### Table 2: Studies identified with costs reported by adherence level and disease group

<table>
<thead>
<tr>
<th>Author, Year, Country</th>
<th>Objective</th>
<th>Study Characteristics</th>
<th>Adherence (as reported in paper)</th>
<th>Outcomes/Indicators</th>
<th>Results (USD, 2015)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular Disease</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>
| Aubert et al [1] 2010 US | To investigate whether compliance during the first 2 years of statin therapy is associated with reduced hospitalization rates and direct medical costs during year 3. | Design: Retrospective cohort study  
Follow Up: 3 years  
Sample Size: 10227  
(A:3512, NA:6715) | Measure: MPR  
Classification: MPR < 80 = non-compliant  
Method of Assessment: pharmacy claims data | Total Healthcare costs  
Medical Costs | Type of Costs: adjusted  
Classification: disease state specific  
Currency Year: USD, 2002  
Cost of Nonadherence: THC:$5289.61 ($6865.90), MC:$4908.09 ($6370.60) | Quality: medium  
Classification: cost description |
Follow Up: 18months  
Sample Size: 13289  
(A:2852, NA:4184, NE:6253) | Measure: PDC  
Classification: PDC <80 = low adherence , 0 = no warfarin exposure  
Method of Assessment: pharmacy claims data | Total Costs  
Inpatient Costs  
Outpatient Costs  
Pharmacy Costs  
Medical Costs | Type of Costs: adjusted  
Classification: all cause  
Currency Year: USD, 2005  
Cost of Nonadherence :  
 TC:$16612.44($19936.70), IC:$9382.56 ($11260.10), OC:$8605.92 ($10328),  
PC:$2388.24 ($2866.20),  
MC:$15235.80($18285) | Quality: medium  
Classification: cost description |
| Dilokthornsakul et al [3] 2012 Thailand | To determine the effects of medication supplies on healthcare costs and hospitalizations in patients with chronic heart failure receiving angiotensin converting enzyme inhibitors or | Design: Retrospective cohort study  
Follow Up: 1 year  
Sample Size: 393  
Classification: MPR < 80 = undersupply, MPR >120 = oversupply  
Method of Assessment: pharmacy claims data | Total Healthcare costs  
Inpatient Costs  
Outpatient Costs | Type of Costs: unadjusted  
Classification: disease state specific  
Currency Year: USD, 2004  
Cost of Nonadherence:  
THC:$1157 ($1433.06),  
IC:$1019 ($1262.13),  
OC:$138 ($170.93) | Quality: high  
Classification: cost description |
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Canada</td>
<td></td>
<td></td>
<td></td>
<td>Method of Assessment: pharmacy claims data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dragomir et al[5]</th>
<th>To evaluate the impact of low adherence to statins on clinical issues and direct healthcare costs.</th>
<th>Design: Retrospective cohort study</th>
<th>Follow Up: 3 years</th>
<th>Sample Size: 55134 (A:28549, NA:26585)</th>
<th>Measure: MPR</th>
<th>Classification: MPR≥80 = adherent, MPR &lt; 80 = nonadherent</th>
<th>Total Healthcare Costs</th>
<th>Pharmacy Costs</th>
<th>Medical Costs</th>
<th>Hospitalization Costs</th>
<th>Type of Costs: unadjusted and predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Canada</td>
<td></td>
<td></td>
<td></td>
<td>Method of Assessment: pharmacy claims data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Quality: medium Classification: cost description | Quality: medium Classification: cost description |
### Pittman et al\([6]\) 2011 US

To examine the relation among statin adherence, subsequent hospitalizations and healthcare costs.

**Design:** Retrospective cohort study  
**Follow Up:** 18 months  
**Sample Size:** 381422 (A:258013, MA:65795, LA:57614)

**Measure:** MPR  
**Classification:**  
- MPR ≥ 80 = adherent, MPR  
- >60<79% = moderate adherence, MPR  
- <59 = low adherence

**Method of Assessment:** pharmacy claims data

<table>
<thead>
<tr>
<th>Total Healthcare Costs</th>
<th>Pharmacy Costs</th>
<th>Medical Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of Costs:</strong> adjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Classification:</strong> all cause and disease state specific</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Currency Year:</strong> USD, 2009</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cost of Nonadherence:</strong> all cause: THC(&gt;80):$6798.67 ($7505.66), THC(60-79):$7072.67 ($7808.16), THC(&lt;59):$7401.33 ($8170.99), PC(&gt;80):$1767.33 ($1951.11), PC(60-79):$1789.33 ($1975.40), PC(&lt;59):$1937.33 ($2138.79), MC(&gt;80):$4472.67 ($4937.78), MC(60-79):$4840.67 ($5344.05), MC(&lt;59):$5138.67 ($5673.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease state specific: PC(&gt;80):$558.67 ($616.77), PC(60-79):$442.67 ($488.70), PC(&lt;59):$325.33 ($359.16), MC(&gt;80):$1596.67 ($1762.71), MC(60-79):$1722 ($1901.07), MC(&lt;59):$1792.67 ($1979.09)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Pittman et al\([7]\) 2010 US

To evaluate the relationship between adherence to antihypertensive medications and subsequent hospitalizations, emergency department visits and

**Design:** Retrospective cohort study  
**Follow Up:** 2 years  
**Sample Size:** 625620(A:467006, MA:96226, LA:62388)

**Measure:** MPR  
**Classification:**  
- MPR ≥ 80 = adherent, MPR  
- >60<79% = moderate adherence, MPR  
- <59 = low adherence

**Method of Assessment:** pharmacy claims data

<table>
<thead>
<tr>
<th>Total Healthcare Costs</th>
<th>Outpatient Costs</th>
<th>ED Costs</th>
<th>Pharmacy Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of Costs:</strong> adjusted and unadjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Classification:</strong> disease state specific</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Currency Year:</strong> USD, 2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cost of Nonadherence:</strong> Adjusted: THC(&gt;80):$7261 ($8077.79), THC(60-79):$7530 ($8377.05), THC(&lt;59):$7370 ($8199.05), OC(&gt;80):$3390 ($3771.34), OC(60-79):$3705 ($4121.77)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Quality:** medium  
**Classification:** cost description

To investigate variations in compliance with four classes of antihypertensive agents: diuretics, ACEIs, CCBs and B-

**Design:** Retrospective cohort study  
**Follow Up:** 12 months  
**Sample Size:** 7211 (P:2668, NC:3101, NP:649, T:793)

**Method of Assessment:** pharmacy claims data

**Costs**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Costs</th>
<th>Unadjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>OC(&lt;59)</td>
<td>$3776 ($4200.76)</td>
<td>$3396 ($3778.01)</td>
</tr>
<tr>
<td>EDC(&gt;80)</td>
<td>$101 ($112.36)</td>
<td>$120 ($134.10)</td>
</tr>
<tr>
<td>EDC(60-79)</td>
<td>$134 ($149.07)</td>
<td>$147 ($162.42)</td>
</tr>
<tr>
<td>EDC(&lt;59)</td>
<td>$172 ($191.35)</td>
<td>$185 ($203.59)</td>
</tr>
<tr>
<td>PC(&gt;80)</td>
<td>$2383 ($2651.06)</td>
<td>$2451 ($2699.14)</td>
</tr>
<tr>
<td>PC(60-79)</td>
<td>$1932 ($2149.33)</td>
<td>$2000 ($2229.50)</td>
</tr>
<tr>
<td>PC(&lt;59)</td>
<td>$1509 ($1678.75)</td>
<td>$1577 ($1755.91)</td>
</tr>
<tr>
<td>HC(&gt;80)</td>
<td>$1386 ($1541.91)</td>
<td>$1454 ($1619.08)</td>
</tr>
<tr>
<td>HC(60-79)</td>
<td>$1759 ($1956.87)</td>
<td>$1827 ($2002.03)</td>
</tr>
<tr>
<td>HC(&lt;59)</td>
<td>$1913 ($2128.19)</td>
<td>$1981 ($2155.35)</td>
</tr>
</tbody>
</table>

**Type of Costs:** unadjusted  
**Classification:** all cause and disease state specific  
**Currency Year:** USD, 1994  
**Cost of Nonadherence:** All cause: THC(>80): $341 ($509.66), THC(30-80): $694 ($1037.26),
blockers and the health care costs associated with various degrees of compliance.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>To evaluate the impact of medication adherence on healthcare utilisation and cost for 4 chronic conditions that are major drivers of drug spending: diabetes, hypertension, hypercholesterolemia, and congestive heart failure.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Design:** Retrospective cohort observational study  
**Follow Up:** 12 months  
**Sample Size:** 137277  

**Measure:** medication supply  
**Classification:** 1-19%, 20-39%, 40-59%, 60-79%, 80-100%  

**Method of Assessment:** pharmacy claims data  

**Total Costs**  
**Pharmacy Costs**  
**Medical Costs**  

**Type of Costs:** adjusted for all cause and disease state specific  
**Classification:** cost description  

**Currency Year:** USD, 1998  

**Cost of Nonadherence:** All cause:  
Diabetes:  
TC(1-19): $16498 ($23071.58),  
TC(20-39): $13077 ($18287.49),  
TC(40-59): $12978 ($18149.05),  
TC(60-79): $11484 ($16059.77),  
TC(80-100): $8886 ($12426.60),  
PC(1-19): $1312 ($1834.76),

| THC(<30): $735 ($1098.53) |
| Disease state specific:  
Renal:  
THC(>80): $2135 ($3190.98),  
THC(30-80): $2488 ($3718.58),  
THC(<30): $2529 ($3779.86),  
Acute MI:  
THC(>80): $1358 ($2029.67),  
THC(30-80): $1711 ($2557.27),  
THC(<30): $1752 ($2618.55),  
Diabetes:  
THC(>80): $770 ($1150.85),  
THC(30-80): $1123 ($1678.44),  
THC(<30): $1164 ($1739.72),  
CHF:  
THC(>80): $698 ($1043.23),  
THC(30-80): $1051 ($1570.83),  
THC(<30): $1092 ($1632.11),  
Angina:  
THC(>80): $702 ($1049.21),  
THC(30-80): $1055 ($1576.81),  
THC(<30): $1096 ($1638.09)  

