DATE: July 2012

Pediatric Prehospital Protocols Grant
Children presenting with Non-Trauma Shock (hypovolemic, septic)
Evidence-Based Practice Summary

Evidence-Based Practice Summary prepared by Elizabeth Crabtree, MPH, Research Specialist and Quinn Franklin, MS, CCLS, Research Specialist

ASK THE QUESTION

Question 1: For the pediatric patient presenting with non-traumatic hypovolemic shock from dehydration in the prehospital setting, does rapid delivery of initial fluid bolus(es) improve quality of care (e.g., decreased intensive care unit [ICU] admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure)?

Question 2: For the pediatric patient presenting with non-traumatic septic shock in the prehospital setting, does rapid delivery of initial fluid bolus(es) improve quality of care (e.g. decreased ICU admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure)?

Question 3: For the pediatric patient presenting with profound non-traumatic septic or hypovolemic shock in the prehospital setting, does a fluid bolus via intraosseous (IO) needle (when peripheral access has failed) result in improved quality of care (e.g. decreased ICU admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure) relative to deferring intravenous (IV) placement at the receiving hospital?

Search Strategy

A comprehensive literature search was conducted to find relevant evidence to support the Prehospital Protocols – Non Traumatic Shock. This search was conducted in January 2012 and included the following databases and websites: Cochrane Collaboration Database, Agency for Healthcare Research and Quality (AHRQ), National Guideline Clearinghouse, Pubmed, Trip Database, American Academy of Pediatrics, Prehospital Emergency Care, Prehospital and Disaster Medicine, Annals of Emergency Medicine, The American Journal of Emergency Medicine, Academic Emergency Medicine, JEMS: A Journal of EMS, Pediatric Emergency Care, and the Canadian Journal of Emergency Medicine. ***Search terms included the following***: hypovolemic shock, hypovolemia, non-traumatic shock, septic shock, sepsis shock, pediatric, children, prehospital, out of hospital, and emergency care. ***Limits placed on the search terms*** were for literature published within the last 10 years, pediatric and adult patients, All Child 0-18 years, All Adult 19+ years, human patients and within the English language.

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Quality and Outcomes Center, Texas Children's Hospital

CRITICALLY ANALYZE THE EVIDENCE

Existing External Order Sets/Guidelines/Clinical Pathways

External Guideline/ Pathway/Order Set	Organization and Author	Last Update
Pediatric Advanced Life Support: 2010 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care	American Heart Association	2010
Pediatric Advanced Life Support Guidelines for Management of Pediatric and Neonatal Septic Shock	American College of Critical Care Medicine	2010

The two published clinical guidelines have been evaluated for this review using the AGREE criteria. AGREE includes evaluation of: Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence. Four reviewers appraised the guideline, and scored each component independently. Domain scores were calculated by summing up all the scores of the individual items in a domain, and standardizing the total as a percentage of the maximum possible score for a particular domain. After appraising the guidelines above using the AGREE instrument, the reviewers recommend using the guidelines with modifcations. The reviewers were: Elizabeth Crabtree, MPH; Quinn Franklin, MS, CCLS; Colleen Jones, MS, RN; and Janelle Smith, MSN, RN.

Question 1: For the pediatric patient presenting with non-traumatic hypovolemic shock from dehydration in the prehospital setting, does rapid delivery of initial fluid bolus(es) improve quality of care (e.g., decreased intensive care unit [ICU] admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure)?

Recommendation: Pediatric patients with non-traumatic hypovolemic shock from dehydration should receive rapid delivery of intravenous (or intraosseous) isotonic fluid in aliquots of 20 ml/kg.

Strength of recommendation: Strong
Grade criteria: Very low quality evidence

There were no studies found directly addressing the PICO question.

The Pediatric Advanced Life Support: 2010 American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care recommend administering a bolus of 20mL/kg of isotonic crystalloid, as the initial fluid treatment. In addition, AHA noted there to be no added benefit in using colloid during the early phase of resuscitation. Subsequently, the University of Texas Southwestern Medical Center at Dallas/BioTel EMS System's guideline for shock mirrors AHA's guideline and notes that 20mL/kg bolus should be administered for children with hypovolvemic shock and repeated once if systolic pressure not above 70 mmHg. Emergency Medical Services for Children Pediatric Protocols recommends administering 20mL/kg set to maximum flow rate, reassess after the 1st bolus and if signs of non-traumatic shock persist, the bolus may be repeated at the same does up to 2 times for a maximum total of 60 mL/kg.

