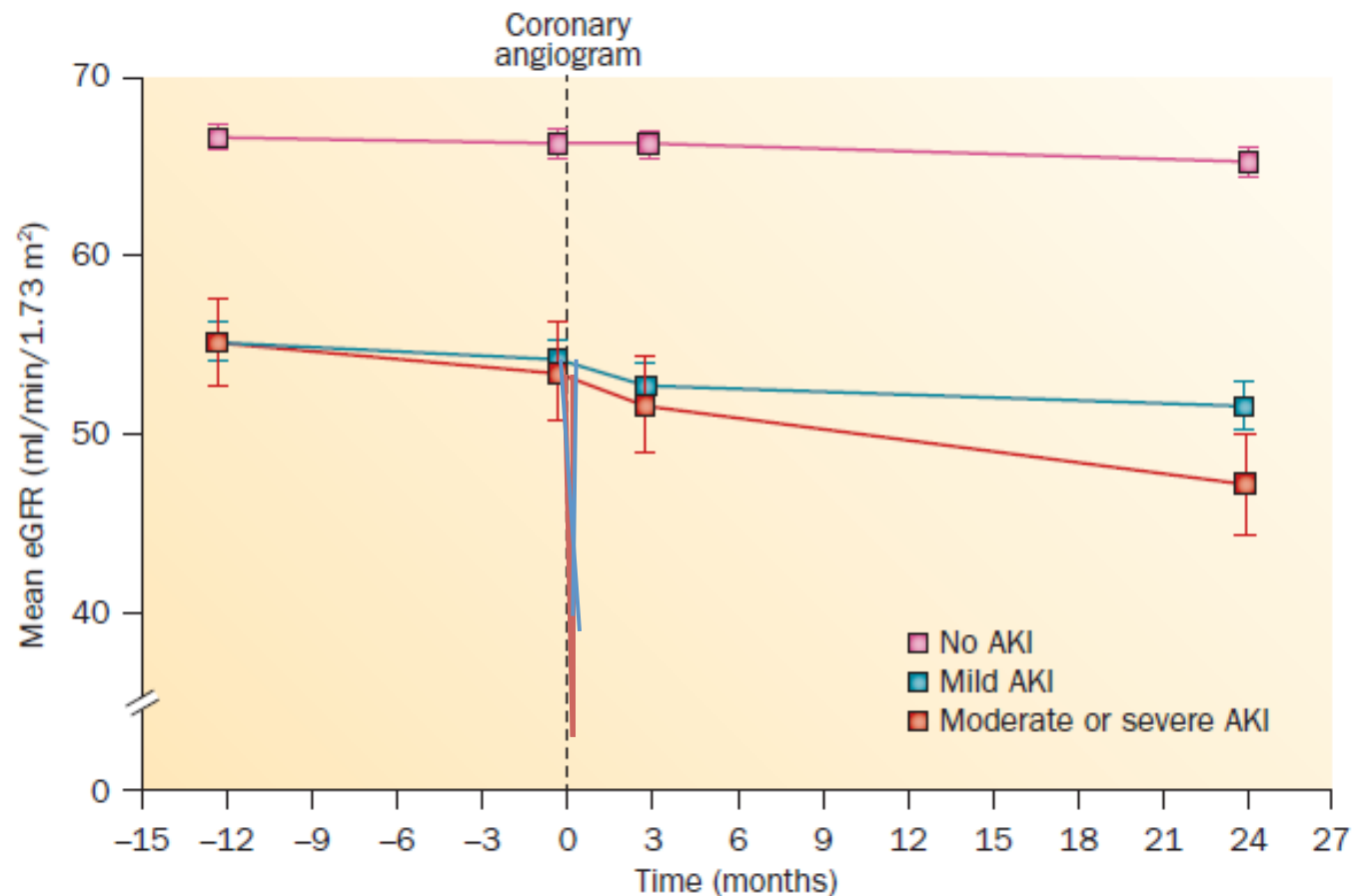
# Consistently Associated with Poor Outcomes



# Consistently Associated with Poor Outcomes

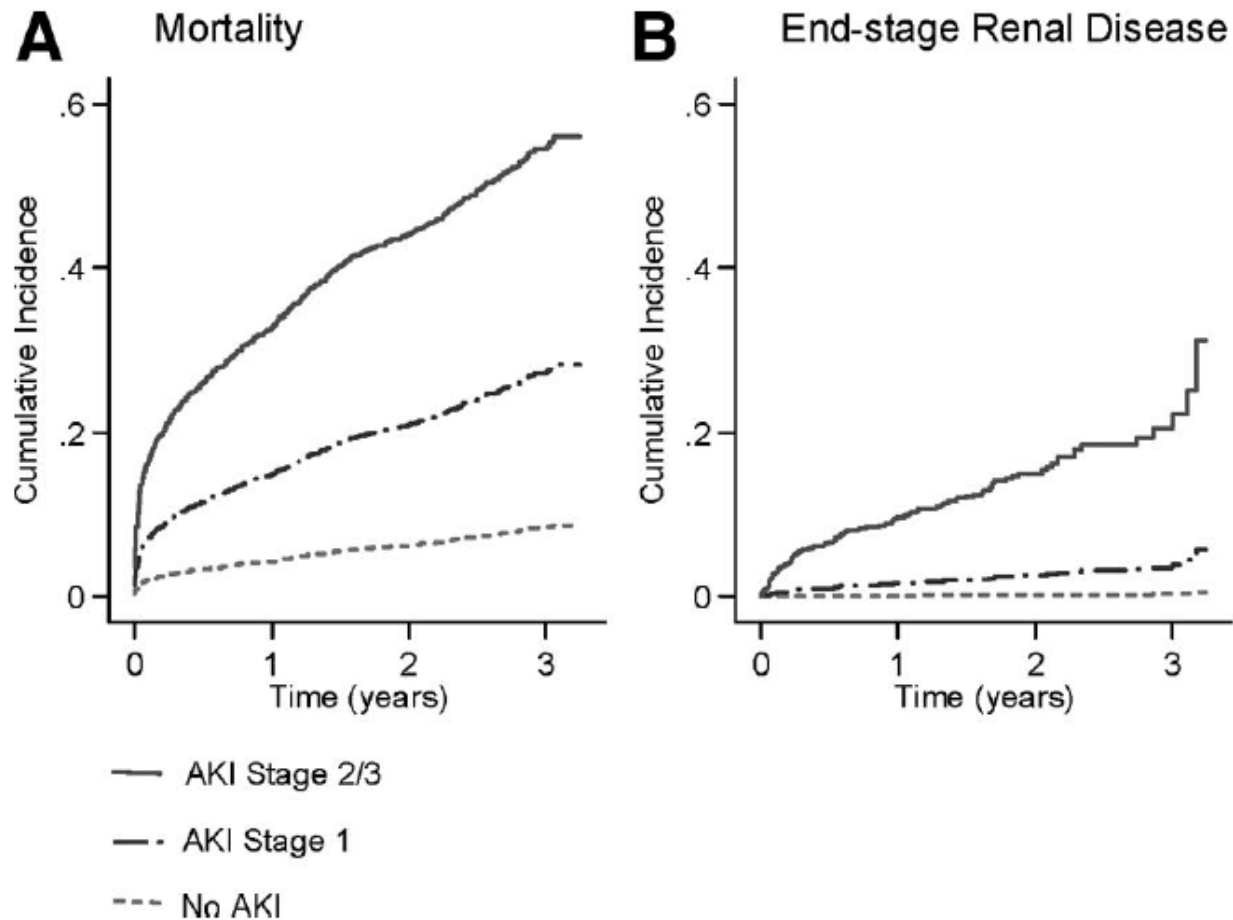
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**Figure 1**

