Pediatric Nontraumatic Seizures

- Recurrent seizure?
  - NO
  - Actively seizing on EMS arrival?
    - YES
    - Diabetic?
      - NO
        - Provide glucose
      - YES
        - Alternative (buccal, intranasal, IM) versus PR: strong recommendation, low evidence
    - NO
      - Check finger stick for hypoglycemia (unless glucose given)
      - Consider other causes.
    - YES
      - Indications for IV access? (extended transport, history of seizure…)
        - YES
          - Obtain IV access
        - NO
          - Monitor and Transport
            Consider calling medical direction for further instructions.

- Actively seizing on EMS arrival?
  - YES
    - Diabetic?
      - NO
        - Provide glucose
      - YES
        - Alternative (buccal, intranasal, IM) versus PR: strong recommendation, low evidence
    - NO
      - Check finger stick for hypoglycemia (unless glucose given)
      - Consider other causes.
    - YES
      - Indications for IV access? (extended transport, history of seizure…)
        - YES
          - Obtain IV access
        - NO
          - Monitor and Transport
            Consider calling medical direction for further instructions.

- Diabetic?
  - NO
    - Provide glucose
  - YES
    - Alternative (buccal, intranasal, IM) versus PR: strong recommendation, low evidence

- Indications for IV access? (extended transport, history of seizure…)
  - YES
    - Obtain IV access
  - NO
    - Monitor and Transport
      Consider calling medical direction for further instructions.

- Continuing (≥5 min) or recurrent seizure?
  - YES
    - Administer 2nd Dose (IV/IO or alternate route) IV diazepam
  - NO
    - Monitor and Transport
      Consider calling medical direction.

- Continuing or recurrent seizure?
  - YES
    - Administer 2nd Dose (IV/IO or alternate route) IV diazepam
  - NO
    - Monitor and Transport
      Consider calling medical direction.
Administer Midazolam for seizure management (buccal, intranasal, IM):

List of Comparisons Contained Below:

1. Buccal Midazolam Compared to IV Diazepam
2. Buccal Midazolam Compared to Rectal Diazepam
3. Intranasal Midazolam Compared to Rectal Diazepam
4. Intramuscular Midazolam Compared to IV Diazepam
5. Intramuscular Midazolam Compared to Rectal Diazepam
6. Intramuscular Midazolam Compared to Intranasal Midazolam
7. Intramuscular Midazolam Compared to Buccal Midazolam
8. Intranasal Midazolam Compared to Buccal Midazolam

1. Buccal Midazolam Compared to IV Diazepam:

PICO Question:
(Efficacy)
In patients < 18 years of age, with or without a prior a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does buccal midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) equivalently compared to IV diazepam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department

(Safety)
In patients < 18 years of age, with or without a prior a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does buccal midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to IV diazepam in randomized controlled trials or quasi-randomized trials (or observational or case-control studies) in the prehospital (preferred) or emergency department

GRADE:
Strength of recommendation: weak;
Level of evidence: weak

Evidence:
Limited data suggests that buccal Midazolam at 0.2 mg/kg may be slightly less effective than intravenous diazepam at 0.3 mg/kg for the cessation of seizures in children who are in the emergency department setting. Very limited data suggests that buccal Midazolam is as safe as intravenous diazepam for the treatment of children with seizures who are in the ED setting. However, data is lacking for the pre-hospital setting

Values and preferences were prioritized in order of
- seizure cessation,
- time to seizure cessation,
- respiratory arrest,
- acceptability by prehospital personnel and parents
- ease of use.

