

Supplementary Online Content

Desai RJ, Mahesri M, Abdia Y, et al. Association of osteoporosis medication use after hip fracture with prevention of subsequent nonvertebral fractures: an instrumental variable analysis. *JAMA Netw Open*. 2018;1(3):e180826. doi:10.1001/jamanetworkopen.2018.0826

eFigure 1. Study Design

eFigure 2. Proportion of Patients Receiving Treatment With Osteoporosis Medications by Instrumental Variable Strata

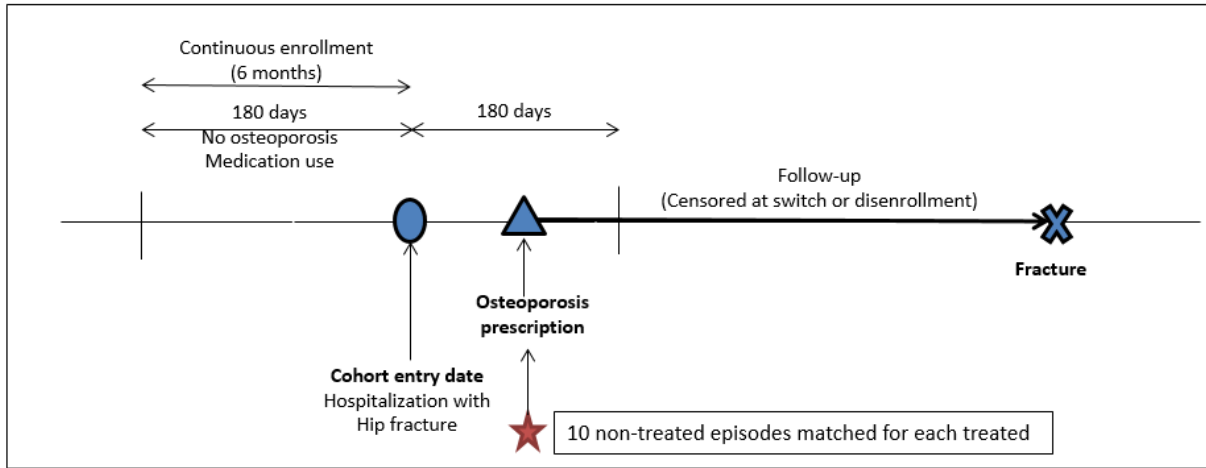
eFigure 3. Cumulative Regression Function With Pointwise 95% Confidence Interval for the Treatment Effect Under the Additive Hazard Model

