**SUPPLEMENTAL CONTENT**

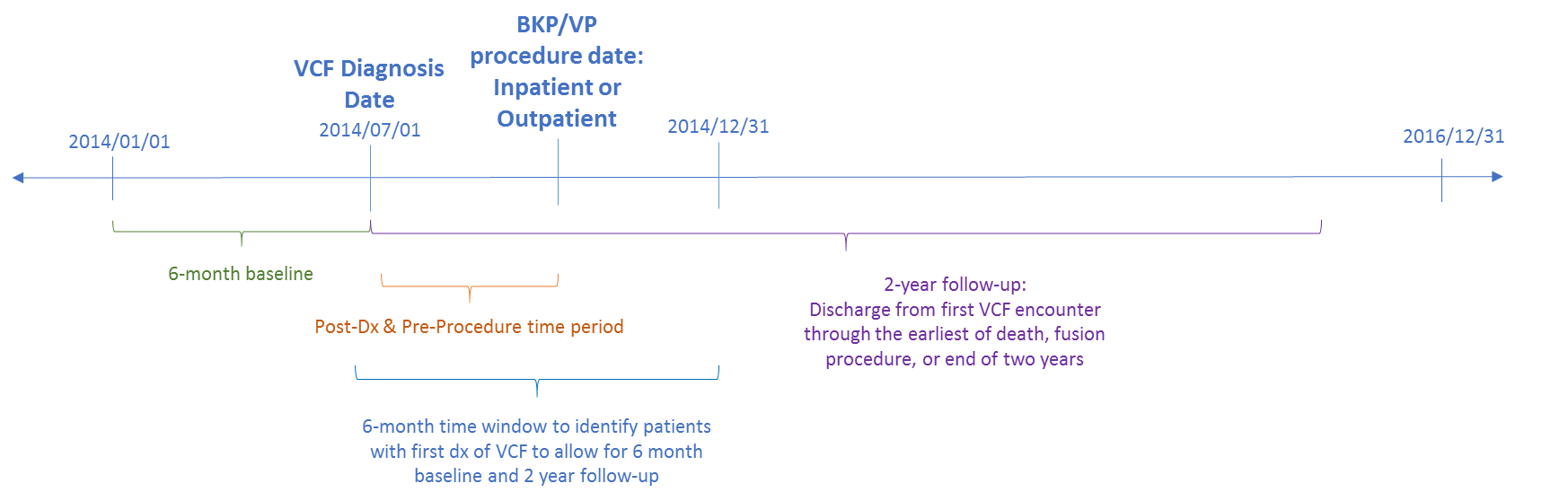
**SUPPLEMENTAL METHODS: RETROSPECTIVE ANALYSIS OF CMS CLAIMS DATA**

**Background:** This retrospective analysis compared medical resource utilization and payments (from a Medicare payor perspective) for patients treated with Balloon Kyphoplasty (BKP), Vertebroplasty (VP), or conservative medical management (CMM) following a diagnosis of Vertebral Compression Fracture (VCF) secondary to osteoporosis. The surgery is conducted either in outpatient or inpatient setting so BKP and VP groups were further categorized in the analysis to account for patient differences in the settings.

**Data Source & Study Time Period:** CMS 100% claims 2014 – 2016.

**Patient Selection:**

Patients were selected based on the date of their first Vertebral Compression Fracture (VCF) diagnosis. For surgical patients, follow-up was evaluated from the day of first VCF diagnosis through two years following discharge from surgery. For CMM patients, follow-up was evaluated over the two years following discharge from their first visit with diagnosis of VCF. Among all patients, follow-up was censored to end at the earliest of death, receipt of a spinal fusion procedure (follow-up censored to the day prior to spinal fusion), or the end of two years follow-up.