See the tables below containing Outcomes A-D for additional information.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative (95% CI)</th>
<th>Absolute</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome A - Seizure cessation (within 5 minutes)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Talukdar 2008</td>
<td>Serious (-1)</td>
<td>Yes (-1)</td>
<td>Yes (-1)</td>
<td>Yes (-1)</td>
<td>51/60 (85%)</td>
<td>56/60 (93.3%)</td>
<td>8.3%</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Outcome B - Time to seizure cessation (from arrival in ED)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Talukdar 2008</td>
<td>Serious (-1)</td>
<td>Yes (-1)</td>
<td>Yes (-1)</td>
<td>2.4 min</td>
<td>3.0 min</td>
<td>0.6 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome C - Respiratory arrest</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talukdar 2008</td>
<td>Serious (-1)</td>
<td>Yes (-1)</td>
<td>Yes (-1)</td>
<td>0/60 - unclear</td>
<td>0/60 - unclear</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome D - Respiratory depression</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talukdar 2008</td>
<td>Serious (-1)</td>
<td>Yes (-1)</td>
<td>Yes (-1)</td>
<td>0/60 - unclear</td>
<td>0/60 - unclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LOE= Level of Evidence
2. Buccal Midazolam Compared to Rectal Diazepam:

**PICO Question:**
(Efficacy)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does buccal midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) more frequently compared to rectal diazepam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) setting or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does buccal midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to rectal diazepam in randomized controlled trials or quasi-randomized trials (or observational or case-control studies) in the prehospital setting (preferred) or emergency department.

**GRADE:**
Strength of recommendation: strong; Level of evidence: moderate

**Evidence:**
Literature suggests that buccal Midazolam is more effective than rectal diazepam for the cessation of seizures in children who are in the emergency department setting. Limited data suggests that buccal Midazolam is as safe as rectal diazepam for children with seizures in the emergency department setting. However, data is lacking for the prehospital setting

*Values and preferences* were prioritized in order of seizure cessation, time to seizure cessation, respiratory arrest, acceptability by prehospital personnel and parents and ease of use. See the tables below containing Outcomes A-E for additional information.
### Outcome A - Seizure cessation (within 10 minutes)

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative (95% CI)</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>RCTs</td>
<td>Serious (-1)</td>
<td>No problems (for 2 of higher quality)</td>
<td>(-1)</td>
<td>No (qualitative combining)</td>
<td>Strong Association (+1)</td>
<td>109</td>
<td>110</td>
<td>Adj OR 4.1 (2.2-7.6) favoring buccal</td>
<td>24% (11.17)</td>
<td>LOE Mod</td>
</tr>
<tr>
<td>MacIntyre (2005)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>(-1) not prehosp, long sz prior to ED</td>
<td>Not really (even at low end of CI, clear advantage)</td>
<td>92 (only 1st episode)</td>
<td>85 (only 1st episode)</td>
<td>18% (4.33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mpimbaza (2008)</td>
<td>RCT</td>
<td>No (not seemingly serious)</td>
<td>(-1) not prehosp, long sz prior, majority with malaria</td>
<td>Not really</td>
<td>165</td>
<td>165</td>
<td>RR 1.42 (1.06-1.90) favors buccal</td>
<td>4.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bayseun (2005)</td>
<td>RCT</td>
<td>Very serious (-2)</td>
<td>(-1) not prehosp, likely long sz prior to ED</td>
<td>Yes</td>
<td>40 (no malaria)</td>
<td>59 (no malaria)</td>
<td>2.11 (1.26, 3.04)</td>
<td>29.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LOE = Level of Evidence
# DRAFT
Not for Distribution

## Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitation(s)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
</table>

### Outcome B – Time to seizure cessation

**Macinlyre (2005)**
- **Design**: RCT
- **Limitation(s)**: Serious (-1)
- **Inconsistency**: (-1) not prehosp, long sz prior to ED
- **Indirectness**: Yes (qualitative combining)
- **Imprecision**: 109 min (5-20)
  - 92 (only 1st episode) 10 min
  - 85 (only 1st episode) 15 min
  - 7 min favors buccal
  - 5 min
- **Quality**: Low

**Mombaza (2009)**
- **Design**: RCT
- **Limitation(s)**: No
- **Inconsistency**: (-1) not prehosp, long sz prior, majority with malaria
- **Indirectness**: Yes
- **Imprecision**: 114 min of those who stopped in <10 min – median
  - 125 min of those who stopped in <10 min – median
  - 0.4 min favoring rectal (but only if stopped within 10 min)
- **Quality**: Strong

