Appendices Guideline Safe Use of Contrast Media - Part 1

Appendices to Chapter 4

Evidence tables

Exclusion after examination of full text (initial search): Risk factors for PC-AKI

Exclusion after examination of fu	ıll text (initial search): Risk factors for PC-AKI
Author and year	Reasons to exclude
Abe, 2011	Does not meet selection criteria
Abujudeh, 2008	Examines risk of PC-AKI in patients who underwent 2 CT-scans within 24 hours,
	not applicable for overall recommendations
Acosta, 2010	Does not meet selection criteria
Agrawal, 2009	Does not meet selection criteria
Aguiar-Suato, 2010	Does not meet selection criteria
Ahuja, 2010	Does not meet selection criteria
Akgullu, 2015	Does not meet selection criteria
Akrawinthawong, 2015	Does not meet selection criteria
Alharazy, 2013	Does not meet selection criteria
Bachorzewska-Gajewska, 2006	Does not meet selection criteria
Balemans, 2012	Does not meet selection criteria
Band, 2007	Does not meet selection criteria
Barbieri, 2014	Does not meet selection criteria
Becker, 2006	Does not meet selection criteria
Canyigit, 2013	Does not meet selection criteria
Caruso, 2011	Does not meet selection criteria
Cely, 2012	Does not meet selection criteria
Chang, 2013	Studies gene polymorphisms and their relation to PC-AKI risk; not applicable in
Chang, 2013	common Dutch clinical practice.
Chavakula, 2013	Does not meet selection criteria
Chen, 2014	Does not meet selection criteria
Cho, 2011	Does not meet selection criteria
Chong, 2009	
O,	Does not meet selection criteria
Chong, 2010_1 Chong, 2010_2	Does not meet selection criteria
	Does not meet selection criteria
Chong, 2012	Does not meet selection criteria
Cheruvu, 2007	Does not meet selection criteria
Crit, 2006	Does not meet selection criteria
Clark, 2011	Does not meet selection criteria
Clec'h, 2013	Does not meet selection criteria
Colling, 2014	Does not meet selection criteria
Conen, 2006	Does not meet selection criteria
Cowburn, 2005	Does not meet selection criteria
Dangas, 2005	Does not meet selection criteria
Davidson, 2008	Does not meet selection criteria
Ding, 2013	Does not meet selection criteria
Diogo, 2010	Does not meet selection criteria
Diogo, 2014	Does not meet selection criteria
Dittrich, 2006	Does not meet selection criteria
Dittrich, 2007	Does not meet selection criteria
Durukan, 2012	Does not meet selection criteria
Elias, 2005	Does not meet selection criteria
Erdogan, 2003	Does not meet selection criteria
Erselcan, 2012	Does not meet selection criteria
Friedewald, 2013	Does not meet selection criteria
From, 2008	Does not meet selection criteria
Fu, 2013	Does not meet selection criteria
Gao, 2011	Does not meet selection criteria
Gao, 2014	Does not meet selection criteria
Garcia, 2014	Does not meet selection criteria
Garcia-Ruiz, 2003	Does not show multivariate model that predicts risk factors of PC-AKI
Goldenberg, 2005	Does not meet selection criteria

Golshahi, 2014	Does not meet selection criteria						
Goo, 2014	Does not meet selection criteria Does not meet selection criteria						
Guevara, 2004	Does not meet selection criteria Does not meet selection criteria						
Gurm, 2011	Does not meet selection criteria Does not meet selection criteria						
Grum, 2013	Does not meet selection criteria						
Hassen, 2014	Does not meet selection criteria						
Haveman, 2006	Does not meet selection criteria						
Hayakawa, 2014	Patient population: patients with hepatocellular carcinoma undergoing trans-						
114 yana 114, 201 1	arterial chemo-embolization. Article too specific to draw overall conclusions						
	over intra-arterial contrast administration and risk of PC-AKI.						
Hernández, 2009	Already included in systematic review Bondi-Zoccai, 2014						
Hipp, 2008	Does not meet selection criteria						
Holscher, 2008	Does not meet selection criteria						
Hoste, 2011	Does not meet selection criteria						
Huang, 2013	Does not meet selection criteria						
Huggins, 2014	Does not meet selection criteria						
Ivanes, 2014	Does not meet selection criteria						
Jaipaul, 2010	Does not meet selection criteria						
Jarai, 2012	Does not meet selection criteria						
Ji, 2015	Does not meet selection criteria						
Jochheim, 2014	Does not meet selection criteria						
Jo, 2015	Does not meet selection criteria						
Kato, 2008	Does not meet selection criteria						
Kian, 2006	Does not meet selection criteria						
Kim, 2011	Does not meet selection criteria						
Kim, 2012	Does not meet selection criteria						
Kim, 2015	Does not meet selection criteria						
Kiski, 2009	Does not meet selection criteria						
Kiski, 2010	Does not meet selection criteria						
Koo, 2013	Does not meet selection criteria						
Kougias, 2014	Does not meet selection criteria						
Kuhn, 2008	Does not meet selection criteria						
Kwasa, 2014	Does not meet selection criteria						
Lameire, 2006	Does not meet selection criteria						
Laskey,2009	Does not meet selection criteria						
Lee, 2014	Does not meet selection criteria						
Lencioni, 2010	Does not meet selection criteria						
Leung, 2014	Model predicts use of cardiac medication after development of PC-AKI, but						
1: 2012	does not predict risk of PC-AKI						
Li, 2013 Li, 2014	Does not meet selection criteria Does not meet selection criteria						
Liebetrau, 2014	Does not meet selection criteria Does not meet selection criteria						
Limbruno, 2014	Does not meet selection criteria Does not meet selection criteria						
Lin, 2014	Does not meet selection criteria Does not meet selection criteria						
Liu, 2012_1	Does not meet selection criteria Does not meet selection criteria						
Liu, 2012_2	Does not meet selection criteria						
Liu, 2013	Does not meet selection criteria						
Liu, 2014	Does not meet selection criteria						
Lodhia, 2009	Does not meet selection criteria						
Lucreziotti, 2014	Does not meet selection criteria						
Lui, 2012	Does not meet selection criteria						
Macaulay, 2015	Does not answer research question, no multivariate analysis performed (n=7)						
Madershahian, 2012	Does not meet selection criteria						
Madershahian, 2012	Does not meet selection criteria						
Madsen, 2009	Does not meet selection criteria						
Mager, 2011	Does not meet selection criteria						
Maioli, 2010	Does not meet selection criteria						
Maioli, 2012	Does not meet selection criteria						
Malyszko, 2009	Does not meet selection criteria						
Marenzi, 2004_1	Does not meet selection criteria						
	5 7						

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Marenzi, 2004_2	Does not meet selection criteria
Matsushima, 2011	Does not meet selection criteria
McCullough, 2006_1	Does not meet selection criteria
McCullough, 2006_2	Does not meet selection criteria
McDonald, 2014_1	Does not meet selection criteria
McDonald, 2014_2	Does not meet selection criteria
Medalion, 2010	Does not meet selection criteria
Mehran, 2004	Does not meet selection criteria
Mehran, 2009	Does not meet selection criteria
Mehta, 2004	Does not meet selection criteria
Mekan, 2004	Does not meet selection criteria
Moos, 2013	Does not meet selection criteria
Moos, 2014	Does not show multivariate model that predicts risk factors of PC-AKI (but tests existing models)
Morabito, 2012	Does not meet selection criteria
Morcos, 2012	Does not meet selection criteria Does not meet selection criteria
Murakami, 2013	
Najjar (ea) 2002	Does not meet selection criteria Does not meet selection criteria
Naruse, 2012	Does not meet selection criteria Does not meet selection criteria
Ng, 2010	Does not meet selection criteria Does not meet selection criteria
Nikolsky, 2004	Does not meet selection criteria Does not meet selection criteria
Nikolsky, 2005	Does not meet selection criteria Does not meet selection criteria
Nozue, 2009	Does not meet selection criteria Does not meet selection criteria
Nyman, 2005	Does not meet selection criteria
Onuigbo, 2008	Does not meet selection criteria
Osman, 2014	Does not meet selection criteria
Owen, 2014	Does not meet selection criteria
Padhy, 2014	Does not meet selection criteria
Pahade, 2011	Does not meet selection criteria
Pakfetrat, 2010_1	Does not meet selection criteria
Pakfetrat, 2010_2	Does not meet selection criteria
Parra, 2004	Does not meet selection criteria
Patel, 2010	Review, not systematic and does not answer research question
Peguero, 2014	Does not meet selection criteria
Peng, 2015	Does not meet selection criteria
Piskinpasa, 2013	Combination of CAG and CT-scan patients (n=70), not analysed separately.
Polena, 2005	Does not meet selection criteria
Prasad, 2014	No multivariate analysis of risk factors for PC-AKI was performed
Rahman, 2005	Does not meet selection criteria
Raingruber, 2011	Does not meet selection criteria
Ranucci, 2013	Does not meet selection criteria
Raposeiras, 2015	Does not meet selection criteria
Raposeiras, 2015	Does not meet selection criteria
Ray, 2013	Does not meet selection criteria No multivariate applysis of rick factors for BC AVI was performed
Reuter, 2014	No multivariate analysis of risk factors for PC-AKI was performed
Sahin, 2014 Saito, 2015	Does not meet selection criteria Does not meet selection criteria
Saritemur, 2014	Does not meet selection criteria Does not meet selection criteria
Sendur, 2013	Does not meet selection criteria Does not meet selection criteria
Sharma, 2013	Does not meet selection criteria Does not meet selection criteria
Shema, 2009	Does not meet selection criteria
Sidhu, 2008	Does not meet selection criteria
Skelding, 2007	Does not answer research question, validation of risk score
Spatz, 2012	Does not meet selection criteria
Spini, 2013	Does not meet selection criteria
Standstede, 2007	Does not meet selection criteria
Stermer, 2001	Does not meet selection criteria
Subedi, 2011	Does not meet selection criteria
Tan, 2013	Does not meet selection criteria
Taniguchi, 2013	Does not meet selection criteria

Thomsen, 2003	Does not meet selection criteria				
Thomsen, 2009	Does not meet selection criteria				
Toprak, 2006_1	Does not meet selection criteria				
Toprak, 2006_2	Does not meet selection criteria				
Toprak, 2007	Does not meet selection criteria				
Trivedi, 2010	Does not meet selection criteria				
Tziakas, 2014	Does not meet selection criteria				
Ucar, 2014	Does not meet selection criteria				
Ugur, 2014	Does not meet selection criteria				
Umruddin, 2012	Does not meet selection criteria				
Utsunomiyama, 2011	Studies risk factors for kidney insufficiency, not risk factors for development of				
	PC-AKI after CT-scan				
Victor, 2014	Does not meet selection criteria				
Wacker-Gusmann, 2014	Does not meet selection criteria				
Wang, 2011	Does not meet selection criteria				
Weisbord, 2006	Does not meet selection criteria				
Wessely, 2009	Does not meet selection criteria				
Wi, 2013	Does not meet selection criteria				
Yamamoto, 2013	Does not meet selection criteria				
Zaytseva, 2009	Does not meet selection criteria				

Exclusion after examination of full text (update 2017): Risk factors for PC-AKI

Exclusion after examination of full text (update 2017): Risk factors for PC-AKI						
Author and year	Redenen van exclusie					
Kanda, 2016	Does not meet selection criteria					
Prasad, 2016.	Does not meet selection criteria					
Abouzeid, 2016	Does not meet selection criteria					
Agarwal, 201	Does not meet selection criteria					
Azzalini, 2016	Does not meet selection criteria					
Cernigliaro, 2016	Does not meet selection criteria					
Briguori, 2016	Does not meet selection criteria					
Chong, 2015	Does not meet selection criteria					
de Francesco, 2015	Does not meet selection criteria					
Dong, 2016	Does not meet selection criteria					
Filomia 2016	Does not meet selection criteria					
Guneyli, 2015	Does not meet selection criteria					
Gurm, 2016.	Does not meet selection criteria					
Subramaniam, 2016	Does not meet selection criteria					
Ye, 2016 / Ye, 2017	Does not meet selection criteria					
Zapata-Chica, 2015	Does not meet selection criteria					
Hinson, 2017	Does not meet selection criteria					
Hong, 2016	Does not meet selection criteria					
Hsieh, 2016	Does not meet selection criteria					
Huber, 2016	Does not meet selection criteria					
Kanbay, 2017,	Does not meet selection criteria					
Khaledifar, 2015	Does not meet selection criteria					
Kim, 2015	Does not meet selection criteria					
Komiyama, 2017	Does not meet selection criteria					
Liu 2015	Does not meet selection criteria					
McDonald 2015	Does not meet selection criteria					
Nijssen, 2017	Does not meet selection criteria					
Nyman, 2015	Does not meet selection criteria					
Ortega, 2015	Does not meet selection criteria					
Park, 2016	Does not meet selection criteria					
Sato, 2015	Does not meet selection criteria					
Shema, 2016	Does not meet selection criteria					
Sigterman, 2016	Does not meet selection criteria					
Salomon, 2015	Does not meet selection criteria					
Tong, 2016,	Does not meet selection criteria					
Turedi, 2016	Does not meet selection criteria					
Usmiani, 2016	Does not meet selection criteria					

Valette, 2017	Does not meet selection criteria
Vontobel, 2015	Does not meet selection criteria
Winther, 2016	Does not meet selection criteria
Xu, 2016	Does not meet selection criteria
Yang, 2014	Does not meet selection criteria
Zeller, 2016	Does not meet selection criteria

Exclusion after examination of full tekst: Measurement instruments for PC-AKI risk

Author and year	Reasons for exclusion					
•	Letter to the editor					
Aguiar, 2008						
Akgullu, 2015	Does not fulfill selection criteria, no risk score is validated/developed					
Balemans, 2012	Does not fulfill selection criteria, no risk score is validated/developed					
Bartholemew, 2004	Already included in systematic review Silver, 2015					
Benko, 2007	Not an original article (guideline)					
Celik, 2015	The diagnostic properties of a laboratory analysis (contrast media volume toe					
	GFR ratio) to predict PC-AKI are examined, not of a non-invasive method.					
Chen, 2014	Already included in systematic review Silver, 2015					
Chong, 2012	Does not fulfill selection criteria, no risk score is validated/developed					
Crit, 2006	Does not fulfill selection criteria, no risk score is validated/developed					
Davenport, 2013	The diagnostic properties of a laboratory analysis (different eGFR cut-off					
	values) to predict PC-AKI are examined, not of a non-invasive method.					
Davenport, 2013_1	The diagnostic properties of a laboratory analysis (different eGFR cut-off					
	values) to predict PC-AKI are examined, not of a non-invasive method					
Erselcan, 2009	The diagnostic properties of a laboratory analysis (eGFR by MDRD formula) to					
	predict PC-AKI are examined, not of a non-invasive method.					
Feldkamp, 2008	Narrative review					
Fu, 2013	Already included in systematic review Silver, 2015					
Gao, 2014	Already included in systematic review Silver, 2015					
Ghani, 2009	Already included in systematic review Silver, 2015					
Gurm, 2013	Already included in systematic review Silver, 2015					
Holscher, 2008	Does not fulfill selection criteria, no risk score is validated/developed					
Kim, 2011	Does not fulfill selection criteria, no risk score is validated/developed					
Kooiman, 2010	Does not fulfill selection criteria, no risk score is validated/developed					
Kowalczyk, 2007	Does not fulfill selection criteria, no risk score is validated/developed					
Lepanto, 2011	Narrative review					
Li, 2013	The diagnostic properties of a laboratory analysis (anemia) to predict PC-AKI					
	are examined, not of a non-invasive method.					
Liu, 2014	Already included in systematic review Silver, 2015					
Maioli, 2011	Already included in systematic review Silver, 2015					
Marenzi, 2004	Already included in systematic review Silver, 2015					
Martainez – Lomakin, 2014	The diagnostic properties of a laboratory analysis (point of care creatinin test)					
	to predict PC-AKI are examined, not of a non-invasive method.					
McCullough, 2001	Narrative review					
McCullough, 2007	Narrative review					
McDonald, 2014	Does not fulfill selection criteria, no risk score is validated/developed					
Mehran, 2004	Already included in systematic review Silver, 2015					
Owen, 2014	Not an original article (guideline)					
Pakfetrat, 2010	Does not fulfill selection criteria, no risk score is validated/developed					
Rainburger, 2011	PC-AKI is not an outcome measure.					
Saito, 2015	The diagnostic properties of a laboratory analysis (proteinuria and to predict					
•	PC-AKI are examined, not of a non-invasive method.					
Sany, 2013	Does not meet selection criteria, no risk score is validated/developed					
Skelding, 2007	Does not fulfill selection criteria, pre-defined outcome variables not reported					
Skluzacek, 2003	The diagnostic properties of a laboratory analysis (eGFR) to predict PC-AKI are					
	examined, not of a non-invasive method.					
Tong, 1996	The diagnostic properties of a laboratory analysis (neutrophil gelatinase					
3,	associated lipoprotein) to predict PC-AKI are examined, not of a non-invasive					
	method.					
Too, 2015	PC-AKI is not an outcome measure. The questionnaire's ability to predict eGFR					
	is examined.					

Tziakas, 2013	Already included in systematic review Silver, 2015						
Wackecker-Guβmann, 2014	The diagnostic properties of a laboratory analysis (cystatin C) to predict PC-AKI						
	are examined, not of a non-invasive method.						
Wang, 2011	The diagnostic properties of a laboratory analysis (contrast media volume to						
	GFR ratio) to predict PC-AKI are examined, not of a non-invasive method.						
Worasuwannarack, 2011	Article not found (Taiwanese journal)						
Zahringer, 2014	PC-AKI is not an outcome measure. The questionnaire's ability to predict eGFR						
	is examined.						

Exclusion after examination of full text (update 2017): Measurement instruments for PC-AKI risk

Author and year	Reasons for exclusion
Akrawinthawong, 2015	Does not meet selection criteria
Ando, 2013	Does not meet selection criteria
Anonymous, 2015	Erratum
Balli, 2016	Does not meet selection criteria
Barbieri, 2016	Does not meet selection criteria
Chatterjee, 2017	Does not meet selection criteria
Garfinkle, 2015	Does not meet selection criteria
Goussot, 2015	Does not meet selection criteria
Grossman, 2017	Does not meet selection criteria
Gurm, 2016	Does not meet selection criteria
Hsieh, 2016	Does not meet selection criteria
Kim, 2015	Does not meet selection criteria
Li, 2016	Does not meet selection criteria
Liu, 2015	Does not meet selection criteria
Oksuz, 2015	Does not meet selection criteria
Osugi, 2016	Does not meet selection criteria
Ozturk, 2016	Does not meet selection criteria
Park, 2017	Does not meet selection criteria
Prasad, 2016	Does not meet selection criteria
Raposeiras-Roubin, 2013	Does not meet selection criteria
Sato, 2015	Does not meet selection criteria
Tao, 2016	Does not meet selection criteria
Victor, 2014	Does not meet selection criteria
Watanabe, 2016	Does not meet selection criteria
Xu, 2016	Does not meet selection criteria
Yin, 2017	Does not meet selection criteria
Yuan, 2017	Does not meet selection criteria
Brown, 2015	Does not meet selection criteria

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate	Comprehensive	Description of	Description of	Appropriate adjustment for	Assessment of	Enough	Potential risk	Potential
	and clearly	and systematic	included and	relevant	potential confounders in	scientific	similarities	of publication	conflicts of
	focused	literature	excluded	characteristics	observational studies?⁵	quality of	between	bias taken into	interest
	question? ¹	search? ²	studies? ³	of included		included	studies to	account? ⁸	reported? ⁹
				studies? ⁴		studies? ⁶	make		
							combining		
							them		
First							reasonable? ⁷		
author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Eng, 2016	Yes	Yes	No	Yes	Yes	No	Yes	No	No

- 1. Research question (PICO) and inclusion criteria should be appropriate and predefined
- 2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
- 3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
- 4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
- 5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)
- 6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
- 7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I²)?
- 8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
- 9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)
Research question:

Study	Describe method of	Bias due to	Bias due to	Bias due to	Bias due to	Bias due to	Bias due to loss	Bias due to violation
(first	randomisation ¹	inadequate concealment of allocation? ²	inadequate blinding of participants to treatment allocation? ³	inadequate blinding of care providers to treatment allocation? ³	inadequate blinding of outcome assessors to treatment allocation? ³	selective outcome reporting on basis of the results? ⁴	to follow-up?°	of intention to treat analysis? ⁶
author, publicatio n year)		(unlikely/likely/unc lear)	(unlikely/likely/uncl ear)	(unlikely/likely/ unclear)	(unlikely/likely/uncl ear)	(unlikely/likely/ unclear)	(unlikely/likely/un clear)	(unlikely/likely/uncle ar)
Chen, 2007	Not described "patients were randomly allocated"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Jurado- Roman, 2014	Not described "patients were randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Kooiman, 2014	Computer generated allocation sequence	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Maioli, 2011	Computer generated, open- label randomization block	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear

- 1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Risk of bias table for intervention studies (observational: non-randomized clinical trials, cohort and case-control studies)
Research question:

Study reference	Bias due to a non-representative or ill- defined sample of patients? ¹	Bias due to insufficiently long, or incomplete follow-up, or differences in follow-up between treatment groups? ²	Bias due to ill-defined or inadequately measured outcome ? ³	Bias due to inadequate adjustment for all important prognostic factors? ⁴
(first author, year of				
publication)	(unlikely/likely/unclear)	(unlikely/likely/unclear)	(unlikely/likely/unclear)	(unlikely/likely/unclear)
Bruce, 2009	Unlikely	Unclear	Unlikely	Likely
Davenport, 2013	Unlikely	Unclear	Unlikely	Likely
McDonald, 2013	Unlikely	Unclear	Unlikely	Likely

- 1. Failure to develop and apply appropriate eligibility criteria: a) case-control study: under- or over-matching in case-control studies; b) cohort study: selection of exposed and unexposed from different populations.
- 2. 2 Bias is likely if: the percentage of patients lost to follow-up is large; or differs between treatment groups; or the reasons for loss to follow-up differ between treatment groups; or length of follow-up differs between treatment groups or is too short. The risk of bias is unclear if: the number of patients lost to follow-up; or the reasons why, are not reported.
- 3. Flawed measurement, or differences in measurement of outcome in treatment and control group; bias may also result from a lack of blinding of those assessing outcomes (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Failure to adequately measure all known prognostic factors and/or failure to adequately adjust for these factors in multivariate statistical analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient	Intervention (I)	Comparison / control	Follow-up	Outcome measures and	Comments
reference	characteristics	characteristics		(C)		effect size	
Eng, 2016	SR and meta-	Inclusion criteria	Describe intervention:	Describe control:	End-point of follow-up:	Outcome measure-1	<u>Facultative</u> :
	analysis of RCTs	SR:			72 hours	Defined as CIN	
[individua		1) RCTs that	LOCM contrast	Iodixanol contrast			Brief description of
I study	Literature search	compared	administration	administration		Intra-arterial contrast	author's conclusion
characteri	up to June 2015	LOCM to IOCM			For how many	administration	
stics		with CIn	Both ia and iv	Both ia and iv	participants were no	Favors iodixanol:	No differences were
deduced	Study design:	incidence as the			complete outcome data	Relative risk (RR): 0.80	found in CIN risk among
from [1st	RCT [parallel]	main outcome			<u>available?</u>	(0.64 – 1.01)	types of LOCM. Iodixanol

atha a.u		and he was in		(into m. o. atio a /o. a. atual)	12 420/ - 0.02)	lead a dialettu lavvan viale
author,	6	as the main		(intervention/control)	I ² =43%, p=0.03)	had a slightly lower risk
year of	Setting and	outcome in		Not described		for CIN than LOCM, but
publicatio	Country: United	patients having			Intra-venous contrast	the lower risk did not
n]	States of	diagnostic			administration	exceed the criterium for
	America	imaging or			Favors iodixanol:	clinical importance.
PS., study		image-based			Relative risk (RR): 0.84	
characteri	Source of	therapeutic			(0.42 - 1.71)	Level of evidence: GRADE
stics and	funding: non-	procedures			I ² =29%, p=0.22)	(per comparison and
results	commercial	2) CIN incidence				outcome measure)
are		is based on sCr				including reasons for
extracted		or eGFR at				down/upgrading
from the		baseline and				
SR (unless		within 72 hours				Most of the included
stated		of injection				studies GRADEd as Low
otherwise		, , , , , , , , , , , , , , , , , , , ,				(due to imprecision)
)		Exclusion				(care co impression,
'		criteria SR:				
		1) language				
		other than				
		English				
		2) mixed route				
		of contrast				
		administration				
		29 studies				
		included				
		Caracana				
		Groups				
		comparable at				
		baseline?				
		Unclear				

AKI: acute kidney injury; CI-AKI: contrast induced acute kidney injury; CIN: contrast induced nephropathy; CT: Computed Tomography; eGFR: estimated glomerular filtration ration; ia: intra-arterial; IOCM: iso-osmolar contrast medium; iv: intravenous; LOCM: low osmolair contrast medium; RCT: randomized controlled trial; sCr: serum creatinine;

Evidence table for intervention studies (randomized controlled trials and non-randomized *observational* studies [cohort studies, case-control studies, case series])¹
This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study	Study	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures	Comments
reference	characteristics					and effect size 4	
		Contr	rast administration versus no co	ntrast administration for Comp	uted Tomography		
Bruce,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2009	retrospective	1) age at least 18	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
	observational	years,			3 days	(include 95%CI and p-	We identified a high
		2) measurement of				value if available):	incidence of acute
	Setting: in-	serum creatinine	administration of	Unenchanced Computed	Loss-to-follow-up:		kidney injury among
	and	concentration within 30	isoosmolarcontrast medium	Tomography	Unclear, only	Acute kidney injury	control subjects
	outpatients,	days before CT, and	(IOCM) (iodixanol) prior to		patients that had	(=a 0.5 mg/dL	undergoing
	multicentre	creatinine measurement	Computed Tomography (CT)		a creatinine	increase in serum	unenhanced CT. The
	study	with result available			measurement at	creatinine	incidence of
		within 3 days after the			baseline and after	concentration or a	creatinine elevation
	Country:	CT examination			3 days were	25% or greater	in this group was
	United States				included in this	decrease in estimated	statistically similar to
	of America	Exclusion criteria:			retrospective	glomerular filtration	that in the
		1) patient received			study.	rate within 3 days	isoosmolar contrast
	Source of	iodinated contrast				after CT)	medium group for all
	funding: not	material as part of			<u>Incomplete</u>		baseline creatinine
	reported	another procedure (e.g.,			outcome data:	In all groups, the	values and all stages
		cardiac catheterization)			As above	incidence of acute	of chronic kidney
		within 30 days before or				kidney injury	disease. These
		3 days after the				increased with	findings suggest that
		reference CT				increasing baseline	the additional risk of
		examination.				creatinine	acute kidney injury
		2) patients with a				concentration. No	accompanying
		preexisting status of				significant difference	administration of
		undergoing long-term				in incidence of	contrast medium
		Dialysis				presumed contrast-	(contrast-induced
		3) any record of dialysis				induced kidney injury	nephrotoxicity) may
		within				was identified	be overstated and
		30 days before or on the				between the	that much of the

day of the CT	isoosmolar contrast	creatinine elevation
· ·		
examination	medium and the	in these patients is
	control groups. The	attributable to
N total at baseline:	incidence of acute	background
Intervention: 337	kidney injury in the	fluctuation,
Control: 6815	low-osmolar contrast	underlying disease,
	medium cohort	or treatment.
Important prognostic	paralleled that of the	
factors ² :	control cohort up to a	Only patients that
For example	creatinine level of 1.8	had a creatinine
age ± SD:	mg/dL, but increases	measurement at
I: 63 ± 16	above this level were	baseline and after 3
C: 59 ± 19	associated with a	days were included in
	higher incidence of	this retrospective
Sex:	acute kidney injury.	study.
I: 65% M		
C: 53% M		IV administration of
C. 35/0 IVI		low-osmolar contrast
Groups comparable at		medium (LOCM)
baseline? Yes		(iohexol) to patients
baselille: 163		with a
		documented serum
		creatinine
		concentration of
		2.0mg/dL or less if
		they did not have
		diabetes and to
		patients with a
		serum creatinine
		concentration of
		1.5 mg/dL if they did
		have diabetes. We
		added a high-risk
		tier, allowing
		administration of iso-
		osmolar contrast
		medium (IOCM)

							(iodixanol) to nondiabetic patients with baseline creatinine values up to a maximum of 2.5 mg/dL and to diabetic patients with values up to a maximum of 2.0 mg/dL. Estimated GFR values are currently computed for all outpatients but have not supplanted serum creatinine concentration for contrast administration decisions.
Davenport,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2013	retrospective	1) CT studies performed	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
	observational	in patients who had			72 hours	(include 95%Cl and p-	Intravenous LOCM is
	Setting: in-	never undergone renal	contrast-enhanced CT	CT examinations without	Loss-to-follow-up:	value if available):	a nephrotoxic risk factor in patients
	and	replacement therapy	examinations	contrast enhancement	Early post- CT SCr	Post CT-AKI	with a stable eGFR
	outpatients,	(eg, dialysis, renal	with LOCM		data were	(= difference between	less than 30
	multicentre	transplantation),			available for	baseline and pre-CT	mL/min/1.73 m2,
	study	2) patients had available			1) 15 724 of 17	SCr within 0.3 mg/dL	with a trend
		data to permit			652 patients	and 50% of baseline)	Toward significance
	Country:	calculation of			(89.1%) 0–24	IV LOCM had a	at 30–44
	United States	the four-variable			hours after CT	significant effect on	mL/min/1.73 m ² . IV
	of America	Modification of Diet in			(7882	the development of	LOCM does not
		Renal Disease formula for eGFR,			nonenhanced, 7842 contrast-	post-CT AKI ($P = .04$).	appear to be a
	Source of	I for alack			/X/I/contract.		nephrotoxic risk

reported	following SCr	2) 12 941 of 17	with decreases in pre-	with a pre-CT eGFR
	measurements	652	CT eGFR (>60 mL/	of 45 mL/min/1.73
	available:	patients (73.3%)	min/1.73 m ² :	m ² or greater.
	(a) baseline SCr (the	25–48 hours after	odds ratio, 1.00; 95%	o o
	most recent SCr	СТ	confidence interval:	
	obtained more than 5	(6450	0.86, 1.16;	
	days before the index	nonenhanced,	45–59 mL/min/1.73	
	(CT);	6491 contrast-	m ² :	
	(b) pre-CT SCr (the most	enhanced),	odds ratio, 1.06; 95%	
	recent SCr obtained	3) 10 213 of 17	confidence interval:	
	between the time of the	652 patients	0.82, 1.38;	
	index CT and 5 days	· (57.9%) 49–72	30-44 mL/min/1.73	
	before);	hours after CT	m ² :	
	(c) at least one of	(5091	odds ratio, 1.40; 95%	
	three early post-CT SCr	nonenhanced,	confidence interval:	
	values (the first SCr	5122 contrast-	1.00, 1.97;	
	obtained in each 24-	enhanced).	<30 mL/min/1.73 m2:	
	hour period for the first		odds ratio, 2.96; 95%	
	72 hours after the index	<u>Incomplete</u>	confidence interval:	
	CT).	outcome data:	1.22, 7.17)	
		As described		
	Exclusion criteria:	above		
	1) CT performed in a			
	patient who had an			
	earlier CT examination			
	that met			
	the inclusion criteria			
	2) missing data			
	regarding contrast			
	material administration			
	3) unstable renal			
	function before the CT			
	study			
	4) calculated eGFR was			
	greater than 200			
	mL/min/1.73 m ²			
	5) patients lacked a 1:1			

		propensity-matched control					
		N total at baseline: Intervention: 8826 Control: 8826					
		Important prognostic factors ² : For example age ± SD: I: 59 ± 17					
		C: 59 ± 18 Sex: I: 48% M					
		C: 48% M Groups comparable at baseline? Yes					
McDonald, 2014	Type of study: retrospective observational	Inclusion criteria: 1) all patients who underwent an	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow- up: 72 hours	Outcome measures and effect size (include 95%Cl and p-	Authors' conclusion: Following adjustment
	Setting: in- and	unenhanced (noncontrast group) or intravenous	contrast-enhanced CT examinations	CT examinations without contrast enhancement	Loss-to-follow-up: Unclear, only	value if available): CIN	for presumed risk factors, the incidence of CIN was not
	outpatients, multicentre study	contrastenhanced (contrast group) abdominal, pelvic,	Scan recipients were stratified with respect to their presumptive risk for	Scan recipients were stratified with respect to their presumptive risk for	patients that had a creatinine measurement at	(=SCr ≥0.5 mg/dL above baseline)	significantly different from contrast material–
	Country: United States of America	and/or thoracic CT scan from January 1, 2000, to December 31, 2010, at our institution;	AKI by baseline SCr level as follows: 1) low risk, SCr ,<1.5 mg/dL; 2) medium risk, SCr 1.5–2.0	AKI by baseline SCr level as follows: 1) low risk, SCr ,<1.5 mg/dL; 2) medium risk, SCr 1.5–2.0	baseline and after 3 days were included in this retrospective	AKI risk was not significantly different between contrast and noncontrast groups in	independent AKI. These two phenomena were clinically
	Source of funding: not	2) who had one or more postscan SCr results during the time period	mg/dL; 3) high risk, SCr > 2.0 mg/dL.	mg/dL; 3) high risk, SCr > 2.0 mg/dL.	study. Incomplete	any risk subgroup after propensity score adjustment by using	indistinguishable with established SCr- defined criteria,
					Incomplete outcome data:		

development of CIN (24–72 hours after CT- scanning) 3) who also had at least one baseline SCr result in the 24-hour window prior to scanning Exclusion criteria: 1) patients who had preexisting renal dialysis requirements; 2) did not have sufficient SCr data to permit detection of AKI; 3) patients who underwent multiple distinct CT-scans or percutaneous cardiac interventions with iodinated contrast material within a 14-day period N total at baseline: Intervention: 10686 Control: 10686 Important prognostic factors ² : For example age (range):	As above	of CIN 1) low risk: odds ratio [OR], 0.93; 95% confidence interval [CI]: 0.76,1.13; $P = .47$; 2) medium risk: odds ratio, 0.97; 95% CI: 0.81, 1.16; $P = .76$; 3) high risk: OR, 0.91; 95% CI: 0.66, 1.24; $P = .58$). Counterfactual analysis revealed no significant difference in AKI incidence between enhanced and unenhanced CT scans in the same patient (McNemar test: x2 = 0.63, $P = 0.43$) (OR = 0.92; 95% CI: 0.75, 1.13; $P =$.46).	intravenous iodinated contrast media may not be the causative agent in diminished renal function after contrast material administration.
factors ² : For example			

		Low risk: 63 (48-74) Medium risk: 71 (59-80) High risk: 68 (56-77)					
		Sex: I: % M Low risk: 48% Medium risk: 65% High risk: 63% C: % M Low risk: 49% Medium risk: 64% High risk: 64%					
		Groups comparable at baseline? Yes					
		buseline, res	Hydration versus no h	ydration at contrast administrat	ion		
Chen,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Author's conclusion:
2008	RCT	Patients with myocardial	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
		ischemia (angina or			6 months	(include 95%CI and p-	Patients with CIN and
	Setting: in-	positive exercise	sCr<1.5mg/dL:	sCr<1.5mg/dL:		value if available):	preexisting renal
	and	treadmill) scheduled for	0.45% saline given	No hydration	<u>Loss-to-follow-up</u> :		insufficiency had
	outpatients,	percutaneous coronary	intravenously at a rate of 1		Not reported	CIN	worse clinical
	multicentre	intervention (PCI) in one	ml/kg/h starting from 12 h			(=increase in SCrN0.5	outcomes. Hydration
	study	of the three	before	sCr ≥1.5mg/dL:	<u>Incomplete</u>	mg/dl at 48 h after	with 0.45% sodium
	Country	participating centers	scheduled time for coronary	twice orally loading dose of	outcome data:	PCI)	chloride alone had no
	Country:	Evaluation aritaria:	angiogram	1200 mg NAC at 12 h before	Not reported	cCr<1 Ema/di.	potential effect on the occurrence of
	China	Exclusion criteria: (1) the coronary		scheduled time for coronary angiogram and immediately		sCr<1.5mg/dL: I: 6.7%	CIN in patients with
	Source of	anatomy not suitable for		after procedure		1: 6.7% C: 7.0%	normal renal
	funding: not	PCI;	sCr ≥1.5mg/dL:	arter procedure		p>0.05	function.
	reported	(2) emergency coronary	1) 0.45% saline given			p>0.03	Combination of
	. cporteu	artery bypassgrafting	intravenously at a rate of 1				hydration with ATLS
		(CABG) being required;	ml/kg/h starting from 12 h			sCr ≥1.5mg/dL:	could reduce the

		(3) patients in chronic	before scheduled time for			I: 21.3%	incidence of CIN in
		peritoneal or	coronary angiogram			C: 34.0%	patients at high risk.
		hemodialytic treatment;	2) twice orally loading dose			P<0.001	
		(4) acute myocardial	of 1200 mg NAC at 12 h				
		infarction (AMI) at	before scheduled time for				Groups comparable
		admission;	coronary angiogram and				at baseline? Unclear
		(5) no written formal	immediately after				(patient data not
		consent from patients	procedure				reported for
		·					intervention and
		N total at baseline:					control group
		sCr<1.5mg/dL					separately)
		Intervention: 330					, ,,
		Control: 330					
		sCr ≥1.5mg/dL					
		Intervention: 188					
		Control: 188					
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		not reported					
		·					
		Sex: %M					
		sCr<1.5mg/dL					
		85%					
		sCr ≥1.5mg/dL					
		82%					
		Groups comparable at					
		baseline? Unclear					
		(patient data not					
		reported for					
		intervention and control					
		group separately)					
Jurado-	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
Roman,	RCT	patients who were	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	

2014		admitted			3 days	(include 95%CI and p-	In conclusion,
	Setting: in-	for STEMI and	Hydration:	No hydration		value if available):	intravenous saline
	and	underwent a PPCI from	isotonic saline at an infusion	Prior to PPCI	<u>Loss-to-follow-up</u> :		hydration during
	outpatients,	July 2012 to	rate of 1 ml/kg/h since the		Not reported	CIN	PPCIreduced the risk
	single centre	November 2013 at our	beginning of the procedure			(=a ≥25% or ≥0.5	of CIN to 48%.
	study	institution.	and during the following 24		<u>Incomplete</u>	mg/dl increase in	Given the higher
			hours.		outcome data:	serum a _25% or _0.5	incidence of CIN in
	Country: Spain	Exclusion criteria:			Not reported	mg/dl increase in	emergentprocedures,
		1) end-stage renal	Prior to PPCI			serum)	and its morbidity
	Source of	failure requiring dialysis,			Crossover		and mortality,
	funding: not	2) cardiac arrest,			between study	CIN was observed in	preventive hydration
	reported	3) severe heart failure			arms: 28%	14% of patients:	should be mandatory
		(Killip III to IV)			How this was	I: 11%	in them unless
					handled in the	C: 21%	contraindicated.
		N total at baseline:			data analysis is	(p=0.016).	
		Intervention: 204			not reported.		
		Control: 204			74 patients	In multivariate	Crossover between
					changed from no	analysis, the only	study arms: 28%
		Important prognostic			hydration to	predictors of CIN	How this was
		factors ² :			hydration group	were:	handled in the data
		For example			because of sever	1) hydration (OR=0.29	analysis is not
		age ± SD:			hypotension	[0.14 to 0.66];	reported.
		1:62 ± 14			42 patients were	p=0.003)	
		C: 64 ± 12			changed from	2) hemoglobin before	
		_			hydration to no	the procedure	
		Sex:			hydration group	(OR=0.69 [0.59 to	
		I: 72% M			because they	0.88]; p <0.0001)	
		C: 75% M			developed heart		
					failure		
		Groups comparable at					
		baseline? Yes				0.1	
Kooiman,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2014	RCT	1) Inpatients and	(treatment/procedure/test):	(treatment/procedure/test):	up:	and effect size	Our manulta
	Cattinania	outpatients with high	Carltona hisanhanata	No bodestion oriente CTDA	96 hours for	(include 95%Cl and p-	Our results suggest
	Setting:in- and	clinical suspicion of	Sodium bicarbonate	No hydration prior to CTPA	laboratory	value if available):	that preventive
	outpatients,	acute PE requiring CTPA	hydration prior to CTPA		parameters	CL AIVI	hydration could be
	single centre	(i.e. Wells score ≥ 4 or			2 months for	CI-AKI	safely withheld in

