Modifiable Contextual Factors and Implementation Processes Associated with Improved Outcomes in the Multisite Spread of a Safety Intervention

Heather C. Kaplan  
University of Cincinnati College of Medicine

Stuart L. Goldstein  
University of Cincinnati College of Medicine

Claude Rubinson  
University of Houston-Downtown

Nancy Daraiseh  
University of Cincinnati College of Medicine

Fang Zhang  
Harvard Medical School, Harvard Pilgrim Health Care Institute

Isabelle M. Rodgers  
Boston Children's Hospital

Devesh S. Dehale  
Southeast Health

David J. Askenazi  
University of Alabama at Birmingham

Michael J.G. Somers  
Boston Children's Hospital

Joshua J. Zaritsky  
St. Chris Hospital for Children

Jason Misurac  
University of Iowa, Stead Family Children's Hospital

Vimal Chadha  
Children's Mercy Hospital

Karyn E. Yonekawa  
Seattle Children's Hospital

Scott Sutherland  
Stanford Medicine

Patricia L. Weng  
UCLA Mattel Children's Hospital

Kathleen E. Walsh (✉ Kathleen.walsh2@childrens.harvard.edu)  
Boston Children's Hospital

Research Article

Keywords: dissemination, context, implementation, acute kidney injury, adverse drug events, patient safety

Posted Date: December 29th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2346684/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background: The national spread of safety interventions has been slow and difficult. While it is widely known that hospital contextual features and implementation factors impact spread of evidence-based interventions, there is little prospective research on modifiable factors that impact implementation at multiple sites. Nephrotoxic Injury Negated by Just-in-Time Action (NINJA) is a system-level patient safety intervention that led to a sustained reduction in nephrotoxic medication–associated acute kidney injury (NTMx-AKI) at one hospital. Our objective was to prospectively characterize the association between context and implementation factors and reduction of NTMx-AKI at nine hospitals implementing NINJA, using mixed methods.

Methods: Grounded in i-PARIHS, we used qualitative comparative analysis (QCA) to assess the association between context and implementation factors, measured quarterly by survey, and reduction of NTMx-AKI, measured using statistical process control and ARIMA modeling. Interviews provided an understanding of causal processes underlying associations identified in QCA. Qualitative and quantitative data were collected and analyzed concurrently and then merged.

Results: Five hospitals reduced AKI, four did not. Overall, the collaborative reduced NTMx-AKI by 8 cases per 1000 patient-days per month (95% CI: 14.6-1.4; p=0.018). QCA analysis revealed that hospitals needed to have a baseline AKI rate > 1.0 to reduce NTMx-AKI (Ncon 1.0, Ncov 0.83). In addition, hospitals that reduced NTMx-AKI had either (a) a pharmacist champion and > 2 pharmacists working on NINJA (Scon 1.0, Scov 0.8) or (b) No other organizational priorities causing implementation delays (Scon 1.0, Scov 0.2). Involving quality improvement coordinators or data analysts did not influence success. Qualitative interviews supported these findings and underscored the importance of how the NINJA implementation team integrated with frontline staff.

Conclusions: We identified two different pathways to successful reduction in NTMx-AKI when implementing NINJA. These findings have implications for the future spread of NINJA and suggest an approach to study spread and scale of safety interventions more broadly.

Contributions To The Literature

- This prospective 9-hospital mixed-methods study used qualitative comparative analysis to assess the association of modifiable context and implementation factors with reduction in acute kidney injury (AKI) when implementing NINJA, a proven intervention.
- While context and implementation factors are known to contribute to the failed spread of interventions, this is one of few prospective studies to identify modifiable factors associated with success or failure to change outcomes.
- Five hospitals that reduced AKI used one of two implementation pathways, each with different critical factors—findings with implications for the spread of NINJA and which suggest an approach to study spread of interventions.

Background

Since the 1999 publication of To Err is Human, reductions in preventable harm to patients caused by healthcare have been slow (1–3). National spread of established safety interventions often proceed incompletely and inconsistently. (3) Complex interventions that greatly improve healthcare quality at one hospital too often fail to achieve the same results when adopted by other hospitals. Singh and Bates in JAMA comment on persistent high rates of harm due to failed spread of effective interventions to reduce healthcare associated infections, adverse drug events, and surgical site infections. (3) To a large extent, failed spread and scale-up of effective interventions contribute to ongoing patient harm and suboptimal healthcare.

The successful spread of complex quality improvement (QI) and safety interventions depend on the context of the health systems where implementation occurs and features of the implementation process itself. (4–8) Despite extensive research on context and implementation factors, methods to overcome barriers to the successful national spread of safety interventions remain elusive. Some experts suggest hospitals only implement interventions developed in similar contexts, (9) but with the spectrum of potential contextual features this proves very limiting. An expert panel could not agree on implementation strategies to overcome contextual barriers, calling for research on determinants of implementation success or failure and how these factors should be addressed. (9)

Accordingly, we had the opportunity to study implementation as part of the dissemination of the Nephrotoxic Injury Negated by Just-in-Time Action (NINJA) safety initiative to nine hospitals. By changing physician and pharmacy practice at the system level, in one hospital, NINJA led to a sustained 62% reduction in nephrotoxic medication-related acute kidney injury (NTMx-AKI) in children hospitalized in a non-ICU setting. (10) Using a mixed methods approach, our aim was to prospectively characterize the contextual factors and implementation processes of hospitals that reduced or failed to reduce NTMx-AKI when implementing NINJA.

