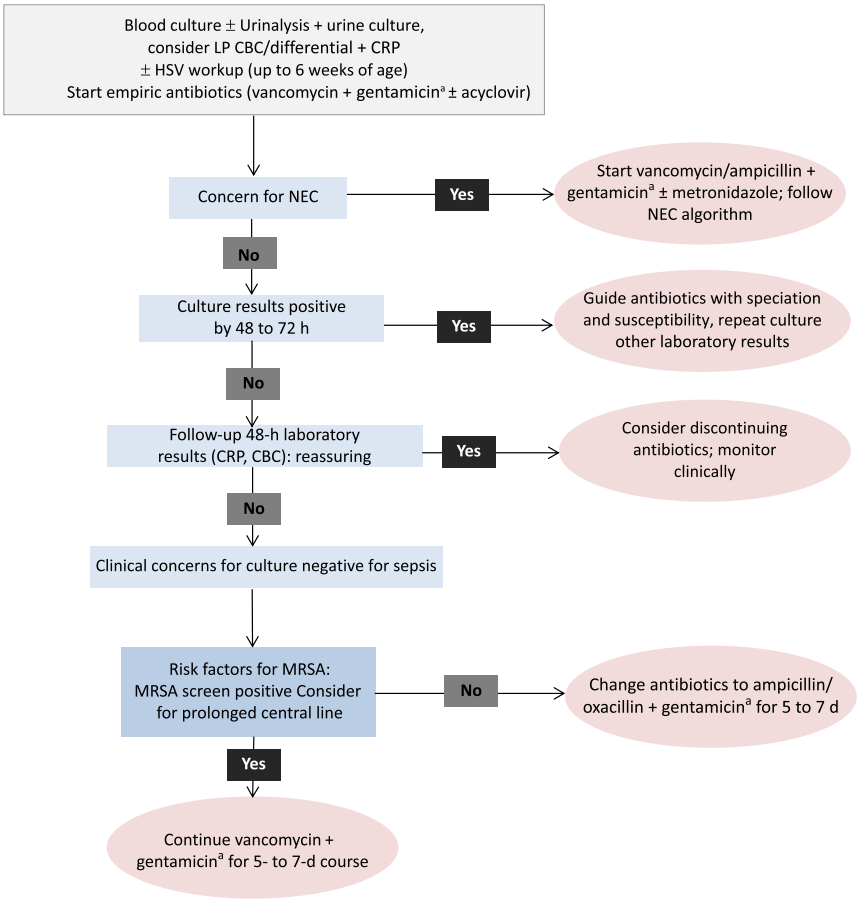
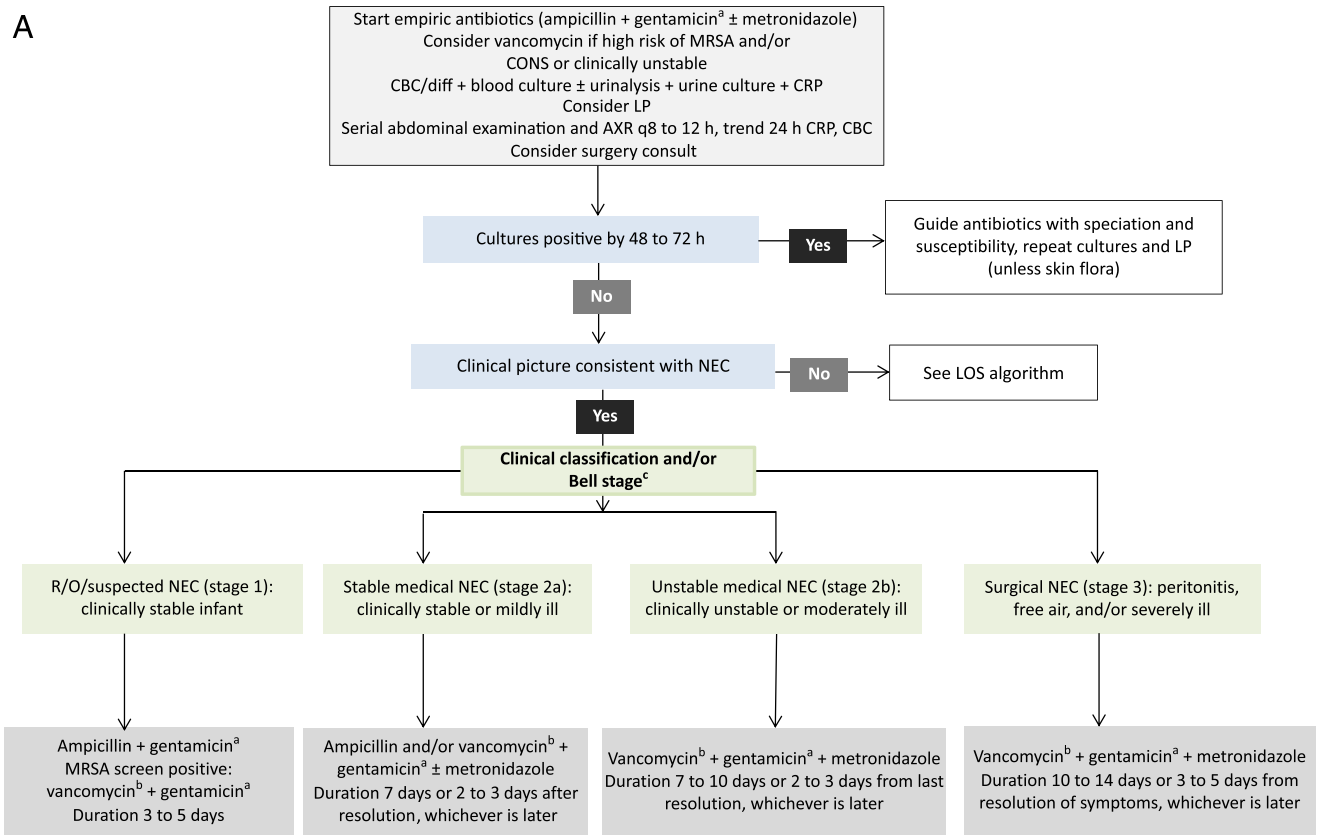
Supplemental Information