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References:
Pediatric Advanced Life Support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care 2010
University of Texas Southwestern Medical Center at Dallas/BioTel EMS System
Emergency Medical Services for Children Partnership for Children/National Association of EMS Physicians Model Pediatric Protocols 2003 Revision 2004

Question 2: For the pediatric patient presenting with septic shock in the prehospital setting, does rapid delivery of initial fluid bolus(es) improve quality of care (e.g. decreased ICU admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure)?

Recommendation: Pediatric patients with presumed septic shock should receive rapid delivery of intravenous (or intraosseous) isotonic fluid in aliquots of 20 ml/kg.

Strength of recommendation: Strong
Grade criteria: Very low quality evidence

There were no studies found directly addressing the PICO question. One cohort study found that less than half of adult patients with severe sepsis treated in the prehospital setting received out-of-hospital fluids and approached but did not attain a statistically significant increase in the likelihood of achieving the goal mean arterial pressure during early goal directed therapy. (Seymour 2010).

The American College of Critical Care Medicine – Pediatric Advanced Life Support Guidelines for Management of Pediatric and Neonatal Septic Shock (2010) and Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Shock (2009) recommend pushing boluses of 20mL/kg isotonic saline or colloid up to and over 60 mL/kg until perfusion improves or unless rales or hepatomegaly develop. In adults, the Surviving Sepsis Campaign (2008) noted that as soon as hypoperfusion is recognized initial resuscitation should begin. Fluid challenges of 1000 ml of crystalloids or 300-500 ml of colloids over 30 minutes. Additionally, the University of Texas Southwestern Medical Center at Dallas/BioTel EMS System's guideline for shock states that 20mL/kg bolus should be administered for children in shock and repeated once if systolic pressure not above 70 mmHg. Similarly, the Houston Fire Department and the Emergency Medical Services for Children Pediatric Protocols recommends 20mL/kg normal saline bolus for non-traumatic shock.

Subsequently, four studies investigated the implementation of a pediatric septic shock protocol. Two of the three studies were conducted in large, freestanding pediatric Emergency Departments and noted that the protocol improved recognition and reductions in time to delivery of rapid, aggressive fluid administration (Cruz 2011, Larsen 2011). Shapiro et al. (2006) reported an association between implementation of a protocol with changes in therapies including intravenous fluid delivery. Han et al (2003) evaluated the use of early septic shock reversal by community physicians and found that aggressive resuscitation can save the lives of children. Shock reversal was found in 24/91 (26%) of patients which was associated with 96% survival and a > 9-fold increased odds of survival (9.49[1.07-83.89]).

Lastly, a retrospective chart review of 90 pediatric patients treated for septic shock in the pediatric intensive care unit found that early fluid resuscitation was associated with a 3-fold reduction in the odds of death (OR: 0.33; 95% CI: 0.13- 0.85) when you control for the risk of mortality (Oliveira 2008).

Additionally, the Pediatric Advanced Life Support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care note that it is reasonable to use isotonic crystalloid solution as the initial fluid for the treatment of septic shock since there appears to be no clinically important difference in survival of children who are treated using a colloid compared with a crystalloid.

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References:

American College of Critical Care Medicine – Pediatric Advanced Life Support Guidelines for Management of Pediatric and Neonatal Septic Shock 2010

Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock: 2007 Update from the American College of Critical Care Medicine

Cruz, A. T., Perry, A. M., Williams, E. A., Graf, J. M., Wuestner, E. R., & Patel, B. (2011). Implementation of goal-directed therapy for children with suspected sepsis in the emergency department. *Pediatrics, 127*(3), e758-e766.

Han, Y. Y., Carcillo, J. A., Dragotta, M. A., Bills, D. M., Watson, R. S., Westerman, M. E., et al. (2003). Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome. *Pediatrics, 112*(4), 793-799.

Houston Fire Department

Larsen, G. Y., Mecham, N., & Greenberg, R. (2011). An emergency department septic shock protocol and care guideline for children initiated at triage. *Pediatrics, 127*(6), e1585-e1592.

