Examining the Seizure Standard for Commercial Motor Vehicle Drivers:

Evidence Report, Systematic Review, and Medical Expert Panel Report

Kurt T. Hegmann, MD, MPH
Professor and Center Director
Dr. Paul S. Richards Endowed Chair in Occupational Safety and Health

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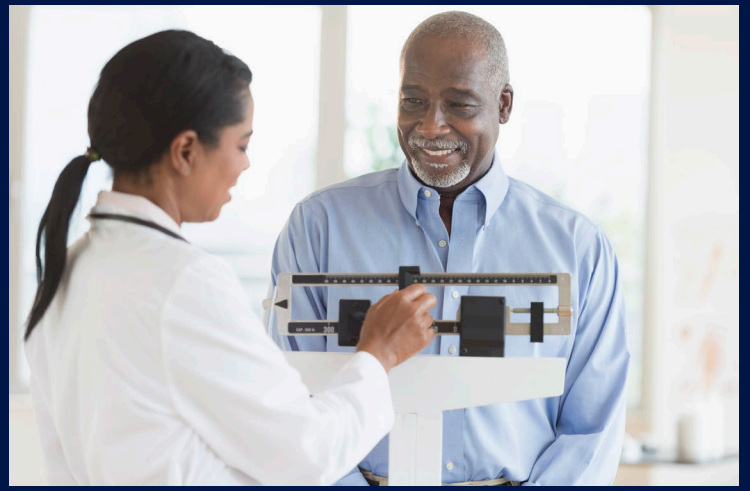

Team to address the Task Order

- Matt Thiese, PhD, MSPH
  University of Utah
- Kurt Hegmann, MD, MPH
  University of Utah
- Jason Bittner
  Applied Research Associates
- Hannah Silber
  Applied Research Associates

Medical Expert Panel (MEP)

- Proleta Datta, MD, PhD
  Oregon Health & Sciences University
- William Greaves, MD, MSPH
  OEM Associates
- Sindhu Richards, MD
  University of Utah
- Matt Rizzo, MD
  University of Nebraska-Omaha
- Jon Tippin, MD
  University of Iowa