SUPPLEMENTAL FIGURE 7

LOS pathway (>3 days of life). Abnormal laboratory results include C-reactive protein (CRP) >1.0 mg/dL or increasing trend after 24 hours (white blood cell count, immature/total ratio, and/or procalcitonin can aid but are unreliable markers by themselves). For blood culture positive, repeat culture to document clearance. Lumbar puncture (LP) is usually indicated unless coagulase negative *Staphylococci*. Adjust duration and choice of antibiotics (narrow spectrum) on the basis of identification and susceptibilities. Use cefotaxime/ceftazidime for Gram-negative bacilli until susceptibilities are available. Consider Herpes Simplex Virus (HSV) evaluation (cerebral spinal, blood, and surface swab polymerase chain reaction tests) and empiric intravenous acyclovir within 6 weeks of life on the basis of risk factors and clinical picture (rash, liver failure, coagulopathy). Consider fluconazole prophylaxis for infants weighing <100 g with surgical NEC/peritonitis. For persistent hyperglycemia and thrombocytopenia, especially after broad-spectrum antibiotic exposure, consider amphotericin B deoxycholate 1 mg/kg per dose intravenous every 24 hours (assuming no renal dysfunction). If perinatal pneumonia is suspected, tracheal aspirate at the time of intubation or within 24 hours can be considered. Delayed tracheal aspirate cultures are not helpful. Consider empirical erythromycin or azithromycin course for chlamydial pneumonia. The following detail duration of treatment, with durations in parentheses noting poor quality or lack of evidence: culture-negative result for clinical sepsis: 5 to 7 days; bacteremia without focus: 7 to 14 days (enterococcus or coagulase negative *Staphylococci* 7 days, Gram-negative 10 days, *S aureus* 14 days); uncomplicated Group B Streptococcus bacteremia (10–14 days) and/or meningitis (14–21 days): switch to penicillin G; Gram-negative meningitis: 21 days or 14 days after clearance, whichever is longer; endocarditis, osteomyelitis: consult infectious diseases. [a] Consider replacing gentamicin with cefotaxime/ceftazidime if there is a concern for nephrotoxicity and/or term corrected age. For meningitis coverage, third-generation cephalosporins are preferred for better central nervous system penetration.



