



Risk of angioedema associated  
with levetiracetam compared  
with phenytoin



# Overview of Research Question

## Purpose:

To evaluate angioedema risk in seizure disorder patients exposed to levetiracetum compared with those exposed to phenytoin sodium. In late 2015, the Food and Drug Administration raised a potential link between levetiracetum and angioedema through their review of spontaneous reporting data.

Angioedema is a rare, rapid swelling of the face, mouth, tongue and throat and is potentially fatal.

Phenytoin is a common first-line anti-seizure treatment with no label warning for angioedema after 60 years on the market.

## Primary hypothesis:

There is no difference in incidence risk of angioedema in new-user, seizure disorder patients of levetiracetum and phenytoin during drug exposure.



# What is angioedema?



Source: Usatine RP, Smith MA, Mayeaux EJ, Chumley HS: *The Color Atlas of Family Medicine, Second Edition*: [www.accessmedicine.com](http://www.accessmedicine.com)  
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# Study Population / design

## *Inclusion:*

Prior diagnosis of seizure disorder

First exposure to levetiracetum or phenytoin (index date)

No prior diagnosis angioedema

At least 183 days of observation time prior to the index date

## *Risk model:*

Propensity-score (variable) matched

Cox proportional hazard models

Time-at-risk censored at end of initial drug exposure era or end of observation

100 negative controls to assess residual bias