National Registry of
Emergency Medical Technicians®
THE NATION'S EMS CERTIFICATION™

2018 EMS Scope of Practice Systematic Reviews

Final Report – March 2017

Commissioned by:

National Association of State EMS Officials (NASEMSO) as defined by the National Highway Traffic Safety Administration (NHTSA)

Prepared by:

The National Registry of Emergency Medical Technicians

Ashish R. Panchal, MD, Ph.D
Research and Fellowship Director, National Registry of Emergency Medical Technicians
Associate Professor of Emergency Medicine
Director, Center for EMS
Department of Emergency Medicine
The Ohio State University Wexner Medical Center

Rebecca E. Cash, MPH, NRP
EMS Research Fellow

Remle P. Crowe, MS, NREMT
EMS Research Fellow

Amanda Broussard, B.ED, NRP, C.T.
Director of Exams and Operations

Jeremy D. Miller, M.Ed, NRP
Chief Certification Officer

Corinne Miesse, MLIS
Certification Specialist, Librarian

City of Columbus (OH), Division of Fire

Eric Cortez, MD, FAEMS
Associate Medical Director

The Ohio State University Wexner Medical Center, Department of Emergency Medicine

Ashley D. Larrimore, MD
Associate Professor of Emergency Medicine

William Krebs, DO
Associate Professor of Emergency Medicine

Table of Contents

Introduction

General Purpose

The National Highway Traffic Safety Administration (NHTSA), Office of Emergency Medical Services (OEMS) primary mission is "To reduce death and disability by providing leadership and coordination to the Emergency Medical Services (EMS) community in assessing, planning, developing, and promoting comprehensive, evidence-based emergency medical services and 9-1-1 systems." As part of this effort, NHTSA's OEMS has supported the revision of the National EMS Scope of Practice Model.

An important aspect of this directed work is the performance of a systematic review of the available literature along with collection of information leading to improvement in clinical outcomes in patients treated and transported by EMS. The key general questions which are to be addressed for specific psychomotor skills through this systematic review are as follows:

1. Is there evidence that the procedure or skill is beneficial to public health?
2. What is the clinical evidence that the new skill or technique as used by EMS practitioners will promote access to quality healthcare or improve patient outcomes?

With the recognition that numerous clinical procedures and practices may be important to be evaluated in this manner, NHTSA chose specific priority areas which need to be addressed for the 2018 EMS Scope of Practice Model.

The topics selected for evaluation included:

1. Hemorrhage control
2. Naloxone
3. Therapeutic hypothermia in cardiac arrest
4. CPAP/BiPAP
5. Pharmacological pain management

Utilizing the above framework provided by NHTSA, a systematic review was prepared for each of these priority areas starting with the development of PICO questions (Population, Intervention, Comparison, and Outcome) for the literature search. With the advice and direction of NHTSA, the following PICO questions were developed:

1. Hemorrhage control
    a. *(P) In patients with severe external limb bleeding in the prehospital setting, (I) does the application of a tourniquet compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, and blood loss (O)?*

    b. *(P) In patients with severe external bleeding, (I) does the application of topical hemostatic dressings plus standard first aid, (C) compared with standard first aid alone, (O) change overall mortality, vital signs, hemostasis, complications, blood loss, and major bleeding?*

2. Naloxone:

   (P) For adults with opiate/opioid toxicity in the prehospital environment, (I) does administration of naloxone (intramuscular or intranasal) by ALS (paramedics/EMT-I/AEMT) responders (C) compared to bystanders, law enforcement or BLS (EMT-B/EMT/EMR) (O) improve patient mental and respiratory status?

3. Therapeutic hypothermia in cardiac arrest

   (P) For patients suffering out of hospital cardiac arrest (OHCA), (I) does induction of prehospital therapeutic hypothermia [targeted temperature management] (C) compared with in-hospital therapeutic hypothermia (O) change survival with favorable neurological/functional outcome?

4. CPAP/BiPAP

   (P) For adult patients requiring non-invasive positive pressure ventilation for respiratory distress in the prehospital setting, (I) does CPAP/BiPAP (C) compared to BVM or supplemental oxygen alone (O) improve respiratory status, death, decompensation leading to further advanced airway intervention, and intubation rates?

5. Pharmacological pain management

   (P) In patients requiring pain management following an acute traumatic event in the prehospital setting, (I) can EMT and AEMT providers administer pharmacological pain medications (C) compared to paramedics (O) safely and effectively?

Strengths and Limitations

Addressing the need for a thorough evaluation of the specific priority areas identified by NHTSA, systematic reviews were conducted on each of the above questions. A strength of this chosen approach is the use of focused questions to drive the search of available literature for each priority area. These were clearly defined *a priori* and reviewed by NHTSA to meet the needs of the EMS Scope of Practice Model. Further, the clear methodology used in the literature review with defined search terms, time periods, and detailed inclusion and exclusion criteria allow clear interpretation of the results. However, a significant limitation of this approach is the innate heterogeneity inherent in many studies which contribute to the analysis. This can be in the form of populations evaluated and statistical approach used by investigators. Finally, another limitation is the possibility of a lack of the literature answering these questions. Even with a well-designed search driven by a detailed PICO question there may not exist literature which satisfies the specific inclusion and exclusion criteria. This concept was an accepted possibility in this evaluation where a lack of evidence in a priority area demonstrates a knowledge gap in the literature. These knowledge gaps would need to be addressed in future evaluations by researchers.

Systematic Review on the Use of Prehospital Tourniquets and Hemostatic Dressings

Concept Problem

For patients with traumatic injuries, hemorrhage is a major concern and a significant cause of preventable death.[1] Tourniquets and hemostatic dressings have been recommended for use in the prehospital setting to assist in control of severe bleeding.[1,2] However, though commonly deployed in the military setting,[3-6] these tools are less frequently used by civilian providers.

The adoption of such interventions in the civilian setting has been slow due to fears of complications such as limb loss, compartment syndrome, and exothermic reactions.[7] Recent evidence has suggested that tourniquets and hemostatic dressings can be safely applied by trained EMS and first aid providers and are effective for severe bleeding.[2,8,9] Though awareness and usage of these tools for trauma patients treated in the civilian setting has started to increase, questions concerning their efficacy still remain.[1,10]

In this systematic review, we evaluate the evidence on the use of tourniquets and hemostatic dressings in the prehospital setting. The specific questions developed with advice from NHTSA for this topic area are the following two PICO questions:

6. *(P) In patients with severe external limb bleeding in the prehospital setting, (I) does the application of a tourniquet compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, and blood loss (O)?*

7. *(P) In patients with severe external bleeding, (I) does the application of topical hemostatic dressings plus standard first aid, (C) compared with standard first aid alone, (O) change overall mortality, vital signs, hemostasis, complications, blood loss, and major bleeding?*

These PICO questions were an extension on the comprehensive work conducted by the American Heart Association through the 2015 Guidelines Process.[2] Utilizing the published PICO questions, we evaluated data from 2013 to current. This work serves as an update to the comprehensive work undertaken through the 2015 Guidelines Process.[2]

These PICO question evaluations were conducted as two separate systematic reviews: Section 1) Use of prehospital tourniquets for hemorrhage control; Section 2) Use of prehospital hemostatic dressings for hemorrhage control. These sections are described below in consecutive order.

Section 1: Use of Prehospital Tourniquets for Hemorrhage Control

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in these searches were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO question. The search dates were from 09/2013 to February 6, 2017.

The search terms were exploded and are as follows: "Hemorrhage" OR "Exsanguination" OR "Shock, Hemorrhagic" OR Hemorrhag* OR Haemorrhag* OR Bleed* OR Exsanguination OR amputat* OR "blood loss" AND "Tourniquets" OR Tourniquet* AND "randomized controlled trial" OR "controlled clinical trial" OR "clinical trial" OR "comparative study" OR random* OR controll* OR "intervention study" OR "experimental study" OR "comparative study" OR trial OR evaluat* OR "Before and after" OR "interrupted time series" NOT "animals" NOT animals AND "humans" OR "Epidemiologic Studies" OR "case control" OR "case-control" OR case OR cases AND control OR controls OR "cohort study" OR "cohort analysis" OR "follow up study" OR "follow-up study" OR "observational study" OR "longitudinal" OR "retrospective" OR "cross sectional" OR "cross-sectional" OR questionnaire OR questionnaires OR survey OR "Emergency Medical Services" OR "Emergency Service, Hospital" OR "Emergency Treatment" OR prehospital OR pre-hospital NOT "Arthroplasty, Replacement, Knee" AND "2013/09/01" : "2017/12/31." Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were human (no basic science or animal models). Exclusion criteria included: studies that did not specifically compare tourniquet to no tourniquet and studies that did not specifically examine severe external limb bleeding in the prehospital setting (no operating room).

Results

A systematic review of the literature from 2013 to 02/2017 was completed with the identification of 466 articles matching search criteria (Figure 1-1). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 415 records were screened by two independent reviewers. Of these, 21 satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 1-1). Five (5) manuscripts for were selected for the final list of manuscripts which met inclusion criteria after full text review (Table 1-3).

Conclusion

In this systematic review, we evaluated the evidence on the use of tourniquets in the prehospital setting answering the following question:

> *(P) In patients with severe external limb bleeding in the prehospital setting, (I) does the application of a tourniquet compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, and blood loss (O)?*

Utilizing a comprehensive search strategy, a total of 466 articles were extracted. After independent evaluation by two reviewers, five (5) manuscripts satisfied inclusion for tourniquet use. In this evaluation, multiple articles were excluded from the final inclusion list due to the lack of a control group (usual care / not applying a tourniquet).

In total, between this review and work done through the 2015 AHA Guidelines Process, 13 total manuscripts have been published that evaluate the stated PICO question concerning prehospital tourniquet use for hemorrhage control.

Section 2: Use of Prehospital Hemostatic Dressings for Hemorrhage Control.

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in this search were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO question. The search dates were from 09/2013 to February 6, 2017.

The search terms were exploded and are as follows: “hemorrhage” OR “bleeding” OR “haemorrhage” OR “combat” OR “trauma” OR “penetrating trauma” OR “bandages” AND “military medicine” OR “emergency medicine” OR “emergency medical services” OR “blood coagulation/drug effects” AND “hemostatic*” OR “haemostatic*” AND “agent” OR “hemostatic techniques” AND “administration, topical” OR “hemcon” OR “quikclot” OR “Celox” OR “bound” AND “state” OR “combat gauze” OR “quikclot” AND “advanced” OR “sponge” OR “QCG” OR “QCX” OR “hemcon” AND “chitoflex” OR “HCF” OR “chitogauze” OR “HCG” OR “chitosan” OR “celow” AND “gauze” OR “CEL” OR “modified” AND “rapid” AND “deployment” AND “hemostat” OR “mRDH” OR “zeolites” AND “mortality” OR “survival” OR outcome OR “wound healing” OR “haemostasis” OR “hemostasis” OR “survival rate” OR “Injury severity scale” OR “war” OR “resuscitation” OR “hemorrhage control” or “burns” AND “2013/09/01”: “2017/12/31” Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were

human (no basic science or animal models). Exclusion criteria included: studies that did not specifically compare hemostatic dressing with first aid to first aid alone and studies that did not specifically examine severe external bleeding in the prehospital setting (no operating room).

Results

A systematic review of the literature from 2013 to 02/2017 was completed with the identification of 356 articles matching search criteria (Figure 1-2). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 351 records were screened by two independent reviewers. Of these, 13 satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 1-3). Four (4) manuscripts were selected for the final list of manuscripts that met inclusion criteria after full text review (Table 1-4).

Conclusion

In this systematic review, we evaluated the evidence on the use of hemostatic dressings in the prehospital setting answering the following question:

> *(P) In patients with severe external bleeding, (I) does the application of topical hemostatic dressings plus standard first aid, (C) compared with standard first aid alone, (O) change overall mortality, vital signs, hemostasis, complications, blood loss, and major bleeding?*

Utilizing a comprehensive search strategy, a total of 356 articles were extracted. After independent evaluation by two reviewers, four (4) manuscripts were included in the final list. In this evaluation, manuscripts were included if the PICO question was satisfied. However, due to the manner in which research in this area was conducted, studies that utilized a failure of standard first aid alone as their inclusion criteria were also included. This precluded a comparison of hemostatic dressings to a standard control group, but it did allow for evaluation of hemostatic dressing efficacy following failure of standard therapy.

In total, between this review and work done through the 2015 AHA Guidelines Process, 15 total manuscripts have been published that evaluate the stated PICO question concerning prehospital hemostatic dressing use.

References

1. Bulger EM, Snyder D, Schoelles K, Gotschall C, Dawson D, Lang E, Sanddal ND, Butler FK, Fallat M, Taillac P, White L, Salomone JP, Seifarth W, Betzner MJ, Johannigman J, McSwain N, Jr. An evidence-based prehospital guideline for external hemorrhage control: American College of Surgeons Committee on Trauma. *Prehosp Emerg Care.* 2014;18(2):163-173.
2. Singletary EM, Charlton NP, Epstein JL, Ferguson JD, Jensen JL, MacPherson AI, Pellegrino JL, Smith WWR, Swain JM, Lojero-Wheatley LF, Zideman DA. Part 15: First Aid. *2015 American Heart Association and American Red Cross Guidelines Update for First Aid.* 2015;132(18 suppl 2):S574-S589.
3. Beekley AC, Sebesta JA, Blackbourne LH, Herbert GS, Kauvar DS, Baer DG, Walters TJ, Mullenix PS, Holcomb JB. Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes. *J Trauma.* 2008;64(2 Suppl):S28-37; discussion S37.
4. Lakstein D, Blumenfeld A, Sokolov T, Lin G, Bssorai R, Lynn M, Ben-Abraham R. Tourniquets for hemorrhage control on the battlefield: a 4-year accumulated experience. *J Trauma.* 2003;54(5 Suppl):S221-225.
5. Cox ED, Schreiber MA, McManus J, Wade CE, Holcomb JB. New hemostatic agents in the combat setting. *Transfusion.* 2009;49(s5):248S-255S.
6. Wedmore I, McManus JG, Pusateri AE, Holcomb JB. A special report on the chitosan-based hemostatic dressing: experience in current combat operations. *J Trauma.* 2006;60(3):655-658.

7. Doyle GS, Taillac PP. Tourniquets: A Review of Current Use with Proposals for Expanded Prehospital Use. *Prehospital Emergency Care.* 2008;12(2):241-256.
8. Kue RC, Temin ES, Weiner SG, Gates J, Coleman MH, Fisher J, Dyer S. Tourniquet Use in a Civilian Emergency Medical Services Setting: A Descriptive Analysis of the Boston EMS Experience. *Prehosp Emerg Care.* 2015;19(3):399-404.
9. Brown MA, Daya MR, Worley JA. Experience with Chitosan Dressings in a Civilian EMS System. *Journal of Emergency Medicine.* 2007;37(1):1-7.
10. Jacobs LM, McSwain NE, Jr., Rotondo MF, Wade D, Fabbri W, Eastman AL, Butler FK, Jr., Sinclair J. Improving survival from active shooter events: the Hartford Consensus. *J Trauma Acute Care Surg.* 2013;74(6):1399-1400.
11. King DR, Larentzakis A, Ramly EP. Tourniquet use at the Boston Marathon bombing: Lost in translation. *J Trauma Acute Care Surg.* 2015;78(3):594-599.
12. Kragh JF, Jr., Dubick MA, Aden JK, McKeague AL, Rasmussen TE, Baer DG, Blackbourne LH. U.S. Military use of tourniquets from 2001 to 2010. *Prehosp Emerg Care.* 2015;19(2):184-190.
13. Kragh JF, Jr., Nam JJ, Berry KA, Mase VJ, Jr., Aden JK, 3rd, Walters TJ, Dubick MA, Baer DG, Wade CE, Blackbourne LH. Transfusion for shock in US military war casualties with and without tourniquet use. *Ann Emerg Med.* 2015;65(3):290-296.
14. Ode G, Studnek J, Seymour R, Bosse MJ, Hsu JR. Emergency tourniquets for civilians: Can military lessons in extremity hemorrhage be translated? *J Trauma Acute Care Surg.* 2015;79(4):586-591.