eTable. Components of the Composite Outcome

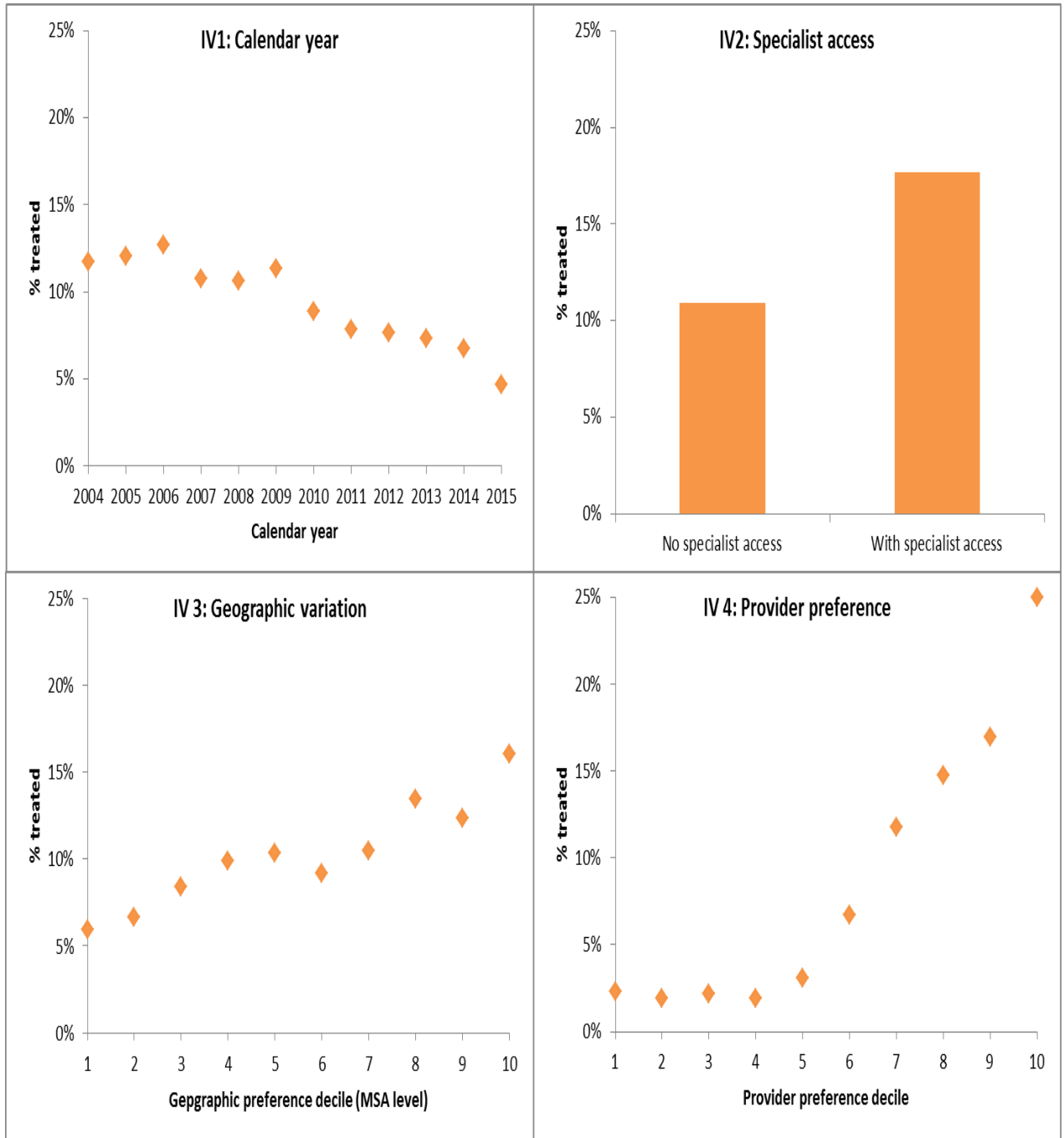
eAppendix. Model Equations

This supplementary material has been provided by the authors to give readers additional information about their work.

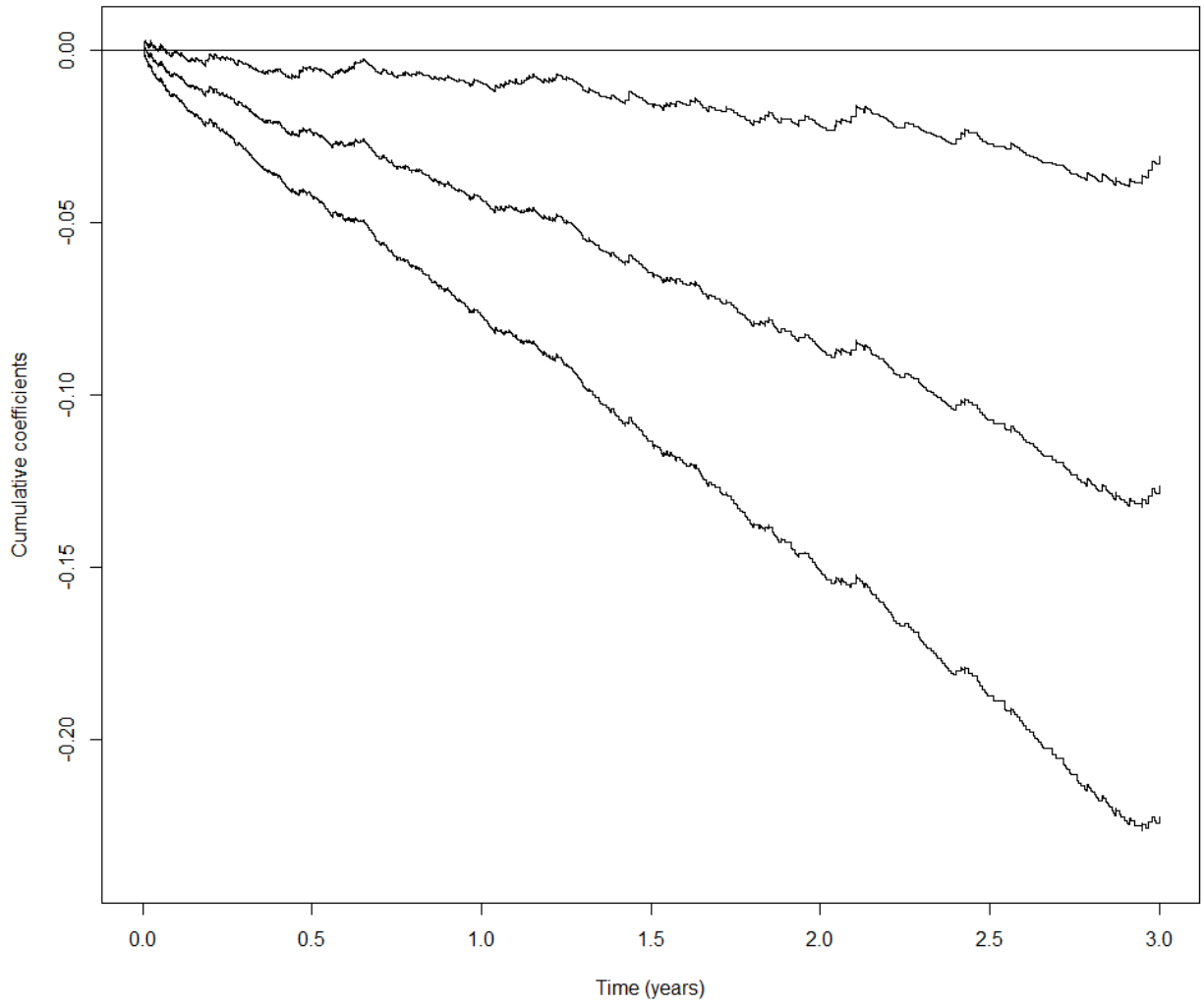
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eTable. Components of the Composite Outcome

