Supplemental Material Table of Contents

Appendix 1. AKI Prevention Toolkit Protocol

The following Appendix 1 details the three interventions included in the AKI Prevention Toolkit Protocol as summarized on Table 2. The AKI Prevention Toolkit was developed through a regional pilot discussed in the Preliminary Data section and supported by the AKI KDIGO guidelines for preventing AKI.

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

Prior Work

1. **Results of previous focus groups[1]:**

Change strategies for evaluation and further consideration

- Nil by mouth (NPO) with clear fluids allowed up to 2-4 h prior to PCI
- N-acetylcysteine 1200 mg orally every 12hX4, first dose 18:00 night before PCI: 1200 mg dose @18:00, 6:00, 18:00, 6:00
- Standardization of volume administration prophylaxis
  - Intravenous NS at 1.5 ml/kg/h at 22:00 night before PCI, continue until intravenous $NaHCO_3$ protocol begins
  - Intravenous $NaHCO_3$ at 3ml/kg/h for 1 h pre PCI (reduce to 1 ml/kg/h if PCI is delayed)
  - Intravenous $NaHCO_3$ at 1 ml/kg/h for 6 h post PCI
- Recommendation: post-discharge follow-up at 3-5 days to determine CI-AKI, if persistent, weekly labs until resolved
- Iopamidol: low-osmolar contrast agent

CI-AKI, contrast-induced acute kidney injury; $NaHCO_3$ = sodium bicarbonate (1000 ml D5W mixed with 150 mEq $NaHCO_3$); NS, normal saline; PCI, percutaneous coronary intervention.

2. **Quality Improvement Project (pilot program)[2]:**

Domain	Key Themes in CI-AKI Performance
Teams	High performance teams had multidisciplinary team members, clinical champions, empowered nurses, multiple team champions, protected time for team meetings and improvement work, regular scheduled meetings, and quality improvement training (LEAN, six-sigma, microsystems)
Intervention Barriers	Challenges included variation in physician ordering, variation in protocols, unlearning old protocols, NPO status of the patient, education, documentation, data collection, working with transferring facilities, physician and patient noncompliance to orders, staffing, resources, time, staff buy-in, trade-ofs with other quality targets
Patient and Process Interventions	Hospitals adopted benchmark hospital protocols, standardized intravenous order sets, reduced NPO status to 2 to 4 h before procedure, stop nephrotoxic drugs before procedure. Hospitals also developed readiness checklists including volume status of the patient and fluid bolus, delayed procedures to allow for fluid bolus, limited contrast volume and exposure, eliminating left ventriculography, and conducted patient education about self-hydration using oral fluids (8x 8 oz glasses of water 12 h pre-and 12 h after procedure)
Factors supporting success	Hospital changes in behavior during the intervention included increased awareness, standardized intravenous fluid order sets, reduced NPO status to 2 to 4 h before procedure, staff and institutional buy-in, hydrating patients before and after the procedure, staff and patient education, limiting contrast volume, precalculated safe contrast dose per patient using the maximum acceptable contrast dose equation (5 mL x body weight in kg/baseline serum creatinine), staging procedures, delaying procedures to allow for fluid bolus, and quality improvement training[34].

3. Consistent guidelines:

Data from SCAI suggest that many cardiac catheterization laboratories do not have protocols for prevention of CA-AKI or inconsistently apply guidelines from the national societies [3]. For example, in one study, 95% of high risk patients were identified by estimated GFR but only 2/3rd received any intravenous volume prophylaxis [4].

Table 3. Current AHA/ACC/SCAI guidelines (2011)[5]

4.4 Contrast-Induced AKI: Recommendations: Class I
1. Patients should be assessed for risk of contrast-induced AKI before PCI.[270,271] *(Level of Evidence: C)* 2. Patients undergoing cardiac catheterization with contrast media should receive adequate preparatory hydration.[272-275] *(Level of Evidence: B)* 3. In patients with CKD (creatinine clearance <60 mL/min), the volume of contrast media should be minimized.[276-278] *(Level of Evidence: B)*

Intervention 1: Standardize pre-cath orders

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

The first guideline of the ACCF/AHA is the assessment of acute kidney risk for pre-catheterization orders. Risk stratification is necessary so that protective interventions are focused on the group of patients who will receive the most benefit.

There are over 12 risk prediction models, however few have been externally validated (i.e. in another setting with a different population) and even fewer have been compared to other risk models. Some risk models consider only patient characteristics that can be known prior to entering the catheterization laboratory, while others use additional variables from the procedure itself such as the amount of contrast given (7/12 models use contrast volume). Although these models defeat the goal of an *a priori* risk assessment, it does focus on risk factors that can be controlled in the catheterization laboratory (see Intervention 8 below). Finally, various risk models are developed from special subgroups such as patients with STEMI or patients only having a PCI.

The risk models also predict different endpoints. The risk models are all relatively strong in predicting acute kidney injury but differ on mortality, long term MACE, or other events[31].

Table 4. List of variables analyzed in risk models

	Study (sample size)											
Variable	**Bartholemew (n = 10481)**	**Chen (n=1500)**	**Fu (n=668)**	**Ghani (n=247)**	**Gao (n=2764)**	**Gurm (n=48001)**	**Liu (n=495)**	**Maioli N=1281)**	**Marenzi (n=218)**	**Mehran (n=5571)**	**Tziakas (n=488)**	**Victor (n=900)**
Demographic												
Age		X	X		X	X	X	X	X	X		
Female sex				X								
Anthropometric data												
Height						X						
Weight						X						
Medical History												
Renal Insufficiency	X	X	X	X	X	X	X	X		X	X	X
Anemia		X	X							X		
Diabetes mellitus	X	X	X	X		X		X		X		X
Hypertension	X				X							
Heart Failure	X				X	X				X		
Impaired LVEF		X	X				X	X				
Previous MI		X	X		X							
Recent cardiac procedure/PCI							X				X	
Peripheral vascular disease	X										X	X
Metformin use											X	
Physical examination/clinical presentation												
Hypotension		X	X							X		X
Shock				X		X						
CAD presentation						X						
Use of IABP	X				X				X	X		
Anterior MI									X			
Time to reperfusion									X			
Procedure												
Urgent/emergent	X	X	X			X						
PCI indication						X						
Contrast volume	X		X		X				X	X	X	X
Multivessel PCI				X								
One procedure in past 72 h								X				
Laboratory values at presentation												
Albuminuria												X
Pre-procedure Cr>baseline Cr								X				
HDL<1		X				X						
CK-MB						X						
Hemoglobin						X						
Troponin I						X						
Troponin T						X						

X=variable included in each model; LVEF=left ventricular ejection fraction, MI=myocardial infarction; PCI=percutaneous coronary intervention; CAD=coronary artery disease; IABP=intra-aortic balloon pump; Cr=creatinine; HDL=high density lipoprotein; CK-MB=creatine kinase isoenzyme-MB.