**Study Time Period**

Three patient groups (BKP, VP, and CMM) were identified using a combination of ICD-9 and ICD-10 diagnosis codes, ICD-9 and ICD-10 procedure codes, CPT procedure codes as follows:

* Diagnosis of VCF – We selected patients with first VCF diagnosis in any setting.
* Balloon Kyphoplasty procedure (BKP) or vertebroplasty (VP) procedure performed for the surgical cohorts; no procedure performed at any time in the study period for the CMM cohort
* Survived through the BKP or VP surgical procedure for the surgical cohorts, survived through the initial visit with a VCF diagnosis for the CMM cohort
* No history of BKP or VP procedures in six months baseline for all cohorts
* No subsequent BKP or VP procedure (repeat procedure) in follow-up
* Aged 65+
* Continuous Medicare enrollment with allowed 30d gap
* No diagnosis of cancer (excluding skin cancers)

Further, surgery groups were divided by place of service – inpatient and outpatient.

**Matching**

A propensity score match was performed for the four surgical cohorts combines (BKP Inpatient, BKP Outpatient, VP Inpatient or VP outpatient) versus patients with non-surgical management (CMM) to control for case selection bias for patients undergoing surgery. The following covariates were included in the propensity score model:

* Age Group
* Gender
* Census Division
* Charlson Score (calculated with diagnoses during 6 months baseline through the index procedure date)
* Osteoporosis diagnosis
* Historic (Baseline) resource use in the six months prior to VCF diagnosis: total number of Inpatient Visits and/or ED visits
* Historic (Baseline) total Medicare payments in the six months prior to VCF diagnosis: categorized as no payments, low (< 25th percentile), medium (25-75th percentile), or high (>75th percentile)

**Post-Acute Care Use**

The proportion of patients with any visit (all-cause) following VCF diagnosis through the end of follow-up or death were identified in the following post-acute care settings: home health, skilled nursing facility, inpatient rehab facility and hospice. Additionally, the proportion of patients with a non-VCF related inpatient readmission (i.e. an inpatient readmission with no diagnosis of VCF and no BKP or VP procedure) was summarized. Finally, to estimate the cost of subsequent fracture for the CMM cohort patients with a follow-up inpatient or outpatient hospital admission with primary diagnosis of VCF were flagged. To estimate the cost of subsequent fracture with treatment for the surgical cohorts, follow-up inpatient or outpatient hospital admissions with a BKP or VP procedure performed were flagged.

**Medicare Payments**

Medicare payments (termed “costs” in the model) were assessed for the following time periods and settings. Conditional payments (i.e. only among patients with the event of interest) were summarized for use in the model.