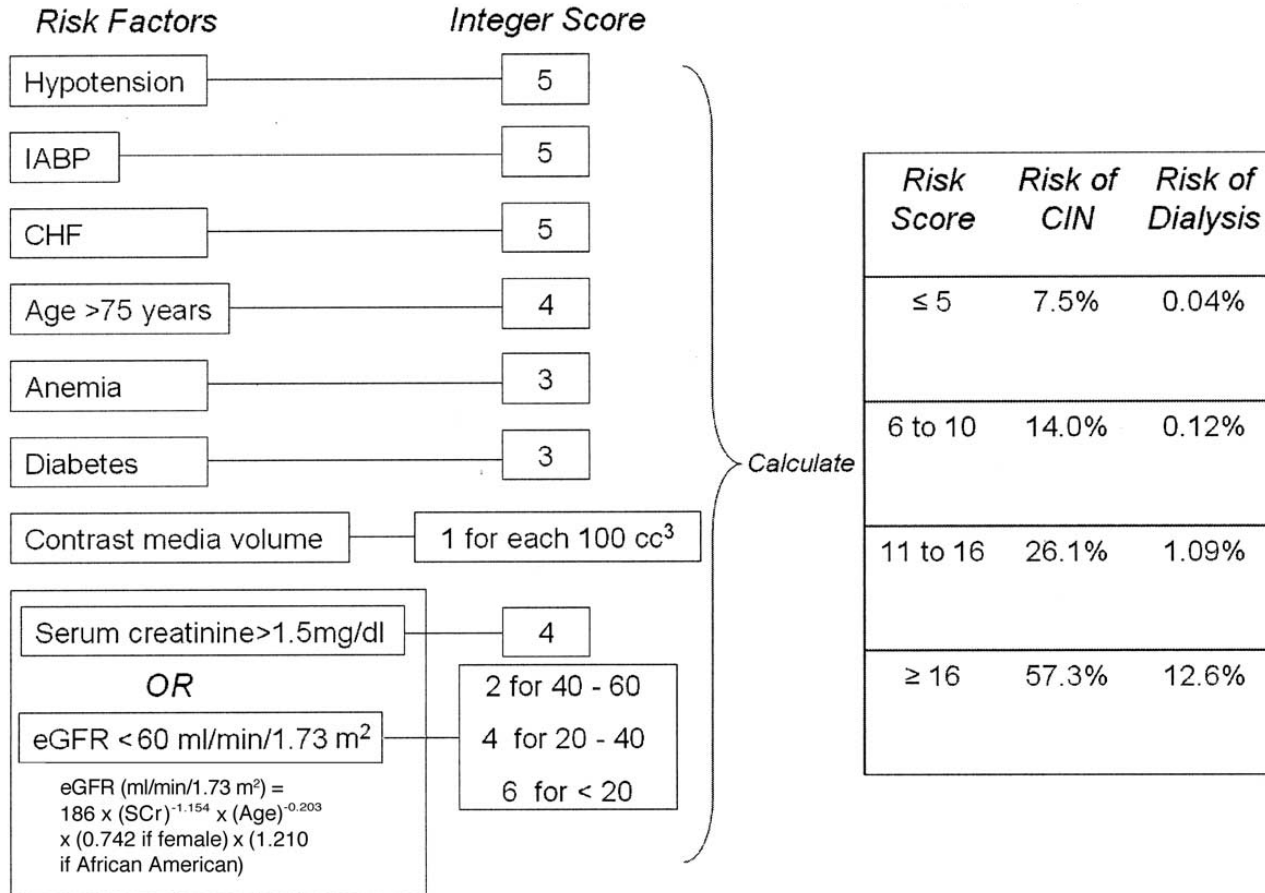


# Consistently Associated with Poor Outcomes

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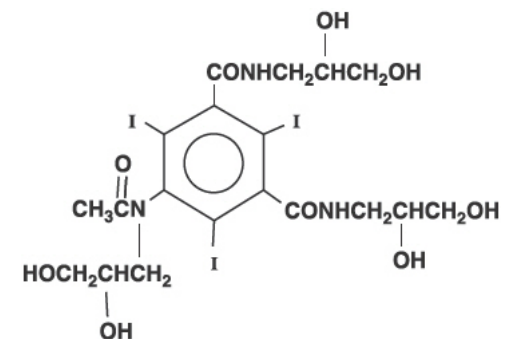
# Risk Factors – Mehran Risk Score



# Iodinated Contrast Agents

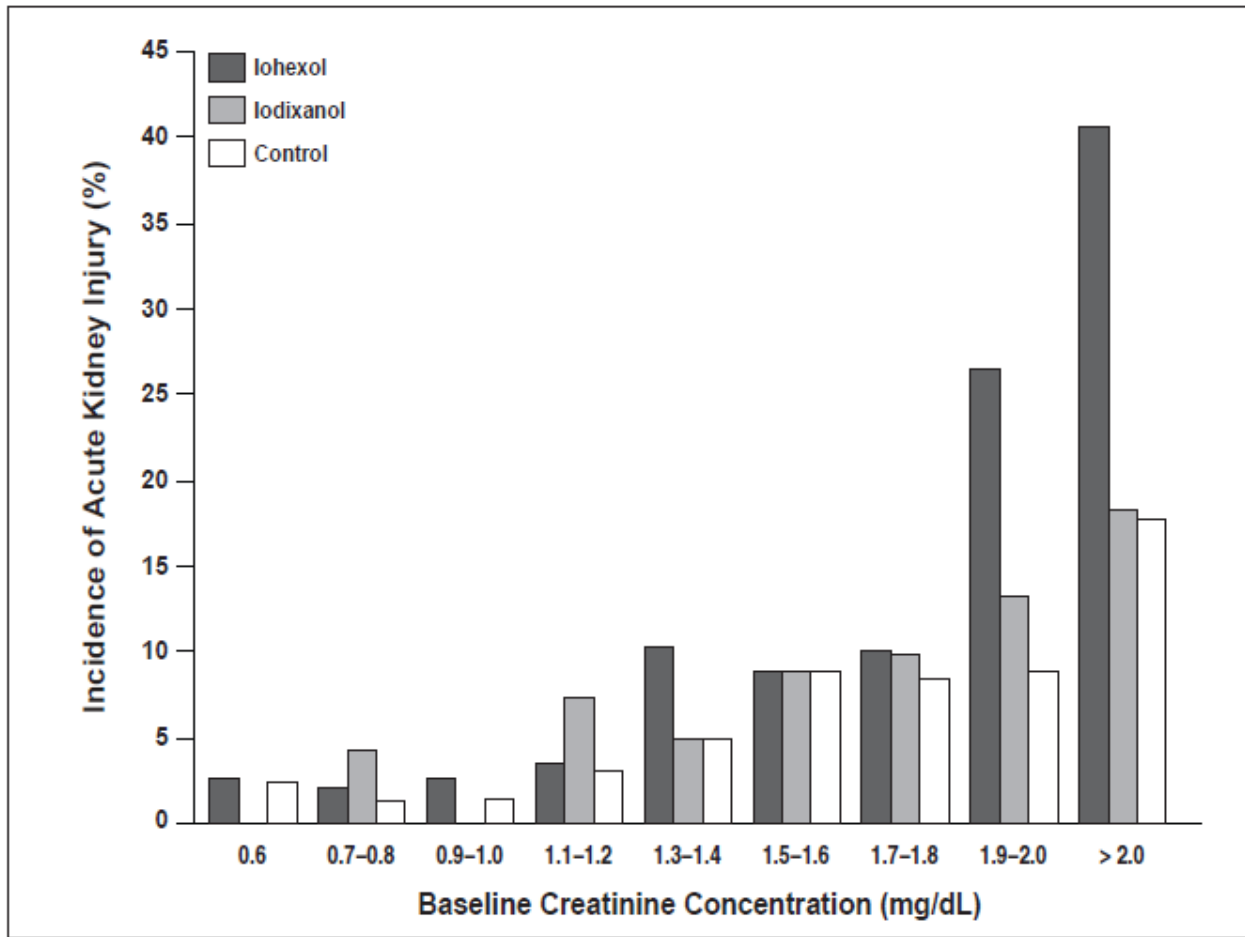
**Table 1.** Properties of Commonly Used Radiocontrast Media

Type	Generic Name	Iodine, mg/mL	Osmolality, mOsm/kg
High osmolar			
Ionic monomer	Sodium iothalamate	325	1843
Ionic monomer	Meglumine diatrizoate	306	1530
Low osmolar			
Ionic dimer	Meglumine ioxaglate	320	580
Ionic dimer	Sodium ioxaglate	320	580
Nonionic monomer	Iopamidol	300	616
Nonionic monomer	Iohexol	300	640
Nonionic monomer	Ioversol	300	645
Nonionic monomer	Iopromide	300	610
Iso osmolar			
Nonionic dimer	Iotrolan	300	320
Nonionic dimer	Iodixanol	320	290



# Risk of AKI Attributable to Contrast Agents

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**Fig. 1**—Incidence of acute kidney injury versus baseline creatinine concentration. Graph shows incidence of acute kidney injury among control patients closely parallels use of iodixanol and parallels use of iohexol for baseline creatinine values up to 1.8 mg/dL.

# Risk of AKI Attributable to Contrast Agents

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## Radiology

### Intravenous Contrast Material Exposure Is Not an Independent Risk Factor for Dialysis or Mortality<sup>1</sup>

*radiology.rsna.org* ■ **Radiology**: Volume 273: Number 3—December 2014

Robert J. McDonald, MD, PhD

Jennifer S. McDonald, PhD

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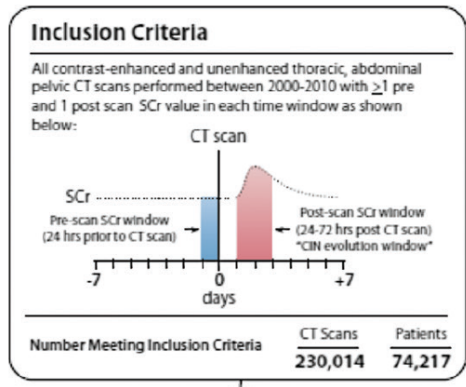
Robert P. Hartman, MD

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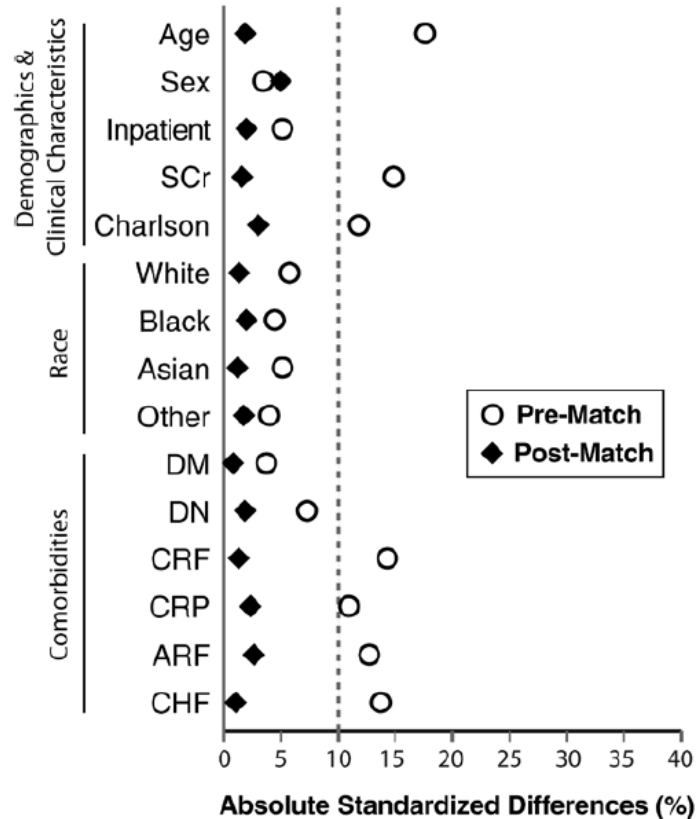
# Risk of AKI Attributable to Contrast Agents