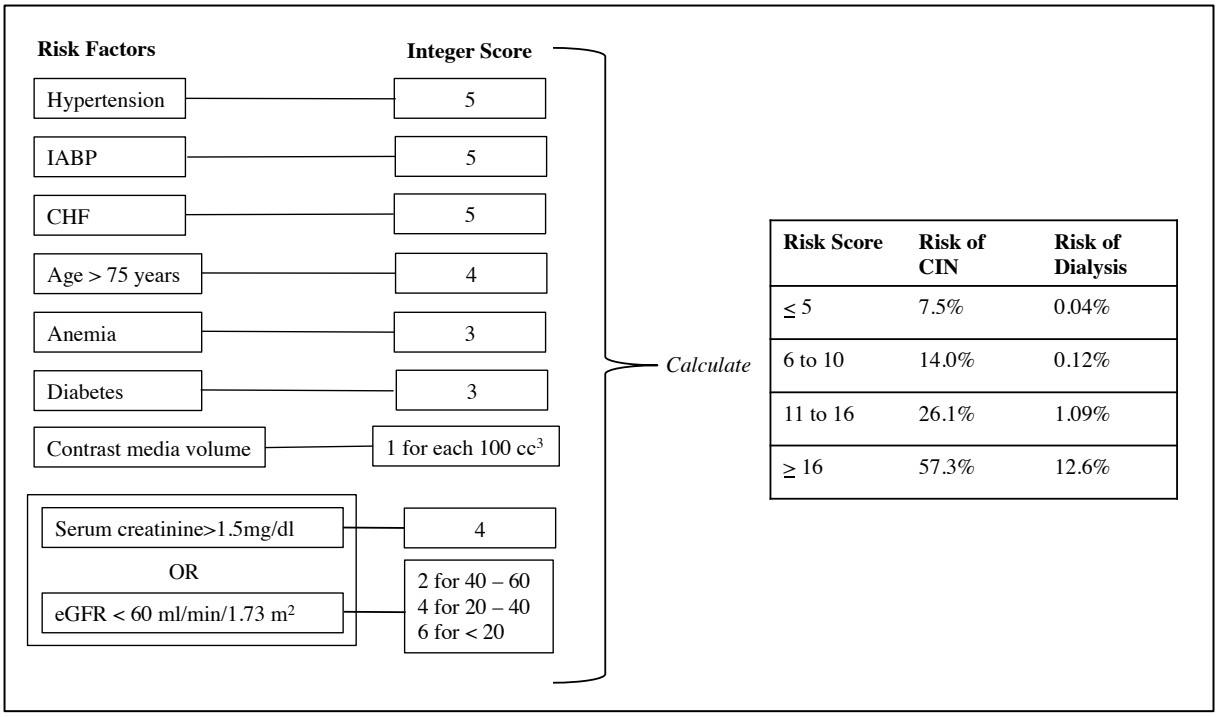
The Mehran risk model is the most widely used (although it does include contrast volume) and is available on such applications as Qx Calculate or on-line at: http://www.zunis.org/Contrast-Induced%20Nephropathy%20Calculator.htm. It has been externally validated in a number of different settings reflecting its generalizability.

The ACEF (Liu) uses only three variables (age, creatinine or eGFR, and ejection fraction) and has been used in cardiac surgery, TAVR, and STEMI/PCI.

We think using any risk model is better than not using one. Mehran is the easiest to use because of its availability on-line. Dose of contrast can be modeled to create multiple scenarios. For example, if only performing a diagnostic study and/or single stent, one calculation using 100 ml of contrast can be performed. If multiple stents are anticipated, a second calculation using 200 mL of contrast can be performed. This allows

the interventional cardiologist to assess the risk of doing multiple procedures ahead of time and supports intervention 8 below.

Figure 1. Scheme to define contrast-induced nephropathy (CIN) risk score.



Risk Score	Risk of CIN	Risk of Dialysis
≤ 5	7.5%	0.04%
6 to 10	14.0%	0.12%
11 to 16	26.1%	1.09%
≥ 16	57.3%	12.6%

Anemia = baseline hematocrit valve <39% for men and <36% for women; CHF = congestive heart failure class III/IV by New York Heart Association classificiation and/or history of pulmonary edema; eGFR = estimated glomerular filration rate; hypotension = systolic blood pressure <80 mm Hg for at least 1 h requiring inotropic support with medications or intra-aortic balloon pump (IABP) within 24 h periprocedurally.

Patients in the upper 2 or 3 risk categories are targeted for prophylactic strategies to prevent AKI (Interventions 2-12 below). At most hospitals, calculation of estimated GFR using either the MDRD or CKD-EPI equation is performed automatically. Serum creatinine should rarely be used.

Intervention 2: IV and Oral fluid orders

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

Although it is well known that adequate hydration/volume expansion (VE) is a key factor in decreasing the risk of AKI, there is currently no standard for the quantity and timing of oral and intravenous fluids.

The guidelines recommend *"adequate preparatory hydration"* in patients at risk of contrast associated acute kidney injury. Although these guidelines suggest intravenous isotonic fluid administration before, during, and after cardiac angiography, evidence supporting a specific protocol is limited. Small, randomized trials have found that administration of IV fluid immediately prior to contrast exposure (<1hr) is inferior to administration given 4-6 hours before exposure. A single trial found isotonic sodium chloride superior to half normal sodium chloride [5]. Many protocols restrict the volume of IV fluid in patients with symptoms of congestive heart failure or depressed LV ejection fractions.

Finally, a goal of IV fluid administration is to produce some mild volume expansion and decrease vasoconstrictor forces acting on the kidney, such as the sympathetic nervous system and the renin-angiotensin system. On the day of the contrast

exposure, diuretics should therefore be held. Evidence from randomized trials support the adverse effects of diuretics in this setting[6].

Guidelines have the following statement:

" Studies of hydration to reduce the risk of contrast-induced AKI suggest that isotonic saline is preferable to half isotonic saline, intravenous (IV) hydration is preferable to oral hydration, hydration for hours before and after exposure to contrast media is preferable to a bolus administration of saline immediately before or during contrast media exposure, and administration of isotonic saline alone is preferable to administration of isotonic saline plus mannitol or furosemide. [272-275, 320] On the basis of these studies, a reasonable hydration regimen would be isotonic crystalloid (1.0-1.5 mL/kg per hour) for 3-12 hours before the procedure and continuing for 6 to 24 hours after the procedure. [272-275, 284, 320, 321]"

We agree with these recommendations although find that they may not be appropriate for all patients. For example, patients with established congestive heart failure (NYHA III or IV) or known depressed LVEF <40 may not tolerate this volume. For those individuals, a reduced administration rate (~50%) might be safer. Likewise, patients needing an urgent intervention (for example, STEMI) would not be afforded sufficient time to meet these volume/rate targets.

Prospective randomized trials comparing sodium bicarbonate vs sodium chloride have shown that bicarbonate is not inferior to chloride. Importantly, these trials compared isotonic sodium bicarbonate to sodium chloride given at a rate of 3 ml/min/h for only 1 hour before catheterization and 1 ml/min/h x 6 hours post catheterization. Because of the short interval between starting the IV infusion and administration of contrast, this protocol may be particularly appropriate for urgent patients.