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Key Question 1

Key Question 1

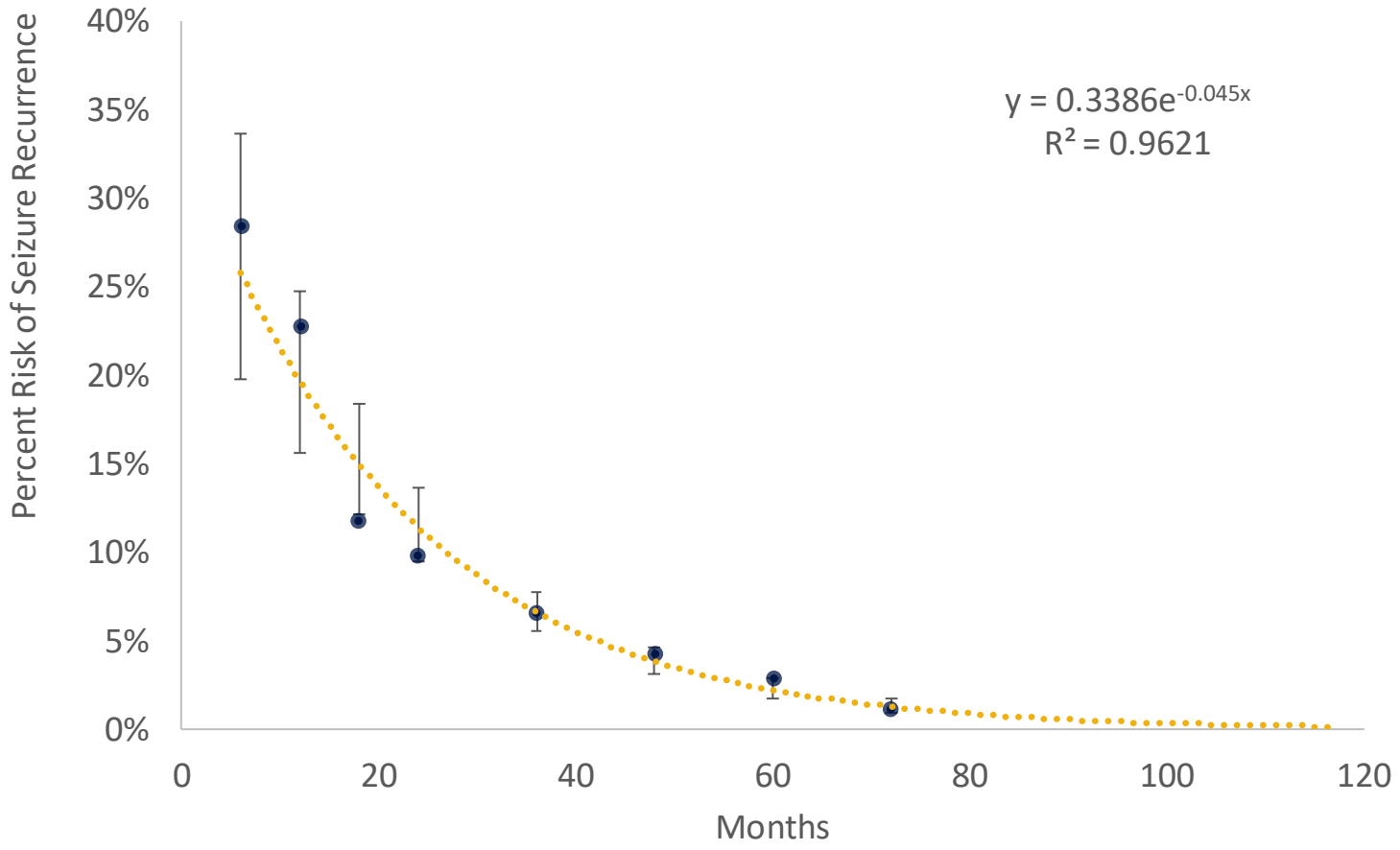
What is the risk for seizure recurrence after an unprovoked first seizure at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and more than 10 years following the first seizure for individuals who (a) are treated with antiepileptic drugs, and (b) are not treated with antiepileptic drugs?

RATIONALE

- 18 studies, 19 reports identified to address Key Question 1
- Study designs mostly prospective cohort studies, although 3 randomized trials