15. Passos E, Dingley B, Smith A, Engels PT, Ball CG, Faidi S, Nathens A, Tien H. Tourniquet use for peripheral vascular injuries in the civilian setting. *Injury.* 2014;45(3):573-577.

16. Leonard J, Zietlow J, Morris D, Berns K, Eyer S, Martinson K, Jenkins D, Zietlow S. A multi-institutional study of hemostatic gauze and tourniquets in rural civilian trauma. *J Trauma Acute Care Surg.* 2016;81(3):441-444.

17. Shina A, Lipsky AM, Nadler R, Levi M, Benov A, Ran Y, Yitzhak A, Glassberg E. Prehospital use of hemostatic dressings by the Israel Defense Forces Medical Corps: A case series of 122 patients. *J Trauma Acute Care Surg.* 2015;79(4 Suppl 2):S204-209.

18. Travers S, Lefort H, Ramdani E, Lemoine S, Jost D, Bignand M, Tourtier JP. Hemostatic dressings in civil prehospital practice: 30 uses of QuikClot Combat Gauze. *Eur J Emerg Med.* 2016;23(5):391-394.

19. Zietlow JM, Zietlow SP, Morris DS, Berns KS, Jenkins DH. Prehospital Use of Hemostatic Bandages and Tourniquets: Translation From Military Experience to Implementation in Civilian Trauma Care. *J Spec Oper Med.* 2015;15(2):48-53.

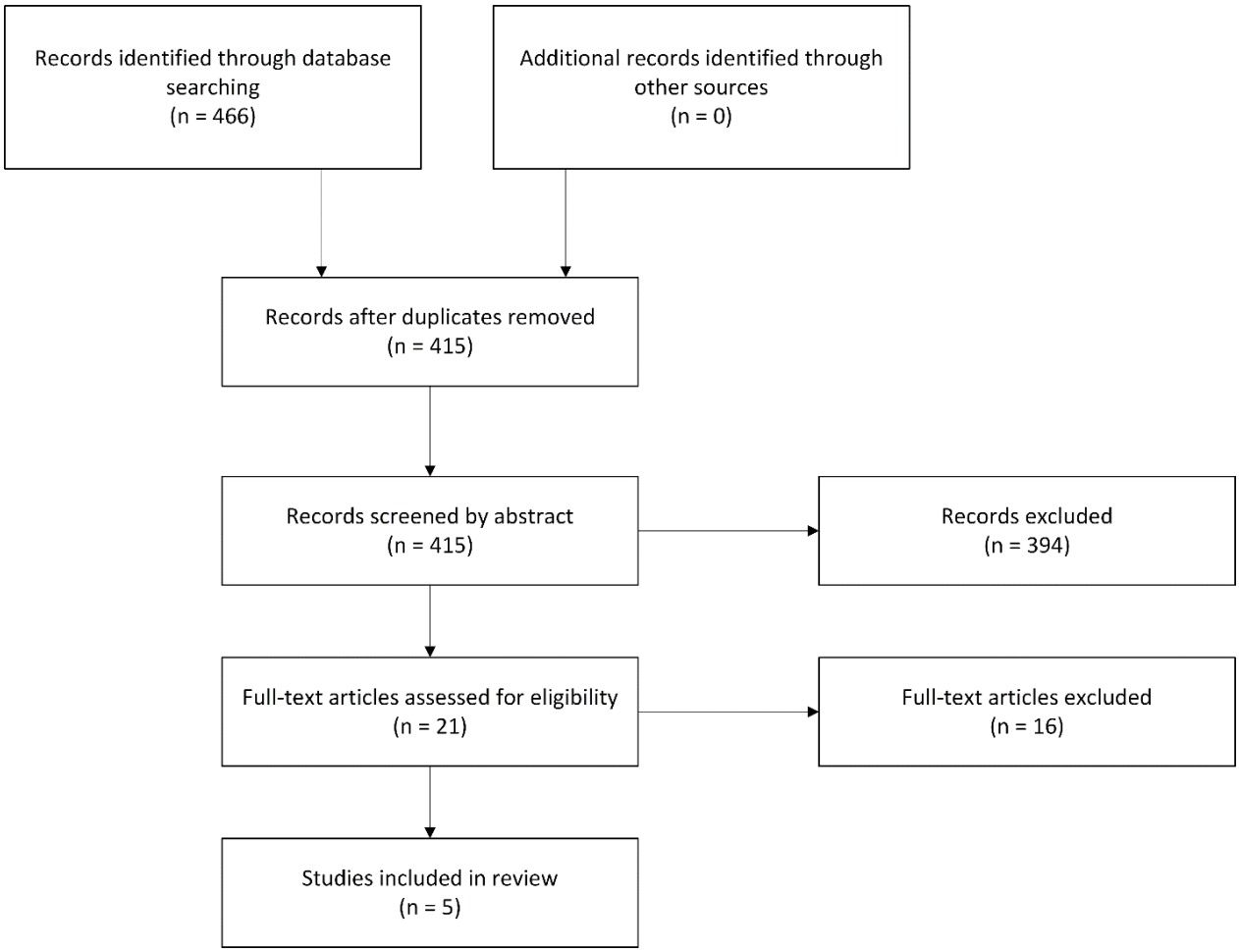

Figure 1-1: Flow diagram of search and review process for the PICO question related to tourniquet use.

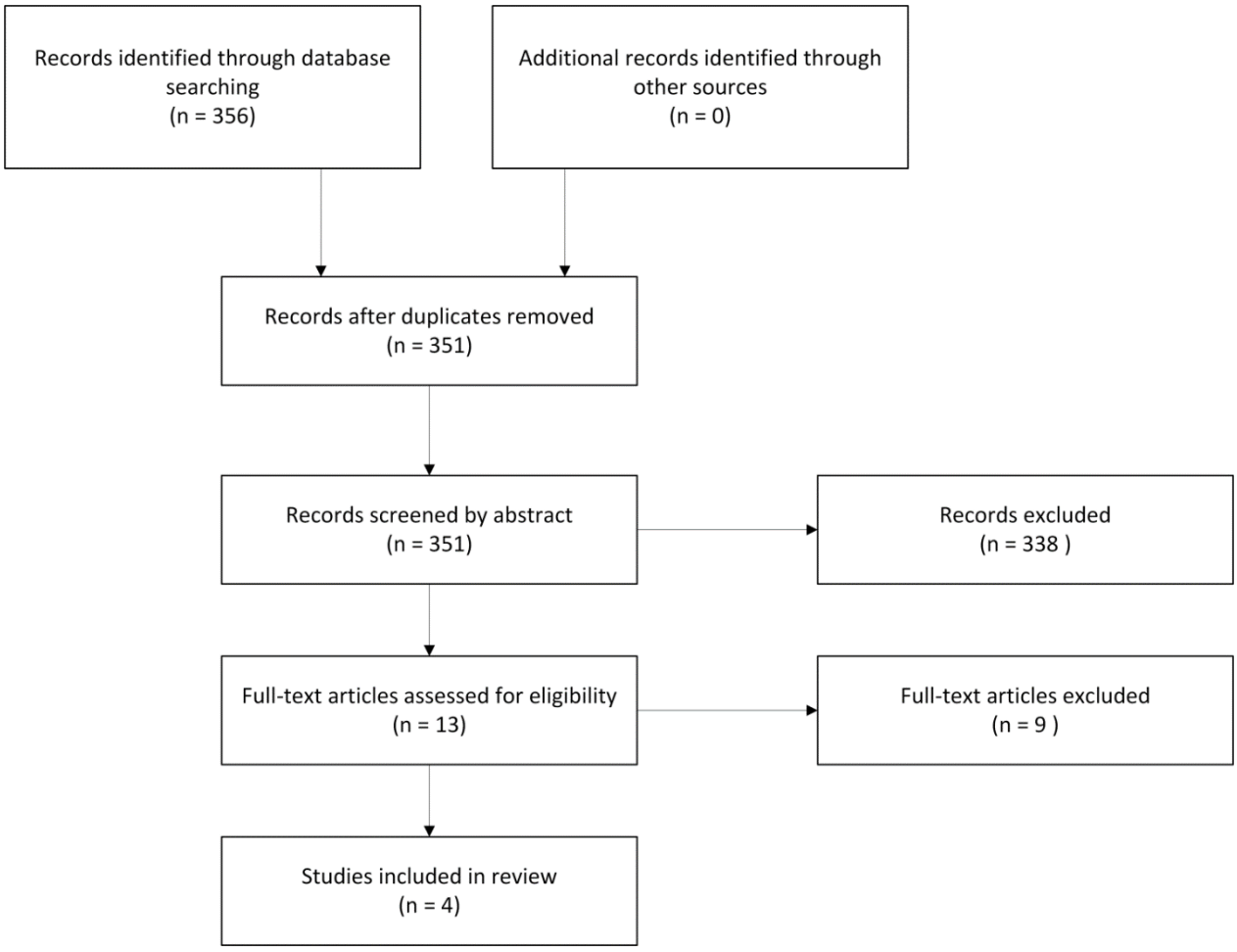

Figure 1-2: Flow diagram of search and review process for the PICO question related to hemostatic dressing use.

Table 1-1: Abstracts that satisfied the PICO question search terms and inclusion criteria for tourniquet. Manuscripts were selected for full text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for exclusion
Beaucreux, C., et al. (2017). "Tourniquet use for treatment of vascular trauma in civilian casualties of terror-related explosions." Journal of Trauma and Acute Care Surgery 82(1): 225.		Letter to the editor
Bulger, E. M., et al. (2014). "An evidence-based prehospital guideline for external hemorrhage control: American College of Surgeons Committee on Trauma." Prehosp Emerg Care 18(2): 163-173.		Evidence-based guideline, no additional records
Callaway, D. W., et al. (2015). "Law enforcement-applied tourniquets: a case series of life-saving interventions." Prehosp Emerg Care 19(2): 320-327.		Case reports
Dunn, J. C., et al. (2016). "Vascular Injuries in Combat-Specific Soldiers during Operation Iraqi Freedom and Operation Enduring Freedom." Ann Vasc Surg 35: 30-37.		No comparison of treatment groups in question
El Sayed, M. J., et al. (2017). "Trends and Predictors of Limb Tourniquet Use by Civilian Emergency Medical Services in the United States." Prehosp Emerg Care 21(1): 54-62.		No comparison of treatment groups in question
Goodloe, J. M., et al. (2014). "Tourniquet utilization patterns & impacts on hemostasis in a large, urban EMS system." Canadian Journal of Emergency Medicine 16: S52.		Conference abstract
Inaba, K., et al. (2015). "Tourniquet use for civilian extremity trauma." J Trauma Acute Care Surg 79(2): 232-237;quiz 332-233.		No comparison of treatment groups in question
King, D. R., et al. (2015). "Tourniquet use at the Boston Marathon bombing: Lost in translation." J Trauma Acute Care Surg 78(3): 594-599.	X	
Kragh, J. F., Jr., et al. (2015). "U.S. Military use of tourniquets from 2001 to 2010." Prehosp Emerg Care 19(2): 184-190.	X	
Kragh, J. F., Jr., et al. (2015). "Transfusion for shock in US military war casualties with and without tourniquet use." Ann Emerg Med 65(3): 290-296.	X	

Kragh Jr, J. F., et al. (2013). "Performance improvement in emergency tourniquet use during the Baghdad surge." American Journal of Emergency Medicine 31(5): 873-875.		Letter to the editor
Kue, R. C., et al. (2015). "Tourniquet Use in a Civilian Emergency Medical Services Setting: A Descriptive Analysis of the Boston EMS Experience." Prehosp Emerg Care 19(3): 399-404.		No comparison of treatment groups in question
Leonard, J., et al. (2016). "A multi-institutional study of hemostatic gauze and tourniquets in rural civilian trauma." J Trauma Acute Care Surg 81(3): 441-444.		No comparison of treatment groups in question
Mawhinney, A. C. and S. J. Kirk (2015). "A systematic review of the use of tourniquets and topical haemostatic agents in conflicts in Afghanistan and Iraq." J R Nav Med Serv 101(2): 147-154.		Systematic review; no additional records
Ode, G., et al. (2015). "Emergency tourniquets for civilians: Can military lessons in extremity hemorrhage be translated?" J Trauma Acute Care Surg 79(4): 586-591.	X	
Passos, E., et al. (2014). "Tourniquet use for peripheral vascular injuries in the civilian setting." Injury 45(3): 573-577.	X	
Sanko, S., et al. (2015). "Tourniquet use in a civilian out-of-hospital setting: The Los Angeles experience." Ann Emerg Med 66(4): S26.		Conference abstract
Scerbo, M. H., et al. (2016). "Safety and Appropriateness of Tourniquets in 105 Civilians." Prehosp Emerg Care 20(6): 712-722.		No comparison of treatment groups in question
Schroll, R., et al. (2015). "A multi-institutional analysis of prehospital tourniquet use." J Trauma Acute Care Surg 79(1): 10-14; discussion 14.		No comparison of treatment groups in question
Wright, G., et al. (2015). "Should civilian pre-hospital emergency care provision include tourniquets for the management of uncontrolled traumatic haemorrhage?" Australasian Journal of Paramedicine 12(4).		Systematic review, no additional records
Zietlow, J. M., et al. (2015). "Prehospital Use of Hemostatic Bandages and Tourniquets: Translation From Military Experience to Implementation in Civilian Trauma Care." J Spec Oper Med 15(2): 48-53.		No comparison of treatment groups in question

Table 1-2: Final list of manuscripts that met inclusion criteria for tourniquet after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
King, D.R., et al. (2015)[11]	Boston, MA Response to mass-casulty event Bystanders, EMS, medical professionals, military	Retrospective review of prehospital and in-hospital records for cohort of patients injured in one event Prehospital tourniquet vs. no tourniquet examined	Location and type of injury Tourniquet usage Vital signs before and after ED arrival Transport time
Kragh, J.F., Jr., et al. (2015)[12]	Military Afghanistan, Iraq	Retrospective observational cohort (trauma registry) September 2001 – December 2010	Injury Severity Score Mortality
Kragh, J.F., Jr., et al. (2015)[13]	Military Afghanistan, Iraq	Retrospective observational cohort of patients requiring transfusion (trauma registry) September 2001 – November 2008	Mortality Length of ICU and hospital stay Vital signs Lab values
Ode, G., et al. (2015)[14]	North Carolina County EMS agency	Retrospective review of prehospital and in-hospital records September 2012 – November 2013	Appropriateness of tourniquet Mortality Vital signs in ED Resuscitative requirements in ED Emergent surgical procedures related to injured extremity Length of hospital stay Tourniquet-related complications
Passos, E., et al.	Canada	Retrospective review of prehospital	Mortality

(2014)[15]	Level I Trauma Center	and in-hospital records and trauma registries January 2001 – December 2010	Length of ICU and hospital stay Compartment syndrome Amputation Units of blood products transfused