Oliveira, C. F., Noguiera de Sa, F. R., Oliveira, D. S. F., Gottschald, A. F. C., Moura, J. D. G., Shibata, A. R. O., et.al. (2008). Time- and fluid-sensitive resuscitation for hemodynamic support of children in septic shock: Barriers to the implementation of the American College of Critical Care Medicine/Pediatric Advanced Life Support Guidelines in a pediatric intensive care unit in a developing world. *Pediatric Emergency Care, 24*(12), 810-815.

Pediatric Advanced Life Support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care 2010

Seymour, C. W., Cooke, C. R., Mikkelsen, M. E., Hylton, J., Rea, T. D., Goss, C. H., et al. (2010). Out-of-hospital fluid in severe sepsis: Effect on early resuscitation in the emergency department. *Prehospital Emergency Care, 14*(2), 145-152.

Shapiro, N., Howell, M., Talmor, D., Lahey, D., Ngo, L., Buras, J., et al. (2006). Implementation and outcomes of the Multiple Urgent Sepsis Therapies (MUST) protocol. *Critical Care Medicine, 34*(4), 1025-1032.

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2008

University of Texas Southwestern Medical Center at Dallas/BioTel EMS System

Recommendation(s): Very Low Quality Evidence
Number of Studies: Total # 1 ☐ Systematic review ☐ RCT ☒ Observational ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size (Seymour 2010) ☒ Lack of blinding (Seymour 2010) ☒ Lack of allocation concealment (Seymour 2010) ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) (Seymour 2010) ☐ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations (Seymour 2010) ☐ Different interventions ☒ Different outcomes measured (Seymour 2010) ☒ Comparisons not applicable to question/outcome (Seymour 2010)	**Dichotomous outcomes** ☒ Sample size lower than calculated optimal information size (Seymour 2010) ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes **Seymour)** ☐ 95% CI includes negligible effect and appreciable benefit or harm **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)

Sample	CI/RR

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Seymour (2010): Retrospective, cohort study of 52 adult patients transported by advanced life support (ALS) and received early-goal directed therapy (EGDT). The study evaluated whether or not the delivery of out-of-hospital fluid in patients with severe sepsis is associated with reduced time to achievement of goal-oriented resuscitation in the emergency department (ED).	**Seymour (2010):** • Patients receiving out-of-hospital fluid had lower out of hospital mean (± SD) systolic blood pressure (95 ± 40 mmHg versus 117 ± 29 mmHg; P=0.03) and a higher median (interquartile range) Sequential Organ Failure Assessment scores in the ED (7 [5-8] versus 4 [4-6], P=0.01) than patients who do not receive out of hospital fluids. • Patients receiving out of hospital fluids approached but did not attain a statistically significant increase in the likelihood of achieving mean arterial pressure (≥ 65 mmHg within 6 hours after ED triage (70% versus 44%; P= 0.09). TABLE 2. Association between the Delivery of Out-of-Hospital Fluid and Achievement of Goal Endpoints of Resuscitation within Six Hours of Emergency Department Triage* Variable / Out-of-Hospital Fluid / No Out-of-Hospital Fluid / Unadjusted Relative Risk (95% CI) MAP ≥65 mmHg: 17/24 (70%) / 12/26 (44%) / 1.53(0.9, 2.65) CVP ≥8 cmH_2O: 18/25 (72%) / 15/25 (60%) / 1.2(0.8, 1.8) $ScvO_2$ ≥70%: 13/24 (54%) / 9/25 (36%) / 1.5(0.8, 2.9) Data are presented as *n/N* (%). *Data not available: MAP, 2 subjects, CVP, 2 subjects, $ScvO_2$, 3 subjects. CI = confidence interval; CVP = central venous pressure; MAP = mean arterial pressure; $ScvO_2$ = central venous oxygen saturation.

Reference:

Seymour, C. W., Cooke, C. R., Mikkelsen, M. E., Hylton, J., Rea, T. D., Goss, C. H., et al. (2010). Out-of-hospital fluid in severe sepsis: Effect on early resuscitation in the emergency department. *Prehospital Emergency Care, 14*(2), 145-152.