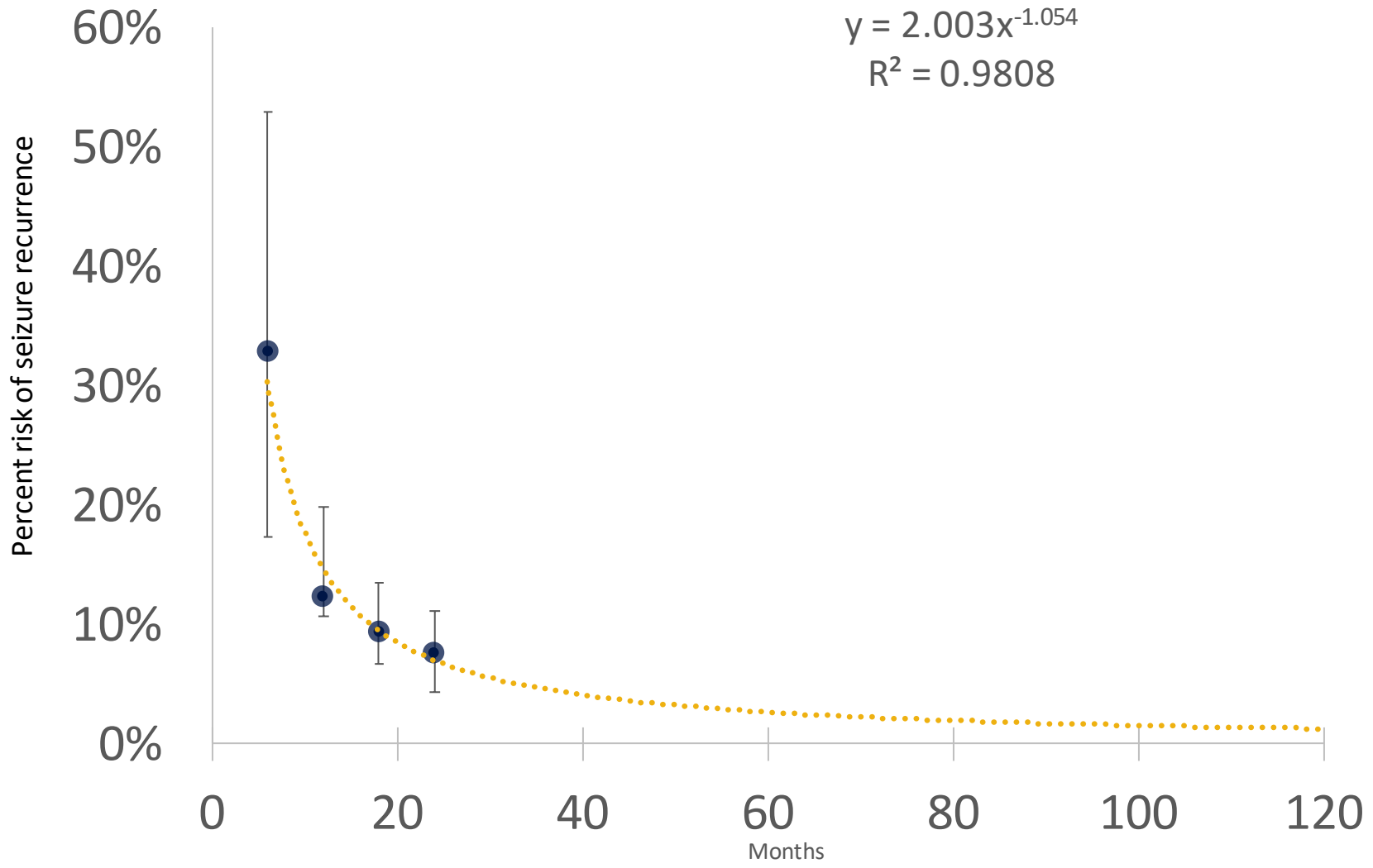
Meta-analysis

Figure 1. Relationship of Seizure Recurrence by Time Since a First Unprovoked Seizure



Meta-analysis

Figure 2. Relationship of Seizure Recurrence by Time Since a First Unprovoked Seizure for Treated Individuals



Key Question 1 Research Findings

Consistent data from multiple different populations. Seizure recurrence after a first unprovoked seizure is a hyperbolic function (See Figures 1-2).

High confidence same mathematical relationship present regardless of treatment with antiepileptic medication or not.

Use of antiepileptic medication results in a somewhat less steep slope as medication appears to particularly reduce short-term seizure risk, but less so over the longer term.

Key Question 2

Key Question 2

What is the risk for seizure recurrence after a provoked first seizure at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and more than 10 years following the first seizure for individuals who (a) are treated with antiepileptic drugs, and (b) are not treated with antiepileptic drugs?

RATIONALE

- Many diverse causes of provoked seizures (defined as an avoidable/reversible cause)
- No quality epidemiological evidence

Key Question 2 Research Findings

No data of sufficient quality to address risk of seizure recurrence after a provoked seizure.

Key Question 3

Key Question 3

What is the risk for seizure recurrence after a seizure caused by stroke at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and more than 10 years following the first seizure for individuals who (a) are treated with antiepileptic drugs, and (b) are not treated with antiepileptic drugs?

