

## Supplementary Online Content

Sacarny AJ, Barnett ML, Le J, Tetkoski F, Yokum D, Agrawal S. Effect of peer comparison letters for high-volume primary care prescribers of quetiapine in older and disabled adults: a randomized clinical trial. *JAMA Psychiatry*. Published online August 1, 2018. doi:10.1001/jamapsychiatry.2018.1867

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

**eTable 1.** Classification Rules for Low-Value and Guideline-Concordant Patients

| <b>Patient Group</b>  | <b>Low-Value</b>  | <b>Guideline-Concordant</b>   |
|---|---|---|
| Inclusion Criteria<br><i>Patient has any of the listed conditions in 2013 or 2014</i>   | Alzheimer’s Disease (54)<br>Dementia (55)                             | Schizophrenia (58)<br>Bipolar Disorders (59)<br>Major Depression (60) |
| Exclusion Criteria<br><i>Patient does not have any of the listed conditions in 2013 or 2014</i>   | Schizophrenia (58)<br>Bipolar Disorders (59)<br>Major Depression (60) | Alzheimer’s Disease (54)<br>Dementia (55)                             |
| <p>Classifications based on FDA labeling for quetiapine.<sup>a,b</sup> Conditions identified using prescription drug hierarchical condition categories (RxHCCs) in Medicare Part D risk-adjustment data, which are based on diagnosis codes submitted by health care providers and Medicare Advantage plans. RxHCC numbers listed in parentheses. See Supplement 1 for more details.</p> <p><sup>a</sup> SEROQUEL (quetiapine fumarate) Prescribing Information. 2016; published online June. <a href="http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020639s0641bl.pdf">http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020639s0641bl.pdf</a></p> <p><sup>b</sup> SEROQUEL XR (quetiapine fumarate) Prescribing Information. 2016; published online June. <a href="http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020639s0641bl.pdf">http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020639s0641bl.pdf</a></p> |   |   |

**eTable 2. Summary Statistics About Patients**

|  | (1)    | (2)       | (3)                  |
|--|--------|-----------|----------------------|
|  | All    | Low-Value | Guideline-Concordant |
| N (No. of Patients)                      | 89,500 | 23,490    | 25,680               |
| Baseline Quetiapine Days Received (mean) | 192.6  | 189.6     | 202.6                |
| Age (mean)                               | 70.4   | 83.6      | 57.9                 |
| Nonwhite Race (%)                        | 29.7   | 27.3      | 31.4                 |
| Female Sex (%)                           | 63.8   | 68.8      | 61.2                 |
| Dementia or Alzheimer's (%)              | 45.1   | 100.0     | 0.0                  |
| Major Psychiatric Illness (%)            | 47.5   | 0.0       | 100.0                |
| Institutionalized in March 2015 (%)      | 15.2   | 25.2      | 4.4                  |
| Qualifies for Medicare by Disability (%) | 37.3   | 4.3       | 72.4                 |
| Dual Eligible in 2014 (%)                | 59.6   | 48.9      | 70.7                 |

Summary statistics describe baseline patients in study. Baseline quetiapine days refers to the quetiapine days received in the 9 months before the study began. Age is as of the study start date (April 2015). Nonwhite race includes anyone classified as Hispanic. Diagnoses are derived from 2013 and 2014 patient encounters with health care providers. Institutionalized indicates residing in a long-term care institution according to risk-adjustment data. Dual eligible defined as eligibility for both Medicare and Medicaid for at least 1 month in 2014.

