Improving Fluconazole Prophylaxis Guideline Adherence in the Neonatal Intensive Care Unit

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Abstract

Problem and Purpose: Invasive candidiasis (IC) has up to a 30% mortality rate in extremely low birth weight (ELBW) infants. Despite evidence supporting fluconazole prophylaxis, adherence to guidelines was inconsistent in a Level IV NICU. A chart audit revealed variability in inclusion criteria and adverse event monitoring related to fluconazole administration. This QI project aimed to standardize fluconazole prophylaxis among ELBW infants in the NICU by implementing and measuring adherence to an updated, evidence-based guideline.

Methods: Implemented from August to December 2024, the revised evidence-based guideline clarified inclusion criteria, dosing, duration, and adverse effect monitoring. Weekly audits to track adherence and provider education were conducted, followed by post-education surveys. Implementation of central line (CL) discussions during daily interdisciplinary rounds were conducted to monitor CL use. The project included 27 infants, NICU providers, and pharmacists.

Results: Overall, weekly guideline adherence improved from 76% to 83%. Fluconazole was initiated within 72 hours for 81.5% (n=22) of infants, with all 27 infants receiving the correct dosing and frequency. Clinical and laboratory findings were unremarkable for 77.8% (n=21) of infants. Mild AST elevation occurred in 18.5% (n=5), and 3.1% had oliguria (n=1). No IC cases were reported. The average CL dwell days decreased from 28 to 18.

Conclusions and Implications: The use of an evidence-based fluconazole prophylaxis protocol may improve guideline adherence. Continued provider engagement, EMR integration, and expansion to satellite NICU sites will be key to sustaining progress and standardizing care.

Keywords: Adherence, antifungal, central line days, ELBW infants, fluconazole, invasive candidiasis, NICU, prophylaxis.

Improving Fluconazole Prophylaxis Guideline Adherence in the Neonatal Intensive Care Unit

Extremely low birth weight (ELBW) infants are at higher risk for invasive candidiasis (IC), which can carry up to a 30% mortality rate (Dermitzaki et al., 2024; Kelly et al., 2015). With the introduction of fluconazole prophylaxis (PPx) and risk factor monitoring, the IC rate has decreased in this population over the last decade (Kilpatrick et al., 2021). Risk factors that indicate the need for fluconazole PPx including hemodynamic instability requiring inotropic support, late-onset sepsis (LOS) or prolonged exposure to broad-spectrum antibiotics, urinary tract infection (UTI), meningitis, feeding intolerance requiring prolonged parenteral nutrition, necrotizing enterocolitis (NEC), spontaneous intestinal perforation (SIP), Histamine Type 2 Receptor Antagonist use, severe intraventricular hemorrhage (IVH), and respiratory decompensation requiring high-frequency ventilation (Dermitzaki et al., 2024).

Between January and March 2024, 17 infants qualified for fluconazole PPx based on risk factors, with an average therapy duration of 25 days. Two of the 17 patients received fluconazole treatment dosing of 12mg/kg/dose in replacement of prophylaxis due to their clinical status in the absence of a known candida infection. The fluconazole administration hospital policy lacked clarity regarding initiating, continuing, or discontinuing therapy for infants ≤1,000g and <28 weeks' gestation, with a hospital guideline adherence rate of 76%. No evidence was embedded within the hospital guideline, and adverse effect monitoring parameters were not included. In addition, internal data showed that the approach to fluconazole PPx administration was inconsistent. Despite having no recent cases of IC at the site, the lack of recent revisions and evidence-based links prompted the need for an updated guideline.

A project site's root cause analysis (RCA) identified key gaps in the existing fluconazole PPx guideline. Gaps identified in the fishbone diagram shown in Figure 1 included the absence of patient-specific instructions and unclear therapy duration, lack of adverse effect monitoring, and inconsistent fluconazole administration practices from provider to provider. The purpose of this quality improvement (QI) project aimed to standardize fluconazole PPx among ELBW infants by implementing an updated evidence-based guideline.

Available Knowledge and Specific Aims

An extensive literature search on neonatal fluconazole PPx was conducted using the keywords “NICU,” “neonatal,” “fluconazole,” “candida,” and “prophylaxis” in the UMD Health Services database (PubMed, CINAHL, and Cochrane Review), yielding 377 articles as shown in the Citation Manager (Appendix A). After applying search filters, 50 articles were screened, and seven studies were selected to support this QI initiative. Based on the Johns Hopkins Evidence-Based Practice Model (Dang et al., 2022), the selected studies ranged from Level 1 to Level 4, Quality A to B. They included systematic reviews, randomized controlled trials (RCTs), cohort studies, and a Clinical Practice Guideline (CPG). The complete PRISMA diagram can be found in Appendix B.

Two Level 1 studies demonstrated that fluconazole PPx reduced IC infections and mortality (Leonart et al., 2017; Manzoni, 2012). Leonart et al. (2017) recommended a 3 mg/kg dosage for its effectiveness and lower hepato- and nephrotoxicity. Studies by Robati et al. (2021), Zhang et al. (2021), and Valenzuela-Stutman et al. (2023) showed that fluconazole PPx reduced IC-associated mortality, colonization, and overall mortality in NICU infants. Valenzuela-Stutman et al. (2023) also found that fluconazole reduced IC in ELBW infants despite a brief rise in liver enzymes. The clinical practice guideline from Pappas et al. (2016)

advises fluconazole PPx for infants <1,000g in nurseries with high IC rates. The CDC recommends monitoring IC risk factors like CL dwell time to reduce the risk of all-cause Central-Line Associated Blood Stream Infection (CLABSI), including candida (Bryant et al., 2022). Tables 1 and 2 provide a detailed evidence review and synthesis.

The literature review's strength and evidence provided good support for clinical practice change. This QI project aimed to implement an updated, evidence-based fluconazole PPx guideline for ELBW infants and improve adherence. The project's elements included increased adherence to guideline recommendations, accurate dosing, appropriate timing of initiation, standardized monitoring, minimized adverse effects, and evaluation of the revised guideline's impact on CL dwell days.

Rationale

The Consolidated Framework for Implementation Research (CFIR) was used to assess the contextual factors influencing the implementation of the revised fluconazole PPx guideline in the NICU. The CFIR evaluates implementation across five domains: intervention characteristics, outer setting, inner setting, characteristics of individuals, and the implementation process. This framework helped identify site-specific barriers and facilitators, guiding the development and execution of the intervention, ensuring it was contextually appropriate and feasible for the NICU setting (Damschroder et al., 2009). As illustrated in Figure 2, the CFIR provided a comprehensive structure that shaped the initiative's design, implementation, and evaluation.

Key elements of the CFIR that influenced the implementation process encompassed intervention characteristics such as adaptability, complexity, and the strength of evidence, in addition to the outer setting that considered external policies and national guidelines. The inner setting uncovered variability in workflow and limited awareness of the original guideline, necessitating the integration of electronic medical record (EMR) prompts and structured tools. The characteristics of the individuals' domain highlighted variability in provider knowledge and confidence, thereby informing targeted educational interventions. The implementation process underscored the importance of stakeholder engagement, which included neonatologists, advanced practice providers, and NICU leadership, to ensure long-term commitment and facilitate sustained adoption.

The application of the CFIR to this project effectively informed the design and execution of the revision of the fluconazole guidelines. Organizational culture and leadership engagement are critical in facilitating implementation within the inner setting. The CFIR framework helped identify barriers, including inconsistent provider awareness and challenges related to workflow, as well as facilitators such as interdisciplinary support and alignment with institutional priorities. Customized strategies, comprising stakeholder meetings, training for providers, and ongoing compliance audits, were developed to address these challenges. As illustrated in Figure 3, integrating CFIR into the project led to achieving sustainable practice changes, thereby enhancing adherence to evidence-based care and fluconazole guidelines through a context-sensitive and collaborative approach.

Methods

Context

The project lead utilized the Safety Attitudes Questionnaire (SAQ) (Sexton et al., 2006) to assess healthcare providers' perceptions of the intervention and its alignment with the NICU's patient safety culture. The assessment revealed a strong sense of teamwork and commitment among staff, but challenges were noted in interdisciplinary communication and resource accessibility for fluconazole PPx (Appendix C). These findings highlighted key barriers to collaboration and efficient communication, which were addressed through targeted interventions aimed at improving access to resources, refining workflows, and enhancing communication during patient care discussions. Periodic reassessments ensured ongoing progress and stakeholder engagement in the practice changes.

This QI project occurred in a 52-bed Level IV NICU at a teaching hospital, where fluconazole PPx practices varied in initiation, maintenance, and discontinuation criteria. Key gaps included inconsistent assessment of infant risk factors, adverse effect monitoring, CL use, and therapy discontinuation (Figure 4).

Intervention

The intervention designed to enhance fluconazole PPx practices and improve provider adherence was executed over 16 weeks, from August to December 2024. The revised fluconazole PPx guideline was formulated by a multidisciplinary team comprising neonatologists, pharmacists, and infection control specialists. The updated guideline created by the project lead provided clear recommendations on therapy initiation, tailored duration, individualized duration, and defined discontinuation criteria to minimize risks such as nephrotoxicity and hepatotoxicity. Following a comprehensive review and formal approval by the medical and pharmacy team, the updated guideline was disseminated electronically to all NICU providers and made available on the hospital's policy website to facilitate accessibility.

Prior to the project implementation in August 2024, the goal was to improve provider education and awareness of fluconazole PPx through targeted training and access to updated guidelines. Providers were encouraged to apply clinical discretion for modifications based on evolving patient status. To support this, a structured educational session was implemented to enhance comprehension of the revised guideline. This initiative incorporated a virtual

PowerPoint presentation directed towards NICU providers and pharmacists, emphasizing the guidelines' key modifications. Pre- and post-education surveys were administered through electronic correspondence to assess provider understanding and confidence in the practical application of the updates.

During implementation, daily multidisciplinary rounds were employed to facilitate discussions regarding the necessity of CL, infection control risk factors, identification of adverse events, laboratory findings, and fluconazole dosing. These rounds promoted collaborative decision-making, ensuring appropriate PPx adjustments were made promptly. A QR code system was added to providers' workstations to simplify and encourage real-time documentation of CL decisions and fluconazole-associated monitoring. This tool streamlined bedside data collection and supported tracking of both adverse effects and guideline adherence.

The intervention additionally included weekly audits of EMR data to monitor compliance with the established guidelines, specifically emphasizing the timing of fluconazole initiation, dosing precision, and reporting of adverse events. Real-time monitoring enabled immediate feedback and targeted provider support, necessitating further education. Throughout the intervention, IC incidence was tracked as a balancing measure to ensure that changes in clinical practice did not lead to unintended increases in infection risk. Figure 6 presents a comprehensive project timeline and outlines key activities and milestones.

Measures

The project utilized a combination of structure, process, and outcome measures to assess the effectiveness of the intervention and track its impact. Structure measures included the implementation of the revised fluconazole PPx guideline, which served as the foundation for the intervention. Staff education was also a key structure measure. Post-implementation assessments measured staff completion of education on fluconazole PPx, current recommendations, adverse effects, and IC knowledge, targeting 100% compliance with online training. Completion rates were evaluated using the REDCap Survey (Appendix F).

Process measures focused on daily interdisciplinary rounds that assessed the necessity of CL and monitored fluconazole-associated adverse effects. A QR code placed on providers' computers streamlined the process of documenting CL discussions during rounds and captured potential adverse effects. Criteria for line removal were based on infant medications, acuity, and the ability to advance enteral feeds. Data collected during this process included CL days and length of fluconazole therapy (Appendix E). The project lead verified data through retrospective chart audits.

Outcome measures reflected adherence to the revised fluconazole PPx guideline elements and included appropriate initiation, dosing, and discontinuation. The goal was to improve adherence to all guideline elements and ensure 100% monitoring for adverse effects, with documentation of any incidents and management strategies. Weekly adherence to the guideline was measured via retrospective chart audits by the project lead and reported (Appendix D).