Table 1-3: Abstracts that satisfied the PICO question search terms and inclusion criteria for hemostatic dressing. Manuscripts were selected for full text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for exclusion
Bulger, E. M., et al. (2014). "An evidence-based prehospital guideline for external hemorrhage control: American College of Surgeons Committee on Trauma." Prehosp Emerg Care 18(2): 163-173.		Evidence-based guideline; no additional records
Butler, F. K. (2015). "Military History of Increasing Survival: The U.S. Military Experience with Tourniquets and Hemostatic Dressings in the Afghanistan and Iraq Conflicts." J Spec Oper Med 15(4): 149-152.		Review article; no additional records
Gegel, B. T., et al. (2013). "An evidence-based review of the use of a combat gauze (QuikClot) for hemorrhage control." Aana j 81(6): 453-458.		Systematic review; no additional records
Grissom, T. E. and R. Fang (2015). "Topical hemostatic agents and dressings in the prehospital setting." Curr Opin Anaesthesiol 28(2): 210-216.		Systematic review; no additional records
Holcomb, J. B., et al. (2015). "Hemorrhage Control Devices: Tourniquets and Hemostatic Dressings." J Spec Oper Med 15(4): 153-156.		Review article; no additional records
Kragh, J. F., Jr., et al. (2015). "Gauze vs XSTAT in wound packing for hemorrhage control." Am J Emerg Med 33(7): 974-976.		Correspondence piece
Leonard, J., et al. (2016). "A multi-institutional study of hemostatic gauze and tourniquets in rural civilian trauma." Journal of Trauma and Acute Care Surgery 81(3): 441-444.	X	
Mawhinney, A. C. and S. J. Kirk (2015). "A systematic review of the use of tourniquets and topical haemostatic agents in conflicts in Afghanistan and Iraq." J R Nav Med Serv 101(2): 147-154.		Systematic review; no additional records
Shina, A., et al. (2015). "Prehospital use of hemostatic dressings by the Israel Defense Forces Medical Corps: A case series of 122 patients." J Trauma Acute Care Surg 79(4 Suppl 2): S204-209.	X	
Smith, A. H., et al. (2013). "Haemostatic dressings in prehospital care." Emerg Med J 30(10): 784-789.		Systematic review; no additional records

Travers, S., et al. (2016). "Hemostatic dressings in civil prehospital practice: 30 uses of QuikClot Combat Gauze." European Journal of Emergency Medicine 23(5): 391-394.	X	
Zhang, Y. J., et al. (2015). "Topical and effective hemostatic medicines in the battlefield." Int J Clin Exp Med 8(1): 10-19.		Systematic review; no additional records
Zietlow, J. M., et al. (2015). "Prehospital Use of Hemostatic Bandages and Tourniquets: Translation From Military Experience to Implementation in Civilian Trauma Care." J Spec Oper Med 15(2): 48-53.	X	

Table 1-4: Final list of manuscripts for hemostatic dressings PICO question that were included after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
Leonard, J., et al. (2016)[16]	10 institutions across MN and WI	Retrospective review of prehospital records for patients who received QuickClot or CAT from 2009 to 2014 Protocol for devices to be applied only after failure of direct pressure to achieve hemostasis	Cessation of visible hemorrhage
Shina, A., et al. (2015)[17]	Israeli Defense Forces Medical Corps	Case series of all documented cases treated with a hemostatic dressing in the prehospital setting from January 2009 through September 2014. For extremity injury, protocol for hemostatic dressing to be used after failure of direct pressure or compression dressing to achieve hemostasis	Cessation of hemorrhage
Travers, S., et al. (2016)[18]	Paris Fire Brigade Prehospital physicians and nurses who work on ambulances	Prospective observational study of prehospital hemostatic dressing use from June 2011 to May 2014 Use of hemostatic gauze recommended only after failure of standard hemorrhage control measures.	Cessation of hemorrhage

Zietlow, J. M., et al. (2015)[19]	Single service ground and rotor-wing rural program	Retrospective review of consecutive patients with hemostatic gauze applications from June 2009 to January 2014. Prehospital protocol dictates that hemostatic gauze be used only after standard compression bandages were unsuccessful.	Cessation of clinically observable bleeding

SUMMARY SECTION 1: Systematic Review on the Use of Prehospital Tourniquets

PICO Question:

(P) In patients with severe external limb bleeding in the prehospital setting, (I) does the application of a tourniquet compared with not applying a tourniquet (C), change hemostasis, overall mortality, vital signs, functional limb recovery, complications, and blood loss (O)?

Date: 09/2013 to 02/2017

Manuscripts
Beekley, A. C., et al. (2008). "Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes." J Trauma 64(2 Suppl): S28-37; discussion S37.
Brodie, S., et al. (2009). "Tourniquet use in combat trauma: U.K. military experience." J Spec Oper Med 9(1): 74-77.
King*, D. R., et al. (2015). "Tourniquet use at the Boston Marathon bombing: Lost in translation." J Trauma Acute Care Surg 78(3): 594-599.
Kragh, J. F., Jr., et al. (2011). "Battle casualty survival with emergency tourniquet use to stop limb bleeding." J Emerg Med 41(6): 590-597.
Kragh, J. F., Jr., et al. (2012). "Survey of trauma registry data on tourniquet use in pediatric war casualties." Pediatr Emerg Care 28(12): 1361-1365.
Kragh*, J. F., Jr., et al. (2015). "Transfusion for shock in US military war casualties with and without tourniquet use." Ann Emerg Med 65(3): 290-296.
Kragh*, J. F., Jr., et al. (2015). "U.S. Military use of tourniquets from 2001 to 2010." Prehosp Emerg Care 19(2): 184-190.
Kue, R. C., et al. (2015). "Tourniquet Use in a Civilian Emergency Medical Services Setting: A Descriptive Analysis of the Boston EMS Experience." Prehosp Emerg Care 19(3): 399-404.
Lakstein, D., et al. (2003). "Tourniquets for hemorrhage control on the battlefield: a 4-year accumulated experience." J Trauma 54(5 Suppl): S221-225.
Ode*, G., et al. (2015). "Emergency tourniquets for civilians: Can military lessons in extremity

hemorrhage be translated?" J Trauma Acute Care Surg 79(4): 586-591.
Passos*, E., et al. (2014). "Tourniquet use for peripheral vascular injuries in the civilian setting." Injury 45(3): 573-577.
Singletary, E.M., et al. (2015). "Part 15: First Aid. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care." 132(18 suppl 2):S574-S589.
Tien, H. C., et al. (2008). "An evaluation of tactical combat casualty care interventions in a combat environment." J Am Coll Surg 207(2): 174-178.

*Included in current review

SUMMARY SECTION 2: Systematic Review on the Use of Prehospital Hemostatic Dressings

PICO Question:

(P) In patients with severe external bleeding, (I) does the application of topical hemostatic dressings plus standard first aid, (C) compared with standard first aid alone, (O) change overall mortality, vital signs, hemostasis, complications, blood loss, and major bleeding?

Date: 09/2013 to 02/2017

Manuscripts
Brown, M. A., et al. (2007). "Experience with Chitosan Dressings in a Civilian EMS System." Journal of Emergency Medicine 37(1): 1-7.
Cox, E. D., et al. (2009). "New hemostatic agents in the combat setting." Transfusion 49(s5): 248S-255S.
Granville-Chapman, J., et al. (2011). "Pre-hospital haemostatic dressings: a systematic review." Injury 42(5): 447-459.
King, D. R., et al. (2004). "Modified rapid deployment hemostat bandage terminates bleeding in coagulopathic patients with severe visceral injuries." J Trauma 57(4): 756-759.
Leonard,* J., et al. (2016). "A multi-institutional study of hemostatic gauze and tourniquets in rural civilian trauma." J Trauma Acute Care Surg 81(3): 441-444.
McManus, J., et al. (2007). "A case series describing thermal injury resulting from zeolite use for hemorrhage control in combat operations." Prehosp Emerg Care 11(1): 67-71.
Ran, Y., et al. (2010). "QuikClot Combat Gauze use for hemorrhage control in military trauma: January 2009 Israel Defense Force experience in the Gaza Strip--a preliminary report of 14 cases." Prehosp Disaster Med 25(6): 584-588.
Rhee, P., et al. (2008). "QuikClot use in trauma for hemorrhage control: case series of 103 documented uses." J Trauma 64(4): 1093-1099.
Shina,* A., et al. (2015). "Prehospital use of hemostatic dressings by the Israel Defense Forces

Medical Corps: A case series of 122 patients." J Trauma Acute Care Surg 79(4 Suppl 2): S204-209.

Singletary, E.M., et al. (2015). "Part 15: First Aid. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care." 132(18 suppl 2):S574-S589.

Sohn, V. Y., et al. (2009). "Efficacy of three topical hemostatic agents applied by medics in a lethal groin injury model." J Surg Res 154(2): 258-261.

Travers,* S., et al. (2016). "Hemostatic dressings in civil prehospital practice: 30 uses of QuikClot Combat Gauze." European Journal of Emergency Medicine 23(5): 391-394.

Wedmore, I., et al. (2006). "A special report on the chitosan-based hemostatic dressing: experience in current combat operations." J Trauma 60(3): 655-658.

Wright, F. L., et al. (2004). "Intracorporeal use of the hemostatic agent QuickClot in a coagulopathic patient with combined thoracoabdominal penetrating trauma." J Trauma 56(1): 205-208.

Zietlow,* J. M., et al. (2015). "Prehospital Use of Hemostatic Bandages and Tourniquets: Translation From Military Experience to Implementation in Civilian Trauma Care." J Spec Oper Med 15(2): 48-53.

*Included in current review

Systematic Review on the Use of Naloxone by Responders in the Prehospital Setting

Concept Problem

Opioid drug-related overdoses are a major cause of death in the US.[1] In 2015, there were 22,000 deaths from prescription opioids, which represents an increase of 16% from 2014.[1] Used to treat these overdoses, naloxone is an opioid antagonist that quickly reverses the associated central nervous system and respiratory depression effects.[2] As naloxone has no abuse potential and few adverse effects, many programs to increase community education and use of naloxone have been recommended and piloted.[3,4] To further address this significant public health threat, some states are expanding the scope of practice for administration of naloxone to include trained firefighters, EMTs and police officers.[5] It is unknown whether outcomes for patients with opioid toxicity vary when administration of naloxone is performed by different types of responders.

In this systematic review, we evaluate the evidence related to naloxone use by different types of responders. The specific question developed with advice from NHTSA for this topic is the following PICO question:

> *(P) For adults with opiate/opioid toxicity in the prehospital environment, (I) does administration of naloxone (intramuscular or intranasal) by ALS (paramedics/EMT-I/AEMT) responders (C) compared to bystanders, law enforcement or BLS (EMT-B/EMT/EMR) (O) improve patient mental and respiratory status?*

This PICO question evaluates all data from 1980 to the date of this search. Thus, the current evaluation serves as a comprehensive evaluation of this PICO question.

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in this search were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO. The search dates were from 1980 to February 2, 2017.

The search terms were exploded and are as follows: Search 1: "ambulance" OR "emergency medical services" OR "pre-hospital care" OR "mobile health units" OR "paramedic" AND "naloxone" OR "narcan" OR "opiate antagonist"; Search 2: "bystander" OR "law enforcement" OR "rescue personnel" OR "untrained" AND "naloxone" OR "narcan" OR "opiate antagonist". Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were human (no basic science or animal models). Exclusion criteria included: studies that did not specifically compare ALS (paramedics/EMT-I/AEMT) responders to bystanders, law enforcement or BLS (EMT-B/EMT/EMR), studies not in the prehospital setting, and studies that examined perceptions of responders only (no clinical patient outcomes).

Results

A systematic review of the literature from 1980 to 02/2017 was completed with the identification of 850 articles matching search criteria (Figure 2-1). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 655 records

were screened by two independent reviewers. Of these, 26 satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 2-1). Zero (0) manuscripts were selected for the final inclusion list after full text review (Table 2-2).

Though all twenty-six (26) articles included in the original extraction were assessed by full text review, none compared the different types of responders as framed in the developed PICO question. Additionally, many studies did not report outcomes of naloxone administration. Interestingly, one article did compare trained to untrained bystanders and their use of naloxone.[6] In this particular study, there were no differences found between trained and untrained individuals in help-seeking, rescue breathing, staying with the victim, or the successful administration of naloxone.

Conclusion

In this systematic review, we evaluate the evidence on the use of naloxone in the prehospital setting answering the following question:

> *(P) For adults with opiate/opioid toxicity in the prehospital environment, (I) does administration of naloxone (intramuscular or intranasal) by ALS (paramedics/EMT-I/AEMT) responders (C) compared to bystanders, law enforcement or BLS (EMT-B/EMT/EMR) (O) improve patient mental and respiratory status?*

Utilizing a comprehensive search strategy, a total of 850 articles were extracted. After independent evaluation by two reviewers, no manuscripts satisfied inclusion. No publications evaluated satisfied the stated PICO question concerning naloxone use between these groups.

Overall, though no literature exists comparing naloxone use by different types of responders as defined by the PICO question, this does not comment on the ability of these providers to administer naloxone. This PICO question was specifically chosen to attempt to address the needs of the update on the EMS Scope of Practice and not on the overall use of naloxone. Future systematic reviews as outlined in a proposal for the AHRQ titled, "Management of suspected opioid overdose with Naloxone by Emergency Medical Services personnel," will address the literature concerning route of administration, titration of dose provided, multi-dose administration, and appropriate transport destinations.

References:

1. Centers for Disease Control and Prevention. Injury Prevention & Control: Opioid Overdose; Opioid Data Analysis. 2017; https://www.cdc.gov/drugoverdose/data/analysis.html. Accessed 3 March 2017.
2. Sporer KA. Acute heroin overdose. *Ann Intern Med.* 1999;130(7):584-590.
3. Lavonas EJ, Drennan IR, Gabrielli A, Heffner AC, Hoyte CO, Orkin AM, Sawyer KN, Donnino MW. Part 10: Special Circumstances of Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2015;132(18 Suppl 2):S501-518.
4. Giglio RE, Li G, DiMaggio CJ. Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. *Inj Epidemiol.* 2015;2(1):10.
5. Davis CS, Ruiz S, Glynn P, Picariello G, Walley AY. Expanded Access to Naloxone Among Firefighters, Police Officers, and Emergency Medical Technicians in Massachusetts. *American Journal of Public Health.* 2014;104(8):e7-e9.
6. Doe-Simkins M, Quinn E, Xuan Z, Sorensen-Alawad A, Hackman H, Ozonoff A, Walley AY. Overdose rescues by trained and untrained participants and change in opioid use among substance-using participants in overdose education and naloxone distribution programs: a retrospective cohort study. *BMC Public Health.* 2014;14:297.