**Patient Demographics: CMS Propensity-Score Matched Claims Analysis**

|  | Matched Group 1:  BKP Inpatient vs. CMM | | | | Matched Group 2:  BKP Outpatient vs. CMM | | | Matched Group 3:  VP Inpatient vs. CMM | | | Matched Group 4:  VP Outpatient vs. CMM | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | BKP Inpatient Matched | | CMM Matched | P-Val | BKP Outpatient Matched | CMM Matched | P-Val | VP Inpatient Matched | CMM Matched | P-Val | VP Outpatient Matched | CMM Matched | P-Val |
| N | | 2,071 | 2,071 |  | 3,708 | 3,708 |  | 710 | 710 |  | 1,042 | 1,042 |  |
| Age |  | |  |  |  |  |  |  |  |  |  |  |  |
| Mean | 81.6 | | 82.2 | 0.028 | 78.9 | 79.3 | 0.015 | 81.4 | 81.8 | 0.287 | 79.5 | 80.4 | 0.006 |
| SD | 7.5 | | 7.1 |  | 7.3 | 7.2 |  | 7.6 | 7.6 |  | 7.5 | 7.2 |  |
| Median | 82 | | 83 |  | 79 | 79 |  | 82 | 83 |  | 80 | 81 |  |
| Age Group |  | |  | 0.526 |  |  | 0.626 |  |  | 0.918 |  |  | 0.800 |
| 65 - 69 | 7.4% | | 6.4% |  | 12.2% | 12.4% |  | 9.9% | 9.7% |  | 11.6% | 10.3% |  |
| 70 - 79 | 29.4% | | 29.7% |  | 39.4% | 40.2% |  | 25.8% | 25.5% |  | 35.6% | 36.1% |  |
| 80 - 89 | 48.2% | | 49.6% |  | 41.7% | 41.3% |  | 49.6% | 51.1% |  | 43.9% | 44.8% |  |
| 90+ | 14.9% | | 14.3% |  | 6.7% | 6.1% |  | 14.8% | 13.7% |  | 8.9% | 8.8% |  |
| Female (%) | 82.3% | | 83.3% | 0.387 | 78.4% | 80.7% | 0.013 | 82.3% | 83.0% | 0.780 | 79.2% | 79.9% | 0.704 |
| Census Division (%) |  | |  | 0.980 |  |  | 0.980 |  |  | 1.000 |  |  | 0.993 |
| EAST\_NORTH\_CENTRAL | 24.1% | | 25.4% |  | 20.4% | 20.8% |  | 21.4% | 21.4% |  | 23.1% | 22.6% |  |
| EAST\_SOUTH\_CENTRAL | 6.3% | | 5.8% |  | 7.9% | 7.8% |  | 6.1% | 5.5% |  | 8.0% | 7.0% |  |
| MIDDLE\_ATLANTIC | 10.5% | | 10.4% |  | 7.8% | 7.6% |  | 8.6% | 9.0% |  | 4.9% | 4.8% |  |
| MOUNTAIN | 3.0% | | 3.2% |  | 3.2% | 3.2% |  | 4.5% | 4.9% |  | 5.1% | 5.0% |  |
| NEW\_ENGLAND | 5.4% | | 4.9% |  | 6.4% | 5.8% |  | 5.1% | 5.5% |  | 5.6% | 6.2% |  |
| PACIFIC | 9.2% | | 9.1% |  | 7.5% | 7.4% |  | 8.2% | 7.6% |  | 5.7% | 5.9% |  |
| SOUTH\_ATLANTIC | 23.9% | | 24.3% |  | 21.5% | 22.4% |  | 19.9% | 19.4% |  | 16.1% | 16.3% |  |
| WEST\_NORTH\_CENTRAL | 6.7% | | 6.5% |  | 9.1% | 8.9% |  | 14.9% | 14.5% |  | 18.2% | 19.2% |  |
| WEST\_SOUTH\_CENTRAL | 11.0% | | 10.5% |  | 16.2% | 16.0% |  | 11.4% | 12.1% |  | 13.3% | 13.1% |  |
| Charlson Score Group (%) |  | |  | 0.630 |  |  | 0.701 |  |  | 0.494 |  |  | 0.985 |
| 0 | 34.3% | | 33.8% |  | 56.6% | 56.3% |  | 30.6% | 32.1% |  | 55.9% | 56.0% |  |
| 1 | 23.5% | | 22.5% |  | 21.3% | 22.0% |  | 22.7% | 20.1% |  | 20.6% | 20.3% |  |
| 2+ | 42.2% | | 43.6% |  | 22.1% | 21.6% |  | 46.8% | 47.7% |  | 23.5% | 23.7% |  |
| Diagnosis of Osteoporosis (%) | 70.8% | | 71.0% | 0.918 | 63.9% | 63.5% | 0.754 | 66.8% | 66.6% | 1 | 56.0% | 56.1% | 0.965 |
| Time from first visit with diagnosis of VCF to surgery (days) |  | |  |  |  |  |  |  |  |  |  |  |  |
| Mean | 13.3 | | N/A |  | 29.1 | N/A |  | 401.7 | N/A |  | 35.0 | N/A |  |
| SD | 47.0 | |  | 93.8 |  | 208.4 |  | 106.4 |  |
| Median | 0.0 | |  | 0.0 |  | 0.0 |  | 0.0 |  |
| Interquartile Range (IQR) | 0-0 | |  | 0-12 |  | 0-37 |  | 0-15.75 |  |
| Baseline Resource Use |  | |  |  |  |  |  |  |  |  |  |  |  |
| Number of Inpatient Visits |  | |  | 0.917 |  |  | 0.782 |  |  | 0.760 |  |  | 0.727 |
| 0 | 68.2% | | 68.5% |  | 78.6% | 79.2% |  | 64.8% | 66.5% |  | 78.9% | 79.8% |  |
| 1 | 21.6% | | 21.7% |  | 16.6% | 16.0% |  | 23.9% | 23.2% |  | 16.7% | 16.5% |  |
| 2+ | 10.2% | | 9.8% |  | 4.8% | 4.8% |  | 11.3% | 10.3% |  | 4.4% | 3.7% |  |
| Number of ED Visits |  | |  | 0.723 |  |  | 0.882 |  |  | 0.912 |  |  | 0.999 |
| 0 | 56.1% | | 56.7% |  | 55.3% | 55.8% |  | 56.5% | 57.6% |  | 55.5% | 55.4% |  |
| 1 | 27.5% | | 27.8% |  | 28.6% | 28.1% |  | 28.0% | 27.3% |  | 28.8% | 28.9% |  |
| 2+ | 16.4% | | 15.5% |  | 16.1% | 16.1% |  | 15.5% | 15.1% |  | 15.7% | 15.7% |  |
| Total Payment Group\* |  | |  | 0.7555 |  |  | 0.8911 |  |  | 0.914 |  |  | 0.943 |
| Low | 24.9% | | 25.0% |  | 19.1% | 18.7% |  | 21.4% | 22.3% |  | 17.4% | 16.9% |  |
| Medium | 49.5% | | 50.5% |  | 64.1% | 64.5% |  | 49.9% | 49.7% |  | 67.8% | 68.4% |  |
| High | 25.5% | | 24.6% |  | 16.7% | 16.8% |  | 28.7% | 28.0% |  | 14.9% | 14.7% |  |
|  |  | |  |  |  |  |  |  |  |  |  |  |  |