## Propensity Score Matching

**Study Population**

Population	Patients	Contrast CTs	Noncontrast CTs
All	21,346	10,673	10,673
Low Risk subset	14,546	7,273	7,273
Medium Risk subset	4,884	2,442	2,442
High Risk subset	1,916	958	958
ARF subset	4,080	2,040	2,040
CRF subset	1,950	975	975
DM subset	3,948	1,974	1,974
CHF subset	2,974	1,487	1,487



# Risk of AKI Attributable to Contrast Agents

## Propensity Score–adjusted Outcomes

Data Set and Outcome	Contrast Group	Noncontrast Group	Statistics	
			ORs and HRs*	P Value
Entire matched data set	10 673	10 673	...	...
AKI	515 (4.8)	544 (5.1)	0.94 (0.83, 1.07) <sup>†</sup>	.38
30-d dialysis	25 (0.2)	27 (0.3)	0.96 (0.54, 1.60) <sup>†</sup>	.89
30-d mortality	850 (8.0)	875 (8.2)	0.97 (0.87, 1.06) <sup>‡</sup>	.45
AKI risk groups <sup>§</sup>				
Low-risk group	7273	7273	...	...
30-d dialysis	7 (0.1)	8 (0.1)	0.88 (0.32, 2.41) <sup>†</sup>	.79
30-d mortality	417 (5.7)	426 (5.9)	0.95 (0.83, 1.09) <sup>‡</sup>	.44
Medium-risk group	2442	2442	...	...
30-d dialysis	7 (0.3)	7 (0.3)	1.00 (0.35, 2.86) <sup>†</sup>	.79
30-d mortality	303 (12.4)	314 (12.9)	0.97 (0.83, 1.14) <sup>‡</sup>	.64
High-risk group	958	958	...	...
30-d dialysis	11 (1.1)	12 (1.3)	0.92 (0.40, 2.09) <sup>†</sup>	.84
30-d mortality	130 (13.6)	135 (14.1)	0.93 (0.73, 1.18) <sup>‡</sup>	.56

# Risk of AKI Attributable to Contrast Agents

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Radiology

## Contrast Material–induced Nephrotoxicity and Intravenous Low-Osmolality Iodinated Contrast Material<sup>1</sup>

*radiology.rsna.org* ▪ **Radiology**: Volume 267: Number 1—April 2013

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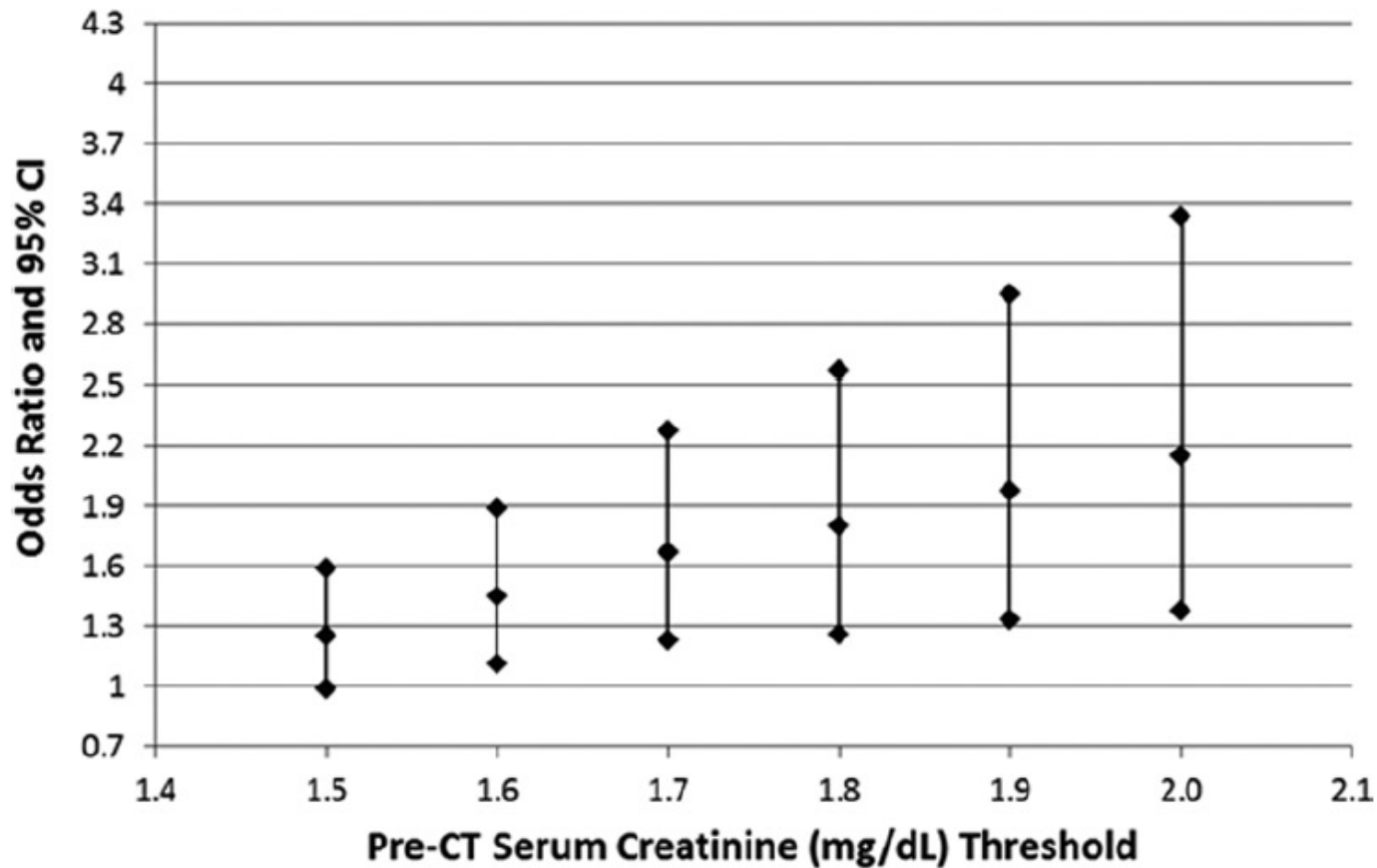
James H. Ellis, MD

# Risk of AKI Attributable to Contrast Agents

Effect of Intravenous Iodinated Contrast Material on the Development of Post-CT AKI							
Pre-CT SCr Subgroup Analysis	AKIN Criteria*						
	No. Patients	No Post-CT AKI	Post-CT AKI	Post-CT AKI Rate	P Value	Odds Ratio	95% CI
SCr <1.5 mg/dL							
With contrast agent	9350	8685	665	7.1%	.25	0.93	0.83, 1.05
Without contrast agent	9025	8368	657	7.3%			
SCr ≥ 1.5 mg/dL							
With contrast agent	771	601	170	22.0%	.06	1.25	0.99, 1.59
Without contrast agent	1096	886	210	19.2%			
SCr ≥ 1.6 mg/dL							
With contrast agent	514	379	135	26.3%	.007	1.45	1.11, 1.89
Without contrast agent	875	703	172	19.7%			
SCr ≥ 1.7 mg/dL							
With contrast agent	333	230	103	30.9%	.001	1.67	1.23, 2.28
Without contrast agent	703	562	141	20.1%			
SCr ≥ 1.8 mg/dL							
With contrast agent	233	151	82	35.2%	.001	1.80	1.26, 2.57
Without contrast agent	537	424	113	21.0%			
SCr ≥ 1.9 mg/dL							
With contrast agent	174	105	69	39.7%	<.001	1.98	1.33, 2.95
Without contrast agent	434	338	96	22.1%			
SCr ≥ 2.0 mg/dL							
With contrast agent	141	80	61	43.3%	<.001	2.15	1.38, 3.34
Without contrast agent	346	268	78	22.5%			
Overall							
With contrast agent	10 121	9286	835	8.3%	.55	0.97	0.87, 1.08
Without contrast agent	10 121	9254	867	8.6%			

# Risk of AKI Attributable to Contrast Agents

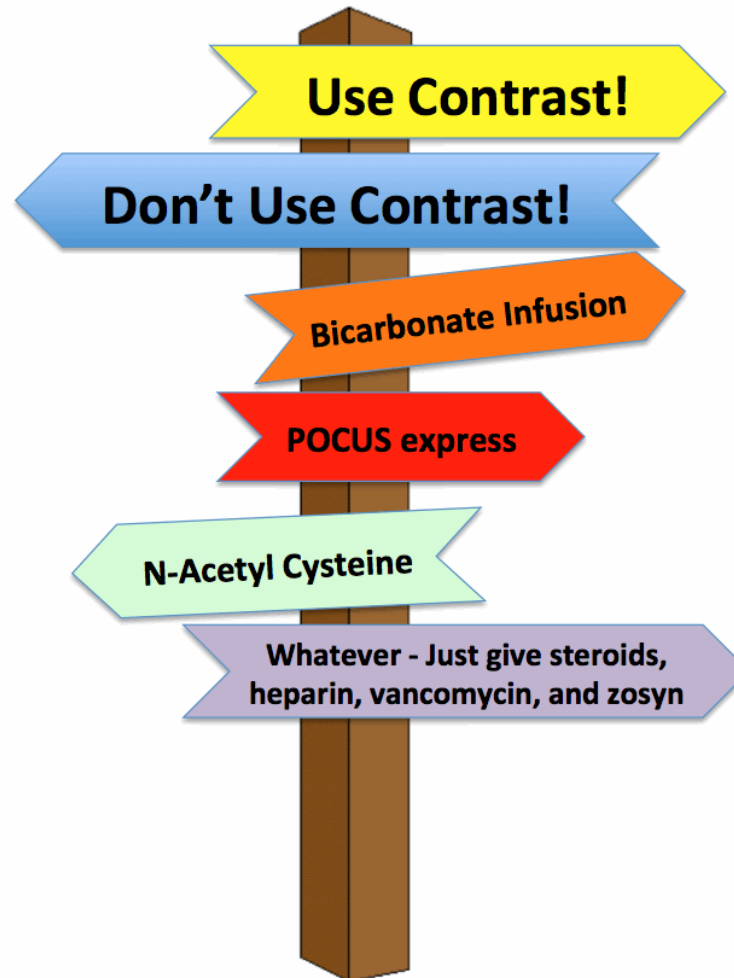
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# Understanding the Actual Risk