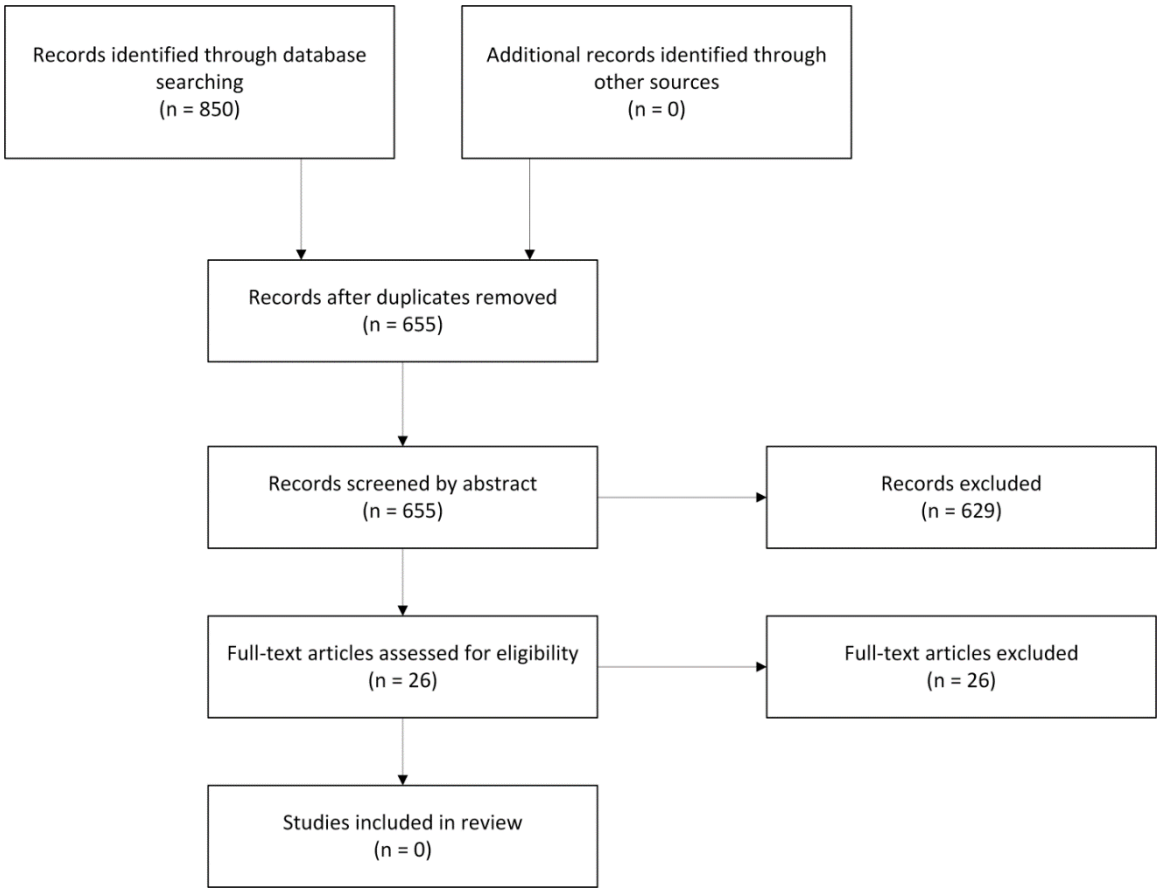

Figure 2-1: Flow diagram of search and review process

Table 2-1: Abstracts that satisfied PICO search terms and inclusion criteria. Manuscripts were selected for full text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for Exclusion
(2005). "Intranasal Naloxone effective in patients who overdose." Nurs Stand 19(24): 10.		News piece
Abarbanell, N. R. (1994). "Prehospital pharmacotherapeutic interventions: recommendations for medication administration by EMT-A and EMT-I personnel." Am J Emerg Med 12(6): 625-630.		No comparison between responders or naloxone administration outcomes reported
Alexander, J. L., et al. (2004). "Suspected opioid-related emergency medical services encounters in a rural state, 1997-2002." Prehosp Emerg Care 8(4): 427-430.		No comparison between responders or naloxone administration outcomes reported
Belz, D., et al. (2006). "Naloxone use in a tiered-response emergency medical services system." Prehosp Emerg Care 10(4): 468-471.		No comparison between responders reported
Dailey, M. W., et al. (2013). "Distributive education can be used to train basic EMTs to treat opioid overdose with intranasal naloxone." Academic Emergency Medicine 20(5): S267-S268.		Conference abstract
Davis, C. S., et al. (2014). "Expanded access to naloxone among firefighters, police officers, and emergency medical technicians in Massachusetts." Am J Public Health 104(8): e7-9.		No comparison between responders or naloxone administration outcomes reported
Doe-Simkins, M., et al. (2014). "Overdose rescues by trained and untrained participants and change in opioid use among substance-using participants in overdose education and naloxone distribution programs: a retrospective cohort study." BMC Public Health 14: 297		Compared trained vs untrained bystanders only
Dong, K. A., et al. (2012). "Community-based naloxone: A Canadian pilot program." CJAM Canadian Journal of Addiction Medicine 3(2): 4-9		No comparison between responders reported
Faul, M., et al. (2015). "Disparity in naloxone administration by emergency medical service providers and the burden of drug overdose in US rural communities." Am J Public Health 105 Suppl 3: e26-32		No naloxone administration outcomes reported

Faul, M., et al. (2014). "Factors that affect naloxone administration by emergency medical services providers following a drug overdose." Academic Emergency Medicine 21(5): S32.	Conference abstract
Fisher, R., et al. (2016). "Police Officers Can Safely and Effectively Administer Intranasal Naloxone." Prehosp Emerg Care 20(6): 675-680.	No comparison between responders
Giglio, R. E., et al. (2015). "Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis." Inj Epidemiol 2(1): 10.	No comparison between responders reported
Horowitz, Z. (1998). "Subcutaneous naloxone: a less rude awakening?" Acad Emerg Med 5(4): 283-285.	Commentary
Hughes, T. (2016). "Expanding access of intranasal naloxone to Columbia county emergency medical technicians." Journal of Investigative Medicine 64(1): 305-306.	Conference abstract
Jeffery, R. M., et al. (2017). "Naloxone administration for suspected opioid overdose: An expanded scope of practice by a basic life support collegiate-based emergency medical services agency." J Am Coll Health: 1-5.	No comparison between responders or naloxone administration outcomes reported
Kelly, A. M. and Z. Koutsogiannis (2002). "Intranasal naloxone for life threatening opioid toxicity." Emerg Med J 19(4): 375.	Conference abstract
Kim, D., et al. (2009). "Expanded access to naloxone: options for critical response to the epidemic of opioid overdose mortality." Am J Public Health 99(3): 402-407.	No comparison between responders or naloxone administration outcomes reported
Kitch, B. B. and R. C. Portela (2016). "Effective Use of Naloxone by Law Enforcement in Response to Multiple Opioid Overdoses." Prehosp Emerg Care 20(2): 226-22.	No comparison between responders reported
Kuehn, B. M. (2014). "Back from the brink: groups urge wide use of opioid antidote to avert overdoses." Jama 311(6): 560-561.	News piece
Perez, A., et al. (2015). "Naloxone availability in the USA: Bystander versus emergency medical services (EMS) administration." Clin Toxicol 53(4): 259	Conference abstract
Robertson, T. M., et al. (2009). "Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose." Prehosp Emerg Care 13(4): 512-515.	No comparison between responders reported
Schoenfeld, D. W., et al. (2012). "Effectiveness of intranasal naloxone by basic life support providers." Academic Emergency Medicine 19: S268.	Conference abstract

Troncoso, A., et al. (2010). "The utilization of pre-hospital advanced life support for toxic ingestions." Clin Toxicol 48(3): 265.	Conference abstract
Walley, A. Y., et al. (2013). "Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis." Bmj 346: f174.	No comparison between responders reported
Weiner, S. G., et al. (2014). "Use of intranasal naloxone by basic life support providers." Ann Emerg Med 64(4): S52.	Conference abstract
Willman, M. W., et al. (2017). "Do heroin overdose patients require observation after receiving naloxone?" Clin Toxicol (Phila) 55(2): 81-87.	No comparison between responders reported

Table 2-2: Final list of manuscripts that met inclusion criteria after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
None found			

Systematic Review on The Use of Naloxone by Responders in the Prehospital Setting

PICO Question:

(P) For adults with opiate/opioid toxicity in the prehospital environment, (I) does administration of naloxone (intramuscular or intranasal) by ALS (paramedics/EMTI/AEMT) responders (C) compared to bystanders, law enforcement or BLS (EMT-B/EMT/EMR) (O) improve patient mental and respiratory status?

Date: 1980 to 02/2017

Manuscripts
No manuscripts identified

Systematic Review on Prehospital Therapeutic Hypothermia

Concept Problem

Cardiac arrest is a significant public health concern affecting more than 400,000 people per year.[1] Even with significant strides in public access defibrillation programs, increased bystander CPR provision, and improved prehospital care by EMS, overall out-of-hospital cardiac arrest survival is low at 12%.[1] Due to the high prevalence of cardiac arrest and low survival rate, a large focus of EMS treatment has been to foster the use of interventions to improve functional neurological outcome post arrest.

One intervention that has been a large focus of prehospital efforts for many years is the use of therapeutic hypothermia. Initially, therapeutic hypothermia was found to significantly improve functional neurological outcomes post arrest.[2,3] However, recently the use of prehospital therapeutic hypothermia has been brought in to questions by a number of investigations that have demonstrated no difference between prehospital and in-hospital treatment.[4,5] Further, even the extent of hypothermia has been questioned leading to the current concept of targeted temperature management where fever prevention is the focus.[6]

Since the use of therapeutic hypothermia has become a major part of EMS care and the changing evidence in this area is significant, as a part of the update to the EMS Scope of Practice, NHTSA purposed an updated systematic review on the use of prehospital therapeutic hypothermia. The specific question developed with advice from NHTSA for this topic area is the following PICO question:

(P) For patients suffering out of hospital cardiac arrest (OHCA), (I) does induction of prehospital therapeutic hypothermia [targeted temperature management] (C) compared with in-hospital therapeutic hypothermia (O) change survival with favorable neurological/functional outcome?

This PICO question was an extension on the comprehensive work conducted by the American Heart Association through the 2015 Guidelines Process.[7] Utilizing the published PICO question, we evaluated data from 2013 to current. This work serves as an update to the comprehensive work undertaken through the 2015 Guidelines Process.[7]

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in this search were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO question. The search dates were from 2013 to present with the search being conducted on February 6, 2017.

The search terms were exploded and are as follows: "paramedic cooling" OR "field hypothermia" OR "Hypothermia, Induced" OR "targeted temperature management" OR "therapeutic hypothermia" OR "hypothermia therapy" OR "whole body cooling" OR "whole-body cooling" OR cool* OR cold AND "Brain Injuries" OR "brain injury" OR "brain injuries" OR "neurological status" OR neuroprotect* OR "Hypoxia-Ischemia, Brain" OR "hypoxic-ischemic encephalopathy" OR impair* OR impare* AND "Heart Arrest" OR "cardiac arrest" OR

“cardiac arrests” OR “cardiovascular arrest” OR “cardiovascular arrests” OR “heart arrest” OR “heart arrests” OR “asystole” OR “pulseless electrical activity” OR “cardiopulmonary arrest” OR “cardiopulmonary arrests” OR “Advanced Cardiac Life Support” OR “Advanced Cardiac Life Support” OR “ACLS” OR “Ventricular Fibrillation” OR “cardiopulmonary resuscitation” OR “cardiopulmonary resuscitation” OR CPR OR “Heart Massage” AND initiat* OR induc* OR early OR earlie* OR late OR later OR length OR prolong* OR hour* OR hrs OR minute* OR rapid* OR fast* OR quick* OR slow* OR time OR timing OR speed OR rate OR “Time Factors” OR “Time-to-Treatment” OR delay* OR “Emergency Medical Technicians” OR “emergency medic” OR “emergency medical” OR “EMS” OR “EMT” OR “pre-hospital” OR prehospital OR paramedic* OR “out-of-hospital” OR “out of hospital” NOT animal NOT humans OR rabbit* OR mouse OR mice OR swine OR pig OR pigs OR dog OR “animal model” OR “animal models” NOT “letter” OR “comment” OR “editorial” or Case Reports AND “2013/12/01” : “2017/12/31.” Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were human (no basic science or animal models). Exclusion criteria included: studies that did not specifically compare prehospital initiation of therapeutic hypothermia to in-hospital initiation, studies using therapeutic hypothermia for reasons other than out-of-hospital cardiac arrest, and studies examining the only efficacy of a specific product.

Results

A systematic review of the literature from 2013 to 02/2017 was completed with the identification of 1,051 articles matching search criteria (Figure 3-1). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 945 records were screened by two independent reviewers. Of these, 65 satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 3-1). Seven (7) manuscripts were selected for the final list of manuscripts that met inclusion criteria after full text review (Table 3-2).

Conclusions

In this systematic review, we evaluate the evidence on the use of therapeutic hypothermia for cardiac arrest in the prehospital setting answering the following question:

> *(P) For patients suffering out of hospital cardiac arrest (OHCA), (I) does induction of prehospital therapeutic hypothermia [targeted temperature management] (C) compared with in-hospital therapeutic hypothermia (O) change survival with favorable neurological/functional outcome?*

Utilizing a comprehensive search strategy, a total of 1,051 articles were extracted. After independent evaluation by two reviewers, seven (7) manuscripts satisfied inclusion. In total, between this review and that done by Callaway (2015)[7], nineteen (19) total manuscripts have been published that evaluate the stated PICO question concerning prehospital therapeutic hypothermia use in cardiac arrest.

References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Després J-P, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jiménez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. Heart Disease and Stroke Statistics—2016 Update. *A Report From the American Heart Association.* 2015.
2. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia. *New England Journal of Medicine.* 2002;346(8):557-563.
3. Hypothermia after Cardiac Arrest Study Group. Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest. *New England Journal of Medicine.* 2002;346(8):549-556.
4. Kim F, Nichol G, Maynard C, Hallstrom A, Kudenchuk PJ, Rea T, Copass MK, Carlbom D, Deem S, Longstreth WT, Jr., Olsufka M, Cobb LA. Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: a randomized clinical trial. *Jama.* 2014;311(1):45-52.
5. Bernard SA, Smith K, Cameron P, Masci K, Taylor DM, Cooper DJ, Kelly AM, Silvester W. Induction of therapeutic hypothermia by paramedics after resuscitation from out-of-hospital ventricular fibrillation cardiac arrest: a randomized controlled trial. *Circulation.* 2010;122(7):737-742.

6. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, Horn J, Hovdenes J, Kjaergaard J, Kuiper M, Pellis T, Stammet P, Wanscher M, Wise MP, Åneman A, Al-Subaie N, Boesgaard S, Bro-Jeppesen J, Brunetti I, Bugge JF, Hingston CD, Juffermans NP, Koopmans M, Køber L, Langørgen J, Lilja G, Møller JE, Rundgren M, Rylander C, Smid O, Werer C, Winkel P, Friberg H. Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest. *New England Journal of Medicine.* 2013;369(23):2197-2206.

7. Callaway CW, Donnino MW, Fink EL, Geocadin RG, Golan E, Kern KB, Leary M, Meurer WJ, Peberdy MA, Thompson TM, Zimmerman JL. Part 8: Post–Cardiac Arrest Care. *2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.* 2015;132(18 suppl 2):S465-S482.

8. Bernard SA, Smith K, Finn J, Hein C, Grantham H, Bray JE, Deasy C, Stephenson M, Williams TA, Straney LD, Brink D, Larsen R, Cotton C, Cameron P. Induction of Therapeutic Hypothermia During Out-of-Hospital Cardiac Arrest Using a Rapid Infusion of Cold Saline: The RINSE Trial (Rapid Infusion of Cold Normal Saline). *Circulation.* 2016;134(11):797-805.

9. Debaty G, Maignan M, Savary D, Koch FX, Ruckly S, Durand M, Picard J, Escallier C, Chouquer R, Santre C, Minet C, Guergour D, Hammer L, Bouvaist H, Belle L, Adrie C, Payen JF, Carpentier F, Gueugniaud PY, Danel V, Timsit JF. Impact of intra-arrest therapeutic hypothermia in outcomes of prehospital cardiac arrest: a randomized controlled trial. *Intensive Care Med.* 2014;40(12):1832-1842.

10. Maynard C, Longstreth WT, Jr., Nichol G, Hallstrom A, Kudenchuk PJ, Rea T, Copass MK, Carlbom D, Deem S, Olsufka M, Cobb LA, Kim F. Effect of prehospital induction

of mild hypothermia on 3-month neurological status and 1-year survival among adults with cardiac arrest: long-term follow-up of a randomized, clinical trial. *J Am Heart Assoc.* 2015;4(3):e001693.

11. Rao MP, Dupre ME, Pokorney SD, Hansen CM, Tyson C, Monk L, Pearson DA, Nelson RD, Myers B, Jollis JG, Granger CB. Therapeutic Hypothermia for Patients with Out-of-Hospital Cardiac Arrest in North Carolina. *Prehosp Emerg Care.* 2016;20(5):630-636.
12. Schenfeld EM, Studnek J, Heffner AC, Nussbaum M, Kraft K, Pearson DA. Effect of prehospital initiation of therapeutic hypothermia in adults with cardiac arrest on time-to-target temperature. *Cjem.* 2015;17(3):240-247.
13. Uray T, Mayr FB, Stratil P, Aschauer S, Testori C, Sterz F, Haugk M. Prehospital surface cooling is safe and can reduce time to target temperature after cardiac arrest. *Resuscitation.* 2015;87:51-56.