<u></u>		,	_		T	
	D-dimer levels	250 mL intravenous 1.4%		clinical outcomes	(=creatinine increase	CKD patients
Country: the	$> 500 \text{ ng mL}^{-1}$).	sodium bicarbonate 1 h			> 25%/> 0.5 mg dL ⁻¹)	undergoing CTPA for
Netherlands	2) at least 18 years old	before CTPA without		Loss-to-follow-up:	I: 5/71 (7%)	suspected acute
	3) CKD (estimated	hydration after CTPA.		Intervention:	C: 6/67 (9%)	pulmonary
Source of	glomerular filtration			2/71 (3%)	RR: 1.29, 95%	embolism. This will
funding: non-	rate			1 withdrew	confidence interval	facilitate
commercial	[eGFR] < 60 mL min			informed consent	0.41-4.03	management of
	$^{-1}/1.73$ m ² estimated by			1 died 24 hours		these patients and
	using the Modification			after CTPA	None of the CI-AKI	prevents delay in
	of Diet in Renal Disease				patients developed a	diagnosis as well as
	formula			Control:	need for dialysis.	unnecessary start of
				2/67 (3%)	,	anticoagulant
	Exclusion criteria:			Lost to follow-up		treatment while
	1) pregnancy,					receiving volume
	2) previous contrast			Incomplete		expansion.
	administration within			outcome data:		
	the past 7 days,			As above		
	3) documented allergy					
	for iodinated contrast					
	media,					
	4) hemodynamic					
	instability (systolic blood					
	pressure < 100 mm Hg)					
	5) participation in					
	another trial					
	N total at baseline:					
	Intervention: 71					
	Control: 67					
	Important prognostic					
	factors ² :					
	For example					
	age ± SD:					
	I: 71 ± 13					
	C: 70 ± 12					
	0.70 ± 12					
		1				l

Maioli, 2011	Type of study: RCT Setting: in- and outpatients, single centre Country: Italy Source of funding: not reported	Sex: I: 48% M C: 52% M Groups comparable at baseline? Yes Inclusion criteria: 1) patients with STEMI who were candidates for primary PCI Exclusion criteria: 1) contrast medium administration within the previous 10 days, 2) end-stage renal failure requiring dialysis, 3) refusal to give informed consent N total at baseline: Intervention: 154 Control: 153 Important prognostic factors ² : For example age ± SD: I:65 ± 13 C: 64 ± 12 Sex:	Describe intervention (treatment/procedure/test): Patients assigned to early hydration were administered a bolus of 3 mL/kg of sodium bicarbonate solution (154 mEq/L in dextrose and water) in 1 hour, starting in the emergency room, followed by infusion of 1 mL/kg per hour for 12 hours after PCI. Hydration rate was reduced to 0.5 mL/kg per hour in patients with left ventricular ejection fraction (EF) <40% or New York Heart Association class III—IV in both groups.	Describe control (treatment/procedure/test): No hydration prior to PCI.	Length of follow-up: 3 days Loss-to-follow-up: Intervention: 4/150 (3%) 1 had emergency procedure 3 no PCI Control: 3/153 (2%) 1 had emergency procedure 2 no PCI Incomplete outcome data: As above	Outcome measures and effect size (include 95%CI and pvalue if available): CI-AKI (=an increase in serum creatinine of ≥25% or 0.5 mg/dL over the baseline value within 3 days after administration of the contrast medium) I: 12% C: 27% P<0.001 Death I: 3 (2%) C: 8 (5%) p>0.05 Hemofiltration I: 2 (1%)	Authors' conclusion: Adequate intravenous volume expansion may prevent CI-AKI in patients undergoing primary PCI. A regimen of preprocedure and postprocedure hydration therapy with sodium bicarbonate appears to be more efficacious than postprocedure hydration only with isotonic saline.
		Sex: I: 77% M C: 73% M Groups comparable at baseline? Unclear					

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

AKI: acute kidney injury; CI-AKI: contrast induced acute kidney injury; CIN: contrast induced nephropathy; CT: Computed Tomography; CTPA: Computed Tomography of the pulmonary artery; eGFR: estimated glomerular filtration ration; ia: intra-arterial; IOCM: iso-osmolar contrast medium; iv: intravenous; LOCM: low osmolair contrast medium; OR: odds ratio; PCI: Percutaneous Coronary Intervention; PE: pulmonary embolism; PPCI: primary Percutaneous Coronary Intervention; RCT: randomized controlled trial; RR: relative risk; sCr: serum creatinine; STEMI: ST-elevation myocardial infarction

Risk of bias assessment diagnostic accuracy studies (QUADAS II, 2011)

Research question:

Study	Patient selection	Index test	Reference standard	Flow and timing	Comments with respect to
reference					applicability
Duan, 2017	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes, consecutive	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		

	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Lian, 2017	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Abellas-	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
Sequeiros,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
2016	Yes, consecutive	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		<u>review question?</u>
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by

	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias?	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	Were all patients included in the analysis? Yes CONCLUSION Could the patient flow have introduced bias?	the reference standard does not match the review question? No
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Araujo, 2016	Was a consecutive or random sample of patients enrolled? Yes, consecutive Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Unclear If a threshold was used, was it pre-specified? Yes	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Unclear	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question?
	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias? RISK: LOW	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW	CONCLUSION Could the patient flow have introduced bias?	
Chou, 2016	Was a consecutive or random sample of patients enrolled? Unclear Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference standard? Unclear	Is the reference standard likely to correctly classify the target condition? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear	Are there concerns that the included patients do not match the review question?
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the

	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	Did the study avoid	<u>pre-specified?</u> Yes	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid inappropriate exclusions?	i tes	index test? Unclear	Did patients receive the same	review question? No
	Yes		Officieal	reference standard?	I NO
	163			Yes	Are there concerns that the
				163	target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Lazaros, 2016	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	<u>Did all patients receive a</u>	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	<u>reference standard?</u>	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard? Yes	A was the suppose as a suppose that the
				Yes	Are there concerns that the target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard.	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		

	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Liu, 2016	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Aykan, 2013	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	<u>Did patients receive the same</u>	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not

				analysis? Yes	match the review question?
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	INO
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
	nave miroduced bids.	have introduced bias?	have introduced bias?	introduced blus.	
		nave introduced blas.	nave introduced blas.		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Bartholomew,	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
2004	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	<u>Did all patients receive a</u>	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	<u>reference standard?</u>	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	<u>Did patients receive the same</u>	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Chen, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or

	Did the study avoid inappropriate exclusions? Yes	pre-specified? Unclear	knowledge of the results of the index test? Yes	Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias?	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	CONCLUSION Could the patient flow have introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Fu, 2012	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Unclear	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias?	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	CONCLUSION Could the patient flow have introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	

Gao, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Unclear	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test have introduced bias?	its conduct, or its interpretation have introduced bias?	introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Gurm, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference standard? Yes	Is the reference standard likely to correctly classify the target condition? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear	Are there concerns that the included patients do not match the review question?
	avoided?	i es	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?	5.1	review question?
	inappropriate exclusions? Yes		Yes	<u>Did patients receive the same</u> <u>reference standard?</u>	No
	163			Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?

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	CONCLUCION	CONCLUCION	CONCLUSION:	Yes	No
	CONCLUSION:	CONCLUSION:		CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Inohara, 2015	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No .
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Ivanes, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	<u>Did all patients receive a</u>	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the

	Did the study avoid inappropriate exclusions? Yes CONCLUSION:	Unclear CONCLUSION:	index test? Yes CONCLUSION:	Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes CONCLUSION	review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Ji, 2015	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Unclear	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question?
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test have introduced bias?	its conduct, or its interpretation have introduced bias?	introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Kul, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the

1	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Maioli, 2010	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
1	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	reference standard? Yes	interpretation differ from the
	Did the study avoid		knowledge of the results of the index test?	Yes	
		pre-specified?	knowledge of the results of the	Yes <u>Did patients receive the same</u>	interpretation differ from the
	Did the study avoid	pre-specified?	knowledge of the results of the index test?	Yes <u>Did patients receive the same</u> <u>reference standard?</u>	interpretation differ from the review question?
	Did the study avoid inappropriate exclusions?	pre-specified?	knowledge of the results of the index test?	Yes <u>Did patients receive the same</u>	interpretation differ from the review question? No Are there concerns that the
	Did the study avoid inappropriate exclusions?	pre-specified?	knowledge of the results of the index test?	Yes Did patients receive the same reference standard? Yes	interpretation differ from the review question? No Are there concerns that the target condition as defined by
	Did the study avoid inappropriate exclusions?	pre-specified?	knowledge of the results of the index test?	Yes Did patients receive the same reference standard? Yes Were all patients included in the	interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not
	Did the study avoid inappropriate exclusions?	pre-specified?	knowledge of the results of the index test?	Yes Did patients receive the same reference standard? Yes	interpretation differ from the review question? No Are there concerns that the target condition as defined by

	T	T	T	T	1
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Mehran, 2004	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes		163	reference standard?	
	163			Yes	Are there concerns that the
				163	target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	NO
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Mizuno, 2015	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
111124110, 2013	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
	163	standard?	Yes	Unclear	No
	Was a case-control design	Yes	163	Officieal	140
	avoided?	163	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	103	pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?	163	review question?
	Did tile Study avoid	Ulicical	index test:		ieview question:

	inappropriate exclusions? Yes		Yes	Did patients receive the same reference standard?	No
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Raposeiras-	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
Roubín, 2013	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	<u>Did all patients receive a</u>	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	<u>Did patients receive the same</u>	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
	CONCLUCION	CONCLUCION	CONCLUCION	Yes	No
	CONCLUSION:	CONCLUSION: Could the conduct or	CONCLUSION: Could the reference standard,	CONCLUSION Could the nationt flow have	
	Could the selection of patients have introduced bias?		1	Could the patient flow have introduced bias?	
	nave introduced bias?	interpretation of the index test have introduced bias?	its conduct, or its interpretation have introduced bias?	mitroduced bias?	
		nave introduced bias:	nave introduced bias:		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Sgura, 2010	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match

	Yes	of the results of the reference standard?	condition? Yes	and reference standard? Unclear	the review question?
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it pre-specified?	results interpreted without knowledge of the results of the	reference standard? Yes	index test, its conduct, or interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION: Could the conduct or	CONCLUSION: Could the reference standard,	CONCLUSION Could the national flow have	
	Could the selection of patients have introduced bias?	interpretation of the index test	its conduct, or its interpretation	Could the patient flow have introduced bias?	
		have introduced bias?	have introduced bias?		
1					
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Tziakas, 2013	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
Tziakas, 2013		Were the index test results interpreted without knowledge	Is the reference standard likely to correctly classify the target	Was there an appropriate interval between index test(s)	included patients do not match
Tziakas, 2013	Was a consecutive or random sample of patients enrolled?	Were the index test results	Is the reference standard likely	Was there an appropriate	
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference	Is the reference standard likely to correctly classify the target condition? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear	included patients do not match the review question? No
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No Are there concerns that the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No Are there concerns that the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not

	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Tziakas, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	Did the extender asset d	pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?	Did actionts access to the	review question?
	inappropriate exclusions? Yes		Yes	<u>Did patients receive the same</u> reference standard?	No
	res			Yes	Are there concerns that the
				Tes	target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Victor, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	<u>Did the study avoid</u>	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	<u>Did patients receive the same</u>	No

	Yes			reference standard?	
	res			Yes	Are there concerns that the
				163	target condition as defined by
				Mana all mationts included in the	the reference standard does not
				Were all patients included in the	
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Lin, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	A to the first constant or an the

Judgments on risk of bias are dependent on the research question: some items are more likely to introduce bias than others, and may be given more weight in the final conclusion on the overall risk of bias per domain:

Patient selection:

- Consecutive or random sample has a low risk to introduce bias.
- A case control design is very likely to overestimate accuracy and thus introduce bias.
- Inappropriate exclusion is likely to introduce bias.

Index test:

- This item is similar to "blinding" in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.
- Selecting the test threshold to optimise sensitivity and/or specificity may lead to overoptimistic estimates of test performance and introduce bias.

Reference standard:

- When the reference standard is not 100% sensitive and 100% specific, disagreements between the index test and reference standard may be incorrect, which increases the risk of bias.
- This item is similar to "blinding" in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.

Flow and timing:

- If there is a delay or if treatment is started between index test and reference standard, misclassification may occur due to recovery or deterioration of the condition, which increases the risk of bias.
- If the results of the index test influence the decision on whether to perform the reference standard or which reference standard is used, estimated diagnostic accuracy may be biased.
- All patients who were recruited into the study should be included in the analysis, if not, the risk of bias is increased.

Judgement on applicability:

Patient selection: there may be concerns regarding applicability if patients included in the study differ from those targeted by the review question, in terms of severity of the target condition, demographic features, presence of differential diagnosis or co-morbidity, setting of the study and previous testing protocols.

Index test: if index tests methods differ from those specified in the review question there may be concerns regarding applicability.

Reference standard: the reference standard may be free of bias but the target condition that it defines may differ from the target condition specified in the review question.

Evidence table for diagnostic test accuracy studies

Research question:

Study	Study	Patient	Index test	Reference test	Follow-up	Outcome measures and	Comments
reference	characteristics	characteristics	(test of interest)			effect size	
Aykan, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference	Time between the index	Outcome measures and	Internal validation only
	study ¹ : cohort	Acute STEMI	SYNTAX score	test ³ :	test en reference test: 72	effect size (include 95%CI	
	study	patients within		≥25% increase of serum	hours	and p-value if available) ⁴ :	Patients with previous
		12 hours of		creatinine			coronary artery bypass
	Setting: in-	symptom onset		concentrations form	For how many	Mehran:	were excluded
	and		Comparator test ² :	baseline within 72 hours	participants were no	Sens: 73%	

¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

² Comparator test is vergelijkbaar met de C uit de PICO van een interventievraag. Er kunnen ook meerdere tests worden vergeleken. Voeg die toe als comparator test 2 etc. Let op: de comparator test kan nooit de referentiestandaard zijn.

	outpatients	Exclusion	Mehran score	after PCI	complete outcome data	Spec: 89%
		criteria:			available?	
	Country:	Patients with			NR	SYNTAX:
	Turkey	previous				Sens: 79%
	,	coronary artery			Reasons for incomplete	Spec: 89%
	Conflicts of	bypass			outcome data described?	
	interest: not				NR	Mehran:
	reported	N= 402				Cut-off value: 12.5
						AUC: 0.68 (95% CI: 0.63 –
		Prevalence: 32%				0.74, p<0.001)
		Mean age ± SD:				SYNTAX:
		63 ± 13				Cut-off value: 31.5
						AUC: 0.66 (95% CI: 0.60 –
		Sex: 76 % M				0.71, p<0.001)
Bartholomew,	Type of study:	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and
2004	cohort	Coronary	RCIN risk score	≥1.0mg/dL increase in	test en reference test: 48	effect size (include 95%Cl
		interventional		serum creatinine from	hours	and p-value if available):
	Setting: in-	procedures		baseline within 48 hours		
	and	(single center)		of PCI	For how many	External validation
	outpatients				participants were no	Cohort 1: patients
		Exclusion			complete outcome data	admitted for elective PCI
	Country:	criteria: -			available?	N=2689
	United States				NR	Discrimination: 0.59
	of America	N= 10 481				Calibration: NR
	0 (1) . (Reasons for incomplete	
	Conflicts of	Incidence of			outcome data described?	Cohort 2: patients
	interest:	events:			NR	admitted for elective or
	commercial	Derivation				emergency PCI
		cohort: 2.8%				N=488
		Validation				Discrimination: 0.58
		cohort: 1.2%				Calibration: NR

³ De referentiestandaard is de test waarmee definitief wordt aangetoond of iemand al dan niet ziek is. Idealiter is de referentiestandaard de Gouden standaard (100% sensitief en 100% specifiek). Let op! dit is niet de "comparison test/index 2".

⁴ Beschrijf de statistische parameters voor de vergelijking van de indextest(en) met de referentietest, en voor de vergelijking tussen de indextesten onderling (als er twee of meer indextesten worden vergeleken).

Chen, 2014	Type of study ⁴ : cohort study Setting: inand outpatients Country: China Conflicts of interest: not reported	Mean age ± SD: 65 ± 12 Sex: 67% M Inclusion criteria: patients receiving PCI, single center Exclusion criteria: - N=1500 ncidence of events: Derivation cohort: 16% Validation cohort: 17% Mean age ± SD: 64 ± 10	Describe index test: "preprocedural risk scoring system"	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creat8inine within 5 days of PCI	Time between the index test en reference test: 5 days For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): Discrimination/calibration: 0.82 P=0.89 Risk score range associated with PC-AKI risk: Low: 5.3% Moderate: 19.9% High: 32.5% Very high: 59.5%	Internal validation only
		Sex:68 % M					
Fu, 2012	Type of study ⁵ : cohort study Setting: in-and	Inclusion criteria: patients undergoing PCI, single center Exclusion	Describe index test: "risk score for contrast induced nephropathy in elderly patients"	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 48-72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no	Outcome measures and effect size (include 95%Cl and p-value if available): External validation Elderly patients at same	

⁴ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

5 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	outpatients Country: China Conflicts of interest: not reported	criteria: - N= 668 Prevalence: 16% Mean age ± SD: 70 ± 6 Sex: 48% M			complete outcome data available? NR Reasons for incomplete outcome data described? NR	institution N=277 Discrimination: 0.79 Calibration: p>0.05	
Gao, 2004	Type of study ⁶ : cohort study Setting: inand outpatients Country: China Conflicts of interest: not reported	Inclusion criteria: Coronary angiography or PCI, single center Exclusion criteria: - N=2764 Incidence of events: Derivation cohort: 5.5% Validation cohort: 5.0% Mean age ± SD: 60 ± 11 Sex: 71% M	Describe index test: "simple risk score for prediction of CIN" Comparator test: Mehran risk score	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%CI and p-value if available): Discrimination / calibration: 0.76 p>0.05 AUC: 1) "simple risk score": 0.75 (95% CI: 0.71 – 0.78) 2) Mehran: 0.57 (95%CI:0.54 – 0.60) Incidence of events: Derivation cohort: 4.6% Validation cohort: 4.2%	Internal validation only
Ghani, 2009	Type of study ⁷ : cohort study	Inclusion criteria: patients undergoing PCI,	Describe index test: "simple risk score for CIN"	Describe reference test: >0.5 mg/dL increase in serum creatinine within	Time between the index test en reference test: 48 hours	Outcome measures and effect size (include 95%Cl and p-value if available):	Internal validation only

⁶ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		single center		48 hours of PCI			
	Setting: in- and outpatients Country:	Exclusion criteria:- N= 247			For how many participants were no complete outcome data available?	Risk score range associated with PC-AKI: <4: 9.2% 5-8: 32% 9-12: 54%	
	Kuwait Conflicts of	Incidence of events:			Reasons for incomplete outcome data described?	>12: 84%	
	interest: not reported	Derivation cohort: 5.5% Validation cohort: 5.0%			NR		
		Mean age ± SD: 63 ± 10					
Gurm, 2014	Type of study ⁸ : cohort study	Sex: 68% M Inclusion criteria: patients undergoing PCI, multiple center	Describe index test: "novel easy-to-use computational tool"	Describe reference test: >0.5 mg/dL increase in serum creatinine within 7 days of PCI	Time between the index test en reference test: 7 days	Outcome measures and effect size (include 95%Cl and p-value if available):	Internal validation only
	Setting: in- and outpatients	Exclusion criteria: 1) patients on		7 days of FCI	For how many participants were no complete outcome data available?	AUC: 0.88 Risk score range associated with PC-AKI:	
	Country: United States of America / the	dialysis 2) patients with missing serum creatinine values			NR Reasons for incomplete outcome data described?	Low: 0.5% Medium: 2.8% High: 13%	
	Netherlands	N= 48001			NR	Incidence of events: Derivation cohort: 2.6%	

⁷ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

8 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

	Conflicts of interest: not	Prevalence: 3%				Validation cohort: 2.5%	
	reported						
	·	Mean age ± SD: 65 ± 12					
		Sex: NR					
Inohara, 2014	Type of study ⁹ : cohort	Inclusion criteria:	Describe index test: "pre-percutaneous	Describe reference test: An increase in serum	Time between the index test en reference test: 30	Outcome measures and effect size (include 95%Cl	
	study	Exclusion criteria:	cornary intervention	creatinine of 50% or 0.3mg/dL compared	days	and p-value if available):	
	Setting: in-		TISK ITIOGEI	with baseline	For how many	External validation:	
	and outpatients	N= 3957			participants were no complete outcome data	N=1979 Discrimination:	
		Prevalence: 9%			available?	c-statistic 0.79	
	Country:	Maar and LCD.			NR		
	Japan	Mean age ± SD: 69 ± 11			Reasons for incomplete		
	Conflicts of	09 1 11			outcome data described?		
	interest: not reported	Sex: 79% M			NR		
Ivanes, 2014	Type of study ¹⁰ : cohort study	Inclusion criteria: PCI, single center	Describe index test: Mehran risk score	Describe reference test: ≥25% or 44.2µmol/L increase in serum	Time between the index test en reference test: 48 hours	Outcome measures and effect size (include 95%CI and p-value if available):	Internal validation only
		Exclusion		creatinine following			
	Setting: in-	criteria: -		contrast administration		AUC: 0.59	
	and 				For how many	CIN incidence: 9%	
	outpatients	N=322			participants were no complete outcome data		
	Country:	Prevalence:9%			available?		
	France	_			NR		
		Mean age ± SD:					

9 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

10 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

	Conflicts of	64 ± 14			Reasons for incomplete		
	interest: not				outcome data described?		
	reported	Sex: 66% M			NR		
Jin, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹¹ :	Acute	Mehran risk score	>0.5 mg/dL	test en reference test: 48	effect size (include 95%CI	
	cohort study	myocardial		(44.2μmol/L) or 25%	hours	and p-value if available):	
		infarction		increase in serum			
	Setting: in-	patients		creatinine within 48	For how many	Risk score range	
	and	undergoing PCI		hours of PCI	participants were no	associated with PC-AKI:	
	outpatients				complete outcome data	Low: 12%	
		Exclusion			available?	Medium: 35%	
	Country:	criteria: -			NR	High: 36%	
	China						
		N= 1041			Reasons for incomplete		
	Conflicts of				outcome data described?		
	interest: not	Prevalence: 14%			NR		
	reported						
		Mean age ± SD:					
		68 ± 12					
		Sex: 52% M					
Kul, 2015	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹² :	patients with	Zwolle risk score	>0.5 mg/dL or 25%	test en reference test: 72	effect size (include 95%CI	
	cohort study	acute STEMI and		increase in serum	hours	and p-value if available):	
		undergoing		creatinine within 72			
	Setting: in-	emergency PCI		hours of PCI	For how many	1) Zwolle score >2	
	and		Comparator test:		participants were no	Sens: 76%	
	outpatients	Exclusion	Mehran risk score		complete outcome data	Spec: 75%	
		criteria: -			available?	AUC: 0.85	
	Country:				NR		
	Turkey	N= 314				2) Mehran score > 5	
					Reasons for incomplete	Sens: 71%	

¹¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

12 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	Conflicts of interest: not reported	Prevalence: 12% Mean age ± SD: 56 ± 11 Sex: 81% M			outcome data described? NR	Spec: 74% AUC:0.79	
Lin, 2015	Type of study ¹³ : cohort study Setting: inand outpatients Country: Taiwan / Egypt Conflicts of interest: not reported	Inclusion criteria: PCI, single center (including emergency PCI) Exclusion criteria: - N= 516 Prevalence: 12% Mean age ± SD: 64 ± 11 Sex: 83% M	Describe index test: 1) "comprehensive risk score model", WHC model 2) Bartholomew model 3) Mehran model 4) Tziakas model 5) Ghain model	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%CI and p-value if available): AUC: 1) own model: 0.92 (95%CI: 0.88 – 0.96) 2) Bartholomew model 0.91 (95%CI: 0.87 – 0.95) 3) Mehran model: 0.90 (95%CI: 0.86 – 0.94) 4) Tziakas model: 0.70 (95%CI: 0.58 – 0.83) 5) Ghain model: 0.65 (95% CI: 0.53 – 0.78) External validation: n=241 Discrimination and calibration NR	
Maioli, 2010	Type of study 14: cohort study Setting: in-and outpatients	Inclusion criteria: patients with an indication for coronary angiography or PCI, single center	Describe index test: Global Registry for Acute Coronary Events (GRACE) risk score Comparator test:	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 5 days of PCI	Time between the index test en reference test: 5 days For how many participants were no complete outcome data	Outcome measures and effect size (include 95%Cl and p-value if available): GRACE Cut-off 160 Sens: 79%	Risk score range associated with PC-AKI risk: 0-1: 0% 2-3: 1% 4: 2% 5: 6%

¹³ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

14 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

		Exclusion	Mehran risk score		available?	Spec: 61%	6: 12%
	Country: Italy	criteria: -	Wieman risk score		NR	Spec. 01/0	7: 19%
	Journal y Heart	or received				Mehran	8: 24%
	Conflicts of	N=1281			Reasons for incomplete	NR	9: 36%
	interest: not				outcome data described?		10: 50%
	reported	Prevalence: 3%			NR	Incidence of events:	
						Derivation cohort: 3.0%	
		Mean age ± SD:				Validation cohort: NR	
		69 ± 10					
						AUC:	
		Sex: 67% M				1) GRACE: 0.72 (0.3) and	
						0.69 (0.5)	
						2) Mehran: 0.78 (0.3) and	
						0.84 (0.5)	
						External validation	
						N=502	
						Discrimination and	
Marenzi,	Tuno of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	calibration NR Outcome measures and	
2004	Type of study ¹⁵ :	patients referred	Marenzi risk score	>0.5 mg/dL increase in	test en reference test: 5	effect size (include 95%Cl	
2004	cohort study	for PCI for	ivialenzi risk score	serum creatinine within	days	and p-value if available):	
	conort study	STEMI, single		5 days of PCI	uays	and p-value if available).	
	Setting: in-	center		3 days of FCI	For how many	External validation	
	and	Certer			participants were no	N=891	
	outpatients	Exclusion			complete outcome data	Discrimination 0.57 and	
	o departernes	criteria:			available?	calibration NR	
	Country: Italy				NR		
	' '	N= 218					
	Conflicts of				Reasons for incomplete		
	interest: not	Incidence of			outcome data described?		
	reported	events:			NR		
		Derivation					
		cohort: 19%					

¹⁵ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		Validation cohort: 14% M					
Mehran, 2004	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
	study ¹⁶ :	patients referred	Mehran risk score	>0.5 mg/dL or 25%	test en reference test: 48	effect size (include 95%CI	
	cohort study	for PCI, single center		increase in serum creatinine within 48	hours	and p-value if available):	
	Setting: in-			hours of PCI	For how many	For Creatinine:	
	and	Exclusion			participants were no	Discrimination: 0.69	
	outpatients	criteria: -			complete outcome data available?	Validation: p=0.43	
	Country:	N= 5571			NR	For eGFR:	
	United States					Discrimination: 0.70	
	of America	Prevalence: 14%			Reasons for incomplete	Validation: p=0.42	
					outcome data described?	-	
	Conflicts of	Mean age ± SD:			NR	External validation	
	interest: not	64 ± 11				Cohort 1: patients	
	reported					undergoing cardiac	
		Sex: 71% M				catheterization or PCI,	
						single center	
						N=3945	
						Discrimination: 0.57	
						Calibration: NR	
						Cohort 2: patients	
						admitted for elective or	
						emergency PCI, single	
						center	
						N=5571	
						Discrimination: 0.59	
						Calibration: NR	
Mizuno, 2014	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹⁷ :	patients	Mehran Risk score	>0.5 mg/dL or 25%	test en reference test: 3	effect size (include 95%CI	
	cohort study	undergoing a PCI		increase in serum	days	and p-value if available):	

¹⁶ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		for STEML single	(and rod coll	creatining within 2 days			
	Setting: in- and outpatients Country: Japan Conflicts of interest: not reported	for STEMI, single center Exclusion criteria: - N= 102 Prevalence: 10% Mean age ± SD: 62 ± 14	(and red cell distribution width)	creatinine within 3 days of PCI	For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	AUC Mehran: 0.72 (0.54 – 0.90)	
		Sex: 78 % M					
Raposeiras- Roubín, 2013	Type of study ¹⁸ : cohort study Setting: inand outpatients Country: Spain Conflicts of interest: not reported	Inclusion criteria: Patients with myocardial infarction after corronary angiography Exclusion criteria: - N=202 Prevalence: 28% Mean age ± SD: 63 ± 13	Describe index test: GRACE risk score	Describe reference test: ≥25% or ≥0.3mg/dL (or 0.5) rise in serum creatinine levels after 72 hours	Time between the index test en reference test: 72 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): GRACE risk score >140 was an independent predictor of CIN	Internal validation only

¹⁷ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

18 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

		Sex: 75% M					
Sgura, 2010	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹⁹ :	patients	Mehran risk score	>0.5 mg/dL	test en reference test: 48	effect size (include 95%CI	
	cohort study	undergoing PCI		(44.2μmol/L) or 25%	hours	and p-value if available):	
		for STEMI, single	Comparator test:	increase in serum			
	Setting: in-	center	Marenzi risk score	creatinine within 48	For how many	AUC	
	and			hours of PCI	participants were no	Mehran: 0.57 (95% CI 0.52	
	outpatients	Exclusion			complete outcome data	-0.62)	
		criteria:			available?	Marenzi: 0.57 (95% CI 0.51	
	Country: Italy	-			NR	- 0.62)	
	Conflicts of	N= 891			Reasons for incomplete		
	interest: not				outcome data described?		
	reported	Prevalence: 14%			NR		
		Mean age ± SD:					
		64 ± 13					
		Sex: 78% M					
Tziakas, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
	study ²⁰ :	Elective or	Tziakas score	>0.5 mg/dL or 25%	test en reference test: 48	effect size (include 95%CI	
	cohort study	emergency PCI,		increase in serum	hours	and p-value if available):	
		single center		creatinine within 48			
	Setting: in-			hours of PCI	For how many	Calibration /	
	and	Exclusion			participants were no	discrimination:	
	outpatients	criteria:			complete outcome data	0.76	
		-			available?	p>0.05	
	Country:				NR		
	Greece	N= 688				External validation	
					Reasons for incomplete	Cohort 1: PCI patient same	
	Conflicts of	Incidence of			outcome data described?	single center	
	interest: not	events:			NR	N=200	

¹⁹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

20 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

Tziakas, 2014	reported Type of study ²¹ : cohort study Setting: in-and outpatients Country: Greece Conflicts of interest: not reported	Derivation cohort: 10% Validation cohort: 14% Mean age ± SD: 64 ± 11 Sex: 74% M Inclusion criteria: PCI, elective or urgent, multiple centers Exclusion criteria: - N=2882 Prevalence: 16% Mean age ± SD: 61 ± 12	Describe index test: Tziakas score	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 48 hours of PCI	Time between the index test en reference test: 48 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Discrimination: 0.86 Calibration: NR Cohort 2: patients admitted for elective or emergency PCI, multiple centers (tertiary care) N=2689 Discrimination: 0.70 Calibration: p=0.18 Outcome measures and effect size (include 95%CI and p-value if available): AUC: 0.70 Risk score range associated with PC-AKI risk: ≤3: <20% >3: ≥20%	Internal validation only
Victor, 2014	Type of study ²² : cohort study Setting: in-	Sex: 70% M Inclusion criteria: patients with an indication for PCI, single center	Describe index test: "simple risk score for CIN"	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 48 hours of PCI	Time between the index test en reference test: 48 hours For how many	Outcome measures and effect size (include 95%Cl and p-value if available): Sens: 94%	

²¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

22 In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

and	Exclusion	participants were no	Spec: 90%	
outpatients	criteria:	complete outcome data		
	-	available?	External validation	
Country: India		NR	N=300	
	N=900		Sens: 92%	
Conflicts of		Reasons for incomplete	Spec: 82%	
interest: not	Incidence of	outcome data described?		
reported	events:	NR		
	Derivation			
	cohort: 9.7%			
	Validation			
	cohort: 8.7%			
	Mean age ± SD:			
	57 v 10			
	Sex: 84% M			

Literature search description

Database	Search terms	Total
	1 exp contrast media/ae or (contrast adj3 iodine).ti,ab. or (contrast adj3 media).ti,ab.	868
	(18687)	
	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or	
	nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
	(537305) 3 1 and 2 (3895)	
	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
	ciaki), ti, ab. (1975)	
	5 3 or 4 (4504)	
	6 limit 5 to (yr="2000 -Current" and (dutch or english)) (2892)	
	7 risk assessment/mj or risk factors/mj or exp Renal Insufficiency/mj or Glomerular Filtration	
	Rate/ (35215)	
	8 (((kidney or renal) adj2 function) or (risk adj2 (assessment or factor* or scor*)) or egfr or	
	gfr or 'glomerular filtration rate').ti,ab. (559159)	
	9 exp contrast media/ad (14851) 10 7 or 8 (570621)	
	11 6 and 10 (1311)	
	12 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or	
	literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature	
	as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or	
	psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data	
	extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not	
	humans/)) (248785)	
	13 11 and 12 (75)	
	14 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or	
	Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii	
	or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or	
	multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or	
	doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not	
	(animals/ not humans/) (1510354)	
	15 11 and 14 (405)	
	16 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled	
	Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or	
	studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross	
	sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time	
	series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en	
	retrospectieve studies] (2212779)	
	17 11 and 16 (574)	
	18 (recommend* or consensus*).ti. (47665)	
	19 guideline*.ab. /freq=2 (47817)	
	20 guideline*.ti. (54427) 21 Guideline/ or Practice Guideline/ or guidelines as topic/ or practice guidelines as topic/	
	(146566)	
	22 or/18-21 (216370)	
	23 11 and 22 (50)	
	24 13 or 15 or 17 or 23 (811)	
	25 13 or 23 (114) – 112 uniek	
	26 15 not 25 (359) – 353 uniek	
	27 25 or 26 (473)	
	28 17 not 27 (338) – 328 uniek	

Literature search for tools to estimate risk of PC-AKI:

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. or	311
(OVID)	ESUR.ti,ab. (113073)	
1995-	2 exp *Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
now	(468614)	
English,	3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
Dutch	ciaki).ti,ab. (2004)	
2 4 6 6	4 (1 and 2) or 3 (8499)	
	10 2 or 3 (468663)	
	11 8 and 10 (3)	
	12 limit 4 to (yr="1995 -Current" and (dutch or english)) (5270) 13 "Contrast Media"/ae [Adverse Effects] (8177)	
	13 Contrast Media 7ae [Adverse Lifects] (8177) 14 "risk factor*".ab. /freq=3 (50816)	
	15 "Mass Screening"/ (86742)	
	16 "Risk Assessment"/ (192736)	
	17 (prediction or (risk adj3 (factor* or score* or marker*)) or screening).ti. (249759)	
	18 exp Questionnaires/ (343170)	
	19 (Questionnaire* or assessment*).ti. (220569)	
	20 Glomerular Filtration Rate/ or Creatinine/ or ("serum creatinine" or "glomerular	
	filltration rate*").ti,ab. (96312)	

21 14 or 15 or 16 or 17 or 18 or 19 (988425)
22 12 and 21 (645)
23 exp "Sensitivity and Specificity"/ or (Sensitiv* or Specific*).ti,ab. or (predict* or ROC-curve or receiver-operator*).ti,ab. or (likelihood or LR*).ti,ab. or exp Diagnostic Errors/ or (inter-observer or intra-observer or interobserver or intraobserver or validity or kappa or reliability).ti,ab. or reproducibility.ti,ab. or (test adj2 (re-test or retest)).ti,ab. or "Reproducibility of Results"/ or accuracy.ti,ab. or Diagnosis, Differential/ or Validation Studies.pt. or *"Practice Guidelines as Topic"/ (4973682)
24 22 and 23 (323)
25 remove duplicates from 24 (311)

Appendices to Chapter 5

Evidence tables

No literature search was performed for this chapter. The working group did not expect to find evidence for this question, since the clinical question could not be answered in a controlled study. Furthermore, the recommendations typically apply for the Dutch healthcare system.

Search conditions

No literature search was performed for this chapter. The working group did not expect to find evidence for this question, since the clinical question could not be answered in a controlled study. Furthermore, the recommendations typically apply for the Dutch healthcare system.