= non-persistence  

Method of Assessment: pharmacy claims data
<table>
<thead>
<tr>
<th>Condition</th>
<th>Age Group 1</th>
<th>Age Group 2</th>
<th>Age Group 3</th>
<th>Age Group 4</th>
</tr>
</thead>
</table>

PC(40-59): $1247 ($1743.86),
PC(60-79): $1736 ($2427.70),
PC(80-100): $1972 ($2757.74),
MC(1-19): $9849 ($13773.30),
MC(20-39): $6830 ($9551.39),
MC(40-59): $5509 ($7704.04),
MC(60-79): $6676 ($9336.03),
MC(80-100): $4780 ($6684.58),
CHF:
TC(1-19): $23964 ($33512.38),
TC(20-39): $19188 ($26833.40),
TC(40-59): $26311 ($36794.54),
TC(60-79): $29785 ($41652.74),
TC(80-100): $22164 ($30995.18),
PC(1-19): $1961 ($2742.35),
PC(20-39): $2055 ($2873.81),
PC(40-59): $2208 ($3087.77),
PC(60-79): $3412 ($4771.50),
PC(80-100): $3107 ($4344.97),
MC(1-19): $22003 ($30770.03),
MC(20-39): $17133 ($23959.59),
MC(40-59): $24103 ($33706.77),
MC(60-79): $26373 ($36881.24),
MC(80-100): $19056 ($26648.81)
Disease state specific: Diabetes:
TC(1-19): $8867 ($12400.03),
TC(20-39): $7124 ($9916.90),
TC(40-59): $6522 ($9120.67),
TC(60-79): $6291 ($8797.63),
TC(80-100): $4570 ($6390.90),
PC(1-19): $55 ($76.91),
PC(20-39): $165 ($230.74),
PC(40-59): $285 ($398.56),
PC(60-79): $404 ($564.97),
PC(80-100): $763 ($1067.02),
MC(1-19): $8812 ($12323.11),
MC(20-39): $6959 ($9731.79),
MC(40-59): $6237 ($8722.11),
MC(60-79): $5887 ($8232.66),
MC(80-100): $3808 ($5325.29),
Hypertension:
TC(1-19): $4878 ($6821.62),
TC(20-39): $6062 ($8477.39),
TC(40-59): $5297 ($7407.57),
TC(60-79): $5262 ($7358.63),
TC(80-100): $4871 ($6811.84),
PC(1-19): $31 ($43.35),
PC(20-39): $89 ($124.46),
PC(40-59): $184 ($257.31),
PC(60-79): $285 ($398.56),
PC(80-100): $489 ($683.84),
MC(1-19): $4847 ($6778.27),
MC(20-39): $5973 ($8352.92),
MC(40-59): $5113 ($7150.26),
MC(60-79): $4977 ($6960.07),
MC(80-100): $4383 ($6129.39),
Hypercholesterolemia:
TC(1-19): $6888 ($9632.50),
TC(20-39): $4999 ($6990.84),
TC(40-59): $3825 ($5349.06),
TC(60-79): $5541 ($7748.79),
TC(80-100): $3924 ($5487.51),
PC(1-19): $78 ($109.08),
PC(20-39): $213 ($297.87),
PC(40-59): $373 ($521.62),
PC(60-79): $603 ($843.26),
To determine the rates of undersupply, appropriate supply, and oversupply of antihypertensive drugs as measured by refill adherence, among patient with complicated and uncomplicated hypertension and to

Design: Retrospective cohort study
Follow Up: 3.3 years
Sample Size: 15206 (not specified)

Measure: MPR
MPR<80 = undersupply, MPR >120 = oversupply

Method of Assessment: pharmacy claims data

Type of Costs: unadjusted
Classification: disease state specific
Currency Year: USD, 2002

Cost of Nonadherence:
THC:$6032.5 ($7830.11), IC:$2067 ($2682.94), OC:$3965 ($5146.52), PC:$130 ($168.74)

Quality: medium
Classification: cost description
examine the association of refill adherence with hospitalization and healthcare costs among these patients.

**Wu et al[11]**

2011

US

To study statin adherence and assess associated medical utilisation and healthcare costs in patients with type 2 diabetes, based on national Medicaid database.

<table>
<thead>
<tr>
<th>Measure: MPR Classification: MPR≥80 = adherent, MPR &lt;80 = nonadherent</th>
<th>Total Healthcare Costs</th>
<th>Type of Costs: adjusted Classification: all cause and disease state specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of Assessment: pharmacy claims data</td>
<td>Pharmacy Costs</td>
<td>Currency Year: USD, 2005</td>
</tr>
<tr>
<td></td>
<td>Medical Costs</td>
<td>Cost of Nonadherence: all cause:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>THC:$17807 ($21370.30), PC:$4915 ($5898.52) MC:$12892 ($15471.77)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disease state specific:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>THC:$2789 ($3347.10), PC:$489 ($586.85) MC:$2300 ($2760.25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quality: medium Classification: cost description</td>
</tr>
</tbody>
</table>

**Zhao et al[12]**

2014

US

To evaluate the associations between statin adherence level, healthcare costs, hospital admissions and emergency room visits after statin therapy is taken for 1 year.

<table>
<thead>
<tr>
<th>Measure: MPR Classification: &lt;40%, 40-59%, 60-69%, 70-79%, 80-84%, 85-89%, 90-95%, 96-100%</th>
<th>Total Healthcare Costs</th>
<th>Type of Costs: unadjusted Classification: all cause and disease state specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of Assessment: pharmacy claims data, census data</td>
<td>Pharmacy Costs</td>
<td>Currency Year: USD, 2010</td>
</tr>
<tr>
<td></td>
<td>Medical Costs</td>
<td>Cost of Nonadherence: all cause:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PC(96-100):$2976.80 ($3247.04), PC(90-95):$2826.99 ($3083.63), PC(85-89):$2795.39 ($3049.16), PC(80-84):$2690.89 ($2935.17), PC(70-79):$2192.83 ($2391.90), PC(60-69):$2323.27 ($2534.18), PC(40-59):$2153.93 ($2349.47), PC(&lt;40):$1749.18 ($1907.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disease state specific:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>THC(96-100):$6536.05 ($7129.40), THC(90-95):$6493.80 ($7083.31), THC(85-89):$6459.40 ($7045.79),</td>
</tr>
</tbody>
</table>
Mental Health

**Bagalman et al[13]**

2010

US

To examine the association between treatment adherence and indirect productivity costs within a cohort of commercially insured employees with bipolar disorder.

**Design:** Retrospective cohort study

**Follow Up:** 1 year

**Sample Size:** 1258 (A:444, NA:814)

**Measure:** MPR

**Classification:**

MPR≥80 = adherent, MPR <80 = nonadherent

**Method of Assessment:** pharmacy claims data

**Type of Costs:** adjusted

**Classification:** disease state specific

**Currency Year:** USD, 2005

**Cost of Nonadherence:** TC:$6894 ($8273.53), STDC:$2134 ($2561.03), WCC:$762 ($914.48), PTOC:$3998 ($4798.03)

**Quality:** medium

**Classification:** cost description

---

**Becker et al[14]**

Examine treatment

**Design:** Retrospective

**Measure:**

**Total Costs**

**Type of Costs:** unadjusted

**Quality:** low

---

| THC(80-84) | $6227.47 ($6792.80) |
| THC(70-79) | $5713.47 ($6232.14) |
| THC(60-69) | $5875.26 ($6408.62) |
| THC(40-59) | $5817.58 ($6345.70) |
| THC(<40)  | $5249.12 ($5725.64) |
| PC(96-100)| $449.86 ($490.70)  |
| PC(90-95) | $439.74 ($479.66)  |
| PC(85-90) | $458.83 ($500.48)  |
| PC(80-84) | $423.15 ($461.56)  |
| PC(70-79) | $356.74 ($389.13)  |
| PC(60-69) | $371.30 ($405.01)  |
| PC(<40)  | $279.21 ($304.56)  |
| MC(96-100)| $3559.25 ($3882.36) |
| MC(90-95) | $3666.81 ($3999.69) |
| MC(85-89) | $3664 ($3996.62)  |
| MC(80-84) | $3586.58 ($3912.17) |
| MC(70-79) | $3520.64 ($3840.25) |
| MC(60-69) | $3551.99 ($3874.44) |
| MC(<40)  | $3663.65 ($3996.24) |
| MC(<40)  | $3499.95 ($3817.68) |

