

Save our Sisyphus Challenge: Week #1 in Review

Yeesuk Kim, Hanyang University Marc Suchard, UCLA



Save our Sisyphus Challenge Team

- Yeesuk Kim, MD PhD, Hanyang University
- Patrick B. Ryan, PhD, Janssen
- Martijn J. Schuemie, PhD, Janssen
- Jon Duke, MD, Georgia Tech
- George Hripcsak, MD, Columbia University
- Christian Reich, MD PhD, IMS Health
- Nigam Shah, MD PhD, Stanford Universtiy
- Marc A. Suchard, MD PhD, UCLA



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.

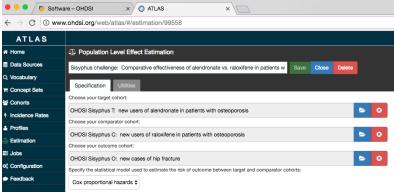
Secondary hypotheses:

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

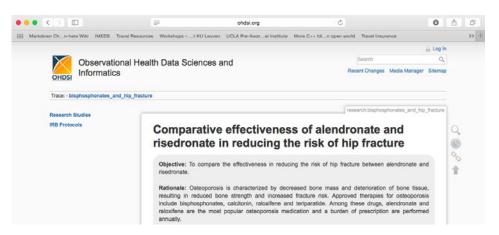


Task for Week #1: Design / Protocol

Specify study design: using ATLAS



Draft protocol





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



Study Cohorts

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

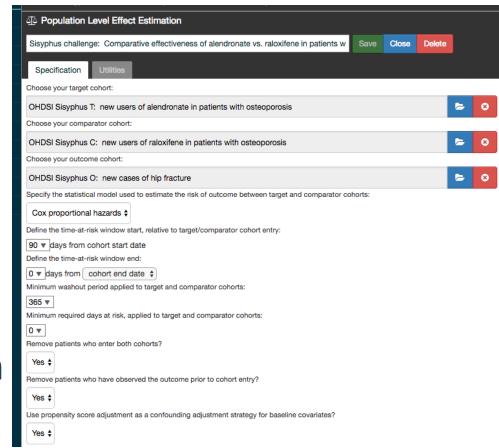
Id	Name	Created	Updated
99321	OHDSI Sisyphus T: new users of alendronate in patients with osteoporosis	3/22/2017	3/28/2017
99322	OHDSI Sisyphus C: new users of raloxifene in patients with osteoporosis	3/22/2017	3/28/2017
99323	OHDSI Sisyphus O: new cases of hip fracture	3/22/2017	3/28/2017
100791	OHDSI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

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



Study Methods

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





Protocol

Available at:

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



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

Version: 0.1

Authors:

Yeesuk Kim, MD PhD, Hanyang University



Upcoming Milestones

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



To Participate...

- Email:
 - estone96@gmail.com
 - msuchard@ucla.edu

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