The Future of Evidence-Based Guidelines in EMS
Today

► The Role of Evidence-Based Guidelines in a People-Centered EMS System
► Reviewing the Relevant Research to Create an EBG
► Creating and using the Naloxone EBG
► What’s Next for Prehospital EBGs
► Questions

In a people-centered EMS system, “EMS care in every community is based on the best available evidence.”
Today’s Speakers

► David Niebuhr, MD, MPH, MSc
   ▶ Medical Officer, Evidence-Based Practice Center Program, Center for Evidence and Practice Improvement, Agency for Healthcare Research and Quality

► Kenneth Williams, MD
   ▶ Medical Director, Rhode Island Department of Health Center for EMS

► Christian Martin-Gill, MD, MPH
   ▶ Associate Professor of Emergency Medicine, University of Pittsburgh
   ▶ Chair, Prehospital Guidelines Consortium

► Max Sevareid, MPH
   ▶ EMS Specialist, NHTSA Office of EMS

Management of Suspected Opioid Overdose With Naloxone by EMS Personnel: A Systematic Review


David Niebuhr, MD, MPH, MSc
Disclosures

► This report is based on research conducted by the Pacific Northwest Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00009-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

► None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

What is Evidence Review?

► Comprehensive review of the world’s literature
► Critical appraisal of the evidence
► Synthesizes and summarizes results from multiple existing studies
Federal agencies, medical professional societies, and health systems can make

► Better healthcare policy
► Better clinical guidelines
► Better health decisions

Leading to longer, healthier lives for all Americans

**Purpose of Systematic Review**

► To compare different routes, doses, and dosing strategies of naloxone administration for suspected opioid overdose by emergency medical services (EMS) personnel in field settings.

► To compare effects of transport to a health care facility versus nontransport following successful reversal of opioid overdose with naloxone.
Key Questions

► What are the comparative benefits and harms of out-of-hospital administration of naloxone by various routes of administration and doses?

► What are the comparative benefits and harms of titration of naloxone until the patient resumes sufficient spontaneous respiratory effort versus regains consciousness?

► What are the comparative benefits and harms of differences in timing of repeat dosing?

► What are the benefits and harms of transporting patients to a health care facility versus not transporting?

Methods

► Topic Refinement and Review Protocol

► Literature Search Strategy

► Search Strategy

► Inclusion and Exclusion Criteria

► Data Extraction

► Risk of Bias Assessment of Individual Studies

► Assessing Research Applicability

► Data Synthesis and Rating the Body of Evidence

► Peer Review and Public Commentary
What evidence is available?

Abstracts of potentially relevant articles identified through searches and other sources: 1,934

Excluded abstracts: 1,752
Full-text articles reviewed: 202
Background articles: 120

Included publications: 13

1,934 Abstracts of potentially relevant articles
13 Included publications

Key Question 1: Routes of Administration

- Higher concentration intranasal naloxone may be similarly effective and safe compared with intramuscular naloxone.
  - IN versus IM
    - 4 Randomized Clinical Trials and 4 cohort studies
    - Low strength of evidence (SOE)
  - IN versus IV
    - 1 RCT and 2 cohort studies
    - Insufficient SOE

- Are there differences in effectiveness between doses and routes of administration?
  - No studies
  - Insufficient SOE
Key Question 2: Titration of Naloxone Until Spontaneous Respiratory Effort Versus Regains Consciousness

► While field administration of naloxone is generally effective in reversing opioid overdoses, there is not strong evidence concerning this question.

▷ No studies
▷ Insufficient SOE

Key Question 3: Timing of Repeat Doses

► More research is needed to determine optimal doses of naloxone, appropriate timing of repeat dosing, and whether it is necessary to dose patients to full consciousness.

▷ No studies
▷ Insufficient SOE
Key Question 4: Transport Versus Not Transported

- More research is needed to determine whether transporting patients to a hospital after successful reversal of overdose is necessary.
  - Six uncontrolled studies in not transported patients found a low death rate
  - Insufficient SOE

Conclusion

- Additional research is urgently needed to optimize administration of naloxone by EMS personnel.
- Future research could leverage existing EMS registries with naloxone administration data, which are available from a number of local and state agencies.
- Research is needed on the comparative effectiveness of the FDA-approved naloxone auto-injectors and highly concentrated IN naloxone formulations, different doses, and dosing strategies.
The Naloxone Evidence-Based Guideline

nasemso.org/projects/naloxone-evidence-based-guidelines/

Ken Williams, MD

Disclosures

- Chaired the NASEMSO/NAEMSP/ACEP Naloxone EBG Project funded by the NHTSA Office of EMS and HRSA EMS for Children program.
- Later retained by Adapt Pharma, makers of Narcan® Nasal Spray, to offer opinions in patent litigation.
- Comments are my own, and do not represent NHTSA or any other entity.
- Some slides are adapted from the Naloxone EBG training module, available at nasemso.org/projects/naloxone-evidence-based-guidelines/.
### Naloxone