---

<table>
<thead>
<tr>
<th>Total Costs</th>
<th>Short term disability cost</th>
<th>Workers compensation cost</th>
<th>Paid time off cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC: $6894</td>
<td>STDC: $2134 ($2561.03)</td>
<td>WCC: $762 ($914.48)</td>
<td>PTOC: $3998 ($4798.03)</td>
</tr>
<tr>
<td>Year</td>
<td>Design</td>
<td>Follow Up</td>
<td>Sample Size</td>
</tr>
<tr>
<td>------</td>
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<td>-----------</td>
<td>-------------</td>
</tr>
<tr>
<td>2007</td>
<td>cohort study</td>
<td>2 years</td>
<td>10330 (&gt;75%:6609, 50-74%:1276, 25-49%:1940, &lt;25%:505)</td>
</tr>
<tr>
<td>2005</td>
<td>Design: Retrospective database analysis</td>
<td>1 year</td>
<td>7864 (&lt;80%:2655, 80-125%:5065, &gt;125%:144)</td>
</tr>
<tr>
<td>2004</td>
<td>Design: Retrospective database analysis</td>
<td>1 year</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Country</td>
<td>Objective</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>Hong et al</td>
<td>2011</td>
<td>UK</td>
<td>To investigate clinical and economic consequences of medication non-adherence in the treatment of bipolar disorder following a manic or mixed episode.</td>
</tr>
<tr>
<td>Jiang et al</td>
<td>2015</td>
<td>US</td>
<td>To estimate the impact of adherence to and persistence with atypical antipsychotics on healthcare costs and risk of hospitalization by controlling potential sources of endogeneity</td>
</tr>
</tbody>
</table>
| **Joe et al[19]** | To investigate the association between psychiatric medication non-compliance and psychiatric and non-psychiatric service utilisation and costs. | **Design:** Retrospective cohort study  
**Follow Up:** 1 year  
**Sample Size:** 7848  
**Measure:** percentage of days of psychiatric prescription (PDP)  
**Classification:** PDP≥80% = adherent, PDP<80% = nonadherent; persistent = continued medication without interruption ≥ 56 day, non-persistent = at least one medication interruption > 56 days  
**Method of Assessment:** health insurance data  
**Total costs** | **Type of Costs:** adjusted  
**Classification:** all cause and disease state specific  
**Currency Year:** USD, 2011  
**Cost of Nonadherence:** all cause: TC:$4961 ($5271.40)  
Disease state specific: TC:$3061 ($3252.50)  
**Quality:** medium  
**Classification:** cost description |
| **Knapp et al[20]** | To assess the relative impact of non-adherence and other factors associated with resource use and costs incurred by people with schizophrenia. | **Design:** Retrospective cohort study  
**Follow Up:** 1 year  
**Sample Size:** 658  
(A:549, NA:109)  
**Measure:** self-report  
**Classification:** adherent vs. nonadherent  
**Method of Assessment:** health insurance data  
**Total costs** | **Type of Costs:** predicted  
**Classification:** disease state specific  
**Currency Year:** GBP, 2001  
**Cost of Nonadherence:**  
TC:£57580 ($116434.12)  
IC:£6714 ($13576.57),  
ESC:£1603 ($3241.47)  
**Quality:** medium  
**Classification:** cost analysis |
<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Classification</th>
<th>Type of Costs</th>
<th>Currency Year</th>
<th>Cost of Nonadherence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offord et al [21] (2013 US)</td>
<td>Retrospective cohort study</td>
<td>1 year</td>
<td>1462 (A:589, NA:873)</td>
<td>time to discontinuation</td>
<td>adherent vs. nonadherent</td>
<td>adjusted</td>
<td>USD, 2008</td>
<td>TC:$15400 ($17132.34), OC:$5773 ($6422.40), PC:$3777 ($4201.87), HC:$5850 ($6508.06)</td>
<td>medium</td>
</tr>
<tr>
<td>Offord et al [22] (2013 US)</td>
<td>Retrospective cohort study</td>
<td>1 year</td>
<td>354 (A:126, NA:228)</td>
<td>MPR</td>
<td>MPR ≥ 70= high adherence, MPR &lt; 70 = low adherence</td>
<td>adjusted</td>
<td>USD, 2008</td>
<td>IC:$9053 ($10071.37), PC:$4267 ($4746.99), HC:$2468 ($2745.62), PC:$1085 ($1207.05)</td>
<td>low</td>
</tr>
<tr>
<td>Robertson et al [23] (2014 US)</td>
<td>Retrospective cohort study</td>
<td>90 days</td>
<td>1376 (90/90:637, 60/90:240, 30/90:174, 0/90:316)</td>
<td>MPR</td>
<td>MPR ≥80% = adherent</td>
<td>unadjusted</td>
<td>USD, 2005</td>
<td>TC(90/90):$28068 ($33495.65), TC(60/90):$21720 ($25920.11), TC(30/90):$21084 ($25161.12), TC(0/90):$12516 ($14936.28)</td>
<td>medium</td>
</tr>
</tbody>
</table>
Robinson et al[24] To determine if the

Design: Retrospective Measure: Total costs Type of Costs: unadjusted Quality: medium
<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Study Title</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Type of Costs</th>
<th>Classification</th>
<th>Cost Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>US</td>
<td>Type of antidepressant drug is related to adherence and assess the 6 month health care costs among newly diagnosed patients.</td>
<td>Pharmacy claims analysis</td>
<td>Follow Up: 6 months</td>
<td>Sample Size: 60386 (A:11526, NA:8860)</td>
<td>Antidepressant medication management measures</td>
<td>Inpatient costs, Outpatient costs, ED visit costs, Pharmacy costs, Physician office visit costs</td>
<td>Classification: all cause and disease state specific</td>
<td>Currency Year: USD, 2004</td>
</tr>
<tr>
<td>2001</td>
<td>US</td>
<td>To examine the relationship of medication non-adherence to hospital use and costs among severely mentally ill clients.</td>
<td>Retrospective database analysis</td>
<td>Follow Up: 1 year</td>
<td>Sample Size: 619 (A:413, NA:206)</td>
<td>Pharmacy claims data, Medicaid data, observational assessment</td>
<td>Hospitalization costs</td>
<td>Type of Costs: unadjusted</td>
<td>Classification: all cause and disease state specific</td>
</tr>
<tr>
<td>2003</td>
<td>US</td>
<td>To evaluate the economic impact of antidepressant</td>
<td>Retrospective database analysis</td>
<td>Follow Up: 6 months</td>
<td>Measure: MPR</td>
<td>Total costs</td>
<td>Pharmacy costs</td>
<td>Classification: disease state specific</td>
<td>Currency Year: USD, 1999</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Research Question</td>
<td>Study Design</td>
<td>Follow Up</td>
<td>Sample Size</td>
<td>Measure</td>
<td>Classification</td>
<td>Type of Costs</td>
<td>Cost of Nonadherence</td>
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<tr>
<td>Diabetes&lt;br&gt; An et al[27] &lt;br&gt; 2014 &lt;br&gt; Korea</td>
<td>This study evaluated the association between medication adherence and clinical/economic outcomes in patients with type II diabetes mellitus in the Republic of Korea over a 3-year period.</td>
<td>Prospective cohort study</td>
<td>3 years</td>
<td>608 (A:472, NA:136)</td>
<td>MPR</td>
<td>MPR≥90% = adherent, MPR&lt;90% = nonadherent</td>
<td>Total costs</td>
<td>Pharmacy claims data</td>
<td>USD, 2007</td>
</tr>
<tr>
<td>Buysman et al[28] &lt;br&gt; 2017 &lt;br&gt; US</td>
<td>To examine the impact of real-world adherence on glycaemic control in type 2 diabetes patients treated with canagliflozin.</td>
<td>Retrospective database analysis</td>
<td>12 months</td>
<td>2261 (A:1215, NA:1046)</td>
<td>PDC</td>
<td>PDC≥80% = highly adherent, PDC&lt;80% = less than highly adherent</td>
<td>Total costs</td>
<td>Healthcare claims data</td>
<td>USD, 2014</td>
</tr>
<tr>
<td>Curtis et al[29] &lt;br&gt; 2017 &lt;br&gt; US</td>
<td>Examine the association between adherence to glucose lowering agents and...</td>
<td>Retrospective analysis</td>
<td>3 years</td>
<td>228074</td>
<td>PDC</td>
<td>PDC≥80% = adherent</td>
<td>Total costs</td>
<td>Pharmacy data</td>
<td>USD, 2014</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Follow Up</td>
<td>Sample Size</td>
<td>Measure</td>
<td>Classification</td>
<td>Type of Costs</td>
<td>Cost of Nonadherence</td>
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<tr>
<td>Egede et al [30] 2012 US</td>
<td>Retrospective cohort study</td>
<td>5 years</td>
<td>740195 (A:427390, NA:312805)</td>
<td>MPR</td>
<td>MPR≥80% = adherent, MPR&lt;80% = nonadherent</td>
<td>unadjusted</td>
<td>TC:$38633 ($39020.09), OC: $16964 ($17134), PC: $9390 ($9484.08), ACC:$12153 ($12274.77)</td>
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<tr>
<td>Gentil et al [31] 2015 Canada</td>
<td>Retrospective, observational cohort analysis</td>
<td>1 year</td>
<td>301 (A:224, NA:77)</td>
<td>MPR</td>
<td>MPR≥80% = adherent, MPR&lt;80% = nonadherent</td>
<td>adjusted and unadjusted</td>
<td>TC:$11124 ($9818.67), OC: $7419 ($6548.43), PC: $2687 ($2371.70), POC:$504 ($444.86), Adjusted disease state specific: TC:$4477 ($3951.65), IC:$2836 ($2503.21), OC: $1518 ($1339.87),</td>
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<tr>
<td>Study</td>
<td>Year</td>
<td>Country</td>
<td>Design</td>
<td>Measure</td>
<td>Type of Costs</td>
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<tr>
<td>Hagen et al [32]</td>
<td>2014</td>
<td>US</td>
<td>Retrospective, observational cohort analysis</td>
<td>PDC</td>
<td>Adjusted and unadjusted</td>
<td>medium</td>
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<td>Follow Up: 1 year</td>
<td>PDC≥80% = compliant, PDC&lt;80% = noncompliant</td>
<td>Classification: all cause and disease state specific</td>
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<td></td>
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<td></td>
<td>Sample Size: 4978 (A:2820, NA:2158)</td>
<td>Method of Assessment: pharmacy claims data</td>
<td>Healthcare costs</td>
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<td>Short term disability costs</td>
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<tr>
<td>Hansen et al [33]</td>
<td>2010</td>
<td>US</td>
<td>Retrospective, cohort study</td>
<td>MPR</td>
<td>Adjusted and unadjusted</td>
<td>medium</td>
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<td>Classification: all cause and disease state specific</td>
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<td>Currency Year: USD, 2003</td>
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<td></td>
<td></td>
<td>Cost of Nonadherence: Adjusted all cause: PC: $1668 ($2065.99),</td>
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<td></td>
<td>Adjusted disease state specific: HC:$7642 ($9465.39), PC:$614 ($760.50), MC:$5974 ($7399.40), STDC:$1840 ($2279.03),</td>
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<td></td>
<td>Unadjusted all cause: PC:$1727 ($2139.06),</td>
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<td></td>
<td>Unadjusted disease state specific: HC:$6919 ($8569.88), PC:$785 ($972.30), MC:$5192 ($6430.82), STDC:$1717 ($2126.68),</td>
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<td>Total Healthcare costs</td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>Objective</td>
<td>Design</td>
<td>Follow Up</td>
<td>Sample Size</td>
<td>Measure</td>
<td>Classification</td>
<td>Method of Assessment</td>
<td>Total Costs</td>
</tr>
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<tr>
<td>US and diabetes mellitus specific health care costs between patients who were adherent or non-adherent to monotherapy with metformin, pioglitazone or a sulfonylurea and to examine whether cost differences varied among patients using these oral antidiabetic drugs.</td>
<td>Follow Up: 2 years Sample Size: 108592 (A:63830, NA:44762)</td>
<td>MPR≥80% = adherent, MPR&lt;80% = nonadherent</td>
<td>Pharmacy claims data</td>
<td>Costs</td>
<td>Hospitalization costs</td>
<td>State specific</td>
<td>USD, 2005</td>
<td>THC:$13258 ($15911.01)</td>
<td>Adjusted all cause: THC:$2284 ($2741.04)</td>
</tr>
<tr>
<td>Hong et al[34] 2011 South Korea</td>
<td>To assess the relationship between initial adherence to oral antihyperglycemic medications and subsequent health outcomes. Design: Retrospective, cohort study Follow Up: 3 years Sample Size: 40082 (A:11800, NA:28282)</td>
<td>Measure: MPR Classification: MPR≥80% = adherent, MPR&lt;80% = nonadherent Method of Assessment: Pharmacy claims data</td>
<td>Total costs</td>
<td>Hospitalization costs</td>
<td>Disease state specific</td>
<td>KRW, 2007</td>
<td>TC:₩765453 ($1142.31), HC:₩397549 ($593.28)</td>
<td>Medium</td>
<td></td>
</tr>
</tbody>
</table>
decreased hospitalizations or emergency department visits? Are there certain subgroups of populations that seem to benefit more than others when they adhere to their medication? What are the financial implications of changes in adherence for the nation at large and for Medicare?