**eTable 3.** Effect of Intervention on Source of Quetiapine by Guideline Conformity

| Patient Group         | (1)         | (2)                     | (3)                            | (4)     | (5)                  | (6)                     | (7)                            | (8)     |
|-----------------------|-------------|-------------------------|--------------------------------|---------|----------------------|-------------------------|--------------------------------|---------|
|                       | Low-Value   |                         |                                |         | Guideline-Concordant |                         |                                |         |
| Source                | All         | Baseline                | Other Prescribers <sup>a</sup> |         | All                  | Baseline                | Other Prescribers <sup>a</sup> |         |
|                       | Prescribers | Prescriber <sup>a</sup> | Non-Psych                      | Pysch   | Prescribers          | Prescriber <sup>a</sup> | Non-Psych                      | Pysch   |
| N                     | 23,490      | 23,490                  | 23,490                         | 23,490  | 25,680               | 25,680                  | 25,680                         | 25,680  |
| Control Mean          | 158.75      | 116.49                  | 37.80                          | 4.46    | 182.14               | 115.65                  | 37.94                          | 28.55   |
| Treatment Mean        | 147.87      | 105.80                  | 37.53                          | 4.54    | 177.86               | 109.45                  | 39.04                          | 29.37   |
| Raw Difference        | -10.88      | -10.69                  | -0.28                          | 0.08    | -4.29                | -6.21                   | 1.10                           | 0.83    |
|                       | (2.12)      | (2.20)                  | (1.70)                         | (0.49)  | (2.62)               | (2.54)                  | (1.47)                         | (1.41)  |
|                       | [<0.001]    | [<0.001]                | [0.870]                        | [0.862] | [0.102]              | [0.014]                 | [0.457]                        | [0.558] |
| Adjusted Difference   | -9.43       | -9.38                   | -0.12                          | 0.02    | -4.46                | -7.18                   | 0.94                           | 1.92    |
|                       | (1.64)      | (1.73)                  | (1.19)                         | (0.37)  | (1.41)               | (1.56)                  | (1.04)                         | (0.84)  |
|                       | [<0.001]    | [<0.001]                | [0.918]                        | [0.968] | [0.002]              | [<0.001]                | [0.366]                        | [0.022] |
| Percent Difference    | -5.94%      | -8.05%                  | -0.32%                         | 0.34%   | -2.45%               | -6.21%                  | 2.48%                          | 6.72%   |
|                       | (1.03%)     | (1.49%)                 | (3.15%)                        | (8.34%) | (0.77%)              | (1.35%)                 | (2.74%)                        | (2.93%) |
|                       | [<0.001]    | [<0.001]                | [0.918]                        | [0.968] | [0.002]              | [<0.001]                | [0.366]                        | [0.022] |
| Contribution to Total | -5.94%      | -5.91%                  | -0.08%                         | 0.01%   | -2.45%               | -3.94%                  | 0.52%                          | 1.05%   |
| Percent Difference    | (1.03%)     | (1.09%)                 | (0.75%)                        | (0.23%) | (0.77%)              | (0.86%)                 | (0.57%)                        | (0.46%) |
|                       | [<0.001]    | [<0.001]                | [0.918]                        | [0.968] | [0.002]              | [<0.001]                | [0.366]                        | [0.022] |

Shows effect of intervention on patients' source of quetiapine separately for low-value and guideline-concordant groups. Columns 1-4 consider only low-value patients while columns 5-8 consider only guideline-concordant patients. Columns 1 and 5 count quetiapine days from all prescribers. Columns 2 and 6 count only days from the patient's baseline study prescriber (i.e. patient received quetiapine from prescriber during the baseline period). Columns 3 and 7 count days from other prescribers without psychiatric specialization, and columns 4 and 8 count days from other prescribers with psychiatric specialization. The contribution to the total percent difference is defined as the column's adjusted difference (and standard error) divided by the all-prescriber control mean. The contributions of the baseline and other prescribers do not sum to exactly the all-prescriber difference because the control variables in each regression are slightly different (see Supplement 1). All outcomes count the days of quetiapine cumulative to 9 months, beginning at the start of the intervention. Standard errors clustered at the baseline prescriber level in parentheses, p-values in brackets.

<sup>a</sup> Exploratory analysis (not pre-specified).

**eTable 4.** Effect of Intervention on Prescribing of Other Psychiatric Drugs

| Drug                | (1)            | (2)          | (3)     | (4)             | (5)      | (6)      | (7)         |
|---------------------|----------------|--------------|---------|-----------------|----------|----------|-------------|
|                     | Antipsychotics |              |         | Benzodiazepines |          | Non-BZD  | Anti-       |
|                     | Quetiapine     | Oth Atypical | 1st Gen | Psych           | Sleep    | Sleep    | Depressants |
| N                   | 5,055          | 5,055        | 5,055   | 5,055           | 5,055    | 5,055    | 5,055       |
| Control Mean        | 2,994.34       | 2,771.61     | 554.25  | 11,254.08       | 1,406.45 | 2,645.77 | 18,900.46   |
| Treatment Mean      | 2,561.18       | 2,416.70     | 472.34  | 11,322.43       | 1,446.75 | 2,606.55 | 18,381.58   |
| Raw Difference      | -433.16        | -354.91      | -81.90  | 68.36           | 40.30    | -39.22   | -518.88     |
|                     | (76.66)        | (109.68)     | (30.48) | (290.24)        | (69.79)  | (68.65)  | (383.52)    |
|                     | [<0.001]       | [0.001]      | [0.007] | [0.814]         | [0.564]  | [0.568]  | [0.176]     |
| Adjusted Difference | -330.39        | -45.15       | -15.52  | -76.58          | 10.64    | -30.75   | -12.91      |
|                     | (30.11)        | (30.26)      | (9.86)  | (83.12)         | (22.41)  | (24.19)  | (96.99)     |
|                     | [<0.001]       | [0.136]      | [0.115] | [0.357]         | [0.635]  | [0.204]  | [0.894]     |
| Percent Difference  | -11.03%        | -1.63%       | -2.80%  | -0.68%          | 0.76%    | -1.16%   | -0.07%      |
|                     | (1.01%)        | (1.09%)      | (1.78%) | (0.74%)         | (1.59%)  | (0.91%)  | (0.51%)     |
|                     | [<0.001]       | [0.136]      | [0.115] | [0.357]         | [0.635]  | [0.204]  | [0.894]     |