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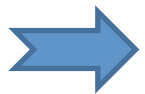
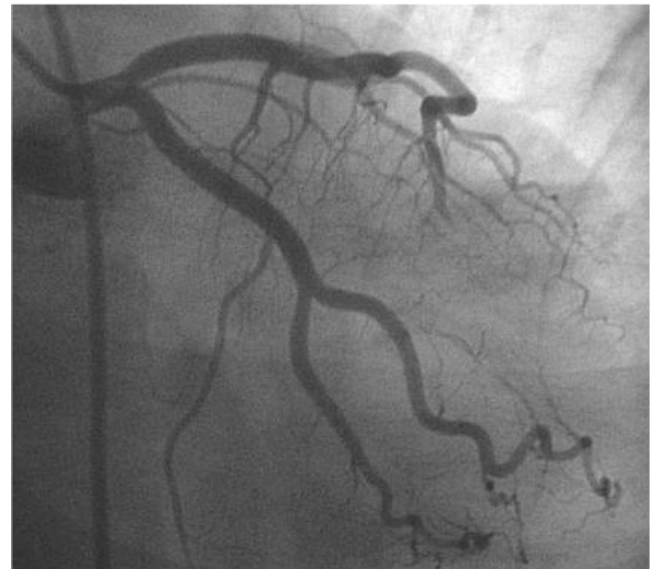
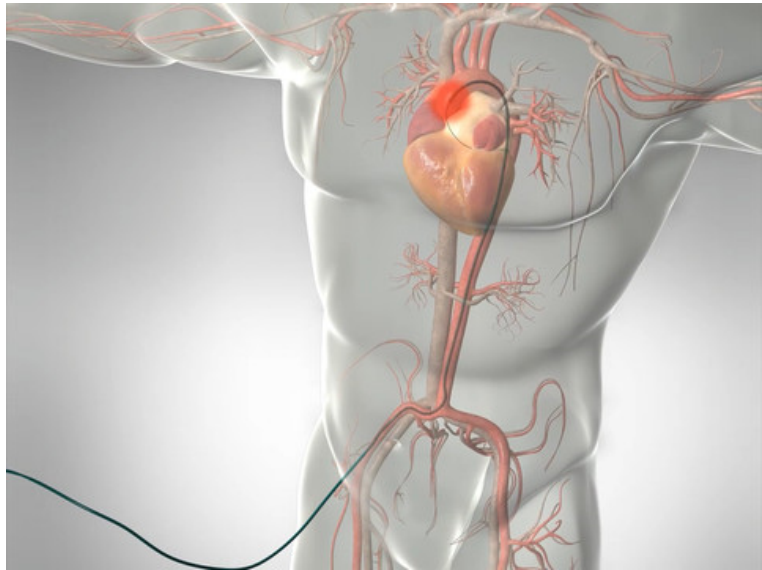
Risk of AKI and complications



Benefit from contrast imaging procedures

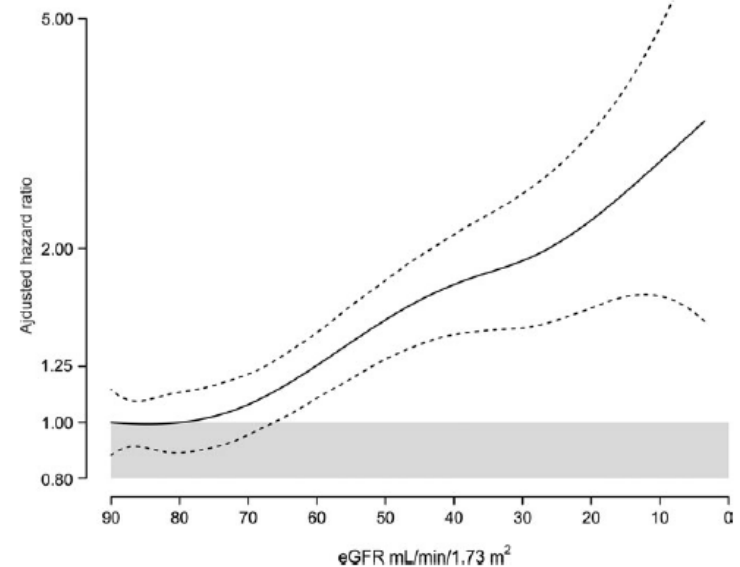
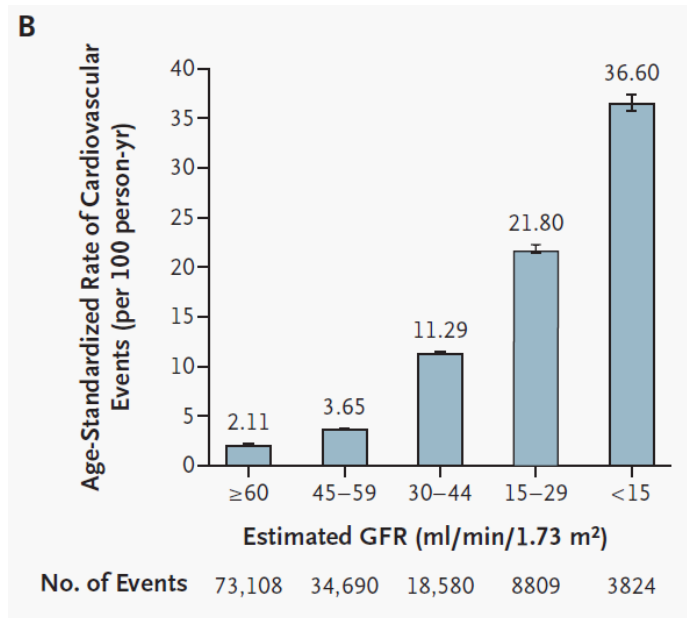
# Understanding the Actual Risk

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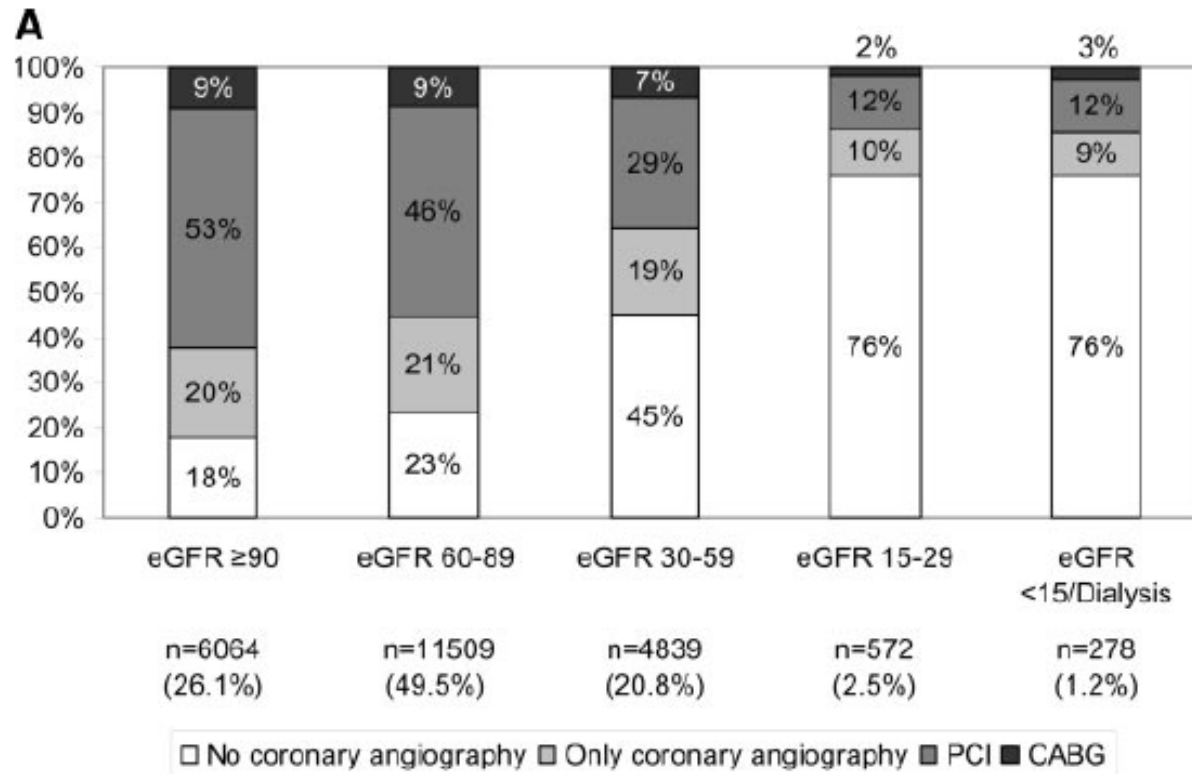
Perspective gained from exploring underutilization of coronary angiography and invasive management of acute coronary syndromes in patients with pre-existing kidney disease