**White et al[36] 2004 US**

To assess the relationship between diabetic medication adherence, total healthcare costs and utilisation with patients with type 2 diabetes mellitus and concomitant diabetes and cardiovascular disease.

| Design: Retrospective, database analysis |
| Follow Up: 1 year |
| Sample Size: 67029 (>95: 20170, 75-95: 14074, <75: 16713) |

**Measure:** MPR

**Classification:**
- MPR≥95%,
- MPR>75%<95%,
- MPR<75%

**Method of Assessment:** pharmacy claims data

<table>
<thead>
<tr>
<th>Total costs Pharmacy costs Non-pharmacy costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Costs: adjusted and unadjusted</td>
</tr>
<tr>
<td>Classification: disease state specific</td>
</tr>
<tr>
<td>Currency Year: USD, 2000</td>
</tr>
<tr>
<td>Cost of Nonadherence: adjusted:</td>
</tr>
<tr>
<td>TC(≥95): $4835 ($6518.17),</td>
</tr>
<tr>
<td>TC(75-95): $5314 ($7163.92),</td>
</tr>
<tr>
<td>TC(&lt;75): $5706 ($7692.38),</td>
</tr>
<tr>
<td>PC(≥95): $1429 ($1926.47),</td>
</tr>
<tr>
<td>PC(75-95): $1157 ($1559.78),</td>
</tr>
<tr>
<td>PC(&lt;75): $762 ($1027.27),</td>
</tr>
<tr>
<td>NPC(≥95): $3406 ($4591.70),</td>
</tr>
<tr>
<td>NPC(75-95): $4157 ($5604.14),</td>
</tr>
<tr>
<td>NPC(&lt;75): $4944 ($6665.11)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total costs Pharmacy costs Non-pharmacy costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Costs: unadjusted</td>
</tr>
<tr>
<td>Classification: disease state specific</td>
</tr>
<tr>
<td>Currency Year: USD, 2000</td>
</tr>
<tr>
<td>Cost of Nonadherence: unadjusted:</td>
</tr>
<tr>
<td>TC(≥95): $4809 ($6483.12),</td>
</tr>
<tr>
<td>TC(75-95): $5333 ($7189.53),</td>
</tr>
<tr>
<td>TC(&lt;75): $5605 ($7556.22),</td>
</tr>
</tbody>
</table>

**Quality:** low

Classification: cost analysis
To examine the predictors of duloxetine compliance and its association with healthcare costs among diabetic peripheral neuropathic pain (DPNP) patients.

**Design:** Retrospective, cohort study

**Follow Up:** 1 year

**Sample Size:** 2354 (A:830, NA:1524)

**Measure:** MPR

**Classification:**
- MPR≥80% = high compliance
- MPR<80% = low compliance

**Subgroup Analysis:**
- commercial
- Medicare supplemental

**Method of Assessment:** pharmacy claims data

**Total healthcare costs**

<table>
<thead>
<tr>
<th>Type of Costs</th>
<th>Classification</th>
<th>US ($1)</th>
<th>US ($2)</th>
</tr>
</thead>
</table>
| Inpatient costs | adjusted all cause and disease state specific | THC(com):$10024 ($11671.20), THC(med):$5015 ($5839.09), IC(com):$2232 ($2598.77), IC(med):$2606 ($3034.23), OC(com):$1989 ($2315.84), OC(med):$1231 ($1433.28), PC(com):$1451 ($1689.44), PC(med):$1179 ($1372.74) | DPNP: THC(com):$3565 ($4150.82), THC(med):$2384 ($2775.75), |}

**Quality:** medium
<table>
<thead>
<tr>
<th>Osteoporosis</th>
<th>To assess rates of osteoporotic fractures and health care utilisation as a function of bisphosphonate compliance in usual clinical practice.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>Retrospective, cohort study</td>
</tr>
<tr>
<td><strong>Follow Up:</strong></td>
<td>3 years</td>
</tr>
<tr>
<td><strong>Sample Size:</strong></td>
<td>17988 (not specified)</td>
</tr>
<tr>
<td><strong>Measure:</strong></td>
<td>MPR</td>
</tr>
<tr>
<td><strong>Classification:</strong></td>
<td>80-100% = adherent, 60-79% = moderate adherence, 40-59% = moderate adherence, 20-39% = nonadherent, 0-19% = nonadherent</td>
</tr>
<tr>
<td><strong>Method of Assessment:</strong></td>
<td>Pharmacy claims data</td>
</tr>
<tr>
<td><strong>Type of Costs:</strong></td>
<td>Adjusted and unadjusted</td>
</tr>
<tr>
<td><strong>Classification:</strong></td>
<td>Disease state specific</td>
</tr>
<tr>
<td><strong>Currency Year:</strong></td>
<td>USD, 2004</td>
</tr>
</tbody>
</table>
| **Cost of Nonadherence:** | Adjusted:  
TC(80-100): $859 ($-1063.96),  
TC(60-79): $474 ($-587.10),  
TC(40-59): $366 ($-453.33),  
TC(20-39): $151 ($187.03),  
IC(80-100): $3233 ($-4004.40),  
IC(60-79): $856 ($-1060.24),  
IC(40-59): $6221 ($-7705.34),  
IC(20-39): $585 ($-724.58),  
OC(80-100): $445 ($-551.18),  
OC(60-79): $538 ($-666.37),  
OC(40-59): $236 ($-292.31),  
OC(20-39): $60 ($74.32),  
PC(80-100): $997 ($1234.89),  
PC(60-79): $923 ($1143.23),  
PC(40-59): $402 ($497.92),  
PC(20-39): $160 ($198.18)  
Unadjusted:  
TC(80-100): $1273 ($-1576.74),  
TC(60-79): $294 ($-364.15),  
TC(40-59): $573 ($-709.72),  
TC(20-39): $101 ($125.10),  
IC(80-100): $883 ($-1093.68), |
| **Quality:**  | Medium                                                                                                                             |
| **Classification:** | Cost description                                                                                                                   |
Eisenberg et al[39]  
2015  
US  
To determine healthcare outcomes associated with compliance and noncompliance to bisphosphonate therapy in women diagnosed with osteoporosis  
Design: Retrospective claims study  
Follow Up: 2 years  
Sample Size: 27905  
(A:11368, NA:16537)  
Measure: MPR  
Classification:  
(≥70% = compliant, <70% = noncompliant)  
Method of Assessment: pharmacy claims data  
Total costs  
Inpatient costs  
Outpatient costs  
ED costs  
Pharmacy costs  
Physician office visit costs  
Type of Costs: unadjusted  
Classification: all cause and disease state specific  
Currency Year: USD, 2012  
Cost of Nonadherence: all cause:  
TC:$7237 ($7550.72),  
IC:$1986 ($2072.09),  
OC:$2057 ($2146.17),  
EDC:$258 ($269.18),  
PC:$2197 ($2292.24),  
POC:$738 ($769.99)  
Disease state specific:  
TC:$674 ($703.22),  
IC:$334 ($348.48),  
OC:$77 ($80.34),  
EDC:$5 ($5.22),  
PC:$213 ($222.23),  
POC:$44 ($45.91)  
Cost of Nonadherence: commercial:  
Quality: medium  
Classification: cost description

Halpern et al[40]  
2011  
US  
To examine the associations of adherence to osteoporosis therapies  
Design: Retrospective analysis  
Follow Up: 540 days  
Sample Size: 21655  
Measure: MPR  
Classification:  
(≥80% = high adherence,  
Medical costs  
Type of Costs: unadjusted  
Classification: all cause  
Currency Year: USD, 2006  
Cost of Nonadherence: commercial:  
Quality: medium  
Classification: cost outcome description
with occurrence of closed fracture, all cause medical costs and all cause hospitalizations.