Analysis

This QI project employed qualitative and quantitative methods to evaluate the effectiveness of the fluconazole PPx intervention. For the quantitative analysis, descriptive statistics were utilized to summarize guideline adherence, provider education completion, adverse effect monitoring, and CL usage. Guideline adherence was gauged on an all-or-nothing basis for each patient each week. Compliance was recorded as 100% if all components were met and 0% if any component was missed. Weekly averages were calculated to assess overall adherence trends during the implementation phase.

Provider education was evaluated by tracking completion of pre- and post-implementation surveys, with the total number of respondents serving as the numerator and total eligible staff as the denominator. Central line utilization was calculated using data from daily rounds and chart audits, measuring the number of days of life during which infants had a CL in place. Weekly averages were derived to evaluate trends over time. Adverse effects, including hepatotoxicity and nephrotoxicity, were identified through QR code submissions during daily rounds and confirmed by chart audits. These events were averaged across the total number of infants receiving fluconazole PPx during the implementation period to monitor safety outcomes.

Provider feedback from surveys and interdisciplinary discussions during rounds informed iterative adjustments to education and workflow strategies. Run charts visualized trends in adherence, education completion, CL usage, and adverse effects, helping the team interpret variations in data over time and refine implementation strategies accordingly.

Ethical Considerations

Participant privacy and data confidentiality were protected following HIPAA guidelines and were CITI compliant. Data was securely entered into the HIPAA-compliant REDCap system at a private location within the hospital. The project lead completed HIPAA and CITI training and declared no conflicts of interest. Patient identifiers could not be imported or downloaded, and access to sensitive information was restricted to the project lead and faculty. The project team verified data for accuracy and fidelity through weekly chart audits. Before project execution, non-human subject research was determined by the University of Maryland, Baltimore Human Research Protections Office (HRPO).

Results

During the 16-week implementation phase (August–December 2024), 27 infants were eligible for fluconazole PPx. Pre-implementation adherence to the fluconazole PPx guideline averaged 76%, which increased to 83% during implementation, with full 100% compliance sustained for ten of the sixteen weeks (Figure 7). Adherence fluctuated between 50% and 100%, with a median adherence of 100%. The most common cause of noncompliance was delayed fluconazole initiation (n=5).

Timely initiation of fluconazole within the recommended 72-hour window was achieved in 88% (n=15) of eligible infants before implementation, while 12% (n=2) experienced delays. During implementation, this rate decreased slightly to 81.5% (n=22), with 18.5% (n=5) experiencing delays (Figure 8). Despite the dip in timely initiation, dosing accuracy remained at 100%, with all infants receiving the appropriate 3 mg/kg/dose twice weekly regimen. Two infants who did not meet the gestational age or birth weight criteria received fluconazole based on provider discretion; one received a single dose before discontinuation, and the other continued therapy due to clinical instability. One infant (3.7%) required a prolonged six-week course due to suspected cutaneous Candida despite negative cultures.

Regarding safety, 77.8% (n=21) of infants had unremarkable clinical and laboratory findings. Mild AST elevations occurred in 18.5% (n=5), but no interventions were necessary. One infant (3.7%) developed transient oliguria that resolved without modifying therapy. Importantly, no cases of IC were identified during either the pre- or post-implementation periods. However, this measure served solely as a balancing metric to ensure that changes in PPx practice did not inadvertently increase infection risk.

The average birth weight of treated infants during pre-implementation was 700g (range: 400g to >1,000g) and 800g (range: 500g to >1,000g) during the implementation phase. The average gestational age was 24 weeks (range: 23–28) during pre-implementation and 26 weeks (range: 22–30) during the project (Figure 9).

Central line use decreased post-implementation. The median CL days decreased from 20 to 15, ranging from 4 to 42 days (Figure 10).

Facilitators of success included consistent interdisciplinary communication throughout the implementation of the project, integration of the guideline into the EMR, and targeted education of the revised guideline. Barriers included provider discretion overriding guideline criteria in select cases, inconsistent documentation contributing to delayed initiation in some instances, and inconsistency with CL discussions during interdisciplinary rounds. Barriers were addressed by ongoing education and reinforcement of the revised guideline by the project lead. While no significant unintended consequences were noted, the slight decrease in timely initiation suggests the need for continued reinforcement of workflow adherence.

Discussion

This QI project demonstrated that implementing a multidisciplinary, evidence-based fluconazole PPx guideline in a NICU was associated with improved provider adherence and decreased CL dwell days among infants receiving prophylaxis. The enhanced consistency in antifungal practices reflects the project's impact on standardizing care and strengthening neonatal antifungal stewardship. Although no cases of IC were observed during the implementation period, this outcome functioned as a balancing measure rather than a targeted outcome. No change was observed in IC rates between pre- and post-implementation phases, suggesting that the new guideline did not inadvertently increase infection risk.

Provider adherence improvements may contribute to potential cost savings by ensuring appropriate fluconazole use and avoiding unnecessary exposure, dosing errors, or prolonged central line utilization. While a formal financial analysis was not conducted, it is reasonable to infer that improved adherence to evidence-based guidelines could reduce costs by minimizing adverse events or unnecessary interventions, which are often expensive in neonatal populations. The results align with existing literature highlighting the importance of establishing a fluconazole PPx guideline and incorporating central line discussions to reinforce adherence, with no observed increase in IC cases during the implementation period. However, this project differed from published studies because it did not directly measure IC reduction or conduct efficacy analyses. Instead, it focused on process improvement and practice standardization, recognizing that institutional differences in workflow, provider education, and pre-existing IC prevalence may influence implementation outcomes.

Several internal validity threats affected the project. Low engagement in QR code-based data collection during rounds and inconsistent documentation limited the evaluation of CL use trends. Similarly, a low provider response to pre- and post-implementation education surveys made it challenging to assess the effectiveness of the educational component or measure sustained knowledge retention. These limitations were partially addressed through manual chart audits, real-time EPIC data monitoring, and multidisciplinary discussions, which helped ensure data accuracy and guideline application. However, variation in provider compliance and documentation practices may still have introduced bias or imprecision.

The project's strengths included developing a clear, accessible, evidence-based guideline, integrating it into daily NICU workflows, and facilitating multidisciplinary collaboration, which facilitated sustained adherence. Limitations included reliance on self-reported education survey data, and implementation barriers such as workload variability and inconsistent technology use of QR codes.

The project emphasizes the significance of structured implementation strategies, real-time feedback loops, and stakeholder engagement in promoting evidence-based practice. Future QI efforts should streamline data collection tools, enhance provider education participation, and utilize automation within the electronic medical record to support ongoing adherence and impact measurement.

Conclusion

This QI project aimed to enhance adherence to the updated fluconazole PPx guideline in the NICU, demonstrating its value in promoting evidence-based antifungal stewardship. Through structured implementation, education, and monitoring, the initiative improved fluconazole use consistency and reduced CL dwell days without increasing IC rates. These findings highlight the need to standardize clinical protocols in high-risk neonatal populations, where practice variation can significantly impact outcomes. Improving provider adherence to guidelines enhances quality, safety, and patient outcomes by minimizing unnecessary medication exposure, reducing complications, and ensuring consistent, high-quality care. The initiative's strengths include practical design, multidisciplinary collaboration, and focus on sustainability. Integrating the fluconazole PPx guideline into the EMR, especially within order sets and ICU navigators for ELBW infants, will promote adherence at critical decision points.

Sustainability is further enhanced through ongoing collaboration with infectious disease (ID) specialists to standardize the protocol across other satellite NICU sites. This initiative aims to reduce practice variation and ensure that all high-risk neonates receive consistent, evidence-based prophylaxis regardless of location. Continued efforts to automate provider reminders, integrate soft stops for therapy reevaluation, and expand educational outreach will reinforce long-term improvements.

While QI outcomes are not inherently generalizable, the project's design may inform fluconazole PPx guidelines in similar neonatal populations. The combination of guideline creation, targeted education, EMR integration, CL discussions, and data audits provides a framework for institutions to implement antimicrobial stewardship initiatives, supporting adherence, enhancing patient safety, and reducing resource use. Future steps include refining provider education to improve survey response rates and knowledge retention. This may involve in-person refresher sessions, mandatory annual training, and point-of-care education. Enhancing real-time data collection with more accessible tools, like bedside tables or integrated EMR prompts, will streamline documentation and improve central line data accuracy.

This QI project shows the value of enhancing fluconazole prophylaxis adherence through multidisciplinary efforts. By aligning practices with evidence, it promotes safer care for vulnerable neonates and paves the way for sustainable antifungal stewardship improvements. Future efforts to scale and measure impact will ensure ongoing progress in neonatal healthcare.

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Table 1

Evidence Review

Citation: Leonart, L. P., Tonin, F. S., Ferreira, V. L., Tavares da Silva Penteado, S., de Araújo Motta, F., & Pontarolo, R. (2017). Fluconazole Doses Used for Prophylaxis of Invasive Fungal Infection in Neonatal Intensive Care Units: A Network Meta-Analysis. *The Journal of Pediatrics*, 185, 129-135.e6. DOI: 10.1016/j.jpeds.2017.02.039		**Level and Quality: 1A**
Purpose or Hypothesis	To compare the effectiveness and safety of different doses of fluconazole for prophylaxis against IC infection in neonates in the NICU/ The hypothesis is that varying doses of fluconazole would have different impacts on the incidence of IC and mortality rates.	
Type of Evidence Research Design	Systematic review/network meta-analysis of multiple RCTs.	
Sample Population, Size, Setting	**Sampling Technique:** Systematic review. **Sample Size:** A total of 1,578 infants across 11 RCT articles. **Eligible Participants:** Neonates weighing < 1,500g at birth who received fluconazole prophylaxis regardless of dose, therapy compared to placebo or another antifungal agent, outcome of interest reported. **Setting:** RCTs in the NICU. **Excluded:** Articles that do not address outcomes of interest, and other types of studies that were not RCTs. **Accepted:** Only RCTs that directly compared fluconazole with placebo or other antifungal agents. **Control:** Infants received placebo or alternative antifungal agents. **Intervention:** Administration of fluconazole at varying doses (3, 4, and 6mg/kg) for IC prophylaxis. **Power analysis/Achieved:** Not specified. **Group Homogeneity:** N/A.	
Intervention Procedures	**Control Protocol:** Received either placebo or alternative antifungal agents depending on the RCT. **Intervention Protocol:** Received fluconazole prophylaxis at different doses, with dosing regimens specified in the respective RCT protocols. **Treatment Fidelity:** N/A.	
Primary Outcome and Measures	**Dependent Variable:** Primary outcome of interest were improved outcomes among neonates receiving fluconazole prophylaxis. **Dependent Variable Measure:** Incidence of IC infection confirmed through laboratory analysis or mortality rates observed during study period.	
Results/Conclusions	**Statistical Results:** Fluconazole at doses 3 and 6mg/kg demonstrated significant reductions in the incidence of IC compared to the control group (odds ratios of 5.48, 95% credible interval 1.81-18.94) and 2.63, 95% credible interval 1.18-7.02 respectively). There were no significant differences between the efficacy of the 3 and 6mg/kg doses. Similarly, for IC related mortality, both fluconazole doses showed superiority over the control group with ORs of 15.32 (95% CI 1.54-54.31) for 3 mg/kg and 9.14 (95% credible interval 1.26-142.7) for 6 mg/kg. Additionally, fluconazole at 4mg/kg showed promising results but requires further investigation due to the limited number of studies utilizing this dose. **Conclusions:** Fluconazole prophylaxis is effective in reducing the incidence of IC and related mortality in high-risk neonates. It is suggested that fluconazole at 3mg/kg is preferred due to its efficacy and potentially lower risk profile compared to higher doses.	