Appendices to Chapter 6

Evidence tables

Table: Exclusion after revision of full text

Author and year	Reason for exclusion
Akyuz. 2014	Patients with normal kidney function
Alessandri, 2014	Patients with normal kidney function
Cho, 2010	Does not fulfill selection criteria
Heguilen, 2013	Not using the most widely used PC-AKI definition of SC rise ≥25% or 44µmol/l
Koc, 2013	Patients with normal kidney function
Kong, 2012	Patients with normal kidney function
Kotlyar, 2005	Does not fulfill inclusion criteria (compares iv hydration with N-acetylcysteïne to
	hydration with placebo, not different hydration strategies)
Lawlor, 2007	Mixture of oral and intravenous hydration, compared to intravenous hydration alone
Mahmoodi, 2014	Patients with normal kidney function
Manari, 2014	The studied hydration infusion mixture is not used in Dutch clinical practice
Martin-Moreno,	Patients with normal kidney function
2015	
Mueler, 2005	Does not fulfill inclusion criteria (no control group)
Pakfetrat, 2009	The studied hydration infusion mixture is not used in Dutch clinical practice
Taylor, 1998	Mixture of oral and intravenous hydration, compared to intravenous hydration alone
Thayssen, 2014	Patients with normal kidney function
Trivedi, 2003	Normal kidney function
Vashegani Ferahani,	The studied hydration infusion mixture is not used in Dutch clinical practice
2009	
Wrobel, 2014	Did not define CIN/CI-AKI/PC-AKI
Yeghanehkah, 2014	The studied hydration infusion mixture is not used in Dutch clinical practice

Evidence table

Research question

Research questions	Describe	Bias due to	Bias due to	Bias due to	Bias due to	Bias due to selective	Bias due to loss	Bias due to violation of
•	method of							
reference		inadequate	inadequate	inadequate	inadequate	outcome reporting	to follow-up? ⁵	intention to treat
	randomisation ¹	concealment of	blinding of	blinding of care	blinding of	on basis of the		analysis? ⁶
		allocation? ²	participants to	providers to	outcome assessors	results? ⁴		
			treatment	treatment	to treatment			
(first			allocation? ³	allocation? ³	allocation? ³			
author,								(unlikely/likely/unclear)
publicatio		(unlikely/likely/un	(unlikely/likely/un	(unlikely/likely/uncl	(unlikely/likely/uncl	(unlikely/likely/unclea	(unlikely/likely/un	
n year)		clear)	clear)	ear)	ear)	r)	clear)	
	•			Hydration versu	is no hydration	•		
Kooiman,	Computer	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
2014	generated	•	•	•			•	·
	allocation							
	sequence							
	(stratified by							
	hospital and							
	renal function)							
Nijssen,	Computer-	Unlikely	Likely	Likely	Unlikely	Unlikely	Unlikely	Unlikely
2017	generated using	Ommery	Lincity	Likery	Omicery	O'mikery	Ommery	Ommery
2017	ALEA screening							
	and enrolment							
	application							
	software.							
	33.6.6.			Oral hy	dration			
Cho, 2010	Not decribed:	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
,	"randomly	,	,	· · · · · · · · · · · · · · · · · · ·				
	assigned"							
Dussol,	Computer	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2006	generated	- CKery	JKery		JKery	······································		
	randomization							
	list							
	1130	Caaliana laisani	La ala auta a da a du d	L	· ·	l phy and/or percutaneous		

Adolph, 2008	Computer- generated randomization schedule	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Boucek, 2013	Computer- generated randomization schedule with the use of numbered opaque envelopes containing identification of assigned medication	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Brar, 2008	Computer- generated randomization schedule	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Gomes, 2012	Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
Huber, 2016	Computer- generated randomization list	Unlikelu	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Manari, 2014	Computer generated balanced randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Ozcan, 2007	Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Ratcliffe, 2009	Not decribed: "randomization	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Unclear

	block"							
Recio- Mayoral,	Not decribed: "randomly	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
2007	assigned"							
		Sodium bicar	bonate short schedule	versus saline long sc	hedule for coronary ang	giography and/or percuta	aneous intervention	
Briguori,	Computer-	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2007	generated							
	randomization							
	schedule							
Castini,	Computer-	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
2008	generated randomization							
	table							
Hafiz,	Random	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2012	allocation table	Officery	Onnikery	Officery	Offinery	Officery	Onnicity	Officical
Klima,	Sealed	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2012	envelopes			,	,	·		
Lee, 2011	Interactive web	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
	response							
	system,							
	computer							
	generated							
	randomization,							
	stratified by participating							
	center							
Maioli,	Computerized	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2008	open-label	O minery	O minically	O'mikery	Onnicity	O'mikery	O minery	Official
	assignment in							
	blinded							
	envelopes used							
	in a consecutive							
	fashion							
Nieto-	Sealed opaque	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Rios, 2014	envelopes							
	(random							
	numbers table)							

Shavit,	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
2009		Sodium I	nicarhonate versus sa	line: "other schedule	" for coronary angiogra	anhy and/or percutaneou	is intervention		\dashv
Chong, 2015	Block randomisation, stratified by site, using aweb- randomisation system or back- up randomisation	Sodium I	Likely	Unclear	" for coronary angiogra Unlikely	aphy and/or percutaneou Unlikely	Unlikely	Unlikely	
Motohiro, 2011	envelopes. Computergenerated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	
Tamura, 2009	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	
Turedi, 2016	Computer- based block randomization.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely	
Ueda, 2011	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	
						e for computed tomograp			
Kooiman, 2014	Computer- generated allocation sequence	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	
				Con	trolled diuresis				
Brar, 2014	Computer- generated concealed	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	

	randomisation schedule							
Barbanti, 2015	Randomization based on computer generated codes	Unlikely	Likely	Likely	Unlikely	Unlikely	Unlikely	Unlikely
Briguori, 2011	Computer- generated randomisation list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Marenzi, 2012	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Qian, 2016	"randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Usmiani, 2015	"randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Usmiani, 2016	Randomly subdivided	Unlikely	Likely	Likely	Unlikely	Unlikely	Unclear	Unlikely
Visconti, 2016	Prospective, non- randomised study	Likely	Unclear	Unclear	Unclear	Unlikely	Unclear	Unclear

- 7. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 8. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 9. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 10. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

- 11. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 12. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1

This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question

Study	Study	Patient	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures	Comments
reference	characteristics	characteristics ²				and effect size 4	
			Hydration v	versus no hydration			
Kooiman,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2014	randomized	1) adult patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	≥18 years with a			96 hours	(include 95%CI and	
		clinical suspicion of	Withholding hydration prior to	250mL iv 1.4% sodium bicarbonate		p-value if	Our results
	Setting:	a pulmonary	СТРА	1 hour before CTPA	Loss-to-	available):	suggest that
	emergency	embolis requiring			follow-up:		preventive
	patients,	computed			3/138 (2.2%)	CI-AKI	hydration could
	multiple	tomography-			2 lost to	(= creatinine	be safely withheld
	centers, both	pulmonary			follow-up	increase >25% /	in CKD patients
	in- and	angiography (CTPA)			1 died	>0.5mg/dL)	undergoing CTPA
	outpatients	2) chronic kidney				I: 6 (9%)	for suspected
		disease (CKD): eGFR				C: 5 (7%)	acute pulmonary
	Country: the	<60mL/min/1.73m ²			<u>Incomplete</u>	RR: 1.29, 95% CI:	embolism.
	Netherlands				<u>outcome</u>	0.41 - 4.03	
		Exclusion criteria:			<u>data</u> :		
	Source of	1) pregnancy			As above	None of the	
	funding: non-	2) previous contrast				patients developed	
	commercial	administration				a need for dialysis	
		within past 7 days					
		3) documented					
		allergy for					
		iodinated contrast					
		media					

		4) hemodynamic					
		instability (systolic					
		blood pressure					
		<100mmHg)					
		5) earlier					
		participation in					
		samen trial					
		N total at baseline:					
		Intervention: 67					
		Control: 71					
		<u>Important</u>					
		prognostic factors ² :					
		For example					
		age ± SD:					
		I: 70 ± 12					
		C: 71 ± 13					
		Sex:					
		I: 52% M					
		C: 48% M					
		eGFR ± SD:					
		I: 50 ± 16					
		C: 48 ± 15					
		Groups comparable					
		at baseline?					
		Yes					
Nijssen,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2017	randomized	1) eGFR: 45-59	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
(AMACING)	controlled trial	mL/min/1.73m ²			2-6 days	(include 95%CI and	
		combined with	Prophylactic hydration protocols	No prophylactic treatment.		p-value if	'We found no
	Setting:	either diabetes, or	according to current guidelines:		Loss-to-	available):	prophylaxis to be
	elective	at least two			follow-up:	,	non-inferior and
			1	1			• • • • • • • • • • • • • • • • • • • •

Г			La. I I			· · · ·
	patients, one	predefined risk	Standard protocol intravenous	I: 68/328	CI-AKI	cost-saving in
	university	factors (age>75y;	0.9% NaCl 3-4 mL/kg per h during	C: 25/332	(25% or 44 μmol/L	preventing
	hospital	anaemia defined as	4 h before and 4 h		within 2–6 days of	contrast-induced
		haematocrit values	after contrast administration; long	<u>Incomplete</u>	contrast exposure)	nephropathy
	Country: the	<0.39L/L for men,	protocol intravenous	<u>outcome</u>	1:8 (2.7%)	compared with
	Netherlands	and <0.36L/L for	0.9% NaCl 1 mL/kg per h during 12	<u>data</u> :	C: 8 (2.6%)	intravenous
		women;	h before and 12 h after	As above	P=0.417	hydration
	Source of	<u>cardiovascular</u>	contrast administration.			according to
	funding:	disease; non-			No hydration was	current clinical
	Stichting de	steroidal anti-			cost-saving relative	practice
	Weijerhorst	inflammatory drug;			to hydration.	guidelines.'
		or diuretic				
		<u>nephrotoxic</u>			No haemodialysis	
		medication).			or related deaths	
					occurred within	
		Exclusion criteria:			35 days.	
		1) Inability to				
		obtain informed				
		consent;				
		2) eGFR lower than				
		30mL per				
		min/1.73m ² ;				
		3) renal				
		replacement				
		therapy;				
		4)emergency				
		procedures;				
		5) intensive care				
		patients;				
		6) known inability				
		to perform primary				
		endpoint data				
		collection;				
		7) no referral to				
		prophylactic				
		hydration;				
		8) participation in				
		-, ps. 00.pat.o III	l		l	L

9) solation due to infection control Notal at baseline: Intervention: 328 ((1: 328, 12: 296) Control: 332 (C1: 332, C2: 307) Important prognositic factors ¹ - For example age ± 5D: I: 71.9 ± 9.3 C: 72.6 ± 9.3 Sex: I: 59% M C: 64% M Baseline SCr: I: 118. 72.28 pmol /L C: 117.72.25 pmol /L C: 117.72.25 pmol /L C: 118.72 pmol /L C:		1	T	T	T	I	I	1
infection control Notal at baseline: Intervention: 328 (II: 328, II: 2296) Control: 332 (II: 328, II: 2296) Control: 332 (II: 328, II: 296) Control: 332 (II: 328, II: 398 M C: 64% M Baseline SCr: II: 159% M C: 64% M Baseline SCr: II: 128, II: 228, III: 22			other RCT; and					
Notal at baseline: Intervention: 328 (II: 328, II: 296) Control: 332 (CI: 332, CI: 296) Control: 332 (CI: 332, CI: 296) Control: 332 (CI: 332, CI: 207) Important prognostic factors ² : For example age ±50: I: 71.9 ±9.3 C: 72.6 ±9.9 C: 71.7 ±25 mol/1. C:								
Intervention: 328 (it: 328, 12: 296) Control: 332 (it: 328, 12: 296) Control: 342 (it: 484 (infection control					
Intervention: 328 (it: 328, 12: 296) Control: 332 (it: 338, 12: 296) Control: 332 (it: 338, 12: 296) Control: 332 (it: 338, 12: 296) Control: 332 (it: 328, 12: 296) Control: 332 C: 72.6 ± 9.3 Sex:								
Cho, 2010 Type of study: randomized randomized randomized controlled trial prognotic lasts seems reactinine Setting: elective patients, one stime, one stime, one stime, one stime, one stime, and the state servine reactinine 1 or all hydration with 50mL of water to be started 4 hours prior to contrast exposure and stopped solar prior to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to procedure prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time to prior) to contrast exposure and stopped control (area time								
Control: 332 (C1: 332, C2: 307) Important prognostic factors ² : For example age ± 5D: 1: 71.9 ± 9.3 C: 72.6 ± 9.3 Sex: 1: 59% M C: 64% M Baseline SCr: 1: 118.7±28 (mol / L) C: 117.7±25 (mol / L) C: 117.7±25 (mol / L) C: 117.7±25 (mol / L) Croups comparable at baseline? Yes Oral hydration Cho, 2010 Type of study: randomized controlled trial andomized controlled trial serious controlled trial serious rolled with stable serious controlled trial serious rolled roll								
Cl: 332, C2: 307) Important prognostic factors*: For example age ± 5D: 1: 71,9 ± 9.3 C: 72.6 ± 9.3 Sex: 1: 59% M C: 64% M								
Important prognostic factors ² : For example age ± 5D: 1: 71.9 ± 9.3 C: 72.6 ± 9.3								
Prognostic factors ² : For example age ± 5D: 17.1.9 ± 9.3 C.72.6 ± 9.3 Sex: 1.59% M C.64% M Baseline SCr:			(C1: 332, C2: 307)					
For example Gog ± 5D: 1: 71.9 ± 9.3 C: 72.6 ± 9.3 Sex: 1: 59% M C: 64% M Baseline 5 Cr: 1:118.7±25 \text{punol}/L C: 117.7±25 \text{punol}/L Groups comparable at baseline? Yes Type of study: Type of st			<u>Important</u>					
Cho, 2010 Type of study: randomized controlled trial restricting: elective patients, one setimated hospital relations of the stable serum creatinine setting: elective patients, one shows the stable serum creatinine hospital creatinine creatinine restimated to the contrast exposure and stopped place in the contrast exposure and stopped place in the contrast exposure and stopped prior to contrast exposure Clin			prognostic factors ² :					
Fig. 17.19 ± 9.3 C: 72.6 ± 9.3 Sex: Fig. 159% M C: 64% M C: 64% M C: 11.11.8 7 ± 25 μmol / L C: 11.7 1 ± 2			For example					
C: 72.6 ± 9.3 Sex: 1: 59% M C: 64% M Baseline SCr: 1:118.7±28µmo1/L C:117.7±25µmo1/L Groups comparable at baseline? Yes Type of study: randomized controlled trial serious reactinine Setting: levels of at least elective patients, one estimated thospital creatinine Setting: levels of at least hospital Controlled trial occurrence in the state of the control occurrence in the state of the control occurrence in the state occurrence in the			age ± SD:					
Sex:			I: 71.9 ± 9.3					
Cho, 2010 Type of study: randomized controlled trial Setting: levels of at least elective elective patients, one patients, one hospital reactions of the patients, one hospital reactions of the patients			C: 72.6 ± 9.3					
Cho, 2010 Type of study: randomized controlled trial Setting: elective elective patients, one patients, one patients, one hospital reactions of the patients of the patien								
C: 64% M Baseline SCr:								
Baseline SCr:								
Cho, 2010 Type of study: randomized controlled trial serum creatinine Setting: levels of at least elective patients, one lective patients, one hospital Setting: levels of at least creating in the serum creatinine Setting: levels of at least creating in the serum creatinine Setting: levels of at least creating in the serum creating Setting: levels of at least creating Setting: levels of at			C: 64% M					
C:117.7±25μmol/L Groups comparable at baseline? Yes Oral hydration			Baseline SCr:					
Groups comparable at baseline? Yes Oral hydration Type of study: randomized controlled trial serum creatinine Setting: levels of at least elective patients, one patients, one hospital creatinine Setting: levels of at least to be started 4 hours prior hospital Type of study: 1) oral hydration with 500mL of to contrast exposure and stopped hospital Oral hydration Describe control (treatment/procedure/test): Describe control (treatment/procedure/test): Describe control (treatment/procedure/test): Type of study: 1) patients 18 years (treatment/procedure/test): Outcome measures and effect size (include 95%Cl and p-value if oral hydration with or without sodium bolus of intravenous saline solution (154mEq/L) over 1 hour prior to contrast exposure Not reported CIN (= >25% increase in to and following)			<i>I:118.7±28</i> μmol/L					
Cho, 2010 Type of study: randomized controlled trial serum creatinine Setting: elective patients, one patients, one hospital creatinine lospital creatinine lossition creatinine lossition contrast exposure lossition contrast exposure lossition contrast exposure lossition lospital lossition lossition lospital losp			C:117.7±25μmol/L					
Cho, 2010 Type of study: randomized controlled trial Setting: levels of at least elective patients, one hospital creatinine lospital creatinine loss control lospication lospital loss control (treatment/procedure/test): losscribe control (treatment/procedure/test): lescribe control (treatment/procedure/test): losscribe control (treatment/procedure/test): long			Groups comparable					
Cho, 2010 Type of study: randomized controlled trial serum creatinine lective patients, one patients, one hospital creatment creatinine loss. Cho, 2010 Type of study: randomized controlled trial controlled trial controlled trial elective patients, one hospital creatment controlled trial creatment creatinine levels of at least controlled trial creatment creatment creatment controlled trial serum creatment levels of at least controlled trial controlled trial serum creatment with 500mL of contrast exposure and stopped solution (154mEq/L) over 1 hour hospital creatment levels of at least control (treatment/procedure/test): Describe control (treatment/procedure/test): Length of follow-up: (include 95%Cl and povalue if control (include 95%Cl and povalue if available): Oral hydration: Oral hydration Oral hydration With or without solution (154mEq/L) over 1 hour hospital creatment with a 3mL/kg bolus of intravenous saline solution (154mEq/L) over 1 hour prior to contrast exposure Power of the control contro								
Cho, 2010 Type of study: randomized controlled trial controlled trial serum creatinine lective patients, one patients, one hospital controlled trial creatinine levels of a least least controlled trial patients and controlled trial creatinine levels of at least lea			at baseline: 163	I Oral	l hvdration		I	
randomized controlled trial controlled trial controlled trial serum creatinine levels of at least patients, one patients, one hospital controlled trial control	Cho, 2010	Type of study:	Inclusion criteria:			Length of	Outcome measures	Authors'
controlled trial or older with stable serum creatinine Setting: levels of at least elective patients, one hospital or older with stable serum creatinine Setting: levels of at least 1) oral hydration with 500mL of to contrast exposure and stopped 2 hours prior to procedure 1) oral hydration with 500mL of to pretreatment with a 3mL/kg bolus of intravenous saline solution (154mEq/L) over 1 hour prior to contrast exposure 72 hours (include 95%Cl and p-value if available): with or without sodium bicarbonate prior to and following								
Setting: levels of at least 1) oral hydration with 500mL of elective patients, one hospital setting: creatinine levels of at least 1) oral hydration with 500mL of 1) pretreatment with a 3mL/kg bolus of intravenous saline solution (154mEq/L) over 1 hour prior to contrast exposure solution (154mEq/L) over 1 hour prior to contrast expos								,
Setting: levels of at least elective elective patients, one hospital election hospital election in the setting is a setting in the setting is election in the setting is election. The setting is election in the setting is election. The setting is election in the setting is election in the setting is election in the setting is election. The setting is election in the setting is election in the setting is election in the setting is election. The setting is election in the settin							,	Oral hydration
elective patients, one hospital creatinine 1.1mg/dL or elective patients, one hospital creatinine 2 hours prior to procedure bolus of intravenous saline solution (154mEq/L) over 1 hour prior to contrast exposure prior to contrast exposure follow-up: Not reported contrast exposure in to and following solution (154mEq/L) over 1 hour prior to contrast exposure		Setting:	levels of at least	1) oral hydration with 500mL of	1) pretreatment with a 3mL/kg	Loss-to-	1 ·	•
patients, one hospital creatinine to contrast exposure and stopped 2 hours prior to procedure solution (154mEq/L) over 1 hour prior to contrast exposure Not reported CIN bicarbonate prior to and following		-	1.1mg/dL or				·	sodium
hospital creatinine 2 hours prior to procedure priori to contrast exposure (= >25% increase in to and following		patients, one			solution (154mEq/L) over 1 hour		CIN	bicarbonate prior
			creatinine				(= >25% increase in	
			clearance less than	followed by oral hydration with	Intravenous infusion of 1mL/kg for	<u>Incomplete</u>	sCr from baseline	CAG is not

		COmpl. Institu	6001	Character and the control of the con			1fi . i k .
	ountry:	60mL/min	600mL water postprocedure	6 hours after procedure	<u>outcome</u>	or an absolute	inferioir to
_	Inited States	scheduled for	2) 11 1 1 1 11 11 11 11 11	2)	data:	increase of	intravenous
Of	f America	diagnostic, elective	2) oral hydration with 500mL of	2) pretreatment with a 3mL/kg	Not reported	0.5mg/dL from	hydration and
		angiography	water to be started 4 hours prior	bolus of intravenous sodium		baseline at 72	sodium
	ource of		to procedure and stopped 2 hours	biacrbonate solution (154mEq/L)		hours following	bicarbonate with
	unding: not	Exclusion criteria:	prior to contrast exposure, with	over 1 hour priori to contrast		exposure to radio-	respect to CIN;
re	eported	1) serum creatinine	the addition of 3.9g (46.4mEq) of	exposure		contrast)	and to date, offers
		levels >8.0mg/dL	oral sodium bicarbonate to be	Intravenous infusion of 1mL/kg for		I1: 1/22	an equivalent and
		2) change in serum	given 20 minutes prior to contrast	6 hours after procedure		I2: 1/22	practical approach
		creatinine levels of	exposure followed by oral			C1: 6/27	in preventing a
		at least 0.5mg/dL	hydration with 600mL of water and			C2: 2/21	decline in renal
		during the previous	1.95g (30.4mEq) of oral sodium			p>0.05	functionafter
		24 hours	bicarbonate 2 hours and 4 hours				contrast exposure
		pre-existing	after the initial dose			There were no in-	without accuring
		dialysis				hospital mortalities	additional delay in
		4) multiple				during this study.	hospital days or
		myeloma or other					in-hospital
		myeloproliferative				Length of hospital	mortality,
		disease				stay did not differ	
		5) current				significantly	
		decompensated				between groups.	
		heart failure or					
		significant change					
		in NYHA					
		6) current					
		myocardial					
		infarction					
		7) symptomatic					
		hypokalaemia					
		8) uncontrolled					
		hypertension					
		9) exposure to					
		radiocontrast					
		within 7 days of					
		enrolment into this					
		study					
		10) emergency					

catheterisation		
11) allergy to		
radiographic		
contrast		
12) pregnancy		
13) administration		
of mannitol,		
feoldapam or NAC		
during the time of		
the study		
14) exacerbation of		
chronic obstructive		
pulmonary disease		
15) serum		
bicarbonate greater		
than 28eEw/L and		
sodium less than		
133mEq/L		
,		
N total at baseline:		
Intervention: 43		
(11: 22, 12: 22)		
Control: 48		
(C1: 27, C2: 21)		
, ,		
<u>Important</u>		
prognostic factors ² :		
For example		
age ± SD:		
I1: 81 ± 7		
12: 79 ± 2		
C1: 77 ± 8		
C2: 78 ± 9		
Sex:		
I1: 45% M		

	C1: 63% M C2: 52 Baseline SCr: I1: 1.38 I2: 1.31 C1: 1.38 C2: 1.41 Groups comparable at baseline? Yes					
Dussol, 2006 Type of study: randomized controlled trial Setting: elective patients, one university hospital Country: France Source of funding: non- commercial	Inclusion criteria: 1) patients referred for any radiological procedures necessitating a contrast medium injection and who had a baseline Cockcroft clearance between 15-60ml/min 2) either chronic renal failure and on a kidney graft Exclusion criteria: 1) <18 years old 2) women of childbearing age not using contraception or breast feeding 3) patients with heart failure and ejection fraction <30% 4) uncontrolled	Describe intervention (treatment/procedure/test): NaCl 1g/10kg/day per os for 2 days	Describe control (treatment/procedure/test): 0.9% saline iv 15ml/kg for 6 hours before the procedure	Length of follow-up: 48 hours Loss-to-follow-up: Not reported per group separately, in total 3/315 (1%) lost to follow-up Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (= increase in the baseline sCr concentration of at least 44µmol/L (0.5mg/dL) within 48 hours after the injection of contrast media) 1: 5/76 (7%) C: 4/77 (5%) p>0.05 None of the patients had fluid overload	Authors' conclusion: Oral saline hydration was as efficient as intravenous saline hydration for the prevention of CIN in patients with stage 3 renal diseases.

arterial			
hypertension			
5) obvious			
extracellular			
overhydration			
6) respiratory			
depression			
7) known prior			
intolerance to			
theophylline or			
furosemide			
8) previous			
exposure to			
contrast media in			
the 14 days before			
randomization			
9) unwilling or			
unable to provide			
informed consent			
10) adequate time			
prior to contrast			
media injection was			
not available to			
perform the study			
procedure			
11) if sCr			
measurements			
varied by >10% in			
the previous weeks			
before referral			
N total at baseline:			
Intervention:			
Control:			
<u>Important</u>			
prognostic factors ² :			
 1 +			L

		- ,				1	
		For example					
		age ± SD:					
		I: 63 ± 15					
		C: 64 ± 11					
		Sex:					
		I: 66% M					
		C:75 % M					
		eGFR ± SD:					
		I: 38 ± 13					
		C: 33 ± 11					
		Groups comparable					
		at baseline? Yes					
	•	Sodium bicarbonate s	short schedule versus saline short sche	edule for coronary angiography and/or	percutaneous in	tervention	
Adolph,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2008	randomized	1) patients >18	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	years with baseline			2 days	(include 95%CI and	
		serum creatinine	Sodium bicarbonate 154mEq/L in	Sodium chloride 154 mEq/L in 5%		p-value if	Renal Insufficiency
	Setting:	concentration	5% dextrose solution	dextrose solution	Loss-to-	available):	following
	elective	greater than	2ml/kg body weight/hour for 2	2ml/kg body weight/hour for 2	follow-up:		radiocontrast
	patients	106μmol/L	hours before	hours before	1 patient	CIN	exposure
		(1.2mg/dL)	And	And	(refused	(= elevation of sCr	demonstrates a
	Country:	undergoing elective	1ml/kg body weight/hour during	1ml/kg body weight/hour during	follow-up)	concentration	homogenously
	Germany	diagnostic or	and for 6 hours after contrast	and for 6 hours after contrast	, ,	>0.5mg/dL	low rate of CIN
	·	interventional	administration	administration	<u>Incomplete</u>	(44µmol/L) or	after exposure to
	Source of	coronary			outcome	25%above baseline	non-ionic, iso-
	funding: not	angiography			data:	between day 0 and	osmolar iodixanol
	reported				3/145 (2%)	days 1 or 2 after	regardless of the
	'	Exclusion criteria:			2 patients	contrast axposure)	use of either
		1) acute myocardial			had an	1: 4.2%	bicarbonate
		infarction			emergency	C: 2.7%	sodium or sodium
		2) allergies to trial			coronary	P=0.61	chloride solution
		medication			bypass and		for volume
		3) exposure to			pulmonary	Dialysis for acute	supplementation.
		contrast			edema	renal failure was	

T				
	mediumwithin the	1 patient	not required	
	last 7 days	refused		
	4) thyroid	follow-up		
	dysfunction			
	5) pregnancy			
	6) uncontrolled			
	hypertension			
	7) life-limiting			
	concomitant			
	disease			
	8) pulmonary			
	edema			
	9) chronic dialysis			
	10) administration			
	of dopamine,			
	mannitol,			
	fenoldopam or NAC			
	during the study			
	N total at baseline:			
	Intervention: 71			
	Control: 74			
	<u>Important</u>			
	prognostic factors ² :			
	For example			
	age ± SD:			
	1: 70 ± 8			
	C: 73 ± 7			
	6.75 ± 7			
	Sex:			
	1: 75% M			
	C: 81% M			
	C. 01/0 IVI			
	cCr (mg/d) + CD)			
	sCr (mg/dL ± SD)			
	l: 1.54 ± 0.51			
	C: 1.57 ± 0.36			

		Groups comparable at baseline? Yes					
Boucek, 2013	Type of study: RCT Setting: elective inpatients, one hospital Country: Czech Republic Source of funding: commercial	Inclusion criteria: 1) presence of diabetes mellitus 2) renal function impairment (screening serum creatinine _100 mmol/L), 3) age of ≥18 years 4) a planned procedure with intra-arterial or intravenous use of contrast Exclusion criteria: 1) endstage renal disease (screening serum creatinine _500 mmol/L, 2) chronic dialysis treatment or presence of kidney transplant), 3) pre-planned dialysis following the contrast-involving procedure, 4) emergency type	Describe intervention (treatment/procedure/test): 1.4% sodium bicarbonate in 5% glucose 3ml/kg/hour 1 hour before contrast administration (limited to a maximum of 330mL) 1mL/kg/hour 6 hours after contrast administration (limited to a maximum of 660mL)	Describe control (treatment/procedure/test): 0.9% saline in 5% glucose 3ml/kg/hour 1 hour before contrast administration (limited to a maximum of 330mL) 1mL/kg/hour 6 hours after contrast administration (limited to a maximum of 660mL)	Length of follow-up: 2 days – laboratory parameters 1 month – clinical parameters Loss-to- follow-up: Intervention: 3/61 (5%) Reasons not described Control: 3/59 (5%) Reasons not described Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (= sCr increase of ≥25% and/or 44µmol/L (0.5mg/dL) within 2 days foillowing administration of contrast) I: 7 (12%) C: 5 (9%) P=0.76 Incidence rate ratio: 1.35 (95% Cl: 0.37 − 5.41) No patients died or experienced severe kidney injury with need for acute dialysis treatment.	Authors' conclusion: In diabetic patients with renal function impairment sodium bicarbonate does not confer protection against contrast-induced nephropathy greater than sodium chloridebased hydration.

(serum creatinine
increase _50
mmol/L during the
previous
24-h period),
5) volume overload
with left ventricular
failure,
6) uncontrolled
hypertension
(systolic BP _180 or
diastolic BP
_110 mmHg),
7) hemodynamic
instability (systolic
BP <90 and
diastolic BP <50
mmHg),
8) contrast use in
the previous 48-h
period,
9) multiple
myeloma,
10) pregnancy or
breastfeeding
11) pre-planned use
of any other
measure for CIN
prevention
apart from the NaCl
or NaHCO3
infusions
N total at baseline:
Intervention: 61
Control: 59
Control 55

		<u>Important</u>					
		prognostic factors ² :					
		For example					
		age ± SD:					
		I: 63 ± 11					
		C: 67 ± 10					
		Sex:					
		I: 75% M					
		C: 75% M					
		eGFR					
		(mL/min/1.73m²) ±					
		SD					
		1: 44 ± 19					
		C: 25 ± 17					
		C. 25 ± 17					
		Groups comparable					
		at baseline? Yes					
Brar, 2008	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized	1) an estimated	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	glomerular			2-3 days for	(include 95%CI and	
		filtration rate (GFR)	1.4% sodium bicarbonate iv		laboratory	p-value if	The results of this
	Setting:	of 60 mL/min per	infusion		parameters	available):	study do not
	elective	1.73m2 or less,	Infusion was begun 1	0.9% saline iv infusion	6 months for		suggest that
	patients, one	2) age 18	hour prior to the start of contrast	Infusion was begun 1	clinical		hydration with
	hospital	years or older,	administration	hour prior to the start of contrast	effects	≥25% reduction in	sodium
		3) at least 1 of the	at3mL/kg for1hour, decreased	administration		estimated eGFR	bicarbonate
	Country:	follwing: -diabetes	to 1.5 mL/kg per hour during the	at3mL/kg for1hour, decreased	Loss-to-	I: 21/158 (13%	is superior to
	United States	mellitus,	procedure	to 1.5 mL/kg per hour during the	follow-up:	C: 24/165 (15%)	hydration with
	of America	-history of	and for 4 hours following	procedure	Intervention:	Absolute	sodium chloride
		congestive heart	completion	and for 4 hours following	17 (10%)	difference: 1.3,	for the prevention
	Source of	failure,	of	completion	Excluded	95% CI: -6.3 to 8.8,	of contrast
	funding:	-hypertension	theprocedure.Forpatientsweighing	of	1 Did not	p=0.75	medium-induced
	commercial	(140/90 mm Hg	more than 100 kg, the bolus and	theprocedure.Forpatientsweighing	undergo		nephropathy in
		treatment with an	infusion	more than 100 kg, the bolus and	coronary	Serum creatinine	patients with
		antihypertensive	rate were limited to those used for	infusion	angiography	>25% or >0.5mg/dL	moderate to

medication),	patients weighing100kg	rate were limited to those used for	16 Did not	increase	severe chronic
-age older than 75		patients weighing100kg	have	I: 26/158 (17%)	kidney disease
years			estimated	C: 30/165 (18%)	who are
'			GFR data	Absolute	undergoing
Exclusion criteria:			1-4 d after	difference: 1.7,	coronary
1) inability to			procedure	95% CI: -6.5 to	angiography.
obtain consent, 2)			,	10.0, p=0.78	
receipt of a sodium			Control:	,	
bicarbonate			13 (7%)	30-day mortality	
infusion prior to			Excluded	I: 3/175 (2%)	
randomization,			2 Did not	C: 3/178 (2%)	
3) emergency			undergo	p>0.05	
cardiac			coronary	P	
catheterization,			angiography	6-month mortality	
4) intra-aortic			11 Did not	1: 34%	
balloon			have	C: 2%	
counterpulsation,			estimated	P=0.54	
5) dialysis,			GFR data	. 0.0	
6) exposure to			1-4 d after	6-month start of	
radiographic			procedure	dialysis	
contrast media			processing.	I: 2/175 (1%)	
within the			Incomplete	C: 4/178 (2%)	
preceding 2 days,			outcome	P-value not	
7) allergy to			data:	reported	
radiographic			As above for		
contrast media,			laboratory		
8) acutely			paramters.		
decompensated			All patients		
congestive heart			were		
failure,			followed up		
9) severe valvular			for clinical		
abnormality (eg,			events.		
severe aortic					
stenosis or					
mitral					
regurgitation),					
10) single					

		functioning					
		kidney,					
		11) history of					
		kidney or heart					
		transplantation,					
		12) change in					
		estimated GFR of					
		7.5% or more per					
		day or a cumulative					
		change of 15% or					
		more over the prior					
		2 or more days					
		2 of more days					
		N total at baseline:					
		Intervention: 175					
		Control: 178					
		2011.1011 27 0					
		Important					
		prognostic factors ² :					
		For example					
		age (IQR range)					
		I: 71 (65-75)					
		C: 71 (65-76)					
		, ,					
		Sex:					
		I: 65% M					
		C: 62% M					
		Groups comparable					
		at baseline? Yes					
Gomes,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2012	randomized	1) patients at	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	moderate to high			48 hours	(include 95%CI and	
		risk for developing				p-value if	Hydration with
	Setting:	CIN who were			Loss-to-	available):	sodium
	elective	referred for elective	154 mEq/l of sodium bicarbonate	0.9% saline infusion	follow-up:		bicarbonate was
	patients, 6	coronary	in 5% dextrose and H ₂ O	3 mL/ kg/ h for 1 hour immediately	Not reported	CIN	not superior to

difference	angiography or PCI	3 mL/ kg/ h for 1 hour immediately	before contrast injection		(=an increase in	saline to prevent
centres	at 6 centers 2) serum creatinine	before contrast injection same fluid at a rate of 1 mL/kg/h	same fluid at a rate of 1 mL/kg/h during contrast exposure and for 6	Incomplete outcome	serum creatinine ≥ 0.5 mg/dL 48 hours	contrast media induced
Country: Br		during contrast exposure and for 6	hours after the procedure	<u>data</u> :	after exposure to	nephropathy in
Country: Bit	glomerular	hours after the procedure	nours after the procedure	Not reported	contrast medium)	patients at risk
Source of	filtration rate (GFR)	The art of the procedure			I: 9/150 (6%)	undergoing
funding: no					C: 9/151 (6%)	cardiac
reported	,				P=0.97	catheterization.
	Exclusion criteria:					
	1) age <18 years,				Dialysis:	
	2) use of				I: 0%	
	radiographic				C: 0%	
	contrast media				P=1.00	
	during the last 21					
	days,				Death: I: 3%	
	3) history of dialysis,				1: 3% C: 5%	
	4) cardiac				P=0.81	
	insufficiency class				F-0.81	
	III-IV NYHA,					
	5) emergency					
	procedures					
	·					
	N total at baseline:					
	Intervention: 150					
	Control: 151					
	Important prognostic factors ² :					
	For example					
	age ± SD:					
	l: 64 ± 12					
	C: 65 ± 12					
	Sex:					
	I: 69% M					
	C: 75% M					

		T	I	1		T	1
		eGFR ± SD I: 51 ± 13					
		C: 52 ± 13					
		Groups comparable					
		at baseline? Yes					
Huber,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2016	randomized	1) >18 years;	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
2010	controlled	2) increased risk of	(treatment, procedure, test).	(treatment, procedure, test).	48h after CM	(include 95%CI and	Concidioni
	controlled	CIN undergoing	Group B received bicarbonate	Control group S received sodium	Ton arter Civi	p-value if	'In patients at
	Setting: single-	administration of	infusion with 200mg theophylline.	chloride infusion with 200mg	Loss-to-	available):	increased risk of
	center	CM. High risk was		theophylline.	follow-up:		CIN receiving
	university	defined by a serum			I:14/91	CIN	prophylactic
	hospital	creatinine level			C: 14/94	as a raise in serum	theophylline,
	'	≥1.1 or ≥0.8 mg/dL				creatinine of 25%	hydration with
	Country:	plus an			<u>Incomplete</u>	or _0.5 mg/dL	sodium
	Germany	additional risk			outcome	within 48 h after	bicarbonate
		factor like diabetes			<u>data</u> :	contrast	reduces contrast-
	Source of	mellitus, renal			Not reported	application	induced renal
	funding:	failure in past				I: 1/74 (1.4%)	impairment
	institutional	medical history, or				C: 7/78 (9%)	compared to
	support	nephrotoxic				P=0.039	hydration with
		medication					saline.'
		(aminoglycoside,				Dialysis:	
		vancomycin,				I: 9%	
		amphotericin B,				C: 17%	
		and diuretic).				P=0.189	
		Exclusion criteria:					
		1) pre-existing renal					
		replacement					
		therapy;					
		2) unstable serum					
		creatinine levels					
		(difference of more					
	1	than _0.4 mg/dL				1	1

within 3
days before
contrast
application);
3) contraindi-
cations for
theophylline
or sodium
bicarbonate
(allergies,
tachycardia,
alkalosis,
and hypokalemia);
and;
4) additional
interventions that
might
influence renal
function.
<u>Important</u>
prognostic factors ² :
For example
age ± SD:
I: 64.4 ± 15.7
C: 66.1 ±13.3
Sex:
I: 59.5% M
C: 66.7% M
Baseline SCr:
I:1.25± 0.69 mg/dL
C:1.38± 0.65 mg/dL
Groups comparable
at baseline? Yes
40 000 cm c 100

Manari,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2014	randomized	1) Patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled	with STEMI within		, , ,	3 days –	(include 95%CI and	
		12 h from symptom	I1:	C1:	laboratory	p-value if	In patients with
	Setting:	onset referred	sodium bicarbonate solution 1	Intravenous normal saline (0.9%)	parameters	available):	STEMI undergoing
	emergency	for primary	ml/kg of body weight per hour for	at a rate of 1 ml/kg of body	12 months –		PPCI, highvolume
	patients,	angioplasty	12 h	weight per hour for 12 h	clinical	sCr increase ≥25%	hydration with
	multicentre	2) age at least 18			events	compared to	normal saline or
	trial	years	12:	C2:		baseline	sodium
		3) chest pain lasting	3 ml/kg of body weight per hour	normal saline at a	Loss-to-	I1: 24 (16%)	bicarbonate
	Country: Italy	for at least 30 min	for 1 h, followed by	rate of 3 ml/kg of body weight per	follow-up:	12: 27 (18%)	administrated at
		associated with	1 ml/kg of body weight per hour	hour for 1 h followed by	Not reported	C1: 29 (19%)	the time of
	Source of	STsegment	for 11 h	1 ml/kg of body weight per hour		C2: 27 (19%)	contrast media
	funding: not	elevation of 0.2mV		for 11 h	<u>Incomplete</u>	P=0.92	administration
	reported	or more in at least			<u>outcome</u>		was not
		two			<u>data</u> :	sCr increase ≥0.5	associated with
		contiguous leads or			Not reported	mg/dL from	any significant
		new left bundle-				baseline	advantage in
		branch block				I1: 5 (3%)	terms
						12: 3 (3%)	of CI-AKI
		Exclusion criteria:				C1: 7 (5%)	prevention.
		1) the concomitant				C2: 8 (6%)	
		detection of				P=0.51	
		mechanical					
		complications,				Mortality did not	
		2) previous				differ at 30 days	
		peritoneal or				and at 12 months	
		hemodialysis				(data not shown).	
		treatment, 3) the					
		presence of					
		postanoxic coma					
		4) pregnancy					
		N total at baseline:					
		Intervention 1: 145					
		Intervention 2: 154					
		Control 1: 142					

