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

Author, Year, Country	Objective	Study Characteristics	Adherence (as reported in paper)	Outcomes/ Indicators	Results (USD, 2015)	Quality
Cardiovascular Disease						
*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
*Casciano et al**[2]*** 2013 US	To assess the economic burden of underuse and nonadherence of warfarin therapy among patients with non-valvular atrial fibrillation in a commercially insured population.	Design: Retrospective, observational, quasi-experimental study 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 (A:168, NA:219, OA:6)	Measure: MPR 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

	angiotensin receptor blockers.					
*Dragomir et al**[4]*** 2010 Canada	To evaluate the impact of low adherence to antihypertensive agents on cardiovascular outcomes and hospitalization costs.	Design: Retrospective cohort study Follow Up: 3 years Sample Size: 56896 (A:38217, NA:18679)	Measure: MPR Classification: MPR≥80 = adherent, MPR < 80 = nonadherent Method of Assessment: pharmacy claims data	Total Healthcare Costs Pharmacy Costs Medical Costs Hospitalization Costs	Type of Costs: unadjusted and predicted Classification: disease state specific and hospitalized patients Currency Year: CAD, 2006 Cost of Nonadherence: Unadjusted Disease state specific: THC:$7165 ($6900.87), PC: $1800 ($1733.64), MC: $1370 ($1319.50), HC: $3995 ($3847.73) Unadjusted Hospitalized patients: THC: $17397 ($16755.67), PC:$2685 ($2586.02), MC:$2608 ($2511.86), HC: $12104 ($11657.79) Predicted disease state specific: HC:$3877 ($3734.08) Predicted hospitalized patient: HC:$11715 ($11283.13)	Quality: medium Classification: cost description
*Dragomir et al**[5]*** 2010 Canada	To evaluate the impact of low adherence to statins on clinical issues and direct healthcare costs.	Design: Retrospective cohort study Follow Up: 3 years Sample Size: 55134 (A:28549, NA:26585)	Measure: MPR Classification: MPR≥80 = adherent, MPR < 80 = nonadherent Method of Assessment: pharmacy claims data	Total Healthcare Costs Pharmacy Costs Medical Costs Hospitalization Costs	Type of Costs: unadjusted and predicted Classification: disease state specific and hospitalized patients Currency Year: CAD, 2005 Cost of Nonadherence: Unadjusted Disease state specific: THC:$6243 ($6175.76), PC:$2506 ($2479.01), MC:$1241 ($1227.63), HC:$2496 ($2469.12) Unadjusted Hospitalized patients: THC:$14725 ($14566.40), PC:$3374 ($3337.66), MC:$2475 ($2448.34), HC:$8876 ($8780.40) Predicted disease state specific:	Quality: medium Classification: cost description

					HC:$2669 ($2640.25) Predicted hospitalized patient: HC$9214 ($9114.76)	
*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	Total Healthcare Costs Pharmacy Costs Medical Costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2009 Cost of Nonadherence*: all cause: THC(>80):$6798.67 ($7505.66), THC(60-79):$7072.67 ($7808.16), THC(<59):$7401.33 ($8170.99), PC(>80):$1767.33 ($1951.11), PC(60-79):$1789.33 ($1975.40), PC(<59):$1937.33 ($2138.79), MC(>80):$4472.67 ($4937.78), MC(60-79):$4840.67 ($5344.05, MC(<59):$5138.67 ($5673.04) Disease state specific: PC(>80):$558.67 ($616.77), PC(60-79):$442.67 ($488.70), PC(<59):$325.33 ($359.16), MC(>80):$1596.67 ($1762.71), MC(60-79):$1722 ($1901.07), MC(<59):$1792.67 ($1979.09)	Quality: medium Classification: cost description
*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	Total Healthcare Costs Outpatient Costs ED Costs Pharmacy Costs Hospitalization	Type of Costs: adjusted and unadjusted Classification: disease state specific Currency Year: USD, 2008 Cost of Nonadherence: Adjusted: THC(>80):$7261 ($8077.79), THC(60-79):$7530 ($8377.05), THC(<59):$7370 ($8199.05), OC(>80):$3390 ($3771.34), OC(60-79):$3705 ($4121.77),	Quality: medium Classification: cost description