Citation: Manzoni, P., Mostert, M., Latino, M. A., Pugni, L., Stolfi, I., Decembrino, L., Vagnarelli, F., Corona, G., Tridapalli, E., Vetrano, G., Memo, L., Priolo, C., Galletto, P., Giovannozzi, C., Gallo, E., Pedicino, R., Barberi, I., Faldella, G., Mosca, F., & Saia, O. S. (2012). Clinical characteristics and response to prophylactic fluconazole of preterm VLBW neonates with baseline and acquired fungal colonisation in NICU: data from a multicentre RCT. *Early Human Development*, 88(s2), S60–S64. DOI: 10.1016/S0378-3782(12)70017-8		**Level and Quality: 1B**
Purpose or Hypothesis	To investigate the clinical characteristics and outcomes associated with fungal colonization by Candida species in VLBW neonates admitted to the NICU. Aims to compare neonates colonized at baseline through vertical transmission with those who acquire colonization during their NICU stay via horizontal transmission.	
Type of Evidence Research Design	Systematic review/secondary analysis of data collection from a multicenter RCT.	
Sample Population, Size, Setting	**Sampling Technique:** Convenience. **Sample Size:** 336 VLBW infants. **Eligible Participants:** VLBW neonates admitted to NICUs. **Setting:** 8 Italian NICUs. **Excluded:** 27 infants ineligible due to liver failure, lack of parental consent, or missing/randomization errors. **Accepted:** 336 infants. **Control:** Neonates not receiving fluconazole prophylaxis. **Intervention:** Fluconazole prophylaxis was administered to VLBW infants. **Power analysis/Achieved:** N/A. **Group Homogeneity:** N/A.	
Intervention Procedures	**Control Protocol:** Neonates who did not receive fluconazole. **Intervention Protocol:** Fluconazole was administered to eligible neonates. **Treatment Fidelity:** N/A.	
Primary Outcome and Measures	**Dependent Variable:** Incidence of IC infections in VLBW neonates. **Dependent Variable Measure:** Measured through cultures.	
Results/Conclusions	**Statistical Results:** Neonates with baseline colonization (4.7%) had significantly higher birth weight and gestational age compared to those with acquired colonization (11.4%) ($p < 0.05$). They were also more likely to be born via vaginal delivery ($p < 0.05$). The overall rate of progression to systemic fungal infection was 0.38, with no significant difference between baseline and acquired colonization groups ($p = 0.5$). Fluconazole prophylaxis significantly reduced progression from baseline colonization to SFI ($p = 0.05$). Candida parapsilosis was significantly more frequent in neonates with acquired colonization compared to those with baseline colonization ($p < 0.05$). **Conclusions:** Neonates with baseline and acquired colonization exhibit differences in demographics, clinical characteristics, and response to fluconazole prophylaxis. Baseline colonization is associated with higher birth weight and gestational age and a better response to fluconazole prophylaxis in preventing the progression to systemic fungal infections. These findings suggest the need for tailored management strategies for different groups of colonized preterm neonates in NICUs.	

Citation: Martin, A., Pappas, A., Lulic-Botica, M., & Natarajan, G. (2012). Impact of "targeted" fluconazole prophylaxis for preterm neonates: efficacy of a highly selective approach? *Journal of Perinatology*, 32(1), 21–26. DOI: 10.1038/jp.2011.27	**Level and Quality: 3B**
Purpose or Hypothesis	To evaluate the effectiveness of targeted fluconazole prophylaxis in reducing the incidence of IC in VLBW infants with multiple risk factors for fungal infections. The hypothesis was that targeted fluconazole prophylaxis would reduce the incidence of invasive fungal infections while minimizing drug exposure.
Type of Evidence Research Design	Observational pre-post cohort study.
Sample Population, Size, Setting	**Sampling Technique:** Non-randomized sampling. **Sample Size:** 524 VLBW infants admitted to the NICU between January 2005 and December 2007. **Eligible Participants:** Infants < 1500g admitted to the NICU during the study period and < 6 weeks of age who received broad spectrum antibiotics for more than 2 days with at least 1 additional risk factor for IC during administration period. **Setting:** NICU in Detroit, MI. **Excluded:** Infants transferred to a different hospital system, severe hepatic dysfunction, or other severe conditions (n=23). **Accepted:** Total of 524 infants, 230 in the control group, 294 in the prophylaxis group. **Control:** No fluconazole prophylaxis was administered to VLBW infants before 2006. **Intervention:** From June 2006 to December 2007, targeted fluconazole prophylaxis 3mg/kg was implemented for selected VLBW infants with significant risk factors for fungal infection (birth weight, gestational age, duration of parenteral nutrition, and previous colonization or candida infection. **Power analysis/Achieved:** N/A. **Group Homogeneity:** N/A.
Intervention Procedures	**Control Protocol:** Standard care practices for VLBW infants admitted to the NICU which did not include routine fluconazole prophylaxis. **Intervention Protocol:** Implementation of targeted fluconazole prophylaxis for selected VLBW infants with specific risk factors. **Treatment Fidelity:** N/A.
Primary Outcome and Measures	**Dependent Variable:** Incidence of IC. **Dependent Variable Measure:** Isolation of Candida species from blood or CSF cultures. Reduction in IC rates seen in control group.
Results/Conclusions	**Statistical Results:** The incidence of IC decreased significantly from 15.3% in the control period to 6.2% in the intervention period ($p = 0.001$), indicating a reduction in the incidence of fungal infections with the implementation of targeted fluconazole prophylaxis. Bivariate regression analysis showed lower birth weight, shorter duration of total parenteral nutrition, and admission during the prophylaxis period were associated with a decreased risk of IC. **Conclusions:** Targeted fluconazole prophylaxis was effective in significantly reducing the incidence of invasive candidiasis in VLBW infants with multiple risk factors for fungal infections. Despite the reduction in fungal infections, no overt adverse effects associated with fluconazole administration were observed during the study period. However duration of parenteral nutrition, central line use, and NEC rates were significantly higher during control period.

Citation: Pappas, P., Kauffman, C., Andes, D., Clancy, C., Marr, K., Ostrosky-Zeichner, L., Reboli, A., Schuster, M., Vazquez, J., Walsh, T., Zaoutis, T., & Sobel, J. (2016). Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of america. *Infectious Diseases Society of America*. 62(1), 1-50. DOI: 10.1093/cid/civ933	**Level and Quality: 4A**
Purpose or Hypothesis	To provide evidence-based recommendations for the management of candidiasis, including prophylaxis with antifungal agents like fluconazole.
Type of Evidence Research Design	Clinical practice guidelines from experts for infectious diseases.
Sample Population, Size, Setting	**Sampling Technique:** Neonates with candidiasis or at risk of developing. **Sample Size:** N/A. **Eligible Participants:** N/A. **Setting:** Various NICU settings. **Excluded:** N/A. **Accepted:** N/A. **Control:** N/A. **Intervention:** Recommendations for the use of fluconazole and other antifungal agents in the management of candidiasis, including prophylaxis strategies. **Power analysis/Achieved:** N/A. **Group Homogeneity:** N/A.
Intervention Procedures	**Control Protocol:** N/A. **Intervention Protocol:** N/A. **Treatment Fidelity:** N/A.
Primary Outcome and Measures	**Dependent Variable:** The effectiveness and safety of fluconazole prophylaxis and treatment for candidiasis. **Dependent Variable Measure:** Various clinical outcomes related to the management of candidiasis such as resolution of infection, adverse events, and mortality rates.
Results/Conclusions	**Statistical Results:** N/A. **Conclusions:** (omitted findings for infection and focused on prophylaxis recommendations). In nurseries with high rates (>10%) of invasive candidiasis, intravenous or oral fluconazole prophylaxis, 3–6 mg/kg twice weekly for 6 weeks, in neonates with birth weights <1000 g is recommended.

Citation: Robati Anaraki, M., Nouri-Vaskeh, M., & Abdoli Oskoei, S. (2021). Fluconazole prophylaxis against invasive candidiasis in very low and extremely low birth weight preterm neonates: a systematic review and meta-analysis. *Clinical and Experimental Pediatrics*, 64(4), 172–179. DOI: 10.3345/cep.2019.01431	**Level and Quality: 2A**
Purpose or Hypothesis	To evaluate the efficacy of different prophylactic fluconazole scheduled in controlling IC colonization infections and mortality in VLBW and ELBW infants in the NICU.
Type of Evidence Research Design	Systematic review and meta-analysis of RCTs and cohort studies.
Sample Population, Size, Setting	**Sampling Technique:** Systematic search though several databases. **Sample Size:** 16 eligible studies (9 RCTs and 8 cohort studies) with total of 4,486 infants. **Eligible Participants:** VLBW and ELBW infants admitted to the NICU who received prophylaxis with fluconazole within 24 hours of birth. **Setting:** NICU where VLBW and ELBW received care. **Excluded:** 3 studies that postponed starting prophylaxis more than 24 hours after birth. **Accepted:** 16 studies. **Control:** Infants who did not receive fluconazole prophylaxis or received a placebo. **Intervention:** Infants who received fluconazole prophylaxis within 24 hours of birth. **Power analysis/Achieved:** N/A. **Group Homogeneity:** Assessed using 12 statistics and Cochrane Q, found to be non-significant for most outcomes.
Intervention Procedures	**Control Protocol:** Not receiving fluconazole prophylaxis or receiving a placebo. **Intervention Protocol:** Administering fluconazole prophylaxis within 24 hours of birth. **Treatment Fidelity:** N/A.
Primary Outcome and Measures	**Dependent Variable:** Colonization, IC, and IC-associated mortality. **Dependent Variable Measure:** Meta-analysis of risk ratios (RRs).
Results/Conclusions	**Statistical Results:** significant reduction in IC-associated mortality among VLBW infants (P=0.011; RR, 0.068; 95% CI, 0.009–0.543), particularly those weighing ≤1,000 g, when administered fluconazole prophylaxis. Additionally, the prophylactic use of fluconazole led to a substantial decrease in colonization by Candida spp. (P<0.001; RR, 0.350; 95% CI, 0.223–0.551), demonstrating its effectiveness in preventing fungal colonization in this high-risk population. Furthermore, the analysis revealed significantly lower overall mortality rates among ELBW infants who received fluconazole prophylaxis (P=0.023; RR, 0.780; 95% CI, 0.629–0.966) compared to those who did not, especially when specific dosing schedules were adhered to. **Conclusions:** VLBW and ELBW infants revealed significant benefits in reducing IC-associated mortality, colonization, and overall mortality rates. The findings underscore the importance of fluconazole prophylaxis as a preventive measure in NICUs, particularly for vulnerable preterm infants. The study provides robust statistical evidence supporting the efficacy of fluconazole prophylaxis in improving outcomes and reducing the burden of fungal infections in this high-risk population.