**SUPPLEMENTAL MODELING TABLES**

Table S1: 6-month probability of vertebral fracture amongst the general US populationa

| **Age category** | **Females (standard error)** | **Males (standard error)** |
| --- | --- | --- |
| 50-54 | 0.032% (0.0033%) | 0.021% (0.0022%) |
| 55-59 | 0.066% (0.0067%) | 0.023% (0.0023%) |
| 60-64 | 0.062% (0.0063%) | 0.089% (0.0091%) |
| 65-69 | 0.116% (0.0119%) | 0.057% (0.0058%) |
| 70-74 | 0.236% (0.0241%) | 0.107% (0.0109%) |
| 75-79 | 0.261% (0.0266%) | 0.175% (0.0178%) |
| 80-84 | 0.311% (0.0317%) | 0.179% (0.0182%) |
| 85+ | 0.546% (0.0557%) | 0.618% (0.0630%) |

aData derived from Ettinger et al. Osteoporos Int. 2010. 21:25-33. Beta distributions used to represent uncertainty. Standard error calculated based on lower and upper confidence limits represented by 20% either side of mean value. Annual rates converted to 6-month probabilities using the formula: probability = 1 – exp (-rate \* 0.5).

Table S2: Relative risk of fracture versus general population, by age at initial vertebral fracture

| Age at initial fracture | Relative risk of subsequent fracture  (standard error) |
| --- | --- |
| 70 | 5.85 (0.597) |
| 71 | 5.59 (0.57) |
| 72 | 5.35 (0.546) |
| 73 | 5.10 (0.521) |
| 74 | 4.85 (0.495) |
| 75 | 4.63 (0.472) |
| 76 | 4.40 (0.449) |
| 77 | 4.18 (0.427) |
| 78 | 3.97 (0.405) |
| 79 | 3.79 (0.386) |
| 80 | 3.66 (0.373) |
| 81 | 3.50 (0.357) |
| 82 | 3.36 (0.342) |
| 83 | 3.23 (0.329) |
| 84 | 3.12 (0.318) |
| 85 | 3.01 (0.308) |
| 86 | 2.99 (0.305) |
| 87 | 2.85 (0.290) |
| 88 | 2.86 (0.292) |
| 89 | 2.84 (0.290) |
| 90 | 2.78 (0.284) |