Methods

In a nine-hospital cohort study, we prospectively, longitudinally measured contextual factors and NINJA implementation processes with quarterly surveys and performed qualitative interviews to discuss barriers and facilitators. We assessed reduction in NTMx-AKI from Spring 2015 to Summer 2017, using statistical process control and interrupted time-series Auto Regressive Integrated Moving Average (ARIMA) modeling. (11) To quantify the association of the reduction in NTMx-AKI with context and implementation factors, we used qualitative comparative analysis (QCA). (12) Qualitative
implementation. We performed Wald tests to select the most parsimonious model and inspected the residual plots to ensure the model assumptions of the time and an auto correlated error term. Model coefficients were used to estimate the trend in NTMx-AKI rates from the beginning of that included a constant term, an integer variable indicating time in two-week increments from the start of the observation period, and a quadratic term autoregressive integrated moving average (ARIMA) modeling and statistical process control (SPC). For the ARIMA modeling, we built a statistical model to recommend daily serum creatinine monitoring for AKI surveillance and work with the team to reduce exposure to NTMx. The NINJA intervention is described in detail elsewhere.(10, 16)

**NINJA Implementation and Fidelity**

Implementation was launched at all sites in Summer 2014. Because hospitals were not monitoring NTMx-AKI, it took several months of implementation before hospitals were able to report data on rates of NTMx-exposure and NTMx-AKI, with all nine sites reporting data beginning in Spring 2015. We used a modified breakthrough series approach to support NINJA implementation across the sites, following established methods.(17) All hospitals adopted common outcome definitions and submitted their data to a central repository. There was a policy of transparent sharing of rates of NTMx-AKI. At the start of the study, senior leaders from each site attended a NINJA implementation workshop and signed a commitment contract. Hospitals participated in monthly teleconference calls and annual in-person learning sessions which were based on an “all teach, all learn” philosophy.(17) Fidelity to the critical features of the intervention was excellent: the entire collaborative implemented the same measurement definitions with the same list of exposures and outcomes, monitored for NTMx-AKI among > 75% non-ICU patients, and collected daily serum creatinines among > 75% non-ICU patients (details published elsewhere)(16).

**Assessment of Contextual Factors and Implementation Processes**

Our assessment of hospital context and implementation processes was grounded in the i-PARIHS (Promoting Action on Research Implementation in Health Services) framework, which describes successful implementation as a function of multiple factors including facilitation, innovation, recipients, and context.(4) To add detail around the NINJA implementation team structure and function, we used the Model for Understanding Success in Quality (MUSIQ). (18–24) An implementation scientist, patient safety expert, and NINJA expert reviewed all factors from i-PARIHS framework, and additional items around facilitation of implementation and motivation to change (25) from MUSIQ framework, and identified specific components relevant to the NINJA study. Additional detail around how specific i-PARIHS context and implementation factors were applied to NINJA for this study is shown in Additional File 1. 1 shows how the i-PARIHS and MUSIQ frameworks this in more detail. Some factors were not relevant to this study. For example, for the external context, there were no relevant incentives, mandates and regulatory frameworks for NTMx-exposure. In another example, all the team leaders were nephrologists so we did not inquire about physician involvement in the team or subject matter expertise, but we did assess experience of the team leaders with quality improvement.

Using these frameworks, we developed a survey and interview guide focused on specific contextual and implementation factors relevant to NINJA. The survey longitudinally measured specific key contextual factors and aspects of implementation hypothesized to affect NINJA effectiveness. The interview characterized the complex relationships between hospital context, implementation processes, and the NINJA intervention. Both the interview guide and the survey were pilot-tested, and changes were made to improve clarity. The final 16-item survey was administered electronically to each site-PI quarterly. Additional File 2 shows this in more detail. The final 27-item semi-structured interview took approximately 45 minutes. Additional File 3 shows the interview guide. We conducted interviews 18 months after starting NINJA implementation anticipating that hospitals should at this time point have insights on the factors contributing to their successes and failures. Because team composition varied by site, the site-PI chose whether additional team members participated in the interview (interviews included one to four people). An experienced physician interviewer with conducted all interviews. Interviews were audio recorded and professionally transcribed.

**Analysis**

**NTMx-AKI Reduction**

Reduction in each hospital’s rate of NTMx-AKI cases per 1000 non-ICU patient-days was assessed using two methods: interrupted time-series autoregressive integrated moving average (ARIMA) modeling and statistical process control (SPC). For the ARIMA modeling, we built a statistical model that included a constant term, an integer variable indicating time in two-week increments from the start of the observation period, and a quadratic term of the time and an auto correlated error term. Model coefficients were used to estimate the trend in NTMx-AKI rates from the beginning of implementation. We performed Wald tests to select the most parsimonious model and inspected the residual plots to ensure the model assumptions.
were roughly met. (26) For the statistical process control analysis, NTMx-AKI rates were plotted biweekly, in real-time, on a U chart. We set an a priori rule that 8 consecutive data points above or below the centerline would constitute a significant change (i.e., we would shift the centerline). (27) Any site that had a reduced NTMx-AKI rate on the SPC as indicated by a centerline shift downwards (lower NTMx-AKI rate) was considered to have improved. All sites that improved on SPC also improved in ARIMA modeling and vice-versa.