**Baysun (2005)**
- **Design**: RCT
- **Limitation(s)**: Very serious (-2)
- **Inconsistency**: (-1) not prehosp
- **Indirectness**: Yes
- **Imprecision**: 16 of those who stopped in <10 min
  - 17 of those who stopped in <10 min
- **Quality**: Weak

### Outcome C – Seizure recurrence within 1 hour

**Macinlyre (2005)**
- **Design**: RCT
- **Limitation(s)**: Serious (-1)
- **Inconsistency**: (-1) not prehosp, long sz prior to ED
- **Indirectness**: No (qualitative combining) Strong Association (+1)
- **Imprecision**: 109 min 14%
  - 92 (only 1st episode) 13%
  - 86 (only 1st episode) 34%
  - 10% (4, 30) favors buccal
  - 22% (4, 40)
- **Quality**: MOD

**Mombaza (2009)**
- **Design**: RCT
- **Limitation(s)**: No
- **Inconsistency**: (-1) not prehosp, long sz prior, majority with malaria
- **Indirectness**: Yes
- **Imprecision**: 114 min (of those who stopped in <10 min) – median
  - 126 min (of those who stopped in <10 min) – median
  - 0.6% (favors buccal)
- **Quality**: Strong

**LOE**: Level of Evidence
## Quality assessment

<table>
<thead>
<tr>
<th>No of</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
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<tbody>
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<td>studies</td>
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</tr>
</tbody>
</table>

### Outcome D - Respiratory arrest

<table>
<thead>
<tr>
<th>No of</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>RCTs</td>
<td>Serious (-1) No problems (-1)</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mowat et al. (2005)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>(-1) not prehosp, long sz prior to ED</td>
<td>Yes</td>
<td></td>
<td></td>
<td>108</td>
<td>(2 arrests, 1.8%)</td>
<td>110</td>
<td>(3 arrests, 2.7%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Mpmboza (2008)</td>
<td>RCT</td>
<td>No</td>
<td>(-1) not prehosp, long sz prior, majority with malaria</td>
<td>Yes</td>
<td></td>
<td></td>
<td>165</td>
<td>165</td>
<td>Unclear (see resp dep)</td>
<td>Unclear</td>
<td>Strong</td>
</tr>
</tbody>
</table>

### Outcome E - Respiratory depression

<table>
<thead>
<tr>
<th>No of</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>RCTs</td>
<td>Serious (-1) No problems (-1)</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mowat et al. (2005)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>(-1) not prehosp, long sz prior to ED</td>
<td>Yes</td>
<td></td>
<td></td>
<td>100</td>
<td>5%</td>
<td>110</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>62 (only 1st episode)</td>
<td>4%</td>
<td>85 (only 1st episode)</td>
<td>7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mpmboza (2006)</td>
<td>RCT</td>
<td>No</td>
<td>(-1) not prehosp, long sz prior, majority with malaria</td>
<td>Yes</td>
<td></td>
<td></td>
<td>165</td>
<td>165</td>
<td>1 (unclear if any arrest vs low sat)</td>
<td>0</td>
<td>Weak</td>
</tr>
</tbody>
</table>

LOE = Level of Evidence
3. Intranasal Midazolam Compared to Rectal Diazepam:

**PICO Question:**

**Efficacy**
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intranasal midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) more frequently compared to rectal diazepam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department?

**Safety**
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intranasal midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to rectal diazepam in randomized controlled trials or quasi-randomized trials (or observational or case-control studies) in the prehospital (preferred) or emergency department?

**GRADE:**
Strength of recommendation: weak; Level of evidence: very weak

**Evidence:**
Very limited data suggests that intranasal Midazolam is at least as effective, and potentially more effective, than rectal diazepam for the cessation of seizures in children who are in the emergency department setting. Very limited data suggests that intranasal Midazolam is as safe as rectal diazepam for the treatment of children with seizures who are in the ED setting. However, data is lacking for the pre-hospital setting.