Citation: Valenzuela-Stutman, D., Romero, A., & Astudillo, P. (2023). Prophylactic fluconazole protocol in very low birth weight infants: Invasive candidiasis prevention in a latin America neonatal intensive care unit. *Journal of Perinatology.* 42 (1139-1144). DOI: 10.1038/s41372-023-01699-0	**Level and Quality: 3B**
Purpose or Hypothesis	To assess the impact of prophylactic fluconazole administration on the incidence of invasive candidiasis (IC) in VLBW infants admitted to the NICU with a high incidence of IC. Prophylactic fluconazole would lead to the reduction in IC incidence, thereby improving patient outcomes.
Type of Evidence Research Design	Interventional pre-post cohort design.
Sample Population, Size, Setting	**Sampling Technique:** Historical cohort approach. **Sample Size:** Pre-prophylaxis control group 228 infants, prophylaxis intervention group 125 infants. **Eligible Participants:** All VLBW infants born at or transferred to hospital. **Setting:** A tertiary NICU. **Excluded:** Infants with congenital candidiasis, prior systemic antifungal therapy, or acute liver failure diagnosis. **Accepted:** All eligible VLBW infants. **Control:** Pre-prophylaxis group who did not receive Fluconazole. **Intervention:** Prophylactic fluconazole administration protocol. **Power analysis/Achieved:** N/A. **Group Homogeneity:** Significant differences were noted in maternal age, maternal morbidity, and prenatal corticosteroid prescription, suggesting some heterogeneity in baseline characteristics.
Intervention Procedures	**Control Protocol:** Pre-prophylaxis control group did not receive prophylactic fluconazole. **Intervention Protocol:** Prophylactic fluconazole administration protocol. Involved the administration of fluconazole at dosage of 3mg/kg IV twice a week for a minimum of 4 weeks, with a possible extension to 6 weeks in high-risk patients. ELBW infants received prophylaxis regardless of risk factors, while BW 1000-1500g were screened for risk factors and colonization cultures to determine prophylaxis eligibility. **Treatment Fidelity:** Implemented a specific protocol for the administration of prophylactic fluconazole, including dosage, duration, and monitoring of liver function tests. The protocol was consistently followed throughout intervention period.
Primary Outcome and Measures	**Dependent Variable:** Incidence of IC in VLBW infants. **Dependent Variable Measure:** Incidence of IC, mortality rates, and liver enzyme levels were measured to assess the effectiveness and the safety of fluconazole.
Results/Conclusions	**Statistical Results:** Substantial reduction in the incidence of IC following the implementation of fluconazole prophylaxis from 7.8% to 2.4% ($p=0.05$) in VLBW infants and 16.7% to 3.7% ($p=0.04$) in ELBW infants. Significant increase in ALT, AST, and GGT levels observed at weeks 5 and 6, extending beyond the initial 4-week period of fluconazole administration ($p < 0.01$). However, no adverse clinical outcomes associated with these increases. **Conclusions:** Evidence supporting the effectiveness and safety of fluconazole prophylaxis in preventing IC in VLBW infants, particularly ELBW. By **significantly reducing the incidence of IC** without adversely affecting mortality outcomes, fluconazole prophylaxis emerges as a valuable preventive strategy in NICU. Fluconazole prophylaxis is generally **well tolerated, with no significant liver function abnormalities observed within the initial 4-week administration**. Although, there were **elevations in liver enzymes beyond 4 weeks, no adverse clinical outcomes were associated with these changes**, suggesting an overall favorable risk benefit profile of fluconazole.

Citation: Zhang, D., Xie, D., Wang, X., Dong, W., & Lei, X. (2021). Prophylactic use of fluconazole in very premature infants. *Frontiers in Pediatrics*. 9. 726769. DOI: 10.3389/fped.2021.726769	**Level and Quality: 3B**
Purpose or Hypothesis	To evaluate the efficacy, safety, and fungal sensitivity of prophylactic fluconazole use in very premature infants.
Type of Evidence Research Design	Non-experimental, retrospective historical comparative analysis.
Sample Population, Size, Setting	**Sampling Technique:** Convenience, retrospective analysis of very premature infants admitted. **Sample Size:** 196 infants – 113 in the prophylaxis group and 83 in the rescue group. **Eligible Participants:** Very premature infants with VLBW admitted to the hospital within the first 24 HOL. **Setting:** NICU at a tertiary care hospital in southwest China. **Excluded:** 41 infants excluded due to fungal infection appearing within 72 hours of hospitalization (n=1), death occurred within 72 hours of hospitalization (n=3), serious congenital structural or chromosomal anomalies (n=6), hepatic insufficiency (n=11), renal insufficiency (n=6), and incomplete data (n=14). **Accepted:** 113 in prophylaxis group and 83 in rescue group (n=196). **Control:** The comparison between infants who received fluconazole prophylaxis and those who received rescue treatment for fungal infections. **Intervention:** Fluconazole IV. 6mg/kg twice a week for 4 weeks in VLBW infants and 6 weeks for ELBW infants. Administration was stopped if significant hepatotoxicity, full enteral feeding, discharge, ect. **Power analysis/Achieved:** N/A. **Group Homogeneity:** Gestational age, gender, birth weight, SGA, endotracheal intubation, use of pulmonary surfactant, early onset sepsis, feeding intolerance, gastric tube and PICC, use of broad-spectrum antibiotics, postnatal steroid use, days of parental nutrition, and duration of hospital stay.
Intervention Procedures	**Control Protocol:** Infants received rescue treatment with IV antifungal agents. **Intervention Protocol:** Infants received prophylactic fluconazole IV. **Treatment Fidelity:** The administration of fluconazole was adjusted based on clinical criteria such as hepatotoxicity, feeding status, or hospital discharge.
Primary Outcome and Measures	**Dependent Variable:** Incidence of nosocomial fungal infection (NCFI) and short-term adverse outcomes. **Dependent Variable Measure:** Comparison of NCFI incidence, fungal sensitivity, short term adverse outcomes, and drug induced liver or renal function disruption.
Results/Conclusions	**Statistical Results:** Prophylactic administration of fluconazole significantly reduced incidence of invasive candidiasis in VLBW infants. Among infants with birth weight < 750gm incidence was 2.4% in prophylaxis group compared to 10.6% in the historical control group (p=0.02). Similarly, in ELBW infants, incidence was 2.2% in prophylaxis group compared to control of 9.4% (p=0.002). Notably, the prophylaxis group exhibited a substantially lower incidence of nosocomial fungal infection (NCFI) compared to the rescue group (15.9% vs. 45.8%), indicating the efficacy of fluconazole in preventing fungal infections in this population. Candida albicans and Candida glabrata were identified as the main pathogens causing NCFI in both groups. However, it is noteworthy that a smaller proportion of fungi isolated from the prophylaxis group were completely sensitive to fluconazole (40% vs. 85%), and the minimum inhibitory concentration of fluconazole was higher in this group, suggesting a potential decrease in sensitivity over time. Despite these findings, no completely resistant fungi were isolated in either group, indicating that fluconazole remained effective in preventing fungal infections, albeit with reduced sensitivity. The analysis also identified

	prolonged antibiotic use as a risk factor for NCFI, highlighting the importance of judicious antibiotic stewardship in preventing fungal infections in very premature infants. **Conclusions:** The use of prophylactic fluconazole administration to significantly reduce the incidence of invasive candidiasis in very premature infants, particularly in those with ELBW. These results have important clinical implications for the management of this vulnerable population, as invasive candidiasis is associated with significant morbidity and mortality. Additionally, efforts to minimize prolonged antibiotic use may further enhance the effectiveness of fluconazole prophylaxis in this vulnerable population. By reducing the incidence of invasive candidiasis, fluconazole prophylaxis may lead to improved clinical outcomes and a decreased need for systemic antifungal therapy, thereby minimizing the risks associated with prolonged medication use. The recommended dose of fluconazole prophylaxis was 6mg/kg every 72 hours, with the duration tailored to individual factors such as gestational age, birth weight (4 weeks VLBW, 6 weeks ELBW), clinical conditions, and risk factors for invasive fungal infections.

Table 2

Evidence Synthesis

Project Title: Fluconazole Prophylaxis Guideline Revision			
PICOT: Does revising the current fluconazole prophylaxis protocol and implementation of central line rounds compared to the current protocol enhance the efficacy and safety of fluconazole and improve patient outcomes?			
JHNEBP Model Level	**Total Number of Sources**	**Author and Quality Rating of each study**	**Synthesis of Findings**
Level 1 Experimental study · Randomized Controlled Trial (RCT) · Systematic review of RCTs with or without meta-analysis	2 systematic reviews of RCTs (Leonart et al., Manzoni et al.)	(Leonart at al., 2017) (Manzoni et al., 2012)	Both studies by Manzoni et al. (2012) and Leonart et al. (2017) investigate the efficacy of fluconazole prophylaxis in preventing IC infections in neonates, particularly those in NICUs. Manzoni et al. focus on Candida colonization patterns in preterm VLBW infants, noting that baseline colonization correlates with higher birth weight and gestational age, leading to a better response to fluconazole prophylaxis. In contrast, infants with acquired colonization have a higher risk of systemic fungal infection despite receiving prophylaxis. Conversely, Leonart et al. compare different fluconazole doses and find both 3 mg/kg and 6 mg/kg doses significantly reduce IC infections and related mortality compared to placebo, recommending the use of the lowest effective dose (3 mg/kg) for its comparable efficacy, lower toxicity risk, and cost-effectiveness. While both studies confirm the efficacy of fluconazole prophylaxis, they diverge in their focus, with Manzoni et al. emphasizing tailored management strategies based on colonization mode and Leonart et al. advocating for dose optimization and cost-effectiveness in neonatal IC prevention.
Level II Quasi-experimental studies · Systematic review of a combination of RCTs and quasi-experimental studies, or quasi-experimental studies only, with or without meta-analysis	1 systematic review of a combination of RCTs and cohort studies with meta-nalysis (Robati et al.)	(Robati et al., 2021)	Robati et al. (2021) highlights the efficacy of fluconazole prophylaxis in reducing IC-associated mortality, colonization, and overall mortality in preterm infants admitted to NICUs. These findings provide strong evidence supporting the consideration of prophylactic fluconazole use as a preventive measure to mitigate the risk of life-threatening fungal infections in this vulnerable population.
Level III Non-experimental study · Systematic review of a combination of RCTs, quasi-experimental, and non-	1 Non-experimental, retrospective comparative	(Zhang et al., 2021) (Valenzuela-Stutman et al., 2023)	Zhang et al. (2021) and Valenzuela et al. (2023) both investigate the efficacy and safety of fluconazole prophylaxis in VLBW infants, but they focus on different aspects and populations. Zhang et al. evaluate the effectiveness, safety, and fungal sensitivity of prophylactic fluconazole in VLBW/ELBW infants, finding a significantly lower incidence of neonatal candida fungal infection (NCFI) in the

experimental studies, or non-experimental studies only, with or without meta-analysis · Qualitative study or systematic review of qualitative studies with or without meta-synthesis	analysis (Zhang et al.) 2 non-experimental cohort studies (Martin et al., Valenzuela et al.)	(Martin et al., 2012)	prophylaxis group compared to the rescue group. Although fewer fungi in the prophylaxis group were completely sensitive to fluconazole and exhibited higher minimum inhibitory concentrations, no completely resistant fungi were isolated. Additionally, the prophylaxis group experienced lower risks of adverse outcomes and NCFI, with no increased risk of serious short-term adverse effects. The recommended dose was 6 mg/kg every 72 hours, with duration tailored to individual factors. In contrast, Valenzuela et al. (2023) assess the impact of prophylactic fluconazole specifically on the incidence of IC in VLBW infants in a high IC incidence NICU setting. Their findings demonstrate a significant decrease in IC incidence with fluconazole prophylaxis, particularly notable in ELBW infants. While mortality rates did not significantly change between groups, analysis of liver enzyme levels indicated a temporary increase post-fluconazole administration within safe ranges. Overall, the study supports the effectiveness and safety of fluconazole prophylaxis in reducing IC in VLBW infants, suggesting its potential as a preventive measure in high-risk NICU environments. Martin et al. (2012) explore targeted intermittent fluconazole prophylaxis in high-risk preterm infants, noting its effectiveness in reducing invasive candidiasis. However, they also highlight increased durations of parenteral nutrition and central line use, along with a higher incidence of necrotizing enterocolitis associated with this approach. Despite these concerns, the study advocates for targeted fluconazole prophylaxis as a valuable strategy for reducing the risk of invasive candidiasis in vulnerable neonatal populations, emphasizing the need for further research and careful monitoring to fully understand its clinical impact.
Level IV Opinion of respected authorities and/or reports of nationally recognized expert committees/consensus panels based on scientific evidence	1 clinical practice guideline from a nationally recognized committee (Pappas et al,)	(Pappas et al. 2016)	Pappas et al. (2016) indicate that in neonatal nurseries where rates of invasive candidiasis are high, particularly exceeding 10%, a specific recommendation is made regarding the prophylactic use of fluconazole. The guideline suggests the use of intravenous or oral fluconazole prophylaxis at a dosage of 3–6 mg/kg given twice weekly for a duration of 6 weeks. This recommendation is specifically targeted towards neonates with birth weights below 1000 grams.