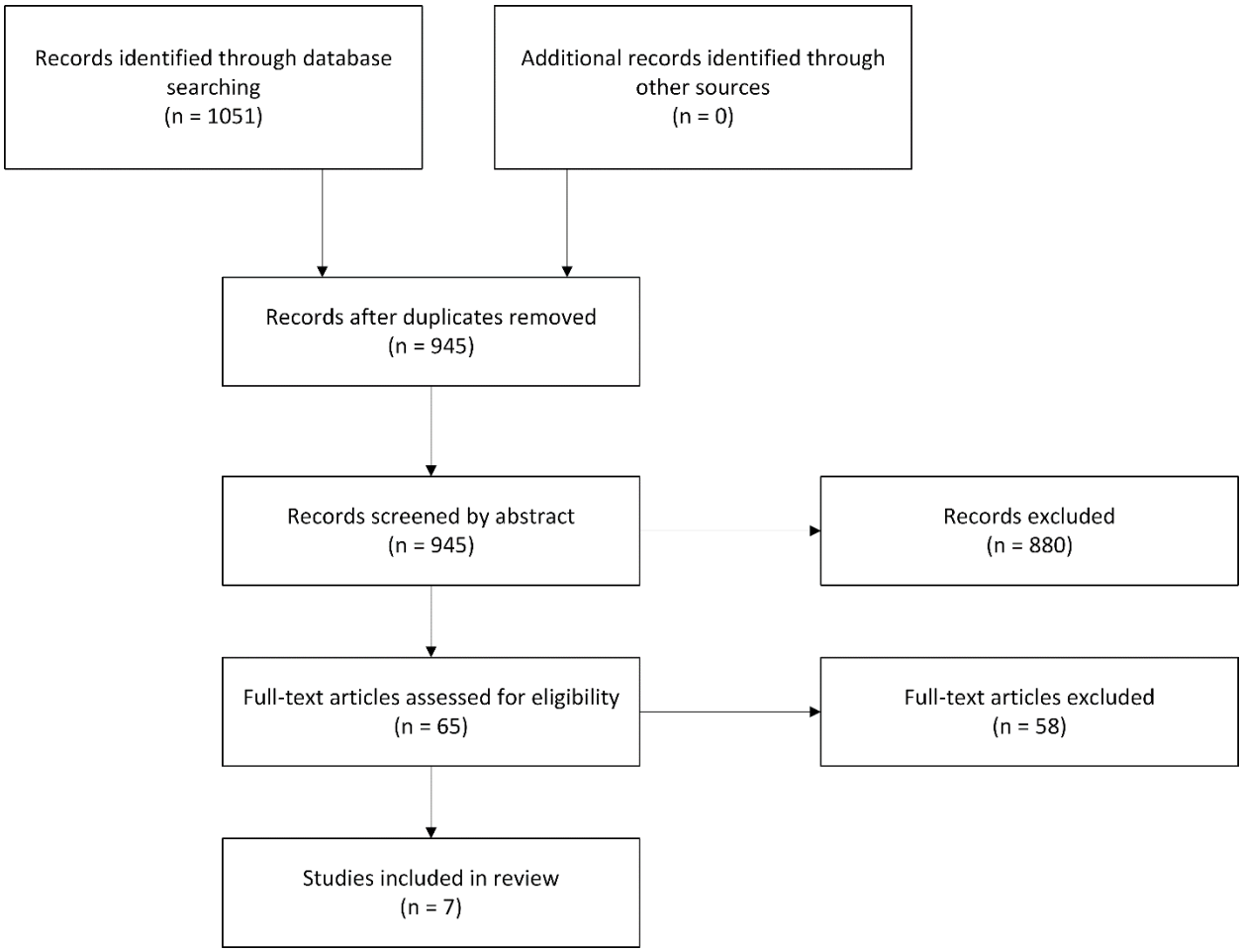

Figure 3-1: Flow diagram of search and review process.

Table 3-1: Abstracts that satisfied the PICO question search terms and inclusion criteria. Manuscripts were selected for full text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for exclusion
Abreu Filho, C. A., et al. (2013). "Comparison of 1-year neurological outcome between intra-hospital and extra-hospital cardiac arrest survivors submitted to mild therapeutic hypothermia in a community-based setting in Brazil." Critical Care 17: S116-S117.		Conference abstract
Adabag, S., et al. (2015). "Outcomes of cardiac arrest in a state-wide integrated resuscitation program: Results from the Minnesota resuscitation consortium." Heart Rhythm 12(5): S461-S462.		Outcomes did not meet inclusion criteria
Alkadri, M. E., et al. (2013). "State-of-the-art paper: Therapeutic hypothermia in out of hospital cardiac arrest survivors." Catheterization and Cardiovascular Interventions 82(4): E482-E490.		Educational review article
Alshimemeri, A. (2014). "Therapeutic hypothermia after cardiac arrest." Ann Card Anaesth 17(4): 285-291.		Educational review article
Arrich, J., et al. (2016). "Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation." Cochrane Database Syst Rev 2: Cd004128		Systematic review, no additional records
Arrich, J., et al. (2016). "Pre-hospital versus in-hospital initiation of cooling for survival and neuroprotection after out-of-hospital cardiac arrest." Cochrane Database Syst Rev 3: Cd010570.		Systematic review, no additional records
Asadi, A., et al. (2015). "Factors predictive of survival after out-of-hospital cardiac arrest." Archives of Cardiovascular Diseases Supplements 7(2): 157.		Conference abstract
Atallah, P. C., et al. (2014). "Induced hypothermia after out-of-hospital cardiac arrest: Body habitus and survival." Circulation 130.		Conference abstract
Avalli, L., et al. (2014). "New treatment bundles improve survival in out-of-hospital cardiac arrest patients: a historical comparison." Resuscitation 85(9): 1240-1244.im		No comparison of treatment groups in question

Bae, K. S., et al. (2015). "The effect of mild therapeutic hypothermia on good neurological recovery after out-of-hospital cardiac arrest according to location of return of spontaneous circulation: a nationwide observational study." Resuscitation 89: 129-136.		No comparison of treatment groups in question
Behringer, W. (2015). "Intra-arrest-cooling CON." BMC Emerg Med 15.		Commentary
Benson-Cooper, K. A. (2015). "Therapeutic hypothermia is independently associated with favourable outcome after resuscitation from out-of-hospital cardiac arrest: a retrospective, observational cohort study." N Z Med J 128(1427): 33-37.		Unable to locate full-text article
Bernard, S., et al. (2015). "Induction of therapeutic hypothermia during out-of-hospital cardiac arrest." Resuscitation 96: 3.		Conference abstract
Bernard, S. A., et al. (2016). "Induction of Therapeutic Hypothermia During Out-of-Hospital Cardiac Arrest Using a Rapid Infusion of Cold Saline: The RINSE Trial (Rapid Infusion of Cold Normal Saline)." Circulation 134(11): 797-805.	X	
Bosson, N., et al. (2014). "Survival and neurologic outcome after out-of-hospital cardiac arrest: results one year after regionalization of post-cardiac arrest care in a large metropolitan area." Prehosp Emerg Care 18(2): 217-223.		No comparison of treatment groups in question
Bravo, P. E. and F. Kim (2014). "Enhancing approaches to therapeutic hypothermia in patients with sudden circulatory arrest." Curr Atheroscler Rep 16(11): 451.		Educational review article
Bucher, J. and A. Koyfman (2015). "Does Initiation of Therapeutic Hypothermia in the Out-of-Hospital Environment Improve Neurologic Outcomes?" Ann Emerg Med 66(4): 379-380.		Educational review article
Choi, S. W., et al. (2016). "Effect of therapeutic hypothermia on the outcomes after out-of-hospital cardiac arrest according to initial ECG rhythm and witnessed status: A nationwide observational interaction analysis." Resuscitation 100: 51-59.		No comparison of treatment groups in question
Cortez, E., et al. (2015). "Clinical Outcomes in Cardiac Arrest Patients Following Prehospital Treatment with Therapeutic Hypothermia." Prehosp Disaster Med 30(5): 452-456.		No comparison of treatment groups in question
Crane, R. D., et al. (2013). "Cardiac arrest post-return of spontaneous circulation emergency medical services initiation of therapeutic hypothermia: Chillingly low rates		Conference abstract

and contributing factors." Canadian Journal of Emergency Medicine 15: S18-S19.		
Debaty, G., et al. (2014). "Impact of intra-arrest therapeutic hypothermia in outcomes of prehospital cardiac arrest: a randomized controlled trial." Intensive Care Med 40(12): 1832-1842.	X	
Debaty, G., et al. (2016). "Hypothermia after cardiac arrest." Praticien en Anesthesie Reanimation 20(5): 234-240.		Unable to locate full-text article in English
DeLia, D., et al. (2015). "Prehospital transportation to therapeutic hypothermia centers and survival from out-of-hospital cardiac arrest." BMC Health Serv Res 15: 533.		No comparison of treatment groups in question
Della Mattia, A., et al. (2015). "Time to target temperature and outcome after out-of-hospital cardiac arrest." Circulation 132.		Conference abstract
Dell'anna, A. M., et al. (2014). "Early neuroprotection after cardiac arrest." Curr Opin Crit Care 20(3): 250-258.		Educational review article
Diao, M., et al. (2013). "Prehospital therapeutic hypothermia after cardiac arrest: A systematic review and meta-analysis of randomized controlled trials." Resuscitation 84(8): 1021-1028.		Systematic review, no additional records
Donnino, M. W., et al. (2015). "Temperature Management After Cardiac Arrest: An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation." Circulation 132(25): 2448-2456.		Systematic review, no additional records
Doshi, P., et al. (2016). "Effect of Therapeutic Hypothermia on Survival to Hospital Discharge in Out-of-hospital Cardiac Arrest Secondary to Nonshockable Rhythms." Acad Emerg Med 23(1): 14-20.		No comparison of treatment groups in question
Drennan, I. R., et al. (2014). "The effect of time to defibrillation and targeted temperature management on functional survival after out-of-hospital cardiac arrest." Resuscitation 85(11): 1623-1628.		No comparison of treatment groups in question
Freese, J., et al. (2014). "Effect of intra-arrest induction of therapeutic hypothermia on out-of-hospital cardiac arrest." Circulation 130.		Conference abstract
Gochnour, J., et al. (2013). "Effectiveness of initiating targeted hypothermia in post-		Conference abstract

cardiac arrest patients by an air medical team." Air Medical Journal 32(5): 251.	
Grenell, W., et al. (2015). "No survival benefit from prehospital induced therapeutic hypothermia in outof-hospital cardiac arrest." Academic Emergency Medicine 22(5): S163-S164.	Conference abstract
Grunau, B. E., et al. (2015). "Targeted temperature management after out-of-hospital cardiac arrest: who, when, why, and how?" Can Fam Physician 61(2): 129-134.	Educational review article
Gupta, C. and K. Parkins (2013). "Therapeutic hypothermia and temperature maintenance during post paediatric cardiac arrest transfers: How good are we?" Intensive Care Med 39: S173.	Conference abstract
Houston, K. and E. S. Lang (2015). "Out-of-hospital cardiac arrest in adults: lowering body temperature." BMJ Clin Evid 2015.	Systematic review, no additional records
Hovdenes, J., et al. (2016). "A low body temperature on arrival at hospital following out-of-hospital-cardiac-arrest is associated with increased mortality in the TTM-study." Resuscitation 107: 102-106.	No comparison of treatment groups in question
Huang, F. Y., et al. (2015). "The efficacy and safety of prehospital therapeutic hypothermia in patients with out-of-hospital cardiac arrest: A systematic review and meta-analysis." Resuscitation 96: 170-179.	Systematic review, no additional records
Hunter, B. R. (2016). "Therapeutic hypothermia during CPR did not improve survival to discharge in out-of-hospital cardiac arrest." Ann Intern Med 165(12): Jc70.	Educational review article
Hunter, B. R., et al. (2013). "The effect of prehospital therapeutic hypothermia on mortality and neurologic outcomes in out-of-hospital cardiac arrest: A systematic review and meta-analysis." Academic Emergency Medicine 20(5): S132-S133.	Conference abstract
Hunter, B. R., et al. (2014). "No benefit to prehospital initiation of therapeutic hypothermia in out-of-hospital cardiac arrest: a systematic review and meta-analysis." Acad Emerg Med 21(4): 355-364.	Systematic review, no additional records
Hwang, W. S., et al. (2015). "A system-wide approach from the community to the hospital for improving neurologic outcomes in out-of-hospital cardiac arrest patients." Eur J Emerg Med.	Outcomes did not meet inclusion criteria
Kim, F., et al. (2013). "Randomized clinical trial of pre-hospital induction of mild	Conference abstract

hypothermia in out-of-hospital cardiac arrest patients using a rapid infusion of 4oC normal saline." Circulation 128(24): 2705.		
Kim, F., et al. (2014). "Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest a randomized clinical trial." JAMA - Journal of the American Medical Association 311(1): 45-52.	X	
Kim, M. J., et al. (2014). "Neurological prognostication by gender in out-of-hospital cardiac arrest patients receiving hypothermia treatment." Resuscitation 85(12): 1732-1738.		No comparison of treatment groups in question
Lee, C. H. and D. C. Cone (2014). "The timing of therapeutic hypothermia initiation." Academic Emergency Medicine 21(4): 462-464		Commentary
Luis, S. S., et al. (2015). "Neurologic outcome in out of hospital cardiac arrest (OCHA) with prolonged downtime and therapeutic hypothermia (TH)." Resuscitation 96: 134.		Conference abstract
Mader, T. J., et al. (2014). "Comparative Effectiveness of Therapeutic Hypothermia After Out-of-Hospital Cardiac Arrest: Insight from a Large Data Registry." Ther Hypothermia Temp Manag 4(1): 21-31.		No comparison of treatment groups in question
Maynard, C., et al. (2015). "Effect of prehospital induction of mild hypothermia on 3-month neurological status and 1-year survival among adults with cardiac arrest: long-term follow-up of a randomized, clinical trial." J Am Heart Assoc 4(3): e001693.	X	
Nie, C., et al. (2016). "Prehospital therapeutic hypothermia after out-of-hospital cardiac arrest: a systematic review and meta-analysis." Am J Emerg Med 34(11): 2209-2216.		Systematic review, no additional records
Nordberg, P., et al. (2015). "Pre-hospital resuscitation INtra-arrest cooling effectiveness survival-The PRINCESS study." Resuscitation 96: 45.		Conference abstract
Pearson, D. A., et al. (2013). "Factors associated with delayed cooling in cardiac arrest patients." Academic Emergency Medicine 20(5): S249-S250.		Conference abstract
Pearson, D. A., et al. (2016). "Rapid cooling to 34°C is not associated with improved neurological outcome among post-cardiac arrest patients." Academic Emergency Medicine 23: S67.		Conference abstract

Randhawa, V., et al. (2015). "Pre-hospital versus in-hospital hypothermia for out-of-hospital cardiac arrest: A meta-analysis of randomized trials." J Am Coll Cardiol 65(10): A164.		Conference abstract
Rao, M. P., et al. (2014). "Pre-Hospital initiation of therapeutic hypothermia associated with better survival and neurologic outcome in a broad population of patients in North Carolina." Circulation 130.		Conference abstract
Rao, M. P., et al. (2016). "Therapeutic Hypothermia for Patients with Out-of-Hospital Cardiac Arrest in North Carolina." Prehosp Emerg Care 20(5): 630-636.	X	
Rotaru, L., et al. (2015). "The impact of telemedicine video vs. data on the cardiorespiratory arrest outcome-in pre-hospital care system in Romania." Resuscitation 96: 80.		Conference abstract
Schenfeld, E. M., et al. (2015). "Effect of prehospital initiation of therapeutic hypothermia in adults with cardiac arrest on time-to-target temperature." Cjem 17(3): 240-247.	X	
Schmid, B., et al. (2015). "Preclinical transnasal cooling during resuscitation in Germany: A look at the PRINCE study." Notfall und Rettungsmedizin 18(7): 588-594.		Unable to locate full-text article in English
Taccone, F. S. (2015). "Intra-arrest-cooling PRO." BMC Emerg Med 15.		Commentary
Tommasi, E., et al. (2014). "Cooling techniques in mild hypothermia after cardiac arrest." J Cardiovasc Med (Hagerstown).		Educational review article
Uray, T., et al. (2015). "Prehospital surface cooling is safe and can reduce time to target temperature after cardiac arrest." Resuscitation 87: 51-56.	X	
Varade, P., et al. (2015). "Earlier cooling in post cardiac arrest patients fails to show benefit." Neurology 84.		Conference abstract
Yajnik, V. and H. Gomez (2014). "Prehospital induction of mild hypothermia with cold normal saline for cardiac arrest: More harm than good?" Critical Care 18(5).		Educational review article
Yannopoiulos, D., et al. (2013). "Improved outcomes of cardiac arrest in a state-wide integrated resuscitation program: Results from the Minnesota resuscitation consortium." Circulation 128(22).		Conference abstract
Zhang, X. W., et al. (2015). "The effect of mild induced hypothermia on outcomes of		Systematic review, no

patients after cardiac arrest: a systematic review and meta-analysis of randomised controlled trials." Crit Care 19: 417.	additional records