This table shows the effect of the intervention on the prescribing of quetiapine and other psychiatric drugs. All outcomes are measured in the total days supplied. The measure of days supply used here is slightly different from that used in the main tables due to its adjustment for multiple fills from the same prescriber and patient on the same day; see the Prescribing of Other Psychiatric Drugs section of Supplement 1. Column 1 shows the days supplied of quetiapine, column 2 considers atypical antipsychotics excluding quetiapine, and column 3 considers first generation antipsychotics. Columns 4 and 5 consider benzodiazepines commonly prescribed for psychiatric and sleep indications, respectively. Column 6 counts non-benzodiazepine sleep aids, and column 7 counts antidepressants. All outcomes count the days of the drug(s) cumulative to 9 months, beginning at the start of the intervention. Robust standard errors in parentheses, p-values in brackets.

**eTable 5.** Effect of Intervention on Patient Receipt of Other Psychiatric Drugs

| Drug                | (1)            | (2)          | (3)     | (4)             | (5)     | (6)     | (7)         |
|---------------------|----------------|--------------|---------|-----------------|---------|---------|-------------|
|                     | Antipsychotics |              |         | Benzodiazepines |         | Non-BZD | Anti-       |
|                     | Quetiapine     | Oth Atypical | 1st Gen | Psych           | Sleep   | Sleep   | Depressants |
| N                   | 89,500         | 89,500       | 89,500  | 89,500          | 89,500  | 89,500  | 89,500      |
| Control Mean        | 178.69         | 25.83        | 7.47    | 75.83           | 8.09    | 12.79   | 119.13      |
| Treatment Mean      | 171.07         | 25.88        | 6.85    | 76.55           | 8.65    | 13.52   | 116.82      |
| Raw Difference      | -7.61          | 0.05         | -0.62   | 0.72            | 0.57    | 0.74    | -2.31       |
|                     | (1.99)         | (0.91)       | (0.39)  | (1.41)          | (0.54)  | (0.47)  | (1.49)      |
|                     | [<0.001]       | [0.955]      | [0.116] | [0.611]         | [0.291] | [0.118] | [0.121]     |
| Adjusted Difference | -6.93          | 0.74         | 0.30    | 0.28            | 0.02    | 0.27    | 0.45        |
|                     | (0.98)         | (0.48)       | (0.18)  | (0.49)          | (0.20)  | (0.23)  | (0.65)      |
|                     | [<0.001]       | [0.125]      | [0.099] | [0.574]         | [0.907] | [0.246] | [0.483]     |
| Percent Difference  | -3.88%         | 2.85%        | 4.03%   | 0.37%           | 0.28%   | 2.12%   | 0.38%       |
|                     | (0.55%)        | (1.86%)      | (2.45%) | (0.65%)         | (2.44%) | (1.83%) | (0.54%)     |
|                     | [<0.001]       | [0.125]      | [0.099] | [0.574]         | [0.907] | [0.246] | [0.483]     |

This table shows the effect of the intervention on patients' receipt of quetiapine and other psychiatric drugs. All outcomes are measured in the total days received. The measure of days supply used here is slightly different from that used in the main tables due to its adjustment for multiple fills from the same prescriber and patient on the same day; see the Receipt of Other Psychiatric Drugs section of Supplement 1. Column 1 shows the days received of quetiapine, column 2 considers atypical antipsychotics excluding quetiapine, and column 3 considers first generation antipsychotics. Columns 4 and 5 consider benzodiazepines commonly prescribed for psychiatric and sleep indications, respectively. Column 6 counts non-benzodiazepine sleep aids, and column 7 counts antidepressants. All outcomes count the days of the drug(s) cumulative to 9 months, beginning at the start of the intervention. Standard errors clustered at the baseline prescriber level in parentheses, p-values in brackets.