# Risks of Cardiovascular Events and Adverse Outcomes with Pre-existing Kidney Disease



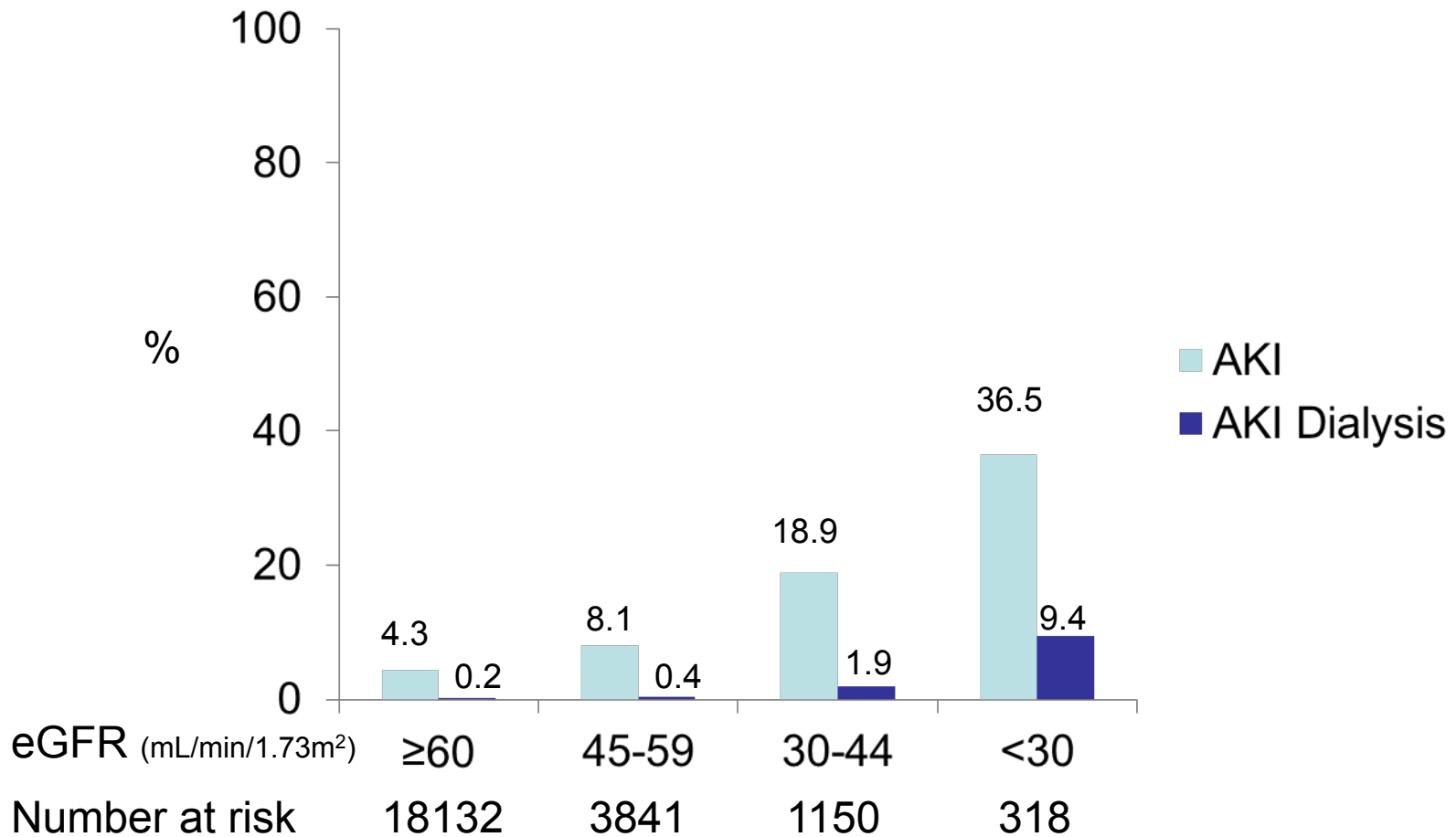
# Inappropriately Low Rates of Imaging and Intervention in Kidney Disease

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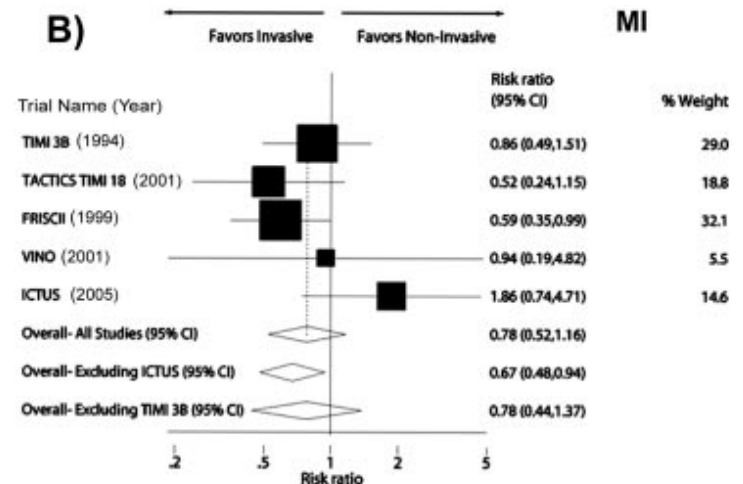
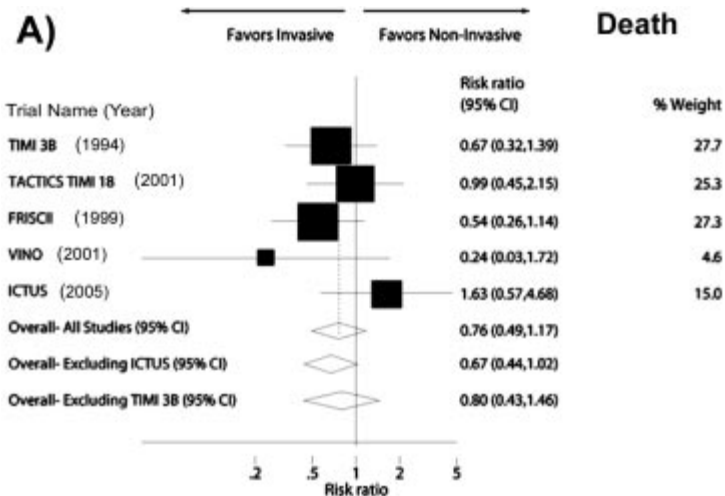


# Risk of AKI According to Baseline Kidney Function

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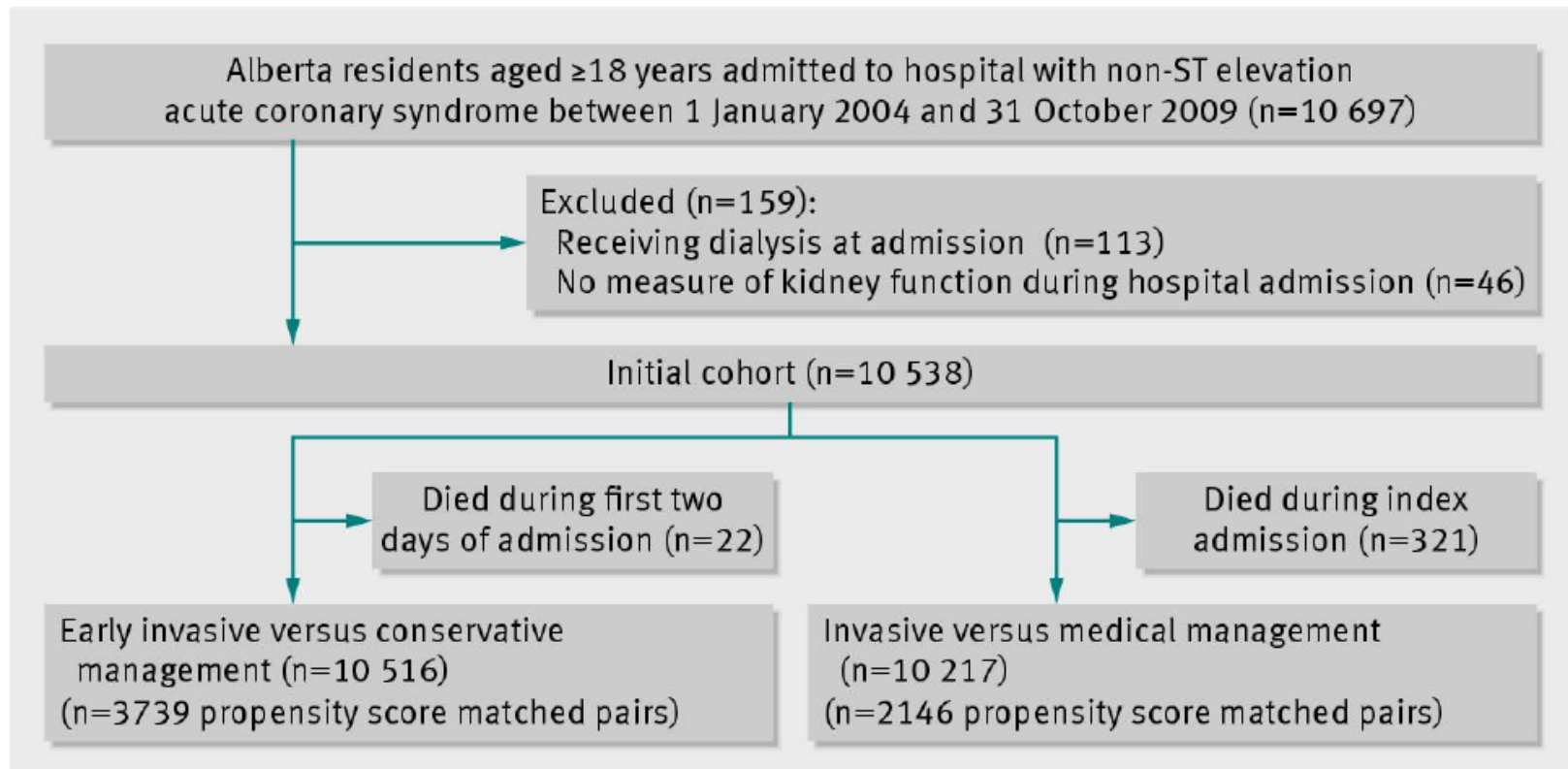