...is an effective part of treatment for opioid overdose  
...takes time to work (2-3 minutes)  
...is temporary (30-90 minutes)  
...has potential side effects (withdrawal and worse)  
...is approved for both *pediatric* and *adult* patients  
...can be given multiple ways

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### How Naloxone Works

- It displaces opioid on receptor  
- Takes about 2-3 minutes to work  
- Takes about 1-2 minutes if given via IV  
- Can be administered via nasal spray, intranasal injection, auto-injector or a standard syringe injection
Fentanyl (And Analogs)

**DO** give

naloxyone if:

the patient is unconscious or semi-conscious,

AND

has abnormally slow, gasping, or absent breathing

**DO NOT** give

naloxyone if:

the patient is breathing normally even if unconscious or semiconscious,

OR

the patient is conscious

---

Okay, so what about EMS?

WIDE variation across the US in:

- Scope of Practice
- Route
- Dose
- Transport Decisions
Partnership and Funding from

Evidence-Based Guideline Development

Expert Panel  Evidence  GRADE Methodology and Tables  Guideline and Other Deliverables
Technical Expert Panel

- Emergency Physicians
- Performance Measure Development
- GRADE Methodology
- Patient Advocate

- EMS Practitioners
- Addiction / Harm Reduction Coalition
- EMS Administration
- Staff Support
- Federal Partners

PICO Questions
(Population, Intervention, Comparison, Outcome)

1. Route
2. Dose
3. Titration
4. Repeat Dosing
5. Transport
**GRADE Table for Recommendation 1 — IN vs IM**

Intranasal naloxone compared to intramuscular naloxone for suspected opioid poisoning

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS &gt; 11 at 8 minutes (GCS &gt; 11 at 6 minutes)</td>
<td>718 per 1,000 0 per 1,000 (0 to 0) not estimable</td>
<td>155 (1 RCT)*</td>
<td>☐☐☐</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Mean Response Time (min) (Mean Response Time)</td>
<td>The mean mean Response Time (min) in the intervention group was 0 (0 to 0)</td>
<td>14 (2 RCTs)</td>
<td>☐☐☐</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Proportion requiring rescue naloxone (Proportion requiring rescue naloxone)</td>
<td>not pooled not pooled not pooled</td>
<td>155 (2 RCTs)</td>
<td>☐☐☐</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Adverse Response (Major; e.g. seizures, agitation, nausea/vomiting)</td>
<td>not pooled not pooled not pooled</td>
<td>155 (2 RCTs)</td>
<td>☐☐☐</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Adverse Response (Minor; e.g. agitation, irritation, nausea/vomiting, headache, sweating)</td>
<td>not pooled not pooled not pooled</td>
<td>155 (2 RCTs)</td>
<td>☐☐☐</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval
Answers

<table>
<thead>
<tr>
<th>Route</th>
<th>Dose</th>
<th>Titration</th>
<th>Repeat Dosing</th>
<th>Transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>(IN=IV)&gt;IM</td>
<td>Varies 0.4 – 4 mg</td>
<td>To adequate respiratory function</td>
<td>2-3 minutes</td>
<td>Yes, or treat at scene</td>
</tr>
</tbody>
</table>

Sample Protocol

Submitted to National Model EMS Clinical Guidelines

Training Module

Narrated version available at vimeo.com/354168233

Recommendations for EMS Use of Naloxone

The important steps are:

► Activation of the 911 System
► Assessment of scene and patient (including safety)
► Start First Aid (CPR, BVM, recovery position, etc., as indicated)
► Naloxone (and AED if indicated)
► Monitor / Further Treatment
The Order Does Not Matter (much)

If your naloxone is closer than your phone...