RATIONALE

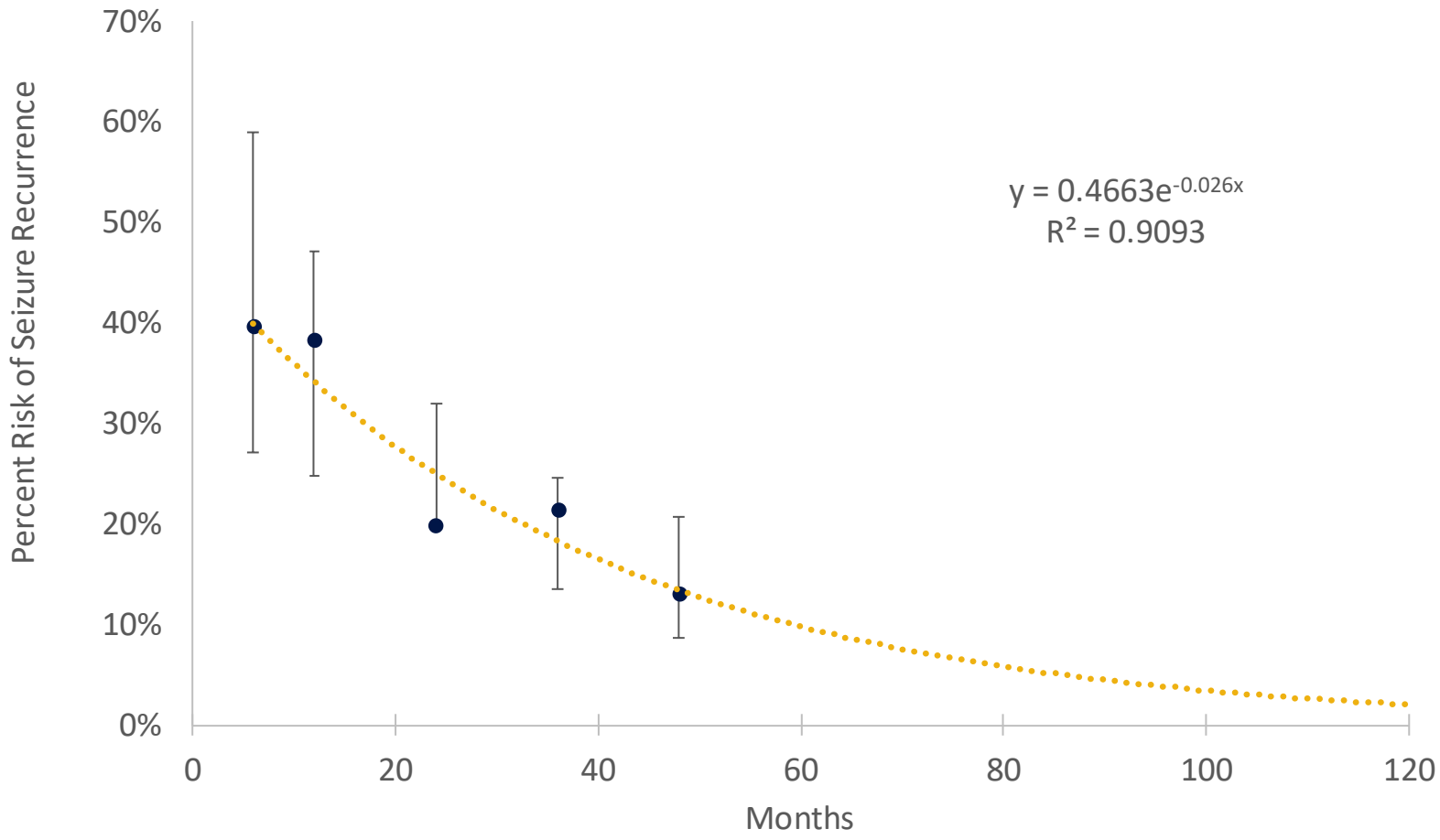
- Total of 8 reports to address Key Question 3

Rationale

- Due to:
  - (i) widely differing underlying causes,
  - (ii) individual case heterogeneity,
  - (iii) rapidly advancing treatment approaches and techniques,
  - (iv) heterogeneity of literature, and
  - (v) notably few studies reporting risk over time in sufficient detail,
- The meta-analysis is limited to the small body of published literature on seizures caused by strokes.

Meta-analysis

Figure 3. Relationship of Seizure Recurrence by Time Since a Seizure caused by a Stroke.



Key Question 3 Research Findings

With few data, low confidence in the risk estimates for Key Question 3.

Low confidence in predictability of seizure recurrence after a stroke.

Some evidence that late occurrence of seizure after stroke predicts higher risk of recurrence.

Key Question 4

Key Question 4

What is the risk for seizure recurrence after a diagnosis of epilepsy at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and more than 10 years following the diagnosis for individuals who (a) are treated with antiepileptic drugs, and
(b) are not treated with antiepileptic drugs?