# Benefits of Intervention in Kidney Disease

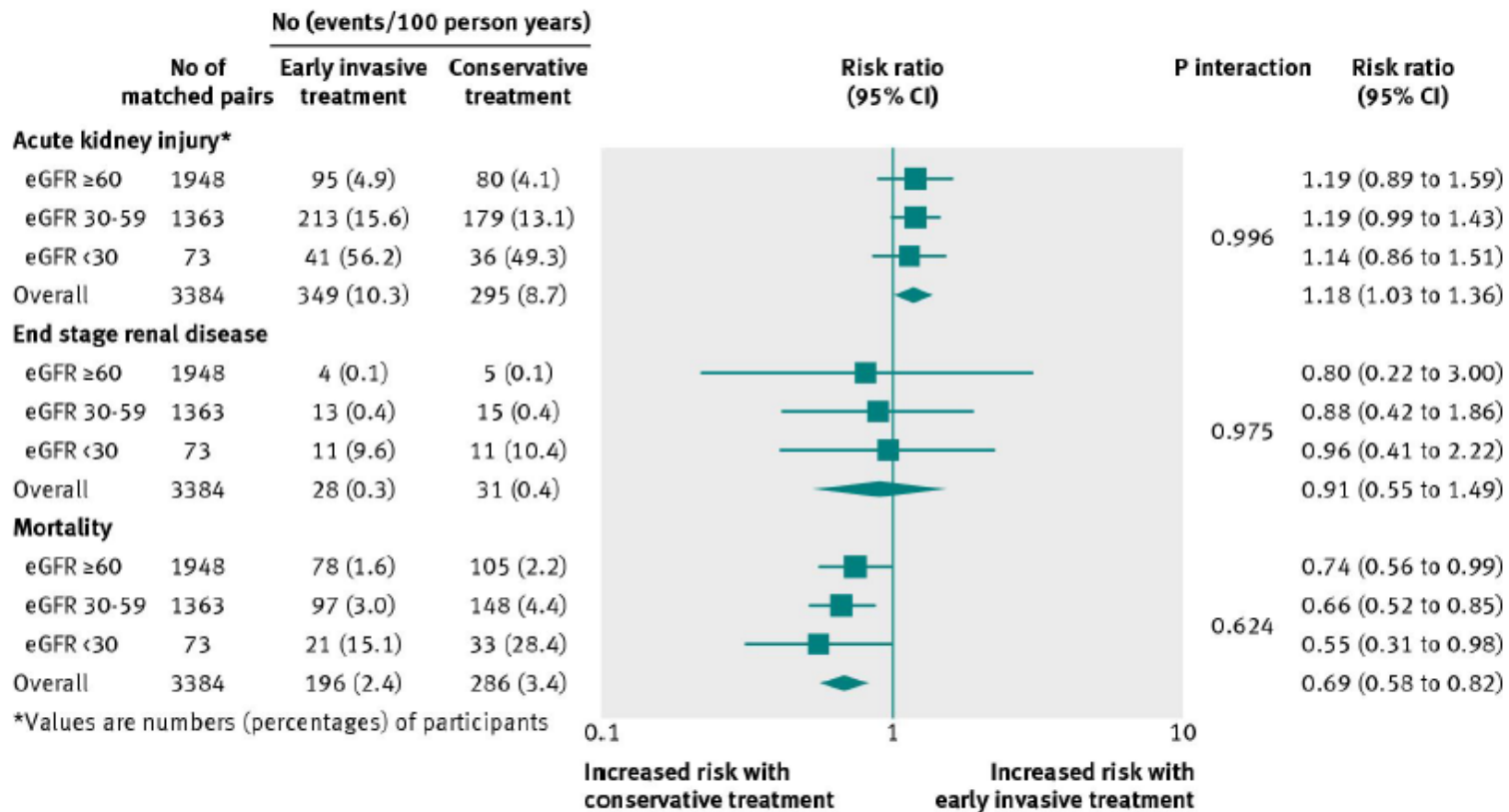


# Risk vs Benefits of Intervention in Kidney Disease

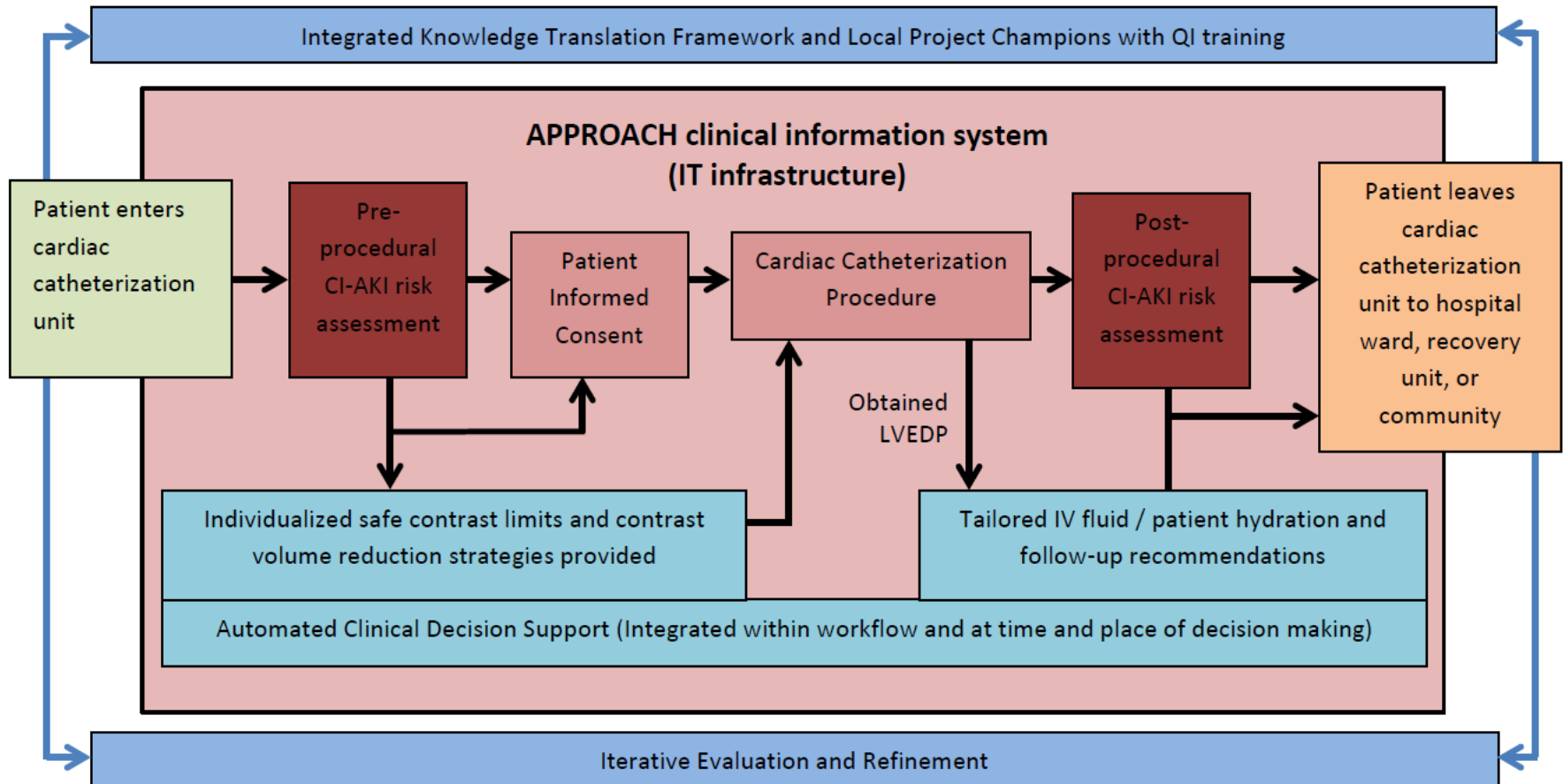
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# Risk vs Benefits of Intervention in Kidney Disease



# Current Initiative for Safe Contrast Imaging



# Implications

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Although contrast exposure is associated with a risk of AKI, the risk attributable to contrast is smaller than is often thought for the majority of patients.

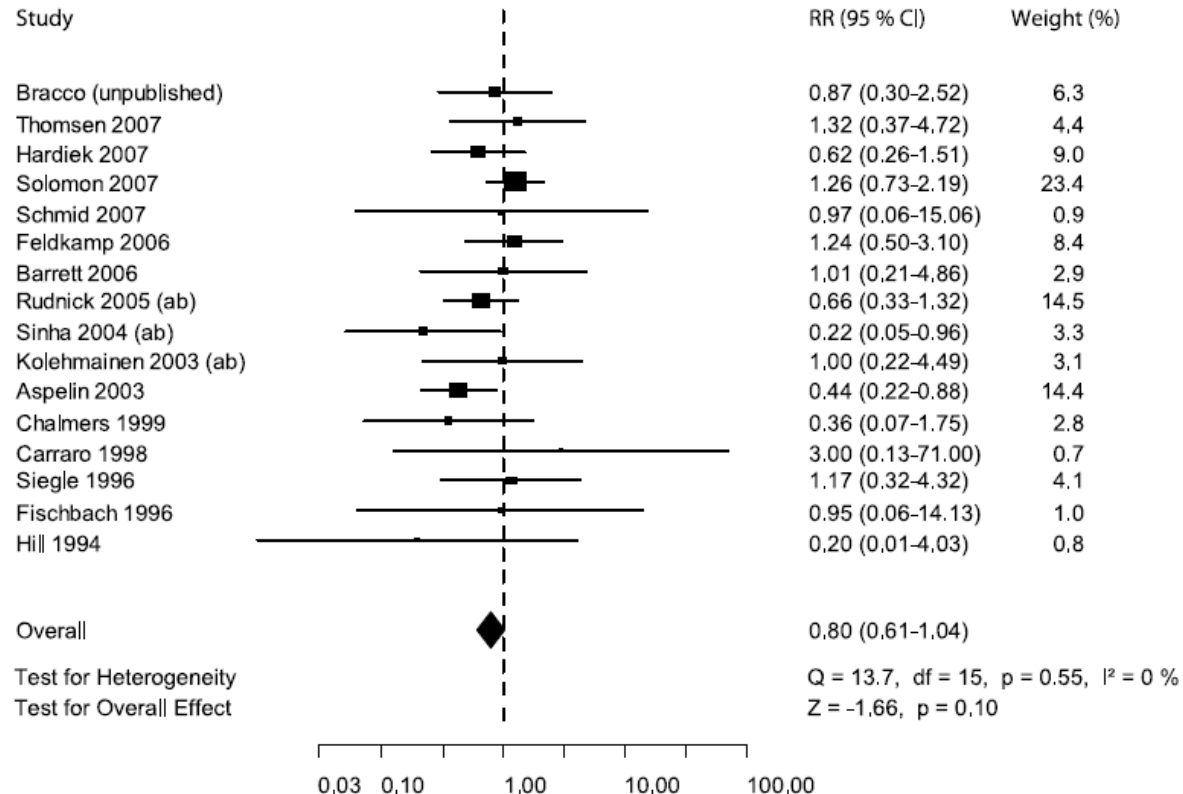
The risk and implications of AKI are most clinically relevant in patients with pre-existing kidney disease.