Lessons

This is how evidence-based EMS enhances respect and professionalism
Facilitating EMS Evidence-Based Guideline Projects: A Pathway to the Future

Christian Martin-Gill, MD, MPH

Disclosures

► Current Grants
  ▶ W81XWH-16-R-0033 Department of Defense 2016-2021 (Co-I)
  Linking Investigators in Trauma and Emergency Services (LITES)
  ▶ 1R01HL137761-01A1 NHLBI 2018-2022 (Co-I)
  Electrocardiographic Detection of Non-ST Elevation Myocardial Events for Accelerated Classification of Chest Pain Encounters (ECG-SMART)
  ▶ PEMF 0061488 PEMF 2018-2020 (PI)
  Pittsburgh Prehospital Care Registry
  ▶ W81XWH18F0426 Department of Defense 2018-2022 (Site PI)
  Prehospital Airway Control Trial (PACT)

► Completed Grants
  ▶ DTNH22-13-H-00435 NHTSA / NAEMSP 2013-2015 (PI)
  National Prehospital Evidence-Based Guidelines Strategy
  ▶ DTNH22-15-C-00029 NHTSA / NASEMSO 2016-2018 (Co-I)
  Developing Fatigue Risk Management Guidelines for Emergency Medical Services
A National Model for Developing, Implementing, and Evaluating Evidence-based Guidelines for Prehospital Care

National Model EMS Clinical Guidelines

An Evidence-based Guideline for Pediatric Prehospital Seizure Management Using GRADE Methodology
An Evidence-based Guideline for the Air Medical Transportation of Prehospital Trauma Patients
An Evidence-based Guideline for Prehospital Anesthesia in Trauma
An Evidence-based Prehospital Care for Emergency Medical Services: A National Compass

A National Model of EMS Clinical Guidelines

Statewide Implementation of an Evidence-based Guideline

Prehospital Guidelines Consortium

A National Compass to Promote Prehospital Evidence-Based Guideline Development, Implementation, and Evaluation
Recent EBG Projects (2018-2019)

Evidence-Based Guidelines for Fatigue Risk Management in Emergency Medical Services


Naloxone Evidence-Based Guidelines

Overview
The National Association of State EMS Officials (NASEMSO), in collaboration with the National Association of EMS Physicians (NAEMSP) and the American College of Emergency Physicians (ACEP), is leading a project to develop and disseminate an evidence-based guideline for the administration of naloxone for opioid overdoses.

The National Prehospital Evidence-Based Guidelines Strategy

Mission: Engage EMS stakeholder organizations, institutions, agencies, and leaders in a sustainable process that promotes the development, implementation, and evaluation of prehospital evidence-based guidelines.

1. Create a Consortium of national organizations and Federal entities that can improve communication and collaboration among EMS stakeholders in EBG-related projects;
2. Promote research supporting prehospital EBGs;
3. Promote development of prehospital EBGs;
4. Improve education related to prehospital EBGs;
5. Facilitate the implementation of prehospital EBGs;
6. Establish standardized evaluation methods for prehospital EBGs; and
7. Promote funding for the development, implementation, and evaluation of prehospital EBGs.
PGC was Formed as Action #1 of the National Prehospital EBG Strategy

Mission:

To engage EMS stakeholder organizations, institutions, agencies and leaders in a sustainable process that promotes the development, implementation and evaluation of evidence-based guidelines for prehospital care.

Comprised of Member Organizations and Liaisons with Federal and Research Entities

- 35 member organizations
  - 11 Executive Committee organizations
- Liaisons with 7 Federal agencies and research organizations
Completed Projects

► Online repository of existing prehospital EBGs and related resources
  ▶ Available at prehospitalguidelines.org

► Educational module for EMS educators on evidenced-based medicine and EBGs
  ▶ Covers required content for NREMT recertification (EMT and Paramedic)
  ▶ Freely available at prehospitalguidelines.org

► Systematic review of literature on implementation of EMS EBGs
  ▶ Fishe et al. Prehosp Emerg Care 2018;22:511-519

► Educational articles related to evidence-based medicine and EBGs for EMS personnel

Ongoing Projects

► Systematic review of all existing EMS evidence-based guidelines
  ▶ Classification by AGREE II and IOM criteria for clinical guidelines

► Update the NASEMSO Statewide EBG Implementation Toolkit
  ▶ National implementation
  ▶ Educational module for implementing new EBGs

► Gap analysis for new or revised EMS EBGs using Delphi process
  ▶ Using stakeholder group from within the PGC

► Piloting a dissemination plan for new EBGs through PGC member organizations

► Collaboration with NEMSQA linking EBGs to performance measures

► 5th Annual Meeting of PGC in San Diego on January 10, 2020
Questions?
Please submit questions through the webinar platform

Get Involved and Learn More

► Get involved with the AHRQ Effective Health care Program:
  ▷ effectivehealthcare.ahrq.gov/get-involved

► Find out more about prehospital EBGs and available resources:
  ▷ prehospitalguidelines.org
  ▷ ems.gov/projects/evidence-based-guidelines.html

► View the naloxone EBG and related resources:
  ▷ nasemso.org/projects/naloxone-evidence-based-guidelines/

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Questions?
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