

# Investigating Imminent Fracture Risk in Elderly Osteoporotic Women

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**Amgen needed expert analysis** regarding the implications behind the longitudinal, healthcare data from the Study of Osteoporotic Fractures (SOF). This study includes 20 years of prospectively collected data, covering periodic exams that assess osteoporosis care and outcomes, and started in 1986, originally including 9,704 Caucasian women from the U.S., aged 65 or older.

Importantly, each qualifying exam measured and assessed potential risk factors for fracture (e.g., bone mineral density [BMD], physical diseases, medications taken, etc.), and the incidence of subsequent fractures was also gathered.

Fractures were of particular interest to Amgen because of a new drug in its pipeline. The SOF was able to differentiate between two types of fracture that adversely affects this population, namely: [1] hip fractures, which served as the study's primary outcome; and [2] non-vertebral fractures, which served as the secondary outcome.

## Approach

After understanding the baseline survival analysis another team had created, our team set out to verify the initial findings by creating a more robust model that could highlight the interaction between certain predictors and fracture events. Exploratory factor analysis (EFA) was first used to identify key variables that would influence the model, and then our team created several *latent constructs*, such as "Cognitive Disease", before validating the structure of these constructs with confirmatory factor analysis (CFA).

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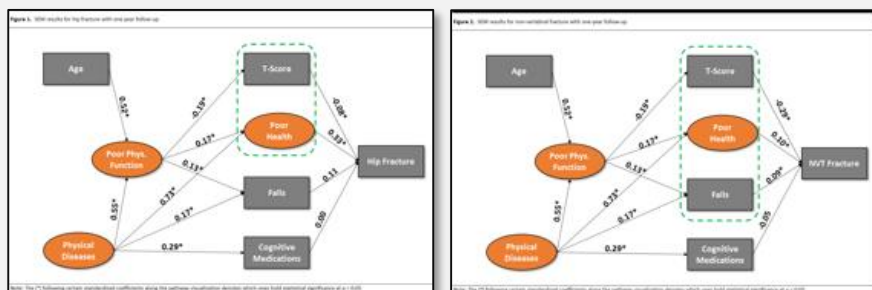
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We then employed structural equation modeling (SEM) to explore the inter-relationships among the latent constructs *as well as* bone fracture. Multiple models were then tested in order to create a model of best fit out of the latent constructs (i.e., Physical Disease, Poor Physical Function, and Poor Health) and the remaining, significant, predictor variables (e.g., age).

## Recommendations

Interestingly, our SEM work simultaneously validated and built upon the previous survival analysis done by another team. Specifically, our model highlighted relationships among variables that had been previously overlooked, mainly because prior work only explored the direct relationships between any two variables.

As such, our team recommended that Amgen reconsider which variables it considered as direct predictors of fracture in elderly women, focusing on a more limited set than previously believed.



## Results

Our SEM results provided Amgen with valuable insights into the market potential for the bone drug Romosozumab – currently not approved by any regulatory body – since this drug increases bone mineral density (BMD), a direct predictor of fracture.

Specifically, an initial Phase 3 study – the STRUCTURE trial – met its primary endpoint, demonstrating a statistically significant difference in favor of Romosozumab in the percent change of total hip BMD through month 12, further reinforcing the SEM findings.

## About Statistics Solutions

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*This study was presented by Rich Barron, Amgen's Director of Global Health Economics, at the American Society for Bone and Mineral Research (ASBMR) 2015 Annual Meeting in Seattle, the poster of which can be viewed on our website.*