		Control 2: 151					
		CONCIOI Z. 131					
		Important					
		Important prognostic factors ² :					
		For example					
		age ± SD:					
		11: 64 ± 13					
		12: 65 ± 13					
		C1: 65 ± 13					
		C2: 65 ± 12					
		Sex:					
		I1: 72% M					
		12: 75% M					
		C1: 75% M					
		C2: 77% M					
		eGFR ml/min					
		11: 80 ± 26					
		12: 82 ± 24					
		C1: 81 ± 23					
		C2: 82 ± 25					
		C2. 02 ± 25					
		Groups comparable					
		at baseline? Yes					
Ozcan,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2007	randomized	patients who were	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled trial	scheduled	,	, , , , , , , , , , , , , , , , , , , ,	48 hours	(include 95%Cl and	
		for coronary	1.4% sodium bicarbonate	0.9% saline		p-value if	Hydration with
	Setting:	angiography or	Iv fluid (1 mL/kg/h,	Iv fluid (1 mL/kg/h,	Loss-to-	available):	sodium
	elective	percutaneous	upper limit 100 mL/h) for 6 hours	upper limit 100 mL/h) for 6 hours	follow-up:	,	bicarbonate
	patients	coronary	before and 6 hours after the	before and 6 hours after the	Not reported	CIN	provides better
	'	intervention	procedure	procedure		(=an increase in	protection against
	Country:	and had a baseline	•	<u>'</u>	Incomplete	serum creatinine	CIN than the
	Turkey	creatinine level			outcome	N25% or 0.5 mg/dL	sodium chloride
	'	N1.2 mg/dL			data:	after 48 hours)	infusion does
	Source of	<u>.</u>			Not reported	I: 12/88	alone.

funding: not	Exclusion criteria:	C: 4/88
reported	1) uncontrolled	P=0.043
	hypertension	RR (adjusted): 0.29
	(systolic and	95% CI: 0.09 – 0.96
	diastolic blood	
	pressure N160 mm	
	Hg and N110 mm	
	Hg, respectively),	
	2) emergency	
	catheterization,	
	3) recent exposure	
	to radiocontrast	
	medium within 2	
	days,	
	4) volume overload,	
	5) serum creatinine	
	levels >4 mg/dL	
	N total at baseline:	
	Intervention: 88	
	Control: 88	
	<u>Important</u>	
	prognostic factors ² :	
	For example	
	age median	
	(minimum –	
	maximum)	
	1: 68 (43-86)	
	C: 70 (40-84)	
	Cove	
	Sex:	
	I: 73% M C: 75% M	
	C. 73% IVI	
	Creatinine	
	clearance (mL/min)	
	cieurunce (mic/min)	

	I: 53 (21 – 81) C: 50 (22-101) Groups comparable at baseline? Yes					
Ratcliffe, 2009 Type of study: randomized controlled trial Setting: elective patients, 1 center Country: United States of America Source of funding: not reported	Inclusion criteria: 1) ambulatory or hospitalized patients who were scheduled for invasive coronary angiography or percutaneous coronary intervention for the evaluation and treatment of coronary artery disease 2) willing to participate in the study, and were able to understand and provide informed written consent 3) patients older than 18 years of age, with renal insufficiency defined by elevated serum creatinine (greater than 132.6 µmol/L in men, and greater than 114.9 µmol/L	Describe intervention (treatment/procedure/test): Iv 0.9% NaHCO3 hydration at an infusion rate of 3 mL/kg/h for 1 h before contrast, and continued at 1 mL/kg/h during the procedure and for 6 h following contrast exposure	Describe control (treatment/procedure/test): Iv 0.9% saline hydration at an infusion rate of 3 mL/kg/h for 1 h before contrast, and continued at 1 mL/kg/h during the procedure and for 6 h following contrast exposure	Length of follow-up: 72 hours Loss-to-follow-up: Intervention: 15/30 (50%) Reasons: 11 lack of complete follow-up 4 other reasons Control: 10/29 (30%) 8 lack of complete follow-up 2 other reasons Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase of greater than 25% in serum creatinine concentration from baseline to 72 h after administration of the contrast media) I: 2/19 (11%) C: 1/15 (7%) p>0.05	Authors' conclusion: CIN in high-risk patients may be effectively minimized solely through the use of an aggressive hydration protocol and an iso-osmolar contrast agent. The addition of NaHCO3 and/or NAC did not have an effect on the incidence of CIN.

in women) or		
reduced calculated		
creatinine		
clearance (less than		
1.002 mL/s) using		
the		
Cockcroft-Gault		
formula, and/or		
diabetes mellitus		
on oral antiglycemic		
or insulin therapy		
Exclusion criteria:		
1) pregnancy or		
lactation; 2) acute		
myocardial		
infarction;		
3) clinical signs of		
heart failure (or		
documented		
ejection fraction of		
less than 35%);		
4) cardiogenic		
shock; 5)		
hypertrophic or		
restrictive		
cardiomyopathy;		
6) contrast medium		
exposure within		
one week before		
the procedure;		
7) previous serious		
reactions to		
contrast medium;		
8) renal		
transplantation;		
dialysis; severe		

		comorbid illness; 9) use of dopamine,					
		mannitol or					
		fenoldopam; 10)					
		newly discovered					
		uncontrolled					
		diabetes mellitus;					
		11) the inability to					
		obtain informed					
		consent or follow-					
		up					
		N total at baseline:					
		Intervention:					
		Control:					
		<u>Important</u>					
		prognostic factors ² :					
		For example					
		age ± SD:					
		I: 67 ± 11					
		C: 64 ± 10					
		Sex:					
		I: 58% M					
		C: 60% M					
		Groups comparable					
		at baseline? Yes					
Recio-	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
Mayoral,	randomized	1) acute coronary	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
2007	controlled trial	syndrome (ACS)			3 days	(include 95%Cl and	
		patients who were				p-value if	Rapid intravenous
	Setting:	admitted to our	Active prophylactic treatment of	Standard treatment:	Loss-to-	available):	hydration with
	emergency	coronary care unit	PCI:	perfusion of isotonic saline (0.9%)	follow-up:		sodium
	patients, one	2) patients with	Intravenous bolus of 5 ml/kg/h of	at rate of 1 ml/kg/h for 12 h after	Not reported	CIN	bicarbonate plus
	hospital	myocardial	alkaline saline solution with 154	PCI plus 2 doses of 600 mg N-AC		(=an absolute	N-AC before

	infarction treated	mEq/I of sodium bicarbonate in 5%	orally the next day	<u>Incomplete</u>	increase in SCr	contrast injection
Country:	with primary PCI or	glucose and H2O (adding 77 ml of		<u>outcome</u>	concentration	is effective and
United	rescue PCI, as well	1,000 mEq/l sodium bicarbonate to		<u>data</u> :	of 0.5 mg/dl or	safe in
Kingdom	as patients with	433 ml of 5% glucose in H2O) plus		Not reported	more from baseline	the prevention of
	high-risk non–ST-	2,400 mg of N-AC in the same			value in the 3 days	CIN in patients
Source of	f segment elevation	solution over 1 hour the bolus was			after	undergoing
funding:	not ACS needing urgent	administered			PCI)	emergency PCI.
reported	revascularization	in the 60 min preceding contrast			I: 1/55 (2%)	
		injection			C: 12/55 (22%)	
	Exclusion criteria:	Afterward, patients received fluid			Odds ratio: 0.065	
	1) end-stage renal	therapy, without N-AC, at 1.5			(95% CI: 0.008 -	
	failure on dialysis,	ml/kg/h perfusion rate in the 12 h			0.521, p=0.01)	
	2) uncontrolled	after the procedure plus 2 doses of				
	hypertension	600 mg N-AC orally the next day			Acute anuric renal	
	(systolic blood				failure	
	pressure				I: 1/55 (2%)	
	>160 mm Hg and/or				C: 7/55 (13%)	
	diastolic blood				P=0.032	
	pressure >100 mm					
	Hg)					
	3) signs of cardiac					
	failure not					
	responding to					
	medical treatment,					
	4) known severe					
	aortic valve stenosis					
	(area >1.0 cm2),					
	5) allergy to iodated					
	contrast or NAC 6)					
	pregnancy					
	N total at baseline:					
	Intervention: 56					
	Control: 55					
	555					
	<u>Important</u>					
	prognostic factors ² :					

		For example					
		age ± SD:					
		I: 65 ± 10					
		C: 64 ± 9					
		0.0723					
		Sex:					
		I: 68% M					
		C: 71% M					
		Glomerular					
		filtration rate					
		(mL/min)					
		I: 75 ± 21					
		C: 74 ± 20					
		Groups comparable					
		at baseline? Yes					
	•	Sodium bicarbonate	short schedule versus saline long sche	dule for coronary angiography and/or	percutaneous int	ervention	
Briguori,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2007	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	chronic kidney			48 hours for	(include 95%CI and	
		disease who	154 mEq/L sodium bicarbonate in	Isotonic saline (0.90%) was given	laboratory	p-value if	The strategy of
	Setting:	underwent	dextrose and H2O,.	intravenously at a rate of 1 mL/kg	parameters	available):	volume
	elective	coronary and/or	The initial intravenous bolus was 3	body weight per hour	5 days for		supplementation
	patients, one	peripheral	mL/kg/h for 1 hour immediately	(0.5 mL/kg for patients with left	clnical events	CIN	by sodium
	hospital	angiography and/or	before contrast injection. After	ventricular ejection fraction _40%)		(=increase _25% of	bicarbonate plus
		angioplasty	this, patients received the same	for 12 hours before and 12 hours	Loss-to-	creatinine	NAC seems to be
	Country: Italy	2) _18 years of age	fluid at a rate of 1 mL/kg/h during	after administration of the contrast	follow-up:	concentration)	superior to the
		3) stable serum	contrast exposure and for 6 hours	agent.	Intervention:	I: 2/108 (2%)	combination of
	Source of	creatinine	after the procedure.		9/117 (8%)	C: 11/111 (10%)	normal saline with
	funding: not	concentration >2.0		NAC orally at a dose of 1200 mg	8 had no	P=0.02	NAC alone or with
	reported	mg/dL and/or or an	NAC orally at a dose of 1200 mg	twice daily on the day before and	follow-up sCr	5 16 3	the addition of
		estimated	twice daily on the day before and	the day of administration of the	value	Renal failure	ascorbic acid in
		glomerular	the day of administration of the	contrast agent (total of 2 days).	1 had no	requiring	preventing CIN in
		filtration rate <40	contrast agent (total of 2 days).		contrast	temporary dialysis:	patients at
		mL/ min/1.73 m ²			exposure	I: 1/108 (1%)	medium to high
						C: 1/111 (1%)	risk.

Exclusion criteria:	Control:	p-value not	
1) serum creatinine	7/118(6%)	reported	
levels >8 mg/dL,	7 had no	•	
2) a history of	follow-up sCr		
dialysis,	value		
3) multiple			
myeloma, 4)	<u>Incomplete</u>		
pulmonary edema,	<u>outcome</u>		
4) acute myocardial	data:		
infarction,	As above		
5) recent exposure			
to radiographic			
contrast within 2			
days of the study,			
6) pregnancy,			
7) administration of			
theophylline,			
dopamine,			
mannitol, or			
fenoldopam			
N total at baseline:			
Intervention: 111			
Control: 108			
<u>Important</u>			
prognostic factors ² :			
For example			
age ± SD:			
1: 70 ± 9			
C: 71 ± 9			
Com			
Sex:			
I: 88% M			
C: 81% M			
Groups comparable			
Groups comparable			

		at baseline? Yes					
Castini, 2008	Type of study: randomized controlled trial Setting: one hospital Country: Italy Source of funding: not reported	Yes Inclusion criteria: 1) patients undergoing coronary angiography and/or percutaneous coronary intervention 2) aged 18 years or older with stable serum creatinine levels ≥1.2 mg/dL Exclusion criteria: 1) serum creatinine levels >4 mg/dL, 2) a history of dialysis, 3) multiple myeloma, 4) pulmonary edema, 5) cardiogenic shock, 6) acute myocardial	Describe intervention (treatment/procedure/test): 154 mL of 1000 mEq/L SB added to 846 mL of 5% dextrose in H2O. The initial intravenous bolus was 3 mL/kg for 1 hour immediately before contrast injection. Thereafter, patients received the same fluid at a rate of 1 mL/kg per hour during contrast exposure and for 6 hours after the procedure.	Describe control (treatment/procedure/test): saline (0.9%) given intravenously at a rate of 1 mL/kg body weight per hour for 12 hours before and 12 hours after administration of the contrast agent	Length of follow-up: 5 days Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN1 (=an increase in serum creatinine concentration≥25% over the baseline value in any of the 3 predefined timepoints: 24 hours, 48 hours and 5 days) I: 7 (14%) C: 7 (14%) P>0.05 CIN2 (=the rate of an absolute increase in serum creatinine concentration ≥0.5 mg/dL at the same	Authors' conclusion: Our findings suggest that neither the addition of NAC nor the administration of SB add further benefit in CIN prevention, compared to standard hydration with isotonic saline infusion.
		infarction, 7) emergency catheterization, 8) recent exposure to radiographic				concentration ≥0.5 mg/dL at the same time-points) I: 6 (12%) C: 4 (8%) p>0.05	
		contrast media within 7 days of the study, 9) allergy to iodinate contrast media or NAC,				No patients required dialysis.	

		10) previous					
		enrollment in the					
		same or other					
		protocols, 11)					
		pregnancy,					
		12) administration					
		of theophylline,					
		mannitol,					
		dopamine,					
		dobutamine,					
		nonsteroidal anti-					
		inflammatory					
		drugs, or					
		fenoldopam.					
		Terioldoparri.					
		N total at baseline:					
		Intervention: 52					
		Control: 51					
		Control. 31					
		<u>Important</u>					
		prognostic factors ² :					
		For example					
		age ± SD:					
		I: 70 ± 8					
		C: 73 ± 8					
		Sex:					
		I: 85% M					
		C: 84% M					
		Groups comparable					
		at baseline? Yes					
Hafiz, 2012	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	coclusion:
	controlled trial	undergoing elective			48 hours	(include 95%CI and	
		coronary and	dextrose 5% in water containing	intravenous 0.9% normal saline		p-value if	Incidence of CI-
	Setting:	peripheral	154 mEq/L of NaHCO3 with or	with or without NAC	Loss-to-	available):	AKI was no

ala atius		ith aut NAC		f-11		d:ff=====t:==th==
elective	angiography and intervention.	without NAC	NAC was used in FOO/ of notice to	follow-up:	CI-AKI	different in the
patients, two		NAC	NAC was used in 50% of patients in	Not reported		NaHCO3 group
tertiary	2) serum creatinine	NAC was used in 50% of patients in	both study arms in a similarly		(=increase in serum	compared to
hospitals	>1.6 mg/dl in non-	both study arms in a similarly	randomized fashion as above;	<u>Incomplete</u>	creatinine	saline group, and
	diabetics and >1.4	randomized fashion as above;	1,200 mg was administered orally	<u>outcome</u>	concentration of	NAC did not
Country:	mg/dl in diabetics	1,200 mg was administered orally	2–12 hr before the procedure	<u>data</u> :	either >25% or >0.5	reduce CI-AKI in
United states	or an estimated	2–12 hr before the procedure	followed by another 1,200 mg oral	Not reported	mg/dl at 48 hr after	the two study
of america	glomerular	followed by another 1,200 mg oral	dose 6–12 hr after the procedure		the procedure)	arms.
	filtration rate	dose 6–12 hr after the procedure			I: 12%	
Source of	(eGFR) of <50				C: 9%	
funding: not	ml/min/1.73 m2,				p>0.05	
reported	calculated by the					
	Modification of Diet				There were no	
	in Renal Disease				deaths or major	
	(MDRD) formula				adverse effects	
	3) age >18 years				noted in our	
					patient population	
	Exclusion criteria:				during	
	(1) were on dialysis;				the study period.	
	(2) had unstable					
	renal function					
	(defined as change					
	in serum creatinine					
	of					
	>0.4 mg/dl within					
	48 hr prior to the					
	index procedure),					
	(3) had pulmonary					
	edema,					
	(4) had serum					
	bicarbonate level					
	>34 mmol/L;					
	(5) received					
	fenoldapam,					
	mannitol,					
	dopamine, or NAC					
	within 48 hr prior to					

		the index procedure; (6) were in cardiogenic shock, (7) were allergic to contrast media, (8) were pregnant, (9) were unable to provide informed consent. N total at baseline: Intervention: 159 Control: 161 Important prognostic factors ² : For example					
		Intervention: 159					
		Control: 161					
		For example					
		age (IQR): I: 74 (65-80)					
		C: 73 (63-80)					
		Sex: I: 56% M					
		C: 57% M					
		eGFR					
		I: 42 (32-51) C: 41 (33-50)					
		Groups comparable at baseline? Yes					
Klima, 2012	Type of study: randomized	Inclusion criteria: All patients	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow-up:	Outcome measures and effect size	Authors' conclusion:
	controlled trial	admitted with renal		tireatineing procedure/test).	48 hours	(include 95%CI and	COLICIUSIOII.
	Sotting:	dysfunction {actual serum creatinine	The initial intravenous bolus was 3 mL/kg/h of 166 mEq/L sodium	The infusion of 0.9% sodium chloride was administered at a	Loss-to-	p-value if available):	Volume
	Setting:	seruiii creatiiiiile	IIIL/ Ng/ II OI 100 IIIEY/ L SOUIUIII	chionide was administered at a	LU33-1U-	available).	supplementation

				•		
elective	level above the	bicarbonate for 1 h immediately	continuous rate of 1 mL/kg/h,	follow-up:		with 24 h sodium
patients,	upper limit of	before radiocontrast injection.	beginning from 8 p.m. on the day	Intervention:	CIN	chloride 0.9% is
multi-center	normal of the	Following this, patients received	before the procedure and for at	6/93 (6%)	(=an increase of	superior to
trial	serum creatinine	the same fluid at a rate of 1	least 12h after the procedure.	5 received no	≥25% or an	sodium
	(0.93 mmol/L for	mL/kg/h during the contrast		radiocontrast	increase of ≥44	bicarbonate for
Country:	women and .117	exposure and for 6 h after the		1 refused	μmol/L in the	the prevention of
Switzerland	mmol/L for men) or	procedure.		participation	baseline serum	CIN.
	estimated				creatinine	
Source of	glomerular			Control:	concentration	
funding:	filtration rate			4/93 (4%)	within 48 h)	
commercial	(eGFR) ,60			4 received no	1: 9%	
and non-	mL/min/1.73 m2			radiocontrast	C:1%	
commerzial	[eGFR calculated				P=0.02	
	using the			<u>Incomplete</u>		
	abbreviated			outcome	No patient	
	Modification of Diet			data:	experienced a	
	in Renal Disease			As above	serious adverse	
	(MDRD) study				event related to	
	equation16]}				the infusion (death,	
	scheduled to				intensive care unit	
	undergo an intra-				admission). Also,	
	arterial or				no patient required	
	intravenous				intravenous	
	radiographic				diuretics or nitrates	
	contrast procedure				due to pulmonary	
	on the next day				congestion.	
	Exclusion criteria:					
	1) age ≥18 years,					
	2) pre-existing					
	dialysis, allergy to					
	radiographic					
	contrast,					
	3) pregnancy,					
	4) severe heart					
	failure (NYHA					
	functional class III					

		and IV), 5) N-acetylcysteine ≤24 h before contrast, 6) clinical condition requiring continuous fluid therapy, e.g. severe sepsis					
		N total at baseline: Intervention: 87 Control: 89					
		Important prognostic factors ² : For example age median (IQR): I: 78 (70-82) C: 75 (70-82)					
		Sex: I: 66% M C: 62% M					
		eGFR ± SD I: 43 ± 11 C: 43 ± 12					
		Groups comparable at baseline? Yes					
Lee, 2011	Type of study: randomized controlled trial	Inclusion criteria: 1) patients undergoing	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow-up: 48 hours for laboratory	Outcome measures and effect size (include 95%Cl and p-value if	Authors' conclusion:
	Setting: elective	coronary or endovascular angiography or	Sodium bicarbonate infusion (154 mEq/L in dextrose and water) was	0.9% sodium chloride 1 ml/kg/hour for 12 hours before and after the	parameters 6 months for	available):	hydration with sodium

	Г	T	T	I	1	T	
	patients,	intervention	begun 1 hour before the start of	procedure	clinical	CIN	bicarbonate is not
	multicentre	2) serum creatinine	contrast injection, starting at 3		parameters	(=a ≥25% increase	superior to
	trial academic	≥1.1 mg/dl,	ml/kg/hour and decreasing to 1	All patients received NAC 1,200 mg		in serum creatinine	hydration with
	hospitals	estimated	ml/ kg/hour during the procedure	2 times/day for 2 days starting the	Loss-to-	concentration	sodium chloride in
		glomerular	and for 6 hours after completion of	day before the index procedure	follow-up:	or a ≥0.5 mg/dl	preventing CIN in
	Country:	filtration rate	the procedure		Intervention:	absolute increase	patients with
	Korea	(eGFR) ≤60			5/193 (3%)	in serum creatinine	diabetic
		ml/min/1.73 m ² ,			All had no	from baseline	nephropathy
	Source of	3) age ≥18 years,	All patients received NAC 1,200 mg		laboratory	within 48 hours	undergoing
	funding: not	4) diagnosis with	2 times/day for 2 days starting the		data	after contrast	coronary or
	reported	diabetes mellitus	day before the index procedure			exposure)	endovascular
					Control:	I: 17 (9%)	angiography or
		Exclusion criteria:			2/189 (1%)	C: 10 (5%)	intervention.
		1) inability to			All had no	P=0.17	
		obtain informed			laboratory		
		consent,			data	Requirement of	Infusion rates
		2) serum creatinine				hemodialysis	were decreased to
		≥8 mg/dl, eGFR ≤15				1: 4 (2%)	0.5 ml/kg/hour in
		ml/min/1.73 m ² at			Incomplete	C: 2 (1%)	patients with left
		rest,			outcome	P=0.69	ventricular
		end-stage renal			data:		ejection fraction
		disease on			As above	Rates of death,	≤45% in the 2
		hemodialysis,				myocardial	treatment arms.
		3) multiple				infarction, and	
		myeloma,				stroke did not	
		4) pulmonary				differ significantly	
		edema,				at 1 month and 6	
		5) uncontrolled				months after	
		hypertension				contrast exposure.	
		(systolic pressure				·	
		>160 mm Hg or					
		diastolic pressure					
		>100 mm Hg),					
		6) acute ST-					
		segment elevation					
		myocardial					
		infarction while					
L	1		1	l .	1	1	1

_		
undergoing primary		
percutaneous		
intervention,		
7) emergency		
coronary		
angioplasty or		
angiography,		
8) use of contrast		
media within the		
previous 2 days,		
9) pregnancy,		
10) allergy to		
contrast medium		
11) medications		
such as		
theophylline,		
dopamine,		
mannitol,		
fenoldopam, and		
NAC		
NAME OF THE OWNER O		
N total at baseline:		
Intervention: 193		
Control: 189		
<u>Important</u>		
prognostic factors ² :		
For example		
age median (IQR)		
I: 69 (63-73)		
C: 68 (67-72)		
Sex:		
I: 70% M		
C: 71% M		
eGFR:		

		I: 46 (34-53) C: 46 (37-53)					
		Groups comparable at baseline? Yes					
Maioli, 2008	Type of study: randomized controlled trial Setting: elective patients, one center Country: Italy Source of funding: not reported	· ·	Describe intervention (treatment/procedure/test): Sodium bicarbonate (154 mEq/l in dextrose and water) received 3 ml/kg for 1 h before contrast medium, followed by an infusion of 1 ml/kg/h for 6 h after the procedure. All patients received 600 mg oral NAC twice a day from the day before to the day after the procedure	Describe control (treatment/procedure/test): 1 ml/kg/h 0.9% sodium chloride for 12 h before and after the procedure	Length of follow-up: 5 days Loss-to-follow-up: Intervention: 4/252 (2%) 3 died 1 acute renal failure Control: 5/250 (2%) 4 died 1 acute renal failure Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an absolute increase of at least 0.5 mg/dl over baseline serum creatinine within 5 days after the administration of the contrast medium) I: 25 (10%) C: 29 (12%) P=0.60 CIN2 (=as a relative increase _25% over baseline serum creatinine within 5 days after contrast agent administration)	Authors' conclusion: Hydration with sodium bicarbonate plus NAC before contrast medium exposure is not more effective than hydration with isotonic saline plus NAC for prophylaxis of CIN in patients with moderate-to-severe renal dysfunction.
		Important prognostic factors ² : For example age median (IQR):				I: 15% C: 21% P=0.13	

		I: 74 (67-79) C: 74 (70-79) Sex: I: 57% M C: 61% M eGFR ± SD: I: 43 ± 11 C: 42 ± 10 Groups comparable at baseline? Yes				Death and acute renal failure, see column "Follow-up" for numbers, no significant difference in clinical events.	
Nieto-Rios,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors
2014	randomized	1) Inpatients in a	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	tertiary center,			5 days	(include 95%CI and	
		scheduled to	3 ml/kg of sodium bicarbonate	1 ml/ kg/hour of normal saline		p-value if	Our investigation
	Setting:	undergo a	solution (150 mEq/L) one hour	solution, starting 12 hours before	Loss-to-	available):	showed that there
	elective	procedure with the	prior to procedure and then drip	and continuing 12 hours after	follow-up:		were no
	patients,	nonionic	rate was decreased to 1 ml/	iohexol contrast	Intervention:	CIN	differences
	single center	radiographic	kg/hour until 6 hours post		7/107 (7%)	(= increase in	between normal
		contrast agent	procedure		3 died	serum creatinine	saline solution
	Country:	iohexol.			1 withdrawed	on 25% or more	(extended
	Colombia	2) serum creatinine levels of at least 1.2			3 technical	within 2 days after administration of	infusion) <i>vs.</i> bicarbonate
	Source of	mg/dL (106.1			difficulties	radiographic con-	solution for
	funding: not	μmol/L) and/or			unneuntes	trast)	nephroprotection.
	reported	type 2 diabetics,			Control:	I: 12 (12%)	nephroprotection.
	reported	type 2 diabetics,			1/113 (1%)	C: 8 (7%)	
		Exclusion criteria:			1 died	RR: 1.68, 95% CI:	
		1) current clinical			Taica	0.72 – 3.94	
		diagnosis of			Incomplete	p>0.05	
		exacerbated			outcome	F 1.00	
		congestive heart			data:	Decompensated	
		failure, 2) ejection			As above	heart failure	
		fraction <35% by				I: 3 (3%)	
		previous				C: 7 (6%)	

echocardiography,		P=0.34	
3) signs of acute		1 -0.54	
pulmonary edema			
within 48 hours			
before the			
procedure,			
4) systolic blood			
pressure <90 mmHg			
or requirement of			
vasopressors			
support,			
5) patients with			
exposure to			
contrast 30 days			
prior to the study,			
6) known allergy to			
contrast dye,			
7) chronic renal			
disease with dialysis			
therapy,			
8) criteria for			
dialytic urgency,			
9) pregnancy,			
10) requirement of			
an emergency			
procedure (e.g.,			
aortography for			
diagnosis of aortic			
aneurism),			
11) patients with			
serum potassium			
<3 mEq/L (because			
of the risk of			
hypokalemia			
induced by			
bicarbonate),			
12) uncompensated			

		T	T		T	T	т — — — — — — — — — — — — — — — — — — —
		diabetes mellitus					
		(four different					
		values >200 mg/dL					
		in the previous 24 hours)					
		13) patient or					
		physician refusal to					
		participate.					
		participate.					
		N total at baseline:					
		Intervention: 107					
		Control: 113					
		Lance and a set					
		Important					
		<u>prognostic factors</u> ² : For example					
		age ± SD:					
		I: 61 ± 17					
		C: 60 ± 17					
		Sex:					
		I: 57% M					
		C: 58% M					
		Baseline sCr					
		(mg/dL):					
		I: 1.3 ± 0.3					
		C: 1.3 ± 0.3					
		Groups comparable					
		at baseline? Yes					
Shavit,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2009	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	chronic kidney		,	2 days	(include 95%CI and	
		disease (CKD) stage	154 mEq/L sodium bicarbonate in	12-hour infusion of 154 mEq/L		p-value if	Hydration with
	Setting:	III–IV undergoing	5% dextrose in water mixed by	(0.9%) sodium chloride at a rate of	Loss-to-	available):	sodium
	elective	cardiac	adding 154 mL of 1,000 mEq/L	1 mL/kg per hour before cardiac	follow-up:		bicarbonate is not

patiens	ıs,	catheterization	sodium bicarbonate to 846 mL of	catheterization and NAC 600 mg ×	Intervention:	CI-AKI	more effective
single-	-center		5% dextrose in water. The initial IV	2/d	0 (0%)	(=an increase of	than hydration
		Exclusion criteria:	bolus was 3 mL/kg for 1 hour	orally the day before and the day		25% or 0.3 mg/dL	with sodium
Countr	ry: Israel	1) plasma	before cardiac catheterization.	of the procedure	Control:	or more in plasma	chloride and oral
		creatinine levels	Following this bolus, patients		5/41 (12%)	creatinine within	NAC for
Source	e of	more than	received the same fluid at a rate of		No	2 days of contrast	prophylaxis of CI-
funding	ng: not	8 mg/dL or eGFR	1 mL/kg per hour during the		laboratory	administration)	AKI in patients
reporte	ted	less than 15	contrast exposure and for 6 hours		evaluation at	I: 5/51 (10%)	with CKD stage III-
		mL/min, change in	after the procedure.		baseline or	C: 3/36 (8%)	IV undergoing
		plasma creatinine			after contrast	p>0.05	cardiac
		levels of ≥0.5 mg/dL	For patients weighing more than		exposure		catheterization.
		during the previous	110 kg, the initial fluid bolus and			CI-AKI2	
		24 hours,	drip were limited to those doses		<u>Incomplete</u>	(=an increase in	
		2) preexisting	administered to patients weighing		<u>outcome</u>	plasma creatinine	
		dialysis, multiple	110 kg.		<u>data</u> :	of 0.3 mg/dL or	
		myeloma,			As above	more from	
		3) pulmonary				baseline)	
		edema,				I: 17%	
		4) uncontrolled				C: 16%	
		hypertension				P>0.05	
		(systolic					
		>160 mmHg,				No patient	
		diastolic >100				developed more	
		mmHg),				than 50%	
		5) recent exposure				increment of	
		to radiographic				creatinine or	
		contrast, or other				required renal	
		nephrotoxic				replacement	
		medications (within				therapy during the	
		2 days of the				hospitalization.	
		study),					
		6) allergy to					
		radiocontrast,					
		7) pregnancy					
		N total at baseline:					
		Intervention: 51					

		Control: 36					
		Important prognostic factors ² : For example age ± SD: I: 72 ± 10 C: 71 ± 9					
		Sex: I: 84% M C: 70% M					
		eGFR (ml/min/1.73m ²) ± SD:					
		I: 43 ± 11 C: 40 ± 10					
		Groups comparable at baseline? Yes					
				for coronary angiography and/or percu	taneous interver		
Chong, 2015	Type of study: randomized controlled trial	Inclusion criteria: 1) adults >21 years of age; 2) glomerular	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow-up: 48 hrs	Outcome measures and effect size (include 95%Cl and p-value if	Authors' conclusion 'The combination
	Setting: University Heart Centre Country: Singapore	filtration rate (GFR) of 15–60 mL/min/1.73m2 – calculated by the abbreviated Modification	I1: High-dose oral NAC with a sustained intravenous sodium chloride infusion (NAC group) I2: Intravenous sodium bicarbonate infusion (SOB	C1: Oral NAC and abbreviated intravenous sodium bicarbonate infusion (COM group)	Loss-to- follow-up: I1: 28/185 I2: 29/182 C1: 25/181	available): CIN, which was defined as ≥25% increase of serum Cr concentration	regimenwas not superior to individual regimens in preventing CIN in patientswith
	Source of funding: not reported	of Diet in Renal Disease (MDRD) formula – 3) scheduled to undergo elective	group)		Death: I1: 0/185 I2: 1/182 C1: 2/181	or a ≥44 µmol/L (0.5mg/dL) increase in serum Cr within 48 h of cardiac	baseline renal impairment. There was a trend suggesting that the 12-hour

cardiac		catheterisation	sustained sodium
catheterisation with		or PCI	chloride
or without PCI		. .	prehydration
4) were able to		I1: 6.5%	regimen was more
receive pre-		12: 12.8%	protective than
hydration for 12 h.		C1: 10.6%	the 1-hour
Trydration for 12 ii.		P=0.214	abbreviated SOB
Exclusion criteria:		F-0.214	regimen.'
1) end-stage renal			regimen.
failure with GFR of			
b15 mL/min/1.73			
m2, acute renal failure			
with a N44 μmol/L			
increase in serum			
Cr levels in the			
previous 24 h;			
2) pre-existing			
dialysis;			
3) pulmonary			
oedema or			
moderate to severe			
congestive heart			
failure			
(New York Heart			
Association III–IV);			
4) inability to			
withstand the fluid			
load;			
5) presence			
of haemodynamic			
compromise,			
uncontrolled			
hypertension			
(untreated systolic			
blood pressure			
N160mmHg, or			
14100111111116, 01			1

diastolic blood		
pressure		
N100mmHg)		
6) emergency		
cardiac		
catheterisation		
7) exposure to		
contrast in the		
previous two days;		
8) allergies to		
contrast or NAC;		
9) administration of		
sodium bicarbonate		
or NAC within 48 h		
of cardiac		
catheterisation;		
10) clinical		
conditions requiring		
continuous fluid		
therapy such as		
severe sepsis;		
11) Use of		
potentially renal-		
toxic drugs;		
12) cisplatin within		
48 h of cardiac		
catheterisation and		
throughout the		
study		
duration;		
<u>Important</u>		
prognostic factors ² :		
For example		
age ± SD:		
I: 69 ± 10		
12: 71 ± 10		

		C: 67 ± 10					
		Sex:					
		11: 72% M					
		11. 72% M 12: 78% M					
		C: 78% M					
		C. 70% IVI					
		Groups comparable					
		at baseline? Yes					
Motohiro,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2011	randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
2011	controlled trial	undergoing	(treatment/procedure/test).	(treatment/procedure/test).	1 months	(include 95%Cl and	CONCIUSION
	controlled trial	coronary	0.9% sodium chloride for 12 hours	0.9% sodium chloride for 12 hours	1 1110111115	p-value if	Sodium chloride
	Setting:	angiography or	before and after the procedure.	before and after the procedure.	Loss-to-	available):	plus sodium
	elective	intervention	before and after the procedure.	before and after the procedure.	follow-up:	avaliable).	bicarbonate is
	patient, 2	2) ≥20 years old	Sodium bicarbonate solution was		Intervention:	CIN	more effective
	hospitals	3) had an estimated	prepared by adding 154 ml of		2/79 (2%)	(=25% increase or	than sodium
	Hospitals	glomerular	sodium bicarbonate 1,000 mEg/L		No	an absolute	chloride alone for
	Country: Japan	filtration rate	to		laboratory	increase of	prophylaxis of CIN
	Country, Japan	(eGFR) <60	846 ml of 5% dextrose in water. In		test results	0.5 mg/dl in	and can lead to
	Source of	ml/min/1.73 m ²	the sodium bicarbonate group the		test results	serum creatinine	retention of
	funding: not	1111/111111/11.75 111	sodium bicarbonate gloup the		Control:	from baseline	better long-term
	reported	Exclusion criteria:	changed 3 hours before contrast		1/79 (1%)	value, which	renal function.
	reported	1) serum creatinine	administration		Angialgia	appeared within 2	Tellai fullction.
		levels >4 mg/dl,	administration		due to	days of the	
		2) changes in serum			sodium	produce)	
		creatinine levels of			bicarbonate	I: 2 (3%)	
		≥0.5 mg/dl during			infusion	C: 10 (13%)	
		the previous 24			iiiusioii	P=0.02	
		hours,			Incomplete	relative risk 0.176,	
		3) pre-existing			outcome	95% confidence	
		dialysis,			data:	interval	
		4) pulmonary			As above	0.037 to 0.83	
		edema,			As above	0.037 10 0.03	
		,				No nationt required	
		5) uncontrolled				No patient required	
		hypertension (treated systolic				Hemodialysis.	
		(treated systolic					

blood pressure >160 mm Hg or diastolic blood pressure >100 mm Hg), 6) emergency catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium N total at baseline:	
diastolic blood pressure >100 mm Hg), 6) emergency catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
pressure >100 mm Hg), 6) emergency catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
Hg), 6) emergency catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
6) emergency catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
catheterization, 7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
7) exposure to radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
radiographic contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
contrast within previous 2 days, 8) any allergy to radiographic contrast medium	
previous 2 days, 8) any allergy to radiographic contrast medium	
2 days, 8) any allergy to radiographic contrast medium	
8) any allergy to radiographic contrast medium	
radiographic contrast medium	
contrast medium	
N total at baseline:	
N total at baseline:	
Intervention: 77	
Control: 78	
<u>Important</u>	
prognostic factors ² :	
For example	
age ± SD:	
1: 74 ± 7	
C: 71 ± 9	
Sex:	
I: 64% M	
C: 76% M	
Groups comparable	
at baseline? Yes	
, , , , , , , , , , , , , , , , , , ,	ıthors'
	nclusion
controlled trial were scheduled for 3 days (include 95%Cl and	
elective coronary Standard hydration with sodium Standard hydration with sodium p-value if In co	

Setting:	arteriography or	chloride plus single-bolus	chloride alone	Loss-to-	available):	single-bolus
elective	percutaneous	intravenous administration of	Chloride alone	follow-up:	avaliable).	intravenous
patients, two	coronary	sodium bicarbonate (20 ml /20	(=intravenous administration with	All patients	CIN	administration of
	intervention	•	1 *		(=an increase ≥25%	sodium
hospitals		mEq; Meyron 84, Otsuka	isotonic saline (0.9%) at a rate of 1	completed	,	bicarbonate in
Carrata a la man	2) age >20 years	Pharmaceutical,	ml/kg/hour (0.5 ml/kg/hour for	the study	or ≥0.5 mg/dl in serum Cr within the	
Country: Japan	3) serum creatinine	Inc., Tokyo, Japan) 5 minutes	patients with left ventricular			addition to
	(Cr) level >1.1 to	before contrast exposure	ejection fraction <40%) for 12	<u>Incomplete</u>	first 3 days after	standard
Source of	<2.0 mg/dl.		hours before and 12 hours after an	<u>outcome</u>	the procedure	hydration can
funding: not			elective coronary procedure. For	<u>data</u> :	compared to	more effectively
reported	Exclusion criteria:		patients weighing >80 kg, infusion	All patients	baseline value)	prevent CIN than
	1) allergy to		rate was limited to 80 ml/hour (40	completed	I: 1.4%	standard
	contrast medium,		ml/hour for patients with left	the study	C: 12.5%	hydration alone in
	pregnancy,		ventricular ejection fraction _40%).		P=0.017	patients with mild
	2) history of					renal insufficiency
	dialysis,				Adverse clinical	undergoing an
	3) exposure to				events (acute	elective coronary
	contrast-medium				pulmonary edema,	procedure.
	within the				acute renal failure	
	preceding 48 hours				requiring dialysis,	
	of the study,				and death within 7	
	4) acute coronary				days of procedure)	
	syndrome within				1: 0%	
	the preceding 1				C: 1.4%	
	month of the study,				p>0.05	
	5) severe symptoms					
	of heart failure					
	(New York Heart					
	Association					
	functional class IV),					
	6) left ventricular					
	ejection fraction					
	>25%,					
	7) severe chronic					
	respiratory disease,					
	8) single					
	functioning kidney,					
	9) administration of					
	J, danimistration of			I	1	1