Table 5. Classification of IV fluid therapy

Type of fluid therapy	**Definition**	**Example of fluid**
Resuscitation	Re-establishes hemodynamic stability through restoring intravascular volume	- Balanced crystalloid - Crystalloid - 0.9% sodium chloride
Replacement	Provides daily maintenance requirements and replacement of any ongoing abnormal losses	- Balanced crystalloid - Crystalloid - 0.9% sodium chloride
Routine maintenance	Provides daily maintenance requirements	- 0.18% sodium chloride / 4$ dextrose - 0.45% sodium chloride - 5% dextrose

Intervention 3: Reducing contrast volume

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

The literature strongly supports that contrast volume is an independent risk factor for CA-AKI [7]. A number of equations have been proposed to calculate a maximum amount of contrast that should be given at any one time[7, 8]. The current guidelines suggest a maximum dose based upon contrast volume/creatinine clearance of <3.7 [9]. The ceiling dose should be determined for every high-risk patient prior to the start of the procedure.

A number of strategies exist to limit the amount of contrast and thus stay below that maximum dose threshold. Treating only the culprit lesion at the initial intervention and staging subsequent interventions for a later time is one strategy in complex multi-vessel cases. Evidence from clinical trials indicates that a reduction in contrast volume occurs when either automated injectors[10, 11] are used or a manifold pressure system (AVERT) is employed [12]. Finally, increased use of IVUS may also limit contrast dose. We do not recommend coronary sinus aspiration or hemodialysis to reduce the amount of contrast that reaches the kidney.

There is less evidence supporting a benefit of isosmolar over low osmolar contrast agents [13, 14]. Because of equipoise, the choice of contrast media should be left up to the individual cath lab personnel and the interventional cardiologist.

Recent, updated guidelines suggest a number of additional approaches to reducing contrast dose [15]:

> "Biplane coronary angiography should be utilized to reduce the contrast load if the equipment is available. Avoiding unnecessary "test" or "puff" injections, eliminating ventriculography and aortography, and taking the least number of angiograms can limit contrast volume. Careful fluoroscopy setup to reduce panning and use of a higher frame rate may also reduce the volume of each contrast injection per image acquisition. Performing ad hoc interventions and combined coronary and peripheral procedures should be carefully reviewed. There should be a low threshold to have the patient return for a repeat procedure to avoid large volumes of contrast during a single procedure. A discussion of maximum contrast limits should be part of the initial "time out" before the procedure" [15]

Intervention 2 continued: NPO Status

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

NPO status: Patients (except those with symptomatic heart failure) are encouraged to drink eight glasses of clear fluids (eight ounces/glass) starting the evening before their procedure until two hours before the procedure. Current practice guidelines for anesthesiology state that patients having a procedure requiring sedation are allowed clear liquids until 2 hours prior to the procedure[32,33]. Referencing these practice guidelines are helpful to reach institutional consensus regarding NPO orders prior to cardiac catheterization.

Evidence supports a beneficial effect of high urine flow rates for the prevention of CA-AKA [16-18]. We recommend restricting NPO to 2-4 hours prior to the expected time of catheterization. Prior to that time, a volume of 20 ml/kg is recommended for ingestion. This volume has been shown to result in maximal dilution of the urine when ingested in a short period of time. We however would recommend ingestion of this amount over hours leading up to the 2-4 hours prior catheterization.

Intervention 2 continued: Patient oral fluids

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

There have been randomized trials that compared oral vs intravenous fluid administration for the prevention of CA-AKI. Five studies randomized patients to oral water intake compared to IV saline [19-23].

The protocols differed significantly with a pre-specified amount of water (e.g 500-1000 ml before CM and 1 ml/kg/h x 12h or 2000 mL post CM) in 4/5 studies. The comparator was IV 0.9% NaCl in all studies given from 1-12 h before CM and 6-24h after CM. One study included NAC in both groups. Studies with a pre-specified amount of water found no difference in the incidence of CIN. The only study in which IV NaCl was more beneficial than oral water had no pre-specified amount of water to be taken or documentation of the amount of water consumed. Patient who received IV fluid gained weight while those randomized to water only lost weight [22]. Dussol randomized 153 CKD patients scheduled for coronary angiography to oral NaCl (1 gm/10 kg/day x 2 days) versus IV (0.9% NaCl @ 15ml/kg over 6 hours) before CM exposure (total 16 g oral vs 12.4 g IV of NaCl). There was no difference in the incidence of nephropathy (6.6% vs 5.2% respectively)[24].

Finally, an observational study by Yoshikawa involving 180 patients with normal kidney function undergoing a CCTA found an inverse correlation between the rise in creatinine at 24h and the amount of oral fluid ingested post CM. No patients met criteria for CIN. However, oral fluid intake was the only independent predictor of the change in serum creatinine[25].

These studies suggest that oral intake of sodium chloride or water may be equally protective as IV fluids for prevention of CIN. The issue may be less about the route of administration and more about the amount of fluid administered and the resulting urine output.

Intervention 2 continued: LVEDP matched hydration

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

The volume of IV fluids is often reduced in patients with a history of congestive heart failure or reduced LVEF because of concerns about volume overloading the patient. As a result many of these patients will receive considerably less volume that may account for the higher incidence of acute kidney injury in these patients. In an attempt to more rigorously determine the correct amount of fluid to administer to a patient, hemodynamic guided fluid therapy has been recommended.

In a trial using an initial measurement of LVEDP, investigators were able to adjust the rate of volume administration based upon the initial pressure (see below) [26]. Using this approach, they were able to give more fluid to patients having LVEDP guided fluid administration. This resulted in a reduction the incidence of CA-AKI compared to the group randomized to receive 1.5 ml/kg/h during and after the procedure (6.7% vs 15.7%).

Table 6. Measurement of LVEDP and stages of catheterization

Pre Cath	During Cath	Post Cath
	LVEDP=<13: 5 ml/kg/h	Continued x 4 h
3 ml/kg/h x 1h	LVEDP= 13-18: 3 ml/kg/h	Continued x 4 h
	LVEDP=>18: 1.5 ml/kg/h	Continued x 4 h

A similar approach using dynamic changes in CVP has also been shown to reduce the incidence of CA-AKI [27]. This approach, however, requires a separate venous catheter and repeated measurements.

Intervention 2 continued: Delay cath if IV fluids not received

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

This may not always be practical, particularly, with STEMI patients in whom door-to-balloon time is critical. As noted above, sodium bicarbonate may be particularly useful in this situation. With elective cases, we think 3 ml/kg delivered over 1-3 hours is a reasonable minimum amount of isotonic volume to be delivered prior to catheterization. A rate of 1 ml/kg/h should be continued during the procedure. In patients without a history of heart failure or LVEF <40%, the rate can be increased up to 3 ml/kg/h to achieve the targeted minimal fluid load.

Intervention 1: Standardize Pre- and Post-Cath Orders - Revisit

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

Intravenous isotonic fluids are to be continued at 1 ml/kg/h x 6 h or 1.5 ml/kg/h x 4h following the procedure. Longer infusion times (up to 24 h) are appropriate for high-risk patients hospitalized overnight. In addition, all patients should be encouraged to consume another 20 ml/kg of water over the 6-12 hours post catheterization (taking into account a requirement to be supine for ~4 hr post femoral sheath removal).