Level V Evidence obtained from literature reviews, quality improvement, program evaluation, financial evaluation, or case reports · Opinion of nationally recognized expert(s) based on experiential evidence			
Overall Quality Rating w/rational and Recommendation: All studies included in this analysis received ratings ranging from A to B, indicating good to high quality of evidence. These ratings reflect the robustness of the methodology employed, the rigor of data collection and analysis, and the relevance of the findings to clinical practice. Studies receiving a B rating demonstrate consistent evidence and provide valuable insights into various aspects of fluconazole prophylaxis, such as Candida colonization patterns and the comparative effectiveness of different dosages. While further research may be needed to address specific uncertainties or gaps identified in these studies, their findings offer important recommendations for improving neonatal care practices. On the other hand, studies rated A provide strong, compelling evidence with definitive recommendations for practice change. These studies employ rigorous methodology, comprehensive data analysis, and a clear focus on addressing key clinical questions related to fluconazole prophylaxis. Their findings support the adoption of specific interventions or protocols, such as tailored management strategies based on colonization patterns, optimal dosing regimens, and the duration of prophylactic therapy. Overall, the quality ratings underscore the reliability of the evidence presented in each study and serve as valuable guidance for clinicians and researchers in optimizing fluconazole prophylaxis protocols for neonatal care.			

Figure 1

Fishbone Diagram

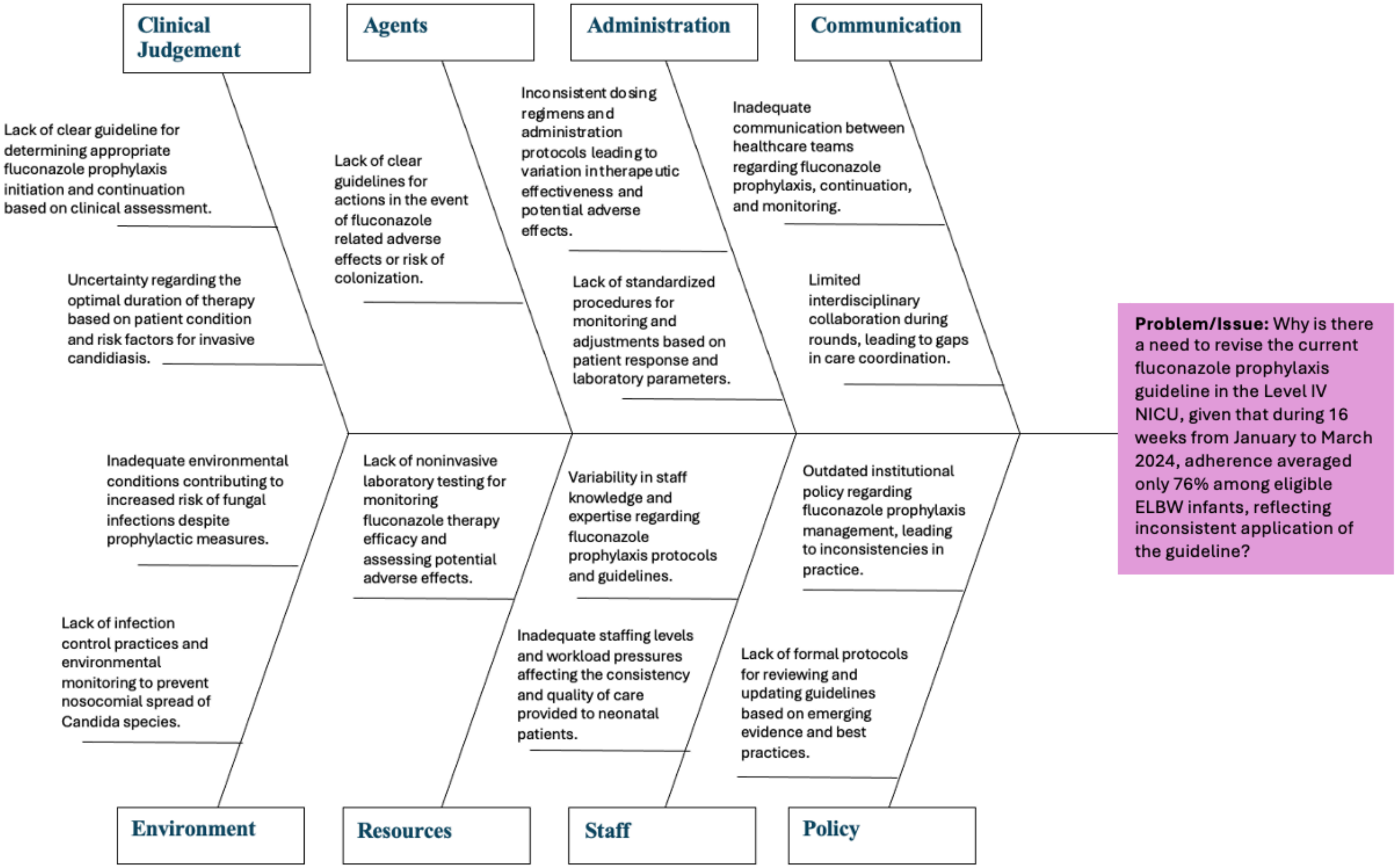
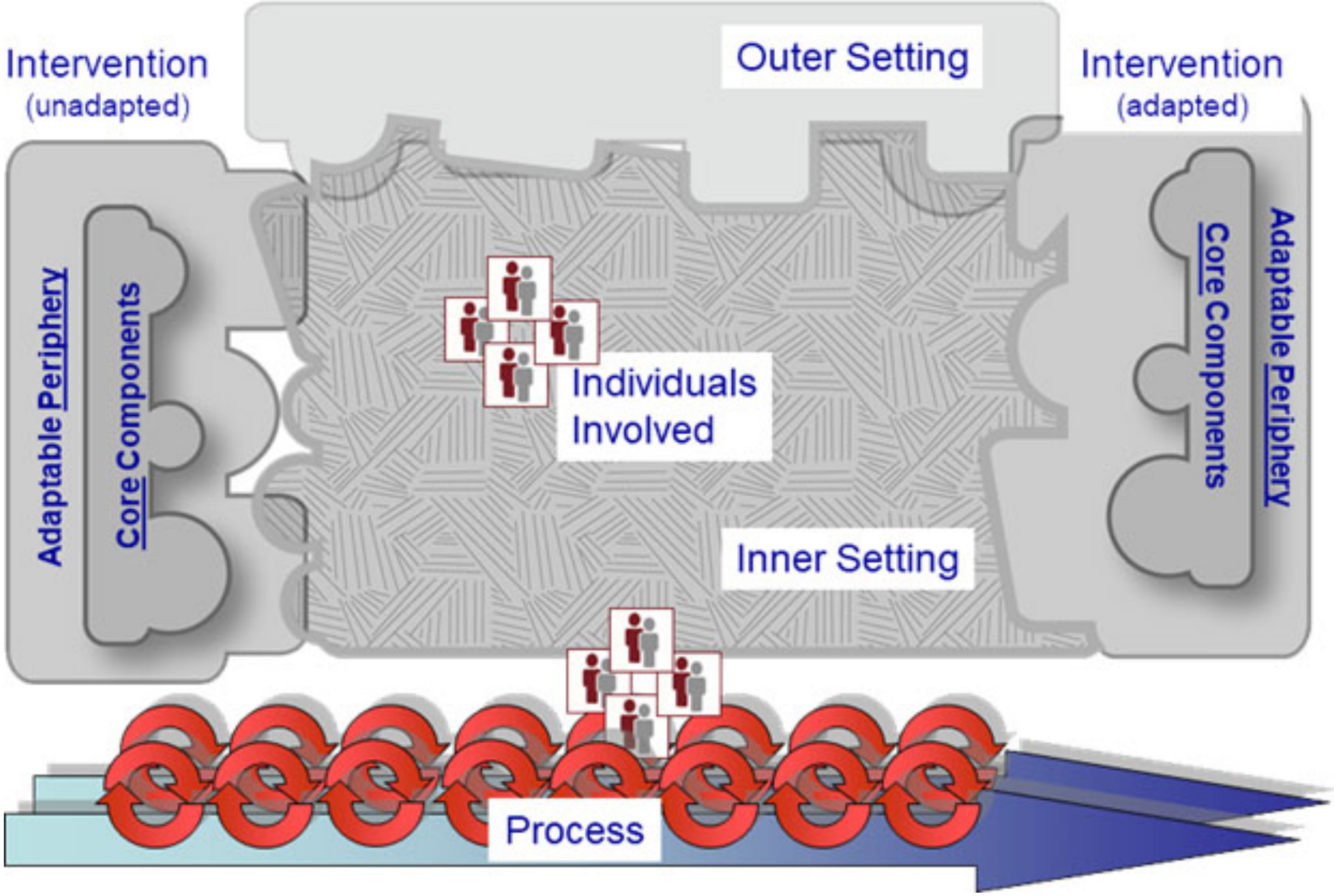


Figure 2

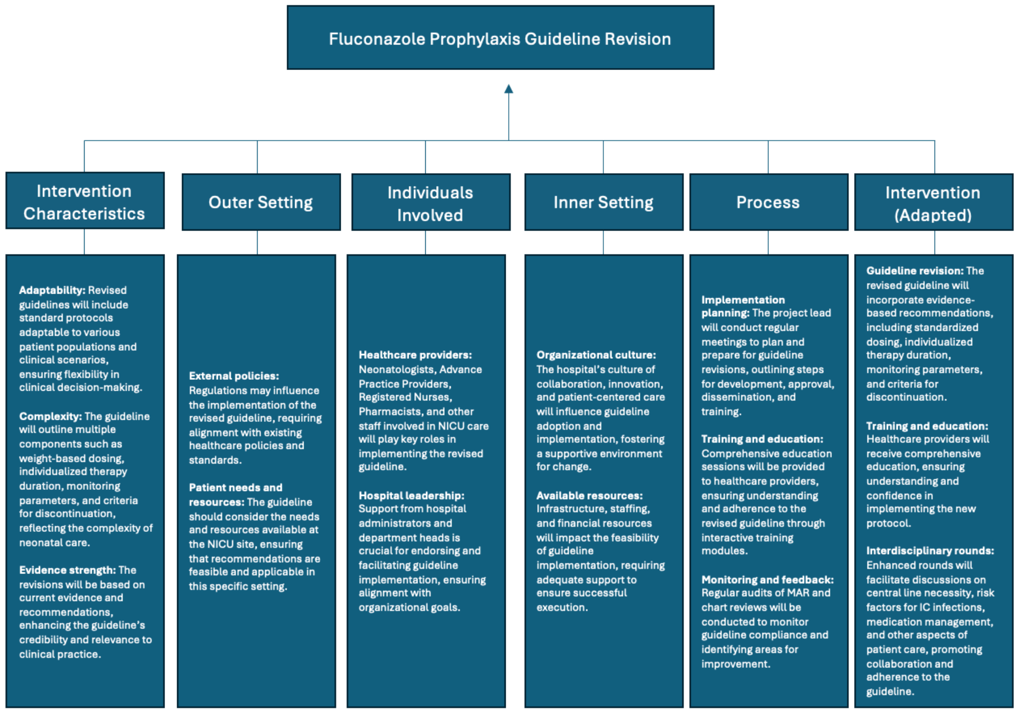
Framework Diagram: Consolidated Framework for Implementation Research (CFIR)



Note: Visual representation of the Consolidated Framework for Implementation Research. From CFIR Research Team Center for Clinical Management Research (2024).