Qualitative Comparative Analysis (QCA)

QCA was used to quantify the association of reduction in NTMx-AKI with specific contextual and implementation factors. QCA, an analytic technique that applies Boolean algebra, is not subject to degrees-of-freedom restrictions because it is based on Boolean algebra as such it is useful with small samples. (12, 28) QCA is increasingly used to study the uptake of public health interventions, because it excels at recognizing different pathways to achieve an outcome by distinguishing among different clusters of conditions under which an outcome does or does not occur. (29–34) QCA identified factors which were necessary, sufficient, or unimportant to reduce NTMx-AKI when implementing NINJA. A necessary condition is required for the outcome to occur. (35) A sufficient condition ensures that the outcome will occur, however, it may not be the only way to achieve the outcome; sometimes different pathways can lead to the same outcome. (35)

Necessity and sufficiency are assessed through two goodness-of-fit metrics: consistency and coverage (range 0 to 1). (35) Consistency, the more crucial metric, reports the strength of a relationship, with 1 indicating that the two conditions are always found together. Coverage describes how frequently the association is seen in the study population, with 1 indicating that all observations are explained by the model. (28, 35) In this study, we employed the “crisp-set” variant of QCA, in which all data are coded with 0, indicating absence of a condition, or 1, indicating its presence. To calibrate quarterly context and implementation survey data we distinguished between the hospital’s initial and established conditions, including both in a single QCA analysis. Hospital context and implementation processes may change over time (36) and we hypothesized that the initial and established conditions may impact outcomes in different ways. We defined initial context and implementation factors as the first six months of implementation and established context and implementation factors as starting after the initial period and ending either: (a) at the hospital’s first reported downward centerline shift in NTMx-AKI rates (SPC) or (b) at the end of the study period, if no downward centerline shift occurred. For established context, a condition was considered present if the hospital reported its presence on at least 75% of the quarterly surveys. QCA analysis was conducted using the Kiq and acq software packages (37), using the most conservative consistency threshold of 1.0 to assess necessity and sufficiency (where 1.0 is the highest possible threshold), as is appropriate for studies with small sample sizes. (12, 28, 35)

Qualitative Interview Analysis

We analyzed interviews to identify any additional contextual and implementation factors that were not previously hypothesized to be important and to characterize complex relationships among the factors influencing the success of NINJA implementation across sites. A clinician researcher and a human factors engineer initiated analysis deductively using the interview guide as a basis for the initial coding framework. Codes and definitions were added in an inductive manner as the analysis progressed. The analysis team met regularly after coding small sets of transcripts, refined the coding framework iteratively, and applied it to the remaining transcripts. All coding decisions were discussed, and differences were resolved by consensus; results were recorded in Microsoft Excel. (38) After coding all interviews, the team examined the electronic record of statements assigned to each code to collapse coding categories as necessary and to ensure that themes in the interviews coded earlier in the process did not require reclassification in light of the later evolution of the coding framework.

Integration of QCA and Qualitative Interview Data

To integrate the quantitative and qualitative components, we used a convergent approach to compare the results that were first obtained and analyzed in parallel. (39, 40) Integration was performed by researchers who analyzed both the quantitative and qualitative findings in collaboration with an expert in NINJA implementation; it involved iterative review, discussion, and interpretation of qualitative and quantitative data, including consideration of how the two kinds of data complemented and contradicted each other. While we anticipated handling contradictions through re-review of data and discussion, this was not an issue. We used qualitative data to add depth and breadth to our understanding of quantitative findings from QCA.

Results

The nine participating hospitals ranged in size from 70 to 298 non-ICU pediatric beds. (Table 1) They included both free-standing children’s hospitals and children’s hospitals within general hospitals, and represented each region of the country. The 9-hospital collaborative contributed 38,695 inpatient hospital-days in which 4,513 patients were exposed to NTMx and experienced 746 NTMx-AKI episodes.
Characteristics of NINJA Implementation Teams

All but one hospital had multidisciplinary NINJA implementation teams. (Table 2). At one hospital (Site C), the nephrologist leading NINJA implementation worked alone. The mean number of pharmacists involved in carrying out the NINJA project was 4 (min 0, max 18). These pharmacists ran reports on exposed patients and daily serum creatinine measurements (AKI), validated reports, reviewed data, entered data and communicated with the clinical teams. Other organizational priorities hindered NINJA implementation at 5 sites, including issues with engagement of specific service lines (e.g. decline to obtain daily creatinines), IRB delays, difficulty obtaining data, and changes in staffing or in hospital EHR. Three hospitals reported that these other priorities severely delayed NINJA implementation (> 6 months).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region of the country, n (%) hospitals Northeast</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>South</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Midwest West</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Median number Non-ICU pediatric beds (min, max)</td>
<td>161 (70, 298)</td>
</tr>
<tr>
<td>Hospital type, n (%) hospitals Freestanding children's hospital</td>
<td>6 (66%)</td>
</tr>
<tr>
<td>Children's hospital within a general hospital</td>
<td>3 (33%)</td>
</tr>
</tbody>
</table>