Question 3: For the pediatric patient presenting with profound non-traumatic septic or hypovolemic shock in the prehospital setting, does a fluid bolus via intraosseous (IO) needle (when peripheral access has failed) result in improved quality of care (e.g. decreased ICU admission rate, decreased hospital LOS, improved mortality, decreased end-organ failure) relative to deferring intravenous (IV) placement at the receiving hospital?

Recommendation: Fluid boluses via the IO route are recommended if administration via the IV route cannot be initiated in a timely manner.

Strength of recommendation: Strong

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Grade criteria: Very low quality evidence

There were no studies found directly addressing the PICO question. One observational study and one single-blinded randomized trial, evaluated the insertion times and success rates of various IO needles (Findlay 2006, Hartholt 2010). The studies concluded that IO devices provide a safe, simple, and fast method for gaining access to the circulation in emergency situations. An observational study of pediatric ED patients found that IO success rates were high despite infrequent use (Nijssen-Jordan 2000). Only one of the studies included pediatric patients in the pre-hospital setting (Hartholt 2010). Three observational studies looked specifically at the use of EZ-IO. They found that EZ-IO requires minimal training, is easy to use, is fast, and has a high success rate even on initial insertion (Levitan 2009, Schalk 2011, Sunde 2010). Two of the studies included pediatric patients (Schalk 2011, Sunde 2010).

While no literature was found evaluating clinical outcomes for pediatric patients with an IO placed in the pre-hospital setting in the last 10 years, a retrospective chart review of prehospital IV placement in pediatric patients published in 1992 found a 57% success rate for IV placement in patients less than 6 years of age, and a 74% success rate in children greater or equal to 6 years (Lillis 1992). Both the American College of Critical Care Medicine – Pediatric Advanced Life Support Guidelines for Management of Pediatric and Neonatal Septic Shock (2010), and the EMSC Partnership for Children/National Association of EMS Physicians Model Pediatric Protocols (2003) recommend obtaining IO access, if IV access is not feasible. However, they caution against delaying transport to obtain vascular access. In addition, the University of Texas Southwestern Medical Center at Dallas/BioTel EMS System's guideline for shock advocates using IO infusion early if the child is unconscious.

Recommendation(s): Fluid boluses via the IO route are recommended if administration via the IV route cannot be initiated in a timely manner. **Strong Recommendation; Very Low Quality Evidence**
Number of Studies: Total # 5 ☐ Systematic review ☒ RCT (1) ☐ Cohort ☒ Observational (4) ☐ Case Reports Publication Bias Evident ☐ Yes ☒ No

Design *Limitations*	Summary of *Consistency*	*Indirectness* of Comparison	*Imprecision* of Results
☐ None ☒ Insufficient sample size (Findlay 2006, Hartholt 2010, Levitan 2009, Nijssen-Jordan 2000, Schalk 2011, Sunde 2010) ☐ Lack of blinding (Findlay 2006, Hartholt 2010, Levitan 2009, Nijssen-Jordan 2000, Schalk 2011, Sunde 2010) ☒ Lack of allocation concealment (Findlay 2006, Hartholt 2010, Levitan 2009, Nijssen-Jordan 2000, Schalk 2011, Sunde 2010) ☐ Large losses to F/U ☐ Incorrect analysis of ITT ☐ Stopped early for benefit ☐ Selective reporting of measured outcomes (e.g., no effect outcome)	☐ No inconsistencies ☐ Wide variation of treatment effect across studies ☒ Populations varied (e.g., sicker, older) ☒ Interventions varied (e.g., doses) ☐ Outcomes varied (e.g., diminishing effect over time)	☐ Head-to-head comparison in correct population ☐ Indirect comparisons (e.g., interventions to placebo but not each other) ☒ Different populations (Findlay 2006, Hartholt 2010, Levitan 2009, Schalk 2011, Sunde 2010) ☐ Different interventions ☒ Different outcomes measured (Findlay 2006, Hartholt 2010, Levitan 2009, Nijssen-Jordan 2000, Schalk 2011, Sunde 2010) ☒ Comparisons not applicable to question/outcome (Findlay 2006, Hartholt 2010, Levitan 2009, Nijssen-Jordan 2000, Schalk 2011, Sunde 2010)	**Dichotomous outcomes** ☒ Sample size lower than calculated optimal information size (Nijssen-Jordan 2000, Schalk 2011, Sunde 2010) ☒ Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes ☐ 95% CI includes negligible effect and appreciable benefit or harm **Continuous outcomes** ☐ 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm ☐ Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size