RATIONALE

- 26 reports addressing seizure recurrence risk among those ON antiepileptic drugs (Key Question 4a)
- 5 reports addressing seizure recurrence risk among those NOT on antiepileptic drugs (Key Question 4b)

Meta-analysis

Figure 4. Seizure Recurrence among Persons with Epilepsy

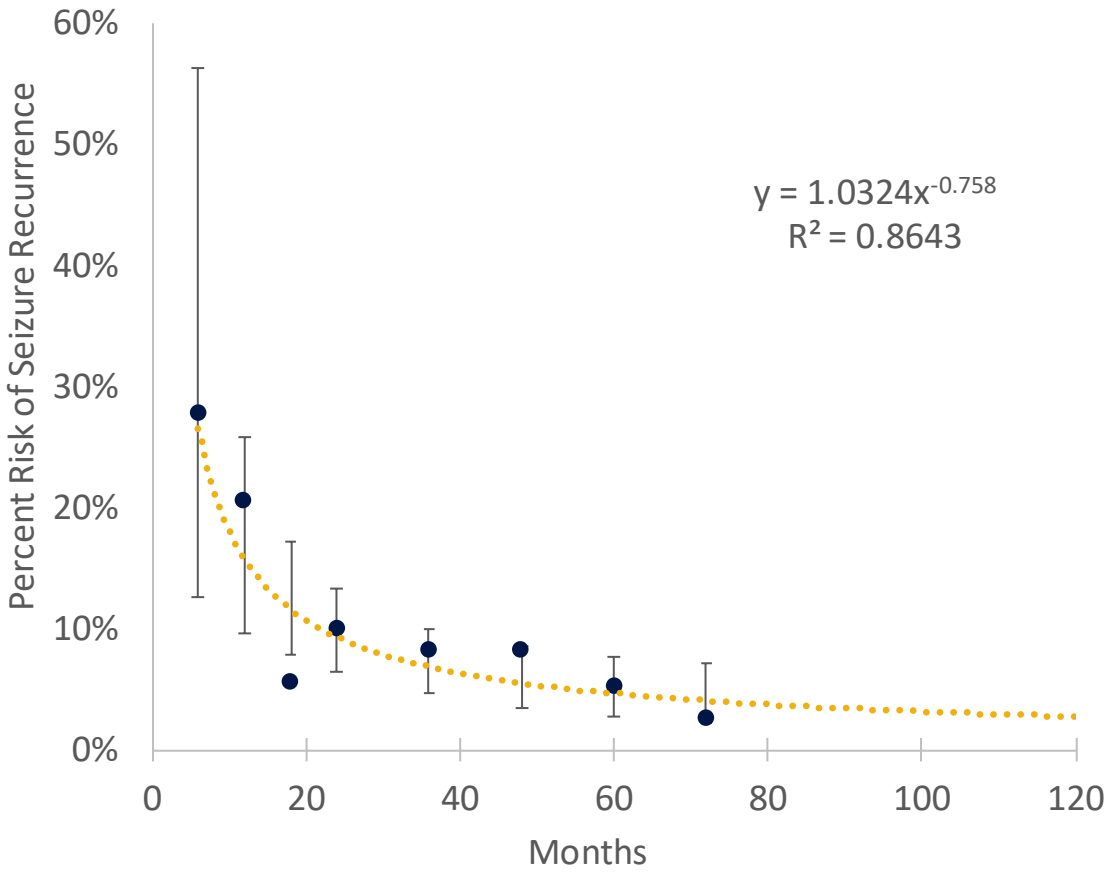
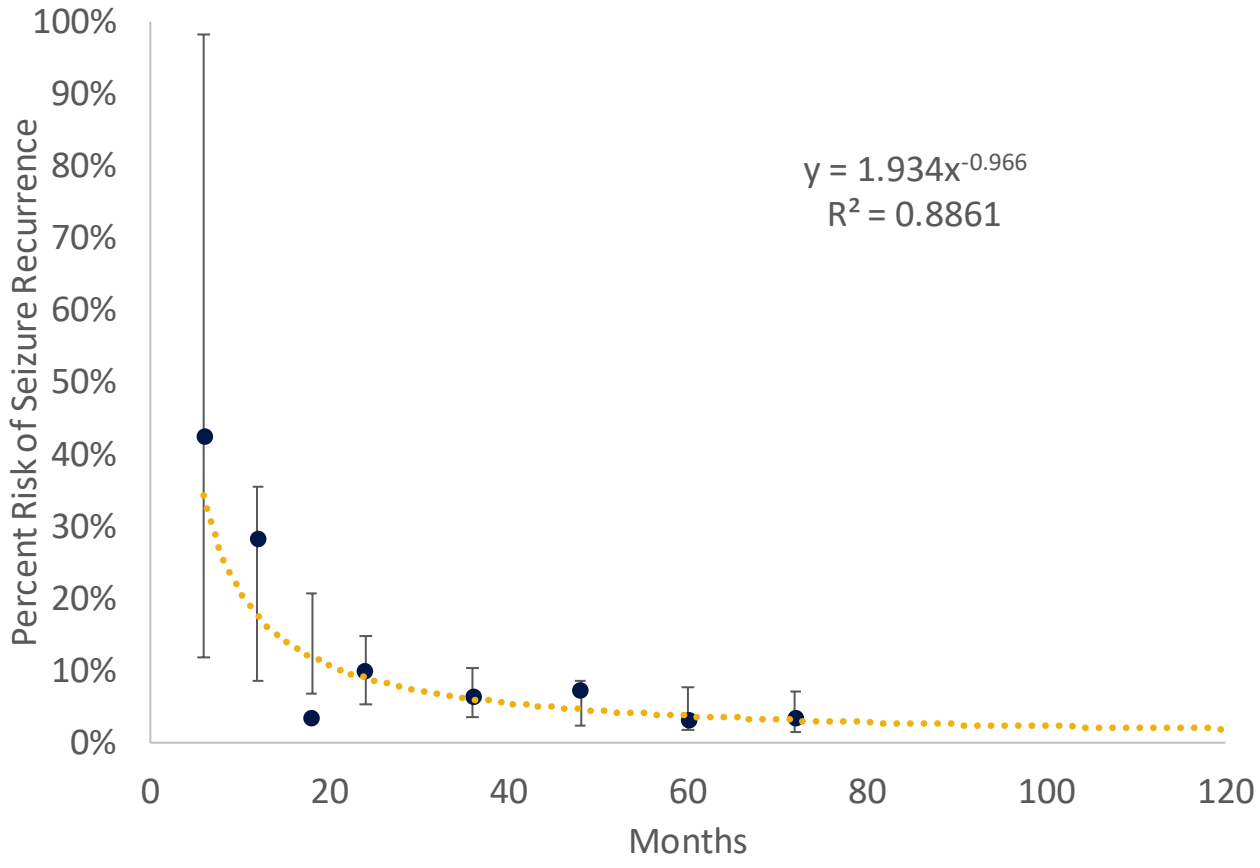