≥80%:8759, ≥50<80%:5237, <50%:7659

≥50<80% = moderate adherence, <50% = low adherence

Method of Assessment: pharmacy claims data

Hazel-Fernandez et al[41] 2013 US

To evaluate the healthcare utilisation patterns of medicare part D beneficiaries newly initiating teriparatide and to assess the association of medication adherence and persistence with bone fracture.

Design: Retrospective cohort study
Follow Up: 12 months
Sample Size: 761
(≥80%:163,
≥50<80%:57,
<50%:541)

≥80% = high adherence,
≥50<80% = moderate adherence, <50% = low adherence

Method of Assessment: pharmacy claims data

Total healthcare costs
Inpatient costs
Outpatient costs
ED costs
Pharmacy costs

Type of Costs: unadjusted
Classification: disease state specific and fracture related
Cost of Nonadherence :

Disease state specific:
THC(≥80):$21033 ($22942.39),
THC(50-80):$25574 ($27895.62),
THC(<50):$15528 ($16937.64),
IC(≥80):$2198 ($2397.54),
IC(50-80):$8448 ($9214.91),
IC(<50):$4897 ($5341.55),
OC(≥80):$5151 ($5618.61),
OC(50-80):$6439 ($7023.54),
OC(<50):$5806 ($6333.07),
EDC(≥80):$211 ($230.15),
EDC(50-80):$330 ($359.96),
EDC(<50):$465 ($507.21),
PC(≥80):$13472 ($14695),
PC(50-80):$10358 ($11298.31),
PC(<50):$4361 ($4756.89)

Fracture related:
THC(≥80):$12670 ($13820.19),
THC(50-80):$9292 ($10135.53),
THC(<50):$4419 ($4820.16),

Quality: medium
Classification: cost outcome description
<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Total costs</th>
<th>Type of Costs</th>
<th>Currency Year</th>
<th>Cost of Nonadherence</th>
<th>Quality</th>
<th>Classification</th>
<th>Cost</th>
</tr>
</thead>
</table>
| Huybrechts et al[42] 2006    | To evaluate non-compliance with osteoporosis medications as well as its implications for health and economic outcomes in actual practice. | Design: Retrospective cohort study
Follow Up: 5 years
Sample Size: 38120 (A:9530, NA:28590) | Design: Retrospective cohort study
Follow Up: 5 years
Sample Size: 38120 (A:9530, NA:28590) | Measure: MPR
Classification: (≥80% = compliant, <50% = noncompliant)
Method of Assessment: pharmacy claims data | Total costs
Medical costs
Institutional costs | Type of Costs: unadjusted
| Kjellberge et al[43] 2016    | To estimate the rate of oral bisphosphonate compliance among Danish women and to examine the association of noncompliance with health care resource use and cost. | Design: Retrospective cohort study
Follow Up: 1 year
Sample Size: 38234 (A:26806, NA:11428) | Design: Retrospective cohort study
Follow Up: 1 year
Sample Size: 38234 (A:26806, NA:11428) | Measure: MPR
Classification: (≥70% = compliant, <70% = noncompliant)
Method of Assessment: pharmacy claims data | Total costs
Medical costs | Type of Costs: adjusted
| Modi et al[44] 2015          | To evaluate compliance with | Design: Retrospective cohort study | Design: Retrospective cohort study | Measure: MPR
Classification: | Total costs
Inpatient costs | Type of Costs: unadjusted
Classification: all cause and disease state specific | Quality: medium | Classification: cost |
<table>
<thead>
<tr>
<th>Country</th>
<th>Study Description</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Classification</th>
<th>Fracture Costs</th>
<th>Type of Costs</th>
<th>Classification</th>
<th>Cost of Nonadherence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Osteoporosis treatments and determine fracture and healthcare burden associated with noncompliance</td>
<td>Retrospective observational study</td>
<td>1 year</td>
<td>27913 (A:23430, NA:34483)</td>
<td>MPR</td>
<td>(≥80% = compliant, &lt;80% = noncompliant)</td>
<td>Outpatient costs: state specific &lt;br&gt;Outpatient costs: Currency Year: USD, 2011 &lt;br&gt;Cost of Nonadherence: all cause: &lt;br&gt;TC: $11749 ($12484.12), IC: $8768 ($9316.60), OC: $3945 ($4191.83), EDC: $104 ($110.51), PC: $2981 ($3167.52), MC: $8768 ($9316.60), OtC: $997 ($1059.38)</td>
<td>Outpatient costs</td>
<td>unadjusted</td>
<td>fracture site specific</td>
<td>DKK, 2010</td>
</tr>
<tr>
<td>Olsen et al[45]</td>
<td>To assess the association between refill compliance and all cause health care costs.</td>
<td>Retrospective observational study</td>
<td>2 years</td>
<td>47176 (not specified)</td>
<td>MPR</td>
<td>(≥80% = optimal compliance, &gt;50%&lt;80% = suboptimal compliance, &lt;50% = low compliance)</td>
<td>Outpatient costs: Hip fracture: FC(50-80): kr81757.50 ($74531.41), FC(&lt;50): kr174700 ($21568.12), FC(&lt;50): kr226472 ($27959.14) &lt;br&gt;Spine fracture: FC(50-80): kr117776.50 ($14540.12), FC(&lt;50): kr795217.50 ($98173.70) &lt;br&gt;Humerus fracture: FC(50-80): kr463024 (-$57162.70), FC(&lt;50): kr45072.50 ($8665.81)</td>
<td>Outpatient costs</td>
<td>unadjusted</td>
<td>fracture site specific</td>
<td>DKK, 2010</td>
</tr>
</tbody>
</table>
Sunyecz et al[46] 2008 US
To examine the relationship between persistence and compliance with bisphosphonate therapy and total and osteoporosis related costs and healthcare resource utilisation in a cohort of female bisphosphonate naïve users.

Design: Retrospective observational study
Follow Up: 3 years
Sample Size: 32944 (A:12186, NA:20758)

Measure: MPR
Classification: (≥80% = compliant, <80% = noncompliant)
Method of Assessment: pharmacy claims data

Other fracture:
FC(50-80): kr19261.50 (-$2377.93), FC(<50): kr84067.50 ($84451.66)

Type of Costs: unadjusted
Classification: all cause and disease state specific
Currency Year: USD, 2005
Cost of Nonadherence:
All cause:
THC: $23660 ($28394.52), IC: $18839 ($22608.81), OC: $10061 ($12074.27), EDC: $832 ($988.49), PC: $6941 ($8329.94), RC: $1079 ($1294.91)
Disease state specific:
THC: $1602 ($1922.57), IC: $14074 ($16890.30), OC: $501 ($601.25), EDC: $452 ($542.45), PC: $918 ($1101.70), RC: $184 ($220.82)

Quality: low
Classification: cost description

Zhao et al[47] 2014 US
To examine the association between teriparatide adherence and healthcare utilisation and costs among hip fracture patients.

Design: Retrospective cohort study
Follow Up: 36 months
Sample Size: 824 (≥80:362, 50-80%:219, <50%:243)

Measure: PDC
Classification: (≥80% = high, 50-80% = medium, <50% = low)
Method of Assessment: pharmacy claims data

Other fracture:
FC(50-80): kr19261.50 (-$2377.93), FC(<50): kr84067.50 ($84451.66)

Type of Costs: adjusted and unadjusted
Classification: disease state specific
Currency Year: USD, 2010
Cost of Nonadherence:
Adjusted:
THC(≥80): $34428 ($37553.4), THC(50-80): $37956 ($41401.68), THC(<50): $31188 ($34019.28), IC(≥80): $7548 ($8233.20), IC(50-80): $11520 ($1256.80), IC(<50): $11556 ($12605.04)

Quality: medium
Classification: cost description
<table>
<thead>
<tr>
<th>Measure</th>
<th>Total healthcare costs</th>
<th>Inpatient costs</th>
<th>Outpatient costs</th>
<th>Pharmacy costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>THC(≥80)</td>
<td>$40212 ($43862.52)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THC(50-80%)</td>
<td>$40512 ($44189.76)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THC(&lt;50%)</td>
<td>$40128 ($43770.84)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IC(≥80)</td>
<td>$8136 ($8874.60)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IC(50-80%)</td>
<td>$12060 ($13154.76)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>IC(&lt;50%)</td>
<td>$15444 ($16283.16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC(≥80%)</td>
<td>$12924 ($14097.24)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC(50-80%)</td>
<td>$14928 ($16283.16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC(&lt;50%)</td>
<td>$17568 ($19162.80)</td>
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</tr>
</tbody>
</table>

Zhao et al[48] 2013 US
To examine the association between teriparatide (TPTD) adherence and healthcare utilisation and costs in real world US kyphoplasty/vertebroplasty (KV) patients.