Table 3-2: Final list of manuscripts that met inclusion criteria after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
Bernard, S.A., et al. (2016)[8]	Australia (Melbourne, Adelaide, Perth) Two-tiered response with BLS and ALS (Melbourne, Adelaide) All ALS (Perth)	Randomized controlled trial	Survival at hospital discharge Shockable/non-shockable rhythms with ROSC Tympanic temperature at hospital arrival Discharge location
Debaty, G., et al. (2014)[9]	France Mobile intensive care units (paramedic, nurse, physician)	Randomized controlled trial, multicenter	Concentration of neuron-specific enolase at 24 hours Concentration of interleukin-6, 8, 10 during first 72 hours ROSC rate ICU length of stay Survival to discharge, 30 days, 1 year
Kim, F., et al. (2014)[4]	Seattle and King County, Washington Two-tiered response with BLS and ALS (paramedics)	Randomized controlled trial	Survival at hospital discharge Neurological status at hospital discharge Various safety endpoints
Maynard, C., et al. (2015)[10]	Seattle and King County, Washington Two-tiered response with BLS	Long-term follow up of randomized controlled trial (Kim, et al. 2014)	Neurological status Mortality

	and ALS (paramedics)		
Rao, M.P., et al. (2016)[11]	North Carolina (CARES registry)	Retrospective review of CARES database	Survival to hospital discharge Neurologic condition at hospital discharge (CPC score)
Schenfeld, E.M., et al. (2015)[12]	Mecklenburg EMS Agency Carolinas Medical Center, Charlotte, NC Two-tiered response BLS and ALS (paramedics)	Prospective review of prehospital charts post-implementation of therapeutic hypothermia protocol compared to retrospective review of pre-implementation historical cohort November 2007 – November 2011	Time-to-target temperature following ROSC Survival to hospital discharge 1-year mortality Neurologic outcome at hospital discharge Transport time
Uray, T., et al. (2015)[13]	Vienna, Austria	Retrospective observation study	Time-to-target temperature following ROSC Hospital admission temperature Time to admission following ROSC Neurological outcome after 12 months

Systematic Review on Prehospital Therapeutic Hypothermia

PICO Question:

(P) For patients suffering out of hospital cardiac arrest (OHCA), (I) does induction of prehospital therapeutic hypothermia [targeted temperature management] (C) compared with in-hospital therapeutic hypothermia (O) change survival with favorable neurological/functional outcome?

Date: 12/2013 to 02/2017

Manuscripts
Bernard*, S.A., et al. (2016). "Induction of Therapeutic Hypothermia During Out-of-Hospital Cardiac Arrest Using a Rapid Infusion of Cold Saline: The RINSE Trial (Rapid Infusion of Cold Normal Saline)." Circulation 134(11): 797-805.
Bernard, S.A., et al. (2002). "Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia." N Engl J Med. 2002;346:557–563.
Callaway, C.W., et al. (2015). "Part 8: Post–Cardiac Arrest Care. 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care." 132(18 suppl 2):S465-S482.
Debaty*, G., et al. (2014). "Impact of intra-arrest therapeutic hypothermia in outcomes of prehospital cardiac arrest: a randomized controlled trial." Intensive Care Med 40(12): 1832-1842.
Dumas, F., et al. (2011). "Is hypothermia after cardiac arrest effective in both shockable and nonshockable patients?: insights from a large registry." Circulation.123:877–886.
Hypothermia after Cardiac Arrest Study Group. (2002). "Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest." N Engl J Med. 346:549–556.
Italian Cooling Experience (ICE) Study Group. (2012). "Early- versus late-initiation of therapeutic hypothermia after cardiac arrest: preliminary observations from the experience of 17 Italian intensive care units." Resuscitation 83(7): 823-828.
Kim*, F., et al. (2014). "Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest a randomized clinical trial." JAMA -

Journal of the American Medical Association 311(1): 45-52.
Mader, T.J., et al. (2014). "Comparative Effectiveness of Therapeutic Hypothermia After Out-of-Hospital Cardiac Arrest: Insight from a Large Data Registry." Ther Hypothermia Temp Manag. 4:21–31.
Maynard*, C., et al. (2015). "Effect of prehospital induction of mild hypothermia on 3-month neurological status and 1-year survival among adults with cardiac arrest: long-term follow-up of a randomized, clinical trial." J Am Heart Assoc 4(3): e001693.
Nichol, G., et al. (2013). "Does induction of hypothermia improve outcomes after in-hospital cardiac arrest?" Resuscitation. 84:620–625.
Nielsen, N., et al. (2009). "Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest." Acta Anaesthesiol Scand 53(7): 926-934.
Nielsen, N., et al. (2013). "Targeted temperature management at 33°C versus 36°C after cardiac arrest." N Engl J Med. 369:2197–2206.
Rao*, M.P., et al. (2016). "Therapeutic Hypothermia for Patients with Out-of-Hospital Cardiac Arrest in North Carolina." Prehosp Emerg Care 20(5): 630-636.
Schenfeld*, E. M., et al. (2015). "Effect of prehospital initiation of therapeutic hypothermia in adults with cardiac arrest on time-to-target temperature." Cjem 17(3): 240-247.
Sendelbach, S., et al. (2012). "Effects of variation in temperature management on cerebral performance category scores in patients who received therapeutic hypothermia post cardiac arrest." Resuscitation 83(7): 829-834.
Testori, C., et al. (2011). "Mild therapeutic hypothermia is associated with favourable outcome in patients after cardiac arrest with non-shockable rhythms." Resuscitation. 82:1162–1167.
Uray*, T., et al. (2015). "Prehospital surface cooling is safe and can reduce time to target temperature after cardiac arrest." Resuscitation 87: 51-56.
Vaahersalo, J., et al. (2013). "Therapeutic hypothermia after out-of-hospital cardiac arrest in Finnish intensive care units: the FINNRESUSCI study." Intensive Care Med. 39:826–837.

*Included in current review

Systematic Review on the Use of Prehospital CPAP/BIPAP

Concept Problem

Management of acute respiratory distress is common for emergency medical services (EMS) professionals in the prehospital setting.[1] The causes of acute respiratory distress are various, and understanding the true underlying etiology of the observed symptoms is a challenge for EMS professionals.[2] However, though the exact etiology may not be known, immediate management and stabilization remains crucial.

One tool available to prehospital providers for management of patients experiencing acute respiratory distress is continuous positive airway pressure (CPAP) devices. The use of these devices started within the hospital setting and has been found to be beneficial in the prehospital setting.[3,4] These devices provide noninvasive positive pressure during spontaneous patient respiration, which decreases patient work of breathing and dyspnea. Preliminary evidence has demonstrated that the use of CPAP may decrease the need for invasive endotracheal intubation and even length of stay in the hospital.[5,6]

In this systematic review, we evaluated the evidence on the use of CPAP in the prehospital setting. The specific question developed with advice from NHTSA for this topic area is the following PICO question:

(P) For adult patients requiring non-invasive positive pressure ventilation for respiratory distress in the prehospital setting, (I) does CPAP/BiPAP (C) compared to BVM or

supplemental oxygen alone (O) improve respiratory status, death, decompensation leading to further advanced airway intervention, and intubation rates?

This PICO question mirrors a previous systematic review that evaluated data prior to 2012. Thus, the current evaluation serves as an update to the comprehensive work by Williams et al.[2]

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in this search were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO question. The search dates were from 2012 to January 31, 2017.

The search terms were exploded and are as follows: Search 1: "acute pulmonary oedema" OR "pulmonary oedema" OR "acute heart failure" OR "acute respiratory failure" AND "continuous positive airway pressure"; Search 2: "ambulance" OR "emergency medical services" OR "pre-hospital care" OR "mobile health units" OR "paramedic" AND "continuous positive airway pressure." Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were human (no basic science or animal models). Exclusion criteria included: studies not specifically examining patients with acute respiratory failure, studies that did not specifically compare the

use of CPAP to standard medical treatment (BVM or supplemental oxygen alone), and studies exclusively including neonatal patients.

Results

A systematic review of the literature from 2012 to 01/2017 was completed with the identification of 553 articles matching search criteria (Figure 4-1). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 434 records were screened by two independent reviewers. Of these, 44 satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 4-1). Eight (8) manuscripts were selected for the final list of manuscripts that met inclusion criteria after full text review (Table 4-2).

Conclusion

In this systematic review, we evaluate the evidence on the use of CPAP in the prehospital setting answering the following question:

> *(P) For adult patients requiring non-invasive positive pressure ventilation for respiratory distress in the prehospital setting, (I) does CPAP/BiPAP (C) compared to BVM or supplemental oxygen alone (O) improve respiratory status, death, decompensation leading to further advanced airway intervention, and intubation rates?*

Utilizing a comprehensive search strategy, a total of 553 articles were extracted. After independent evaluation by two reviewers, eight (8) manuscripts satisfied inclusion. In total,

between this review and that done by Williams 2012, from 01/1980 to 01/2017, fifteen (15) total manuscripts have been published that evaluate the stated PICO question concerning prehospital CPAP use.

References

1. Prekker ME, Feemster LC, Hough CL, Carlbom D, Crothers K, Au DH, Rea TD, Seymour CW. The epidemiology and outcome of prehospital respiratory distress. *Acad Emerg Med.* 2014;21(5):543-550.
2. Williams TA, Finn J, Perkins GD, Jacobs IG. Prehospital continuous positive airway pressure for acute respiratory failure: a systematic review and meta-analysis. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors.* 2013;17(2):261-273.
3. Knox N, Chinwe O, Themba N, Joseph F, Hormoz A. Relationship between intubation rate and continuous positive airway pressure therapy in the prehospital setting. *World Journal of Emergency Medicine.* 2015;6(1):60-66.
4. Aguilar SA, Lee J, Dunford JV, Castillo E, Lam B, Choy J, Patel E, Pringle J, Serra J. Assessment of the addition of prehospital continuous positive airway pressure (CPAP) to an urban emergency medical services (EMS) system in persons with severe respiratory distress. *J Emerg Med.* 2013;45(2):210-219.
5. Thompson J, Petrie DA, Ackroyd-Stolarz S, Bardua DJ. Out-of-hospital continuous positive airway pressure ventilation versus usual care in acute respiratory failure: a randomized controlled trial. *Ann Emerg Med.* 2008;52(3):232-241, 241.e231.
6. Roessler MS, Schmid DS, Michels P, Schmid O, Jung K, Stöber J, Neumann P, Quintel M, Moerer O. Early out-of-hospital non-invasive ventilation is superior to standard medical treatment in patients with acute respiratory failure: A pilot study. *Emergency Medicine Journal.* 2012;29(5):409-414.

7. Cheskes S, Turner L, Thomson S, Aljerian N. The impact of prehospital continuous positive airway pressure on the rate of intubation and mortality from acute out-of-hospital respiratory emergencies. *Prehospital emergency care : official journal of the National Association of EMS Physicians and the National Association of State EMS Directors.* 2013;17(4):435-441.

8. Garrote JI, Aylagas D, Gutierrez JM, Sinisterra JA, Gowran BM, Medina A, Díaz-Tendero J, Gómez-Calcerrada P, Crespo R. Noninvasive Mechanical Ventilation in Helicopter Emergency Medical Services Saves Time and Oxygen and Improves Patient and Mission Safety: A Pilot Study. *Air Medical Journal.* 2015;34(4):218-222.

9. Nielsen VM, Madsen J, Aasen A, Toft-Petersen AP, Lubcke K, Rasmussen BS, Christensen EF. Prehospital treatment with continuous positive airway pressure in patients with acute respiratory failure: a regional observational study. *Scand J Trauma Resusc Emerg Med.* 2016;24(1):121.

10. Willmore A, Dionne R, Maloney J, Ouston E, Stiell I. Effectiveness and safety of a prehospital program of continuous positive airway pressure (CPAP) in an urban setting. *Canadian Journal of Emergency Medicine.* 2015;17(6):609-616.

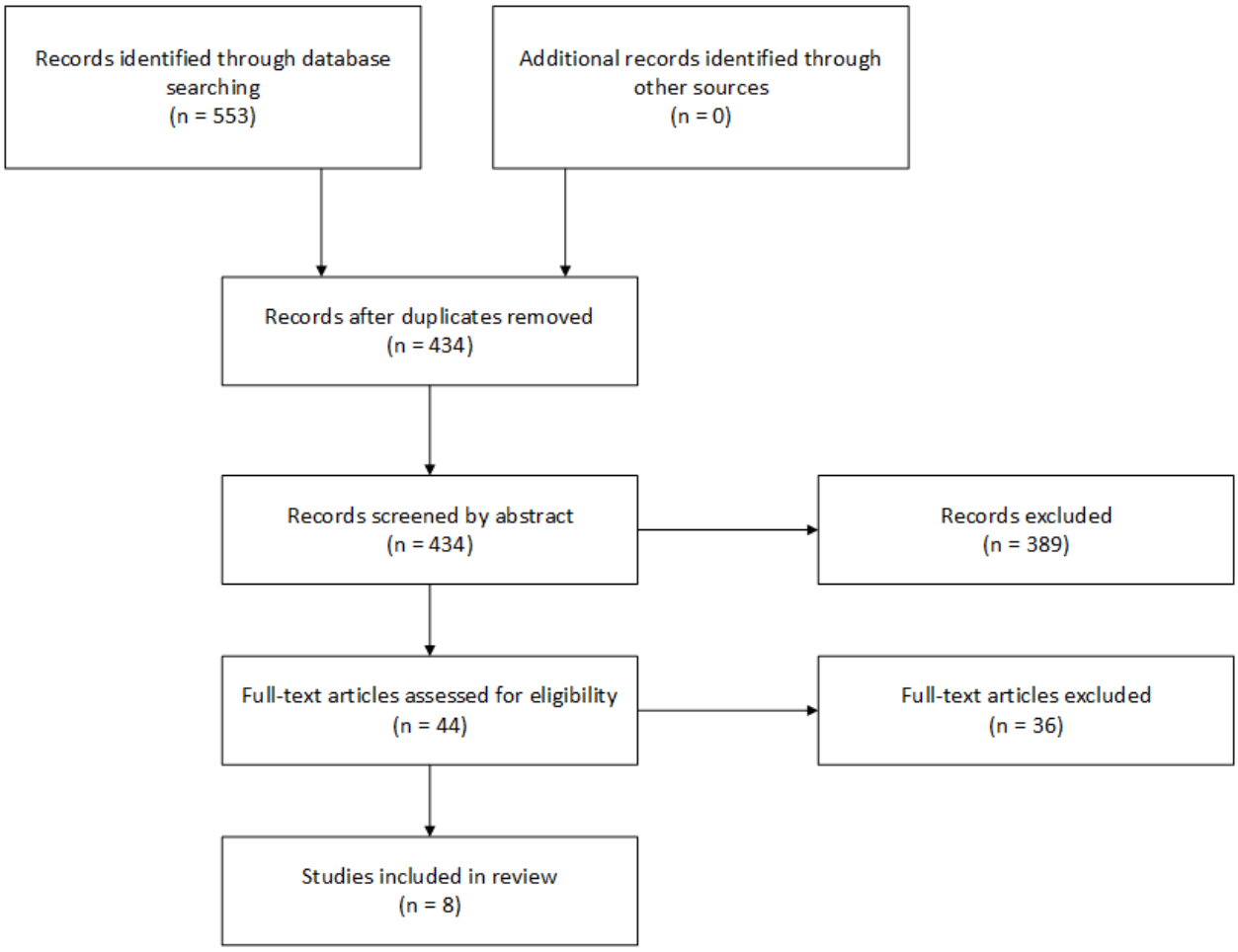

Figure 4-1: Flow diagram of search and review process.