Table 1
Characteristics of the nine participating hospitals implementing NINJA in this study

<table>
<thead>
<tr>
<th>Site</th>
<th>Initial AKI Rate</th>
<th>Pharmacy champion w/time devoted to NINJA</th>
<th>Mean # pharmacists carrying out NINJA</th>
<th>QI expert/project manager*</th>
<th>Data analyst*</th>
<th>Other organizational priorities delayed NINJA implementation</th>
<th>IT stage in developing automated exposure and AKI report+</th>
<th>Monthly exposure and AKI data report</th>
<th>Leader collaborative attendance</th>
<th>Team member collaborative attendance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.0</td>
<td>Y Y 2</td>
<td>N N N Y Y N c c N Y Y Y Y Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>1.9</td>
<td>Y Y 15</td>
<td>N N N N N N N N N e e N Y Y Y N N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>5.4</td>
<td>N N 0</td>
<td>N N N N Y Y N b d N Y Y Y N/A N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>2.6</td>
<td>Y Y 1.5</td>
<td>N N N N Y Y Y e e N Y Y Y N Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>1.6</td>
<td>Y Y 2</td>
<td>Y Y Y N N N b b N Y N N Y Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>1.6</td>
<td>Y Y 1</td>
<td>Y Y Y N N N d d Y Y Y Y Y N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>0.9</td>
<td>N N 0</td>
<td>Y N Y Y Y Y d d Y Y Y Y Y Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>1.5</td>
<td>Y Y 4</td>
<td>Y Y Y Y Y Y b b Y Y Y Y Y Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0.5</td>
<td>Y Y 1</td>
<td>Y Y Y N N N c c N Y Y Y Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Sites with this resource always provided salary support; +Meaning of letter responses as follows: a. has not talked to IT, b. has not started building the report, c. build in progress, d. IT/EHR generates report but needs manual refinement, e. Automated report is complete and accurate.

Reduction in NTMx-AKI

Overall, across the collaborative, in interrupted time-series ARIMA modeling, there was a statistically significant decline of 8 cases of NTMx-AKI per 1,000 non-ICU patient-days per month throughout the study period (95% CI: 1.44, 14.57; p = 0.018). Using a network-wide SPC chart, we observed a 23% reduction in NTMx-AKI across the collaborative. However, within these global results, there was striking variability; five hospitals reduced NTMx-AKI considerably, while four did not reduce it at all (Fig. 1). The reduction of NTMx-AKI by individual hospitals ranged from 30–57%. In ARIMA modeling each of the five hospitals had a statistically significant reduction in NTMx-AKI over the study period, with p values that ranged from 0.03 to 0.007 and the other four hospitals had no change.
QCA Analysis

We found that only hospitals with a baseline AKI rate > 1.0 were able to reduce NTMx-AKI; this was the only necessary condition. (Table 3) See Additional File 4 for the Truth Table. Ncon and ncov were 1.0 and 0.83, respectively, indicating that the baseline rate of AKI greater than 1.0 is highly relevant to understanding the conditions under which NINJA was successful. This was the only necessary condition and the only baseline factor associated with reduction in NTMx-AKI.

Table 3. Fiss chart presenting necessary and sufficient conditions for successful reduction in NTMx-AKI when implementing the NINJA intervention.* †

<table>
<thead>
<tr>
<th>Recipes</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AKI &gt; 1.0</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Pharmacist champion with hours dedicated to NINJA</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>Mean number of pharmacist assigned to NINJA &gt; 2</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>QI expert or project manager</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Data analyst</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>No other organization priorities delayed NINJA implementation</td>
<td>○</td>
<td>●</td>
</tr>
</tbody>
</table>

Consistency 1.00
Solution coverage: 1.00

- ● Presence/absence of condition is necessary
- ● Core/ contributory condition present
- ○ Core/ contributory condition absent

* "Core conditions" are those that belong to both the paramorous and intermediate models;
"contributory conditions" belong exclusively to the intermediate model. The absence of a glyph indicates that the condition is irrelevant to explaining the outcome; some cases possess the condition while others do not. Consistency scores report the consistency of each recipe with the realization of the outcome. Solution consistency reports the consistency of all recipes combined.

**Raw/unique coverage scores report the proportion of cases of successful AKI reduction explained by each recipe. Solution coverage reports the proportion of cases of successful AKI reduction explained by all recipes combined.**

The sufficiency analysis revealed two distinct pathways ("recipes") to reduction in NTMx-AKI, both of which used factors from the established time period. The first pathway (Recipe 1, Table 3) identified that four of the five hospitals that reduced AKI shared two conditions: (a) a pharmacist champion with time devoted to NINJA implementation, and (b) a mean of more than two pharmacists involved in carrying out the NINJA project throughout the implementation period. The second pathway (Recipe 2, Table 3) describes a single hospital that reduced its NTMx-AKI rate with no pharmacist, QI support, project manager, or data analyst. The key explanatory factor here was that there were no other organizational priorities which caused delays in NINJA implementation efforts.