Sample	CI/RR
Findlay (2006): Observational study of 10 paramedics that participated in a training program on the use of the FAST1 System (Adult IO Intraosseous Infusion System), and then used the system in 3 simulated prehospital scenarios. The study evaluated the ease and use and compatibility of the training method using a visual analog scale. **Hartholt (2010):** Single-blinded randomized trial of 65 adults and 22 pediatric patients requiring acute administration of fluids or medication without successful insertion of IV catheter. Patients randomized to either Jamshidi 15G, BIG	**Findlay (2006):** • Mean duration of the procedure from opening package to initiation of fluid flow was 92 +/= 32 seconds • Mean displacement of 2 mm (0.08 in) and 1 mm (0.04 in) in the vertical and horizontal planes, respectively • Paramedics rated the system highly in all areas

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18G or FAST1 IO needle. **Levitan (2009):** Prospective study of EZ-IO with operators performing insertions on cadavers **Nijssen-Jordan (2000):** Retrospective chart review of a tertiary pediatric ED identifying number of ED resuscitations from 1989-1995 that involved IO access. **Schalk (2011):** Prospective study of all cases of prehospital IO access during a 24 month period; study included 69 adults and 5 infants and children **Sunde (2010):** Retrospective review of 70 prehospital patients with 78 insertion attempts using either manual needle, bone injection gun or EZ-IO	**Hartholt (2010):** • Median insertion times ranted from 38 seconds for the Jamshidi 15G to 49 seconds for the BIG 15G and 62 seconds for the FAST1 (p=0.004) • Devices did not differ with respect to success rates (adults overall 80% and children overall 86%) **Levitan (2009):** • 289 of 297 (97.3%) insertions were successful • Median insertion time was 6 seconds (range 3-25 seconds) • Mean ease of use rating was 4.8 (95% CI: 4.7-4.9) **Nijssen-Jordan (2000):** • IO access was successful in 36 of 42 (86%) patients • There were 68 attempts (or 1.6 attempts per child) • Median time to successful IO placement was 8 minutes • Two complications observed: 2 fractures in one 10-day-old neonate **Schalk (2011):** • IO access was successful at first attempt in all but 2 adults • Of 22 responsive patients, 18 reported pain upon fluid administration via the needle • Rescuers median subjective rating of handling device and ease of needle was 10 on an analogue scale of (0=entirely unsatisfied, 10=most satisfied) **Sunde (2010):** • Overall success rates were 50% using the manual needle, 55% using the bone injection gun and 96% using the EZ-IO (p<0.001) • Nearly 1/3 of all insertions were made on children younger than 2 years

References:

Findlay, J., Johnson, D., Macnab, A., MacDonald, D., Shellborn, R., & Susak, L. (2006). Paramedic evaluation of adult intraosseous infusion system. *Prehospital and Disaster Medicine, 21*(5), 329-335.

Hartholt, K. A., van Lieshout, E. M. M., Thies, W. C., Patka, P., & Schipper, I. B. (2010). Intraosseous devices: A randomized controlled trial comparing three intraosseous devices. *Prehospital Emergency Care, 14*(1), 6-13.

Levitan, R. M., Bortle, C. D., Snyder, T. A., Nitsch, D. A., Pisaturo, J. T., & Butler, K. H. (2009). Use of a battery-operated needle driver for intraosseous access by novice users: Skill acquisition with cadavers. *Annals of Emergency Medicine, 54*(5), 692-694.

Nijssen Jordan, C. (2000). Emergency department utilization and success rates for intraosseous infusion in pediatric resuscitations. *CJEM, 2*(1), 10-14.

Schalk, R., Schweigkofler, U., Lotz, G., Zacharowski, K., Latasch, L., & Byhahn, C. (2011). Efficacy of the EZ-IO(R) needle driver for out-of-hospital intraosseous access - a preliminary, observational, multicenter study. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 19*(1), 65.

Sunde, G., Heradstveit, B., Vikenes, B., & Heltne, J. (2010). Emergency intraosseous access in a helicopter emergency medical service: A retrospective study. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 18*(1), 52.

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