		N-acetylcysteine, theophylline, dopamine, or mannitol					
		N total at baseline: Intervention: 72 Control: 72					
		Important prognostic factors ² : For example age \pm SD: I: 73 \pm 8 C: 72 \pm 10					
		Sex: I: 83% M C: 92% M					
		Groups comparable at baseline? Yes					
Turedi, 2016	Type of study: randomized controlled trial	Inclusion criteria: 1) Undergoing contrastenhanced thoracic CT due to	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Length of follow-up: 48-72 hrs	Outcome measures and effect size (include 95%CI and p-value if	Authors' conclusion
	Setting: academic emergency center	suspected PE; 2) aged over 18 years; 3) with measure-	I1: 3 mL/kg intavenous NAC+NS solution (3 g NAC was made up to 1000 mL with NS),	C1: NS alone 1 hour before CTPA and 1 mL/kg intavenous per hour for a minimum of 6 hour after CTPA.	Loss-to- follow-up: I1: 7/85 I2: 8/85	available): CIN development creatinine levels	there were no statistically significant differences
	Country: Turkey	able basal creatinine levels pretomography and;	I2: NaHCO3 + NS solution (132 mEq NaHCO3 was made up to 1000 mL with NS)		C1: 11/87 Death: I1: 4/85	and post-CTPA creatinine levels measured 48–72 hours	observed among prophylactic NAC, NaHCO3, and NS
	Source of funding: not reported	4) measureable serum creatinine levels 48–72 hours			12: 2/85 C1: 6/87	following contrast exposure and an increase	in prevention of CIN following contrast-enhanced

	posttomography,		≥25% or 0.5 mg/dL	CTPA.'
	and with one or		223/0 OF 0.3 HIg/UL	CITA.
	more of the		I1: 23.5%	
	risk factors for CIN.		I2: 21.2%	
	The risk		C1: 26.4%	
	factors were		P=0.719	
			P-0.719	
	preexisting renal			
	dysfunction (Cr 1.4			
	mg/dL or a high or			
	calculated			
	glomerular			
	filtration rate			
	[GFR] < 60			
	mL/min/1.73 m ²),			
	diabetes mellitus,			
	hypertension			
	receiving			
	treatment,			
	hypotension			
	(systolic blood			
	pressure < 90 mm			
	Hg), coronary artery			
	disease, history of			
	nephrotoxic drug			
	use (nonsteroidal			
	anti-inflammatory			
	drugs, cisplatin,			
	aminoglycoside,			
	amphotericin B),			
	liver disease,			
	congestive heart			
	failure (active or			
	history thereof),			
	age 75 or over, and			
	anemia (hematocrit			
	< 30%).			
	,			

	Exclusion criteria:
	1) end-stage renal
	disease already in
	peritoneal dialysis;
	2) hemodialysis;
	3) pregnant
	women;
	4) subjects with a
	known allergy to
	NAC or NaHCO3;
	5) patients
	requiring NAC
	therapy or NaHCO3
	therapy
	for existing
	additional disease;
	6) exposed to
	contrast
	material for any
	reason in the
	previous 10 days or
	7) during the in-
	hospital follow-up
	period
	8) patients
	who refused to
	participate
	<u>Important</u>
	prognostic factors ² :
	For example
	age ± SD:
	I: 76 (72-80)
	12: 77 (71-80)
	C: 74 (73-76)
	Sex:
l l	

		I1: 48% M I2: 51% M C: 53% M Groups comparable at baseline? Yes					
Ueda, 2011	Type of study: randomized controlled trial Setting: emergency patients, single center Country: Japan Source of funding: not reported	Inclusion criteria: 1) patients undergoing an emergent (within 60 minutes of admission) diagnostic or interventional coronary procedure, such as coronary angiography or percutaneous coronary intervention 2) >20 years old 3) had renal insufficiency, defined by a serum creatinine (Cr) concentration of >1.1 mg/dl or estimated glomerual filtration rate (eGFR) of <60 ml/min Exclusion criteria: 1) change in the serum Cr	Describe intervention (treatment/procedure/test): Intravenous bolus injection of 154 mEq/L of sodium bicarbonate at a dose of 0.5 ml/kg, as soon as possible after they were admitted, before the administration of the contrast medium Intravenous infusion of 154 mEq/L sodium bicarbonate at 1 ml/kg/hour during and for 6 hours after the coronary procedure	Describe control (treatment/procedure/test): Intravenous bolus injection of 154 mEq/L of sodium chloride at a dose of 0.5 ml/kg, as soon as possible after they were admitted, before the administration of the contrast medium Intravenous infusion of 154 mEq/L sodium bicarbonate at 1 ml/kg/hour during and for 6 hours after the coronary procedure	Length of follow-up: 2 days Loss-to-follow-up: Intervention: 0 (0%) Control: 1/30 (3%) Circulatory failure Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase by >25% or >0.5 mg/dl of the serum creatinine level within 2 days after the procedure) I: 1 (3%) C: 8 (28%) RR: 0.12, 95% Cl: 0.016 – 0.91 P=0.01 Congestive heart failure I: 5/30 (17%) C: 6/29 (21%) p>0.05 Death I: 2/30 (7%) C: 2/29 (7%) p>0.05	Authors' conclusion In conclusion, rapid alkalization by bolus injection of sodium bicarbonate was effective for the prevention of CIN in patients with CKD undergoing emergent procedures.
		concentration of				No patients	

Т		T	
	>0.5 mg/dl during		developed acute
	the 24 hours before		renal failure
	the procedure,		requiring
	2) pre-existing		hemodialysis.
	dialysis, exposure		
	to the contrast		
	media within 2 days		
	before the study,		
	3) allergy to the		
	contrast media,		
	pregnancy,		
	4) previous or		
	planned		
	administration of		
	mannitol,		
	fenoldopam, N-		
	acetylcysteine,		
	theophylline,		
	dopamine, or		
	nonstudy sodium		
	bicarbonate		
	N total at baseline:		
	Intervention: 30		
	Control: 29		
	<u>Important</u>		
	prognostic factors ² :		
	For example		
	age ± SD:		
	1: 77 ± 9		
	C: 75 ± 10		
	Sex:		
	I: 79% M		
	C: 77% M		
	I I	I I	

		sCr (mg/dL) ± SD: I: 1.32 ± 0.46 C: 1.51 ± 0.59					
		Groups comparable at baseline? Yes					
	1			saline long schedule for computed to		T	1
Kooiman, 2014	Type of study: randomized	Inclusion criteria: 1) In- and	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	<u>Length of</u> <u>follow-up</u> :	Outcome measures and effect size	Authors' conclusion
	controlled trial	outpatients			96 hours	(include 95%CI and	
		electively	250 mL intravenous 1.4% sodium	2000 mL of intravenous 0.9%		p-value if	Short hydration
	Setting:	scheduled for CE-CT	bicarbonate 1 h prior to CE-CT	saline, 1000 mL prior to and 1000	Loss-to-	available):	with sodium
	elective	regardless of the	without hydration post-CE-CT	mL post-CE-CT	follow-up:		bicarbonate prior
	patients,	indication			Intervention:	CI-AKI	to CE-CT was non-
	multi-center	2) least 18 years of			15/267(6%)	(=serum creatinine	inferior to peri-
	trial	age, had CKD (eGFR			2 treated	increase >25%/>44	procedural saline
		<60 mL/min/1.73			according to	μmol/L (0.5 mg/dL)	hydration with
	Country: the	m ² estimated by			protocol	I: 8 (3%)	respect to renal
	Netherlands	the Modification of			5 CT without	C: 14 (5%)	safety and may
		Diet in Renal			iv contrast	P=0.23	result in
	Source of	Disease formula			6 CT		healthcare
	funding: non-	3) eligible for the			cancelled and	Recovery of kidney	savings.
	commercial	fluid challenge of			no hydration	function:	
		saline hydration				I: 75%	
					Control:	C: 69%	
		Exclusion criteria:			20/281 (7%)	P=0.81	
		1) pregnancy,			7 treated		
		2) previous contrast			according to	Acute heart failure	
		administration			protocol	due to volume	
		within the last 7			7 CT	expansion (based	
		days,			cancelled and	on the	
		3) documented			no hydration	treating physician's	
		allergy for			4 CT without	clinical judgement)	
		iodinated contrast			iv contrast	occurred in none of	
		media,			2 treated	the patients in the	
		4) haemodynamic			with sodium	sodium	
		instability (systolic			bicarbonate	bicarbonate group	

		blood pressure <100 mmHg) 5) previous participation in the trial N total at baseline: Intervention: 267 Control: 281 Important prognostic factors ² : For example age ± SD: I: 72 ± 10 C: 73 ± 10 Sex: I: 60% M C: 61% M Mean eGFR: I: 50 ± 13 C: 51 ± 14 Groups comparable at baseline? Yes			Incomplete outcome data: As above	versus 6 of 281 patients in the saline group (P = 0.03) None of the CI-AKI patients developed a need for dialysis.	
		at baseline? Yes	Controlled digresis for coronary angi	ography and/or percutaneous interven	l ition		
Barbanti,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2016	randomized controlled trial	1) All patients with symptomatic severe	(treatment/procedure/test):	(treatment/procedure/test):	follow-up: 78 hrs	and effect size (include 95%CI and	conclusion
	Setting: university hospital	aortic stenosis undergoing TAVI were considered eligible Exclusion criteria:	RenalGuard therapy received hydration with a normal saline solution; with an initial bolus (priming) of 250 ml was infused over 30 min (preprocedural. Urine	control group received sodium normal saline solution at a rate of 1 ml/kg/h 12 h before TAVR, during contrast exposure, and for 6 h after the	Loss-to- follow-up: No loss to follow-up	p-value if available): AKI (defined: absolute	'In summary, furosemide- induced diuresis with matched isotonic

Country: Italy	1) chronic end-	flow was monitored and	procedure.	reduction in kidney	intravenous
	stage renal failure	maintained at the target value		function (<72 h)	hydration using
Source of	on dialysis;	throughout the procedure		and defined as: 1)	the RenalGuard
funding: not	2) episode of acute	and during the following 4 h.		stage 1: increase in	system
reported	congestive heart	phase).		serum creatinine to	is an effective
	failure with left			150% to 200% (1.5	therapeutic tool to
	ventricular ejection			to 2.0x increase	reduce the
	fraction <30% in the			compared with	occurrence of AKI
	past 30 days			baseline) or	in patients
	before			increase of >0.3	undergoing TAVR.'
	randomization;			mg/dl (≥26.4	
	3) contraindica-			mmol/l); 2) stage 2:	
	tions to placement			increase in serum	
	of a Foley catheter;			creatinine to 200%	
	4) urgent TAVI			to 300% (2.0 to	
	5) unavailability of			3.0x increase	
	the RenalGuard			compared with	
	system.			baseline); and 3)	
				stage 3: increase in	
	<u>Important</u>			serum creatinine to	
	prognostic factors ² :			≥300% (>3_	
	For example			increase compared	
	age ± SD:			with baseline) or	
	I: 82 (78-83)			serum creatinine of	
	C: 81 (78-84)			≥4.0 mg/dl	
				(≥354 mmol/l) with	
	Sex:			an acute increase	
	I: 61% F			of at least 0.5	
	C: 59% F			mg/dl (44 mmol/l).)	
	Serum creatine ± SD			I: 4 (5.4%)	
	I: 1.0 (0.85-1.15)			C: 13 (25.2%)	
	C: 0.97 (0.83-1.16)			RR: 0.21, 95% CI:	
	, ,			0.06 - 0.71	
	Groups comparable			P=0.014	
	at baseline? Yes				
				Cardiovascular	

	, do not be
	death
	1: 0/56(0%)
	C: 1/56 (1.8%)
	P=0.306
	Death
	I: 1/56 (1.8%)
	C: 2/56 (3.6%)
	P=0.537
Brar, 2014 Type of study: <u>Inclusion criteria</u> : Describe interve	
randomized 1) patients referred (treatment/prod	
controlled trial to the cardiac	2-8 weeks for (include 95%Cl and
catheterisation	laboratory p-value if Left ventricular
, , , , , , , , , , , , , , , , , , , ,	The state of the
-/ -/ -/ -/ -/ -/ -/ -/ -/ -/ -/ -/ -/	manage of the same
patients, 1 glomerular fi 3 mL/kg for 1 h	1 , 0
center Itration rate (GFR)	events (=a greater than seems to be safe
of 60 mL/min per 1 The fl uid rate w	•
Country: • 73 m ² or lower; according to the	
, , ,	sure as follows: 5 of the procedure (before contrast follow-up: serum creatinine contrast-induced
of America older; mL/kg/h for left	
4) at least one of diastolic pressur	
Source of the following: mmHg,	4 h post-procedure. C: 28/172 (16%) undergoing
funding: not diabetes mellitus, 3 mL/kg/h for pr	
reported history of mmHg, and	0 (0%) $0.22 - 0.79$, catheterisation.
congestive heart 1.5 mL/kg/h for	ressure higher p=0.005
failure, than 18 mmHg.	ne fl uid rate was <u>Incomplete</u>
hypertension set at the start of	the procedure outcome 6-months mortality
(blood pressure (before contrast	xposure), data: I: 0.5%
>140/90 mm Hg or continued for th	duration of the Intervention: C: 4%
treatment with procedure, and	
antihypertensive procedure.	12 had 1 sCr
medication), or age	value No significant
older than 75 years.	6 had no sCr difference in other
	value adverse clinical
Exclusion criteria:	events at 30 days
1) inability to	Control: or 6 months

Г	<u> </u>	T	1
	obtain consent	28/200 (14%)	
	from participants,	24 had 1 sCr	In total, six patients
	2) emergency	value	(1 • 5%)—three in
	cardiac	4 had no sCr	each group—
	catheterisation (eg,	value	terminated the
	primary		intravenous fl uids
	percutaneous		early, the reason
	coronary		for which was
	intervention for ST-		shortness of breath
	segment elevation		in all six patients.
	myocardial		
	infarction),		
	3) renal		
	replacement		
	therapy,		
	4) exposure to		
	radiographic		
	contrast media		
	within the previous		
	2 days,		
	5) allergy to		
	radiographic		
	contrast media,		
	6) acute		
	decompensated		
	heart failure,		
	7) severe valvular		
	heart disease,		
	8) mechanical		
	aortic prosthesis,		
	9) left ventricular		
	thrombus,		
	10) history of		
	kidney or heart		
	transplantation,		
	11) change in		
	estimated GFR of		
	commuted of it of		<u>l</u>

		7.5% or more per day or a cumulative change of 15% or more during the pre ceding 2 or more days. N total at baseline: Intervention: 196 Control: 200 Important prognostic factors²: For example age ± SD: I: 71 ± 9 C: 72 ± 8 Sex: I: 64% M C: 59% M eGFR ± SD I: 48 ± 9 C: 48 ± 9 Groups comparable at baseline?					
Briguori,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2011	randomized controlled trial	patients with chronic kidney	(treatment/procedure/test):	(treatment/procedure/test):	follow-up: 1 week	and effect size (include 95%CI and	conclusion:
	Some officer trial	disease scheduled	hydration with normal saline plus	154 mEq/L sodium bicarbonate in		p-value if	RenalGuard
	Setting:	for coronary and/or	NAC controlled by the RenalGuard	dextrose and H2O.	Loss-to-	available):	therapy is
	elective	peripheral	system	The initial intravenous bolus was 3	follow-up:		superior to
	patients,	angiography and/or		mL/kg per hour for at least 1 hour	0 (0%) in	CI-AKI	sodium
	multicenter	angioplasty with an	NAC was administered only iv	before contrast injection. Then, all	both groups	(=an increase in sCr	bicarbonate and
		estimated	(1500 mg in 1L saline) during the 3	patients received the same fluid at		concentration ≥0.3	N-acetylcysteine

	Т.	Ι	1	T	T	T
Country: Italy	glomerular	phases (preprocedural,	a rate of 1 mL/kg per hour during	<u>Incomplete</u>	mg/dL above the	in preventing
	filtration rate	intraprocedural, and	contrast exposure and for 6 hours	<u>outcome</u>	baseline value at 48	contrast-induced
Source of	(eGFR) ≤30mL	postprocedural) of the RenalGuard	after the procedure.	<u>data</u> :	hours after	acute kidney
funding: not	/min/ 1.73 m ²	therapy.		Intervention:	administration of	injury in high-risk
reported	and/or a risk score		NAC orally at a dose of 1200 mg	0 (0%)	Contrast or the	patients.
	≥11)		twice daily the day before and the		need fordialysis)	
			day of administration of the	Control:	I: 16/146 (11%)	
	Exclusion criteria:		contrast agent (for a total of 2	3/147 (2%)	C: 30/146 (21%)	The risk score for
	1) acute myocardial		days)	2	Odds ratio: 0.47,	predicting CI-AKI
	infarction;		additional NAC dose (1200 mg	discontinued	95% CI 0.24 – 0.92	was calculated
	2) acute pulmonary		diluted in 100 mL normal	treatment	P<0.05	according to the
	edema;		saline) was administered	1 did not		following
	3) cardiogenic		intravenously during the	receive		algorithm:
	shock;		procedure.	allocated		hypotension
	4) dialysis;		The total NAC dose was 6 g.	treatment		(integer score 5),
	5) multiple					intra-aortic
	myeloma;					balloon pump
	6) administration of					support (integer
	sodium					score 5),
	bicarbonate,					congestive heart
	theophilline,					failure (integer
	dopamine,					score 4), age >75
	mannitol,					years (integer
	and/or					score 4), diabetes
	fenoldopam;					mellitus (integer
	7) recent (<48					score 3), eGFR _60
	hours)					mL/min/1.73 m ²
	administration of					(integer score 2 to
	iodinated contrast					6), preexisting
	medium					anemia(integer
	8) enrollement in					score 3), and CM
	another study					volume (integer
						score 1 for each
	N total at baseline:					100 cm ³).
	Intervention: 146					The global scores
	Control: 146					≥5, 6 to 10, 11 to
						16, and _16
L	1			I	1	10, 4114 _10

		Important prognostic factors ² : For example age ± SD: I: 76 ± 8 C: 75 ± 9 Sex: I: 61% M C: 71% M eGFR ± SD: I: 32 ± 7 C: 32 ± 9					predict a CI-AKI risk of 7.5%, 14%, 26.1%, and 57.3%, respectively.
		Groups comparable at baseline? Yes					
Marenzi,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2012	randomised	1) age ≥18 years	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	and ≤85 years, and	,	,	72 hours	(include 95%Cl and	
		elective or urgent		continuous intravenous infusion of		p-value if	In patients with
	Setting:	(within 24 h from	Approximately 90 min before the	isotonic saline at a rate of 1	Loss-to-	available):	CKD undergoing
	elective and	hospital admission	coronary procedure, Furosemide	ml/kg/h (0.5ml/kg/h in case of left	follow-up:		coronary
	emergency	because of non–ST-	with matched hydration treatment	ventricular ejection fraction ≤40%)	Intervention:	CIN	procedures,
	patients	segment elevation	was started with an initial	for at least 12 h before and 12 h	2/89 (2%)	(=a ≥25% or ≥0.5	furosemide-
		[acute] myocardial	intravenous bolus (250 ml) of	after the procedure.	Failed to	mg/dl rise in serum	induced high urine
	Country: Italy	infarction	normal saline solution over 30 min.		insert foley	creatinine over	output with
		[NSTEMI]) coronary	Furosemide was then administered		catheter	baseline during the	matched
	Source of	angiography and,	as a single intravenous bolus of 0.5			first 72 h post-	hydration
	funding: not	when indicated,	mg/kg (up to a maximum of 50		Control:	procedure)	significantly
	reported	percutaneous	mg).		2/85 (2%)	I: 4 (5%)	reduces the risk of
		coronary	Urine output was calculated		Withdrawal	C: 15 (18%)	CIN and may be
		intervention (PCI).	continuously by the system, and		of treatment	P=0.005	associated with
			when a urine output rate >300		due to	_	improved in-
		Exclusion criteria:	ml/h was achieved, patients were		pulmonary	Cumulative in-	hospital outcome.
		1) primary or	brought to the catheterization		edema	hospital	
		rescue PCI and	laboratory and underwent			complications	

angiography coronary angiography. Matched <u>Incomplete</u> I: 8%	
procedures hydration was continued outcome C: 18%	
requiring a direct throughout the catheterization <u>data</u> : P=0.052	
renal injection of procedure and for 4 h after the last As described	
contrast, contrast dose. At this time, therapy above)	
2) cardiogenic was discontinued.	
shock, overt Additional doses of furosemide (up	
congestive heart to a maximal cumulative dose of	
failure, 2.0 mg/kg) were given in cases	
3) acute respiratory where the urine output was below	
insufficiency, 300 ml/h during treatment. The	
4) recent acute Foley catheter was removed 24 h	
kidney injury, after the procedure.	
5) chronic	
peritoneal	
or hemodialysis	
treatment,	
6) known	
furosemide	
hypersensitivity,	
7) receipt of	
intravenous	
contrast within 10	
days before the	
procedure or	
another planned	
contrast-enhanced	
procedure in the	
following 72 h,	
8) contraindications	
to placement of a	
Foley catheter in	
the bladder.	
N total at baseline:	
Intervention: 87	
Control: 83	

Qian, 2016	Type of study: randomised controlled trial Setting: elective patients, multiple centers Country: Japan Source of funding: not reported	Important prognostic factors²: For example age ± SD: I: 73 ± 7 C: 74 ± 8 Sex: I: 78% M C: 78% M eGFR ± SD: I: 1.8 ± 0.6 C: 1.7 ± 0.5 Groups comparable at baseline? Yes Inclusion criteria: 1) patients with CKD and chronic heart failure undergoing coronary procedures Exclusion criteria: - N total at baseline: Intervention: 132 Control: 132 Groups comparable at baseline? Yes	Describe intervention (treatment/procedure/test): Central-venous pressure guided hydration group	Describe control (treatment/procedure/test): Standard hydration group	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase by >25% or >0.5 mg/dl of the serum creatinine level within 2 days after the procedure) I: 16% C: 30% P=0.006 Acute heart failure: I: 3.8%	Authors' conclusion: Controlled vnous pressure guided fluid administration can safely and effectively reduce the risk of CIN in patients with CKD and chronic heart failure.
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						C: 3.0% P=0.50	
Usmiani,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2015	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	chronic kidney	(**************************************	(, , , , , , , , , , , , , , , , , , ,	2 days	(include 95%CI and	
		disease (CKD)	iv 250 mL isotonic saline bolus,	Standard saline and bicarbonate	,	p-value if	In patients with
	Setting:	undergoing	followed by a 0.5 mg/kg	hydration	Loss-to-	available):	CKD undergoing
	elective	coronary	furosemide i.v. bolus to forced	•	follow-up:	,	coronary
	patients	procedures	diuresis. A dedicated device		Not reported	CI-AKI	procedures,
			automatically matched the isotonic		·	(=an increase by	furosemide-
	Country: Brazil	Exclusion criteria:	saline i.v. infusion rate to the		Incomplete	>25% or >0.5 mg/dl	induced high urine
		-	urinary output for 1 h before,		<u>outcome</u>	of the serum	output with
	Source of		during and 4h after the procedure.		<u>data</u> :	creatinine level	matched
	funding: not	N total at baseline:			Not reported	within 2 days after	hydration
	reported	Intervention: 65				the procedure)	significantly
		Control: 68				I: 7%	reduces the risk of
						C: 25%	CIN and may be
						P=0.01	associated with
		Groups comparable					improved in-
		at baseline? Yes				Major adverse	hospital outcome.
						cardiovascular	
						events	
						1: 7%	
						C: 32%	
						P<0.01	
Usmiani,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2016	randomized	1) Elgibile for voth	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled trial	procedures 2) eGFR			7 days	(include 95%CI and	(2.5.) (
	6	of less than 60 mL/	Matched hydration was to be	BS-NAC intravenous hydration		p-value if	'Matched
	Setting:	min/1.73m2	performed with the Renal-	(isotonic saline/	Loss-to-	available):	hydration was
	university	Freely of an authority	Guard System.	N-acetylcysteine/vitamin C)	follow-up:	A 1/1	more effective
	hospital	Exclusion criteria:	250 ml i u icatania salina	1000!	9 loss to	AKI	than BS-NAC in CIAKI
	Carrata u Italia	1) primary PCI	250 mL i.v. isotonic saline	1000 mL isotonic saline i.v.	follow-up	(CIAKI after	
	Country: Italy	(emergency	bolus is given in 30 min, followed	administration 12 h before	1: 8/67	coronary	prevention.'
	Source of	procedure);	by 0.5 mg/kg i.v. furosemide to forced diuresis. Isotonic saline i.v.	procedure (rate-adjusted according to LVEF 20–40mL/h if	C: 1/66	angiography/PCI as	
		2) cardiogenic		_ ·		defined by an increase of sCr +0.3	
	funding: not	shock;	infusion proceeds automatically,	LVEF<30%, 80–120 mL/h if LVEF		increase of scr +0.3	

reported	3) acute heart	rate-matched with diuresis	30-50%, 200 mL/h if LVEF >50%).	mg/dL in 48 h or	
1.555.354	failure;			+50% in 7 days)	
	4) endstage		Plus 3 mL/kg/h 1.4% SB solution		
	renal disease on		i.v. infusion for 1 h before	I: 4 (6%)	
	haemodialysis;		Plus: 5000mg p.o. Vitamin C	C: 16 (24%)	
	5) urinary tract		Plus: 1200mg p.o. N-acetylcysteine	P=0.01	
	infections				
	within the last 3			Cardiovascular	
	months;			death	
	6) benign prostatic			I: 1/59(1.7%)	
	hyperplasia			C: 7/65 (10.8%)	
	and;				
	7) previously known				
	difficulties in				
	urinary				
	catheterization.				
	<u>Important</u>				
	prognostic factors ² :				
	For example				
	age ± SD:				
	<i>I1: 76 ± 9</i>				
	C: 75 ± 8				
	Sex:				
	I1: 22% F				
	C: 29% F				
	6				
	Serum creatine ± SD				
	11: 1.54 ±0.43				
	C: 1.42 ±0.41				
	Groups comparable				
	at baseline? Yes				
	at paseille: 168				

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

CAG: Cardiac angiography; CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; CKD: chronic kidney disease; CT: computed tomography; CTPA: computed tomography – pulmonary angiography; ia: intra-arterial; IQR: intra quartile range; iv: intra-venous; NAC: N-acetylcysteine; PCI: percutaneous coronary intervention; sCr: serum creatinine

Search description

Systematic reviews							
Database	Search terms	Total					
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	177					
(OVID)	(108416) 2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or						
	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or						
2000-	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post adj1						
heden	hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2						
Engels,	(chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2 catheterization*)).ti,ab. (262412)						
Nederlands	3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or						
	nephropath* or (renal adj2`(insufficienc* or function* or disease* or failure*))).ti,ab.						
	(525125) 4 1 and 2 and 3 (911)						
	5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or						
	cin or ciaki).ti,ab. (8859)						
	6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or						
	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or posthydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post adj1						
	hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2						
	(chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2						
	catheterization*)).ti,ab. (262412)						
	7 5 and 6 (644) 8 4 or 7 (1049)						
	9 limit 8 to (yr="2000 -Current" and (dutch or english)) (775)						
	10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or						
	((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or						
	medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or						
	((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or						
	Editorial/ or Letter/ or (animals/ not humans/)) (236842)						
	11 9 and 10 (69) – 66 uniek 12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or						
	randomized controlled trials as topic/ or Random Allocation/ or Double-Blind						
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or						
	clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or						
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj						
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)						
	(1459903) 13 9 and 12 (333)						
	14 13 not 11 (278)						
Embase	'contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3						
(Elsevier)	medi*):ab,ti						
,	AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1						
	hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR						
	(sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR						
	cardiac) NEAR/2 catheterization):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR						
	'hydration'/exp						
	AND ('kidney disease'/exp OR 'kidney function'/exp OR ((kidney or renal) NEAR/2						
	(disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)						
	(insufficience on functions on disease on failure)).ab,ti)						
	OR ('contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2						
	(nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR cin:ab,ti OR						
	ciaki:ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR						
	'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1						
	hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR						
	(sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR 'sodium chloride'/exp OR 'heart						
	catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR						
	'hydration'/exp))						
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py						
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR						
	'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR						
	'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR						
	'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it (484)						
	יים ביים אינון איניים א						
-							

Cochrane	AND 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT (animal* NOT human*)), (137) - 82 uniek ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR	
(Wiley)	nephrotoxicity)):ab,ti OR cin:ab,ti OR ciaki:ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization)) 15 CDR, 45 DARE	
	11 CR's niet relevant (CIN-HPV) >4 uniek, DARE 25 uniek, 2 niet relevant	

RCTs

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	572
(OVID)	(110323)	RCTS
(- /	2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
Engels,	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	6 SRs
Nederlands	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	new
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium	(177 SRs
2000-juni	adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	in earlier
2015	catheterization*)).ti,ab. (263883)	search
	3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*))	strategy)
	or nephropath* or (renal adj2 (insufficienc* or function* or disease* or	
	failure*))).ti,ab. (527891)	
	4 1 and 2 and 3 (918)	
	5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity))	
	or cin or ciaki).ti,ab. (8912)	
	6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	
	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid*)) or (sodium	
	adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	
	catheterization*)).ti,ab. or Water/ or water.ti,ab. or D5w.ti,ab. or Isotonic	
	Solutions/ or Hypotonic Solutions/ or (ringer* adj3 (lactate or solution*)).ti,ab. or	
	((hypotonic or isotonic) adj3 solution*).ti,ab. or Hydroxyethyl Starch Derivatives/	
	or (Hydroxyethy* adj3 starch*).ti,ab. (818303)	
	7 5 and 6 (733) 8 4 or 7 (1140)	
	9 limit 8 to (yr="2000 -Current" and (dutch or english)) (818)	
	10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or	
	((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw.	
	or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or	
	embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or	
	cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not	
	(Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (240088)	
	11 9 and 10 (72)	
	12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/	
	or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind	
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii	
	or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or	
	randomized controlled trial or multicenter study or clinical trial).pt. or	
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj	
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not	
	humans/) (1471469)	
	13 9 and 12 (341)	
	14 13 not 11 (283) – 265 uniek	
	17 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or	
	Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or	
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or	
	(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw.	
	or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically	

controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2160769) 22 21 not 19 (134) – vanaf 2007: 105 – 103 uniek –in afzonderlijk document **Embase** 'contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 (Elsevier) medi*):ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid*)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR water:ab,ti OR d5w:ab,ti OR (ringer* NEAR/3 (lactate OR solution*)):ab,ti OR ((hypotonic OR isotonic) NEAR/3 solution*):ab,ti OR (hydroxyethy* NEAR/3 starch*):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp OR 'water'/exp OR 'isotonic solution'/exp OR 'ringer lactate solution'/exp OR 'hetastarch derivative'/exp OR 'fluid balance'/exp) AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti) OR ('contrast induced nephropathy'/exp/dm pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR cin:ab,ti OR ciaki:ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid*)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR water:ab,ti OR d5w:ab,ti OR (ringer* NEAR/3 (lactate OR solution*)):ab,ti OR ((hypotonic OR isotonic) NEAR/3 solution*):ab,ti OR (hydroxyethy* NEAR/3 starch*):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp OR 'water'/exp OR 'isotonic solution'/exp OR 'ringer lactate solution'/exp OR 'hetastarch derivative'/exp OR 'fluid balance'/exp)) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it NOT 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR

Observational studies

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	103
(OVID)	(110323)	obs.
	2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
Engels,	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	
Nederlands	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2	
2007-juni	(chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	
2015	catheterization*)).ti,ab. (263883)	
	3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*))	

'systematic review'/de NOT (animal* NOT human*)) (517) - 307 uniek

or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab. (527891)

4 1 and 2 and 3 (918)

5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (8912)

6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid*)) or (sodium adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2 catheterization*)).ti,ab. or Water/ or water.ti,ab. or D5w.ti,ab. or Isotonic Solutions/ or Hypotonic Solutions/ or (ringer* adj3 (lactate or solution*)).ti,ab. or ((hypotonic or isotonic) adj3 solution*).ti,ab. or Hydroxyethyl Starch Derivatives/ or (Hydroxyethy* adj3 starch*).ti,ab. (818303)

7 5 and 6 (733)

8 4 or 7 (1140)

9 limit 8 to (yr="2000 -Current" and (dutch or english)) (818)

10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (240088)

11 9 and 10 (72)

12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1471469)

13 9 and 12 (341)

14 13 not 11 (283) - 265 uniek

17 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2160769)

22 21 not 19 (134) – vanaf 2007: 105 – 103 uniek –in afzonderlijk document

Appendices to chapter 7.1

Evidence tables

Table: Exclusion after revision of full text

Table: Exclusion after r	
Author and year	Reason for exclusion
Aggarwal, 2014	Article not found
Atallah, 2004	Published before the SR of Liu, 2015
Ball, 2014	Review, not systematic
Barbieri, 2014	Did not include subgroup analyses with patients with renal dysfunction
Bidram, 2015	Patients with eGFR<60 excluded
Bouzas-Mosquera,	Published before the search date of SR of Liu, 2015
2009	
Cheungpasitporn,	Did not include subgroup analyses with patients with renal dysfunction
2015	
Gandhi, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Giacoppo, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Han, 2014	Included in the review of Liu, 2015
Hoshi, 2014	Renal function not compromised, observational study
Jo, 2015	Article not available
Jo, 2008	Included in the review of Liu, 2015
Kandula, 2010	Published before the SR of Liu, 2015
Kaya, 2013	Published before the SR of Liu, 2015
Kenaan, 2014	Renal function not compromised, observation study
Lee, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Leoncini, 2014	Outcomes were the cardioprotective effects
Leoncini, 2014	Included in the review of Liu, 2015
Li, 2012	Published before the SR of Liu, 2015
Liu, 2014	Patients with eGFR of 30-90 mL/min/1.73m ² included, compared rosuvastatin with
	atorvastatin
Mao, 2014	Did not include subgroup analyses with patients with renal dysfunction
Marenzi, 2015	Did not include subgroup analyses with patients with renal dysfunction
Munoz, 2011	Published before the SR of Liu, 2015
Ozhan, 2010	Published before the SR of Liu, 2015
Pappy, 2011	More recent SR available
Patti, 2014	Letter to the editor, substantial subgroup of patients has no renal dysfunction
Patti, 2008	Published before the SR of Liu, 2015
Patti, 2011	Included in the review of Liu, 2015
Peruzzi, 2014	No separate analysis for patients with renal dysfunction
Qiao, 2015	Patients with eGFR of 30-89 mL/min/1.73m ² included
Quintavalle, 2012	Included in the review of Liu, 2015
Sanadgol, 2012	Published before the SR of Liu, 2015
Sanei, 2014	Patients with normal renal function included
Shehata, 2015	Patients with eGFR of 30-90 mL/min/1.73m ² included
Singh, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Takagi, 2011	More recent SR available
Toso, 2014	Used the data of Leoncini, 2013
Toso, 2010	Included in the review of Liu, 2015
Ukaigwe, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Wu, 2015	Article not found
Xie, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Xinwei, 2009	Published before the SR of Liu, 2015
Yoshida, 2009	Published before the SR of Liu, 2015
Yun, 2014	Observational study

Zhang, 2011	More recent SR available
Zhao, 2008	Published before the SR of Liu, 2015
Zhou, 2011	More recent SR available

Table: Exclusion after revision of full text (update 2017)

Author and year	Reason for exclusion
Ali-Hassan-Sayegh, 2016	Does not meet selection criteria, references were checked
Chalikias, 2016	Does not meet selection criteria, references were checked
Fan, 2016	No studies included after original search
Gadapa, 2016	Full text not available
Giacoppo, 2015	Full text not available
Jo, 2015	Does not meet selection criteria
Li, 2016	Does not meet selection criteria
Navarese, 2017	Does not meet selection criteria
Rabbat, 2015	Abstract
Subramaniam, 2016	Does not meet selection criteria, references were checked
Thompson, 2016	No studies included after original search
Vanmassenhove, 2016	No studies included after original search
Wang, 2016	No studies included after original search
Zografos, 2016	Full text not available
Zografos, 2016	No studies included after original search
Zografos, 2016	No studies included after original search
Fu, 2015	Full text not available
Gaskina, 2016	Abstract
Gaskina, 2016	Abstract
Maskon, 2016	Abstract
Park, 2016	Full text not available
Kohsravi, 2016	Does not meet selection criteria
Li, 2016	Does not meet selection criteria

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study First author,	and clearly focused	Comprehensive and systematic literature search? ²	Description of included and excluded studies? ³	relevant	Appropriate adjustment for potential confounders in observational studies? ⁵	Assessment of scientific quality of included studies? ⁶	Enough similarities between studies to make combining them reasonable? ⁷	of publication bias taken into	Potential conflicts of interest reported? ⁹ Yes/no/unclear
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	
Liu, 2015	yes	Yes	No (excluded studies not referenced)	yes	NA	Yes	Unclear (different definitions of PC-AKI used among included studies)	plot not provided for	Yes (none of the studies were sponsored by industry)

- 1. Research question (PICO) and inclusion criteria should be appropriate and predefined
- 2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
- 3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
- 4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
- 5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)
- 6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
- 7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?
- 8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
- 9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials) Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year)		(unlikely/likely/un clear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncle ar)
Shehata, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Qiao, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Abaci, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	unlikely	Unclear	unclear

- 1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the process of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

nescaren q	nessentin questioni										
Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments				
reference	characteristics			control (C)		effect size					
Liu, 2015	SR and meta-	Inclusion criteria SR:	Describe intervention:	Describe control:	End-point of follow-up	Outcome measure-1: PC-	<u>Facultative</u> :				
	analysis of RCTs	RCTs investigating the			<u>(PC-AKI)</u> :	AKI, defined as an					