Figure 3

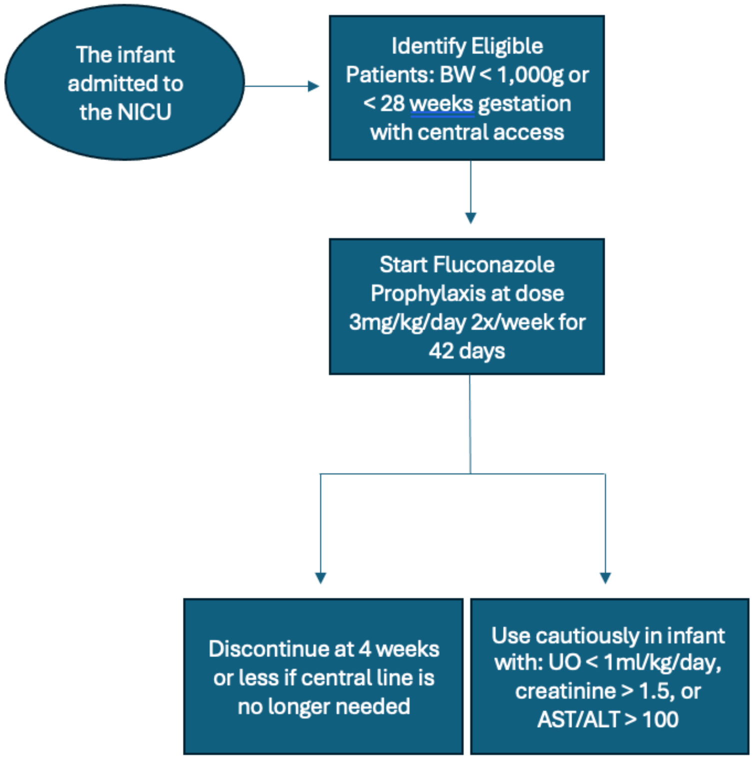
Adaptation of Theoretical Framework



Note: Adaptation from Damschroder, L. J., Reardon, C. M., Opra Widerquist, M. A., & Lowery, J. (2022). The updated consolidated framework for implementation research is based on user feedback. *Implementation Science.* DOI: 10.1186/s13012-022-01245-0

Figure 4

Current Process Flow Map



*Note: The c*urrent state flow map is based on a discussion with Victoria Beltran about the current unit protocol.