**Design:** Retrospective observational cohort study
**Follow Up:** 36 months
**Sample Size:** 1568
(≥80: 783, 50-80%: 382, <50%: 403)

**Measure:** PDC
**Classification:**
(≥80% = high, 50-80% = medium, <50% = low)

**Method of Assessment:** pharmacy claims data

**Total healthcare costs**

**Inpatient costs**

**Outpatient costs**

**Pharmacy costs**

**Type of Costs:** adjusted and unadjusted
**Classification:** disease state specific

**Currency Year:** USD, 2010

Cost of Nonadherence:

**Adjusted:**
THC(≥80): $40212 ($43862.52),
THC(50-80): $40512 ($44189.76),
THC(<50): $40128 ($43770.84),
IC(≥80): $8136 ($8874.60),
IC(50-80): $12060 ($13154.76),
IC(<50): $15444 ($16283.16),
OC(≥80): $12924 ($14097.24),
OC(50-80): $14928 ($16283.16),
OC(<50): $17568 ($19162.80),

**Quality:** medium
**Classification:** cost description
To assess the association between adherence levels to different inhaled corticosteroid/long acting β₂-adrenergic agonist and COPD exacerbation rates and costs in commercially insured population.

**Design:** Observational cohort study  
**Follow Up:** 12 months  
**Sample Size:** 13657 (≥80%: 1898, ≥50<80%: 1971, ≥30 <50%: 2443, <30% :7345)  

**Measure:** PDC  
**Classification:** (≥80 = adherent, ≥50<80% = mildly nonadherent, ≥30 <50% = moderately nonadherent, <30% highly nonadherent)  

**Type of Costs:** adjusted  
**Classification:** all cause and disease state specific  
**Currency Year:** USD, 2014  

**Cost of Nonadherence:**  
All cause:  
TC(≥80):$22546 ($22772.24),  
TC(50-80):$25545 ($25800.95),  
TC(30-50):$24303 ($24546.51),  
TC(<30):$25148 ($25399.98),  
OC(≥80):$7816 ($7894.31),  
OC(50-80):$8225 ($8307.41),  
OC(30-50):$8365 ($8448.81),  
OC(<30):$8857 ($8945.74),  
PC(≥80):$7954 ($8033.70),  
PC(50-80):$13908 ($15170.52),  
PC(<50):$8700 ($9843.24)  

Unadjusted:  
THC(≥80):$42768 ($46650.48),  
THC(50-80):$36780 ($40118.88),  
THC(<50):$39792 ($43404.36),  
IC(≥80):$7620 ($8311.80),  
IC(50-80):$12228 ($13338.12),  
IC(<50):$15768 ($17199.48),  
OC(≥80):$14580 ($15903.60),  
OC(50-80):$12108 ($13207.20),  
OC(<50):$15324 ($16715.16),  
PC(≥80):$20568 ($22435.20),  
PC(50-80):$12444 ($13573.68),  
PC(<50):$8700 ($9489.84)
Delea et al[50]  
2008 US

To assess the association between adherence with fluticasone propionate/salmeterol combination product in a single inhaler and asthma care utilisation and costs in asthma

<table>
<thead>
<tr>
<th>Design</th>
<th>Retrospective longitudinal cohort study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow Up</td>
<td>24 months</td>
</tr>
<tr>
<td>Sample Size</td>
<td>12907 (≥75: 2612, 50-75%: 3608, 25-50%: 5035, &lt;25%: 1652)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Measure</th>
<th>MPR Classification: (≥75, 50-75%, 25-50%, &lt;25%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of Assessment</td>
<td>pharmacy claims data</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Costs</th>
<th>unadjusted costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>disease state specific</td>
</tr>
<tr>
<td>Cost of Nonadherence</td>
<td>TC(≥80): $1564 ($1990.27), TC(50-80): $1155 ($1166.57), TC(30-50): $1619 ($1635.22), TC(&lt;30): $1405 ($1419.08)</td>
</tr>
<tr>
<td>Cost of Nonadherence Classification</td>
<td>disease state specific</td>
</tr>
<tr>
<td>Currency Year</td>
<td>USD, 2003</td>
</tr>
<tr>
<td>Quality</td>
<td>medium</td>
</tr>
</tbody>
</table>

Total costs:
- PC(50-80): $6862 ($6930.76), PC(30-50): $5485 ($5539.96), PC(<30): $4395 ($4439.04), HC(≥80): $6106 ($6167.51), HC(50-80): $9391 ($9485.09), HC(30-50): $9171 ($9262.89), HC(<30): $10849 ($10957.70) |
- Disease state specific:
patients in typical US clinical practice

**Diehl et al [51]**

2010

US

To evaluate respiratory-related medical outcomes and cost for infants who were prescribed and received palivizumab in accordance with the dosing schedule recommended by the American Academy of Paediatrics in 2006 versus those who did not.

**Design:** Retrospective claims analysis

**Follow Up:** 7 months

**Sample Size:** 245 (A:73, NA:172)

**Measure:** 37 day gap in claims

**Classification:** (>37 day gap in claims = noncompliant)

**Method of Assessment:** pharmacy claims data

**Total costs**

**Pharmacy costs**

**Services costs**

**Type of Costs:** unadjusted

**Classification:** disease state specific

**Currency Year:** USD, 2007

**Cost of Nonadherence:**

TC: $19093.46 ($21656.12),

PC: $7647.40 ($8673.81),

SC**: $11604.03 ($13161.45)

**Quality:** medium

**Classification:** cost description

**Joshi et al [52]**

2006

US

Examine the association of medication adherence with workplace productivity and health-related quality of life in asthma patients.

**Design:** quantitative analysis

**Follow Up:**

**Sample Size:** 385

(high:150, medium:73, low: 162)

**Measure:** Morisky scale

**Classification:** (0= high adherence, 1-2 = medium adherence, >2 = low adherence)

**Method of Assessment:**

**Total productivity cost**

**Absenteeism costs**

**Presenteeism costs**

**Type of Costs:** unadjusted

**Classification:** disease state specific

**Currency Year:** USD, 2002

**Cost of Nonadherence**: 

TPC(0): $1210.90 ($1571.73),

TPC(1-2): $1428.50 ($1854.17),

TPC(>2): $1073.10 ($1392.87),

AbC(0): $633.70 ($822.53),

AbC(1-2): $608.90 ($790.34),

**Quality:** medium

**Classification:** cost outcome description
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Classification</th>
<th>Method of Assessment</th>
<th>Type of Costs</th>
<th>Cost of Nonadherence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miravitlles et al.[53] 2013 Spain</td>
<td>multicentre, retrospective, observational study</td>
<td>18 months</td>
<td>1365 (A:246, NA:1119)</td>
<td>GOLD 2007 Guidelines</td>
<td>(adherent, nonadherent)</td>
<td>GOLD guidelines</td>
<td>unadjusted</td>
<td>ED costs Pharmacy costs Physician office visit costs Hospitalization costs Primary care costs Interdisciplinary visit costs Medical test costs Radiology costs Laboratory costs</td>
<td>medium</td>
</tr>
<tr>
<td>Quittner et al.[54] 2014 US</td>
<td>retrospective, cohort study</td>
<td>2 years</td>
<td>3287 (≥80%: 663, 50-80%: 949, &lt;50%: 1675)</td>
<td>MPR</td>
<td>(≥80% = high adherence, 50-80% = moderate adherence, &lt;50% = low adherence)</td>
<td>pharmacy claims data</td>
<td>unadjusted</td>
<td>All cause and disease state specific</td>
<td>medium</td>
</tr>
</tbody>
</table>
### Gastrointestinal Disease

**Carter et al [55]**

**2011**

**US**

To further evaluate the impact of adherence to infliximab on CD related utilisation and inpatient costs in the first year of treatment using a different definition of adherence and a larger more diverse claims database.

**Design:** retrospective, observational cohort claims analysis

**Follow Up:** 12 months

**Sample Size:** 638 (A:466, NA:172)

**Measure:** number of infusions in 12 month period

**Classification:** (7-9 infusions = adherent, <7 infusions = nonadherent)

**Method of Assessment:** health claims data

**Type of Costs:** unadjusted

**Classification:** disease state specific

**Currency Year:** USD, 2007

**Cost of Nonadherence:**

- THC(50-80): $33132.50 ($35444.44)
- THC(<50): $33894 ($36259.07)

**Quality:** medium

**Classification:** cost outcome description

---

**Gosselin et al [56]**

**2009**

**US**

To examine the effects of gastroesophageal reflux disease (GERD) patients compliance with PPI therapy on health care resource utilisation and costs.

**Design:** retrospective cohort study

**Follow Up:** 12 months

**Sample Size:** 41837 (A:28321, NA:13516)

**Measure:** MPR

**Classification:** (≥80% = adherent, <80% = nonadherent)

**Method of Assessment:** pharmacy claims data

**Type of Costs:** adjusted

**Classification:** disease state specific

**Currency Year:** USD, 2003

**Cost of Nonadherence:**

- TC: $9497 ($12085.43),
- IC: $2116 ($2692.72),
- OC: $5458 ($6945.59),
- PC: $1922 ($2445.85),
- MC: $7575 ($9639.58)

**Quality:** medium

**Classification:** cost description

---

**Kane et al [57]**

**2009**

**US**

To evaluate adherence to infliximab maintenance therapy and the impact of medication adherence on healthcare utilisation and costs by patients.