Figure 5. Seizure Recurrence among Persons with Epilepsy who are Treated



Key Question 4 Research Findings

- Consistent data from many populations.
- Risk of seizure recurrence is a hyperbolic function.
- Highest risk for recurrence is in the first years after seizure.
- High degree of confidence that the same mathematical risk relationship is present regardless of whether the person is treated with an antiepileptic medication or not.
- Recurrence risks are higher among those untreated.
- Use of an antiepileptic medication results in a less steep slope.

Key Question 5

Key Question 5

What is the risk for seizure recurrence for individuals who have undergone surgery for a structural brain abnormality or a seizure disorder, to include epilepsy, at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and more than 10 years following the surgery?

RATIONALE

- 8 studies to address Key Question 5.
- Include varying diagnoses, most lack seizure incidence/recurrence data.
  - Highest quality study included surgeries performed prior to 1999.

Rationale

- Most studies did not report antiepileptic medication use.
- Due to:
  - (i) widely differing underlying causes,
  - (ii) rapidly advancing surgical approaches and techniques,
  - (iii) varying surgical procedures used,
  - (iv) some reporting of outcomes as improvement in epilepsy without absolute seizure rates,
  - (v) unclear antiepileptic medication use, and
  - (vi) heterogeneity of the literature,

A meta-analysis while technically feasible using some of these data was not judged to be scientifically sound for Key Question 5.