	T		T	1			
[individua		efficacy of statins in	A: Simvastin 40mg, 12	A: Placebo	A: within 48h after	increase of ≥25%SCr or	The result presented here
l study	Literature search	preventing CIN	hours for 2 days,		contrast administration	SCr ≥0.5mg/dL within 48-	involves a subgroup
characteri	up to Feb 2014	compared with	80mg before		B : within 5 days	120h.	analyses of patients with
stics		placebo, the treatment	procedure, 80mg after		C: 48h after PCI		impaired kidney function.
deduced	A : Jo, 2008	groups received statins	the procedure		D : 48h after from baseline	Effect measure: RR (95%	
from [1st	B : Toso, 2010	before the contrast	B: Atorvastatin	B: Oral NAC	value	CI:	The results of the study of
author,	C : Patti, 2011	exposure at any dose,	80mg/d for 48 hours	1200mg 2 times	E: within 72h after	A : 0.75 (0.17;3.28)	Quintavalle, 2012 are
year of	D : Quintavalle,	for any length of time.	before and after the	day before to the	contrast administration	B : 0.94 (0.48;1.83)	adapted (secondary
publicatio	2012	Studies were only	procedure versus	day after	F: within 72h after	C : 0.56 (0.21;1.47)	outcome measure is the
n	E : Han, 2013	included if none of the	placebo, oral NAC	procedure	contrast administration	D : 0.44 (0.17;1.13)	correct PC-AKI definition)
]]	F: Leoncini, 2013	arms or both received	1200mg 2 times day			E : 0.82 (0.33;2.04)	
		N-acetylcysteine.	before to the day		For how many	F : 0.41 (0.20;0.85)	Liu, 2015 include a fixed
PS., study	Study design:		after procedure		participants were no		analyses, the use of
characteri	RCT [parallel]	Exclusion criteria SR:	C: Atorvastatin 80 mg	C: Placebo	complete outcome data	Pooled effect (fixed	random analyses might
stics and		Trials comparing 2	12 hours before and		available?	effects model): 0.51	be preferred given the
results	Setting and	different doses of	further 40mg 2 hours		Not reported	(0.37;0.70) favouring	heterogeneity found
are	Country:	statins. Only studies	before angiography			intervention. I ² =44%	(I ² =44%)
extracted	Not reported	that included patients	D : 80mg within 24h	D : Placebo, oral			,
from the		with renal dysfunction	before exposure, oral	NAC 1200mg ²		Outcome measure-2:	For the outcome
SR (unless	Source of	(defined as eGFR≤60	NAC 1200mg ²	times/day before		Mortality (cases)	measures mortality, start
stated	funding:	mL/min/1.73m ² or	times/day before and	and the day of		A: intervention=0,	of dialysis and ICU
otherwise	None was	creatine clearance ≤60	the day of procedure	procedure		placebo=0	admission, data
)	sponsored by	mL/min/1.73m ²) were	E: Rosuvastatin 10mg	•		B: intervention=1,	extraction took place
	industry	included here.	from 2 days before to			placebo=0	using the original articles
	,		3 days after	E: placebo		C: NR	of the studies included in
		6 studies included	procedure			D: NR	Liu, 2015.
			F: Rosuvastin 40mg			E: NR	ŕ
		Important patient	followed by 20mg/d,	F : oral NAC 1200		F: NR	
		characteristics at	oral NAC 1200 mg 2	mg 2 times/d			
		baseline:	times/d before and	before and day		Outcome measure-3:	
		·	day after procedure	after procedure		Start dialysis	
		<u>N</u>	, ,	'		A: intervention=0,	
		A: 236				placebo=1	
		B : 304				B : intervention=0,	
		C : 74				placebo=1	
		D : 410				C: NR	
		E : 450				D: NR	
		F : 210				E: NR	
						F: NR	
		Groups comparable at				Outcome measure-4: ICU	
		baseline? Unclear				(not reported in any of	
	1		I .	I	I	,p	

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1
This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study referenc	Study characteristic	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
е	S						
Shehata,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	follow-up:	Outcome measures and	The current study results
2015	RCT	Diabetic patients, carrying	(treatment/procedure	(treatment/proced	10 days	effect size (include 95%CI	identify a high-risk
		the diagnosis of chronic	/test):	ure/test):		and p-value if available):	population showing a
	Setting:	stable angina and			Loss-to-follow-up:		pronounced benefit upon
	Catheterizatio	suffering from mild or	Oral atorvastatin (80	Intravenous	Intervention: 0	Incidence of PC-AKI	adopting the high dose
	n laboratory	moderate	mg daily) for 48 h	infusion of		(increase in serum	atorvastatin
		CKD. (eGFR 30–<90	before PCI, in addition	isotonic saline and	Control: 0	creatinine of ≥0.5 mg/dL	pretreatment approach
	Country:	mL/min/1.73 m ²	to periprocedural	oral N-		or an absolute increase of	before contrast exposure.
	Egypt		intravenous infusion	acetylcysteine, in	Incomplete outcome	≥25% from baseline <48	
		Exclusion criteria:	of isotonic saline and	addition to	<u>data</u> :	or72h after contrast	
	Source of	Severe CKD (e GFR <30	oral N-acetylcysteine.	placebo formula.	No	exposure)	
	funding: not	mL/min/1.73 m) [9], end-	Standard parenteral				
	reported, no	stage renal disease (or	hydration protocol in			Intervention group: 5/65	
	conflicts of	patients on hemodialysis),	both groups.			events, control group	
	interest	intake of potentially				13/65 events, p<0.05	
		nephrotoxic drugs, acute					
		myocardial infarction				Mortality, initiation of	
		requiring emergency				dialysis and ICU-	
		coronary intervention,				admission not reported	
		cardiogenic shock.					
		See article for a complete					
		overview of exclusion					
		criteria.					
		N total at baseline:					
		Intervention: 65					
		Control: 65					
		Important prognostic factors ² :					

		For everyone			I	I	
		For example					
		age ± SD:					
		1: 55 (6)					
		C:57 (5)					
		Sex:					
		1: 53% M					
		C: 56% M					
		C. 30% W					
		Contrast (mL) (mean± SD)					
		1: 274 (8)					
		C: 278 (11)					
		- ,					
		Contrast nephropathy risk					
		score (mean± SD)					
		I: NR					
		C: NR					
		Groups comparable at					
		baseline? yes, no					
		statistical significant					
		differences					
Qiao,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	follow-up:	Outcome measures and	
2015	RCT	1. Diabetic patients; 2.	(treatment/procedure	(treatment/proced	Between 48-72h after	effect size (include 95%CI	
		Mild to moderate CKD,	/test):	ure/test):	procedure, up to 30 days.	and p-value if available):	
	Setting:	which was defined as					
	Hospital	estimated glomerular	The rosuvastatin	Received no	Loss-to-follow-up:	Incidence of PC-AKI	
		filtration rate (eGFR) 30 to	group received 10 mg	statins during the	Intervention: 0	(increase in serum	
	Country:	89 ml/min per 1.73 m2; 3.	everyday for at least	trial. All patients		creatinine of ≥0.5 mg/dL	
	China	Total CM administrated	48 hours before and	received	Control: 0	or an absolute increase of	
		dose of volume ≥ 100 ml.	72 hours after CM	intravenous		≥25% from baseline <48	
	Source of		administration.	hydration with	Incomplete outcome	or72h after contrast	
	funding: not	Exclusion criteria:		isotonic saline	<u>data</u> :	exposure)	
	reported, no	Pregnancy, lactation,		(0.9% sodium	No	lataniation and 2/50	
	conflicts of	Ketoacidosis, Lactic		chloride 1-1.5		Intervention group: 2/60	
	interest	acidosis, prior CM		ml/kg/hour for 3-		events, control group	
		administration within 7		12 hours before		2/60 events, p<0.05	
		days of study entry.		and 6-24 hours		Mantalita, initiation -f	
		Importantly, all patients		after the		Mortality, initiation of	
		who were recent statin		procedure).		dialysis and ICU-	
		users (with 14 days before				admission not specifically	

	1	I				T	
		the procedure) were				reported, but no post	
		excluded.				procedural adverse	
		See article for a complete				events occurred.	
		overview of exclusion					
		criteria.					
		N total at baseline:					
		Intervention: 60					
		Control: 60					
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		1: 62 (8)					
		C:62 (8)					
		Sex:					
		1: 68% M					
		C: 73% M					
		Contrast (mL) (mean± SD)					
		1: 204 (75)					
		C: 212 (85)					
		Contrast nephropathy risk					
		score (mean± SD)					
		I: NR					
		C: NR					
		C. IVI					
		Groups comparable at					
		baseline? Yes, average					
		eGFR 60 ml/min/1.73 m ²					
Abasi	Type of study:		Docaribo intomiontico	Doscribo control	follow up:	Outcome messures and	All patients received
Abaci,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	follow-up:	Outcome measures and	All patients received
2015	RCT	Patients naïve to statins	(treatment/procedure	(treatment/proced	Between 48-72h after	effect size (include 95%Cl	intravenous hydration
	6	and scheduled for	/test):	ure/test):	angiography, 6 months	and p-value if available):	with isotonic saline
	Setting:	coronary angiography			and 1 year.		(14mL/kg/h, 0.9% sodium
	University	with EGFR between 30	Patients were given	No statin		Incidence of PC-AKI	chloride) for 12h before
	cardiology	and 60 mL/min/1.73m ² .	40mg rosuvastatin	treatment	Loss-to-follow-up:	(increase in serum	and 24h after contrast
	institute,		<24 h before coronary		Intervention: 7 (6%)	creatinine of ≥0.5 mg/dL	exposure.
	inpatients	Exclusion criteria:	angiography and		Reasons unknown	or an absolute increase of	

		Emergency coronary	hereafter 20mg/day		≥25% from baseline <48	Statistical analyses not
	Country:	angiography, acute renal	for 2 days.	Control: 5 (5%)	or72h after contrast	clear. Secondary
	Turkey	failure or end-stage renal		Reasons unknown	exposure.	outcomes (death and
		failure requiring dialysis.				decrease in eGFR of ≥25%
	Source of	See article for a complete		Incomplete outcome	Intervention group: 6/103	or renal failure requiring
	funding: not	overview of exclusion		<u>data</u> :	events, control group	dialysis at 12 months)
	reported, no	criteria.		See loss to follow-up	9/105 events. Relative	were reported as a
	conflicts of				risk (95%CI)= 0.71 (0.25;-	composite outcome and
	interest	N total at baseline:			2.0)	exact data was not
		Intervention: 110				shown.
		Control:110			Mortality, initiation of	
					dialysis and ICU-	
		Important prognostic			admission not reported	
		<u>factors</u> ² :				
		For example				
		age ± SD:				
1		1: 67.5 (8.9)				
		C:67.7 (8.9)				
		Sex:				
		I: 64% M				
		C: 73.4% M				
		Contrast (mL) (mean± SD)				
1		I: 139.2 (77.4)				
ļ		C: 117.7 (56.8)				
		Contrast nephropathy risk				
		score (mean± SD)				
		<i>I:</i> 9.3 (3.9)				
		C: 7.7 (3.4)				
		Groups comparable at				
		baseline? Not completely,				
		see contrast volume and				
		contrast nephropathy risk				
		(above)				

Notes:

1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures

- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Search description								
Database	Search terms	Total						
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	131						
(OVID)	(112282)							
1995-aug.	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.							
2015	(536907)							
2013	3 1 and 2 (8955)							
Engels	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or							
Engels,	ciaki).ti,ab. (1969)							
Nederlands	5 3 or 4 (9449)							
	6 limit 5 to (yr="1995-Current" and (dutch or english)) (5521)							
	7 exp hydroxymethylglutaryl-coa reductase inhibitors/ or (statin* or lovastatin* or meglutol* or pravastatin* or simvastatin* or rosuvastatin* or							
	atorvastatin*).).ti,ab,kw. or (hydroxymethylglutaryl* adj4 inhibitor*).ti,ab,kw.							
	(45277)							
	8 6 and 7 (131)							
	9 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic*							
	or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review							
	Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection							
	criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or							
	Letter/ or (animals/ not humans/)) (248141)							
	10 8 and 9 (32) – 31 uniek							
	11 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or							
	randomized controlled trials as topic/ or Random Allocation/ or Double-Blind							
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or							
	randomized controlled trial or multicenter study or clinical trial).pt. or							
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj							
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)							
	(1508278)							
	12 8 and 11 (71)							
	13 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or							
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or							
	(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or							
	prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically							
	controlled study/ or interrupted time series analysis/ [Onder exp cohort studies							
	vallen ook longitudinale, prospectieve en retrospectieve studies] (2209511) 14 8 and 13 (38)							
	15 12 not 10 (45)							
	22 (12 or 14) not 10 (58) – 56 uniek							
Embase	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2							
(Elsevier)	(nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR							
(Lisevier)	('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3							
	medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2							
	(disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti))							
	The second of th							
	AND ('hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR							
	statin*:ab,ti OR lovastatin*:ab,ti OR meglutol*:ab,ti OR pravastatin*:ab,ti OR							
	simvastatin*:ab,ti OR rosuvastatin*:ab,ti OR atorvastatin*:ab,ti OR							
	(hydroxymethylglutaryl* NEAR/4 inhibitor*):ab,ti)							
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [1995-2015]/py							
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR							
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1							
	analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR							
	'systematic review /de NOT ('animai experiment /exp OK 'animai model /exp OK 'nonhuman'/exp NOT 'human'/exp)) (34) – 6 uniek							
	nomanan jeng nor naman jengij (54) o aniek							
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR							
	'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR							
	'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR							
	'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR							
	placebo*:ab,ti) NOT 'conference abstract':it OR 'clinical study'/exp (87) – 38 uniek	<u>l</u>						

Appendices to chapter 7.2

Evidence tables

Table: Exclusion after revision of full text

Table: Exclusion after i	evision of full text
Author and year	Reason for exclusion
ACT Investigators,	description of study design, not an original article
2009	
Amini, 2009	Prehydration only, not comparable to Dutch clinical practice
Ashworth, 2010	overlaps with Loomba, 2013 and is a less recent review
Azmus, 2005	Not specifically patients with normal or abnormal kidney function (mix of impaired kidney function and diabetics)
Bagshaw, 2006	review, not systematic
Berwanger, 2012	Sub-analysis of ACTT studty (which is already included in literature analysis)
Briguori, 2011	Does not compare N-acetylcysteine to placebo
Briguori, 2007	Not specifically patients with normal or abnormal kidney function (mix of impaired kidney function and diabetics)
Brown, 2009	overlaps with Loomba, 2013 and is a less recent review
Burns, 2010	Not specifically patients with normal or abnormal kieny function (mix of impaired kidney function and diabetics)
Busch, 2013	overlaps with Loomba, 2013 and is a less recent review
Buyukhatipoglu,	outcome measures as described in PICO not reported
2010	
Calabro, 2011	observational study
Carbonell, 2010	already included in Loomba 2013, and Sun, 2013
Carbonell, 2007	already included in Loomba 2013, and Sun, 2013
Chen, 2008	does not compare no NAC to NAC (both treatment arms recieve NAC)
Coyle, 2006	Not specifically patients with normal or abnormal kidney function (mix of impaired kidney function and diabetics)
Duong, 2005	overlaps with Loomba, 2013 and is a less recent review
Gomes, 2005	Not specifically patients with normal or abnormal kidney function (mix of impaired
- Coco, 2000	kidney function and diabetics)
Gonzales, 2007	overlaps with Loomba, 2013 and is a less recent review
Gouveira, 2015	review, not systematic
Gulel, 2005	already included in Loomba 2013
Gurm, 2011	Does not answer study question
Hafiz, 2012	Acetylcysteine not compared to control
Hassan, 2011	observational study
Housseinjani, 2013	review, not systematic
Hsu, 2012	already included in review Wu 2013
Hsu, 2007	already included in review Wu 2013
Izcovich, 2015	systematic review, poor quality (no clear description of included studies)
Jo, 2009	does not compare no NAC to NAC
Juergens, 2010	does not compare no NAC to NAC (both treatment arms recieve NAC)
Khalili, 2006	Prehydration only, not comparable to Dutch clinical practice
Kim, 2010	already included in Loomba 2013
Kotlyar, 2005	Dubbel met Kotlyar, 2005
Lee, 2011	does not compare no NAC to NAC (both treatment arms recieve NAC)
Liu, 2006	overlaps with Loomba, 2013 and is a less recent review
Marenzi, 2006	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Mittal, 2014	review, not systematic
Momeni, 2012	Observational study
O'Sullivan 2013	Does not answer reseach question broadly enough, used for cross refernecing
Ratcliffe, 2009	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Ritz, 2006	letter to the editor, not an original article
Sandhu, 2006	Unclear if patients were hydrated next to the NAC administration or not
Sar, 2010	Not specifically patients with normal or abnormal kidney function (mix of impaired

	kidney function and diabetics)
Shabbir, 2015	Article not found
Shalansky, 2006	review, not systematic
Solomon, 2014	review, not systematic
Staniloae, 2009	subanalysis of trial, observational data
Thiele, 2010	already included in Loomba 2013
Trivedi, 2009	overlaps with Loomba, 2013 and is a less recent review
Zagler, 2006	overlaps with Loomba, 2013 and is a less recent review

Risk of bias table for intervention studies (randomized controlled trials) Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio		(unlikely/likely/	(unlikely/likely/uncl	(unlikely/likely/uncle	(unlikely/likely/uncl	(unlikely/likely/un	(unlikely/likely/uncle	(unlikely/likely/uncle
n year)		unclear)	ear)	ar)	ear)	clear)	ar)	ar)
Herr 2012	Communitari	Lindilani.	Lielikeli.	CT scan, normal kid		Lindiilanka	Lindiilanka	Lindan
Hsu, 2012	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
				CT scan, decreased k	idney function			_
Kama, 2014	By website randomization.c om	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Kitzler, 2012	Not reported	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	Unclear
Poletti, 2007	Randomized by serial enrolment	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Poletti, 2013	Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
Tepel, 2000	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
				CAG or PCI, normal k	didney function			
Carbonell, 2007	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Jaffery,	"Randomly	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Unlikely	Unclear

2012	assigned"							
Kim, 2010	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Kinbara, 2010	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Lawlor, 2004	"randomization was performed by the hospital clinical trials pharmacist"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Sadat, 2011	Computer generated randomization scheme	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Tanaka, 2011	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Thiele, 2010	Computer generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
CAG or PCI, decreased kidney function								
ACT, 2011	24-hour Web- based automated randomization system	Unlikely						
Castini, 2010	Computer generated randomization table	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Ferrario, 2009	Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Gulel,	Random	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear

2005	allocation table							
Habib,	Patients were	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
2016	randomized							
	into three							
	groups							
Izani Wan	Computer	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
(Mohame	generated							
d), 2008	randomization							
	list							
Koc, 2012	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Kotlyar,	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
2005								
Sadineni,	Patients were	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
2017	randomly							
	assigned							
Seyon,	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
2007								

- 1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1

This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study	Study	Patient characteristics ²	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments				
reference	characteristic			control (C) 3		effect size ⁴					
	S										
	CT scan, normal kidney function										
Hsu, 2012	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:				
	Randomized	1) all adult patients who	intervention	(treatment/proced	72 hours	effect size (include 95%CI	A singe dose of NAC				
	controlled	received chest or	(treatment/procedu	ure/test):		and p-value if available):	before CECT imagingcan				
	trial	abdominal contrast-	re/test):				prevent CIN in an ED				
		enchanced computed		0.9% sodium	Loss-to-follow-up:	CIN05:	setting. However it does				
	Setting:	tomography (CECT)	600mg NAC	chloride (3	Not reported	(=a rise in SCr ≥0.5mg/dL	not improve mortality				
	emergency		In 0.9% sodium	mL/kg/h) for 60		within 48-72 hours after	rate or the need for				
	department,	Exclusion criteria:	chloride (3 mL/kg/h)	minutes prior to	Incomplete outcome	CECT imaging)	dialysis.				
	medical	1) patients undergoing	for 60 minutes prior	the CECT	<u>data</u> :	I: 7.5%					
	teaching	long-term hemodialysis or	to the CECT		Not reported	C: 14.6%	Patients with congestive				
	center	peritoneal hemodialysis		0.9% sodium		Odds Ratio (OR): 0.31	pulmonary edema				
		2) patients who received	0.9% sodium	chloride (1		(95% CI: 0.10 – 0.96,	received an adjusted				
	Country:	another dose of contrast	chloride (1 mL/kg/h)	mL/kg/h) for 6		p=0.04)	hydration schedule				
	Taiwan	medium within 72 hours	for 6 hours after	hours after CECT			where the rates of fluid				
		3) patient refused to sign	CECT			CINor:	loading were decreased				
	Source of	concent forms				(=a rise in SCr ≥0.5mg/dL	by 50%.				
	funding: non-	4) patients had a knon				or 25% within 48-72					
	commercial	allergic reaction to N-				hours after CECT imaging)					
		acetlycysteine (NAC)				I: 11.3%					
						C: 19.4%					
		N total at baseline:				OR: 0.35 (95% CI: 0.13 -					
		Intervention: 106				0.91, 0=0.03)					
		Control: 103									
						Mortality:					
		Important prognostic				I: 7.5%					
		<u>factors</u> ² :				C: 12.6%					
		For example				OR: 0.49 (95% CI: 0.15 –					
		age ± SD:				1.55, p=0.22)					

	I: 80 ± 9 C: 80 ± 11 Sex: I: 74% M C: 76% M Baseline SCr (mg/dL) ± SD I: 1.40 ± 0.58 C: 1.26 ± 0.43 Groups comparable at baseline?				Permanent renal replacement therapy: 0% in both groups	
		CT so	can, decreased kidney f	unction		
Kama, Type of study: randomized controlled trial Setting: emergency department, academic tertiary hospital Country: Turkey Source of funding: not reported	Inclusion criteria: 1) adult patients (≥18 years) who presented to the emergency department 2) patients who received CECT as part of their emergency care 3) moderate or high risk for contrast induced nephropathy (CIN) according to Mehran score (>5) Exclusion criteria: 1) CIN risk determine as Low by Mehran score 2) history of contrast- related allergies 3) hemodynamically unstable patients requiring resuscitation or surgery 4) patients receiving renal replacement therapy	Describe intervention (treatment/procedu re/test): 150mg/kg NAC In 1000mL in 0.9% saline at the rate of 350ml/hour for 3 hours Before, after and during administration of contrast	Describe control (treatment/proced ure/test): 1000mL 0.9% saline at the rate of 350ml/hour for 3 hours Before, after and during administration of contrast	Length of follow-up: 48-72 hours Patients who were diagnosed with CIN – 1 months Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=25% increase or greater than 0.5mg/dL (44µmol/L) increase in the serum creatinine level, 48-72 hours after administration of the contrast agent compared with the baseline creatinine measurement) I: 7 (19%) C: 5 (14%) p>0.05 No contrast- or treatment-induced adverse events were detected during emergency department	Authors'conclusion: None of the short-term protocols with normal saline or NAC was superior in the emergency department pateints requiring CECT who had a moderate or high risk of CIN.

		infomed consent					
		N total at baseline: Intervention: 36 Control: 35					
		Important prognostic factors ² : For example age (95% CI): I: 69 (65-73) C: 67 (62-72)					
		Sex: I:69 % M C: 65% M					
		eGFR <20 mL/min/1.73m ² I: 25% C: 9%					
		eGFR 40-20 mL/min/1.73m ² I: 36%					
		C: 46% eGFR 60-40mL/min/1.73m ² I: 11%					
		C: 14% Groups comparable at baseline? Yes					
Kitzler, 2012	Type of study: randomized controlled trial	Inclusion criteria: -patients with chronic kidney disease stage 1-4 undergoing elective	Describe intervention (treatment/procedu re/test):	Describe control (treatment/proced ure/test):	Length of follow-up: Not reported Loss-to-follow-up:	Outcome measures and effect size (include 95%Cl and p-value if available):	Authors' conclusion: Following radiocontrast administration neither vitamin E nor NAC in
	Setting: single-center,	computer-assisted tomography with non-ionic radiocontrast agents when	N-acetylcysteine 4800mg per os	0.45% saline, 1mL/kg/h over 24 hours	Not reported Incomplete outcome	No patients developed contrast induced acute kidney injury.	addition to saline demonstrated an additional beneficial

	elective	compared to 0.45% saline			<u>data</u> :		effect on kidney
	patients	alone	0.45% saline,		Not reported	There was no significant	fi=unction when
			1mL/kg/h over 24			difference in serum	compared to saline alone.
	Country:	Exclusion criteria:	hours			creatinine change	
		-				between the three study	
	Source of					arms.	
	funding:	N total at baseline:					
		Intervention: 10					
		Control: 10					
		Important prognostic					
		<u>factors</u> ² :					
		For example					
		age ± SD: mean: 75 years					
		(not reported per group)					
		Sex:					
		38% M					
		(not reported per group)					
		Groups comparable at					
		baseline? Unc;ear					
Poletti,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2007	randomized	1) patients admitted	intervention	(treatment/proced	4 days	effect size (include 95%Cl	
	controlled	consecutively to the	(treatment/procedu	ure/test):		and p-value if available):	On the basis of the serum
	trial	emergency department	re/test):		Loss-to-follow-up:	Nephrotoxicity	creatinine concentration,
		during daytime hours		placebo in 5%	7 (8%)	(=≥25% increase in serum	iv administration of NAC
	Setting:	2) serum creatinine	900mg NAC diluted	glucose solution	3 died, 3 left hospital 1	creatinine value)	appears protective
	emergency	>1.2md/dL	in 5% glucose	administered iv 1	transferred to another	I: 2/44 (5%)	against the
	patients	Fuel veien enitenie	solution	hour before CT	hospital (not reported	C: 9/43 (21%)	nephrotoxicity of
	Countra	Exclusion criteria:	administered iv 1 hour before CT	0.45% saline iv at a	per group)	P=0.026	contrast medium.
	Country: Switzerland	1) pregnancy	nour before C1		Incomplete outcome		
	Switzerialiu	2) end stage renal failure with dialysis	0.45% saline iv at a	rate of 5mL/kg body weight over	Incomplete outcome data:		
	Source of	3) suspicion of acute renal	rate of 5mL/kg body	the course of an	As above		
	funding: not	obstruction	weight over the	hour before CT	AS above		
	reported	4) asthma	course of an hour	noul before Ci			
	reported	+) u3011110	course of all float	l	l		

		5) severe cardiac failure 6) hemodynamically unstable condition contraindicating iv hydration 7) nonurgent indications for CT	before CT 900mg NAC mixed into the 0.45% saline perfusion administered iv after completion of CT at a rate of	placebo mixed into the 0.45% saline perfusion administered iv after completion of CT at a rate of 1mL/kg body weight per hour for			
		N total at baseline: 87 Intervention: 44 Control: 43	1mL/kg body weight per hour for 12 hours	12 hours			
		Important prognostic factors ² : For example age ± SD: I: 70 ± 19 C: 73 ± 17					
		Sex: I: 59% M C: 67% M					
		Groups comparable at baseline? Yes					
Poletti, 2013	Type of study: randomized controlled trial	Inclusion criteria: 1) patients admitted consecutively to the emergency department 2) estimated creatinine	Describe intervention (treatment/procedu re/test):	Describe control (treatment/proced ure/test): placebo diluted in	Length of follow-up: 10 days Loss-to-follow-up: Intervention:	Outcome measures and effect size (include 95%CI and p-value if available): Nephropathy	Authors' conclusion: An ultra-high dose of intravenous NAC is ineffective at preventing
	Setting: emergency department patients	clearance by MDRD of <60ml/min/1.73m ² Exclusion criteria: 1) asthma	6000mg NAC iv diluted in 100mL saline, administered in the 60 minutes before the CT-scan	100mL saline, administered in the 60 minutes before the CT-scan	3 (5%) Reasons not reported Control: 1 (2%)	(=increase of at least 25% or 44µmol/l in serum creatinine level at day 2,4 or 10 compared to day 0) I: 8 (15%)	nephrotoxicity in patients with renal impairment undergoing emergency contrast CT.
	Country: Switzerland	2) pregnancy 3) obstructive nephropathy	Hydration of 250mL	Hydration of 250mL of 0.45%	Reasons not reported	C: 10 (17%) P=0.99	

	Source of funding: not reported	4) patient's refusal N total at baseline: 104 Intervention: 55 Control: 59 Important prognostic factors ² : For example age ± SD: I: 78 ± 12 C: 78 ± 12 Sex:	of 0.45% saline before CT-scan 1000mL saline 0.45% after CT-scan	saline before CT- scan 1000mL saline 0.45% after CT- scan	Incomplete outcome data: As above	Composite event of death or acute kidney injury I: 33% C: 24% p-value not reported	
		I: 49% M C: 51% M					
		C: 51% W					
		Groups comparable at baseline? Yes					
Tepel,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2000	Randomized	1) patients with a serum	intervention	(treatment/proced	48 hours, 6 days	effect size (include 95%CI	
	controlled	creatinine >1.2mg/dL or	(treatment/procedu	ure/test):		and p-value if available):	Prophylactic
	trial	creatinine clearance	re/test):		Loss-to-follow-up:		administration of the
		<50mL/min		Saline (0.45%) iv.	Not reported	Increase of at least	antioxidant
	Setting:	2) known chronic renal	Acetylcycsteine	1ml/kg/h for 12		0.5mg/dL (44μmol/L) in	acetylcysteine, along with
	elective	failure and a stable serum	orally 600mg twice	hours before and	Incomplete outcome	serum creatinine	hydration, prevents the
	patients	creatinine concentration	daily on the day	12 hours after	data:	concentration 48 hours	reduction in renal
	receiving CT-	3) patients receiving	before and on the	contrast	Not reported	after administration of	function induced by
	scan at	elective CT-scans	day of administration of	administration		contrast agent: I: 1/41 (2%)	iopromide, a non-ionic, low-osmolality contrast
	hospital	Exclusion criteria:	the contrast agent			C: 9/42 (21%)	agent, in patients with
	Country:	1) acute renal failure	the contrast agent			RR: 0.1 (95% CI: 0.01 –	chronic renal
	Germany	1, acate renariance	Saline (0.45%) iv.			0.9)	insufficiency.
		N total at baseline:	1ml/kg/h for 12			P=0.01	
	Source of	Intervention: 41	hours before and 12				
	funding: not	Control: 42	hours after contrast			None of the patients	
	reported		administration			required dialysis	

		Important prognostic factors ² : For example age ± SD: I: 66±11 C: 65 ± 15 Sex: I:59 % M C: 55% M Groups comparable at baseline? Yes					
			CAG	or PCI, normal kidney f	unction		
Carbonell , 2007	Type of study: randomized controlled trial Setting: tertiary hospital, cardiac unit Country: Spain Source of funding: not reported	Inclusion criteria: 1) patients with acute coronary syndrome and normal renal function, admitted to the cardiac unit and referred for cardiac catheterization 2) angina at rest or postmyocardial infarction Or they had received thrombolytic therapy with failed recanalization so the cardiac catheterisation was an emergency procedure Exclusion criteria: 1) chronic renal failure or acute renal dysfunction 2) hemodynamic instability (systolic blood pressure <90mmHg) 3) known allergy to NAC or	Describe intervention (treatment/procedu re/test): NAC (600mg diluted in 50mL of 0.9% saline) iv for 30 minutes twice daily for a total of 4 times Starting at least for 6 hours before the administration of contrast media 0.9% saline iv at least 6 hours before procedure, maintained for 12 hours after contrast dosing	Describe control (treatment/proced ure/test): placebo (diluted in 50mL of 0.9% saline) iv for 30 minutes twice daily for a total of 4 times Starting at least for 6 hours before the administration of contrast media 0.9% saline iv at least 6 hours before procedure, maintained for 12 hours after contrast dosing	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): Contrast induced nephropathy (=an acute increase in the serum creatinine concentration ≥0.5mg/dL and/or >25% increase above baseline level at 48 hours after contrast dosing) I; 10.3% C: 10.1% P=0.50 None of the patients required dialysis.	Patients with congestive heart failure received a reduced hydration volume. Authors' conclusion: The prophylactic administration of intravenous NAC provides no additional benefit to saline in high-risk coronary patients with normal renal function.

		4) untreated gastrointestinal bleeding 5) previous treatment with theophylline, mannitol or					
		N total at baseline: Intervention: 107 Control: 109					
		Important prognostic factors ² : For example age ± SD: I: 63 ± 14 C: 61 ± 12					
		Sex: I: 80% M C: 73% M					
		Creatinine clearance (ml/min) I: 86 ± 29 C: 88 ± 30					
		Groups comparable at baseline?					
Jaffery, 2012	Type of study: randomized controlled trial	Inclusion criteria: 1) patients hospitalized with a primary diagnosis of acute coronary syndrome 2) scheduled for coronary	Describe intervention (treatment/procedu re/test):	Describe control (treatment/proced ure/test):	Length of follow-up: 72 hours for lab parameters 30 days for mortality and hospital stay	Outcome measures and effect size (include 95%Cl and p-value if available):	Patients with clinical evidence of heart failure received only NAC iv or placebo
	Setting: single-center inpatients, emergency	angiography (CAG) or intervention during this hospitalization 3) age ≥18 years	NAC: 1200mg bolus followed by 200mg/h for 24	Placebo in 500ml 5% dextrose solution of water iv	Loss-to-follow-up: Not reported	(=increase in serum creatinine concentration ≥25% above the baseline level within 72 hours of	Authors' conclusion: In acute coronary syndrome patients undergoing CAG with or

	procedure		hours	Normal saline	Incomplete outcome	the administration of	without percutaneous
		Exclusion criteria:		(0.9%) iv; 1/ml/kg	<u>data</u> :	intravenous contrast)	intervention (PCI), high-
	Country:	1) end stage renal disease	In 500ml 5%	for 24 hours	Not reported	I: 16%	dose intravenous NAC
	United States	requiring dialysis	dextrose solution of			C:	failed to reduce the
	of America	2) hypersensitivity to NAC	water iv			13%	incidence of CIN.
		3) history of life-				P=0.40	
	Source of	threatening contrast	Normal saline				
	funding: not	reaction	(0.9%) iv; 1/ml/kg			Outcomes of mortality	
	reported		for 24 hours			and length of hospital not	
		N total at baseline:				reported.	
		Intervention: 192					
		Control: 206					
		Important prognostic					
		<u>factors</u> ² :					
		For example					
		age ± SD:					
		I: 66 ± 13					
		C: 65 ± 13					
		Sex:					
		I: 67 % M					
		C: 59 % M					
		Baseline creatinine					
		clearance (ml/min)					
		I: 87 ± 41					
		C: 92 ± 44					
		Groups comparable at					
		baseline? Yes			_		
Kim, 2010	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
	randomized	1) patients scheduled for	intervention	(treatment/proced	48 hours	effect size (include 95%CI	
	controlled	elective CAG and/or PCI	(treatment/procedu	ure/test):		and p-value if available):	Not relevant – based on
	trial	with apparently normal	re/test):		Loss-to-follow-up:		cystatin-C defined CIN
		renal function		0.9% saline	Not reported	CIN	results and not the sCR
	Setting:		Oral acetylcysteine	1/mL/kg/h for 12		(=increase in sCR of at	based CIN.

elective	Evaluaion aritaria	600mg twice a day	hours before and	Incomplete outcom-	least 0.5mg/dL or >25%	
	Exclusion criteria:		6hours after CAG	Incomplete outcome	within 48 hours of	
patients, o		on the day before	bhours after CAG	data:		
hospital	syndrome requiring	and the day of		Not reported	contrast exposure)	
	emergency CAG/PCI	coronary			1: 3.8%	
Country:	2) cardiogenic shock	angiography			C: 8.1%	
South Kor	*				p>0.05	
	media administration	0.9% saline				
Source of	within a monthor NAC	1/mL/kg/h for 12				
funding: n	ot within 48 hours before	hours before and				
reported	study entry	6hours after CAG				
	4) current dialysis or a					
	serum creatinine					
	>1.4mg/dL for men or					
	>1.2mg/dL for women					
	5) thyroid diseases					
	6) allergy to the study					
	medication					
	N total at baseline:					
	Intervention: 80					
	Control: 86					
	common co					
	Important prognostic					
	factors ² :					
	For example					
	age ± SD:					
	I: 62 ± 11					
	C: 62 ± 10					
	C: 62 ± 10					
	Sow					
	Sex: I: 79% M					
	C: 67% M					
	60 ((11)					
	SCr (mg/dL)					
	<i>I:</i> 1.03 ± 0.17					
	C: 1.03 ± 0.14					

		Groups comparable at baseline? Yes					
2010 ra co tri Se ele pa hc Cc Ja So fu	ype of study: andomized ontrolled rial etting: lective atients, one ospital ountry: apan ource of unding: not eported	Inclusion criteria: 1) Patients with stable coronary artery disease scheduled to undergo CAG and/or PCI, with stable serum creatinine concentrations Exclusion criteria: 1) acute myocardial infarction 2) use of vasopressors before PCI 3) cardiogenic shock 4) current peritoneal or hemodialysis 5) planned post-contrast dialysis 6) allergies to ths study medications 7) congestive heart disease 8) severe valvular disease 9) pregnancy 10) multiple myeloma 11) amyloidosis N total at baseline: Intervention: 15 Control: 15 Important prognostic factors ² : For example age ± SD: 1: 70 ± 10	Describe intervention (treatment/procedu re/test): NAC 704mg orally twice daily on the day before ond on the day of CAG and/or PCI 0.9% saline iv 1/ml/kg/hour For 30 minutes before and 10 hours after angiography	Describe control (treatment/proced ure/test): 0.9% saline iv 1/ml/kg/hour For 30 minutes before and 10 hours after angiography	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=SCr increase of >0.5mg/dL from baseline to 48 hours to angiography) I: 0 (0%) C: 4 (27%) 96% CI: 0.10 – 5.991, p=0.011	Authors' conclusion: These results suggest that both prophylactic NAC and aminophylline administration are effective in preventing CIN, but not with hydration alone.