Table 4-1: Abstracts that satisfied the PICO question search terms and inclusion criteria. Manuscripts were selected for full text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for Exclusion
(2014). "Positive airway pressure therapy for heart failure." World J Cardiol 6(11): 1175-1191.		Conference abstract
Aguilar, S. A., et al. (2013). "Assessment of the addition of prehospital continuous positive airway pressure (CPAP) to an urban emergency medical services (EMS) system in persons with severe respiratory distress." Journal of Emergency Medicine 45(2): 210-219.	X	
Austin, M. A., et al. (2013). "Effect of continuous positive airway pressure (CPAP) on mortality in the treatment of acute cardiogenic pulmonary oedema (ACPO) in the pre-hospital setting: Randomised controlled trial." EMA - Emergency Medicine Australasia 25: 5.		Conference abstract
Baird, J. S. and T. M. Ravindranath (2012). "Out-of-hospital noninvasive ventilation: Epidemiology, technology and equipment." Pediatric Reports 4(2).		Educational review article
Bakke, S. A., et al. (2014). "Continuous positive airway pressure and noninvasive ventilation in prehospital treatment of patients with acute respiratory failure: a systematic review of controlled studies." Scand J Trauma Resusc Emerg Med 22: 69.		Systematic review, no additional records
Berg, K. M., et al. (2012). "Noninvasive ventilation for acute respiratory failure: A review of the literature and current guidelines." Intern Emerg Med 7(6): 539-545.		Educational review article
Bledsoe, B. E., et al. (2012). "Low-fractional oxygen concentration continuous positive airway pressure is effective in the prehospital setting." Prehosp Emerg Care 16(2): 217-221.		No comparison of treatment groups in question
Budd, R., et al. (2014). "Noninvasive positive pressure ventilation. Changing the respiratory distress prehospital paradigm of ventilation & intubation." Jems 39(11): 22-27.		Educational review article
Cappiello, J. L. and M. B. Hocker (2014). "Noninvasive ventilation in severe acute asthma." Respir Care 59(10): e149-e152.		Case report

Cheskes, S., et al. (2012). "Feasibility of continuous positive airway pressure by primary care paramedics." Prehosp Emerg Care 16(4): 535-540.		No comparison of treatment groups in question
Cheskes, S., et al. (2013). "Does prehospital continuous positive airway pressure impact the rate of intubation and mortality of acute respiratory emergencies?" Canadian Journal of Emergency Medicine 15: S52.		Conference abstract
Cheskes, S., et al. (2013). "The impact of prehospital continuous positive airway pressure on the rate of intubation and mortality from acute out-of-hospital respiratory emergencies." Prehosp Emerg Care 17(4): 435-441.	X	
Cheskes, S., et al. (2013). "The safety of prehospital continuous positive airway pressure use by primary care paramedics." Canadian Journal of Emergency Medicine 15: S17.		Conference abstract
Cooper, T., et al. (2014). "Emergency medical services initiation of non-invasive positive pressure ventilation in urban acute congestive heart failure patients." Ann Emerg Med 64(4): S51-S52.		Conference abstract
Cudini, D., et al. (2013). "The use of Continuous Positive Airway Pressure for management of Acute Respiratory Failure in the COPD Patient: Time for Pre Hospital Intervention." Australasian Journal of Paramedicine 10(3): 14.		Conference abstract
Cuny, J., et al. (2012). "Management of acute bronchospasm respiratory distress with CPAP ventilation associated with nebulization in the prehospital emergency setting." Critical Care 16: S48.		No comparison of treatment groups in question
Esquinas, A. M. and B. Mina (2013). "Early out-of-hospital non-invasive ventilation vs. standard medical treatment in patients with acute respiratory failure. Patient selection is the first priority." J Emerg Med 45(4): 618.		Letter to the Editor
Garrote, J. I., et al. (2015). "Noninvasive Mechanical Ventilation in Helicopter Emergency Medical Services Saves Time and Oxygen and Improves Patient and Mission Safety: A Pilot Study." Air Med J 34(4): 218-222.	X	
Goodacre, S., et al. (2014). "Prehospital noninvasive ventilation for acute respiratory failure: Systematic review, network meta-analysis, and individual patient data meta-analysis." Academic Emergency Medicine 21(9): 960-970.		Systematic review, no additional records

Groner, K., et al. (2012). "Observational study on the safety of out-of-hospital BLS application of CPAP in the dyspneic patient." Ann Emerg Med 60(4): S43.		Conference abstract
Hess, D. R. (2013). "Noninvasive ventilation for acute respiratory failure." Respir Care 58(6): 950-972.		Educational review article
Hess, R., et al. (2013). "Discussion: Pre-hospital oxygen therapy." Respir Care 58(1): 95-97.		Educational review article
Knox, N., et al. (2015). "Relationship between intubation rate and continuous positive airway pressure therapy in the prehospital setting." World Journal of Emergency Medicine 6(1): 60-66.	X	
Kovala, C. M., et al. (2013). "Compliance and opportunity in the use of a prehospital continuous positive airway pressure protocol in acute decompensated heart failure." Academic Emergency Medicine 20(5): S268.		Conference abstract
Lee, J. S., et al. (2015). "Factors Associated with Failure of Non-invasive Positive Pressure Ventilation in a Critical Care Helicopter Emergency Medical Service." Prehosp Disaster Med 30(3): 239-243.		No comparison of treatment groups in question
Luiz, T., et al. (2016). "Prehospital CPAP Therapy by Emergency Physicians in Patients with Acute Respiratory Failure due to Acute Cardiogenic Pulmonary Edema or Acutely Exacerbated COPD." In Vivo 30(2): 133-139.		Physician-level providers
Mal, S., et al. (2013). "The impact of prehospital non-invasive positive pressure support ventilation in adult patients with severe respiratory distress: A systematic review and meta-analysis." Academic Emergency Medicine 20(5): S210.		Conference abstract
Mal, S., et al. (2014). "Effect of out-of-hospital noninvasive positive-pressure support ventilation in adult patients with severe respiratory distress: A systematic review and meta-analysis." Ann Emerg Med 63(5): 600-607.e601.		Systematic review, no additional records
Mal, S., et al. (2013). "The impact of prehospital noninvasive positive pressure support ventilation in adult patients with acute respiratory distress: A systematic review and meta-analysis." Canadian Journal of Emergency Medicine 15: S3.		Conference abstract
Mal, S. and B. H. Rowe (2014). "Review: Prehospital noninvasive ventilation for severe respiratory distress reduces hospital mortality." Ann Intern Med 160(10): JC2.		Summary article

Mazzeo, B., et al. (2017). "Management of Hospitalized Asthmatic Children Before Transport." Air Med J 36(1): 30-33.		No comparison of treatment groups in question
Nielsen, V. M., et al. (2016). "Prehospital treatment with continuous positive airway pressure in patients with acute respiratory failure: a regional observational study." Scand J Trauma Resusc Emerg Med 24(1): 121.	X	
Pandor, A., et al. (2015). "Pre-hospital non-invasive ventilation for acute respiratory failure: A systematic review and cost-effectiveness evaluation." Health Technology Assessment 19(42): 1-8.		Systematic review, no additional records
Roessler, M. S., et al. (2012). "Early out-of-hospital non-invasive ventilation is superior to standard medical treatment in patients with acute respiratory failure: A pilot study." Emergency Medicine Journal 29(5): 409-414.	X	
Salturk, C. and A. M. Esquinas (2016). "CPAP Devices for Emergency Prehospital Use: Looking Inside of It." Respir Care 61(5): 719.		Letter to the editor
Sen, A. (2015). "ACP Journal Club: review: in acute respiratory failure, prehospital CPAP reduces mortality and intubation rates." Ann Intern Med 162(8): Jc5.		Summary article
Spijker, E. E., et al. (2013). "Practical use, effects and complications of prehospital treatment of acute cardiogenic pulmonary edema using the Boussignac CPAP system." Int J Emerg Med 6(1).		Device specific study
Strnad, M., et al. (2016). "Bedside lung ultrasound for monitoring the effectiveness of prehospital treatment with continuous positive airway pressure in acute decompensated heart failure." Eur J Emerg Med 23(1): 50-55		Not relevant to PICO question
Vital, F. M., et al. (2013). "Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema." Cochrane Database Syst Rev 5: CD005351.		Systematic review, no additional records
Williams, B., et al. (2013). "When pressure is positive: A literature review of the prehospital use of continuous positive airway pressure." Prehosp Disaster Med 28(1): 52-60.		
Williams, T. A., et al. (2013). "Prehospital continuous positive airway pressure for acute respiratory failure: a systematic review and meta-analysis." Prehosp Emerg Care 17(2):		Systematic review used for basis of search

261-273.	
Willmore, A., et al. (2015). "Effectiveness and safety of a prehospital program of continuous positive airway pressure (CPAP) in an urban setting." Canadian Journal of Emergency Medicine 17(6): 609-616.	X

Table 4-2: Final list of manuscripts which met inclusion criteria after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
Aguilar, S. A., et al. (2013)[4]	San Diego, CA Paramedics	Retrospective review of prehospital charts pre- and post-implementation of CPAP protocol September 2005 – September 2010	Vital signs Need for prehospital intubation Acuity on admission Level of admission Length of hospital stay Mortality
Cheskes, S., et al. (2013)[7]	Peel, Ontario, Canada Advanced care paramedics and primary care paramedics	Retrospective review of prehospital charts pre- and post-implementation of CPAP protocol June 2008 – June 2010	Admission to hospital Admission to ISU Length of hospital stay In-hospital intubation In-hospital mortality DNR status
Garrote, J. I., et al. (2015)[8]	Spain Helicopter EMS Nurse and physician team	Prospective non-randomized controlled trial	Vital signs Patient comfort Stabilization time Oxygen consumption In-flight complications
Knox, N., et al. (2015)[3]	New Jersey Paramedics	Retrospective cohort study	Rate of intubation
Nielsen, V. M., et al. (2016)[9]	North Denmark Three tier system: primary	Prospective review of prehospital charts post-implementation of CPAP protocol compared to retrospective	For prospective CPAP group: Adverse events Hospital length of stay

	ambulance, paramedic response vehicles, physician staffed mobile emergency care units	review of pre-implementation historical cohort	ICU admission In-hospital and 30-day mortality For pre/post: Vital signs (SpO2, respiratory rate)
Roessler, M. S., et al. (2012)[6]	Goettingen, Germany Two-tiered system: paramedics and emergency physicians	Randomized controlled trial (standard medical therapy or CPAP)	Vital signs Frequency and length of ICU stay Hospital length of stay Mortality
Willmore, A., et al. (2015)[10]	Eastern Ontario Basic life support and advanced life support paramedics	Retrospective review of prehospital charts pre- and post-implementation of CPAP protocol	Mortality Protocol adherence Prehospital and ED intubation rates Non-invasive ventilation in the ED ED disposition Hospital length of stay

Systematic Review on the Use of Prehospital CPAP/BIPAP

PICO Question:

(P) For adult patients requiring non-invasive positive pressure ventilation for respiratory distress in the prehospital setting, (I) does CPAP/BiPAP (C) compared to BVM or supplemental oxygen alone (O) improve respiratory status, death, decompensation leading to further advanced airway intervention, and intubation rates?

Date: 01/1980 to 01/2017

Manuscripts
Aguilar*, S.A., et al. (2013). "Assessment of the addition of prehospital continuous positive airway pressure (CPAP) to an urban emergency medical services (EMS) system in persons with severe respiratory distress." Journal of Emergency Medicine 45(2): 210-219.
Cheskes*, S., et al. (2013). "The impact of prehospital continuous positive airway pressure on the rate of intubation and mortality from acute out-of-hospital respiratory emergencies." Prehosp Emerg Care 17(4): 435-441.
Dib, J.E., et al. (2012). “Prehospital use of continuous positive airway pressure for acute severe congestive heart failure.” J Emerg Med. 42:553–8.
Ducros, L., et al. (2011). “CPAP for acute cardiogenic pulmonary oedema from out-of-hospital to cardiac intensive care unit: a randomized multicentre study.” Intensive Care Med. 37:1501–9.
Frontin, P, et al. (2011). “Continuous positive airway pressure for cardiogenic pulmonary edema: a randomized study.” Am J Emerg Med. 29:775–81.
Garrote*, J.I., et al. (2015). "Noninvasive Mechanical Ventilation in Helicopter Emergency Medical Services Saves Time and Oxygen and Improves Patient and Mission Safety: A Pilot Study." Air Med J 34(4): 218-222.
Hastings, D., et al. (1998). “CPAP. A supportive adjunct for congestive heart failure in the prehospital setting.” JEMS. 23(9):58–65.
Hubble, M.W., et al. (2006). “Effectiveness of prehospital continuous positive airway pressure in

the management of acute pulmonary edema. Prehosp Emerg Care." 10:430–9.
Knox*, N., et al. (2015). "Relationship between intubation rate and continuous positive airway pressure therapy in the prehospital setting." World Journal of Emergency Medicine 6(1): 60-66.
Nielsen*, V.M., et al. (2016). "Prehospital treatment with continuous positive airway pressure in patients with acute respiratory failure: a regional observational study." Scand J Trauma Resusc Emerg Med 24(1): 121.
Roessler*, M.S., et al. (2012). "Early out-of-hospital non-invasive ventilation is superior to standard medical treatment in patients with acute respiratory failure: A pilot study." Emergency Medicine Journal 29(5): 409-414.
Thompson, J., et al. (2008). "Out-of-hospital continuous positive airway pressure ventilation versus usual care in acute respiratory failure: a randomized controlled trial." Ann Emerg Med. 52:232–41.
Warner, G.S. (2010). "Evaluation of the effect of prehospital application of continuous positive airway pressure therapy in acute respiratory distress." Prehosp Disaster Med. 25:87–91.
Williams, T.A., et al. (2013). "Prehospital continuous positive airway pressure for acute respiratory failure: a systematic review and meta-analysis." Prehosp Emerg Care 17(2): 261-273.
Willmore*, A., et al. (2015). "Effectiveness and safety of a prehospital program of continuous positive airway pressure (CPAP) in an urban setting." Canadian Journal of Emergency Medicine 17(6): 609-616.

*Included in current review

Systematic Review on the Use of Pharmacological Pain Management for Trauma-Related Pain

Concept Problem

Management of acute pain in the prehospital setting has been recognized as a key management step in emergency care.[1] However, a number of evaluations have demonstrated that acute pain is undermanaged in the prehospital setting.[2-4] This issue has also been noted in the vulnerable pediatric patient population where implementation of best practice recommendations did not improve pain management [5,6] Most concerning, the continued high severity of patient pain levels may cause complications and worsening patient outcomes for adults and children alike.[1,7]

As part of the update to the EMS Scope of Practice, particular attention was placed on the importance of improving pain management in the prehospital setting. Specifically, due to this significant issue, NHTSA seeks to understand whether providers below the paramedic level can safely and effectively provide analgesia to patients experiencing acute pain. Thus, in this systematic review, we evaluate the evidence related to pharmacological pain management for trauma-related pain in the prehospital setting. The specific question developed with advice from NHTSA for this topic area is the following PICO:

> *(P) In patients requiring pain management following an acute traumatic event in the prehospital setting, (I) can EMT and AEMT providers administer pharmacological pain medications (C) compared to paramedics (O) safely and effectively?*

This PICO question evaluates all data from 1980 to the date of this search. Thus, the current evaluation serves as a comprehensive evaluation of this PICO question.

Search Strategy

To identify studies eligible for review, an information specialist performed computerized searches of bibliographic databases: MEDLINE/PubMed (National Library of Medicine, Washington, DC), Embase (Elsevier B.V., Amsterdam, The Netherlands), and the Cochrane Library (The Cochrane Collaboration, Oxford, England). Terms used in this search were mapped to Medical Subject Headings (MeSH), and other terms were defined for the PICO. The search dates were from 1980 to February 14, 2017.