**Design:** retrospective cohort analysis

**Follow Up:** 12 months

**Sample Size:** 571 (A:375, NA:196)

**Measure:** number of infusions in 12 month period

**Classification:** (≥8 infusions = adherent, <7 infusions = nonadherent)

**Method of:**

**Type of Costs:** unadjusted

**Classification:** all cause and disease state specific

**Currency Year:** USD, 2004

**Cost of Nonadherence:**

- OC: $6679 ($8272.62),
- ED: $314 ($388.92),
- PC: $16129 ($19974.85),
- MC: $7575 ($9639.58)

**Quality:** medium

**Classification:** cost outcome description
<table>
<thead>
<tr>
<th><strong>Mitra et al[58]</strong></th>
<th>To assess the association between adherence to oral 5-aminosalicylates (5-ASAs) and all cause costs and health care utilisation among patients with active ulcerative colitis.</th>
</tr>
</thead>
</table>
| **2012**          | **Design:** retrospective, observational cohort study  
|                   | **Follow Up:** 12 months  
|                   | **Sample Size:** 1693 (A:476, NA:1216)  
| **Measure:**      | **MPR**  
|                   | **Classification:** (≥80% = adherent, <80% = nonadherent)  
| **Method of**     | **Assessment:** pharmacy claims data  
| **Type of Costs:**| **adjusted**  
| **Classification:**| **all cause and disease state specific**  
| **Currency Year:**| **USD, 2010**  
| **Cost of Nonadherence:** | 
|                   | **All cause:**  
|                   | **PC:** $4494 ($5566.27)  
|                   | **HC:** $6893 ($8537.68)  
|                   | **Disease state specific:**  
|                   | **OC:** $3931 ($4868.94)  
|                   | **EDC:** $91 ($112.71)  
|                   | **MC:** $10243 ($12686.99)  
|                   | **HC:** $4494 ($5566.27)  
| **Quality:**      | **high**  
| **Classification:**| **cost description** |

<table>
<thead>
<tr>
<th><strong>Wan et al[59]</strong></th>
<th>To examine the effect of adherence versus non-adherence on healthcare costs in patients with inflammatory bowel disease.</th>
</tr>
</thead>
</table>
| **2014**          | **Design:** retrospective cohort analysis  
|                   | **Follow Up:** 360 days  
|                   | **Sample Size:** 1646 (A:674, NA:972)  
| **Measure:**      | **MPR**  
|                   | **Classification:** (≥80% = adherent, <80% = nonadherent)  
| **Method of**     | **Assessment:** pharmacy claims data  
| **Type of Costs:**| **adjusted**  
| **Classification:**| **all cause and disease state specific**  
| **Currency Year:**| **USD, 2009**  
| **Cost of Nonadherence:** | 
|                   | **All cause:**  
|                   | **PC:** $1541.60 ($1681.55)  
|                   | **TC:** $47411 ($52341.27)  
|                   | **THC:** $32522 ($35903.96)  
|                   | **IC:** $17634 ($19467.76)  
|                   | **OC:** $10909 ($12043.43)  
|                   | **EDC:** $458 ($505.63)  
|                   | **MC:** $10923 ($12686.99)  
|                   | **HC:** $4494 ($5566.27)  
| **Quality:**      | **high**  
<p>| <strong>Classification:</strong>| <strong>cost description</strong> |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Measure</th>
<th>Total costs</th>
<th>Type of Costs</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al [60]</td>
<td>retrospective claims analysis</td>
<td>MPR Classification: (≥80% = adherent, &lt;80% = nonadherent)</td>
<td>Inpatient costs, ED costs, Pharmacy costs, Other pharmacy costs</td>
<td>unadjusted classification</td>
<td>medium classification</td>
</tr>
<tr>
<td>Ettinger et al [61]</td>
<td>retrospective claims analysis</td>
<td>MPR Classification: (≥80% = adherent, &lt;80% = nonadherent)</td>
<td>Inpatient costs, ED costs, Pharmacy costs, Office visit costs, Ancillary costs, Other pharmacy costs</td>
<td>unadjusted classification</td>
<td>medium classification</td>
</tr>
<tr>
<td>Faught et al [62]</td>
<td>retrospective observational open cohort design</td>
<td>MPR Classification: (≥80% = adherent)</td>
<td>Inpatient costs, Outpatient costs</td>
<td>unadjusted classification</td>
<td>medium classification</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Country</td>
<td>Objective</td>
<td>Design</td>
<td>Follow Up</td>
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<tr>
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<tr>
<td>Barnett et al [63]</td>
<td>2011</td>
<td>US</td>
<td>To characterise the cost of HIV care including combination antiretroviral treatment.</td>
<td>Retrospective observational cohort study</td>
<td>1 year</td>
</tr>
<tr>
<td>Cooke et al [64]</td>
<td>2014</td>
<td>US</td>
<td>To measure adherence to antiretroviral therapy regimens in commercially insured patients with HIV infection and analyse the clinical and demographic factors associated with ≥90% adherence.</td>
<td>Retrospective claims analysis</td>
<td>1 year</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Measure</td>
<td>Total costs</td>
<td>Type of Costs</td>
<td>Quality</td>
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<td>---------</td>
</tr>
<tr>
<td><strong>Pruitt et al[65]</strong></td>
<td>retrospective cohort study</td>
<td>MPR</td>
<td>Inpatient costs</td>
<td>unadjusted</td>
<td>medium</td>
</tr>
<tr>
<td>2015</td>
<td>Follow Up: 2 years</td>
<td>(≥90% = adherent, &lt;90% = nonadherent)</td>
<td>Outpatient costs</td>
<td>disease state specific</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Other pharmacy costs</td>
<td>Cost of Nonadherence:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Behavioural health inpatient costs</td>
<td>HIV:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TC:$15360 ($16957.32),</td>
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<td></td>
<td>IC:$3864 ($4265.76),</td>
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<td></td>
<td></td>
<td>OC:$3948 ($4358.52),</td>
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<td></td>
<td></td>
<td>PC:$4956 ($5471.40),</td>
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<td></td>
<td>OtPC:$1764 ($1947.48),</td>
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<td></td>
<td></td>
<td>BHIC:$840 ($927.36)</td>
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<td>AIDS:</td>
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<td></td>
<td></td>
<td>TC:$27648 ($30523.08),</td>
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<td>IC:$13008 ($14360.76),</td>
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<td>OC:$5880 ($6491.52),</td>
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<td></td>
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<td>PC:$5640 ($6226.56),</td>
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<td>OtPC:$2580 ($2848.32),</td>
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<td></td>
<td></td>
<td>BHIC:$528 ($582.96)</td>
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<tr>
<td><strong>Parkinson’s Disease</strong></td>
<td>retrospective administrative claims study</td>
<td>MPR</td>
<td>Total costs</td>
<td>unadjusted</td>
<td>medium</td>
</tr>
<tr>
<td><strong>Davis et al[66]</strong></td>
<td>Follow Up: 12 months</td>
<td>(≥80% = adherent, &lt;80% = nonadherent)</td>
<td>Pharmacy costs</td>
<td>disease state specific</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td></td>
<td></td>
<td></td>
<td>Cost of Nonadherence:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TC:$18511 ($24262.36),</td>
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<td></td>
<td>PC:$2684 ($3537.36),</td>
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<td></td>
<td>MC:$15827 ($20859.12)</td>
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<tr>
<td><strong>Delea et al[67]</strong></td>
<td>retrospective historical cohort study</td>
<td>PDC</td>
<td>Total costs</td>
<td>adjusted and unadjusted</td>
<td>high</td>
</tr>
<tr>
<td>2011</td>
<td>Follow Up: 12 months</td>
<td>(≥80% = adherent)</td>
<td>Pharmacy costs</td>
<td>all cause and disease state specific</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td></td>
<td></td>
<td></td>
<td>Classification: cost description</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quality: medium</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Follow Up</td>
<td>Sample Size</td>
<td>Measure</td>
<td>Classification</td>
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<tr>
<td>Wei et al [68] 2014 US</td>
<td>Retrospective cross-sectional study</td>
<td>19 months</td>
<td>7583 (90-100%:3948, 80-89%:1456, ≤79%:2179)</td>
<td>MPR</td>
<td>(&gt;90&lt;100% = high, &gt;80&lt;89% = moderate, ≤79% = low)</td>
</tr>
</tbody>
</table>

To examine the associations of adherence to antiparkinson drugs with healthcare utilisation and economic outcomes.

Sample Size: 1215 (A:617, NA:598)

Method of Assessment: pharmacy claims data

Cost of Nonadherence:
- Adjusted all cause:
  - TC:$19686 ($23625.30), IC:$5954 ($7145.43), PC:$6391 ($7669.88), OtC:$8795 ($10554.94)
  - Adjusted disease state specific:
    - TC:$8574 ($10289.71), IC:$3705 ($4446.39), PC:$3850 ($4620.41), OtC:$1884 ($2261)
- Unadjusted all cause:
  - TC:$19362 ($23236.46), IC:$5463 ($6556.18), PC:$6158 ($7390.26), OtC:$7740 ($9288.82)
  - Unadjusted disease state specific:
    - TC:$9156 ($10988.18), IC:$3238 ($3885.94), PC:$3789 ($4547.20), OtC:$2129 ($2555.03)
To compare the rates of severe relapse and total direct and indirect costs over a 2 year period between US based employees with MS who were adherent and non-adherent to disease modifying drugs.