	C: 70 ± 8 Sex: I: 80% M C: 80% M SCr (mg/dL) I: 1.00 ± 0.36 C: 0.94 ± 0.21 Groups comparable at					
	baseline? Yes					
Lawlor, 2004 Type of study: randomized controlled trial Setting: elective patients, single center Country: United Kingdom Source of funding: not reported	Inclusion criteria: 1) patients with peripheral vascular disease going for elective angiography or angioplasty to participate in this trial Exclusion criteria: N total at baseline: Intervention: 46 Control: 48 Important prognostic factors ² : For example age ± SD: I: 72 ± 12 C: 69 ± 12 Sex: I: 59% M C: 69% M	Describe intervention (treatment/procedu re/test): 1g of NAC in each bag of 0.9% saline 0.9% saline (500mL over 4-6 hours) 6-12 hours prior to angiography and again after angiography	Describe control (treatment/proced ure/test): 0.9% saline (500mL over 4-6 hours) 6-12 hours prior to angiography and again after angiography with placebo	Length of follow-up: 7 days Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=a rise of 25% or 0.5mg/dL in sCR at 48 hours after contrast administration) Patients with normal kidney function: I: 0/29 (0%) C: 0/27 (0%) p>0.05 Patients with decreased kidney function: I: 3/17 (18%) C: 3/21 (14%) p>0.05	Authors' conclusion: NAC pre-contrast and post-contrast does not confer any benefit in preventing radiocontrast induced nephropathy in vascular patients

		SCr (μ mol/L) I: 110 ± 42 C: 124 ± 63 Groups comparable at baseline? Yes					
Sadat, 2011	Type of study: randomized controlled trial Setting: elective patients, single center Country: United Kingdom Source of funding: no funding	Inclusion criteria: 1) patients undergoing peripheral angiography for peripheral artery disease Exclusion criteria: 1) patients with established renal failure – on renal replacement therapy N total at baseline: Intervention: 21 Control: 19 Important prognostic factors ² : For example age ± SD: I: 75 ± 11 C: 70 ± 14 Sex: Not reported Groups comparable at baseline? Unclear	Describe intervention (treatment/procedu re/test): NAC 600mg twice daily orally on the ay before and on the day of CAG (2.4g in total) Iv hydration 0.9% saline 1L over 12 hours before CAG 1L over 12 hours after CAG	Describe control (treatment/proced ure/test): Iv hydration 0.9% saline 1L over 12 hours before CAG 1L over 12 hours after CAG	Length of follow-up: 72 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=0.5mg/dL or 25% increase in sCr from baseline value within 48 hours of exposure to intravascular radiographic contrast media that is not attributable to other causes) I: 1/21 (5%) C: 3/19 (16%) P=0.33	Authors' conclusion: A clear conclusion is not formulated.
Tanaka, 2011	Type of study: randomized controlled trial	Inclusion criteria: 1) patients admitted for ST-segment elevation acute myocardial infarction	Describe intervention (treatment/procedu re/test):	Describe control (treatment/proced ure/test):	Length of follow-up: 36 hours Loss-to-follow-up:	Outcome measures and effect size (include 95%Cl and p-value if available):	Authors' conclusion: While N=acetylcysteine might have the possibility

Thiele,	Setting: emergency patients, single center Country: Japan Source of funding: not reported	treated with primary PCI Exclusion criteria: 1) dialysis 2) known allergy to NAC 3) inability to take NAC orally N total at baseline: Intervention: 38 Control: 38 Important prognostic factors ² : For example age ± SD: I: 63 ± 13 C: 61 ± 14 Sex: I: 82% M C: 82% M SCr (mg/dL) I: 0.95 ± 0.34 C: 0.88 ± 0.25 Groups comparable at baseline? Yes Inclusion criteria:	NAC 705mg orally before and 12, 24, 26 pours after intervention (2.8g in total) Hydration with iv Ringer lactate solution at a rate of 1-2ml/kg/hour for more than 12 hours after primary CAG	Hydration with iv Ringer lactate solution at a rate of 1-2ml/kg/hour for more than 12 hours after primary CAG	Not reported Incomplete outcome data: Not reported Length of follow-up:	CIN (=an increase in sCr level of 25% or more from baseline value within 72 hours after primary angioplasty) I: 2/38 (5%) C: 5/38 (13%) P=0.21 No major adverse events (death, acute renal failure requiring temporary replacement therapy, need for mechanical ventilation) occurred in either group during the in-hospital follow-up period. Outcome measures and	to reduce the incidence of contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction, the in-hospital mortality and morbidity were not significantly different between the two groups.
2010	randomized	1) patients with acute	intervention	(treatment/proced	Laboratory parameters:	effect size (include 95%Cl	Authors Conclusion.
	controlled	myocardial infarction	(treatment/procedu	ure/test):	72 hours	and p-value if available):	High-dose iv NAC does
	trial	undergoing primary PCI	re/test):		Clinical endpoints: 6	CIN	not provide additional
	Setting:	2) symptoms <12 hours and ST-segment elevation		10mL of 0.9%	months	CIN (=increase in sCr of ≥25%	clinical benefit to placebo with respect to CIN in
	emergency	≥0.1mV in ≥2 extremity	NAC intravenous	saline at each	Loss-to-follow-up:	from baseline within 72	non-selected patients
	patients, one	leads or ≥0.2 mV in ≥2 ore-	bolus	injection	none	hours after PCI)	undergoing angioplasty

	tertiary hospital Country: Germany Source of funding: not reported	Exclusion criteria: 1) previous fibrinolysis <12 hours 2) known NAC allergy 3) chronic dialysis 4) pregnancy 5) contra-indications for magnetic resonance imaging N total at baseline: Intervention: 126 Control: 125 Important prognostic factors ² : For example age (interquartile range): I: 68 (57-75) C: 68 (56-76) Sex: I: 71% M C: 66% M SCr (µmol/L; interquartile range) I: 81 (69-97) C: 78 (67-90)	1200mg before CAG And 1200mg twice daily for 48 hours (total dose 6g) Hydration with intravenous 0.9% saline; infusion rate 1ml/kg/hour for 12 hours (or 0.5mg/kg/h in overt heart failure)	Hydration with intravenous 0.9% saline; infusion rate 1ml/kg/hour for 12 hours (or 0.5mg/kg/h in overt heart failure)	Incomplete outcome data: none	I: 18/126 (14%) C: 25/125 (20%) P=0.28 Mortality after 6 months I: 12/126 (14%) C: 12/125 (14%) p>0.05 New congestive heart failure I: 11/126 (9%) C: 7/125 (6%) p>0.05	with moderate doses of contrast medium and optimal hydration.
		Groups comparable at baseline? Yes	6000	PCI degreesed kider	function		
				PCI, decreased kidney			
ACT, 2011	Type of study: randomized	Inclusion criteria: 1) patients undergoing	Describe intervention	Describe control (treatment/proced	<u>Length of follow-up:</u> 48-96 hours for	Outcome measures and effect size (include 95%CI	Authors' conclusion

	ontrolled rial	CAG or peripheral arterial angiography 2) at least one risk factor	(treatment/procedu re/test):	ure/test):	laboratory parameters 30 days for clinical events	and p-value if available): CI-AKI	In this large randomized trial we found that acetylcysteine does not
Se	etting:	for CI-AKI:	NAC 2x600mg orally	placebo orally	Loss-to-follow-up:	(=a 25% elevation of sCr	reduce the risk of
in	npatients,	-age >70 years	every 12 hours for 2	every 12 hours for	Intervention:	above baseline 48-986	contrast-induced acute
el	lective,	-chronic renal failure	days	2 days	56 (5%)	hours after angioplasty)	kidney injury or other
m	nulti-centre	-diabetes mellitus	(2 doses before and	(2 doses before	12 did not receive study		clinically relevant
		-clinical evidence of	2 doses after	and 2 doses after	drug before angiography	All participants	outcomes in at-risk
C	Country:	congestive heart failure	contrast	contrast	15 were not submitted to	I: 147/1153 (12.7%)	patients undergoing
В	razil	-left ventricular ejection	administration, total	administration)	angiography	C: 142/119 (12.7%)	coronary or peripheral
		fraction < 0.45	dose 4800mg)		19 were lost to 48-96	RR: 1.00 (95% CI: 0.81 –	vascular angiography.
So	ource of	-hypotension			hour serum creatinine	1.25, p=0.97)	
fu	unding: non-		Hydration with 0.9%		follow-up		
Co	ommercial	Exclusion criteria:	saline 1mg/kg/hour	Hydration with	4 died before 48-96 hours	Patients with serum	
		-patients on dialysis	from 6-12 hours	0.9% saline	15 did not return to	creatinine >1.5mg/dL:	
		-patients with ST-segment	before to 6-12	1mg/kg/hour from	collect serum creatinine	I: 12/188 (6%)	
		elevation myocardial	hours after	6-12 hours before	1 was lost to 30-day	C: 10/179 (6%)	
		infarction	angiography	to 6-12 hours after	follow-up	P=0.75	
		-pregnancy or		angiography			
		breastfeeding			Control:	Patients with eGFR 30 –	
		-women <45 years who did			54 (5%)	60 mL/min	
		not use contraceptive			7 did not receive study	I: 30/425 (7%)	
		methods			drug before angiography	C: 27/398 (7%)	
					12 were not submitted to	RR: 1.04 (0.63 – 1.72)	
		N total at baseline:			angiography	P=0.73	
		Intervention: 1172			17 were lost to 48-96		
		Control: 1136			hour serum creatinine	Patients with	
					follow-up	eGFR<30ml/min	
		With eGFR<30 ml/min			3 died before 48-96 hours	I: 6/56 (11%)	
		I: 68			14 did not return to	C: 3/48 (6%)	
		C: 63			collect serum creatinine	RR: 1.71 (0.45 – 6.49)	
					1 was lost to 30-day	P=0.92	
		With eGFR 30 to 60 ml/min			follow-up		
		I: 515			-		
		C: 492					
					Incomplete outcome	Composite outcome of	
		Important prognostic			data:	death or need for dialysis:	

		factors ² : For example age ± SD: I: 68 ± 10 C: 68 ± 10 Sex: I: 62% M C:61 % M Groups comparable at baseline? Yes			Intervention: 1153 (98%) had data included in laboratory parameters analysis 1171 (99.9%) had data included in secondary outcome analysis Reasons not reported Control: 1119 (98%) had data included in laboratory parameters analysis 1135 (99.9%) had data included in secondary	I: 2,2% C: 2.3% Hazard ratio (HR): 0.97 (95% CI: 0.56 – 1.69, p=0.92) Cardiovascular deaths: HR: 0.99 (95% CI: 0.51 – 1.99, p=0.97) There was also no difference in the risk of these outcomes defined post hoc.	
					outcome analysis Reasons not reported		
Castini,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion
2008	randomized	1) patients undergoing	intervention	(treatment/proced	5 days	effect size (include 95%CI	
	controlled	CAG and/or PCI	(treatment/procedu	ure/test):		and p-value if available):	Our findings suggest that
	trial	2) age ≥18 years	re/test):	,	Loss-to-follow-up:	,	the addition of NAC does
		3) stable sCr ≥1.2mg/dL			none	CIN1	not add further benefit in
	Setting:			0.9% saline iv		(=increase in sCr ≥25%	CIN prevention,
	elective	Exclusion criteria:	NAC 600mg orally	1ml/kg/hour for 12	Incomplete outcome	over the baseline value in	compared to standard
	patients,	1) sCr >4mg/dL	every 12 hours for 2	hours before and	<u>data</u> :	any of the time points:	hydration with isotonic
	single centre	2) a history of dialysis,	days	12 hours after	Not reported	24, 48 and 120 hours	saline infusion.
		multiple myeloma,	(2 doses before and	contrast		after contrast	
	Country: Italy	pulmonary edema,	2 doses after	administration		administration)	
	Source of	cardiogenic shock, acute	contrast			I: 7 (14%) C: 9 (17%)	
	funding: not	myocardial infarction 3) emergency	administration, total dose 2400mg)			p>0.05	
	reported	catheterization	400111g)			μ/0.03	
	. aported	4) recent exposure to	0.9% saline iv				
		radiographic contrast	1ml/kg/hour for 12				
		media within 7 days of the	hours before and 12			CIN2	
		study	hours after contrast			(=increase in sCr	
		5) allergy to iodinate	administration			≥0.5mg/dL over the	

contrast media or NAC 6) previous enrolment in the same or other protocols 7) administration of mannitol, theophylline, dopamine, dobutamine, nonsteroidal anti- infammatory drugs or fenoldopam Notatl at baseline: Intervention: 52 Control: 51 Important prognostic factors: For example age ± 5D: 1: 71 ± 7 C:73 ± 8 Sex: 1: 99% M C: 84% M Sc (mg/alt.) 1: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Ferrario, 2009 randomized controlled trial 7 type of study: 10 patients scheduled for controlled trial 10 patients scheduled for controlled trial 20 page 215: 10 patients scheduled for controlled trial 20 page 218 pars Describe control (treatment/proced pre/test): 10 patients scheduled for controlled controlled trial 10 patients scheduled for controlled controlled controlled trial 10 patients scheduled for contrast administration) 1: 4 (8%) C: 5 (9%) p>0.05 No acute renal failure necessitating renal replacement therapy coccurred. No acute renal failure necessitating renal replacement therapy coccurred. No acute renal failure necessitating renal replacement therapy coccurred. Cutome measures and effect size (include 99%CI and p-value if available): and p-value if available): on our experience, NAC did not prevent CIN in patients receiving iso-							handler of the second	
the same or other protocols 7) administration of mannitol, theophylline, dopamine, dobutamine, nonsteroidal anti-inflammatory drugs or fenoldopam No acute renal failure necessitating renal replacement therapy occurred. No acute renal failure necessitating renal replacement therapy occurred. Important prognostic factors: For example age ± 5D: 1: 71 ± 7 1: 72 : 73 ± 8 Sex: 1: 94% M 1: 43% M 1: 43% M 1: 43% M 1: 1.57 ± 0.38 1: 1.57 ± 0.								
protocols 7) administration of mamitol, theophyline, dopamine, dobutamine, nonsteroidal anti- inflammatory drugs or fenoldopam Notatal at baseline: intervention: 52 Control: 51 Important prognostic factors: For example age ± SD: 1: 71 ± 7 C:73 ± 8 Sex: 1: 94% M C: 84% M SCr (mg/dL) 1: 1.57 = 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Ferrario, 2009 Type of study: randomized controlled trial Type of study: randomized controlled and/or PCI and/or PCI and/or PCI bescribe control (treatment/procedu re/test): refets): refets								
7) administration of mannitol, theophylline, dopamine, dobutamine, nonsteroidal anti-inflammatory drugs or fenoldopam N total at baseline: intervention: 52								
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dopamine, dobutamine, nonsteroidal anti- inflammatory drugs or fenoldopam Notal at baseline: Intervention: 52 Control: 51 Important prognostic factors; For example age ± 5D: I: 71 ± 7 C: 73 ± 8 Sex: I: 94% M C: 84% M SC? (mg/dL) I: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Ordinated controlled trial Inclusion criteria: I) patients scheduled for elective or diagnostic CAG trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI (treatment/procedu trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI In our experience, NAC did not prevent CIN in our experience, NAC did not prevent CIN in control (and prev			7) administration of				1: 4 (8%)	
dopamine, dobutamine, nonsteroidal anti- inflammatory drugs or fenoldopam Notal at baseline: Intervention: 52 Control: 51 Important prognostic factors; For example age ± 5D: I: 71 ± 7 C: 73 ± 8 Sex: I: 94% M C: 84% M SC? (mg/dL) I: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Ordinated controlled trial Inclusion criteria: I) patients scheduled for elective or diagnostic CAG trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI (treatment/procedu trial and/or PCI and/or PCI Describe control (treatment/procedu trial and/or PCI In our experience, NAC did not prevent CIN in our experience, NAC did not prevent CIN in control (and prev			mannitol, theophylline,				C: 5 (9%)	
nonsteroidal anti- inflammatory drugs or fenoldopam N total at baseline: Intervention: 52 Control: 51 Important prognostic factors': For example age ± 5D: F. 71 ± 7 C.73 ± 8 Sex: F. 94% M C: 84% M C: 84% M C: 84% M C: 84% M C: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Type of study: Indiusion criteria: Indiusion criteria: I) patients scheduled for elective or diagnostic CAG and p-value if available): In our experience, NAC did not prevent CIN in								
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Important prognostic factors ² : For example age ± 5D:								
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Sex: 1: 94% M C: 84% M SCr (mg/dL) 1: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Inclusion criteria: 1) patients scheduled for controlled controlled trial and/or PCl and/or PCl and/or PCl Loss-to-follow-up: Loss-to								
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Sex: I: 94% M C: 84% M SCr (mg/dL) I: 1.57 ± 0.38 C: 1.49 ± 0.30 Groups comparable at baseline? Yes Ferrario, 2009 Tandomized controlled trial Type of study: randomized controlled and/or PCI Type of study: randomized controlled trial Describe intervention (treatment/proced ure/test): Describe control (treatment/proced ure/test): Length of follow-up: 3 days Outcome measures and effect size (include 95%CI and p-value if available): In our experience, NAC did not prevent CIN in								
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Ferrario, 2009 Tandomized controlled trial Tile 4 % M C: 84% M C: 84% M SCr (mg/dL)								
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Errario, 2009 Type of study: randomized controlled elective or diagnostic CAG trial and/or PCI Type of study: re/test): Describe control (treatment/proced ure/test): Length of follow-up: 3 days Outcome measures and effect size (include 95%Cl and p-value if available): In our experience, NAC did not prevent CIN in Controlled								
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controlled elective or diagnostic CAG (treatment/procedu ure/test): and p-value if available): In our experience, NAC did not prevent CIN in								Authors' conclusion
trial and/or PCI re/test): Loss-to-follow-up: did not prevent CIN in	2009					3 days		
		controlled	elective or diagnostic CAG	(treatment/procedu	ure/test):		and p-value if available):	In our experience, NAC
		trial	and/or PCI	re/test):		Loss-to-follow-up:		did not prevent CIN in
			2) age ≥18 years			Intervention:	CIN	patients receiving iso-

Setting:	3) creatinine clearance		Placebo (glucose	4 (4%)	(=increase in sCr	osmolar (iodixanol)
elective	<55ml/min and a stable	NAC 600mg orally	tablets) orally	Reasons not reported	≥0.5mg/dL or >25%	contrast media and
patients,	renal function	every 12 hours for 2	every 12 hours for	·	within 3 days after the	adequate hydration.
university		days	2 days	Control:	procedure)	, ,
hospital	Exclusion criteria:	(2 doses on the day	(2 doses on the day	4 (3%)	I: 8/99 (8%)	
	1) ongoing acute	before and 2 doses	before and 2 doses	Reasons not reported	C: 6/101 (6%)	
Country: Italy	myocardial infarction or	on the day of	on the day of	·	P=0.60	
, ,	acute coronary syndrome	contrast	contrast	Incomplete outcome		
Source of	2) renal replacement	administration, total	administration)	data:		
funding: not	therapy	dose 2400mg)		Not reported		
reported	3) allergy to NAC	-	0.9% saline			
	4) need for administration	0.9% saline	1ml/kg/h in 12-24			
	of mannitol, theophylline,	1ml/kg/h in 12-24	hours before the			
	dopamine, dobutamine,	hours before the	procedure and 24			
	fenoldopam or nephrotoxic	procedure and 24	hours after			
	drugs within 1 week of	hours after				
	procedure					
	5) clinical signs of					
	dehydration and systemic					
	hypotension					
	N total at baseline:					
	Intervention: 99					
	Control: 101					
	Important prognostic					
	<u>factors</u> ² :					
	For example					
	age ± SD:					
	I: 75 ± 8					
	C: 75 ± 7					
	Sex:					
	I: 68% M					
	C: 62% M					
	Creatinine clearance					

Gulel, 2005	Type of study:	(mL/min) I: 37 ± 11.5 C: 40 ± 9.3 Groups comparable at baseline? Yes Inclusion criteria: 1) patients scheduled for	Describe intervention	Describe control (treatment/proced	Length of follow-up: 48 hours	Outcome measures and effect size (include 95%CI	Authors' conclusion:
2005	controlled trial Setting: elective, single centre Country: Turkey Source of funding: not reported	1) patients scheduled for elective diagnostic CAG 2) chronic renal impairement: sCr >1.3mg/dL 3) stable renal function Exclusion criteria: 1) acute renal failure 2) end-stage renal failure on regular dialysis 3) clinically evident heart failure 4) allergy against contrast agents 5) serious hepatic dysfunction 6) planned PCI N total at baseline: Intervention: 25 Control: 25 Important prognostic factors ² : For example age ± SD:	Intervention (treatment/procedu re/test): NAC 600mg orally every 12 hours for 2 days (2 doses on the day before and 2 doses on the day of contrast administration, total dose 2400mg) 0.9% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	ure/test): 0.9% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	errect size (include 95%Cl and p-value if available): Contrast nephropathy (= an increase more than 0.5 mg/dL 48 hours after the procedure compared with baseline values-) I: 3/25 (12%) C: 2/25 (8%) p>0.05	Our results show that oral acetylcysteine does not reduce the risk of contrast nephropathy when used before elective diagnostic CAG in patients with renal dysfunction.
		I: 61 ± 12 C: 62 ± 12					

Habib, 2016	Type of study: randomized controlled trial Setting: European Gaza Hospital, Gaza, Palestine (Israel) Source of	Sex: I: 80% M C: 72% M Creatinine clearance (mL/min) I: 46.5 ± 4.2 C: 43.2 ± 3.9 Groups comparable at baseline? Yes Inclusion criteria: Patients had at least one risk factor for CIN (age >70 years, baseline creatinine level >1.5 mg/dL, heart failure, diabetes mellitus or contrast media volume >300 mL) Exclusion criteria: Not stated N total at baseline: Group A: 40	Describe intervention (treatment/procedu re/test): Group A (n = 30), NAC 1200 mg orally before angiography and 1200 mg orally twice daily for three doses along with good hydration	Describe control (treatment/proced ure/test): Group C (n = 45), hydration with 0.9% saline started just before contrast media injection and continued for 12 h at a rate 1.0 mL/kg/min after	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): Contrast nephropathy (= an increase more than 0.5 mg/dL 48 hours after the procedure compared with baseline values-) I: 2/30 C: 8/45 P=0.001	Authors' conclusion: Our study indicates that high doses of NAC plus hydration provide better protection against CIN than combination therapy of NAC and ascorbic acid plus hydration, or hydration alone.
	Source of funding: not reported						

	Groups comparable at baseline? Yes					
Izani Wan, 2008 (Mohame d) Setting: elective patients, single cent Country: Malaysia Source of funding: no reported	1) patients electively admitted for CAG 2) calculated creatinine clearance 40-90ml/min 3) age ≥18 years Exclusion criteria: 1) severe renal failure 2) presence of acute or reversible component of renal failure 3) severe peptic ulcer disease	Describe intervention (treatment/procedu re/test): NAC 600mg orally every 12 hours for 2 days (2 doses on the day before and 2 doses on the day of contrast administration, total dose 2400mg) 0.45% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Describe control (treatment/proced ure/test): 0.45% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Length of follow-up: 48 hours Loss-to-follow-up: Intervention: 4 (8%) 1 early discharge 2 procedure cancellation 1 procedure complication Control: 4 (7%) 2 early discharge 2 procedure cancellation Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (= increase of >25% in the sCr level 48 hours after the procedure) I: 2/49 (4%) C: 6/51 (12%) P=0.27 None of the patients who developed CIN required dialysis.	Authors' conclusion: Addition of NAC to standard hydration therapy is not associated with reduction in incidence of CIN in patients with mild to moderate renal impairment undergoing elective CAG.

Koc, 2012	Type of study: randomized	SCr (µmol/L) I: 124 ± 17 C: 124 ± 22 Groups comparable at baseline? Yes Inclusion criteria: 1) patients about to	Describe intervention	Describe control (treatment/proced	Length of follow-up: 48 hours	Outcome measures and effect size (include 95%CI	Authors'conclusion:
	controlled trial	undergo CAG and/or PCI 2) calculated creatinine clearance <60ml/min or	(treatment/procedu re/test):	ure/test):	Loss-to-follow-up: Not reported	and p-value if available): CIN	The results of this study suggest that NAC plus high-dose hydration was
	Setting: elective patients,	sCr≥1.1mg/dL 3) age ≥18 years	NAC 600mg intravenously every	0.9% saline iv 1ml/kg/h in on the day before, on the	Incomplete outcome data:	(=baseline sCr ≥25% and/or an absolute increase in sCr of ≥0.5	superior to high-dose hydration alone as well as standard hydration for
	single centre Country:	Exclusion criteria: 1) contrast-agent hypersensitivity	12 hours for 2 days (2 doses on the day before and 2 doses	day of, and on the day after the procedure	Not reported	mg/dL 48 hours after the procedure) I: 2 (3%)	the protection of renal function in patients with mild to moderate renal
	Turkey	pregnancy or lactation decompensated heart	on the day of contrast	procedure		C: 13 (16%) P=0.006	dysfunction who are undergoing CAG and/or
	Source of funding: not	failure 4) pulmonary edema	administration, total dose 2400mg)				PCI.
	reported	5) emergency catheterisation 6) acute or end-stage renal failure	0.9% saline iv 1ml/kg/h in on the day before, on the day of, and on the			No patients needed hemodialysis.	
		N total at baseline: Intervention: 80 Control: 80	day after the procedure				
		Important prognostic factors ² : For example age ± SD: I: 62 ± 10 C: 65 ± 11					

1 day Countr Austral Source funding comme (pharm	I) day-stay elective patients scheduled for CAG and/or PCI Exclusion criteria: 1) allergy to the study medication 2) unstable renal function 3) undergoing chronic dialysis 4) uncontrolled asthma 5) pregnancy or breastfeeding The ce of ong: Ing: Ing: Ing: Ing: Ing: Ing: Ing: I	Describe intervention (treatment/procedu re/test): I1: NAC 300mg intravenously, once 1-2 hours before procedure and once 2-4 hours after procedure (total dose 600mg) Hydration iv: 0.9% saline 100ml/hour 2 hours before procedure and 5hours after procedure	Describe control (treatment/proced ure/test): Hydration iv: 0.9% saline 100ml/hour 2 hours before procedure and 5hours after procedure	Length of follow-up: 2-4 days and 30 days Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): None of the patients developed CIN (= None of the patients developed a need for dialysis.	Authors' conclusion: For day-saty patients with mild to moderate renal impairement undergoing CAG and/or PCI, prehydration alone is less complicated and more cost-effective than a combination of IV NAC (at doses used) and hydration.
	For example age ± SD: I1: 66 ± 14 I2: 67 ± 12	NAC6300mg intravenously, once 1-2 hours before				

		C: 69 ± 9 Sex: I1: 75% M I2: 86% M C: 89% M SCR (mmol/L) I1: 0.16 ± 0.03	procedure and once 2-4 hours after procedure (total dose 1200mg) Hydration iv: 0.9% saline 100ml/hour 2 hours before procedure and 5hours after				
		I2: 0.16 ± 0.03 C: 0.15 ± 0.02 Groups comparable at baseline? Yes	procedure				
Sadineni, 2017	Type of study: randomized controlled trial Setting: Department of Nephrology, Nizam's	Inclusion criteria: Age more than 30 years + Patients should have their serum creatinine ≥1.2 mg/dl on their most recent sample drawn within 3 months of planned procedure Exclusion criteria:	Describe intervention (treatment/procedu re/test): NAC + NS: Group of patients who received NS and NAC	Describe control (treatment/proced ure/test): Placebo + NS: Group of patients who received NS only	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN, defined as either a relative increase in serum creatinine from baseline of ≥25% or an absolute increase of ≥0.3 mg/dl (44.2 µmol/L) during days	Authors' conclusion: The major finding of this study was there was no significant difference between NAC and placebo in the prevention of contrast nephropathy.
	Institute of Medical Sciences, Hyderabad, Telangana, India	Patients with acute renal failure, endstage renal disease requiring dialysis, intravascular administration of contrast material within previous 6 days, pregnancy, lactation,				1 and 2 NAC: 7/35 Placebo: 11/30 P > 0.05	
	Source of funding: not reported	emergent coronary angiography, history of hypersensitivity reaction to contrast media, cardiogenic shock, pulmonary edema,					

		mechanical ventilator, parenteral use of diuretics, recent use of NAC, recent use of ascorbic acid, and use of metformin or NSAIDS within 48 h of procedure were excluded from the study. N total at baseline: NAC: 35 Placebo: 30 Important prognostic factors ² : For example age ± SD: NAC: 61 ± 11 Placebo: 63 ± 12 Sex: Group A: 77% M Group C: 87% M Groups comparable at baseline? Yes					
Seyon, 2007	Type of study: randomized controlled trial Setting: emergency patients, one centre Country:	Inclusion criteria: 1) patients admitted with a diagnosis of acute coronary syndrome 2) scheduled for CAG and/or PCI 3) impaired renal function defined as: -calculated creatinine clearance <50ml/min or -sCr≥1.4mg/dL for males or	Describe intervention (treatment/procedu re/test): 600mg NAC orally four doses in total (1 before procedure and 3 after every 12 hours)	Describe control (treatment/proced ure/test): Iv hydration 0.45% saline1ml/kg/hour 4-6 hours before and 12 hours after procedure	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=increase in sCr >44µmol/L (0.5mg/dL) and/or 25% above baseline within 48 hours) I: 1/20 (5%) C: 2/20 (10%)	Authors' conclusion These results suggest that this cohort gained no added protection to renal function with the use of NAC

Canada	sCr≥1.3mg/dL for females	Iv hydration 0.45%		p<0.05	
	4) age ≥18 years	saline1ml/kg/hour		•	
Source of		4-6 hours before			
funding: not	Exclusion criteria:	and 12 hours after		No patients required	
reported	1) hemodynamic instability	procedure		dialysis therapy.	
	requiring inotropic support				
	2) pregnancy				
	3) acute gastrointestinal				
	disorder				
	4) Killip class III or IV or				
	NYHA III or IV, or patients				
	deemed by cardiologist				
	unsuitable for iv hydration				
	5) known sensitivity to NAC				
	6) current treatment with				
	theophylline or mannitol				
	7) dialysis therapy				
	8) participation in another				
	study or use of				
	experimental drugs				
	N total at baseline:				
	Intervention: 20				
	Control: 20				
	Important prognostic				
	factors ² :				
	For example				
	age ± SD:				
	1: 76 ± 6				
	C: 75 ± 10				
	Sex:				
	I: 60% M				
	C: 70% M				
	Groups comparable at				

haseline? Ves				
		V		
	l baseline?	Yes		

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

CAG: coronary angiography; CECT: contrast-enhanced computed tomography; CI: confidence interval; CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; iv: intravenous; NAC: N-acetylcysteine; NYHA: New York Heart Association; OR: odds ratio; PCI: percutaneous coronary intervention; SCr: serum creatinine

Search description

Search des	ch description								
Database	Search terms	Total							
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	302							
(OVID)	(111910) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or								
	nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.								
2005-juli	(535114)								
2015	3 1 and 2 (8902) 4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or								
	ciaki), ti, ab. (1951)								
English	5 3 or 4 (9390)								
	6 limit 5 to (yr="2005 -Current" and (dutch or english)) (3922)								
	7 Acetylcysteine/ or ('acetyl cysteine' or acetylcysteine or (n adj1 acetyl*)).ti,ab. (71339)								
	8 6 and 7 (356)								
	9 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic*								
	or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab.								
	or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection								
	criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or								
	Letter/ or (animals/ not humans/)) (245460)								
	10 8 and 9 (50) – 49 uniek 11 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or								
	randomized controlled trials as topic/ or Random Allocation/ or Double-Blind								
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or								
	clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or								
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj								
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)								
	(1499747) 12 8 and 11 (184)								
	13 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or								
	Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or								
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or								
	prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically								
	controlled study/ or interrupted time series analysis/ [Onder exp cohort studies								
	vallen ook longitudinale, prospectieve en retrospectieve studies] (2196775) 14 8 and 13 (107)								
	15 12 not 10 (144) – 141 uniek								
	16 14 not (10 or 12) (23)								
Embase	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2								
(Elsevier)	(nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3								
	medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2								
	(disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2								
	(insufficienc* OR function* OR disease* OR failure*)):ab,ti)) NOT 'conference abstract':it AND [english]/lim AND [embase]/lim AND [2005-2015]/py								
	abstract iterato [english]/intrato [embase]/intrato [2005 2015]/py								
	AND ('acetylcysteine'/exp/mj OR 'acetyl cysteine':ab,ti OR acetylcysteine:ab,ti OR (n								
	NEAR/1 acetyl*):ab,ti)								
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR								
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1								
	analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR								
	'nonhuman'/exp NOT 'human'/exp))) (70) – 21 uniek								
	AND 'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR								
	'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR								
	'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR								
	placebo*:ab,ti NOT 'conference abstract':it)) (171) – 56 uniek								
	AND 'major clinical study'/de (25) – 12 uniek								

Appendices to Chapter 7.3

Evidence tables

Table: Exclusion after revision of full text

Table: Exclusion after revision of full text								
Author and year	Reason for exclusion							
Albabtain, 2013	Included in systematic review by Sadat, 2013							
Alexopoulos, 2010	No vitamin C administration in one of the treatment groups							
Au, 2014	review, not specifically focussed on vitamin C (review of Sadat, 2013 of better							
	quality and includes same literature)							
Boscheri, 2005	Included in systematic review by Sadat, 2013							
Briguori, 2006	review, not systematic							
Briguori, 2007_1	vitamin C group not being compared to hydration only or no hydration group (does							
	not comply with PICO)							
Briguori, 2007_2	vitamin C group not being compared to hydration only or no hydration group (does							
	not comply with PICO)							
Bruerck, 2013	Included in systematic review by Sadat, 2013							
De Bie, 2011	review, not systematic							
Generali, 2012	review, not systematic							
Itoh, 2005	review, not systematic							
Jo, 2009	Included in systematic review by Sadat, 2013							
Joannidis, 2007	review, not systematic							
Kayan, 2012	Not a clinical study							
McCullough, 2008	Letter to editor							
McCullough, 2013	Letter to editor							
Naziroglu, 2013	review, not specifically focussed on vitamin C (review of Sadat, 2013 of better							
	quality and includes same literature)							
Oudemans – van Straaten,	review, not systematic							
2005								
Pattharanitima, 2014	review, not systematic							
Reiner, 2009	review, not systematic							
Sadat, 2015	review, not systematic							
Shakeryan, 2013	oral administration of vitamin C in combination with pentoxyfilline in treatment							
	group (does not comply with PICO)							
Sinert, 2007	more recent review by Sadat, 2013 available							
Sinert, 2013	review, not systematic							
Spargias, 2005	Included in systematic review by Sadat, 2013							
Stacul, 2006	more recent review by Sadat, 2013 available							
Wang, 2014	Article not found							
Zhou, 2012	Included in systematic review by Sadat, 2013							

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10;doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question? ¹	Comprehensive and systematic literature search? ²	Description of included and excluded studies? ³	Description of relevant characteristics of included studies? ⁴	Appropriate adjustment for potential confounders in observational studies? ⁵	Assessment of scientific quality of included studies? ⁶	Enough similarities between studies to make combining	bias taken into	Potential conflicts of interest reported? ⁹
First author,	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	them reasonable? ⁷ Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
year Sadat,	Yes	Yes	No No	Yes	Not applicable	Yes	Yes		Yes
2013									

- 1. Research question (PICO) and inclusion criteria should be appropriate and predefined
- 2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
- 3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
- 4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
- 5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)
- 6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
- 7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?
- 8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
- 9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)

Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year)		(unlikely/likely/un clear)	(unlikely/likely/un clear)	(unlikely/likely/un clear)	(unlikely/likely/uncle ar)	(unlikely/likely/unc lear)	(unlikely/likely/uncle ar)	(unlikely/likely/uncle ar)
Komiyama 2017	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear
Dvoršak, 2013	Not reported	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear

- 1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments
reference	characteristics			control (C)		effect size	
Sadat,	SR and meta-	Inclusion criteria SR:	Describe intervention:	Describe control:	End-point of	Outcome measure-1	<u>Facultative</u> :
2013	analysis of	1) RCTs assessing the use of			follow-up:	Defined as. Risk of CI-AKI	
	[RCTs]	ascorbic acid in reducing CI-		A: placebo with IV	Not reported	(risk ratio)	Brief description of
[individua		AKI compared with placebo	A: Ascorbic acid, oral	hydration as in			author's conclusion:
l study	Literature search	or other pharmacological	administration,	ascorbic acid arm		Effect measure: relative	Ascorbic acid provides
characteri	up to May 15 th	treatments in patients	3g at least 2 hours after	B : placebo with IV	For how many	risk [95% CI]:	effective
stics	2013	undergoing coronary	procedure, 2g night	hydration as in	<u>participants</u>	A : 0.46 (0.23 – 0.90)	nephroprotection against
deduced		angiography	before and morning	ascorbic acid arm	were no	B : 1.55 (0.39 – 6.26)	CI-AKI and may form a
from [1st	A: Sparglas,	2) route of administration of	after procedure.	C : 1200mG NAC	<u>complete</u>	C : 3.65 (0.42 – 31.99)	part of effective
author,	2004	ascorbic acid: oral or	Hydration with saline	orally 2x/daily on	outcome data	D : 1.35 (0.40 – 4.61)	prophylactic
year of	B : Boscheri,	intravenous or both	50-125mg/hr IV from	day of procedure	<u>available?</u>	E : 0.25 (0.08 – 0.81)	pharmacological
publicatio	2007	3) Incidence of CI-AKI	time of randomization	and day before	(intervention/co	F : 0.76 (0.51 – 1.14)	regiments.
n	C : Jo, 2009	(absolute increase in serum	to at least 6 hours after	procedure	ntrol)	G : 1.14 (0.32 – 4.07)	
]]	D : Zhou, 2011	creatinine of ≥0.5 mg/dl	procedure	D : IV saline	Not reported	H : 0.46 (0.32 – 2.30)	Personal remarks on
	E: Komiyama,	(44µmol/L) or a relative	B: 1g ascorbic acid	hydration		I: 0.49 (0.09 – 2.30)	study quality,
PS., study	2011	increase of ≥25% from the	orally 20 minutes before	1mg/kg/hour for 4			conclusions, and other
characteri	F: Bruerck, 2011	baseline value after	exposure to contrast	hours before and at		Pooled effect (random	issues (potentially)
stics and	G : Li, 2012	administration of contrast	medium, 500mL saline,	least 12 hours after		effects model): risk ratio:	relevant to the research
results	H : Albabtain,	media during angiography)	2 hours before and	angiography		0.672 [95% CI 0.466 to	question:
are	2013	was reported as outcome	500ml during	E: IV saline		0.969] favoring ascorbic	
extracted	I:Hamdi, 2013	measure	angiography and	hydration 1.5 – 2.5L		acid	When studies on oral
from the			subsequent 6 hours	F : placebo (per		Heterogeneity (I ²): 27%	ascorbic acid
SR (unless	Study design:	Exclusion criteria SR:	C: ascorbic acid, 3g	ascorbic acid dose)			administration and IV
stated	RCT [parallel]	-	(night before) and 2g	and IV saline		Outcome measure-2	ascorbic acid
otherwise			morning of procedure;	(1/mg/kg/hour) for		Risk of publication bias	administration were
)	Setting and	9 studies included	2g night before and	12 hours before to		Egger's regression	pooled separately, the
	Country:		morning after	12 hours after		intercept:	ascorbic acid
	Outpatients		procedure, oral	contrast medium		1.086 (95% CI: -2.57 –	administration was as
	England and	Important patient	administration, all doses	exposure		4.74)	effective as control in
	Pakistan	characteristics at baseline:	12 hours apart	G : IV saline		df = 4	prevention of CI-AKI.
		Number of patients;	D : ascorbic acid, IV	hydration		p=0.455	
	Source of	characteristics important to	administration, 3g	H: IV saline			Level of evidence: GRADE
	funding:	the research question and/or	morning of procedure,	hydration			(per comparison and

Not reported	for statistical adjustment (confounding in cohort studies); for example, age,	oral 0.5g on the night of procedure and next morning (all doses 12	I:IV saline hydration		outcome measure) including reasons for down/upgrading:
	sex, bmi,	hours apart). IV saline			For the outcome risk of
		hydration1mg/kg/hr for			CI-AKI the level of
	<u>N,</u>	4 hours before and at			evidence was reduced to
	A: 238	least 12 hours after			moderate, due to
	B : 143	angiography			inconsistency of results.
	C : 212	E: ascorbic acid, IV			
	D : 174	administration, 3g			
	E : 70	before procedure, 2g			
	F : 520	night and morning after			
	G : 149	procedure (12 hours			
	H : 243	apart). Saline hydration			
	1:202	1.5 – 2.5L			
		F: ascorbic acid, IV			
		administration			
	Groups comparable at	G : ascorbic acid, IV 3g 2-			
	baseline?	4 hours before			
	Unclear	procedure and oral 1g			
		on days 1 and 2 after			
		procedure. IV saline			
		hydration			
		H: ascorbic acide, oral			
		administration, 3g 2			
		hours before procedure,			
		2g after angiogram and			
		2g 24 hours after			
		angiogram. IV saline 50-			
		125 ml/hour from			
		randomization until at			
		least 6 hours after			
		procedure			
		I: ascorbic acid 3g 2			
		hours before procedure,			
		2g day after procedure			
		and next day, mode of			

_				
		 administration not		
		reported		

Ascorbic acid = vitamin C;CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; IV: intravenous; NAC: N-acetyl-cysteine; NR: not reported; RCT: randomised controlled trial