Fluid administration is required in high-risk patients to increase urine output, dilute the concentration of contrast within the tubule lumen, and reduce vasoconstrictive effects of contrast on the kidney. The importance of fluid management in prevention of CA-AKI, including mechanisms of action and clinical trial results, is reviewed in depth in a paper by Rojkovskiy [28].

Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast – Revisit

Table 2. Virtual Learning Collaborative and Technical Assistance Call Topics

Month	Clinical Topic	Quality Improvement Implementation Component
1	Getting Started, team members/roles, Project timeline. Overview of bundle interventions from the AKI Prevention Toolkit	Components of a learning collaborative, Problem identification, Model for Improvement, Setting Global and Specific Aim Statements
2	**Intervention 1: Standardize Pre- and Post-Cath Orders**	Planning Process Improvements (Process Maps/Flowcharts): What is the problem? What process will you focus on? What is the current process?
3	**Intervention 2: IV and Oral Fluid Orders**	Effective Communication
4	**Intervention 3: Reducing contrast volume**	Causation: Fishbone diagrams
5	Intervention 2 continued: NPO status	Change Ideas: Plan, Do, Study, Act (PDSAs)
6	Intervention 2 continued: Patient oral fluids	Measurement: Process changes and outcome measures
7	Review Pre-PCI Interventions, lessons learned, Case 1, 2	Lessons learned from Interventions 1-4
8	Intervention 2 continued: LVEDP matched hydration	Measures, use of playbooks
9	Intervention 2 continued: Delay Cath if IV fluid bolus not received	Ladder of inference
10	Review of Peri-Cath interventions trialed, case study, lessons learned	Lessons learned from Interventions 5-6
11	Intervention 1: Standardize Pre- and Post-Cath Orders - revisit	Accomplishments: What is going well or be improved?
12	Intervention 2 and 3: IV and Oral Fluids and Reducing Contrast -revisit	Revisit improvement methods
13	Review of interventions trialed, lessons learned, Case 3-5	Lessons learned from interventions 7-8
14	Review of Process Changes Implemented	Planning for sustainability: PDSA/SDSA
15	How to sustain and spread changes in practice	NHS Sustainability Model
16	Sustainability/Spread: NHS Model for Sustainability	NHS Sustainability Model
17,18	Final Team Reports and Plans for next 18 months post-intervention	Lessons Learned

REFERENCES:

1. Brown JR, McCullough PA, Splaine ME, Davies L, Ross CS, Dauerman HL, Robb JF, Boss R, Goldberg DJ, Fedele FA, Kellett MA, Phillips WJ, Ver Lee PN, Nelson EC, MacKenzie TA, O'Connor GT, Sarnak MJ, Malenka DJ and Northern New England Cardiovascular Disease Study G. How do centres begin the process to prevent contrast-induced acute kidney injury: a report from a new regional collaborative. *BMJ Qual Saf*. 2012;21:54-62. PMCID:PMC4872501.
2. Brown JR, Solomon RJ, Sarnak MJ, McCullough PA, Splaine ME, Davies L, Ross CS, Dauerman HL, Stender JL, Conley SM, Robb JF, Chaisson K, Boss R, Lambert P, Goldberg DJ, Lucier D, Fedele FA, Kellett MA, Horton S, Phillips WJ, Downs C, Wiseman A, MacKenzie TA, Malenka DJ. Northern New England Cardiovascular Disease Study G. Reducing contrast-induced acute kidney injury using a regional multicenter quality improvement intervention. *Circ Cardiovasc Qual Outcomes*. 2014;7:693-700. PMCID:PMC4869689.
3. Prasad A, Sohn A, Morales J, Williams K, Bailey SR, Levin D, McCullough PA, Mehran R, Lopez-Cruz G and Harder J. Contemporary practice patterns related to the risk of acute kidney injury in the catheterization laboratory: Results from a survey of Society of Cardiovascular Angiography and Intervention (SCAI) cardiologists. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2016. PMID:27315581.
4. Schilp J, de Blok C, Langelaan M, Spreeuwenberg P, Wagner C. Guideline adherence for identification and hydration of high-risk hospital patients for contrast-induced nephropathy. *BMC nephrology*. 2014 Jan 6;15. PMCID:PMC3890484.
5. Mueller C, Buerkle G, Buettner H, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H. Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angiography. *Arch Int Med*. 2002;162:329-336. PMID:11822926.
6. Solomon R, Werner C, Mann D, D'Elia J, Silva P. Effects of saline, mannitol, and furosemide to prevent acute decreases in renal function induced by radiocontrast agents. *N Engl J Med*. 1994;331:1416-1420. PMID:7969280.
7. Gurm HS, Dixon SR, Smith DE, Share D, Lalonde T, Greenbaum A, Moscucci M and Registry BMC. Renal function-based contrast dosing to define safe limits of radiographic contrast media in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol*. 2011;58:907-14. PMID:21851878.
8. Cigarroa RG, Lange RA, Williams RH, Hillis LD. Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. *The American journal of medicine*. 1989;86:649-652. PMID:2729314.
9. Laskey WK, Jenkins C, Selzer F, Marroquin OC, Wilensky RL, Glaser R, Cohen HA, Holmes DR, Jr. and Investigators NDR. Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention. *J Am Coll Cardiol*. 2007;50:584-90. PMID:17692741.
10. Gurm HS, Smith D, Share D, Wohns D, Collins J, Madala M, Koneru S, Menees D and Chetcuti S. Impact of automated contrast injector systems on contrast use and