Figure 5

Desired Process Flow Map

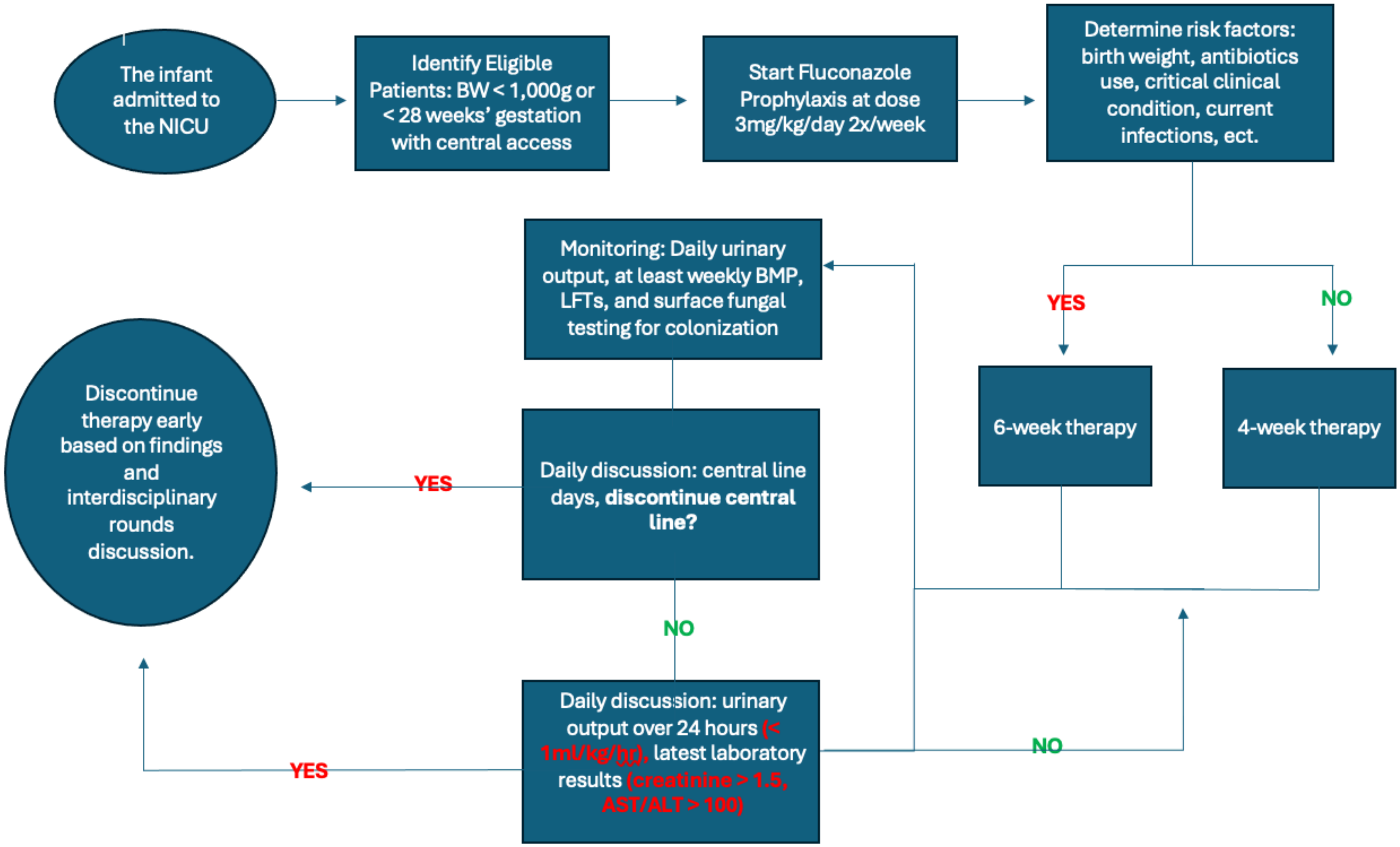


Figure 6
Timeline GANTT Chart

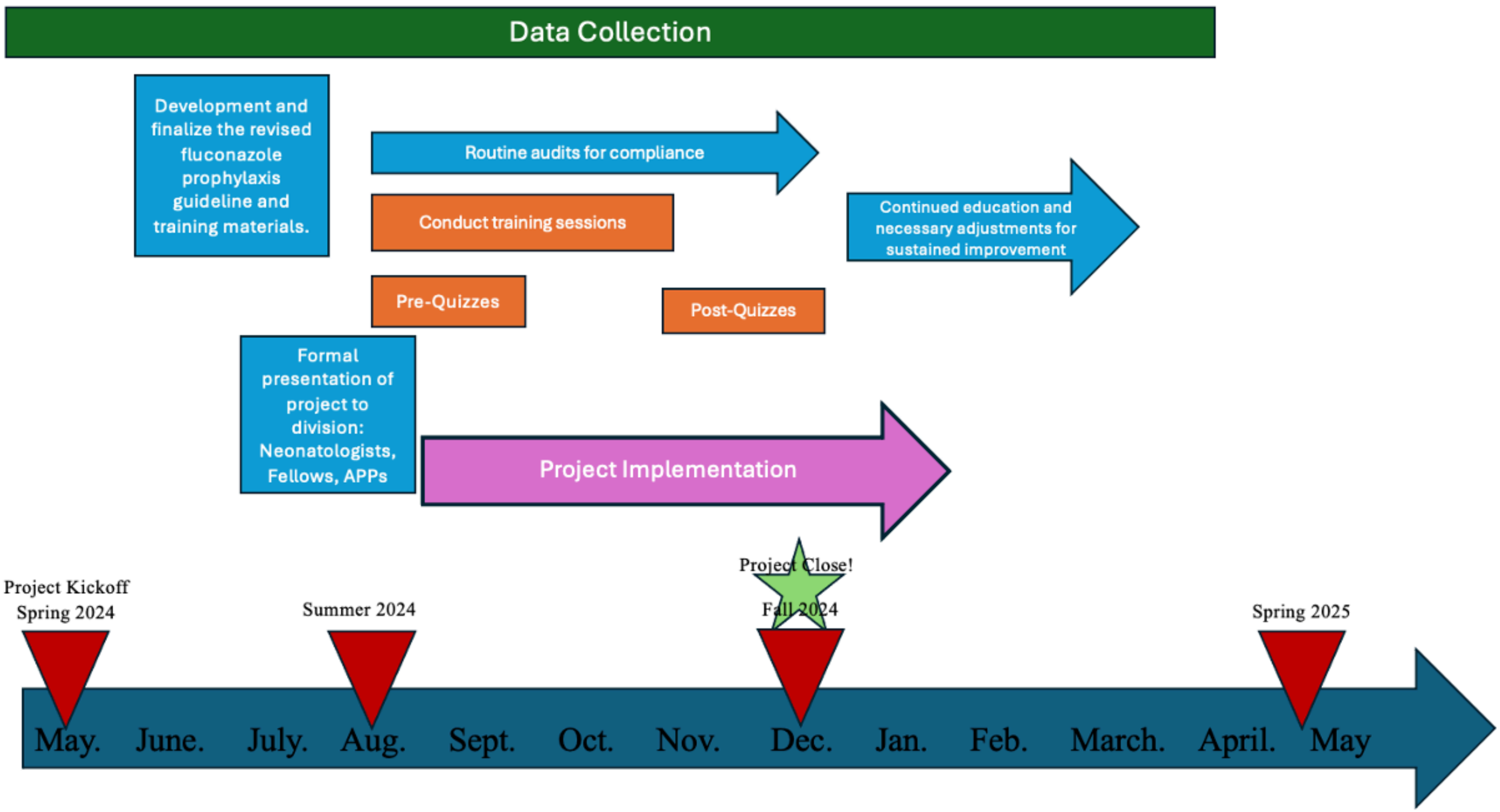


Figure 7

Run Chart of Fluconazole Prophylaxis Guideline Compliance

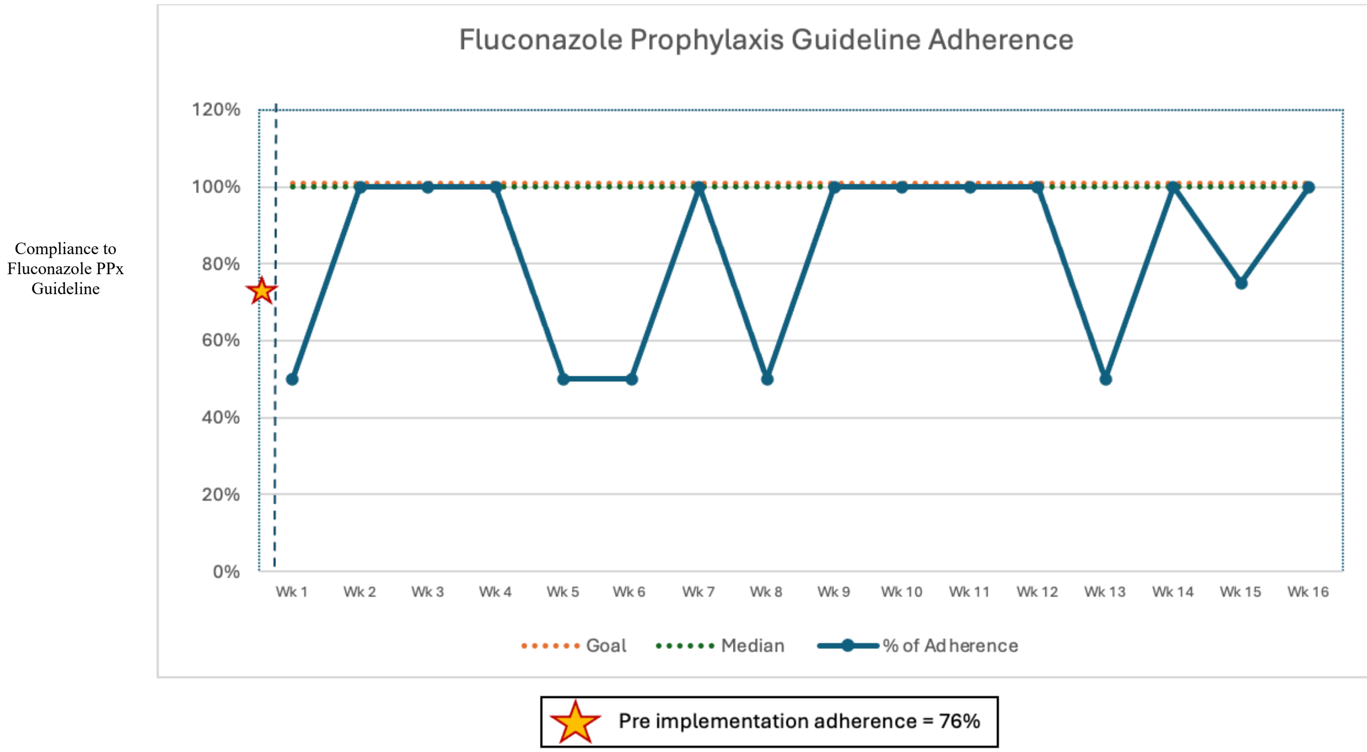
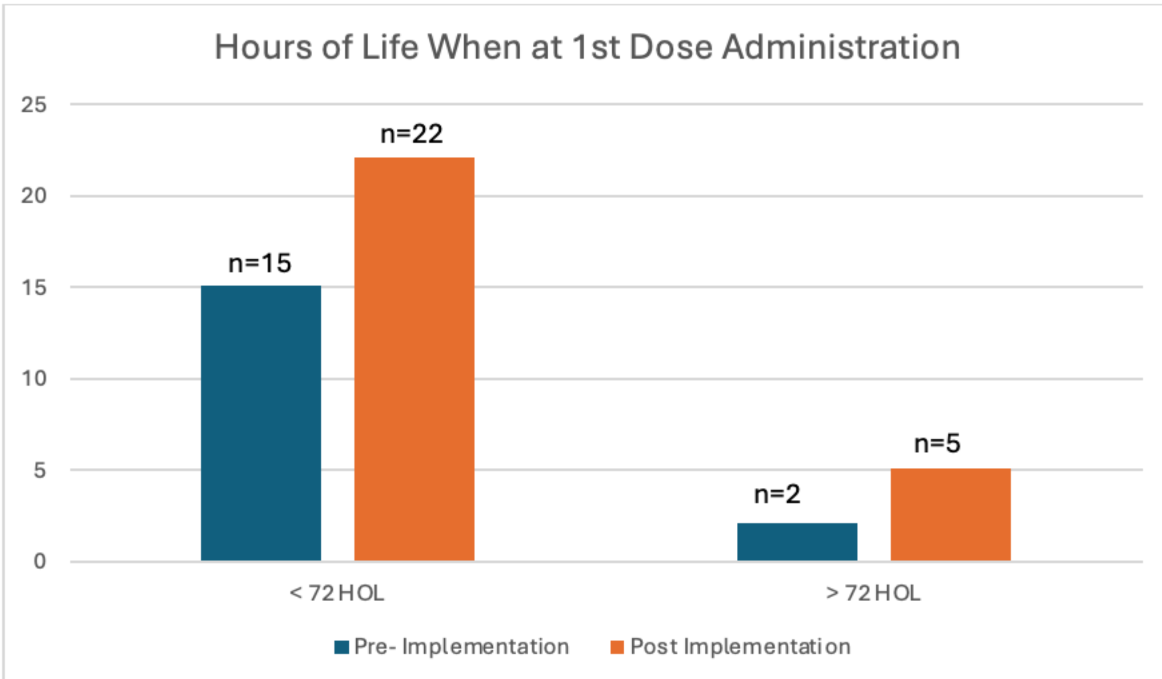


Figure 8

Bar Graph of Hour of Life at 1st Dose Administration of Fluconazole

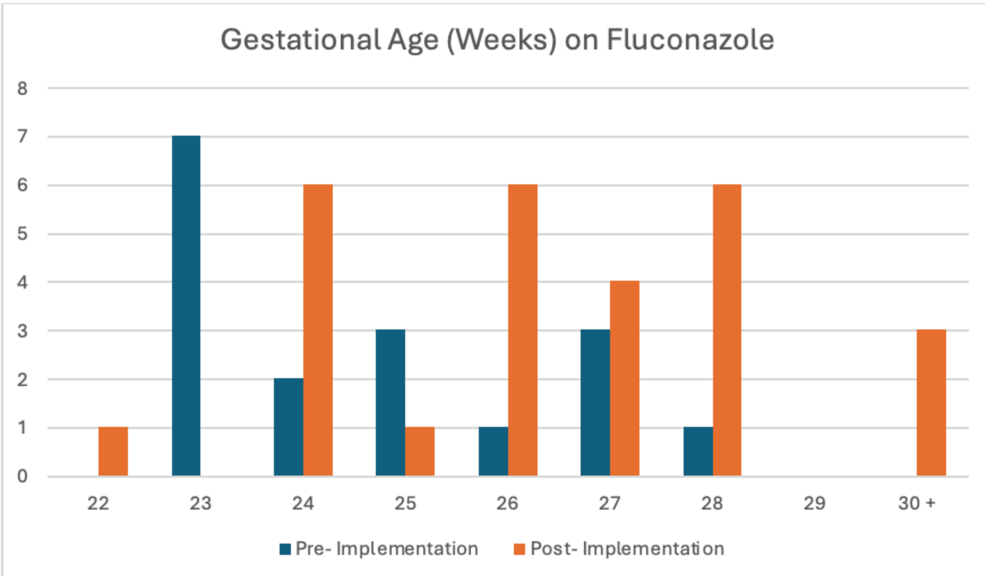
Number of Patients



HOL at 1st Dose

Figure 9

Bar Graphs of Gestational Age and Birth Weight for Patients on Fluconazole



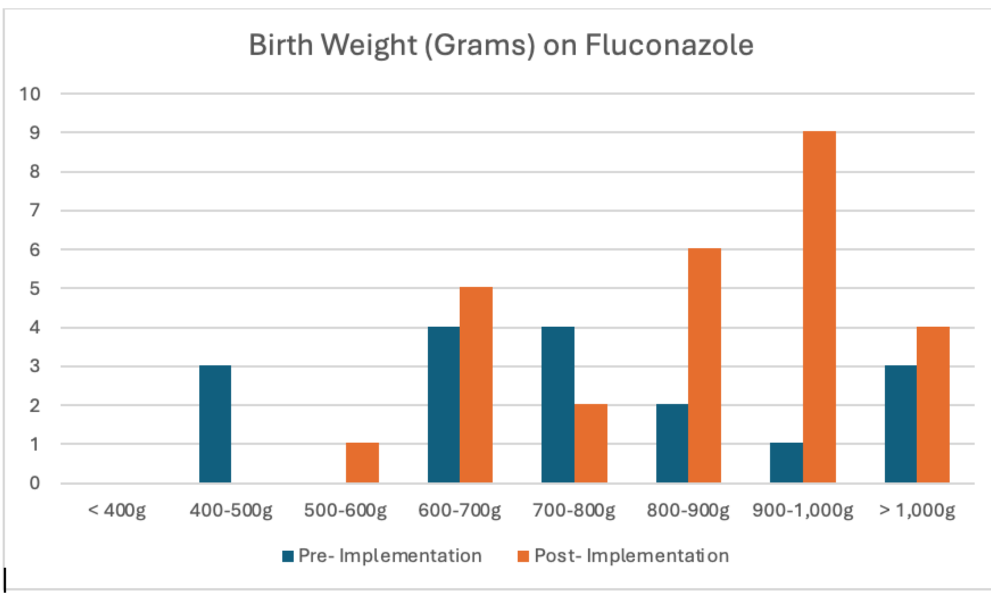
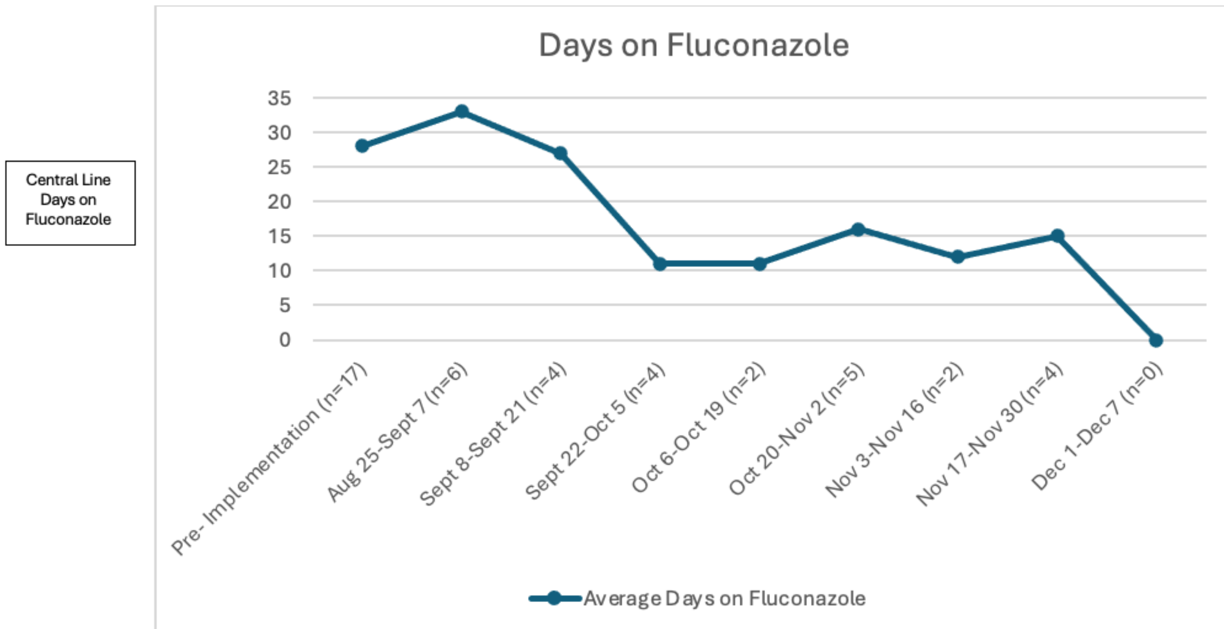


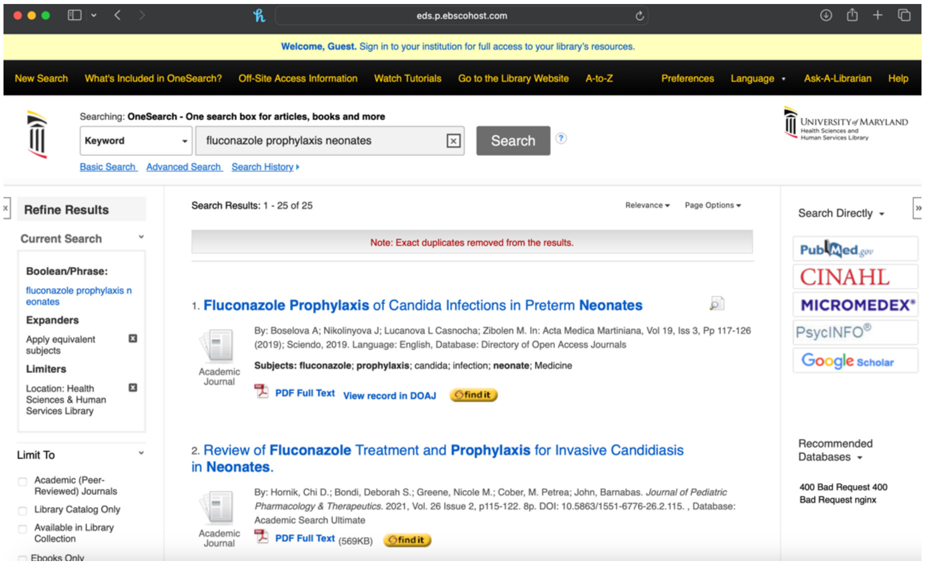
Figure 10

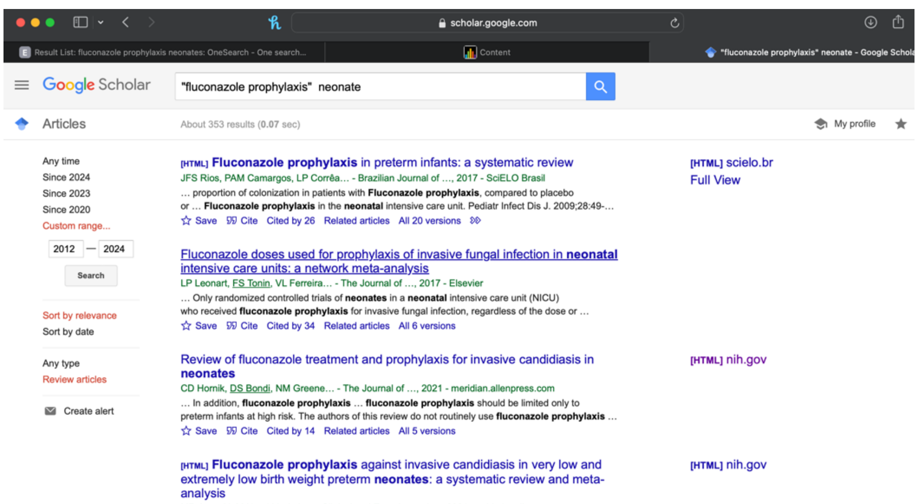
Line Graph of Average Central Line Days on Fluconazole Prophylaxis