The QCA additionally revealed several resources that were not required to reduce NTMx-AKI when implementing NINJA. Having a QI coordinator/project manager on the implementation team did not make a difference nor did having a data analyst. Of the five hospitals that reduced NTMx-AKI, one had a QI coordinator and two had a data analyst. (Table 2)

Qualitative Interviews

The qualitative interviews identified several themes related to key aspects of context and implementation that affected success, including factors related to the external environment, hospital macrosystem, work environment, individual hospital unit microsystems, and the NINJA implementation team. (Table 4) Within the external environment, the only contextual factor consistently raised in interviews was the influence of and support from outside organizations (e.g., the lead site, Solutions for Patient Safety Network). For example, one team mentioned: "It was difficult because none of us were really QI trained...and through you know the support of [The study lead site], we kind of learned how to do it."
### Emerging themes organization by PARIHS/MUSIQ factor, with representative quotes among sites that reduced NTMx-AKI versus those that did not. (See Additional File 3 for additional information on methods)

<table>
<thead>
<tr>
<th>External level context</th>
<th>Site Reduced NTMx-AKI</th>
<th>Site Did Not Reduce NTMx-AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outside organizations supported the importance of NTMx-AKI or NINJA</td>
<td>It was difficult because none of us were really QI trained... and through you know the support of Cincinnati Children's [leading modified breakthrough series collaborative], we kind of learned how to do it</td>
<td>Actually, we were hoping to get more buy-in from [hospital leader] with the Solutions for Patient Safety, you know that [planned future] involvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organizational level context</th>
<th>Site Reduced NTMx-AKI</th>
<th>Site Did Not Reduce NTMx-AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Project aligned with organizational priorities</td>
<td>It just provided some...sense to the hospital that, you know, this was part of the mission of the entire center</td>
<td>So, they don't have the capacity to do it internally and it was, to our children's hospital administration credit, they said 'this is a priority for us'</td>
</tr>
<tr>
<td>Specific senior leader sponsor</td>
<td>The Chief Medical Officer... he kind of helped me kind of steer the ship, through...some of the med safety committee, the QI committee...</td>
<td>Although supportive, there's not really anybody who's going to go to that point and say, 'alright, this is an exception. You guys need to get on board.' So, it is really up to us and we don't really have the teeth to make it stick if somebody</td>
</tr>
<tr>
<td>Hospital culture of quality improvement and safety</td>
<td>Just in terms of the culture of quality in the hospital and what's already expected from all of the divisions in terms of having quality programs ongoing. The hospital tends to be reactive to things, so when our CLABSI rate goes up, they will institute procedures to reduce that. When the US News and World Report gave points for having a dedicated antibiotic stewardship pharmacist, they created that position.</td>
<td>It's a challenge because the individual service lines are quite used to functioning independently and...not being as cooperative, so certain things, certain groups like [specific subspecialty/service line] have their own ideas about how things should be done, and so it's a little challenging to get cooperation.</td>
</tr>
<tr>
<td>Structure and systems: Sophistication of QI program</td>
<td>All the divisions have quality triads that consist of the physician leader, nurse leader, and a Quality Specialist. I [NINJA leader] was the Physician leader of our triad.</td>
<td>The QI department here in general seems underfunded and understaffed.</td>
</tr>
<tr>
<td>Structure and systems: Systems in place to support NTMx-AKI monitoring prior to NINJA</td>
<td>It [NINJA] worked pretty well and the reason that I think we like it is because its integrated with a program the pharmacists are already using.</td>
<td>We already had a system in place. I think what was a little difficult was trying to figure out how to adapt the NINJA protocol to what we had already done because our pharmacy refuses to participate in terms of daily monitoring.</td>
</tr>
<tr>
<td>Structure and systems: Manual versus automated identification of patients exposed to nephrotoxic medications and their serum creatinines</td>
<td>The report gets automatically generated and there's a little bit of verification that they [pharmacists] have to still do that we're still tinkering with but it's pretty automated... We have a group that understands the data, a great IT team that's helped us to create data that we feel very strong about... It was just easier for me to go through all the charts. [Health system]is a pretty small hospital there are only about 120 beds that are non-ICU. So, you know every day it would be me clicking on 20 charts.</td>
<td>It is a manual process now- still for me. I [NINJA lead] get a report but I have to count- I get a report of everyone on the service line but I have to manually change that so I can filter out the ICU... So there's a lot of manual work that I do. We got behind on the data, we you know it all fell on me... and we got behind on data entry... it kind of spiraled from there. Yeah, it [automating identification of patients at risk] worked out [with IT] but it had its challenges. Yeah, it's like pushing a bulldozer.</td>
</tr>
<tr>
<td>Learning networks: Communication approach to ensure system-wide engagement</td>
<td>We went to all of the divisions, and I [NINJA leader] met with each division, and...gave them a 15-minute walkthrough...my main purpose of doing it that way was because I wanted to make sure that, it was a lot of mystique about what NINJA was, so kind of from the very beginning...[I] was very upfront and open about this is what it is, and this is what it is not.</td>
<td>So pharmacy buy-in I think is good. They're on the ball with getting us the reports [of patients exposed and with AKI]. But the communication could improve. And I guess we don't have regular meetings. That could certainly help that.</td>
</tr>
</tbody>
</table>

**Both organizational level and inner context**

---

**Table 4**
Several themes emerged around the role of the hospital macrosystem. One key theme was the importance of senior management support. At some hospitals senior leaders guided the NINJA team leader: “he kind of helped... steer the ship.” At other hospitals senior leaders gave verbal support but did not provide ongoing support to remove barriers. Participants from a hospital that did not reduce NTMx-AKI indicated: “We really don’t hear too much from senior leadership on this project.”