contrast-associated complications in patients undergoing percutaneous coronary interventions. *JACC Cardiovascular interventions*. 2013;6:399-405. PMID:23523450.
11. Minsinger KD, Kassis HM, Block CA, Sidhu M and Brown JR. Meta-analysis of the effect of automated contrast injection devices versus manual injection and contrast volume on risk of contrast-induced nephropathy. *Am J Cardiol*. 2014;113:49-53. PMCID:PMC4848037.
12. Prasad A, Ortiz-Lopez C, Kaye DM, Byrne M, Nanayakkara S, Ahmed SH, Bailey SR, Mehran R, Sethi S, Banerjee A and Eng M. The use of the AVERT system to limit contrast volume administration during peripheral angiography and intervention. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2015;86:1228-33. PMID:26389534.
13. Heinrich M, Haberle L, Muller V, Bautz W, Uder M. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology*. 2009;250:68-86. PMID:19092091.
14. Reed M, Meier P, Tamhane UU, Welch KB, Moscucci M and Gurm HS. The relative renal safety of iodixanol compared with low-osmolar contrast media: a meta-analysis of randomized controlled trials. *JACC Cardiovascular interventions*. 2009;2:645-54. PMID:19628188.
15. Bashore TM, Balter S, Barac A, Byrne JG, Cavendish JJ, Chambers CE, Hermiller JB, Jr., Kinlay S, Landzberg JS, Laskey WK, McKay CR, Miller JM, Moliterno DJ, Moore JW, Oliver-McNeil SM, Popma JJ, Tommaso CL and Members ATF. 2012 American College of Cardiology Foundation/Society for Cardiovascular Angiography and Interventions expert consensus document on cardiac catheterization laboratory standards update: A report of the American College of Cardiology Foundation Task Force on Expert Consensus documents developed in collaboration with the Society of Thoracic Surgeons and Society for Vascular Medicine. *J Am Coll Cardiol*. 2012;59:2221-305. PMID:22575325.
16. Briguori C, Visconti G, Focaccio A, Airoldi F, Valgimigli M, Sangiorgi GM, Golia B, Ricciardelli B and Condorelli G. Renal Insufficiency After Contrast Media Administration Trial II (REMEDIAL II): RenalGuard System in high-risk patients for contrast-induced acute kidney injury. *Circulation*. 2011;124:1260-9. PMID:21844075.
17. Marenzi G, Ferrari C, Marana I, Assanelli E, De Metrio M, Teruzzi G, Veglia F, Fabbiocchi F, Montorsi P and Bartorelli AL. Prevention of contrast nephropathy by furosemide with matched hydration: the MYTHOS (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention) trial. *JACC Cardiovascular interventions*. 2012;5:90-7. PMID:22230154.
18. Stevens MA, McCullough PA, Tobin K, Speck JP, Westveer DC, Guido-Allen DA, Timmis GC, O'Neill WW. A prospective randomized trial of prevention measures in patients at high risk for contrast nephropathy. *J Am Coll Cardiol*. 1999;33:403-411. PMID:9973020.
19. Cho R, Javed N, Traub D, Kodali S, Atem F, Srinivasan V. Oral hydration and alkalinization is noninferior to intravenous therapy for prevention of contrast-induced nephropathy in patients with chronic kidney disease. *J Interven Cardiol*. 2010;23:460-466. PMID:20796166.

20. Kong D, Hou YF, Ma LL, Yao, DK, Wang LX, . Comparison of oral and intravenous hydration strategies for the prevention of contrast-induced nephropathy in patients undergoing coronary angiography or angioplasty: a randomized clinical trial. *Acta Cardiol*. 2012;67:565-569. PMID:23252007.
21. Lawlor D, Moist DK, Derose L, Harris KA, Lovell MB, Kribs S, Elliot J, Forbes TL. Prevention of contrast-induced nephropathy in vascular surgery patients. *Ann Vasc Surg*. 2007;21:593-597. PMID:17823041.
22. Trivedi HS, Moore H, Nasr S, Aggarwal K, Agrawal A, Goel P and Hewett J. A Randomized Prospective Trial to Assess the Role of Saline Hydration on the Development of Contrast Nephrotoxicity. *Nephron Clinical Practice*. 2003;93:c29-c34. PMID:12411756.
23. Wrobel W, Sinkiewicz W, Gordon M, Wozniak-Wisniewska A. Oral versus intravenous hydration and renal function in diabetic patients undergoing percutaneous coronary interventions. *Kardiol Pol*. 2010;68:1015-1020. PMID:20859892.
24. Dussol B, Morange S, Loundoun A, Auguier P, Berland Y. A randomized trial of saline hydration to prevent contrast nephropathy in chronic renal failure patients. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2006;21:2120-2126. PMID:16611682.
25. Yoskikawa D, Isobe S, Sato K, Ohashi T, Fujiwara Y, Ohyama H, Ishii H, Murohara T. Importance of oral fluid intake after coronary computed tomography angiography: an observational study. *Eur J Radiol*. 2011;77:118-122. PMID:19695806.
26. Brar SS, Aharonian V, Mansukhani P, Moore N, Shen AYJ, Jorgensen M, Dua A, Short L and Kane K. Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial. *The Lancet*. 2014;383:1814-1823. PMID:24856027.
27. Qian G, Fu Z, Guo J, Cao F and Chen Y. Prevention of Contrast-Induced Nephropathy by Central Venous Pressure-Guided Fluid Administration in Chronic Kidney Disease and Congestive Heart Failure Patients. *JACC Cardiovascular interventions*. 2016;9:89-96. PMID:26685074.
28. Rojkovskiy I and Solomon R. Intravenous and Oral Hydration. *Interventional Cardiology Clinics*. 2014;3:393-404. PMID:28582224.
29. Washam JB, Herzog CA, Beitelshees AL, Cohen MG, Henry TD, Kapur NK, Mega JL, Menon V, Page RL, 2nd, Newby LK, American Heart Association Clinical Pharmacology Committee of the Council on Clinical Cardiology CoCS, Anesthesia CoFG, Translational Biology CotKiCD, Council on Quality of C and Outcomes R. Pharmacotherapy in chronic kidney disease patients presenting with acute coronary syndrome: a scientific statement from the American Heart Association. *Circulation*. 2015;131:1123-49. PMID:25712269.
30. Washam JB, Herzog CA, Beitelshees AL, Cohen MG, Henry TD, Kapur NK, Mega JL, Menon V, Page RL, 2nd, Newby LK, American Heart Association Clinical Pharmacology Committee of the Council on Clinical Cardiology CoCS, Anesthesia CoFG, Translational Biology CotKiCD, Council on Quality of C and Outcomes R. Pharmacotherapy in chronic kidney disease patients presenting with acute coronary syndrome: a scientific statement from the American Heart Association. *Circulation*. 2015;131:1123-49. PMID:25712269.

31. Silver SA, Shah PM, Chertow GM, Harel S, Wald R, Harel Z. Risk prediction models for contrast induced nephropathy: systematic review. BMJ 2015;351:h4395. PMCID:PMC4784870.
32. Apfelbaum JL, Caplan RA, Connis RT, et al. Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures An Updated Report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology.* 2011;114(3):495-511. PMID:21307770.
33. Cigarroa RG, Lange RA, Williams RH, Hillis LD. Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. *Am J Med.* 1989;86(6 Pt 1):649-652. PMID:2729314.
34. Lambert P, CHaisson K, Horton S, et al. Reducing Acute Kideny Injury DUe to Contrast Material: How Nurses Can Improve Patient Safety. Am J Med. 1989;86(6)(pt 1):649-652. PMID:28148611.