Values and preferences were prioritized in order of seizure cessation, time to seizure cessation, respiratory arrest, acceptability by prehospital personnel and parents and ease of use. See the tables below containing Outcomes A-E for additional information.

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative (95% CI)</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome A - Seizure cessation (within 10 minutes)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>RCT</td>
<td>(-3), including multiple episodes per patient</td>
<td>(2) Outpt and ED, 37% gen T-C</td>
<td>(-1)</td>
<td></td>
<td></td>
<td>92 episodes (not pts) 85.7%</td>
<td>96 episodes (not pts) 83.8%</td>
<td></td>
<td>6% favors intranasal</td>
<td>LOE Weak</td>
</tr>
<tr>
<td>Shattahsrya (2006)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flsgin (2002)</td>
<td>RCT</td>
<td>(-2)</td>
<td>(-1) ED</td>
<td>(-1)</td>
<td></td>
<td></td>
<td>23 (97%)</td>
<td>22 (60%)</td>
<td></td>
<td>27%</td>
<td>LOE Weak</td>
</tr>
</tbody>
</table>

| Outcome B – Time to seizure cessation | | | | | | | | | | |
| 2 | RCT | (-2), including multiple episodes per patient | (2) Outpt and ED, 37% gen T-C | (-1) | | | 92 episodes (not pts) 178 sec SD 179 | 96 episodes (not pts) 115 sec SD 127 | | 62 sec | LOE Weak |
| Shattahsrya (2006) | | | | | | | | | | |
| Flsgin (2002) | RCT | (-2) | (-1) ED | (-1) | | | 23 min 5% min | 23 min 6% min | | | LOE Weak |

LOE= Level of Evidence
## Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
</table>
| 1 Bhattachar 
 yya (2006) | RCT    | (-2), including multiple episodes per patient | (-2) Outcome and ED, 37% gen T-C | (-1) | | | 92 episodes (not pts) 3% | 96 episodes (not pts) 6.25% | 3.25% (favors IN 
micaz) | GRADE Very Low | LOE Very weak |

## Summary of findings

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>92 episodes (not pts) 3%</td>
<td>96 episodes (not pts) 6.25%</td>
</tr>
</tbody>
</table>

## Outcome C – Seizure recurrence within 1 hour

### Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
</table>
| 2 Bhattachar 
 yya (2006) | RCT    | (-2), including multiple episodes per patient | (-2) Outcome and ED, 37% gen T-C | (-1) | | | 92 episodes (not pts) 0-unclear | 96 episodes (not pts) 0-unclear | 0 | GRADE Very Low | LOE Very weak |

### Summary of findings

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>92 episodes (not pts) 0-unclear</td>
<td>96 episodes (not pts) 0-unclear</td>
</tr>
</tbody>
</table>

## Outcome D – Respiratory arrest

### Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
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<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
</table>
| 1 Bhattachar 
 yya (2006) | RCT    | (-2), including multiple episodes per patient | (-2) Outcome and ED, 37% gen T-C | (-1) | | | 92 episodes (not pts) 0-unclear | 96 episodes (not pts) 0-unclear | 0 | GRADE Very Low | LOE Very weak |

### Summary of findings

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>92 episodes (not pts) 0-unclear</td>
<td>96 episodes (not pts) 0-unclear</td>
</tr>
</tbody>
</table>

## Outcome E – Respiratory depression

### Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Intervention</th>
<th>Control</th>
<th>Relative</th>
<th>Absolute</th>
<th>Quality</th>
</tr>
</thead>
</table>
| 1 Bhattachar 
 yya (2006) | RCT    | (-2), including multiple episodes per patient | (-2) Outcome and ED, 37% gen T-C | (-1) | | | 92 episodes (not pts) 0-unclear | 96 episodes (not pts) 0-unclear | 0 | GRADE Very Low | LOE Very weak |