Patients with pre-existing kidney disease have among the highest risk of cardiovascular event and adverse outcomes and potential to benefit from these procedures. Avoiding contrast imaging and interventions in these patients is unlikely to improve their outcomes.

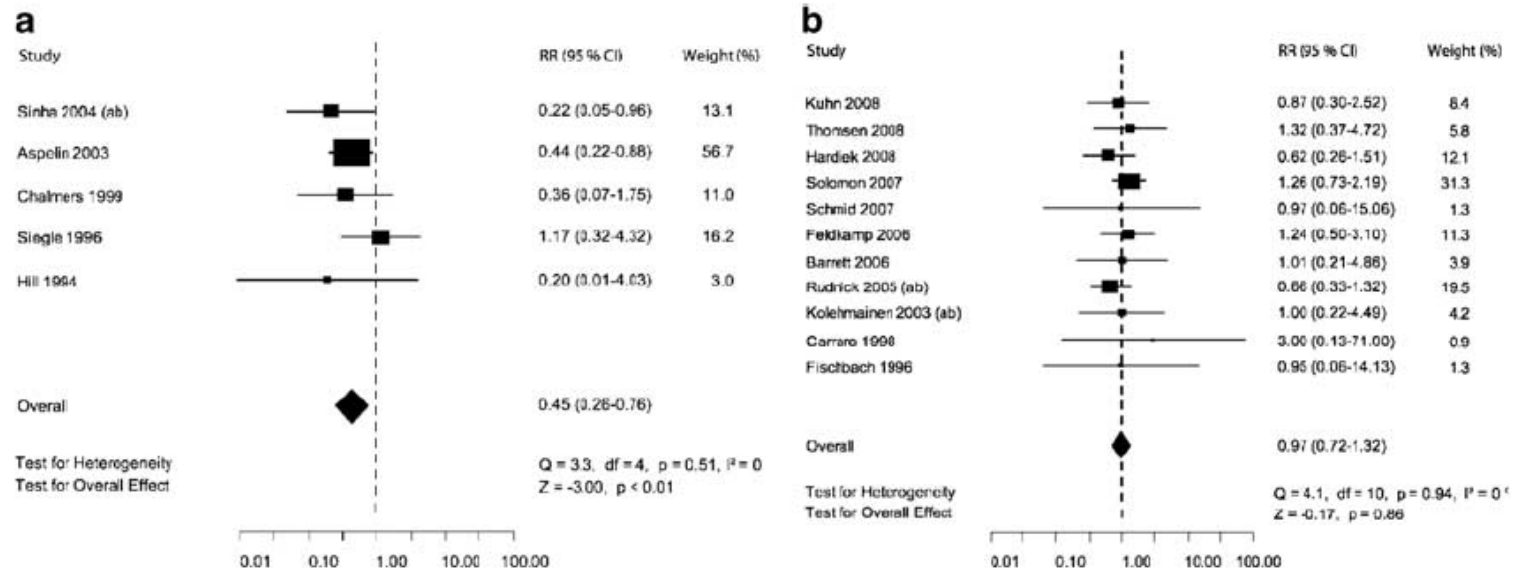
# Questions / Discussion

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# Iso-osmolar versus Low Osmolar Agents



# Iso-osmolar versus Low Osmolar Agents

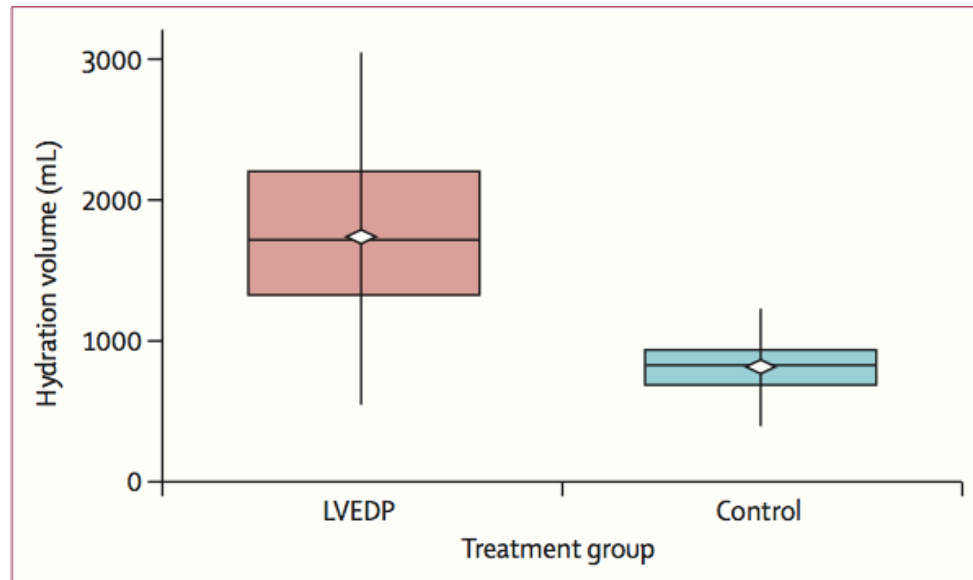


**Figure 14 | Risk for contrast-induced nephropathy.** (a) Iodixanol vs. iohexol and risk for contrast-induced nephropathy; (b) iodixanol vs. nonionic low-osmolar contrast media other than iohexol and risk for contrast-induced nephropathy. Reprinted from Heinrich MC, Haberle L, Muller V *et al.* Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology* 2009; 250: 68-86 with permission, copyright 2009, from Radiological Society of North America<sup>457</sup>; accessed <http://radiology.rsna.org/content/250/1/68.long>

# Intravenous Fluids

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**Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial**