Appendix A

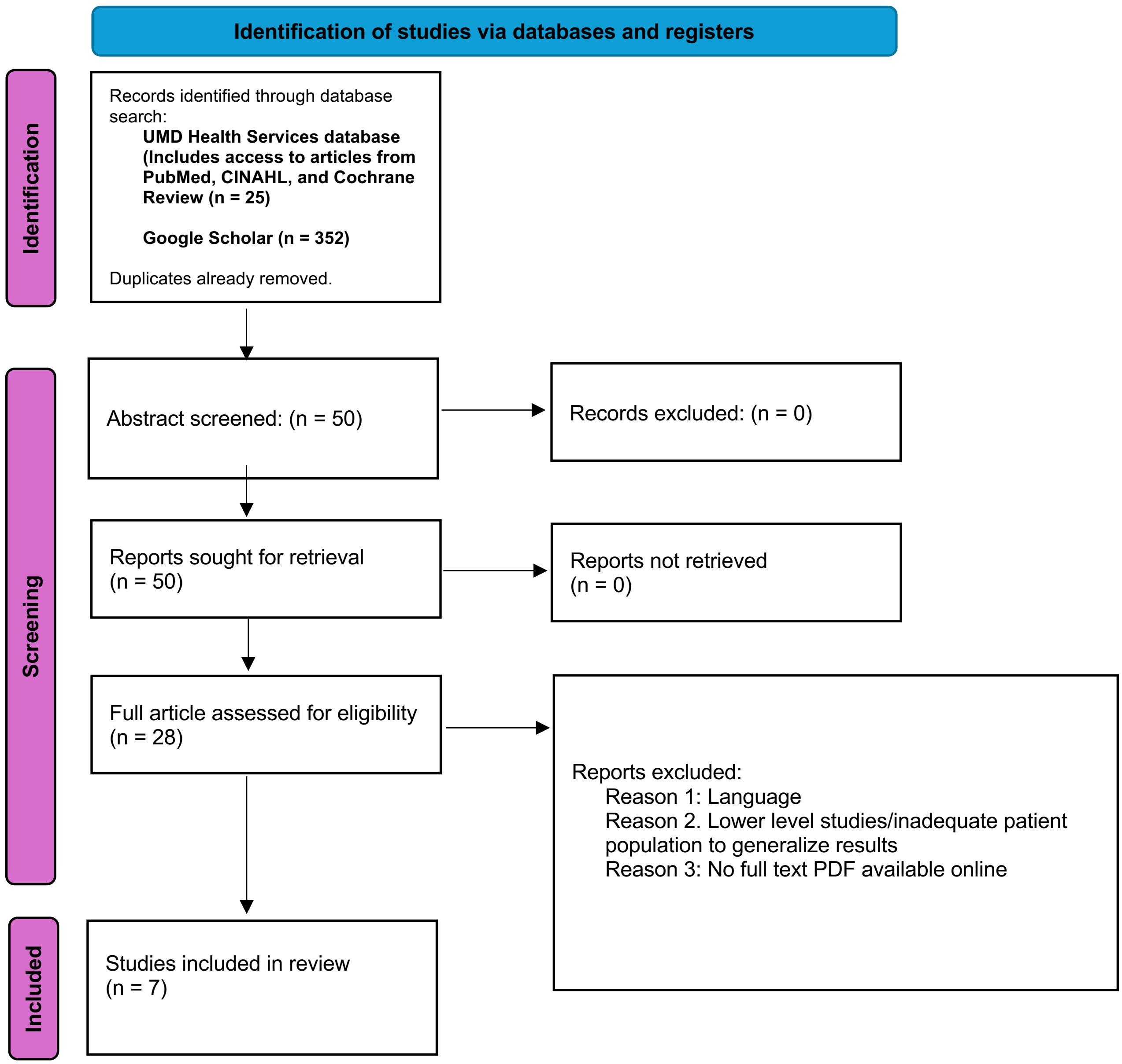
Citation Manager





Appendix B

PRISMA Diagram



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71 DOI: 10.1136/bmj.n71 http://www.prisma-statement.org/

Appendix C

Safety Attitudes Questionnaire

Scale: Definition	Example items
Teamwork climate: perceived quality of collaboration between personnel	–Disagreements are appropriately resolved (i.e., not *who* is right, but *what* is best for the patient) –Our doctors and nurses work together as a well coordinated team
Job satisfaction: positivity about the work experience	–I like my job –This ICU is a good place to work
Perceptions of management*:* approval of managerial action	–Management supports my daily efforts in this ICU –Management is doing a good job
Safety climate: perceptions of a strong and proactive organizational commitment to safety	–I would feel perfectly safe being treated here –ICU personnel frequently disregard rules or guidelines
Working conditions: perceived quality of the work environment and logistical support (staffing, equipment etc.)	–Our levels of staffing are sufficient to handle the number of patients –The equipment in this ICU is adequate
Stress recognition: acknowledgement of how performance is influenced by stressors	–I am less effective at work when fatigued –When my workload becomes excessive, my performance is impaired

From: Sexton, J. B., Helmreich, R. L., Neilands, T. B., Rowan, K., Vella, K., Boyden, J., Roberts, P. R., & Thomas, E. J. (2006). The Safety Attitudes Questionnaire: psychometric properties, benchmarking data, and emerging research. *BMC health services research*, *6*, 44. DOI: 10.1186/1472-6963-6-44

Appendix D

REDCap Measurement Tool: Chart Audit Tool

Fluconazole Prophylaxis Guideline
Page 1

Fluconazole Prophylaxis Audit Tool

Record ID	__________________________________
Date of Collection	__________________________________
MRN	__________________________________
Date of Birth	__________________________________
Gestational Age (At birth)	◯ 22-23 weeks ◯ 23-24 weeks ◯ 24-25 weeks ◯ 25-26 weeks ◯ 26-27 weeks ◯ 27-28 weeks ◯ > 28 weeks
Birth weight in grams	◯ 300-500g ◯ 500-700g ◯ 700-900g ◯ 900-1,100g ◯ 1,100-1,300g ◯ 1,300-1,500g ◯ > 1,500g
Days of life with a central line	__________________________________
Indication to initiate fluconazole prophylaxis per guideline	◯ Yes ◯ No
Days of life on fluconazole prophylaxis	__________________________________
Discussion during morning interdisciplinary rounds	◯ Yes ◯ No
Any related abnormal laboratory/assessment findings over the last 24 hours?	☐ Urinary output < 1ml/kg/day ☐ Creatinine > 1.5 ☐ AST/ALT > 100 ☐ Positive cultures (specify in next question) ☐ Other (specify in next question) ☐ Laboratory testing/assessment WNL ☐ No laboratory testing was obtained
Specify organism for positive culture (if any) AND/OR other abnormal findings in the last 24 hours	____

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Page 2

Indication for central line	◯ Continue with the current central line ◯ Discontinue the central line and switch to a less invasive access ◯ Discontinue IV therapy, no longer indicated
Indication to discontinue fluconazole prophylaxis	◯ Yes ◯ No

Appendix E

REDCap Measurement Tool: Interdisciplinary Rounds Audit Tool

Fluconazole Prophylaxis Guideline
Page 1

Central Line Overview Audit Tool

Record ID	__________________
Date of Collection	__________________
MRN	__________________
Date of Birth	__________________
Central Line Days	__________________
Any related abnormal laboratory/assessment findings over the last 24 hours?	☐ Urinary output < 1ml/kg/day ☐ Creatinine > 1.5 ☐ AST/ALT > 100 ☐ Positive cultures (specify in the next question) ☐ Other (specify in next question) ☐ Laboratory testing/assessment WNL ☐ No laboratory testing was obtained
Specify organism for positive culture (if any) AND/OR other abnormal findings in the last 24 hours.	__________________
Indication for central line	○ Continue with the current central line ○ Discontinue the central line and switch to a less invasive access ○ Discontinue IV therapy, no longer indicated
List of medication(s)	__________________
Indication to discontinue fluconazole	○ Yes ○ No

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Appendix F

REDCap Measurement Tool: Staff Survey

Page 1

Pre- and Post-implementation Staff Survey

Hi NICU team! Please take a moment to complete the brief survey below for me to collect valuable insight for my DNP Quality Improvement initiative. All surveys remain anonymous.

Thank you for your time!

1) Are you completing this survey during the pre- or post-implementation?
- ◯ Pre-implementation phase
- ◯ Post-implementation phase

2) The discipline most closely related with my role in the hospital is:
- ◯ Physician
- ◯ Nurse Practitioner
- ◯ Physician Associate
- ◯ Other

3) If "Other" to the previous question, please specify your appropriate discipline.

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4) Which pharmacological agent is typically administered as prophylaxis against candida infection in neonates?
- ◯ Ampicillin and Gentamicin
- ◯ Fluconazole
- ◯ Miconazole
- ◯ Amphotericin B
- ◯ All of the above
- ◯ None of the above

5) Choose one of the following dose and frequency that is typical for candida prophylactic treatment.
- ◯ 3mg/kg once daily
- ◯ 12mg/kg every 72 hours
- ◯ 3mg/kg every 72 hours
- ◯ 8mg/kg once daily

6) Assuming that the central line is not discontinued early, what is the typical course of prophylactic treatment?
- ◯ 1 week
- ◯ 2, weeks
- ◯ 3 weeks
- ◯ 4 weeks
- ◯ 5 weeks
- ◯ 6 weeks

7) What are risk factors for candida infections in neonates? SELECT ALL THAT APPLY
- ☐ Prematurity
- ☐ Immature immune system
- ☐ Maternal antibiotic use
- ☐ GI dysmotility
- ☐ Broad-spectrum antibiotics
- ☐ CVC access

8) What is a potential concern or side effect for candida prophylaxis in neonates?
- ◯ Increased risk for blood clots
- ◯ Allergic reaction
- ◯ Increased diuresis
- ◯ Hepatotoxicity

9) Do you prescribe candida prophylaxis?
- ◯ Yes
- ◯ No

10) I have encountered barriers and challenges while initiating or maintaining candida prophylaxis (if applies to your discipline).
- ◯ Strongly disagree
- ◯ Disagree
- ◯ Neutral
- ◯ Agree
- ◯ Strongly agree

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11) I believe the candida prophylaxis guideline is effectively communicated to healthcare staff.
- ◯ Strongly disagree
- ◯ Disagree,
- ◯ Neutral
- ◯ Agree
- ◯ Strongly agree

12) I have observed an improvement in the management of infants at risk for candida infections since the implementation of the revised prophylaxis guideline.
- ◯ Strongly disagree
- ◯ Disagree,
- ◯ Neutral
- ◯ Agree
- ◯ Strongly agree

13) I am satisfied with the adherence of healthcare staff to the candida prophylaxis guideline.
- ◯ Strongly disagree
- ◯ Disagree,
- ◯ Neutral
- ◯ Agree
- ◯ Strongly agree

14) What suggestions do you have for optimizing the implementation and effectiveness of this QI initiative?

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