## Supplemental Table 1. Sensitivity analysis — Average costs per patient per year: Hyperprolactinemia Cohort vs. Hyperprolactinemia-free Cohort

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Direct healthcare costs1,**  **2016 USD** | **Commercially insured patients** | | | | **Medicaid-insured patients** | | | |
| **HPRL Cohort [A]** | **HPRL-free Cohort [B]** | **Cost difference (95% CI) [A] - [B]** | **P-value** | **HPRL Cohort [A]** | **HPRL-free Cohort [B]** | **Cost difference (95% CI) [A] - [B]** | **P-value** |
| **N = 3,144** | **N = 3,144** | **N = 1,360** | **N = 1,360** |
| **Medical service costs** | 11,406 ± 23,830 | 8,190 ± 23,946 | $3,216  (1,927 - 4,463) | 0.004\* | 11,731 ± 22,666 | 10,122 ± 22,632 | $1,608  (430 - 3,089) | 0.012\* |
| **HPRL-related2** | 1,356 ± 6,545 | 357 ± 7,812 | $999  (637 - 1,330) | 0.004\* | 822 ± 3,053 | 199 ± 1,952.67 | $623  (422 - 814) | 0.004\* |
| **Mental health-related** | 4,338 ± 14,807 | 3,310 ± 15,973 | $1,028  (191 - 1,763) | 0.020\* | 8,543 ± 22,641 | 8,381 ± 21,304 | $161  (-1,456 - 1,784) | 0.904 |
| **Pharmacy costs** | 6,636 ± 12,467 | 4,768 ± 8,704 | $1,868  (1,416 - 2,385) | 0.004\* | 7,798 ± 10,180 | 6,618 ± 17,395 | $1,180  (336 - 1,961) | 0.012\* |
| **Total healthcare costs** | **18,042 ± 28,794** | **12,957 ± 26,548** | **$5,084**  **(3,652 - 6,471)** | **0.004\*** | **19,529 ± 26,560** | **16,740 ± 29,418** | **$2,788**  **(1,243 - 4,545)** | **0.008\*** |

*CI: confidence intervals; HPRL: hyperprolactinemia*

**Notes:**

**[1]** Healthcare costs were measured during the 12-month period following the index date.

**[2]** The main HPRL-related costs driver were hypothyroidism, sexual dysfunction, and amenorrhea.

## Supplemental Table 2. Sensitivity analysis — Comparison of the risk of hyperprolactinemia

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Number of treatment episodes with HPRL** | | **No/Low Prolactin Elevation Cohort vs. High/Moderate Prolactin Elevation Cohort** | |
| **No/Low Prolactin Elevation Cohort** | **High/Moderate Prolactin Elevation Cohort** |
| **Commercially insured patients** | **N = 446,673** | **N = 77,532** | **Odds ratios**  **(95% CI)** | **P-value** |
| Episodes with HPRL | 2,099 | 702 | 0.53 (0.49 ; 0.58) | <0.001\* |
| **Medicaid-insured patients** | **N = 177,379** | **N = 58,447** | **Odds ratios**  **(95% CI)** | **P-value** |
| Episodes with HPRL | 664 | 459 | 0.46 (0.40 ; 0.51) | <0.001\* |

*CI: confidence intervals; HPRL: hyperprolactinemia*

## Supplemental Table 3. Excess costs of atypical antipsychotics associated with high/moderate prolactin elevation compared to no/low prolactin elevation

|  |  |  |
| --- | --- | --- |
| **Variable** |  | **Estimate** |
| Commercial health plan population size | **[A]** | 1,000,000 |
| Prevalence of antipsychotic use in the US1 | **[B]** | 2.16% |
| Estimated number of individuals receiving antipsychotics | **[C]** | 21,649 |
| Estimated proportion of antipsychotic users receiving AAs | **[D]** | 84.2% |
| Estimated number of individuals receiving AAs | **[E]** | 18,222 |
| Estimated proportion of AA users receiving AAs associated with high/moderate prolactin elevation | **[F]** | 14.8% |
| Estimated number of individuals receiving AAs associated with high/moderate prolactin elevation | **[G]** | 2,697 |
| Prevalence of HPRL among individuals receiving AAs associated with high/moderate prolactin elevation2 | **[H]** | 35.2% |
| Estimated number of individuals with HPRL receiving AAs associated with high/moderate prolactin elevation | **[I]** | 992 |
| Estimated relative risk of HPRL among individuals receiving AAs associated with no/low vs. high/moderate prolactin elevation | **[J]** | 0.21 |
| Estimated number of individuals with HPRL should individuals receiving AAs associated with high/moderate prolactin elevation have received AAs associated with no/low prolactin elevation | **[K]** | 208 |
| Estimated excess number of individuals with HPRL associated with AAs associated with high/moderate prolactin elevation | **[L]** | 784 |
| Estimated excess annual costs of HPRL (USD 2016) per individual | **[M]** | $5,732 |
| **Total excess costs of HPRL associated with AAs associated with high/moderate prolactin elevation** | **[N]** | **$4,494,139** |

*AA: atypical antipsychotic; HPRL: hyperprolactinemia, US: United States, USD: United States dollars*

**Notes:**

**[1]** IMS, Vector One: National (VONA) and Total Patient Tracker (TPT) Database, Year 2013, Extracted April 2014

**[2]** Prevalence of HPRL is based on Fleischhacker et al. "A randomized trial of paliperidone palmitate and risperidone long-acting injectable in schizophrenia." International Journal of Neuropsychopharmacology, Invega sustenna® prescribing information [Online]. Available: Available at: <https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022264s015lbl.pdf> [Accessed 14 August 2017], and Potkin et al. "Efficacy and tolerability of asenapine in acute schizophrenia: a placebo-and risperidone-controlled trial." The Journal of clinical psychiatry.