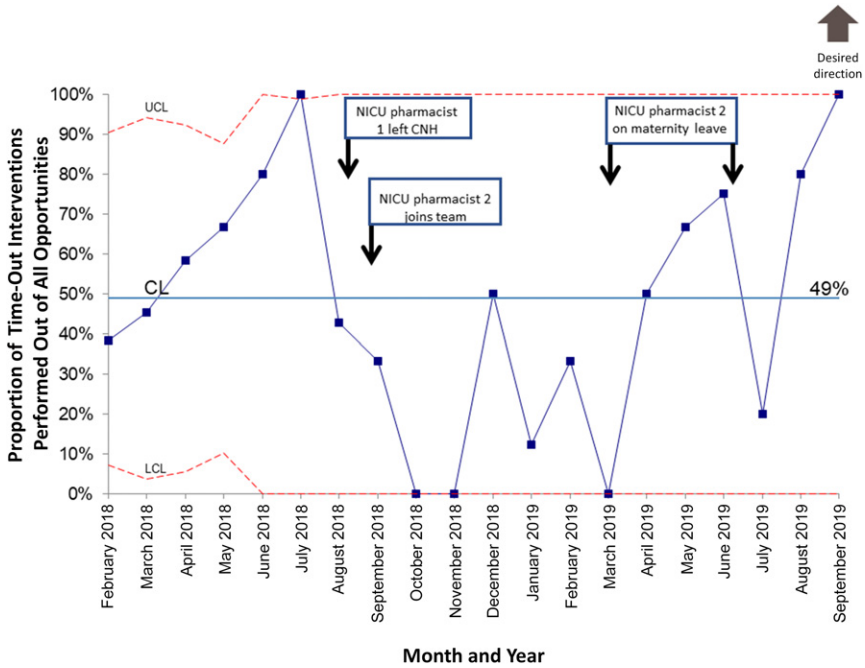
SUPPLEMENTAL FIGURE 8

A, NEC pathway. B, Modified Bell staging criteria for NEC. The blood culture should be at least 1 mL of peripheral blood sample collected with aseptic technique. For positive blood culture, repeat culture to document clearance. Lumbar puncture is usually indicated unless coagulase negative *Staphylococci* (CONS). Adjust duration and choice of antibiotics (narrow spectrum) on the basis of identification and susceptibilities. Use cefotaxime/ceftazidime for Gram negative bacilli until susceptibilities available. Spontaneous intestinal perforation may be adequately treated with 7 days (±2 days after drain removal and/or clinical resolution, whichever is later). Consider fluconazole prophylaxis for infants weighing <1000 g with surgical NEC and/or peritonitis. For persistent hyperglycemia and thrombocytopenia, especially after broad-spectrum antibiotic exposure, consider amphotericin B deoxycholate 1 mg/kg per dose intravenous every 24 hours (assuming no renal dysfunction). Rule out (R/O) NEC is defined as radiographs showing no pneumatosis, but signs of bowel wall thickening, with feeding intolerance and abdominal distention. Medical NEC that is stable is defined as pneumatosis on radiograph, +/− thrombocytopenia, and no bloody stools; the neonate is hemodynamically stable with symptoms that clear quickly (# modified Bell staging criteria for NEC). Medical NEC that is unstable is defined as pneumatosis, hypotension requiring pressors, respiratory deterioration, thrombocytopenia, and +/− bloody stools. Surgical NEC is defined as NEC with perforation, free air, bowel resection; the neonate is severely ill. [a] Consider replacing gentamicin with cefotaxime/ceftazidime if there is a concern for nephrotoxicity and/or term corrected age. For meningitis coverage, third-generation cephalosporins are preferred for better central nervous system penetration. [b] Consider starting with or switching to ampicillin/oxacillin if cultures produce negative results after 48 hours in neonates with an MRSA screen negative, low risk for CONS, and who are clinically stable. [c] Bell stage description is shown in panel B. AXR, abdominal radiograph; diff, differential; q8 to 12 hours, every 8 to 12 hours. Panel B is adapted from Lee JS, Polin RA. Treatment and prevention of necrotizing enterocolitis. Semin Neonataol. 2003;8(6):449–459.

