Background
Atypical Femur Fractures (AFF) have been associated with antiresorptive therapies for osteoporosis. Studies evaluating AFF have varied in methodology and AFF definition. The ASBMR Task Force on Atypical Femur Fractures published revised criteria for AFF definitions in 2014. We conducted a retrospective case-control study, evaluating femur subtrochanteric/diaphyseal fractures for features of AFF using ASBMR 2014 criteria.

Methods
Inclusion criteria: Women and men age 30 and over with low trauma femur shaft fracture from January 1, 2005 to June 30, 2014, and assessable plain radiographs.

Exclusion criteria: Evidence of major trauma; periprosthetic fracture; Pagets, or other bone lesions in the femur.

Design: Retrospective case-control study using electronic health records from a multi-institution health information database. The earliest occurrence of the above criteria was the index date.

Fracture evaluation (see Figure 1):
- Radiographs were identified using ICD9 codes for femur shaft fractures (821.XX and 733.97). CT scans or other imaging modalities were not utilized.
- Pre-screening was performed by a radiologist physician assistant for exclusion criteria.
- Two musculoskeletal radiologists blinded to treatment status then reviewed and scored each radiograph using the ASBMR 2014 AFF feature definitions. Any radiographs with exclusion criteria missed on pre-screening were removed by the radiologists. All discrepancies on individual AFF features were jointly adjudicated.
- AFF features were summed to determine whether a fracture was an AFF or a non-AFF femur shaft fracture.
- Radiologists also measured shaft diameter, lateral and medial cortical thickness 5 cm below the lesser trochanter.

Figure 1. Flowchart of radiograph evaluation.

Case-control study:
- Patients with AFF were matched for race and sex to two patients with low-trauma “control” femur fractures, from radiographs evaluated during radiologist review, including shaft, hiptrochanteric or distal femur fractures; excluding periprosthetic fractures or bone lesions.
- Chart review was performed for structured (coded) and unstructured (text) data in the health record. Comorbidities were obtained via ICD9 codes. Medication use was confirmed as low-trauma by review of text notes surrounding the fracture event.
- Medication use (osteoporosis medications, glucocorticoids, proton pump inhibitors, etc.) was determined primarily from dispensing records and augmented by chart review.

Results
- 98 patients had low-trauma fracture in the correct location for possible AFF. Table 1 describes AFF features.
- 57 patients had AFF, 53 (93%) white, 49 (86%) female.
- 54 AFF cases matched to 108 non-AFF fracture controls (see Table 2).
- Control fractures (19 proximal; 29 shaft; 56 distal) could be outside AFF location due to low number of controls in shaft.
- Clinical variables were similar between control fractures in the femoral shaft (n=29) and non-shaft regions (n=79).
- Age, cortical thickness, prior fracture, other medical conditions and proton pump inhibitors were not associated with AFF.

Table 2. Univariate odds ratios

Table 1. Low-trauma subtrochanteric/diaphyseal fracture features (*marks those counted as meeting criteria)

Conclusions
Over half of the low-energy trauma femoral shaft fractures met the ASBMR 2014 AFF criteria. Notably almost half of the AFFs occurred without bisphosphonate exposure. AFFs were associated with osteoporosis diagnosis, bisphosphonates within 5 years, glucocorticoid use at fracture occurrence, prodromal pain and lower alkaline phosphatase.