Alignment of NINJA with hospital strategic priorities also emerged as a theme with one center noting: “It provided some... sense in the hospital that... this was part of the mission of the entire center.” However, some hospitals did not decrease NTMx-AKI despite having alignment with the hospital’s strategic priorities. There was some evidence that a strong culture of safety within the hospital supported successful implementation, though findings were not always consistent. One team suggested that one of the key factors for their success was “in terms of [having a] culture of quality in the hospital and
what's expected from all the divisions” and a site that did not reduce NTMx-AKI reported: “It's a challenge because the individual service lines are quite used to functioning independently and...not being as cooperative.” However, there were also examples of sites that reduced NTMx-AKI and lacked elements of a strong culture of quality and safety. In the area of resource availability and work environment, a key facilitator was already having systems in place to support AKI monitoring prior to NINJA: “It [NINJA] worked pretty well and the reason... is because its integrated with a [IT] program the pharmacists are already using." Conversely, another hospital reported “what was a little difficult was trying to adapt the NINJA protocol to what we had already done..." In addition, monetary support and dedicated personnel for NINJA implementation were highlighted as important by some sites.

While there were numerous features of the individual hospital microsystems that impacted success, one of the key themes that emerged was the importance of integrating the work of the NINJA team with the activities occurring on the frontline: "Our approach from the beginning was that this was going to work best for us if we empower the [frontline] pharmacists... So how we've built our system and our tools were really to make sure that the pharmacist who is walking around (with the team on rounds) can have the tools." (Table 4) Another team reported: "We wanted the [frontline] teams to own the process.”

The characteristics of the NINJA implementation team itself seemed to be less important. There were a few comments from teams about the role of effective team functioning in success. For example, one hospital that reduced NTMx-AKI stated: “we've got a great multi-disciplinary team that's been working for two-plus years now”. Another hospital that did not reduce NTMx-AKI had only one person on the implementation team who was able to access and analyze exposure and outcome data; and when that person left the institution the team's effectiveness was severely affected: "I guess, making sure that the knowledge of how to run those reports is not all contained with one person? That would have been helpful.”

We additionally identified several instances in which teams adapted their local context to facilitate successful implementation. In one example, "We initially struggled to get pharmacy support, but they have actually now been the biggest proponents of the NINJA project, and we are just about to get a dedicated renal pharmacist." In another example: “when the US News and World Report gave points for a dedicated antibiotic stewardship pharmacist, they created that position... They're carving out time to allow this person to help on kidney stuff.”

**Integration of Qualitative and Quantitative data**

Qualitative data supported and enriched the relationships found through the QCA between context and implementation factors and outcomes. (Table 5) For example, while the QCA points to the critical need for adequate pharmacy support, one site PI without any pharmacy help or help from any other paid staff, leveraged unfunded resources, including help from medical students and the support of the division directors. “For a year and a half, I had a med student...So that really helped.” The interview also explained why pharmacists did not participate: “There are two pharmacists that are dedicated to pediatrics only, but they can’t [help with NINJA implementation], I mean I went to the CMO and there was no way...” Qualitative data also identified themes that may be important for reduction in NTMx-AKI, though not directly included in the QCA pathways, such as: support of a specific senior leader, having a coordinated approach to communication about NINJA across the system, obtaining buy-in and overcoming resistance to change at the unit/division (microsystem) level, and close integration between the NINJA implementation team and staff on the frontlines.
Qualitative interviews revealed that hospitals sometimes spread. Gathering data from a small pilot group of hospitals about specific factors critical to success can provide important information for future national MARQUIS and then adapted the intervention before further spread to address these issues. (48, 49) This study and ours suggest that prospectively gathering data from a small pilot group of hospitals about specific factors critical to success can provide important information for future national spread.

Most studies of context in the implementation of safety initiatives have employed retrospective case analyses, interviews, or surveys. (9, 36, 40, 46) For example, a study of 60 AHRQ-funded patient safety implementation studies, found that "surprisingly few projects actually planned for or expected the medical student" did it for my vacations. (140) Another hospital: "We switched from Cerner to EPIC and monitoring and not a whole lot of intervention. [Team with no pharmacy FTE for NINJA"