The search terms were exploded and are as follows: “prehospital” OR ”emergency medical services” OR “emergency treatment” OR “emergency care” AND “pain management” OR “pain” OR “acute pain” OR “analge*” OR “morphine” OR “fentanyl” OR “ketamine” or “nitrous” OR “opiate” AND “trauma” OR “injury” OR “traumatic injury” OR “acute injury” OR “acute trauma.” Additionally, review articles were hand searched for relevant papers.

Inclusion criteria used for the evaluation of this search were manuscripts that satisfied the PICO question, were published in English, in peer-reviewed journals, and whose subjects were human (no basic science or animal models). Exclusion criteria included: studies not specifically comparing EMT/AEMT and paramedic provider levels and studies examining pain relief for non-acute traumatic events or non-traumatic pain.

Results

A systematic review of the literature from 1980 to 02/2017 was completed with the identification of 2,086 articles matching search criteria (Figure 5-1). No additional records were identified by hand searching relevant review articles. Duplicates were removed and 1,838 records were screened by two independent reviewers. Of these, forty-one (41) satisfied inclusion criteria and underwent full text review for eligibility in the analysis (Table 5-1). Zero (0) manuscripts were selected for the final list of manuscripts which met inclusion criteria after full text review (Table 5-2).

Though all forty-one (41) articles included in the original extraction were assessed by full text review, none compared administration between levels of providers as framed in the developed PICO question. Additionally, some studies did not report outcomes related to prehospital pain management.

Conclusion

In this systematic review, we evaluate the evidence on the use of naloxone in the prehospital setting answering the following question:

> *(P) In patients requiring pain management following an acute traumatic event in the prehospital setting, (I) can EMT and AEMT providers administer pharmacological pain medications (C) compared to paramedics (O) safely and effectively?*

Utilizing a comprehensive search strategy, a total of 2,086 articles were extracted. After independent evaluation by two reviewers, no manuscripts satisfied inclusion. No publications

evaluated satisfied the stated PICO question concerning EMT and AEMT providers administering pharmacological pain management for acute trauma in the prehospital setting. This question addressed the needs of the update on the EMS Scope of Practice to understand whether practice levels other than paramedic may safely provide pharmacological pain management. This review does not comment on the overall use of pharmacological pain management following an acute traumatic event.

References

1. Gausche-Hill M, Brown KM, Oliver ZJ, Sasson C, Dayan PS, Eschmann NM, Weik TS, Lawner BJ, Sahni R, Falck-Ytter Y, Wright JL, Todd K, Lang ES. An Evidence-based Guideline for prehospital analgesia in trauma. *Prehosp Emerg Care.* 2014;18 Suppl 1:25-34.
2. White LJ, Cooper JD, Chambers RM, Gradisek RE. Prehospital use of analgesia for suspected extremity fractures. *Prehosp Emerg Care.* 2000;4(3):205-208.
3. Abbuhl FB, Reed DB. Time to analgesia for patients with painful extremity injuries transported to the emergency department by ambulance. *Prehosp Emerg Care.* 2003;7(4):445-447.
4. Galinski M, Ruscev M, Gonzalez G, Kavas J, Ameur L, Biens D, Lapostolle F, Adnet F. Prevalence and management of acute pain in prehospital emergency medicine. *Prehosp Emerg Care.* 2010;14(3):334-339.
5. Samuel N, Steiner IP, Shavit I. Prehospital pain management of injured children: a systematic review of current evidence. *Am J Emerg Med.* 2015;33(3):451-454.
6. Browne LR, Shah MI, Studnek JR, Ostermayer DG, Reynolds S, Guse CE, Brousseau DC, Lerner EB. Multicenter Evaluation of Prehospital Opioid Pain Management in Injured Children. *Prehosp Emerg Care.* 2016;20(6):759-767.
7. Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. *Arch Pediatr Adolesc Med.* 1998;152(2):147-149.

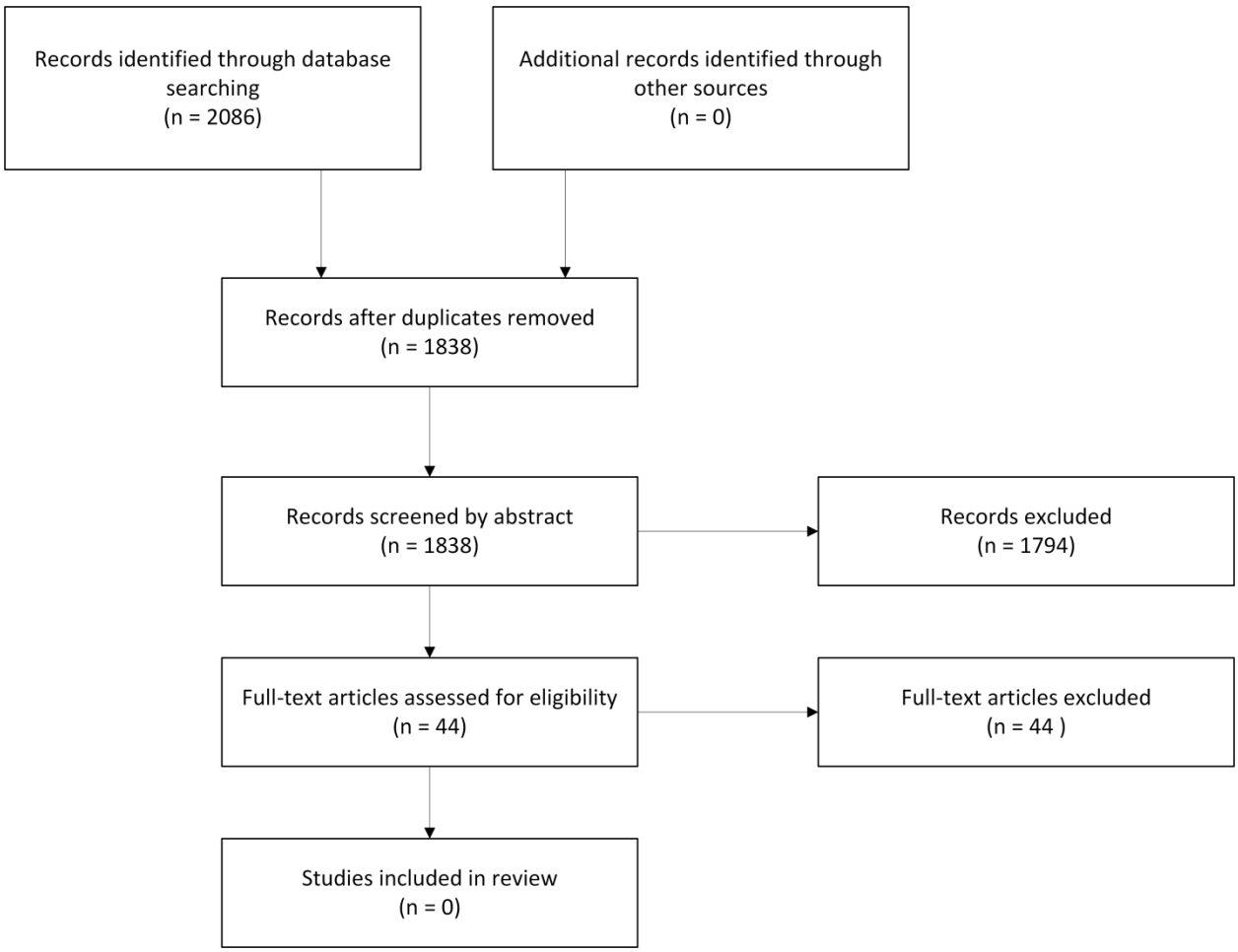

Figure 5-1: Flow diagram of search and review process

Table 5-1: Abstracts that satisfied PICO search terms and inclusion criteria. Manuscripts were selected for full-text review and marked as included or excluded with reasons for exclusion.

Study	Included	Reason for Exclusion
Ardeel, E. (2012). "Adverse effects following prehospital use of ketamine by paramedics." Academic Emergency Medicine 19: S269-S270.		Conference abstract
Berben, S. A., et al. (2012). "Facilitators and barriers in pain management for trauma patients in the chain of emergency care." Injury 43(9): 1397-1402.		Qualitative study with no report on outcomes of interest
Berben, S. A., et al. (2011). "Prevalence and relief of pain in trauma patients in emergency medical services." Clin J Pain 27(7): 587-592.		No comparison between provider levels reported
Blackman, V. S., et al. (2016). "Prevalence and Predictors of Prehospital Pain Assessment and Analgesic Use in Military Trauma Patients, 2010-2013." Prehosp Emerg Care 20(6): 737-751.		No comparison between provider levels reported
Bowman, W. J., et al. (2012). "The effects of standardized trauma training on prehospital pain control: have pain medication administration rates increased on the battlefield?" J Trauma Acute Care Surg 73(2 Suppl 1): S43-48.		No comparison between provider levels reported
Bradford, P., et al. (2013). "Analysis of prehospital treatment of pain in the multisystem trauma patient at a community level 2 trauma centre." Canadian Journal of Emergency Medicine 15: S36.		Conference abstract
Brown, K. M., et al. (2014). "The implementation and evaluation of an evidence-based statewide prehospital pain management protocol developed using the national prehospital evidence-based guideline model process for emergency medical services." Prehosp Emerg Care 18 Suppl 1: 45-51.		No comparison between provider levels reported
Browne, L. R., et al. (2016). "Multicenter Evaluation of Prehospital Opioid Pain Management in Injured Children." Prehosp Emerg Care 20(6): 759-767.		No comparison between provider levels reported
Browne, L. R., et al. (2016). "Prehospital Opioid Administration in the Emergency Care of Injured Children." Prehosp Emerg Care 20(1): 59-65.		No comparison between provider levels reported

Byyny, R., et al. (2010). "Safety of prehospital single-dose fentanyl in adult trauma patients." Academic Emergency Medicine 17: S175.	Conference abstract
Carlson, J. N., et al. (2016). "Procedures Performed by Emergency Medical Services in the United States." Prehosp Emerg Care 20(1): 15-21.	No outcomes or comparison between provider levels reported
Castle, N. and R. Naidoo (2012). "Achieving prehospital analgesia." Emerg Med J 29(9): 765-766.	Reflection piece
Devellis, P., et al. (1998). "Prehospital fentanyl analgesia in air transported pediatric trauma patients." Pediatr Emerg Care 14(5): 321-323	No comparison between provider levels reported
Dijkstra, B. M., et al. (2014). "Review on pharmacological pain management in trauma patients in (pre-hospital) emergency medicine in the Netherlands." Eur J Pain 18(1): 3-19.	Systematic review; no new records identified
Fullerton-Gleason, L., et al. (2002). "Prehospital administration of morphine for isolated extremity injuries: a change in protocol reduces time to medication." Prehosp Emerg Care 6(4): 411-416.	No comparison between provider levels reported
Galinski, M., et al. (2011). "Out-of-hospital emergency medicine in pediatric patients: prevalence and management of pain." Am J Emerg Med 29(9): 1062-1066.	No comparison between provider levels reported
Galinski, M., et al. (2010). "Prevalence and management of acute pain in prehospital emergency medicine." Prehosp Emerg Care 14(3): 334-339.	No comparison between provider levels reported
Gausche-Hill, M., et al. (2014). "An Evidence-based Guideline for prehospital analgesia in trauma." Prehosp Emerg Care 18 Suppl 1: 25-34.	No comparison between provider levels reported
Gray, A., et al. (1997). "Paramedic use of nalbuphine in major injury." Eur J Emerg Med 4(3): 136-139.	Conference abstract
Haley, K., et al. (2012). "Assessment and treatment of pain in adult prehospital patients after pediatric focused pain management education and pain protocol implementation." Academic Emergency Medicine 19: S268.	Conference abstract
Haley, K. B., et al. (2016). "Effect of System-Wide Interventions on the Assessment and Treatment of Pain by Emergency Medical Services Providers." Prehosp Emerg Care 20(6): 752-758.	No comparison between provider levels reported
Infinger, A. E. and J. R. Studnek (2014). "An assessment of pain management among	No comparison between

patients presenting to emergency medical services after suffering a fall.	provider levels reported
Izsak, E., et al. (2008). "Prehospital pain assessment in pediatric trauma." Prehosp Emerg Care 12(2): 182-186.	No comparison between provider levels reported
Jennings, P., et al. (2013). "Ketamine is superior to morphine alone for the management of traumatic pain in the prehospital setting: A randomized controlled trial." Australasian Journal of Paramedicine 10(2): 14-15.	Conference abstract
Jennings, P. A., et al. (2011). "Ketamine as an analgesic in the pre-hospital setting: a systematic review." ActaAnaesthesiol Scand55(6): 638-643.	Systematic review; no new records identified
Jennings, P. A., et al. (2012). "Morphine and ketamine is superior to morphine alone for out-of-hospital trauma analgesia: a randomized controlled trial." Ann Emerg Med 59(6): 497-503.	No comparison between provider levels reported
Losvik, O. K., et al. (2015). "Ketamine for prehospital trauma analgesia in a low-resource rural trauma system: a retrospective comparative study of ketamine and opioid analgesia in a ten-year cohort in Iraq." cand J Trauma Resusc Emerg Med 23: 94.	Review article; no new records identified
Maddock, A. and J. Ferris (2013). "Prehospital analgesia." Br J Anaesth 110(5): 848.	Correspondence piece
Madeira, F., et al. (2013). "Prehospital pain management: Do we have to learn more about it?" Eur J Anaesthesiol 30: 203-204.	Conference abstract
McCarthy, D. T. (2013). "Prehospital analgesia: multimodal considerations." Br J Anaesth 110(5): 849.	Correspondence piece
McEachin, C. C., et al. (2002). "Few emergency medical services patients with lower-extremity fractures receive prehospital analgesia." Prehosp Emerg Care 6(4): 406-410.	No comparison between provider levels reported
Murphy, A. P., et al. (2016). "Intranasal fentanyl for the prehospital management of acute pain in children." European Journal of Emergency Medicine.	Conference abstract
Petz, L. N., et al. (2015). "Prehospital and en route analgesic use in the combat setting: a prospectively designed, multicenter, observational study." Mil Med 180(3 Suppl): 14-18.	No comparison between provider levels reported
Risgaard, O. and S. Mikkelsen (2010). "Fentanyl in a prehospital setting in Denmark: A retrospective study." Resuscitation 81(2): S72.	Conference abstract
Samuel, N., et al. (2015). "Prehospital pain management of injured children: a systematic review of current evidence." Am J Emerg Med 33(3): 451-454.	Systematic review; no new records identified

Scholten, A. C., et al. (2015). "Pain management in trauma patients in (pre)hospital based emergency care: current practice versus new guideline." Injury 46(5): 798-806.	No comparison between provider levels reported
Shackelford, S. A., et al. (2015). "Prehospital pain medication use by U.S. Forces in Afghanistan." Mil Med 180(3): 304-309.	No comparison between provider levels reported
Slomer, A., et al. (2014). "A retrospective review of time-to-analgesia for the direct from scene trauma patients transported to a level-1 trauma centre by a single EMS provider." Canadian Journal of Emergency Medicine 16: S108.	Conference abstract
Thomas, S. H. and S. Shewakramani (2008). "Prehospital trauma analgesia." J Emerg Med 35(1): 47-57.	Systematic review; no new records identified
Watkins, N. (2006). "Paediatric prehospital analgesia in Auckland." Emerg Med Australas 18(1): 51-56.	No outcome or comparison between provider levels reported
White, L. J., et al. (2000). "Prehospital use of analgesia for suspected extremity fractures." Prehosp Emerg Care 4(3): 205-208.	No comparison between provider levels reported

Table 5-2: Final list of manuscripts that met inclusion criteria after full text review.

Study	Type of EMS	Study Design	Outcomes Evaluated
None found			

Systematic Review on the Use of Pharmacological Pain Management for Trauma-Related Pain

PICO Question:

(P) In patients requiring pain management following an acute traumatic event in the prehospital setting, (I) can EMT and AEMT providers administer pharmacological pain medications (C) compared to paramedics (O) safely and effectively?

Date: 1980 to 02/2017

Manuscripts
No manuscripts identified