ELEMENTS OF QUALITY IMPROVEMENT PROJECT

- Infrastructure:
  - Multidisciplinary teams, champion
  - Protocol for managing patients based upon risk
  - Data collection and periodic review
- Pre cardiac angiography
  - NPO 4 hours before procedure
  - Encourage patient hydration with water before NPO period (1 L)
  - Assess risk of AKI: baseline kidney function, review of medications, presence of heart failure, diabetes
  - For high risk patients
    - Obtain baseline creatinine
    - Establish maximum contrast volume, for example (3.7 x eGFR)
    - IV isotonic sodium chloride at 1 ml/kg/h for 4 hr pre angiography

      or
    - IV isotonic sodium bicarbonate at 3 ml/kg/h x 1 h
  - Delay start of procedure when possible to permit IV fluid target to be reached
  - In patients with a history of congestive heart failure, adjust rate of fluid infusion based upon LVEDP or CVP
  - Hold diuretics and metformin
  - Continue statin therapy (if patient not on statin, start statin therapy)
  - Physician discretion regarding continuation of ACEi or ARB. Note that ACC/AHA guidelines indicate that ACEi should be started in all ACS patients with LVEF ≤40% [29].
- During procedure (high risk patients)
  - Continue IV fluid at rate of 1 ml/kg/h
  - Reduce contrast volume by avoiding 'puffs', LVgram
  - Use automated injectors, manifold pressure device
  - Stage multi-vessel procedures; culprit lesion first
- After procedure (high risk patients)
  - Continue IV fluid at 1.0 ml/kg/h for 6-12 hours
- After procedure (all patients)
  - Encourage patient hydration with water after procedure (1 L)
  - Obtain repeat creatinine 12-48 h post angiography
  - Identify those with CA-AKI by KDIGO criteria
  - Refer all patients with CA-AKI for nephrology follow-up within 3 months

VA and CART Catheterization Data Elements Captured through the Data Core:

Table A1*: Summary of the utilized data elements. All of these data elements are synthesized from a combination of CDW (EHR) and CART program data sources, as noted above.*

Data Element
Demographics: Age, Race, Gender, Marital Status, Service Connection, Primary VA Hospital, PCP, Admit/Discharge Date
Pre-Procedural Medical History: Blood Pressure, Hypertension, Hyperlipidemia, Diabetes, Stroke, Peripheral Vascular Disease, Cerebral Vascular Disease, Sleep Apnea, Heart Failure, Prior LVEF assessment, Chronic Obstructive Pulmonary Disease, Prior MI, CABG, PCI, Valve Surgery, Valve Replacement, Prior angina, Cardiac Transplant, Stress Test, Prior Cath with ≥1 one coronary stenosis ≥50%, Chronic Kidney Disease or Dialysis, Prior renal insufficiency, PTSD, Depression, Tobacco Use history, Family history of CAD
Peri-Procedural Catheterization Lab Data: Presentation Factors, Indication, Physical Exam, Laboratory Tests, Sedation, Procedures Performed, Devices Implanted, Complications, Summary Variables
Medication Usage: Pre-Admission, During admission, at Discharge
Outcomes: AKI, Death, Readmission, Post-Procedural CABG or PCI
Medical Center: VA region and VISN, Procedure Volume, Distance to Academic Affiliate, Number of Catheterization Rooms

Table 7. Definition of AKI

Stage	**Serum Creatinine**	**Urine Output**
1	1.5 – 1.9 x baseline OR ≥ 0.3 mg/dL increase	< 0.5 mL/kg/h for 6 – 12 h
2	2.0 – 2.9 x baseline	< 0.5 mL/kg/h for ≥ 12 h
3	3.0 x baseline OR increase to ≥4.0 ml/dL	<0.3 mL/kg/h for ≥ 24 h OR anuria for ≥ 12 h

Appendix 2. Implementation Strategies, Data Collection, and Data Coordinating Center

DETAILED MATERIALS AND METHODS

Data Collection and Data Coordinating Center

The Tennessee Valley Healthcare System VA served as the Data Coordinating Center for this trial. Data were collected from the source electronic health record (EHR) systems and components, which included the EHR (VistA, CPRS) and the VA Clinical Assessment, Reporting, and Tracking System for Cath Labs (CART) program quality initiative data collection modules to capture all patient and procedural characteristics, comorbidities, and outcomes in order to identify patients for pre-existing chronic kidney disease (CKD), ascertain acute kidney injury (AKI) outcomes, and to provide the data infrastructure to support the Automated Surveillance Reporting (Surveillance) intervention.

Retrospective data collection on all 76 Veterans Affairs medical centers with cardiac catheterization laboratories was performed for all patient procedures starting January 1st, 2017 and then updated prospectively on a monthly basis from the EHR data sources. As part of a prior research project (VA HSR&D IIR 11-292), we established a comprehensive automated data center with monthly feeds from the CART program and daily to weekly feeds from the data domains in the VA Corporate Database Warehouse, which extract data from the production EHR. These data are transformed and merged through a validated process into an analytic data cube that can be analyzed to provide reports to operators and hospitals as well as providing data for review. Individual clinical registry elements conform to the American College of Cardiology National Clinical Data Repository data element definitions.[1, 2]

Implementation Strategies

Two strategies for implementing the AKI Prevention Toolkit were evaluated – basic technical assistance (Assistance) and a coaching-based Virtual Learning Collaborative

(Collaborative) – with and without information support through Surveillance. Assistance served as the active study control.

Technical Assistance was offered to the 10 teams (5 with and 5 without information support through Surveillance).[3, 4] An AKI improvement specialist led monthly scheduled calls (60 minutes each) with each Assistance site team individually to review and discuss the bundle interventions (as is done in the Collaborative group) and allowed for consultation on implementing the AKI Prevention Toolkit. Assistance sites were encouraged to ask questions, review their implementation progress, and discuss challenges in implementing the AKI Prevention Toolkit. If additional expertise was needed for specific questions, the Assistance expert either scheduled a follow-up call or responded via email. Teams were able to reach out to the Assistance expert at any point during the 18 months.

Virtual Learning Collaborative served as an enhanced implementation strategy for the AKI Prevention Toolkit and was offered to 10 teams (5 with and 5 without information support through Surveillance).[3, 4] The research team supported each participating site established a multidisciplinary team charged with continuously improving AKI. Teams were composed of interventional cardiologists, cardiac catheterization lab managers and technicians, nursing representatives from the intensive care unit and/or holding areas, cardiology administration, nephrology, and representation from the quality improvement department (VA Clinical Application Coordinator [CAC] and Systems Redesign). Collaborative sites were assigned two expert coaches from Dartmouth: AKI quality improvement specialist and Virtual Learning Collaborative improvement specialist. A 60-minute Collaborative training call was held monthly during the 18-month trial. Sites randomized to the Collaborative and Collaborative + Surveillance interventions were coached independently to avoid contamination. Each Collaborative sessions used a structured agenda and consisted of the following components: education on one of the clinical interventions in the Toolkit, team updates, quality improvement knowledge, and review of the Surveillance dashboard (Collaborative + Surveillance only). In

addition, we measured fidelity to the Collaborative, including participation on monthly calls, submission of key documents and a general active participation in the learning community.

Information Support with Automated Surveillance Reporting (Surveillance)

Ten teams (5 with Collaborative and 5 with Assistance) were provided with information support through the Surveillance dashboard, which provided insight into site-level AKI performance over time. The Surveillance tools executed a monthly updated estimation of each site's risk-adjusted performance, populating a series of tables and graphs for each site (**Figure 1**). There were four primary sets of content delivered within a single view: 1) an 18-month lookback of month-by-month observed to expected ratio estimate for each site compared to the national risk adjusted benchmark, with 95% confidence intervals; 2) risk-adjusted rankings reporting the cumulative overall performance of each site over the last 18 months relative to multiple benchmarks: national, regional, and Veterans Integrated Services Networks level site groupings; 3) a site-specific performance summary control chart which highlighted whether the site was out of expectation with regards to the statistical process control risk-adjusted sequential probably ratio testing; and 4) a site-specific patient list, which provided patient-level risk factors, observed outcomes, and predicted AKI risk.