**eTable 6.** Effect of Intervention on Patient Receipt of Antipsychotics by Guideline Conformity

| Patient Group       | (1)                           | (2)                           | (3)                         | (4)                         | (5)                          | (6)                          | (7)                         | (8)                         |
|---------------------|-------------------------------|-------------------------------|-----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------|-----------------------------|
|                     | Low-Value                     |                               |                             |                             | Guideline-Concordant         |                              |                             |                             |
| Source              | All Anti-                     | Quetiapine                    | Other Antipsychotics        |                             | All Anti-                    | Quetiapine                   | Other Antipsychotics        |                             |
|                     | Psychotics                    |                               | Atypicals                   | 1st Gen                     | Psychotics                   |                              | Atypicals                   | 1st Gen                     |
| N                   | 23,490                        | 23,490                        | 23,490                      | 23,490                      | 25,680                       | 25,680                       | 25,680                      | 25,680                      |
| Control Mean        | 186.38                        | 167.29                        | 15.64                       | 3.46                        | 244.07                       | 192.48                       | 39.23                       | 12.35                       |
| Treatment Mean      | 175.39                        | 155.60                        | 16.54                       | 3.26                        | 236.52                       | 186.59                       | 38.99                       | 10.94                       |
| Raw Difference      | -10.99<br>(2.51)<br>[<0.001]  | -11.69<br>(2.37)<br>[<0.001]  | 0.90<br>(0.90)<br>[0.318]   | -0.20<br>(0.36)<br>[0.578]  | -7.55<br>(3.86)<br>[0.051]   | -5.90<br>(2.95)<br>[0.046]   | -0.24<br>(1.84)<br>[0.895]  | -1.41<br>(0.90)<br>[0.120]  |
| Adjusted Difference | -8.00<br>(1.83)<br>[<0.001]   | -9.70<br>(1.75)<br>[<0.001]   | 1.43<br>(0.65)<br>[0.029]   | 0.26<br>(0.26)<br>[0.320]   | -3.62<br>(1.73)<br>[0.037]   | -4.84<br>(1.51)<br>[0.001]   | 0.89<br>(0.86)<br>[0.299]   | 0.14<br>(0.38)<br>[0.719]   |
| Percent Difference  | -4.29%<br>(0.98%)<br>[<0.001] | -5.80%<br>(1.05%)<br>[<0.001] | 9.12%<br>(4.17%)<br>[0.029] | 7.43%<br>(7.47%)<br>[0.320] | -1.48%<br>(0.71%)<br>[0.037] | -2.51%<br>(0.78%)<br>[0.001] | 2.28%<br>(2.20%)<br>[0.299] | 1.11%<br>(3.07%)<br>[0.719] |

Shows effect of intervention on patients' receipt of antipsychotics separately for low-value and guideline-concordant groups. All outcomes are measured in the total days received. The measure used here is slightly different from that used in the main tables due to its adjustment for multiple fills from the same prescriber and patient on the same day; see the Sensitivity and Robustness section of Supplement 1. Columns 1-4 consider only low-value patients while columns 5-8 consider only guideline-concordant patients. Columns 1 and 5 count all antipsychotics (quetiapine, other atypical antipsychotics, and first generation antipsychotics). Columns 2 and 6 count quetiapine only. Columns 3 and 7 count atypical antipsychotics excluding quetiapine, and columns 4 and 8 look at first generation antipsychotics. All outcomes count the days of the drug(s) cumulative to 9 months, beginning at the start of the intervention. Standard errors clustered at the baseline prescriber level in parentheses, p-values in brackets.

These analyses are exploratory (not pre-specified).