**Design:** retrospective cohort study  
**Follow Up:** 2 years  
**Sample Size:** 648 (A:448, NA:200)  
**Measure:** MPR  
**Classification:** (≥80% = adherent, <80% = nonadherent)  
**Method of Assessment:** pharmacy claims data  
**Total costs**  
**Type of Costs:** unadjusted  
**Classification:** all cause, disease state specific and indirect  
**Currency Year:** USD, 2007  
**Cost of Nonadherence:**  
- All cause:  
  - TC:$8079 ($9276.76),  
  - THC:$6022 ($6830.25),  
  - IC:$1030.50 ($1168.81),  
  - OC:$3231 ($3664.65),  
  - EDC:$143.50 ($162.76),  
  - PC:$1617 ($1834.03),  
  - MC:$4405.50 ($4996.79)  
- Disease state specific:  
  - TC:$3005 ($3408.32),  
  - IC:$505 ($572.78),  
  - OC:$1710 ($1939.51),  
  - EDC:$37 ($41.97),  
  - PC:$753 ($854.07),  
  - MC:$2252 ($2554.26)  
- Indirect:  
  - STDC:$1231 ($1396.22),  
  - Absenteeism cost: $826 ($936.86)  
**Quality:** high  
**Classification:** cost outcome description

**Tan et al[70]**  
2011  
US  
To assess the impact of treatment adherence on MS related hospitalizations  
**Design:** retrospective cohort study  
**Follow Up:** 12 months  
**Sample Size:** 2446  
**Measure:** MPR  
**Classification:** (≥80% = adherent, <80% = nonadherent)  
**Medical costs**  
**Type of Costs:** adjusted and unadjusted  
**Classification:** disease state specific  
**Currency Year:** USD, 2007  
**Cost of Nonadherence:**  
**Quality:** medium  
**Classification:** cost outcome description
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Classification</th>
<th>Method of Assessment</th>
<th>Type of Costs</th>
<th>Cost of Nonadherence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al[71] 2011 US</td>
<td>retrospective cohort analysis</td>
<td>12 months</td>
<td>5435 (A:1459, NA:987)</td>
<td>MPR</td>
<td>≥80% = adherent, &lt;80% = nonadherent</td>
<td>pharmacy claims data</td>
<td>Total healthcare costs</td>
<td>Commercial: $20323 ($22609.12), Medicare: $25282 ($28125.96),</td>
<td>medium</td>
</tr>
<tr>
<td>Cancer Darkow et al[72] 2007 US</td>
<td>retrospective observational cohort analysis</td>
<td>12 months</td>
<td>267 (≥95%:120, 90-95%:25, 50-90%:69, &lt;50%:53)</td>
<td>MPR</td>
<td>≥95% = very high, &gt;90&lt;95% = high, &gt;50&lt;90% = intermediate, &lt;50% = low</td>
<td>pharmacy claims data</td>
<td>Total healthcare costs</td>
<td>Commercial: $42250 ($52330.90), Medicare: $39236 ($48597.76),</td>
<td>high</td>
</tr>
</tbody>
</table>
**Wu et al[73]**

2010

US

To examine the association between adherence with imatinib and direct healthcare costs and resource utilisation

**Design:** retrospective observational cohort analysis

**Follow Up:** 12 months

**Sample Size:** 592 (A:350, NA:242)

**Measure:** MPR

**Classification:** (≥85% = high adherence, <85% = low adherence)

**Method of Assessment:** pharmacy claims data

**Total costs**

<table>
<thead>
<tr>
<th>Type of Costs</th>
<th>Classification</th>
<th>Total Costs</th>
<th>Unadjusted Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient costs</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Outpatient costs</td>
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<tr>
<td>ED costs</td>
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<tr>
<td>Pharmacy costs</td>
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<tr>
<td>Other pharmacy costs</td>
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</tr>
</tbody>
</table>

**Type of Costs:** unadjusted

**Classification:** disease state specific

**Currency Year:** USD, 2008

**Cost of Nonadherence:**

- TC: $107341 ($119415.73)
- IC: $44498 ($49503.55)
- OC: $34097 ($37932.55)
- EDC: $248 ($275.90)
- PC: $22846 ($25415.93)
- OtPC: $5652 ($6287.79)

**Quality:** medium

**Classification:** cost description
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Follow Up</th>
<th>Sample Size</th>
<th>Measure</th>
<th>Classification</th>
<th>Total Healthcare Costs</th>
<th>Type of Costs</th>
<th>Cost of Nonadherence</th>
<th>Currency Year</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leider et al</td>
<td>retrospective claims based analysis</td>
<td>12 months</td>
<td>2100 (A:442, NA:1658)</td>
<td>urine testing</td>
<td>(positive test = nonadherent, negative test = adherent)</td>
<td>Total healthcare costs</td>
<td>unadjusted</td>
<td>THC: $26433 ($29406.43), IC: $6361 ($7076.55), OC: $9734 ($10828.97), EDC: $421 ($468.36), PC: $7960 ($8855.42), MC: $1957 ($2177.14)</td>
<td>USD, 2008</td>
<td>medium</td>
</tr>
<tr>
<td>Ruetsch et al</td>
<td>cross sectional, retrospective analysis</td>
<td>12 months</td>
<td>477 (A:172, NA:305)</td>
<td>MPR</td>
<td>(≥80% = adherent, &lt;80% = nonadherent)</td>
<td>Total healthcare costs</td>
<td>unadjusted</td>
<td>THC: $16555 ($16995.62), IC: $5657 ($5807.57), OC: $5594 ($5742.89), EDC: $1147 ($1177.53), PC: $2365 ($2427.95), POC: $1765 ($1811.98), MC: $14190 ($14567.68)</td>
<td>USD, 2013</td>
<td>medium</td>
</tr>
<tr>
<td>Tkacz et al</td>
<td>retrospective cohort analysis</td>
<td>12 months</td>
<td>455 (A:146, NA:309)</td>
<td>MPR</td>
<td>(≥80% = adherent, &lt;80% = nonadherent)</td>
<td>Total healthcare costs</td>
<td>adjusted and unadjusted</td>
<td>THC: $49051 ($53503.88), IC: $26470 ($28872.96), OC: $14570 ($15892.67), EDC: $4439 ($4841.98)</td>
<td>USD, 2010</td>
<td>medium</td>
</tr>
</tbody>
</table>
Metabolic conditions other than diabetes mellitus

Lee et al[77] 2011 US
To assess the relationship between medication adherence and healthcare costs among US patients on dialysis given cinacalcet to manage secondary hypoparathyroidism.

Design: retrospective cohort study
Follow Up: 12 months
Sample Size: 4923
(A:1372, NA:1304)

Measure: MPR
Classification: (≥80% = high adherent, <80% = low adherent)
Method of Assessment: pharmacy claims data

Total costs
Type of Costs: unadjusted
Classification: all cause and disease state specific
Currency Year: USD, 2010
Cost of Nonadherence:
All cause:
PC:$3581 ($3906.09)
Unadjusted:
THC:$47868 ($52213.49),
IC:$26043 ($28407.20),
OC:$14173 ($15459.63),
EDC:$4058 ($4426.39),
PC:$3557 ($3879.91)

Quality: medium
Classification: cost description

Blood
Candrilli et al[78] 2011 US
To investigate the relationships among hydroxyurea adherence, healthcare utilisation and healthcare costs.

Design: retrospective longitudinal study
Follow Up: 12 months
Sample Size: 312
(A:110, NA:202)

Measure: MPR
Classification: (≥80% = adherent, <80% = nonadherent)
Method of Assessment: pharmacy claims data

Total costs
Type of Costs: adjusted
Classification: all cause and disease state specific
Currency Year: USD, 2008
Cost of Nonadherence:
All cause:
TC:$20436 ($22734.83),

Quality: medium
Classification: cost description
<table>
<thead>
<tr>
<th>Pharmacy claims data costs</th>
<th>Ancillary costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC: $9780 ($10880.15),</td>
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<tr>
<td>EDC: $837 ($931.15),</td>
<td></td>
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<tr>
<td>PC: $2579 ($2869.11),</td>
<td></td>
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<tr>
<td>POC: $3483 ($3874.80),</td>
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<tr>
<td>AC: $3911 ($4350.95)</td>
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</tr>
<tr>
<td>Disease state specific:</td>
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</tr>
<tr>
<td>TC: $12097 ($13457.78),</td>
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</tr>
<tr>
<td>IC: $7315 ($8137.86),</td>
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</tr>
<tr>
<td>EDC: $552 ($614.09),</td>
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</tr>
<tr>
<td>PC: $158 ($175.77),</td>
<td></td>
</tr>
<tr>
<td>POC: $1865 ($2074.79),</td>
<td></td>
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<tr>
<td>AC: $2466 ($2743.40)</td>
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</tr>
</tbody>
</table>

To determine the profile of patients who are admitted to hospital as a result of non-adherence and to obtain an estimate of the economic impact for the hospital.

Design: retrospective observational study
Follow Up: 1527 days
Sample Size: 87 (A: 21, NA: 66)

Measure: pharmacy records
Classification: (>75% = adherent, ≤75% = nonadherent)
Method of Assessment: pharmacy and hospital claims data

Hospitalization costs

Type of Costs: unadjusted
Classification: all cause
Currency Year: EUR, 2012
Cost of Nonadherence: €6275.80 ($8893.94)

Quality: low
Classification: cost outcome description

costs, OtC: other costs, com: commercial patients, med: Medicare supplemental patients, USD: United States dollar, GBP: Great British Pound, EUR: Euro, DKK: Danish krone, CAD: Canadian dollar, KRW: South Korean won

*: extrapolated annual cost; **: subgroups averaged; ***: national estimate of cost; ****: negative value as costs modelled against lowest adherence group; 
#: extrapolated annual cost and subgroups averaged; ##: cost represents losses in workplace productivity; ###: negative value as costs modelled against adherent group; ####: cost per episode of nonadherence


26. White TJV, Ann; Ory, Caron; Dezii, Christopher M.; Chang, Eunice. Economic Impact of Patient Adherence with Antidepressant Therapy Within a Managed Care Organization. Disease Management & Health Outcomes 2003;11(12):817-22 doi: 10.2165/00115677-200311120-00006[published Online First: Epub Date]


34. Hong JS, Kang HC. Relationship between oral antihyperglycemic medication adherence and hospitalization, mortality, and healthcare costs in adult ambulatory care patients with type 2 diabetes in South Korea. Medical care 2011;49:378-84 doi: 10.1097/MLR.0b013e31820292d1[published Online First: Epub Date]]