Table 5
Integration of QCA and Qualitative Interview Data

<table>
<thead>
<tr>
<th>Recipe</th>
<th>Critical Factors</th>
<th>Quote from site that reduced AKI</th>
<th>Quote from site that did not reduce AKI</th>
<th>QCA Consistency and Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>QCA recipe 1</td>
<td>1. Pharmacist Champion with time devoted to NINJA implementation</td>
<td>They [pharmacy leadership] have actually now been the biggest proponents of the NINJA project, and we are just about to get a dedicated renal pharmacist who's going to help with NINJA and all other aspects of renal related medication delivery.</td>
<td>They [pharmacy leadership] were just like no. Right up front, they're like: we're not going to help you. They were very clear. They were like, unless you can support our FTEs; you give us money for FTE, then we'll do it but we don't have any extra time to give you.</td>
<td>Scon 1.0, Scov 0.80</td>
</tr>
<tr>
<td></td>
<td>2. A mean of more than two pharmacists assigned to the project throughout the implementation period</td>
<td>When they're rounding there is a pharmacist...we were not going to the floor. The pharmacist from the central pharmacy, disseminates the information to the respective teams and then those pharmacists on the floor... they took the initiative [to communicate with the team about risk for NTMx-AKI, serum creatinines, and regimen changes]</td>
<td>It's a black box how much the pharmacist would approach the team about nephrotoxins. From an outsider's perspective, it seems that it's mostly what we're doing is monitoring and not a whole lot of intervention. [Team with no pharmacy FTE for NINJA]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Baseline AKI rate &gt; 1</td>
<td>N/A</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>QCA recipe 2</td>
<td>1. No QI Coordinator or analyst but</td>
<td>It's basically just a one-woman show... This is a pretty small hospital, there</td>
<td>We switched from Cerner to EPIC and that set us back probably 6 to 9 months.</td>
<td>Scon 1.0, Scov 0.2</td>
</tr>
<tr>
<td></td>
<td>2. NINJA team had no major competing priorities that took time away from implementation efforts</td>
<td>are only about 120 beds that are non-ICU. So, you know every day it would be me clicking on 20 charts. The weekends I'm on call, I just do it... You know the weekend when I leave I talk to the health staff... For a year and a half, I had a med student... It was fantastic. So that really helped. So, she [the medical student] did it for my vacations.</td>
<td>Another hospital: I don't always have the time! want to commit to all the projects I agree to, but I'm happy to help.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Baseline AKI implementation efforts</td>
<td>do it... You know the weekend when I leave I talk to the health staff... For a year and a half, I had a med student... It was fantastic. So that really helped. So, she [the medical student] did it for my vacations.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion
In this collaborative, similar to other multisite safety collaboratives, there was an overall reduction in harm across the collaborative, but impact at individual hospitals was variable. (40) By prospectively studying this variable impact, we were able to identify two distinct pathways that led to improvements when spreading a safety intervention. We also determined members of the implementation team that were critical to reduction in NTMx-AKI and those that are less so. Taken together, these findings have the potential to inform and improve national NINJA spread to maximize reduction in NTMx-AKI. This study also suggests a possible approach to future spread, where critical contextual factors and multiple successful pathways for implementation are identified before national spread to optimize the likelihood of improved outcomes at as many hospitals as possible during national spread.

Quality improvement collaboratives and multisite dissemination studies typically report aggregated results (17, 41–45), which does not provide information about variation between individual or groups of hospitals. By studying variation in outcomes, we found two distinct pathways to reduce NTMx-AKI. One pathway relied on obtaining pharmacy resources and a pharmacy leader to serve as a champion for NINJA. The other pathway relied less on resources and more on strategic prioritization, dedication, and grit. Commonly utilized is resources, such as data analysts, were potentially not necessary for hospitals to reduce NTMx-AKI when implementing NINJA. This funding could be redirected to functions more directly valuable to the implementation effort, such as pharmacy staff or protected time for the NINJA team leader.

Most studies of context in the implementation of safety initiatives have employed retrospective case analyses, interviews, or surveys. (9, 36, 40, 46) For example, a study of 60 AHRQ-funded patient safety implementation studies, found that "surprisingly few projects actually planned for or expected many of the barriers and facilitators they experienced during their project implementation" (47) One exception is a multisite study of a medication reconciliation intervention (MARQUIS) which identified several reasons why some hospitals failed to reduce errors in reconciliation when implementing MARQUIS and then adapted the intervention before further spread to address these issues. (48, 49) This study and ours suggest that prospectively gathering data from a small pilot group of hospitals about specific factors critical to success can provide important information for future national spread.

Qualitative interviews revealed that hospitals sometimes changed their context to facilitate implementation. For example, on hospital that did not initially dedicate pharmacy resources to NINJA was able, over time, to identify resources through another program. In another example, several hospitals
worked with division directors to change culture, including clinician attitudes and resistance to NINJA. These prospective findings are aligned with those of Kirsh et al., who used in-depth retrospective case analysis at one site to demonstrate that both the intervention and the local context co-adapted and evolved to ensure sustainability.(36) What are the implications of this research for the spread and scale-up of safety interventions? Our study suggests a practical approach to improve the national spread of safety interventions. Leveraging lessons from small pilot implementation studies - information on specific critical modifiable contextual factors and implementation pathways that lead to improved outcomes - may inform and potentially improve national spread. For example, based on our data, collaboratives interested in implementing NINJA can encourage hospitals to consider the critical contextual factors we identified then select one of the two pathways and modify contextual barriers as needed, using mitigation strategies employed by pilot hospitals. While there are sporadic examples where hospitals have changed context to enable implementation of patient safety interventions, we are proposing the prospective study of implementation in a small number of hospitals to inform and improve the national spread of patient safety interventions. The strategy that we propose encourages planning for critical contextual barriers and using multiple implementation pathways to allow for a more tailored approach to implementation that improves the current “one size fits all” approach. Systematically examining variation in success in pilot implementation studies would allow collaboratives to identify critical factors and design approaches to overcome barriers before spreading safety interventions nationally.