**eTable 7.** Effect of Intervention on Mortality and Health Care Utilization

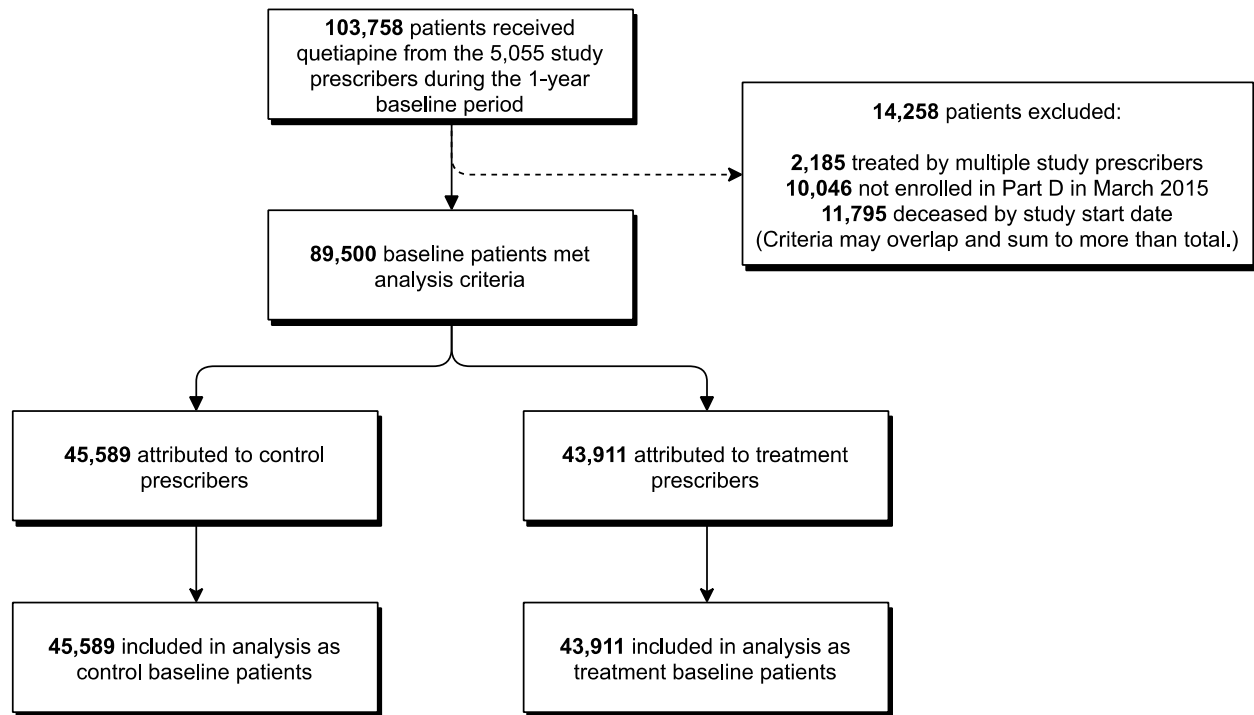
| Patient Group       | (1)     | (2)                  | (3)     | (4)         | (5)                    | (6)                  | (7)     | (8)         | (9)                               | (10)                 | (11)    | (12)        |
|---------------------|---------|----------------------|---------|-------------|------------------------|----------------------|---------|-------------|-----------------------------------|----------------------|---------|-------------|
|                     | All     |                      |         |             | Low-Value <sup>a</sup> |                      |         |             | Guideline-Concordant <sup>a</sup> |                      |         |             |
|                     | Outcome | Utilization Outcomes |         |             | Death                  | Utilization Outcomes |         |             | Death                             | Utilization Outcomes |         |             |
|                     | Death   | Inpatient            | ED      | Psychiatric | Death                  | Inpatient            | ED      | Psychiatric | Death                             | Inpatient            | ED      | Psychiatric |
| N                   | 89,500  | 60,425               | 60,425  | 60,425      | 23,490                 | 16,718               | 16,718  | 16,718      | 25,680                            | 16,241               | 16,241  | 16,241      |
| Control Mean        | 0.104   | 0.528                | 0.854   | 0.791       | 0.196                  | 0.44                 | 0.53    | 0.55        | 0.031                             | 0.627                | 1.38    | 1.11        |
| Treatment Mean      | 0.100   | 0.509                | 0.867   | 0.779       | 0.192                  | 0.449                | 0.558   | 0.605       | 0.032                             | 0.583                | 1.332   | 1.086       |
| Raw Difference      | -0.004  | -0.018               | 0.013   | -0.012      | -0.004                 | 0.01                 | 0.02    | 0.06        | 0.001                             | -0.04                | -0.05   | -0.03       |
|                     | (0.003) | (0.013)              | (0.024) | (0.041)     | (0.005)                | (0.02)               | (0.02)  | (0.05)      | (0.002)                           | (0.03)               | (0.06)  | (0.06)      |
|                     | [0.248] | [0.156]              | [0.578] | [0.763]     | [0.442]                | [0.728]              | [0.254] | [0.233]     | [0.701]                           | [0.095]              | [0.359] | [0.638]     |
| Adjusted Difference | -0.002  | -0.015               | -0.008  | -0.010      | -0.005                 | 0.01                 | 0.02    | 0.03        | 0.001                             | -0.04                | -0.09   | -0.04       |
|                     | (0.002) | (0.010)              | (0.015) | (0.021)     | (0.005)                | (0.01)               | (0.02)  | (0.03)      | (0.002)                           | (0.02)               | (0.04)  | (0.04)      |
|                     | [0.411] | [0.132]              | [0.605] | [0.625]     | [0.371]                | [0.700]              | [0.299] | [0.183]     | [0.677]                           | [0.060]              | [0.034] | [0.276]     |
| Percent Difference  | -1.66%  | -2.79%               | -0.93%  | -1.29%      | -2.36%                 | 1.22%                | 3.35%   | 6.20%       | 2.96%                             | -5.97%               | -6.24%  | -3.91%      |
|                     | (2.02%) | (1.85%)              | (1.80%) | (2.63%)     | (2.63%)                | (3.15%)              | (3.22%) | (4.65%)     | (7.09%)                           | (3.17%)              | (2.94%) | (3.59%)     |
|                     | [0.411] | [0.132]              | [0.605] | [0.625]     | [0.371]                | [0.700]              | [0.299] | [0.183]     | [0.677]                           | [0.060]              | [0.034] | [0.276]     |