In order to conduct national risk-adjusted surveillance for participating sites, we collected data from January 1, 2017, in each of the 76 Veterans Affairs medical centers with cardiac catheterizations laboratories.[5] We implemented a published VA-specific model for post-procedural AKI for risk adjustment of procedures captured by the Surveillance dashboard.[5] An L-1 penalized logistic regression model was trained to predict 7-day post-procedural AKI, the same target outcome as the current study. The model retained the following predictors: age at procedure, race, tobacco use, prior myocardial infarction, peripheral vascular disease, prior percutaneous coronary intervention, prior coronary artery bypass graft surgery, hypertension, diabetes, anemia, congestive heart failure, prior stroke, shock, chronic kidney disease,

estimated glomerular filtration rate, urgency of presentation, unstable angina, ejection fraction, and myocardial infarction in week prior to procedure. Due to sample size restrictions, the race variable was dichotomized as Asian American, Black, American Indian, Pacific Islander, and Unknown vs White. Race information was sourced from the EHR system. Ethnicity was not incorporated into this variable as it was not present in the original dataset. Thrombolytic use, which was selected in the published model, was excluded here due to small samples sizes. We extracted the model coefficients for all retained predictors and designed the data underlying our Surveillance dashboard with parallel inclusion criteria and variable definitions, allowing application of the published model to our study population.

As the model was developed on data between 2009 and 2013, we conducted an initial update of the model to account for recent changes in patient characteristics or practice patterns based on data from the 12 months prior to the initial Surveillance display period. Thus, data from February 2017 – March 2018 was used to update the model prior to the start of the study in October 2019, at which point the Surveillance dashboard displayed 18 months of information covering April 2018 – September 2019. We applied the update recommended by a testing procedure designed to select between available updating methods, including recalibration and retraining, while maximizing performance of the updated model and minimizing overfitting.[6] After this initial update, we applied a monthly surveillance-based updating approach from April 2018 through the end of the study intervention in March 2021.[7] This updating approach monitored model calibration on a monthly basis and updated in response to any detected deterioration in model performance.[6, 8] Updates were applied prospectively such that all data in the Surveillance dashboard displayed risk-adjusted information based on the version of the model active at the time of each observation. With monthly monitoring and data-driven updating, calibration of model predictions was improved over the original model and stable across the action phase of the study.

Data security access was tied to the EHR through VIA (VistA Integration Adapter), an approved EHR application programming interface using the provider's CPRS (Computerized Patient Record System) login credentials. Logging and tracking were conducted in accordance with VA patient access controls. All computing and data storage resources hosted onsite within the Tennessee Valley Healthcare System's secured environment.

Supplement 3 References

1. Byrd JB, Vigen R, Plomondon ME, Rumsfeld JS, Box TL, Fihn SD, et al.: Data quality of an electronic health record tool to support VA cardiac catheterization laboratory quality improvement: the VA Clinical Assessment, Reporting, and Tracking System for Cath Labs (CART) program. *Am Heart J,* 165**:** 434-440, 2013 10.1016/j.ahj.2012.12.009
2. Cannon CP, Battler A, Brindis RG, Cox JL, Ellis SG, Every NR, et al.: American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes. *J Am Coll Cardiol,* 38**:** 2114-2130, 2001 S0735109701017028 [pii]
3. Brown JR, McCullough PA, Splaine ME, Davies L, Ross CS, Dauerman HL, et al.: How do centres begin the process to prevent contrast-induced acute kidney injury: a report from a new regional collaborative. *BMJ Qual Saf,* 21**:** 54-62, 2012 10.1136/bmjqs-2011-000041
4. Brown JR, Solomon RJ, Sarnak MJ, McCullough PA, Splaine ME, Davies L, et al.: Reducing Contrast-Induced Acute Kidney Injury Using a Regional Multicenter Quality Improvement Intervention. *Circulation Cardiovascular quality and outcomes,* 114**:** 000903 (In Press), 2014 10.1161/CIRCOUTCOMES.114.000903
5. Brown JR, MacKenzie TA, Maddox TM, Fly J, Tsai TT, Plomondon ME, et al.: Acute Kidney Injury Risk Prediction in Patients Undergoing Coronary Angiography in a National Veterans Health Administration Cohort With External Validation. *J Am Heart Assoc,* 4, 2015 10.1161/JAHA.115.002136
6. Davis SE, Greevy RA, Fonnesbeck C, Lasko TA, Walsh CG, Matheny ME: A nonparametric updating method to correct clinical prediction model drift. *J Am Med Inform Assoc,* 26**:** 1448-1457, 2019 10.1093/jamia/ocz127
7. Davis SE, Brown JR, Dorn C, Westerman D, Solomon RJ, Matheny ME: Maintaining a National Acute Kidney Injury Risk Prediction Model to Support Local Quality Benchmarking. *Circ Cardiovasc Qual Outcomes,* 15**:** e008635, 2022 10.1161/circoutcomes.121.008635
8. Davis SE, Greevy RA, Jr., Lasko TA, Walsh CG, Matheny ME: Detection of calibration drift in clinical prediction models to inform model updating. *J Biomed Inform,* 112**:** 103611, 2020 10.1016/j.jbi.2020.103611

Appendix 3. Sample Size Estimates and Power Calculation

Specific Aim 1: Compare the efficacy of a Virtual Learning Collaborative (Collaborative) and/or Automated Surveillance Reporting (Surveillance) compared to Technical Assistance (Assistance) to reduce the incidence of AKI. Our working hypothesis is that multi--disciplinary clinical teams in a Collaborative with team--based coaching in implementation methods will reduce the incidence of AKI following cardiac catheterization, compared to an Assistance intervention, both with or without Surveillance. We hypothesize Surveillance will have a larger impact with Collaborative than Assistance.

Randomization. Randomization will occur at the hospital level in a 2x2 factorial design.35 We have enrolled a convenience sample of 12 Veteran Affairs (VA) hospitals with cardiac catheterization laboratories from across the United States (see Letters of Support) that meet the medical center inclusion/exclusion criteria. We will use a random number generator and block--randomize centers by size of eligible CKD patient volume, total procedure volume, number of catheterization rooms, VA region, size of city, and distance from academic medical center to ensure balanced sample size within each randomized cluster.