This multisite prospective study has some limitations. While QCA is ideally suited for a study of different combinations of conditions associated with an outcome, it is a descriptive technique for identifying associations rather than inferring causation. It is the case knowledge developed from the qualitative interviews that allows an understanding of the causal processes underlying these associations.(50) Furthermore, QCA is not designed for longitudinal analyses. To accommodate this limitation, we distinguished between “initial” and “established” contexts, with the latter averaged across multiple quarters of context data. One strength of QCA is that it works well with purposively collected data such as ours, which included a variety of hospital types. Because our sample is non-random, however, the results might not be generalizable to all hospitals. In addition, the 38,695 inpatient hospital-days from the nine participating hospitals make it a relatively small study of spread and scale-up.

Conclusions

Having a high baseline rate of NTMx-AKI in combination with either pharmacy support or engagement of a team leader without competing institutional demands was critical for the successful implementation of NINJA. Early understanding of these critical factors may inform future spread and scale-up of NINJA. We are currently testing approaches to help hospitals planning to implement NINJA not only select one of the two pathways identified in this study but also modify factors pertaining to context to better facilitate NINJA implementation. More generally, this approach provides a model for the prospective study of the association of critical contextual and implementation factors and the scale-up of evidence-based interventions nationally.

Abbreviations

NINJA
Nephrotoxic Injury Negated by Just-in-Time Action
NTMx-AKI
Nephrotoxic Medication-Associated Acute Kidney Injury
QCA
Qualitative Comparative Analysis
ARIMA
Auto Regressive Integrated Moving Average Modeling
QI
Quality Improvement
IRB
Institutional Review Board
AKI
Acute Kidney Injury
EHR
Electronic Health Record
PARIHS
Promoting Action on Research Implementation in Health Services
MUSIQ
Model for Understanding Success in Quality
SPC
Statistical Process Control
AHRQ
Agency for Healthcare Research and Quality
MARQUIS
Multisite Study of a Medication Reconciliation Intervention

Declarations

Ethics approval

All methods were carried out in accordance with relevant guidelines and regulations. The study was deemed exempt from human subjects research by the institutional review boards (IRB) at all sites (Cincinnati Children's Hospital Medical Center IRB, Boston Children's Hospital IRB, University of Alabama at Birmingham IRB, Lucille Packard Stanford Children's Hospital IRB, Stead Family Children's Hospital IRB, Children's Mercy Hospital IRB, Seattle Children's Hospital IRB, UCLA Mattel Children's Hospital IRB, Helen DeVos Children's Hospital at Spectrum Health IRB. Informed consent was obtained from all subjects involved in the interview.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

S.G. is currently receiving funding from the Agency for Healthcare Research and Quality Grant 1R18HS023763-01. D.A. within the past 36 months has received grants or contracts from the NIH, Baxter, and Medtronic. He is a paid consultant for Baxter, Medtronic, Seastar, Nuwellis, Bioporte, and the AKI foundation. He has patents planned for Advancements in CRRT for small children and in an external urine collection device for neonates. He is the unpaid Board Chair of the Neonatal Kidney Collaborative. K.W. within the past 36 months has served as a consultant for Sanofi and Research Triangle Institute. The remaining authors have no conflicts of interest.

Funding

This study was funded by Agency for Healthcare Research and Quality 1R18HS023763.

Author’s contributions

K.W. designed the study, led the analysis and interpretation of data, wrote the manuscript and approved the final version, S.G., H.K., N.D. contributed to study design, analysis, interpretation of data, manuscript writing, and approved the final version, C.R. and F.Z. contributed to design, performed data analysis, contributed to interpretation of the data and manuscript writing, and approved the final version, I.R. contributed to analysis and interpretation of data as well as manuscript writing and approved the final version. D.D. contributed to data analysis and interpretation, edited the manuscript and approved the final version. D.A., M.S., J.Z., J.M., V.C., K.Y., S.S., P.W. contributed to data acquisition, analysis and interpretation, and edited the manuscript as well as approving the final version.

Acknowledgements

We would like to thank Stephen Muething, M.D. for his encouragement, support, and advice throughout this work, Julia Steinke, M.D. and Traci Henderson, R.Ph., for their work on NINJA implementation.

References

5. Reed J, Kaplan HC, editors. Qualitative exploration of context using the Model for Understanding Success in Quality (MUSIQ). 10th International Organisational Behaviour in Healthcare; 2015; Cardiff. Wales, UK.


**Figures**
Figure 1

ARIMA modeling (right) and U chart (left) figures showing NTMx-AKI over the study period among the five sites that reduced NTMx-AKI (p=0.006) and those that did not.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- NINJAQCAISAdditionalfile1.docx
- NINJAQCAISAdditionalfile2.docx
- NinjaQCAISAdditionalfile3.docx
- NINJAQCAISAdditionalfile4.docx