Shows effect of intervention on patients' mortality and health care utilization separately for all patients (columns 1-4), the low-value patient subgroup (columns 5-8), and the guideline-concordant patient subgroup (columns 9-12). For columns 1, 5, and 9, the outcome is an indicator for being deceased at 9 months after the start of the intervention. These columns use the main study sample. The utilization outcomes (columns 2-4, 6-8, and 10-12) count the number of provider encounters cumulative to 9 months, beginning at the start of the intervention. Multiple encounters with the same provider on the same day only count as one encounter. Utilization outcomes use the subset of main study sample that was enrolled in Original Medicare (Parts A and B) in March 2015. Columns 2, 6, and 10 count inpatient stays. Columns 3, 7, and 11 count emergency department visits. Columns 4, 8, and 12 count visits with psychiatric providers (physicians with psychiatric specialization and psychiatric nurse practitioners). Standard errors clustered at the baseline prescriber level in parentheses, p-values in brackets.

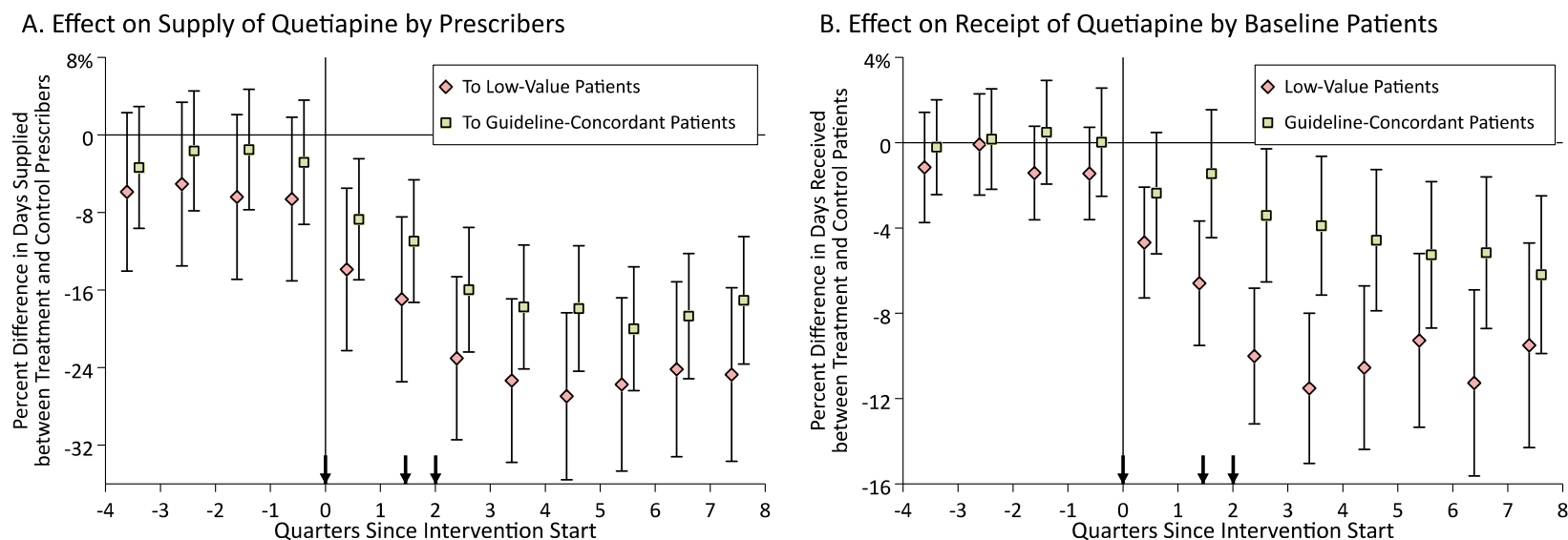
<sup>a</sup> Exploratory analysis (not pre-specified).