Data based on model reported by Svedbom et al. Osteoporos Int. 2013. 24(1):355-367. Lognormal distributions used to represent uncertainty, with standard error estimated by specifying confidence intervals for each relative risk based on 20% variation either side of the mean.

Table S3: Hazard ratio for treatment effect on mortalitya

| **Treatment comparison** | **Hazard ratio for mortality in surgery group** | **95% CI** | **p-value** |
| --- | --- | --- | --- |
| BKP vs. CMM, inpatient | 0.70 | 0.64 – 0.78 | <0.0001 |
| BKP vs. CMM, outpatient | 0.72 | 0.65 – 0.80 | <0.0001 |
| VP vs. CMM, inpatient | 0.64 | 0.54 – 0.77 | <0.0001 |
| VP vs. CMM, outpatient | 0.76 | 0.62 – 0.92 | 0.0050 |

aLognormal distributions used to represent uncertainty

Table S4: Initial procedure cost (facility + physician) by intervention and setting (USD)a

| **Intervention & setting** | **Mean cost per patient** | **Standard Deviation** |
| --- | --- | --- |
| BKP, inpatient | 15,696 | 14,037 |
| BKP, outpatient | 5,586 | 1,514 |
| VP, inpatient | 16,162 | 15,252 |
| VP, outpatient | 2,304 | 803 |

aGamma distributions used to represent uncertainty

Values based on Propensity-Score matched cohorts in an analysis of CMS claims data.

Table S5: Two-year post-acute care costs per patient (Mean ± SD), and the proportion (%) with any utilization by care settinga

| **Treatment comparison and setting** | **Treatment group** | **Home health** | **Skilled nursing facility** | **Hospice** | **Inpatient rehabilitation** | **Totalb** |
| --- | --- | --- | --- | --- | --- | --- |
| BKP vs. CMM, inpatient | BKP | 8,467 ± 7,728 (70.8) | 24,651 ± 18,627 (66.4) | 12,996 ± 19,441 (19.1) | 23,908 ± 14,978  (16.1) | 28,694 |
| CMM | 7,883: 7,106 (59.2) | 24,217 ± 17,753 (58.3) | 13,533 ± 22,067 (24.0) | 22,647 ± 11,388  (8.9) | 24,049 |
| BKP vs. CMM, outpatient | BKP | 7,485 ± 5,519 (42.7) | 20,035 ± 14,967 (23.9) | 14,343, 19,780 (8.5) | 22,170 ± 11,529  (5.7) | 10,467 |
| CMM | 7,990 ± 7,916 (42.1) | 22,402 ± 17,042 (27.0) | 16,987 ± 23,955 (11.0) | 22,780 ± 11,309 (4.3) | 12,261 |
| VP vs. CMM, inpatient | VP | 9,489 ± 8,459 (73.8) | 23,892 ± 17,854 (66.5) | 12,106 ± 18,906 (20.6) | 26,426 ± 19,473 (14.5) | 29,210 |
| CMM | 7,854 ± 7,034 (54.1) | 22,927 ± 17,523 (58.2) | 14,990 ± 22,715 (22.1) | 22,147 ± 9,709 (6.2) | 22,271 |
| VP vs. CMM, outpatient | VP | 7,003 ± 6,465 (43.6) | 20,877 ± 18,429 (26.8) | 13,863: 21,334 (9.5) | 22,068 ± 8,383 (6.6) | 11,422 |
| CMM | 7,408 ± 6,829 (41.4) | 21,380 ± 16,667 (28.7) | 16,044 ± 20,742 (12.0) | 22,228 ± 11,398 (4.2) | 12,062 |

adata are presented as mean ± SD (%). Gamma distributions used to represent uncertainty

bTotal cost after adjusting for the proportion with care by setting

Values based on Propensity-Score matched cohorts in an analysis of CMS claims data.

