



# Save our Sisyphus Challenge: Week #1 in Review

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# Save our Sisyphus Challenge Team

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# Overview of Research Question

## Purpose:

To compare the effectiveness in reduction of osteoporotic hip fracture between alendronate and raloxifene and to evaluate the adverse outcomes in using osteoporotic medication

## Primary hypothesis:

There is no difference in incidence rate of osteoporotic hip fracture between alendronate and raloxifene.

## Secondary hypotheses:

There is no difference in incidence rate of vertebral fracture and atypical femoral fracture between alendronate and raloxifene.



# Task for Week #1: Design / Protocol

- Specify study design: using ATLAS

ATLAS

Population Level Effect Estimation

Sisyphus challenge: Comparative effectiveness of alendronate vs. raloxifene in patients w Save Close Delete

Specification Utilities

Choose your target cohort:

OHDSI Sisyphus T: new users of alendronate in patients with osteoporosis

Choose your comparator cohort:

OHDSI Sisyphus C: new users of raloxifene in patients with osteoporosis

Choose your outcome cohort:

OHDSI Sisyphus O: new cases of hip fracture

Specify the statistical model used to estimate the risk of outcome between target and comparator cohorts:

Cox proportional hazards

- Draft protocol

Observational Health Data Sciences and Informatics

Trace: bisphosphonates\_and\_hip\_fracture

research:bisphosphonates\_and\_hip\_fracture

## Comparative effectiveness of alendronate and risedronate in reducing the risk of hip fracture

**Objective:** To compare the effectiveness in reducing the risk of hip fracture between alendronate and risedronate.

**Rationale:** Osteoporosis is characterized by decreased bone mass and deterioration of bone tissue, resulting in reduced bone strength and increased fracture risk. Approved therapies for osteoporosis include bisphosphonates, calcitonin, raloxifene and teriparatide. Among these drugs, alendronate and raloxifene are the most popular osteoporosis medication and a burden of prescription are performed annually.



# Study Population

## *Inclusion:*

Women over 45 years (postmenopause)

Exposure to alendronate or raloxifene

At least 365 days of observation time prior to the index date

At least 90 days of observation time after to the index date

## *Exclusion:*

Prior hip fracture on or preceding the index date

Prior hip replacement on or preceding the index date

No other bisphosphonates or SERMs preceding the index date

High energy trauma (open fracture, pelvic bone fracture)

Pathologic fracture (metastatic tumor, Paget's disease)



# Outcome Definitions

- Hip fracture: femur neck fracture, femur intertrochanteric fracture, femur trochanteric fracture.
- Vertebral fracture: thoracic vertebral (spine) fracture, lumbar vertebral (spine) fracture, compression fracture (thoracic or lumbar), burst fracture (thoracic or lumbar)
- Atypical fracture: subtrochanteric fracture of femur, femur midshaft fracture, fatigue fracture of femur, insufficiency fracture of femur



## Other Possible Safety Outcomes

- Adverse effect associated with alendronate:  
Osteonecrosis of jaw, Esophageal cancer
  
  - Adverse effect associated with Raloxifene:  
Deep vein thrombosis, Pulmonary embolism
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# Study Cohorts

- [www.ohdsi.org/web/atlas/#/cohortdefinitions](http://www.ohdsi.org/web/atlas/#/cohortdefinitions)
- T (alendronate), C (raloxifene), O (hip fracture)

Id	Name	Created	Updated
99321	<a href="#">OHDSI Sisyphus T: new users of alendronate in patients with osteoporosis</a>	3/22/2017	3/28/2017
99322	<a href="#">OHDSI Sisyphus C: new users of raloxifene in patients with osteoporosis</a>	3/22/2017	3/28/2017
99323	<a href="#">OHDSI Sisyphus O: new cases of hip fracture</a>	3/22/2017	3/28/2017
100791	<a href="#">OHDSI Sisyphus O2: new cases of vertebral fracture</a>	3/28/2017	12/31/1969
100792	<a href="#">OHDSI Sisyphus O3: new cases of non-hip non-vertebral fracture</a>	3/28/2017	12/31/1969
100793	<a href="#">OHDSI Sisyphus O4: new cases of osteonecrosis of jaw</a>	3/28/2017	12/31/1969
100794	<a href="#">OHDSI Sisyphus O5: new cases of esophageal cancer</a>	3/28/2017	12/31/1969
100795	<a href="#">OHDSI Sisyphus O6: new cases of atypical femoral fracture</a>	3/28/2017	12/31/1969

- O2 (vertebral fracture), O3 (non-hip, non-vertebral fracture), O4 (osteonecrosis of jaw), O5 (esophageal cancer), O6 (atypical femoral fractures)





# Study Methods

- Propensity score stratified
- Cox survival model
- Fully specified:
  - In ATLAS
- Complete with
  - diagnostics
- Uses CohortMethod
- Empirical calibration
  - Negative controls

**Population Level Effect Estimation**

Sisyphus challenge: Comparative effectiveness of alendronate vs. raloxifene in patients w Save Close Delete

Specification Utilities

Choose your target cohort:

OHDSI Sisyphus T: new users of alendronate in patients with osteoporosis 🗑️

Choose your comparator cohort:

OHDSI Sisyphus C: new users of raloxifene in patients with osteoporosis 🗑️

Choose your outcome cohort:

OHDSI Sisyphus O: new cases of hip fracture 🗑️

Specify the statistical model used to estimate the risk of outcome between target and comparator cohorts:

Cox proportional hazards ⌵

Define the time-at-risk window start, relative to target/comparator cohort entry:

90 ▾ days from cohort start date

Define the time-at-risk window end:

0 ▾ days from cohort end date ⌵

Minimum washout period applied to target and comparator cohorts:

365 ▾

Minimum required days at risk, applied to target and comparator cohorts:

0 ▾

Remove patients who enter both cohorts?

Yes ⌵

Remove patients who have observed the outcome prior to cohort entry?

Yes ⌵

Use propensity score adjustment as a confounding adjustment strategy for baseline covariates?

Yes ⌵



# Protocol

- Available at:

- <https://docs.google.com/document/d/1ldRAh45uUWs7pzKThBx7KhWaSpkYcD7T-QG0phbxDys> and
- <http://www.ohdsi.org/web/wiki>



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## Comparative effectiveness of alendronate and raloxifene in reducing the risk of hip fracture

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**Version:** 0.1

**Authors:**

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# Upcoming Milestones

- Week 1: Protocol drafted and posted on OHDSI wiki.
  - Week 2: R package posted on github and tested at  $\geq 2$  sites; all participating sites signed up.
  - Week 3: Results from all sites shared back to study coordinator.
  - Week 4: Draft manuscript under preparation.
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# To Participate...

- Email:
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Yeesuk, what has been your favorite part so far?  
What has been the most frustrating?