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1
This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study reference	Study characteristic s	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
Dvoršak,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	We found no statistically
2013	randomized	1) patients with stable	intervention	(treatment/proced	4 days	effect size (include 95%CI	significant impact of
	controlled	serum creatinine levels	(treatment/procedu	ure/test):		and p-value if available):	ascorbic acid on the
	trial	(>107μmol/L / 1.2 mg/dL)	re/test):		Loss-to-follow-up:		incidence of CIN in
		2) undergoing elective			Intervention:	Contrast-induced	patients with chronic
	Setting: not	coronary angiography or		Placebo	2/42 (5%)	nephropathy	renal impairment
	clear	angioplasty	Ascorbic acid in		Reasons: lost to follow-up	(+an increase in serum	undergoing coronary
			500mg capsules		(?)	creatinine level >25%	arteriography or
	Country:	Exclusion criteria:	3g orally before			from baseline or increase	angioplasty.
	Slovenia	1) regular medication	procedure		Control:	of serum cystatin C levels	
	_	containing vitamin C	2g after the		0/41 (0%)	>25%, measured 3-4 days	
	Source of	2) acute renal failure	procedure in the		Reasons: not applicable	after procedure)	
	funding: no	3) end-stage renal disease	evening and the				
	funding	4) radiocontrast procedure	next morning		Incomplete outcome	1: 2/40	
		in the last 3 months			data:	C: 3/41	
		5) cardiogenic shock			Not reported	P=0.51	
		6) acute myocardial					
		infarction					
		N total at baseline:					
		Intervention: 42					
		Control: 41					
		Control. 41					
		Important prognostic					

		factors ² :					1
		For example					
		•					
		age ± SD:					
		1: 71 ± 9					
		C: 71 ± 9					
		Carri					
		Sex:					
		1: 78% M					
		C: 68% M					
		Consumer and the st					
		Groups comparable at					
		baseline? Yes					
Komiyam	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Use of i.v. sodium
a 2017	randomized	patients with renal	intervention	(treatment/proced	3 days	effect size (include 95%Cl	bicarbonate and ascorbic
	controlled	dysfunction undergoing	(treatment/procedu	ure/test):		and p-value if available):	acid and a saline
	trial	elective angiography	re/test):		Loss-to-follow-up:		hydration protocol in
		(including coronary			Intervention:	Contrast-induced	patients with CKD
	Setting:	angiography, aortography,	Sodium bicarbonate	The control group	None reported	nephropathy	undergoing elective
	hospital	and venography)	(20 mL=20 mEq;	received 0.9%	Reasons: not applicable	(+an increase in serum	procedures can prevent
		or intervention (including	Meyron 84, Otsuka	physiological saline		creatinine level >25%	CIN more effectively than
	Country:	percutaneous coronary	Pharmaceutical,	6–15 h before, and	<u>Control:</u>	from baseline or increase	saline hydration alone.
	Japan	intervention and	Tokyo, Japan) and	during, the	None reported	of serum cystatin C levels	
		endovascular treatment)	ascorbic acid (3 g)	procedure at a rate	Reasons: not applicable	>25%, measured 3 days	
	Source of	with a catheter	were given i.v.	of 1.5 mL/kg/h.		after procedure)	
	funding: no		before the	This rate was then	Incomplete outcome		
	funding	Exclusion criteria:	procedure. Ascorbic	increased to 2.5	<u>data:</u>	I: 6/211	
		1) aged <20 years	acid (2 g) was then	mL/kg/h for 6 h	Not reported	C: 19/218	
		pregnant or undergoing	administered after	after the		P=0.008	
		maintenance dialysis. 3)	the procedure,	procedure. The			
		acute conditions such as	followed by another	total amount of			
		acute myocardial infarction	2 g of ascorbic	saline administered			
		and unstable angina	acid 12 h later after	was 1,500–2,500			
		3) severe cardiac failure	the procedure; this	mL			
		(New York Heart	group also received				
		Association class III or	the same saline				
		<u>higher)</u>	hydration protocol				
		4) severe respiratory	as the control				

l.			
<u>disease</u>	group.		
5) undergone catheter			
procedures involving the			
use of a contrast agent			
within the previous 48 h			
N total at baseline:			
Intervention: 218			
<u>Control: 211</u>			
Important prognostic			
<u>factors2:</u>			
<u>For example</u>			
age ± SD:			
<u>1: 73 ± 10</u>			
<u>C: 74 ± 10</u>			
<u>Sex:</u>			
<u>I: 79% M</u>			
<u>C: 82% M</u>			
Groups comparable at			
baseline? Yes			

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Search de	scription	
Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	113
(OVID)	(110542) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
1995-june	(528935)	
English, Dutch	3 1 and 2 (8818) 4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or ciaki).ti,ab. (1925)	
	5 3 or 4 (9301) 6 limit 5 to (yr="1995 -Current" and (dutch or english)) (5402) 9 "Ascorbic Acid"/ (36223)	
	10 ("vitamine C" or ascorbate or "ascorbic acid*").ti,ab. (36094) 11 9 or 10 (52727) 12 6 and 11 (32)	
	14 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (241238) 15 12 and 14 (8) – 7 uniek	
	16 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase ii or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1475337)	
	17 12 and 16 (19) 18 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2167237) 19 12 and 18 (8) 20 15 or 17 or 19 (21) 21 17 or 19 (19) not 15 (13)	
Embase (Elsevier)	'ascorbic acid'/exp OR 'vitamine c':ab,ti OR ascorbate:ab,ti OR (ascorbic NEAR/2 acid*):ab,ti AND ('contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti))) NOT 'conference abstract':it AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [1995-2015]/py	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT (animal* NOT human*) – 31 – 27 uniek	
	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti OR 'clinical study'/exp) – 79 – 66 uniek	

Appendix 1 Additional meta-analyses

Figure 7.9 Meta-analysis also including the studies published in abstract form only

Chudy or Cubaroup	vitamin C plus		hydration		Mojaht	Risk Ratio		Risk Ratio
Study or Subgroup /	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI
Albabtain 2013	2	57	5	66	4.4%	0.46 [0.09, 2.30]		
Boscheri 2007	5	74	3	69	5.7%	1.55 [0.39, 6.26]		
Brueck 2011	24	98	62	193	43.1%	0.76 [0.51, 1.14]		-■
Dvorsak 2013	2	40	3	41	3.8%	0.68 [0.12, 3.88]		
Komiyama 2011	5	78	4	71	6.8%	1.14 [0.32, 4.07]		
Li 2012	3	35	12	35	7.9%	0.25 [0.08, 0.81]		
Spargias 2004	11	118	23	113	21.0%	0.46 [0.23, 0.90]		
Zhou 2011	6	82	4	74	7.3%	1.35 [0.40, 4.61]	annone.	- •
Total (95% CI)		582		662	100.0%	0.68 [0.48, 0.96]	ananan a	•
Total events	58		116					
Heterogeneity: Tau ² = 0.03; Chi ² = 7.85, df = 7 (P = 0.35); I ² = 11%								<u>la</u>
Test for overall effect: Z = 2.19 (P = 0.03)							0	0.01 0.1 1 10 100 Favours vitamin C Favours placebo

Figure 7.10 Meta-analysis including all RCTs on vitamin C (both impaired kidney function and kidney function not reported)

5 Total 11 118 5 74 6 82 3 35 5 78	4 3 2 4 5 12	Total 113 69 74 35	17.1% 4.4% 5.6%	1.55 [0.39, 6.26]	M-H, Random, 95% CI
5 74 6 82 3 35	4 3 2 4 5 12	69 74	4.4% 5.6%	1.55 [0.39, 6.26]	-
6 82 3 35	2 4	74	5.6%		4 · · · · · · · · · · · · · · · · · · ·
3 35	12	-		1.35 [0.40, 4.61]	
		35			
5 78			6.1%	0.25 [0.08, 0.81]	-
	3 4	71	5.2%	1.14 [0.32, 4.07]	
2 57	7 5	66	3.4%	0.46 [0.09, 2.30]	· · · · · · · · · · · · · · · · · · ·
2 40	3	41	2.9%	0.68 [0.12, 3.88]	-
11 107	7 20	95	16.6%	0.49 [0.25, 0.97]	<u> </u>
24 98	62	193	38.6%	0.76 [0.51, 1.14]	
689	9	757	100.0%	0.65 [0.48, 0.87]	•
69	136				
					0.01 0.1 10 100 Favours ascorbic acid Favours placebo
	2 40 11 107 24 98	24 98 62 689	2 40 3 41 11 107 20 95 24 98 62 193 689 757	2 40 3 41 2.9% 11 107 20 95 16.6% 24 98 62 193 38.6% 689 757 100.0%	2 40 3 41 2.9% 0.68 [0.12, 3.88] 11 107 20 95 16.6% 0.49 [0.25, 0.97] 24 98 62 193 38.6% 0.76 [0.51, 1.14] 689 757 100.0% 0.65 [0.48, 0.87]

Appendices to Chapter 7.4

Evidence Tables

Table: exclusion after examination of full text

	examination of full text
Author and year	Reasons for exclusion
Aspelin, 2014	Exam questions, not an original article
Baris, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Cirit, 2006	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Del Veccio	Narrative review
Diogo, 2010	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Duan, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Goo, 2014	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Gu, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Gu, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Jo, 2015	Only abstract available (full tekst nogmaals aangevraagd bij Sanne, aan de hand hiervan
	alsnog inclusie mogelijk)
Kalyesubula, 2014	Narrative review
Kellum, 2001	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Kiski, 2010	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Lapi, 2014	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
11 2044	radiological examination with intravasal contrast)
Li, 2011	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
1: 2042	radiological examination with intravasal contrast)
Li, 2012	Narrative review
Li, 2012b	Only abstract available (full tekst nogmaals aangevraagd bij Sanne, aan de hand hiervan
Managari 2012	alsnog inclusie mogelijk)
Marenzi, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
Mauer, 2002	injury)
Mauer, 2002	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney injury)
Oguzhan, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
Oguziiaii, 2013	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Onuigbo, 2008	No control group
Onuigbo, 2009	Narrative review
Onuigbo, 2012	Narrative review
Onuigbo, 2015	Editorial comment, not an original article
Patel, 2011	Narrative review
Peng, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
. 5116, 2013	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Rim, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
, 2022	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Rim, 2013	Erratum of Rim, 2012; not an original article
Ryan, 2008	Narrative review
,,	

Saudan, 2008	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination but started, with the hypothesis that this will prevent kidney injury)
Schetz, 2004	Narrative review
Shehata, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Shemirani, 2012	Patients with normal kidney function
Spatz, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Umruddin, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Wolak, 2013	Patients with normal kidney function
Wu, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Zhou, 2013	Narrative review

Risk of bias table for intervention studies (randomized controlled trials)
Research question:

Study reference (first author, publicatio n year)	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ² (unlikely/likely/un clear)	Bias due to inadequate blinding of participants to treatment allocation? ³ (unlikely/likely/un clear)	Bias due to inadequate blinding of care providers to treatment allocation? ³ (unlikely/likely/un clear)	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³ (unlikely/likely/uncl ear)	Bias due to selective outcome reporting on basis of the results? ⁴ (unlikely/likely/uncle ar)	Bias due to loss to follow-up? ⁵ (unlikely/likely/uncle ar)	Bias due to violation of intention to treat analysis? ⁶ (unlikely/likely/unclea r)
Bainey, 2015	Permuted block- randomization; computerized intractive voice- response system	Unlikely	Unlikelu	Unclear	Unclear	Unlikely	Unclear	Unlikely
Rosenstoc k, 2008	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

- 1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1
This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study reference	Study characteristics	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
Bainey,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	<u>Length of</u>	Outcome	Contrast induced AKI
2015	Randomized	1) presented for	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	measures and	defined as an
	controlled trial	cardiac			72±24 hours	effect size (include	absolute rize in
	(pilot)	catheterization				95%Cl and p-value	serum creatinine of
		2) using an ACEi or	Angiotensin II blockade	No discontinuation of angiotensin		if available):	≥25% (44µmol/L)
	Setting:	ARB	medication was stopped at least	II blockade medication	Loss-to-		from baseline and/or
	outpatients and	3) moderate	24 hours prior to catheterisation		follow-up:	Mean serum	a relative rise of
	inpatients	chronic kidney	and restarted after up to 96	Intravenous normal saline at 3	not reported	creatinine change	serum creatinine of
	Constant	disease (≥1.7	hours after.	mL/kg/hour for at least an hour	In a constant	I: 0.1±0.3	≥25% compared with
	Country:	mg/dL within 3	lataria a la compania de la compania del compania de la compania de la compania del compania de la compania del compania de	before contrast injection,	Incomplete	C: 0.3±0.5	baseline at any time
	Canada	months or ≥1.5	Intravenous normal saline at 3	intravebous normal saline at 1	<u>outcome</u>	P=0.03	between 48 and 96
	Causes of	within one week	mL/kg/hour for at least an hour	mL/kg/hour during contrast	data: not	Combined in divised	hours post
	Source of	of cardiac	before contrast injection,	exposure and 6 hours after the	reported	Contrast induced	procedure.
	funding: both	catheterisation)	intravebous normal saline at 1	procedure or until discharge.		AKI:	
	commercial and	Fralmaian anikania.	mL/kg/hour during contrast			I: 10.9%	
	non- commercial	Exclusion criteria:	exposure and 6 hours after the			C: 18.4%	
	commercial	1) end-stage renal	procedure or until discharge.			HR: 0.59, 95% CI: 0.30 – 1.19.	
		disease				0.30 – 1.19, p=0.16	
		emergency cardiac				p=0.16	
		catheterisation				Mortality:	
		with insufficient				1: 0 (0%)	
		time to hold ACEi				C: 1 (1%)	
		3) pulmonary				C. 1 (176)	
		oedema				Ischemic stroke:	
		ocacina				1: 0 (0%)	
		N total at baseline:				C: 1 (1%)	
		208				C. 1 (1/0)	
		Intervention: 106				Rehospitalization	

		Control: 102				for cardiovascular	
						cause:	
		Important				I: 0 (0%)	
		prognostic				C: 3 (2%)	
		factors ² :				, ,	
		For example					
		age ± SD:					
		1: 73 ± 9					
		C: 72 ± 8					
		Sex:					
		1: 74% M					
		C: 73 % M					
		C: 73 % IVI					
		Groups					
		comparable at					
		baseline? yes					
Rosenstock,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome	Measurements of
2008	Randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up: 24	measures and	creatinine 24 hours
	controlled trial	undergoing			hours	effect size (include	post-procedure;
		coronary		1) No Discontinuation of ACE		95%CI and p-value	various ACE-inhibitor
	Setting: unclear	angiography		inhibitor use around coronary		if available):	subgroups not
		2) chronic use (>2	Discontinuation of ACE inhibitor	angiography	Loss-to-	Incidence of CIN	compared due to
	Country:	months) of ACE-	use		follow-up:		small sample size.
	unclear	inhibitor	Morning of procedure up to 24	2) ACE-inhibitor naïve patients	unclear	ACE-inhibitors	
			hours after coronary angiography	undergoing coronary angiography		discontinued:	
	Source of	Exclusion criteria:			Intervention:	3.7%	
	funding:	unclear	Patients were hydrated based on	Patients were hydrated based on	N (%)	ACE-inhibitors not	
	unclear		the institution's policies and	the institution's policies and	Reasons	discontinued:	
		N total at baseline:	medications such as diuretics and	medications such as diuretics and	(describe)	6.2%	
		Intervention: 107	metformin were held prior to	metformin were held prior to		ACE-inhibitor	
		Control: 113	procedure	procedure	Control:	naïve group: 6.3%	
		ACE-naïve			N (%)	P=0.66	
		patients: 68			Reasons		
					(describe)		
		<u>Important</u>					
		prognostic			<u>Incomplete</u>		

		<u>factors</u> ² : unclear			<u>outcome</u>		
		For example			data: unclear		
		age ± SD:					
		I:			Intervention:		
		C:			N (%)		
					Reasons		
		Sex:			(describe)		
		I: % M					
		C: % M			Control:		
					N (%)		
		Groups			Reasons		
		comparable at			(describe)		
		baseline?					
		Incidence of					
		diabetes and					
		hypertension was					
		significantly lower					
		in the ACE-naïve					
		group					
1st author,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome	
year of			(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	measures and	
publication	Setting:	Exclusion criteria:				effect size (include	
						95%CI and p-value	
	Country:	N total at baseline:			Loss-to-	if available):	
		Intervention:			follow-up:		
	Source of	Control:			Intervention:		
	funding:				N (%)		
		<u>Important</u>			Reasons		
		prognostic			(describe)		
		factors ² :					
		For example			Control:		
		age ± SD:			N (%)		
		l:			Reasons		
		C:			(describe)		
		Sex:			<u>Incomplete</u>		
1	ĺ	I: % M			outcome		

		C: % M Groups comparable at			data: Intervention: N (%) Reasons		
		baseline?			(describe) Control: N (%) Reasons		
1st author, year of publication	Type of study: Setting: Country: Source of funding:	Inclusion criteria: Exclusion criteria: N total at baseline: Intervention: Control: Important prognostic factors ² : For example age ± SD: I: C: Sex: I: % M C: % M	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	(describe) Length of follow-up: Loss-to-follow-up: Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe) Incomplete outcome data: Intervention:	Outcome measures and effect size (include 95%Cl and p-value if available):	
		Groups comparable at baseline?			N (%) Reasons (describe) Control: N (%) Reasons		

l .			
		/ al a a a a: la a \	
		(describe)	
		(acseribe)	

ACEi: angiotensin converting enzyme inhibitor; AKI: acute kidney injury; ARB: angiotensin receptor blocker; CIN: contrast induced nephropathy; HR: hazard ratio

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search terms

Search to		
Database	Search terms 1 aug Contract Madia / aug // contract adi3 indina) aug/contract adi3 madi*\\ ti ab // (413533)	Total
	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. (112523) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab. (537836)	320
	3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9122) 4 1 and 2 (8979)	
	10 3 or 4 (16547)	
	12 exp "Angiotensin Receptor Antagonists"/ (18363) 13 exp Angiotensin-Converting Enzyme Inhibitors/ (40094)	
	13 exp Angiotensin-Converting Enzyme inhibitors/ (40094) 14 exp Diuretics/ (72995)	
	15 exp Anti-Inflammatory Agents, Non-Steroidal/ (164802)	
	16 12 or 13 or 14 or 15 (279958) 17 ((Angiotensin* adj3 (Antagonist or Inhibitor* or blocker*)) or Diuretic* or "Non-Steroidal Anti-Inflammatory Agent*" or NSAID* or (nephrotoxic adj3 medic*)).ti,ab. (74424) 18 12 or 13 or 14 or 15 or 17 (307695)	
	19 10 and 18 (641)	
	20 limit 19 to (yr="2000 -Current" and (dutch or english)) (266)	
	21 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not	
	humans/)) (249387)	
	22 20 and 21 (26) - 25 uniek 23 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii	
	or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1512514)	
	24 20 and 23 (75) 25 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy\$,tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2216587)	
	26 20 and 25 (81)	
	27 24 or 26 (128)	
	28 27 not 22 (109) – 107 uniek 'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti))	
	AND ('angiotensin receptor antagonist'/exp/mj OR 'dipeptidyl carboxypeptidase inhibitor'/exp/mj OR 'diuretic agent'/exp/mj OR 'nonsteroid antiinflammatory agent'/exp/mj OR (angiotensin* NEAR/3 (antagonist OR inhibitor* OR blocker*)):ab,ti OR diuretic*:ab,ti OR 'non-steroidal anti-inflammatory agent':ab,ti OR 'non-steroidal anti-inflammatory agents':ab,ti OR nsaids:ab,ti OR (nephrotoxic NEAR/3 medic*):ab,ti)	
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp)) (38) – 26 uniek	
	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	
	OR 'clinical study'/exp NOT 'conference abstract':it (225) – 162 uniek	

Appendices to Chapter 7.5

Evidence tables

Table: Exclusion after revision of full text

Table: Exclusion after revision of full text					
Author and year	Reason for exclusion				
Chang, 2013	Does not fulfill selection criteria				
Choi, 2014	Does not fulfill selection criteria				
Cruz, 2006	Does not fulfill selection criteria				
Cruz, 2008	Does not fulfill selection criteria				
Deray, 2006	Does not fulfill selection criteria				
Frank, 2003	Already included in systematic review Cruz, 2012				
Furukawa, 1996	Does not fulfill selection criteria				
Gabutti, 2003	Does not fulfill selection criteria				
Ghani, 2011	Does not fulfill selection criteria				
Hsieh, 2005	Already included in systematic review Cruz, 2012				
Huber, 2002	Does not fulfill selection criteria				
Joannidis, 2010	Does not fulfill selection criteria				
Lee, 2007	Already included in systematic review Cruz, 2012				
Lehnert, 1998	Already included in systematic review Cruz, 2012				
Marenzi, 2003	Already included in systematic review Cruz, 2012				
Marenzi, 2004	Does not fulfill selection criteria				
Marenzi, 2006	Already included in systematic review Cruz, 2012				
Marenzi, 2007	Does not fulfill selection criteria				
Moon, 1995	Does not fulfill selection criteria				
Ono, 2004	Does not fulfill selection criteria				
Reinecke, 2007	Already included in systematic review Cruz, 2012				
Schindler, 2001	Does not fulfill selection criteria				
Shinoda, 2002	Does not fulfill selection criteria				
Song, 2010	Does not fulfill selection criteria				
Song, 2011 Does not fulfill selection criteria					
Sterner, 2000	Already included in systematic review Cruz, 2012				
Vogt, 2001	Already included in systematic review Cruz, 2012				

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and	Comprehensive	Description of	Description of	Appropriate adjustment for	Assessment of	Enough	Potential risk	Potential
	clearly focused	and systematic	included and	relevant	potential confounders in	scientific	similarities	of publication	conflicts of
	question? ¹	literature	excluded	characteristics	observational studies? ⁵	quality of	between studies	bias taken into	interest
		search? ²	studies? ³	of included		included	to make	account? ⁸	reported? ⁹
				studies? ⁴		studies? ⁶	combining them		
							reasonable? ⁷		
First author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Cruz, 2012	Yes	Yes	No	Yes	No	Yes	Yes	No	No

- 10. Research question (PICO) and inclusion criteria should be appropriate and predefined
- 11. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
- 12. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
- 13. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
- 14. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)
- 15. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
- 16. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I²)?
- 17. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
- 18. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)
Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year) Spini, 2013	Not randomised	(unlikely/likely/un clear) Unlikely	(unlikely/likely/un clear) Unclear	(unlikely/likely/uncl ear) Unclear	(unlikely/likely/uncl ear) Unclear	(unlikely/likely/uncl ear) Unlikely	(unlikely/likely/unclea r) Unlikely	(unlikely/likely/uncle ar) Unclear

- 13. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
- 14. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..
- 15. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 16. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 17. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 18. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Risk of bias table for intervention studies (observational: non-randomized clinical trials, cohort and case-control studies) Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments
reference	characteristics			control (C)		effect size	
Cruz,	SR and meta-	Inclusion criteria SR:	Describe	Describe control:	End-point of follow-	Outcome measure-1	<u>Facultative</u> :
2012	analysis of RCTs	1) studies that ecaluated the	intervention:		<u>up</u> :	Defined as RCIN	
	/ cohort studies	use of periprocedural renal		For all studies:		Reported for CKD stage 4-	Brief description of
individual		replacement therapy (RRT)	A: hemodialysis	Standard medical	Not reported	5 patients only	author's conclusion: In
study	Literature search	for the prevention of	(HD)	therapy, depending			this updated meta-
characteri	up to March	radiocontrast induced	B: HD	on hospital either		Effect measure: RR [95%	analysis periproceural
stics	2011	nephropathy (RCIN) as	C: HD	pre-hydration or	For how many	CI]:	RRT did not decrease the
deduced		compared with standard	D : HD	pre- and	participants were no	J : 3.43 (0.45 – 25.93)	incidence of RCIN
from [1st	A : Lee, 2007	medical treatment (SMT)	E: HD	posthydration	complete outcome	G : 1.56 (0.66 – 3.72)	compared with SMT. HD
author,	B : Reinecke,	2) 10 or more human	F: HD		data available?	D : 0.33 (0.01 – 7.72)	appears to actually
year of	2007	subjects	G : HD		Not reported	E : 0.12 (0.05 – 0.32)	increase RCIN risk.
publicatio	C : Marenzi, 2006	3) primary outcome: RCIN	H : HD			C : 0.48 (0.27 – 0.88)	
n	D : Hsieh, 2005	(sCR ≥0.5mg/dL / 44	I: Hemofiltration			I: 1.70 (0.59 – 4.90)	Personal remarks on
	E: Marenzi, 2003	umol/L); secondary	(HF)			H : 1.27 (0.80 – 2.01)	study quality,
	F : Frank, 2003	outcomes: need for	J: HF				conclusions, and other
PS., study	G : Gabutti, 2003	temporary acute RRT, need	K: Hemodiafiltration			Pooled effect (random	issues (potentially)
characteri	H : Vogt, 2001	for permanent RRT, long-				effects model):	relevant to the research
stics and	I: Sterner, 2000	term changes in renal				0.81 [95% CI 0.37 to 1.76]	question:
results	J: Berger, 2001	function, death				favoring RRT.	In our own literature
are	K: Lehnert, 2008					Heterogeneity (I ²): 79%	analysis the observational
extracted		Exclusion criteria SR:					studies were excluded
from the	Study design:					Outcome measure-2	from the systematic
SR (unless	A: Randomized	11 studies included				Risk for acute RRT	review and only the RCTs
stated	trial						with patients CKD stage
otherwise	B : Randomized					HDF/HF	4-5 were included.
)	trial	Important patient				G : 2.89 (0.12 – 67.75)	
	C: Randomized	characteristics at baseline:				E : 0.14 (0.03 – 0.58)	Level of evidence: GRADE
	trial	Number of patients;				C : 0.16 (0.05 – 0.55)	Low to Very low for most
	D : Observational	characteristics important to				Pooled effect (random	studies due to high risk of
	E: Randomized	the research question and/or				effects model):	bias in several studies,
	trial	for statistical adjustment				0.22 [95% CI 0.06 to 0.74]	wide confidence intervals
	F : Randomized	(confounding in cohort				favoring RRT.	(imprecision) and

trial	studies); for example, age,		Heterogeneity (I ²): 36%	heterogeneity of included
G : Observational	sex, bmi,			studies
H: Randomized			HD	
trial	Number of patients, age		A: 0.07 (0.01 – 0.49)	
I: Randomized	(years)		B: 2.05 (0.29 – 14.41)	
trial	A : 82; 65-66		H: 2.81 (0.70 – 10.06)	
J: Randomized	B : 424; 67-68		Pooled effect (random	
trial	C : 92; 71-72		effects model):	
K: Randomized	D : 40; 66-69		0.78 [95% CI 0.07 to 8.43]	
trial	E : 114; 69		favoring RRT.	
	F : 17; 58-67		Heterogeneity (I ²): 83%	
	G : 49; 70			
Setting and	H : 113; 69-70			
Country: Italy	I:32; 65-72		Outcome measure-3	
	J: 15; 62-68		Risk for chronic RRT	
Source of	K: 30; 60-63			
<u>funding:</u>			HDF/HF	
No funding	<u>Sex</u> : not reported		E: 0.32 (0.03 – 3.00)	
	Groups comparable at		HD	
	baseline?		F: 1.43 (0.26 – 7.86)	
	Unclear		D: 1.33 (0.34 – 5.21)	
			A: 0.09 (0.00 – 1.52)	
			H: 2.11 (0.20 – 22.61)	
			Pooled effect (random	
			effects model):	
			0.87 [95% CI 0.33 to 2.29]	
			favoring RRT.	
			Heterogeneity (I ²): 19%	
			Outcome measure-4	
			Mortality	
			Not reported per study.	
			Pooled analysis for 5	
			studies.	
			I: 2.6%	

			C: 3.7% RR: 0.65, 95% CI: 0.17 –	
			2.49	

CIN: contrast induced nephropathy; NAC: N-acetyl-cysteine; NR: not reported

Evidence table for intervention studies (randomized controlled trials and non-randomized *observational* studies [cohort studies, case-control studies, case series])¹
This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study reference	Study characteristics	Patient characteristics 2	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
Spini,	Type of study:	<u>Inclusion</u>	Describe intervention	Describe control	Length of follow-up:	Outcome measures and	A limitation of using PC-
2013	prospective	<u>criteria</u> :	(treatment/procedure/test):	(treatment/procedure/test):	Creatinine levels – 72	effect size (include	AKI / CIN as an
	controlled	patients			hours	95%CI and p-value if	endpoint, is that
	trial	admitted to			Mortality 12 months, 18	available):	creatinine, which forms
		the cardiac	Continuous renal	CRRT only after	months		the base of the PC-AKI
	Setting:	stepdown at	replacement therapy (CRRT)	percutaneous intervention		Contrast induced	definition, is removed
	cardiac	the	at least 6 hours before and		Loss-to-follow-up: not	nephropathy (CIN):	by RRT. However,
	stepdown	participating	24 hours after contrast		reported	I: 0/25 (0%)	creatinine is removed by
		hospital	medium administration			C: 13/21 (62%)	CRRT.
	Country: Italy	-eGFR			Incomplete outcome	p-value not reported	
		<30mL/min			<u>data</u> :		
	Source of	-needed to be			Not reported	Worsening renal failure:	
	funding: not	submitted to				I: 3/25 (12%)	
	reported	percutaneous				C: 9/25 (43%)	
		intervention				p-0.042	
		Exclusion				Dialysis:	
		criteria: -				I: 2/25 (8%)	
						C: 9/21 (19%)	
		N total at				P=0.50	
		baseline: 46					
		Intervention:				Long-term mortality:	
		25				I: 4/25 (16%)	
		Control: 21				I: 12/21 (57%)	

			P0.009	
Impo	<u>portant</u>			
prog	ognostic		Cardiovascular deaths:	
facto	tors ² :		I: 0/25 (0%)	
For e	· example		C: 5/21 (24%)	
age	e ± SD:		p-value not reported	
l: 73	3 ± 11			
C: 74	74 ± 8			
Sex:	c:			
1: 84	4% M			
C: 67	57% M			
Grou	oups			
	mparable at			
	seline? Yes			

Notes:

- 5. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 6. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 7. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 8. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Search d	escription	
Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	194
(OVID)	(113850) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
1995- okt. 2015	(543550) 3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9272)	
English	4 1 and 2 (9076) 5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9272) 6 4 or 5 (16764)	
	7 exp Hemofiltration/ or exp Renal Dialysis/ (103123) 8 (Hemofiltrat* or Haemofiltrat* or Haemodiafiltrat* or Hemodiafiltrat* or Dialysis or hemodialysis or haemodialysis).ti,ab. (130690) 9 7 or 8 (153364)	
	10 6 and 9 (918) 11 (prophyla* or prevent*).ti,ab. or pc.fs. (1907859) 12 10 and 11 (356)	
	13 limit 12 to (english language and yr="1995 -Current") (302) 14 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or	
	Editorial/ or Letter/ or (animals/ not humans/)) (254827) 15 13 and 14 (59) 16 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase ii or clinical trial or	
	randomized controlled trial or multicenter study or clinical trial).mp. or comparative study.pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2605774)	
	17 13 and 16 (149) 18 The prevention of radiocontrast-agent-induced nephropathy by hemofiltration.m_titl. (1) 19 Effects of two different treatments with continuous renal replacement therapy in	
	patients with chronic renal dysfunction submitted to coronary invasive procedures.m_titl. (1) 20 "Renal replacement therapies for prevention of radiocontrast-induced nephropathy: a systematic review.".m_titl. (1)	
	21 18 or 19 or 20 (3) 22 15 or 17 (166) 23 21 and 22 (3) 24 17 not 15 (107)	
	25 remove duplicates from 15 (56) 26 remove duplicates from 24 (104)	
Embase (Elsevier)	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)) AND [english]/lim AND [1995-2015]/py AND ('hemodiltration'/exp/mj OR 'hemodialysis'/exp/mj OR hemodiltrat*:ab,ti OR haemodiafiltrat*:ab,ti OR	
	haemodialysis:ab,ti) AND ('prophylaxis'/exp OR prophyla*:ab,ti OR prevent*:ab,ti OR prevention:lnk) 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR	
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp)) (26) – 9 uniek	
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it - (57) – 25 uniek	

Appendices to Chapter 8

Evidence tables

Table: Exclusion of article after	examination of full tekst.
Author and year	Reason for exclusion
Aronson, 2007	Does not meet selection criteria
Baerlocher, 2013	Review, not systematic
Blickle, 2007	Does not meet selection criteria
Bloomgarten, 1996	Does not meet selection criteria
Boscheri, 2007	Does not meet selection criteria
Chan, 1999	Does not meet selection criteria
Chong, 2004	Does not meet selection criteria
Cicero, 2012	Does not meet selection criteria
Dawson, 2002	Does not meet selection criteria
Dichtwald, 2011	Case series, no control group
Douros, 2015	Does not meet selection criteria
Elder, 2003	Does not meet selection criteria
Erley, 2006	Does not meet selection criteria
Goergen, 2010_1	Does not meet selection criteria
Gomez-Herrerp, 2013	Does not meet selection criteria
Gupta, 2002	Does not meet selection criteria
Hammond	Does not meet selection criteria
Heikkinen, 2007	Does not meet selection criteria
Heupler, 1998	Does not meet selection criteria
Hoste, 2013	Does not meet selection criteria
Jain, 2008	Included in systematic review Goergen, 2010
Jones, 2003	Does not meet selection criteria
Kdoqi, 2007	Does not meet selection criteria
Khurana, 2010 1	Review, not systematic
Khurana, 2010_2	Letter to editor
Klepser, 1997	Does not meet selection criteria
Koc, 2013	Does not meet selection criteria
Lalau, 2001	Systematic review, however more recent systematic (Georgen, 2010) present
	and included in literature summary
Landewe-Cleuren, 2000	Review, not systematic
Leow, 2015	Does not meet selection criteria
Longeran, 2008	Does not meet selection criteria
McCartney, 1999	Systematic review, however more recent systematic (Georgen, 2010) present
	and included in literature summary
Millican, 2004	Does not meet selection criteria
Morcos, 2001	Does not meet selection criteria
Morcos, 2005	Does not meet selection criteria
Nawaz, 1998	Included in systematic review Goergen, 2010
Nolan, 1997	Does not meet selection criteria
Parra, 2004	No control group.
Pond, 1996	Does not meet selection criteria
Quasny, 1997	Does not meet selection criteria
Radwan, 2011	Does not meet selection criteria
Rakovac, 2005	Does not meet selection criteria
Rasuli, 1998_1	Does not meet selection criteria
Rasuli, 1998_2	Does not meet selection criteria
Safadi, 1996	Does not meet selection criteria
Sayer, 2006	Letter to the editor
Schweiger, 2007	Does not meet selection criteria
Senior, 2012	Does not meet selection criteria
Setter, 2003	Does not meet selection criteria
Stacul, 2006	Does not meet selection criteria
Stacul, 2011	Guideline tekst, not an original article

Thompson, 2000	Does not meet selection criteria	
Thomsen, 2003	Guideline tekst, not an original article	
Thomsen, 2010	Does not meet selection criteria	
Thomson 2010	Does not meet selection criteria	
Tonolini, 2012	Does not meet selection criteria	
Tzakias, 2013	Does not meet selection criteria	
Tzakias, 2014	Does not meet selection criteria	
Van Dijk, 2008 Does not meet selection criteria		
Widmark, 2007 Does not meet selection criteria		

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

	clearly focused question? ¹	and systematic literature	Description of included and excluded studies? ³	relevant	Appropriate adjustment for potential confounders in observational studies? ⁵	Assessment of scientific quality of included studies? ⁶	Enough similarities between studies to make combining them reasonable? ⁷	of publication	Potential conflicts of interest reported? ⁹
First author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Goergen, 2010	Yes	Yes	Yes	Yes	Not applicable	Yes	Yes	No	No

- 1. Research question (PICO) and inclusion criteria should be appropriate and predefined
- 2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched
- 3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons
- 4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported
- 5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)
- 6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)
- 7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?
- 8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
- 9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)

Evidence table for systematic review of RCTs and observational studies (intervention studies)

Research question:

	······································							
Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments	
reference	characteristics			control (C)		effect size		
Goergen,	SR and meta-	Inclusion criteria SR:	Describe	Describe	End-point of follow-	Outcome measure-1	<u>Facultative</u> :	
2010	analysis of [RCTs	1) English language publication	intervention:	control:	<u>up</u> :	Defined as presence of		

	/ cohort / case-	2) administration of iodinated				metformin associated	Brief description of
[individua	control studies]	contrast medium in adult	A: metformin and	A: not	A: not reported	lactic acidosis (MALA), or	author's conclusion:
l study		patients who were tacing	undergoing	applicable	B: not reported	relation between MALA	It is not clear whether
characteri	Literature search	metformin	angiography	B: not	C: not reported	and iodinated contrast	cessation of metformin in
stics	up to March	3) lactic acidosis was outcome	B: patients who had	applicable	D : not reported	medium administration	patient undergoing
deduced	2009	measure	metformin-	C: not applicable			intravascular contrast
from [1st			associated lactic	D : not		Effect measure: RR, RD,	administration for
author,	A : Nawaz, 1998	Exclusion criteria SR:	acidosis after use of	applicable	For how many	mean difference [95% CI]:	radiological examination
year of	B: MacCartney,	1) studies in children (<18	intravenous		participants were no	A: 4 patients died (2	is effective for decreasing
publicatio	1999	years)	iodinated contrast		complete outcome	attributed to acute renal	the risk of lactic acidosis
n]	C : Stades, 2004	2) procedures in which	medium		data available?	failure and lactic	and hyperglycemia.
	D : Jain, 2008	administration of contrast	C: patients who had		(intervention/control)	acidosis), in 29 patients	
PS., study		medium was not used	metformin-		A: not reported	with normal renal	
characteri	Study design:	3) lactic acidosis was not one	associated lactic		B: not reported	function no change was	Level of evidence:
stics and	RCT [parallel /	of the outcomes assessed	acidosis, 26% of		C: not reported	observed after procedure	GRADE:
results	cross-over],	4) publications that were	them received		D : not reported	B : in 16-17 out of 18	All included studies had a
are	cohort	letters, narratives, editorials,	contrast medium			cases renal dysfunction or	very low quality of
extracted	[prospective /	reviews based on only expert	prior			other contra-indication	evidence (summaries of
from the	retrospective],	opinion, draft reports	D : metformin-			was present	case-reports, case-series,
SR (unless	case-series,		associated lactic			C: 25% of cases had	case-report)
stated	case-control	4 studies included	acidosis,			intravascular contrast	-no studies with control
otherwise	A: case-series					medium administered	group
)	B : summary of					D : metformin-associated	
	case-reports	Important patient				lactic acidosis, developed	For study C (stades, 2004)
	C: summary of	characteristics at baseline:				in patient with normal	contrast medium was
	case-reports					renal function	administered in 26% of
	D : case report	N, mean age					the cases.
		A: 33, not reported					
		B: 18, not reported				Pooled effect (random	
	Setting and	C: 47, not reported				effects model / fixed	
	Country:	D: 1, not reported				effects model):	
	Australia, in- and					No pooling was possible	
	outpatiennts	<u>Sex</u> :				due to heterogeneity of	
		A: not reported				included studies	
	Source of	B : not reported					
	funding:	C: not reported					
	Not reported	D: not reported					

Impaired renal function: A; 4/33 (12%)			
B:16/18 (89%) (unclear if this is			
correct number) C: not reported			
D: 0/1 (0%)			
Groups comparable at			
baseline? Not applicable (no			
control group)			

Search description

Database	Search terms	Total
Medline (OVID)	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. (111686) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	202
1995-now	(534205) 3 1 and 2 (8890) 4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or ciaki).ti,ab. (1942)	
English Dutch	5 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (244003) 6 3 or 4 (9377) 7 limit 6 to (yr="1995 -Current" and (dutch or english)) (5451) 8 Metformin/ or (metformin* or glucophage).ti,ab. (12587) 9 7 and 8 (53) – 52 uniek	
	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)) NOT 'conference abstract':it AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [1995-2015]/py AND ('metformin'/exp OR metformin*:ab,ti OR glucophage:ab,ti) (191) – 150 uniek	