### Summary of findings

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>92 episodes (not pts) 0-unclear</td>
<td>96 episodes (not pts) 0-unclear</td>
</tr>
</tbody>
</table>

LOE= Level of Evidence
4. Intramuscular Midazolam Compared to IV Diazepam:

**PICO Question:**

(Efficacy)
In patients < 18 years of age, with or without a prior a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does IM midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) equivalently compared to IV diazepam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intramuscular midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to IV diazepam in randomized controlled trials or quasi-randomized trials (or observational or case-control studies) in the prehospital (preferred) or emergency department

**GRADE:**
Strength of recommendation: weak; Level of evidence: very weak

**Evidence:**
Very limited data suggests that intramuscular Midazolam is as effective as intravenous diazepam for the cessation of seizures in children who are in the emergency department setting. Very limited data suggests that intramuscular Midazolam is as safe as intravenous diazepam for the treatment of children with seizures who are in the emergency department setting. However, data are lacking for the pre-hospital setting

Values and preferences were prioritized in order of seizure cessation, time to seizure cessation, respiratory arrest, acceptability by prehospital personnel and parents and ease of use. See the tables below containing Outcomes A-E for additional information.

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>Summary of findings</th>
<th>GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of studies</td>
<td>Design</td>
<td>Limitations</td>
</tr>
<tr>
<td>Outcome A - Seizure cessation (within 10 minutes)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Chamberlain (1997) | RCT | Serious (-1) | Yes (-1) | Yes (-1) | 13 (92.3%) | 11 (91%) | RR 0.85, (95% CI 0.66, 1.21) | 1.3% favors IM | LOE Mod |
| Shah (2005) | RCT | Very serious (-2) | Yes (-2), ED, admitted and PICU, severe underlying diseases | Yes (-1) | 50 (90%) | 31 (93.5%) | Only those w/o IV initially | -3.5% favors diazepam | LOE Very weak |

LOE= Level of Evidence
### Quality assessment

<table>
<thead>
<tr>
<th>No of studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Impression</th>
<th>Other considerations</th>
<th>No of patients</th>
<th>Effect</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Outcome B – Time to seizure cessation if no IV line

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Impression</th>
<th>No of patients</th>
<th>Effect</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamberlain (1997)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>Yes (-1) not prehosp, long sz prior to treatment</td>
<td>Yes (-1)</td>
<td>13</td>
<td>11</td>
<td>7.8 min (time to cessation after ED arrival)</td>
</tr>
<tr>
<td>Shah (2005)</td>
<td>RCT</td>
<td>Very serious (-2)</td>
<td>Yes (-2), ED admitted and PICU, severe underlying diseases</td>
<td>Yes (-1)</td>
<td>50</td>
<td>31</td>
<td>97 sec</td>
</tr>
</tbody>
</table>

**GRADE: VERY WEAK**

**LOE: Mod**

#### Outcome C – Seizure recurrence within 1 hour

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Impression</th>
<th>No of patients</th>
<th>Effect</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamberlain (1997)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>Yes (-1) not prehosp, long sz prior to treatment</td>
<td>Yes (-1)</td>
<td>13</td>
<td>11</td>
<td>30.7%</td>
</tr>
</tbody>
</table>

**GRADE: VERY WEAK**

**LOE: Mod**

### Outcome D – Respiratory arrest

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Impression</th>
<th>No of patients</th>
<th>Effect</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamberlain (1997)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>Yes (-1) not prehosp, long sz prior to treatment</td>
<td>Yes (-1)</td>
<td>13</td>
<td>11</td>
<td>RR 0.85, (95% CI 0.66, 1.201)</td>
</tr>
<tr>
<td>Shah (2005)</td>
<td>RCT</td>
<td>Very serious (-2)</td>
<td>Yes (-2), ED, admitted and PICU, severe underlying diseases</td>
<td>Yes (-1)</td>
<td>50</td>
<td>31</td>
<td>0/50</td>
</tr>
</tbody>
</table>