**eFigure 1. CONSORT Flow Diagram of Baseline Patients in Study**

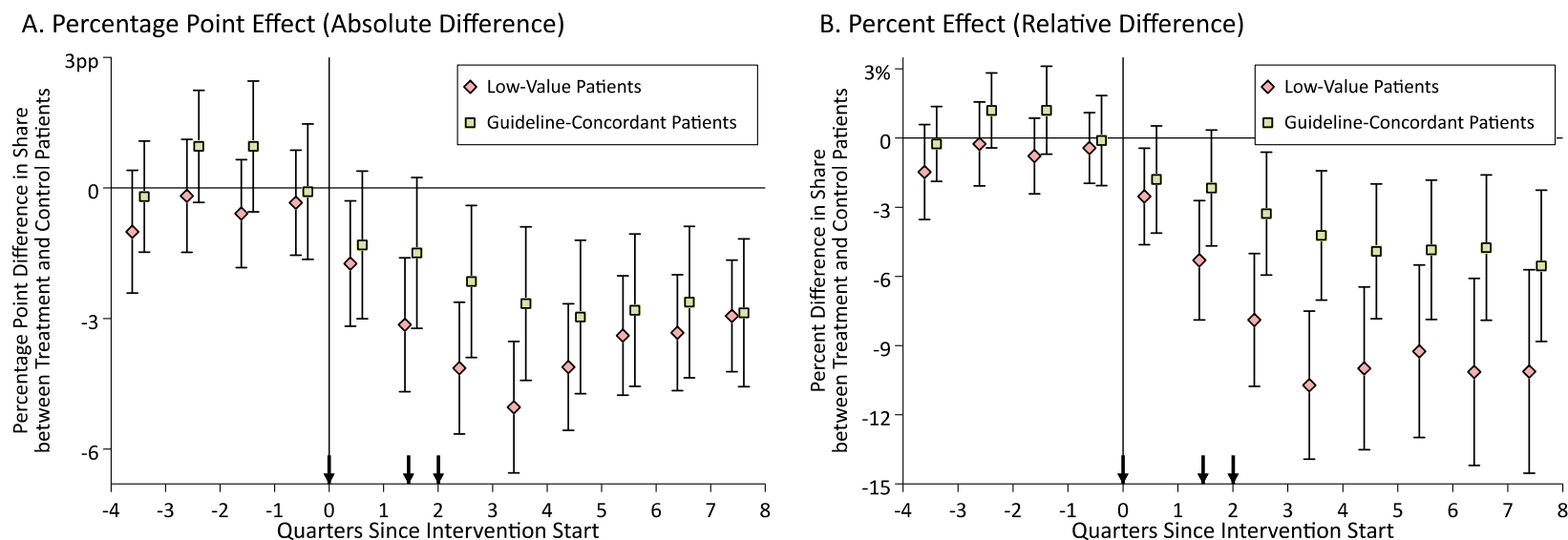


**eFigure 2. Quarterly Effect of Intervention on Prescribers and Patients, by Guideline Conformity**



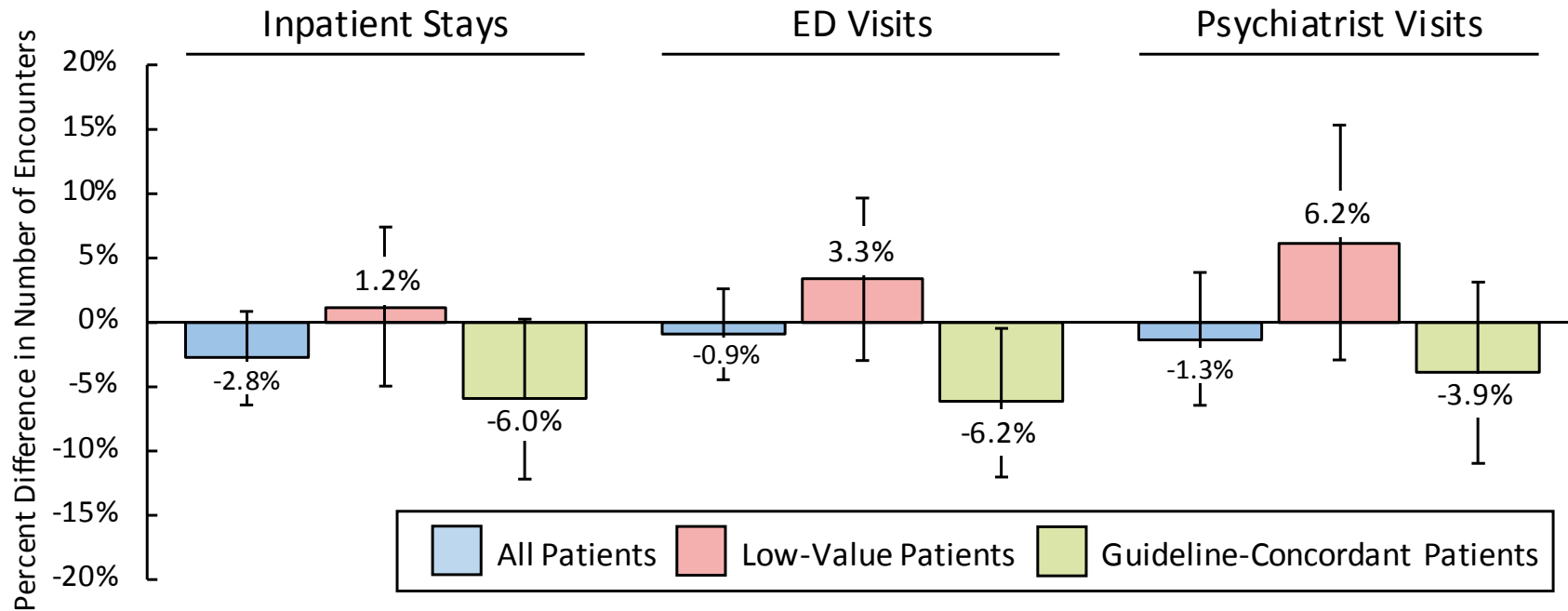
Each point shows the percent difference in days of quetiapine supplied/received between treatment and control groups in each quarter relative to the intervention start date, subdivided by the guideline-conformity of the prescription/patient. Panel A displays effects on days supplied by the prescribers to low-value (red diamonds) and to guideline-concordant (green squares) patients. Panel B displays effects on days received by baseline patients classified as low-value (red diamonds) and guideline-concordant (green squares). The percent difference is defined as the absolute difference between treatment and control means divided by the control mean. Error bars indicate 95% CIs. Arrowheads denote when letters were sent to prescribers.

**eFigure 3. Quarterly Effect of Intervention on Any Receipt of Quetiapine**



Each point shows the (absolute or relative) difference in the share of patients receiving at least 1 day of quetiapine between treatment and control groups during the quarter relative to the intervention start date, subdivided by the guideline-conformity of the patients. Panel A displays absolute differences, i.e. the percentage point difference in the share receiving any quetiapine between treatment and control groups. Panel B displays relative differences, i.e. the percent difference in the share receiving any quetiapine between treatment and control groups. The percent difference is defined as the absolute difference divided by the control mean. Error bars indicate 95% CIs. Arrowheads denote when letters were sent to prescribers.

**eFigure 4.** Cumulative Effect on Health Care Utilization for All, Low-Value, and Guideline-Concordant Patients Over 9 Months



Bars show the percent difference in the number of healthcare encounters between treatment and control patients for all, (blue), low-value (red), and guideline-concordant (green) patients in the 9 months after the start of the intervention. Each bar reports an adjusted percent difference (difference between treatment and control means, adjusting for baseline receipt and other characteristics described in text and Supplement 1, divided by the control mean). Error bars indicate 95% CIs. See **eTable 7** in Supplement 2 for coefficients.