B

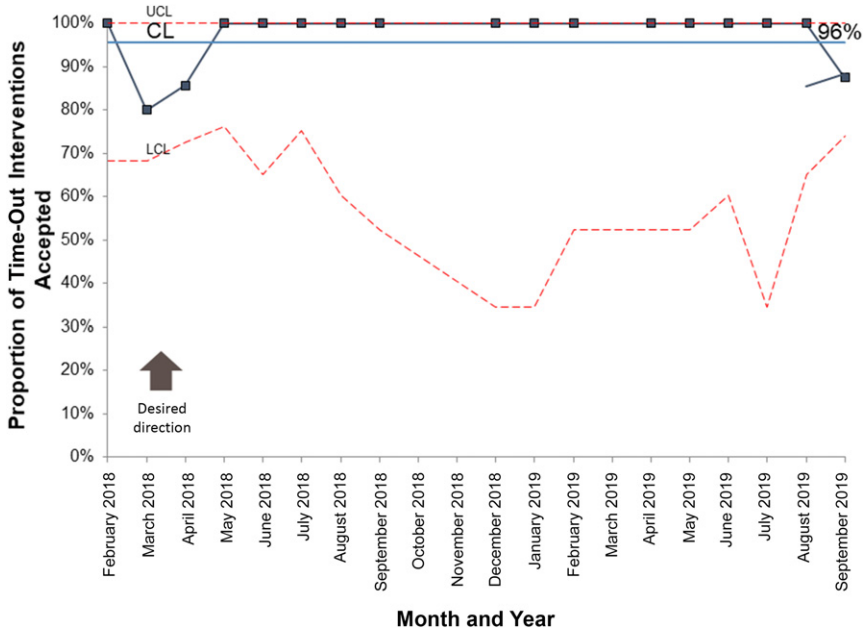
Stage	Classification	Systemic signs	Intestinal signs	Radiologic signs
IA	Suspected NEC	Temperature instability, apnea, bradycardia, lethargy	Increased pregavage residuals, mild abdominal distention, emesis, guaiac-positive stool	Normal or intestinal dilation, mild ileus
Stage	**Classification**	**Systemic signs**	**Intestinal signs**	**Radiologic signs**
IB	Suspected NEC	Same as above	Bright red blood from rectum	Same as above
IIA	Proven NEC (mildly ill)	Same as above	Same as above, plus absent bowel sounds, with or without abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis
IIB	Proven NEC (moderately ill)	Same as above, plus mild metabolic acidosis, mild thrombocytopenia	Same as above, plus absent bowel sounds, definite abdominal tenderness, with or without abdominal cellulitis or right lower quadrant mass	Same as IIA, plus portal venous gas, with or without ascites
IIIA	Advanced NEC (severely ill, bowel intact)	Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, disseminated intravascular coagulation, and neutropenia	Same as above, plus signs of generalized peritonitis, marked tenderness, and distention of abdomen	Same as IIB, plus definite ascites
IIIB	Advanced NEC (severely ill, bowel perforated)	Same as IIIA	Same as IIIA	Same as IIB, plus pneumoperitoneum

SUPPLEMENTAL FIGURE 8
Continued.



SUPPLEMENTAL FIGURE 9

Pharmacist-initiated 48-hour time-out interventions for vancomycin: proportion of interventions performed on rounds of total vancomycin courses >48 hours. P-chart shows the proportion of pharmacist-initiated 48-hour time-out interventions for vancomycin documented out of total vancomycin courses >48 hours Monday through Friday. Only the first intervention documented per course was included. The chart is annotated with significant changes to NICU pharmacist personnel. CL, centerline; LCL, lower control limit; UCL, upper control limit.



SUPPLEMENTAL FIGURE 10

Proportion of time-out interventions accepted. Shown is the proportion of pharmacist-initiated 48-hour time-out interventions documented that were documented as followed by the primary team. CL, centerline; LCL, lower control limit; UCL, upper control limit.