**GRADE: VERY WEAK**

**LOE: Mod**

### Outcome E – Respiratory depression

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Limitations</th>
<th>Indirectness</th>
<th>Impression</th>
<th>No of patients</th>
<th>Effect</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamberlain (1997)</td>
<td>RCT</td>
<td>Serious (-1)</td>
<td>Yes (-1) not prehosp, long sz prior to treatment</td>
<td>Yes (-1)</td>
<td>13</td>
<td>11</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

**GRADE: VERY WEAK**

**LOE: Mod**

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LOE = Level of Evidence
5. Intramuscular Midazolam Compared to Rectal Diazepam

PICO Question:
(Efficacy)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intramuscular (IM) midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) more frequently than rectal diazepam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intramuscular midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to rectal diazepam in randomized controlled trials or quasi-randomized trials (or observational or case-control studies) in the prehospital (preferred) or emergency department

Evidence:
No literature included in final pool.
No useful comparative data exist on which to recommend or not recommend IM midazolam compared to rectal diazepam for patients < 18 years of age with acute seizures in the prehospital setting.
6. Intramuscular Midazolam Compared to Intranasal Midazolam

**PICO Question:**
(Efficacy)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does IM midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) equivalently to intranasal midazolam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does IM midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to intranasal midazolam in randomized controlled trials, quasi-randomized trials, observational or case-control studies in the prehospital (preferred) or emergency department.

**Evidence:**
No literature included in final pool.
No useful comparative data exist on which to recommend or not recommend IM midazolam compared to intranasal midazolam for patients < 18 years of age with acute seizures in the prehospital setting.
7. Intramuscular Midazolam Compared to Buccal Midazolam

_PICO Question:

(Efficacy)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does IM midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) equivalently to buccal midazolam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does IM midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to buccal midazolam in randomized controlled trials, quasi-randomized trials, observational or case-control studies in the prehospital (preferred) or emergency department.

_Evidence:
No literature included in final pool.
No useful comparative data exist on which to recommend or not recommend IM midazolam compared to buccal midazolam for patients < 18 years of age with acute seizures in the prehospital setting.
8. Intranasal Midazolam Compared to Buccal Midazolam

**PICO Question:**
(Efficacy)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intranasal midazolam lead to seizure cessation (secondary outcomes: time to cessation, recurrence in 1 hour) equivalently to buccal midazolam in randomized controlled trials or quasi-randomized trials performed in the prehospital (preferred) or emergency department.

(Safety)
In patients < 18 years of age, with or without a prior history of epilepsy, with an acute tonic-clonic seizure (including those in status epilepticus), does intranasal midazolam have equivalent likelihood of respiratory arrest (secondary outcomes: any respiratory depression, other severe events) compared to buccal midazolam in randomized controlled trials, quasi-randomized trials, observational or case-control studies in the prehospital (preferred) or emergency department.

**Evidence:**
No useful comparative data exist on which to recommend or not recommend Intranasal midazolam compared to buccal midazolam for patients < 18 years of age with acute seizures in the prehospital setting.
Administer 2nd Dose (IV/IO or alternate route) IV diazepam

If short (<=5 mins) transport time, use alternative routes:
Strong recommendation, Low evidence

*Values/Preferences:*
- Skill competency of EMS provider

Administer second dose of lorazepam or midazolam:
Weak Recommendation, Low Evidence,

*Values/Preferences:*
- Seizure cessation in field
- Prompt transfer of child
- Avoid respiratory distress
- Acceptability by prehospital personnel
- Ease of use of therapies in prehospital setting
- Simplicity of algorithm
- Continuum of care between EMS and ED

IV diazepam or lorazepam:
Weak recommendation, Low evidence

*Values/Preferences:*
- seizure cessation
- respiratory depression

Use of IV Midazolam:
Weak recommendation, Very low evidence

*Values/Preferences:*
- need to only carry one benzo
- low risk respiratory depression