Key Question 5 Research Findings

High rates of seizure recurrences, ranging from 34% to 70%, with the best results apparently likely due to only 2 years of follow-up data.

Moderately high confidence that seizure recurrences are common among post-operative patients treated surgically for refractory epilepsy.

Key Question 6

Key Question 6

What are the requirements in each state concerning seizures? What are the requirements for select countries?

- **Detailed findings are available in the report.**

Key Question 7

Key Question 7

What are the professional recommendations regarding seizures and driving for commercial drivers including (a) following a first unprovoked seizure, (b) following a first provoked seizure, (c) following a diagnosis of epilepsy, and (d) following a diagnosis of sleep epilepsy (defined as epilepsy with seizures only while asleep or upon awakening)?

Sleep Epilepsy

- **Sleep Epilepsy:** Additional systematic review was performed.
  - Research findings:
    - Risk of subsequent awake seizures estimated at 13% to 31%.

Recommendations of the MEP

Regulation

- No evidence-based data to recommend major changes to FMCSA's regulation, but one minor change was advised.
- Regulation could be clarified for the driver to not have *a current* diagnosis of epilepsy or seizure disorder.

Seizure Exemption Criteria

- No evidence-based data to recommend major changes to FMCSA's exemption criteria, but several minor changes were advised.
- **First unprovoked seizure:** MEP confirmed research findings. There is no major identifiable, strong bias in the available studies, likely producing reasonably reliable risk estimates.

Recommendations of the MEP

- **First provoked seizure:** (i.e., caused by reversible/avoidable factor such as a medication known to lower the seizure threshold or severe hypoglycemia): Many specific, individual factors.
  - MEP confirmed: there is no significant recurrence risk when seizure due to both reversible factor and/or that factor is eliminated or otherwise avoided.

- **Stroke:** Many causes. Quite heterogenous. For nearly all causes, there is a limited ability to quantify seizure recurrence.
  - Regardless, a late seizure due to stroke results in a diagnosis of presumptive epilepsy.

- **Epilepsy:** Clarify criteria regarding not having had a seizure *for at least* 8 years prior to certification.

Recommendations of the MEP

- **Sleep Epilepsy:**
  - Data are consistent with high risk of conversion from only sleep epilepsy to awake seizure(s).
  - Risks too high to advise changes to current FMCSA seizure exemption criteria.
- **Multiple epileptogenic:**
  - Advised this should be a criterion.
  - If present, advised that person is not an appropriate candidate for commercial driving.
- **Surgery for seizures:**
  - Many surgical procedures. Most unstudied in quality studies.
  - Temporal lobe epilepsy surgery studies show high seizure recurrent risks.
    - Temporal lobe epilepsy surgery may also cause visual field deficits (e.g., quadrantanopia) that should be considered.

Further Considerations from the MEP

- Regarding provoked seizures and a provoking factor
  - Advised should specify no use of provoking factor for X amount of time (e.g., alcohol for an alcohol-induced seizure).
  - Clarify need to be off illicit drug(s)/alcohol for a certain amount of time, as well as under control by treatment.
  - For medication-induced provoked seizures, clarify need to be off the medication.
- Define the term “provoked seizure” as a seizure caused by a reversible and/or avoidable factor.
- Provide more examples of low risk for seizure recurrence (e.g., on a provoking medication and now off that medication).

Further Considerations from the MEP

- Online seizure risk calculators may be helpful in some circumstances, especially after validated.
- Antiepileptic drugs may cause cognitive impairment.
  - Potential impairments should be assessed and integrated into decisions by a qualified neurologist.
- Drug-drug interactions should be considered and evaluated by a qualified neurologist, as these could compound impairments.
- Definitions of seizures and epilepsy continue to evolve.
  - Recommended these be considered to clarify existing exemption criteria (existing studies will have to rely on older terminology).

Further Considerations from the MEP

- There are several surgical procedures and devices used for epilepsy.
  - Recommended that these undergo systematic searches for seizure recurrence risks including Responsive Neurostimulation (RNS).
  - RNS feedback systems have objective measures of seizures. These need to be integrated, both from neurology and FMCSA standpoints, into driving decisions.