Sample Size and Power. To be conservative, power calculations assume the two-factor ANOVA with interaction. The target enrollment of 1,983 is planned in each of the four arms of the study (Assistance, Assistance + Surveillance, Collaborative, Collaborative + Surveillance) with three hospitals within each arm (average 661 patients per hospital). Based on national VA catheterization data for CKD patients,[1] the proportion of AKI in the Collaborative and Collaborative + Surveillance arms are assumed to be 0.2700 under the null hypothesis and 0.2025 under the alternative hypothesis. The proportion of AKI in Assistance and Assistance + Surveillance arms are projected at 0.2700 for the intervention period. We further assume an

intra--cluster correlation coefficient (the ratio of variation between hospitals to the sum of variation within and between hospitals) of 0.0009 – this is implied by the intervention arm of the pilot study.[2] We plan to conduct 0.05--level tests and desire power of at least 80%. Although we plan to perform hierarchical logistic regression models, the power for the analysis can be approximated using an F--test based on a normal approximation of the distribution of the proportion of AKI cases under each of the four intervention strategies. Under these assumptions, our power to detect any difference at all across the four intervention strategies against the null of no difference is above 99%. We also compute power for illustrative individual contrasts of interest. The power to test for a significant effect of Collaborative within a level of Surveillance (i.e., either for Surveillance used or Surveillance not used) assuming a z--test is just under 98% (this is lower than for the test of any difference across the four groups as sample size is halved). If the proportion of AKI under Collaborative arm was 0.27 under the alternative hypothesis (so that an interaction effect was present), the power to test whether the effect of VLR differs with Surveillance than without Surveillance is just above 80%. Power is substantially reduced for the interaction contrast due to four groups being compared as opposed to only two groups. In summary, we have overwhelming power to detect a difference among any of the four intervention strategies, very high power to find a difference between the levels of one factor within a level of the other factor, and acceptable power (i.e., above 80%) to detect a significant interaction between the effect of the factors. Finally, assuming a Bonferroni correction for multiple testing and a 25% effect size for each difference, testing the full set of 6 pairwise differences among the four intervention
strategies has power >90% implying we will be adequately powered to infer the optimal interven tion strategy.

The research design and analytic plan are described in the manuscript.

References

1. Brown JR, Solomon RJ, Sarnak MJ, et al. Reducing Contrast--Induced Acute Kidney Injury Using a Regional Multicenter Quality Improvement Intervention. Circulation. Cardiovascular quality and outcomes. 2014;;7(5):693--700. PMID: 25074372;; PMCID: PMC4869689.

2. Brown JR, MacKenzie TA, Maddox TM, et al. Acute Kidney Injury Risk Prediction in Patients Undergoing Coronary Angiography in a National Veterans Health Administration Cohort With External Validation. Journal of the American Heart Association. 2015;;4(12). PMID: 26656858;; PMCID: PMC4845295.

Supplemental Table 1. Sensitivity Analysis of 30-day AKI rates during the action phase and in the prior 12 months by intervention group and CKD status.

	All patients		CKD subset	
Population	**Prior 12m**	**Action phase**	**Prior 12m**	**Action phase**
All VA sites	19%	20%	33%	33%
All study sites	21%	20%	34%	32%
Intervention group				
Assistance	17%	24%	30%	35%
Assistance + Surveillance	22%	20%	35%	34%
Collaborative	25%	22%	38%	33%
Collaborative + Surveillance	17%	15%	30%	27%

AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease, VA: Veterans Affairs,

Assistance: Technical Assistance, Surveillance: Automated Surveillance

Reporting, Collaborative: Virtual Learning Collaborative

Supplemental Figure 1. Sensitivity Analysis of multilevel logistic models for AKI at 30-days with site-level random effects for all cardiac catheterization patients and those patients with chronic kidney disease.

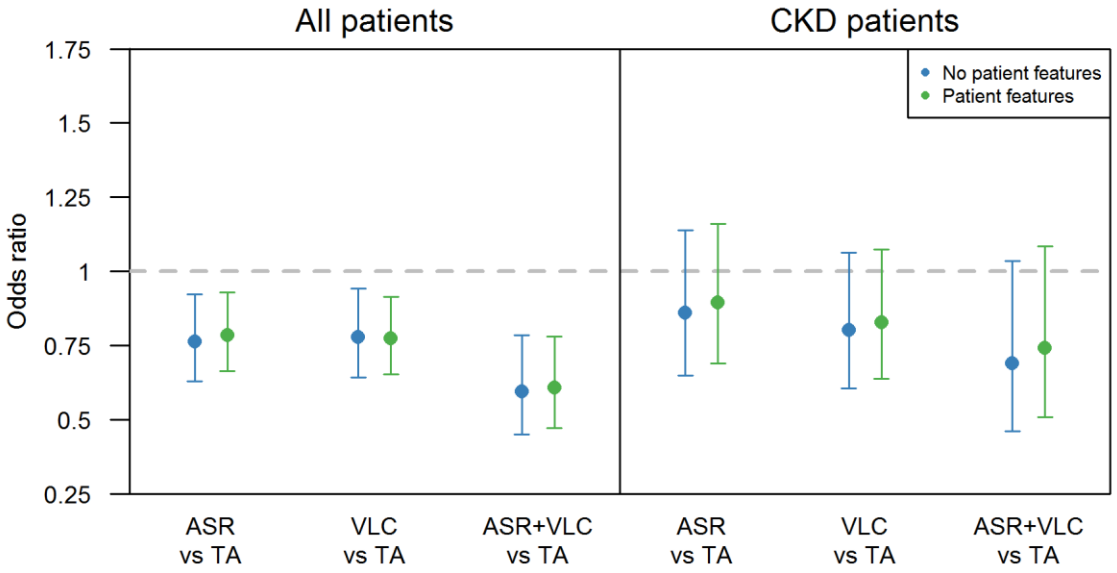


Figure S1 Legend:

AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease, ASR: Automated Surveillance Reporting, TA: Technical Assistance, VLC: Virtual Learning Collaborative. The following patient characteristics were included for adjustment: age, race, tobacco use, anemia, heart failure, CKD, diabetes, hypertension, prior percutaneous coronary intervention, and site baseline performance. *In all patients, the VLC+ASR intervention cluster compared to TA alone showed a statistically significant reduction in AKI with an adjusted and unadjusted odds ratio of 0.61 [0.47, 0.78] and 0.59 [0.45, 0.78], respectively.

Supplemental Table 2. Site compliance to the IMPROVE AKI Trail Action Phase and AKI Prevention Toolkit interventions.

	Collaborative + Surveillance	**Collaborative**	**Assistance + Surveillance**	**Assistance**
Monthly call attendance	69 (81%)	35 (41%)	32 (50%)	42 (53%)
Cardiologist attendance	41%	37%	22%	26%
Cath-lab leadership* attendance	22%	3%	6%	12%
# ASR dashboard hits	82	NA	64	NA
Intervention 1 Implemented	5 out of 5 sites	3 out of 5 sites	3 out of 4 sites	3 out of 5 sites
Intervention 2 Implemented	5 out of 5 sites	3 out of 5 sites	3 out of 4 sites	5 out of 5 sites
Intervention 3 Implemented	4 out of 5 sites	3 out of 5 sites	2 out of 4 sites	4 out of 5 sites
Total interventions implemented	93%	60%	67%	80%

AKI: Acute Kidney Injury, CKD: Chronic Kidney Disease, Assistance: Technical Assistance, Surveillance: Automated Surveillance Reporting, Collaborative: Virtual Learning Collaborative. The AKI Prevention Toolkit include interventions 1. Standardize order sets, 2. Increase intravenous and oral fluids, and 3. Reduce contrast volume.

*Cath-lab leadership includes the Cath lab director, Cath lab manager, or MD Chief of Medicine.