Fracture	Definition/codes
1. Humerus	Humerus fracture diagnosis (ICD-9: 812.xx, 733.11) AND procedure within 30 days of fracture date (ICD-9: 78.52, 79.01, 79.11, 79.21, 79.31, 79.61; CPT-4: 23600, 23605, 23610, 23615, 23620, 23625, 23630, 23665, 23670, 23680, 24500, 24505, 24506, 24510, 24515, 24530, 24531, 24535, 24536, 24538, 24540, 24542, 24545, 24560, 24565, 24570, 24575, 24581, 24583, 24585-8, 24516)
2. Radius and/or Ulna	Radius/ulna fracture diagnosis (ICD-9: 813.xx, 733.12) AND procedure within 30 days of fracture date (ICD-9: 78.53, 79.02, 79.12, 79.22, 79.32, 79.62; CPT-4: 24620, 24625, 24635, 24650, 24655, 24660, 24665-6, 24670, 24680, 24685, 25500, 25505, 25510, 25515, 25530, 25535, 25540, 25545, 25560, 25565, 25570, 25575, 25600, 25605, 25610-1, 25615, 25620, 25650)
3. Hip	Hip fracture diagnosis (ICD-9 code: 820.xx, 733.14) during hospitalization AND procedure code during hospitalization (ICD-9: 78.55, 79.05, 79.15, 79.25, 79.35, 79.65; CPT-4: 27230-27248)
4. Pelvis	Pelvis fracture diagnosis (ICD-9: 808.xx)

Codes used for identification of confounding variables: Osteoporosis diagnosis (ICD-9-CM codes 733.0x), presence of bone mineral density test (CPT code 77080, 77085), Parkinson's disease (ICD-9-CM codes 332.xx or 333.0x), Alzheimer's disease or other dementia (ICD-9-CM codes 290.xx, 294.xx, 330.xx, 331.xx), obesity (ICD-9-CM codes 278.0x, 649.1x, V85.3x, V85.4x), diabetes mellitus (ICD-9-CM codes 250.xx), rheumatoid arthritis (ICD-9 codes 714.x), or history of falls, syncope, or gait abnormality (ICD-9-CM codes E885, E885.9x, E888.xx, 780.2x, 458.0x, 781.2x, 782.3x)

eAppendix. Model Equations

1. Mixed effect models for calculating adjusted rates of treatment for creating geographic and provider preference IVs

$$\text{logit} \left(P(Y_{ij} = 1 | \text{Age}_i, \text{Gender}_i, \text{Random effect}_j^*) \right) = \beta_0 + \beta_1 \text{Age}_i + \beta_2 \text{Gender}_i + \beta_{3j}$$

* MSA Region was the random variable for IV3 and Primary provider was the random variable for IV4

Y_{ij} = treatment initiation status in individual i in region j (or with provider j)

β_0 = Fixed intercept

β_1 = Age coefficient

β_2 = Gender coefficient

β_{3j} = Random intercept specific to region j (or provider j)

2. First stage instrumental variable models

$$\Pr(A_i = 1 | IV = IV_i, X = x_i) = \frac{\exp(\beta_0 + \beta_1 IV_i + \sum_{k=2}^n \beta_k x_{k,i})}{\{1 + \exp(\beta_0 + \beta_1 IV_i + \sum_{k=2}^n \beta_k x_{k,i})\}}$$

$$\Pr(A_i = 1|IV = IV_i, X = x_i)$$

= Probability of osteoporosis medication initiation given covariates and instrumental variable values for each individual i

$\beta_0 =$ Intercept

$\beta_1 =$ IV co-efficient

$\beta_k =$ Co-efficient (β_2 through β_n) for predictor variables

$x_{k,i} =$ Covariate values for individual i

3. Second stage instrumental variable model (Additive hazards model)

$$h(t|A, X) = h_0(t) + \beta_1(t)A + \beta_2(t)\Delta + \sum_{k=3}^n \beta_k(t)x_k$$

$h_0(t) =$ baseline hazard

$\beta_1 =$ Treatment effect estimate

$A =$ Actually received treatment

$\beta_2(t)\Delta$

= Control function which is meant to capture variation in the hazard function due to unobserved correlates of the treatment;

where $\Delta = A - \Pr(A_i = 1|IV = IV_i, X = x_i)$

$\beta_k =$ Co-efficient for other covariates in the model