Table S6: Mean 2-year costs of post-fracture outpatient care (USD)a

| **Treatment comparison and setting** | **Treatment group** | **2-year outpatient costs** | **Per-cycle outpatient costsb** |
| --- | --- | --- | --- |
| BKP vs. CMM, inpatient | BKP | 4,221 ± 5,765 | 1,055 |
| CMM | 3,043 ± 5,884 | 761 |
| BKP vs. CMM, outpatient | BKP | 5,326 ± 6,823 | 1,332 |
| CMM | 4,250 ± 6,206 | 1,062 |
| VP vs. CMM, inpatient | VP | 4,412 ± 6,305 | 1,103 |
| CMM | 3,821 ± 6,050 | 955 |
| VP vs. CMM, inpatient | VP | 5,250 ± 6,645 | 1,313 |
| CMM | 3,980 ± 5,897 | 995 |

aData presented as mean ± SD. Gamma distributions used to represent uncertainty

bApplied in the first four model cycles

Values based on Propensity-Score matched cohorts in an analysis of CMS claims data.

Table S7: Mean inpatient cost for repeat fracture, USDa

| **Treatment comparison and setting** | **Treatment group** | **Inpatient cost for repeat fracture** |
| --- | --- | --- |
| BKP versus CMM, inpatient | BKP | 14,718 ± 7,194 |
| CMM | 7,698 ± 4,017 |
| BKP versus CMM, outpatient | BKP | 13,457 ± 5,519 |
| CMM | 7,349 ± 4,292 |
| VP versus CMM, inpatient | VP | 14,833 ± 6,138 |
| CMM | 7,654 ± 2,823 |
| VP versus CMM, outpatient | VP | 16,320 ± 9,931 |
| CMM | 7,349 ± 4,292 |

aData presented as mean ± SD. Gamma distributions used to represent uncertainty

Values based on Propensity-Score matched cohorts in an analysis of CMS claims data.

Table S8: Mean utility weights by treatment group and time since fracture, based on data from the FREE-2 trial, adjusted to US utility values.a

| **Time since fracture** | **BKP/VP** | **CMM** |
| --- | --- | --- |
| 0-6 months | 0.68 ± 0.018 | 0.60 ± 0.020 |
| 6-12 months | 0.73 ± 0.018 | 0.65 ± 0.020 |
| 12-18 months | 0.72 ± 0.018 | 0.66 ± 0.021 |
| 18-24 months | 0.72 ± 0.018 | 0.67 ± 0.021 |
| 24-30 months | 0.70 ± 0.019 | 0.67 ± 0.021 |
| 30-36 months | 0.69 ± 0.020 | 0.67 ± 0.021 |
| Beyond 36 months | 0.67 ± 0.021 | 0.67 ± 0.021 |

aData are presented as mean ± SD. Derived from Wardlaw et al. Lancet. 2009. 373:1016-1024 and Fryback et al. Med Care. 2007. 45:1162-1170. Beta distributions used to represent uncertainty.

Table S9: Age-specific population utilities from the general US population.a These factors were used to adjust the treatment-specific utilities according to patient age.

| **Age group** | **Utility** |
| --- | --- |
| 18-24 | 0.92 ± 0.01 |
| 25-34 | 0.91 ± 0.01 |
| 35-44 | 0.89 ± 0.01 |
| 45-54 | 0.86 ± 0.01 |
| 55-64 | 0.83 ± 0.01 |
| 65-74 | 0.82 ± 0.01 |
| 75+ | 0.76 ± 0.01 |

aData are presented as mean ± SE and are derived from Szende et al. 2014., DOI 10.1007/978-94-007-7596-1. Beta distributions used to represent uncertainty.