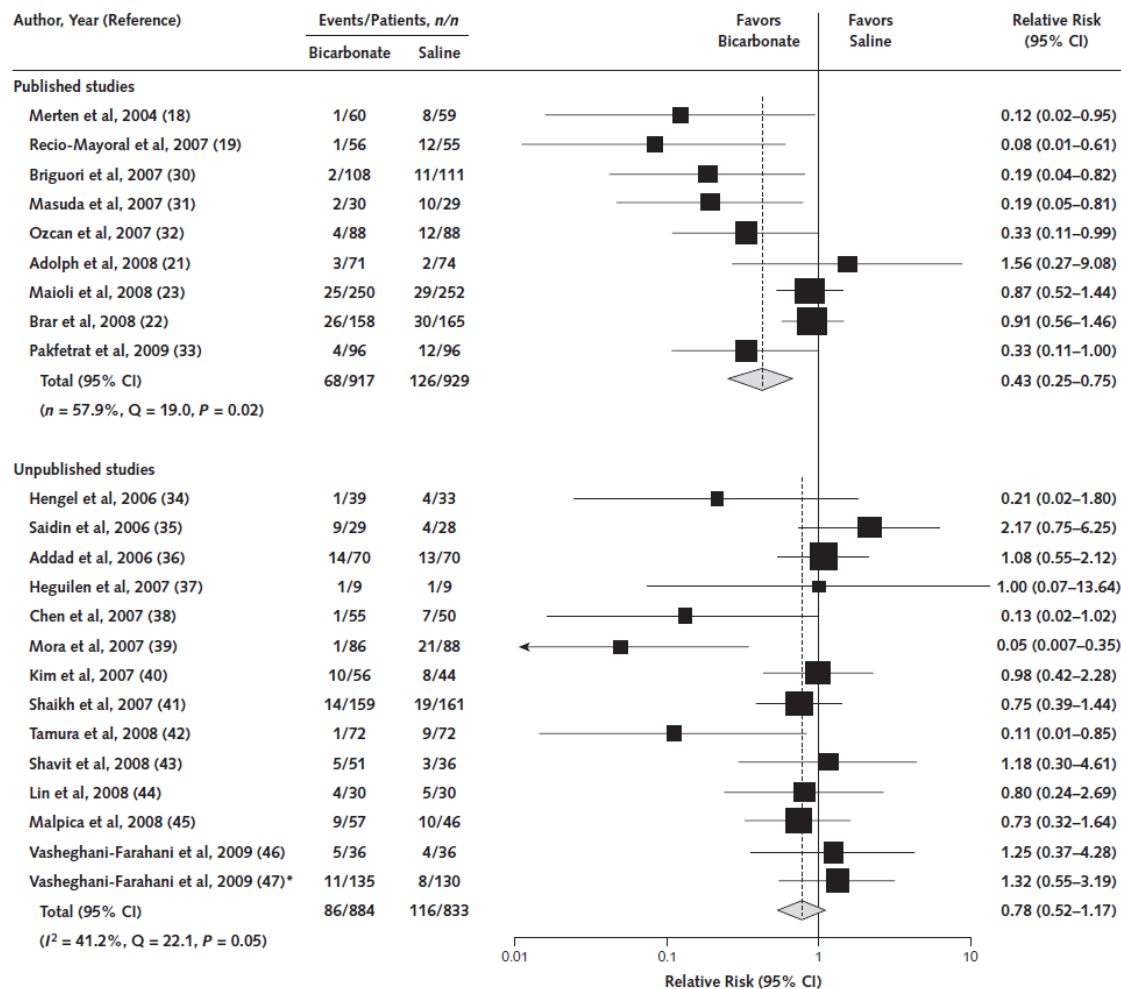


# Intravenous Fluids

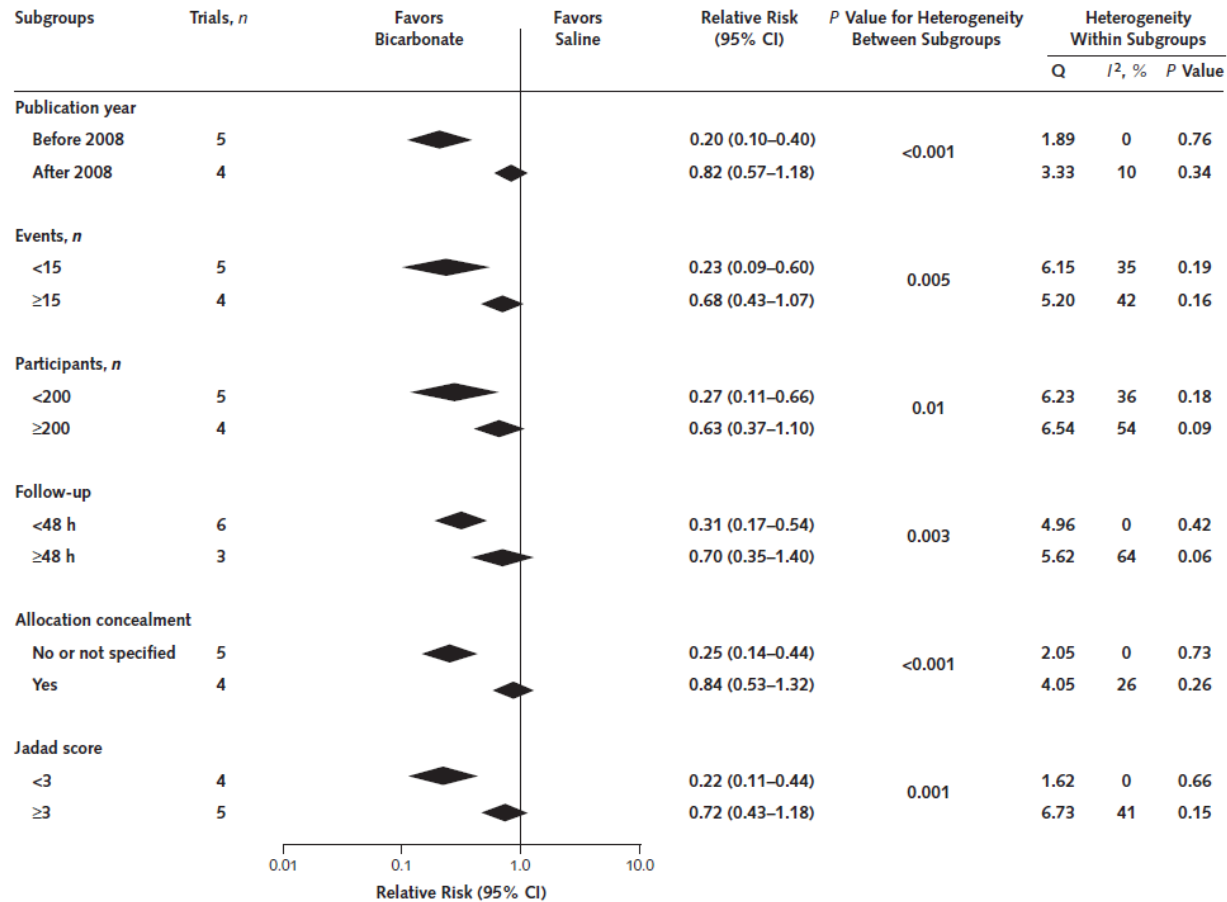
## Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial

	LVEDP hydration-guided group	Control group	Relative risk (95% CI)	Risk difference (95% CI)	p value
<b>Primary endpoint</b>					
>25% or 0.5 mg/dL increase in serum creatinine	12/178 (6.7%)	28/172 (16.3%)	0.41 (0.22–0.79)	–9.5 (–2.9 to –16.2)	0.005
<b>Secondary endpoints</b>					
>25% increase in serum creatinine	12/178 (6.7%)	27/172 (15.7%)	0.43 (0.22–0.82)	–9.0 (–2.5 to –15.5)	0.008
>0.5 mg/dL increase in serum creatinine	5/178 (2.8%)	11/172 (6.4%)	0.44 (0.16–1.24)	–3.6 (–8.0 to 0.8)	0.11
<b>Sensitivity analyses</b>					
≥0.3 mg/dL increase in serum creatinine	24/178 (13.5%)	43/172 (25.0%)	0.54 (0.34–0.85)	–11.5 (–3.3 to –19.7)	0.006
>25% or 0.5 mg/dL increase in serum creatinine in participants with ≥1 serum creatinine value available	12/190 (6.3%)	28/196 (14.3%)	0.44 (0.23–0.84)	–8.0 (–2.0 to –14.0)	0.01

# IV Bicarbonate versus Saline



# IV Bicarbonate versus Saline



# N-Acetylcysteine

## Acetylcysteine in the Prevention of Contrast-Induced Nephropathy

### *A Case Study of the Pitfalls in the Evolution of Evidence*

**Table 2. Publication History and Summary of Findings for Meta-analyses on the Efficacy of Acetylcysteine for Prevention of Contrast-Induced Nephropathy**

Source	Clinical Scope	Studies Included*	No. of Trials Included	No. of Patients Included	Heterogeneity ( <i>P</i> Value)	Pooled Estimate (95% CI)	Author Conclusions
Birck et al <sup>24</sup>	CT or angiography	A	7	805	Present ( <i>P</i> = .02)	RR, 0.44 (0.22-0.88)	Treatment beneficial
Isenbarger et al <sup>25</sup>	CT or angiography	A	7	805	Present ( <i>P</i> = .01)	OR, 0.37 (0.16-0.84)	Treatment beneficial
Alonso et al <sup>26</sup>	CT or angiography	A, B	8	885	Not reported	RR, 0.41 (0.22-0.79)	Treatment beneficial
Kshirsagar et al <sup>27</sup>	CT or angiography	A, B	16	1538	Present ( <i>P</i> < .001)	Not reported	Inconclusive
Pannu et al <sup>28</sup>	CT or angiography	A, B, D	15	1776	Present ( <i>P</i> = .02)	RR, 0.65 (0.43-1.0)	Inconclusive
Guru and Fremes <sup>29</sup>	CT or angiography	A, C	11	1213	Present ( <i>P</i> = .01)	OR, 0.46 (0.32-0.66)	Treatment beneficial
Bagshaw and Ghali <sup>30</sup>	Angiography	A	14	1261	Present ( <i>P</i> = .03)	OR, 0.54 (0.32-0.91)	Inconclusive
Misra et al <sup>31</sup>	Angiography	A	5	643	Present ( <i>P</i> = .05)	RR, 0.30 (0.11-0.82)	Treatment beneficial
Nallamothu et al <sup>32</sup>	CT or angiography	A, D	20	2195	Present ( <i>P</i> = .01)	RR, 0.73 (0.52-1.0)	Inconclusive
Liu et al <sup>33</sup>	CT or angiography	A, B	9	1028	Present ( <i>P</i> = .03)	RR, 0.43 (0.24-0.75)	Treatment beneficial
Duong et al <sup>34</sup>	CT or angiography	A, C	14	1584	Present ( <i>P</i> = .01)	RR, 0.57 (0.37-0.84)	Treatment beneficial

Abbreviations: CI, confidence interval; CT, computed tomography; OR, odds ratio; RR, relative risk.

\*Source(s) of data for meta-analyses: A indicates published articles describing randomized controlled trials; B, published abstracts describing randomized controlled trials; C, published articles describing nonrandomized clinical trials; and D, unpublished data.

# N-Acetylcysteine

## Acetylcysteine for Prevention of Renal Outcomes in Patients Undergoing Coronary and Peripheral Vascular Angiography Main Results From the Randomized Acetylcysteine for Contrast-Induced Nephropathy Trial (ACT)

Table 3. End Points

Outcomes	Acetylcysteine	Placebo	Relative Risk (95% CI)	P
Primary end point, No. of events/total No. (%)				
Contrast-induced acute kidney injury	147/1153 (12.7)	142/1119 (12.7)	1.00 (0.81–1.25)	0.97
Other end points, No. of events/total No. (%)				
End points in 48 to 96 h				
Doubling in serum creatinine	13/1153 (1.1)	17/1119 (1.5)	0.74 (0.36–1.52)	0.41
Elevation $\geq 44.2 \mu\text{mol/L}$ (0.5 mg/dL) in serum creatinine	45/1153 (3.9)	42/1119 (3.8)	1.04 (0.69–1.57)	0.85
Elevation $\geq 13.3 \mu\text{mol/L}$ (0.3 mg/dL) in serum creatinine	140/1153 (12.1)	123/1119 (11.0)	1.10 (0.88–1.39)	0.39
End points at 30 d				
Deaths or need for dialysis*	26/1171 (2.2)	26/1135 (2.3)	0.97 (0.56–1.69)	0.92
Death, need for dialysis, or doubling in serum creatinine	38/1171 (3.2)	41/1135 (3.6)	0.90 (0.58–1.39)	0.63
Deaths*	23/1171 (2.0)	24/1135 (2.1)	0.97 (0.54–1.73)	0.92
Need for dialysis*	3/1171 (0.3)	3/1135 (0.3)	0.87 (0.17–4.35)	0.86
Cardiovascular deaths*	18/1171 (1.5)	18/1135 (1.6)	0.99 (0.51–1.90)	0.97

# N-Acetylcysteine