	costs of care.		Method of Assessment: pharmacy claims data	Costs	OC(<59):$3776 ($4200.76), EDC(>80):$101 ($112.36), EDC(60-79):$134 ($149.07), EDC(<59):$172 ($191.35), PC(>80):$2383 ($2651.06), PC(60-79):$1932 ($2149.33), PC(<59):$1509 ($1678.75), HC(>80):$1386 ($1541.91), HC(60-79):$1759 ($1956.87), HC(<59):$1913 ($2128.19) Unadjusted: THC(>80):$7182 ($7989.90), THC(60-79):$7560 ($8410.42), THC(<59):$7995 ($8894.35), OC(>80):$3396 ($3778.01), OC(60-79):$3635 ($4043.90), OC(<59):$3887 ($4324.25), EDC(>80):$102 ($113.47), EDC(60-79):$131 ($145.74), EDC(<59):$172 ($191.35), PC(>80):$2317 ($2577.64), PC(60-79):$2034 ($2262.80), PC(<59):$1880 ($2091.48), HC(>80):$1366 ($1519.66), HC(60-79):$1759 ($1956.87), HC(<59):$2057 ($2288.39)	
*Rizzo et al**[8]*** 1997 US	To investigate variations in compliance with four classes of antihypertensive agents- diuretics, ACEIs, CCBs and ß-	Design: Retrospective cohort study Follow Up: 12 months Sample Size: 7211(P:2668, NC:3101, NP:649, T:793)	Measure: ordinary least square regression analysis Classification: >80% = persistent, ≥30<80% = non-compliance, <30%	Total Healthcare Costs	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),	Quality: low Classification: cost description

	blockers and the health care costs associated with various degrees of compliance.		= non-persistence Method of Assessment: pharmacy claims data		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)	
*Sokol et al**[9]*** 2005 US	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.	Design: Retrospective cohort observational study Follow Up: 12 months Sample Size: 137277 Diabetes:(≥80: 1801, 60-79: 599, 40-59: 419, 20-39: 259, <19: 182) Hypertension:(≥80: 5804, 60-79: 921, 40-59: 562, 20-39: 344, <19: 350)	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 Classification: all cause and disease state specific 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),	Quality: medium Classification: cost description

	Hypercholesterolemia: (≥80: 1754, 60-79: 520, 40-59: 324, 20-39: 216, <19: 167) CHF: (≥80: 518, 60-79: 107, 40-59: 82, 20-39: 70, <19: 86)	PC(20-39):$1877 ($2624.89), PC(40-59):$1970 ($2754.94), PC(60-79):$2121 ($2966.11), PC(80-100):$2510 ($3510.10), MC(1-19):$15186 ($21236.82), MC(20-39):$11200 ($15662.61), MC(40-59):$11008 ($15394.10), MC(60-79):$9363 ($13093.66), MC(80-100):$6377 ($8917.90), Hypertension: TC(1-19):$9747 ($13630.66), TC(20-39):$11238 ($15715.75), TC(40-59):$9491 ($13272.66), TC(60-79):$8929 ($12486.73), TC(80-100):$8386 ($11272.38), PC(1-19):$916 ($1280.98), PC(20-39):$952 ($1331.32), PC(40-59):$1123 ($1570.46), PC(60-79):$1271 ($1777.43), PC(80-100):$1817 ($2540.98), MC(1-19):$8831 ($12349.69), MC(20-39):$10286 ($14384.43), MC(40-59):$8368 ($11702.20), MC(60-79):$7658 ($10709.31), MC(80-100):$6570 ($9187.80), Hypercholesterolemia: TC(1-19):$10916 ($15265.45), TC(20-39):$7982 ($11162.40), TC(40-59):$6756 ($9447.91), TC(60-79):$8412 ($11763.74), TC(80-100):$6752 ($9442.31), PC(1-19):$1067 ($1492.14), PC(20-39):$1152 ($1611.01),

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),

					PC(80-100):$801 ($1120.16), MC(1-19):$6810 ($9523.42), MC(20-39):$4786 ($6692.97), MC(40-59):$3452 ($4827.44), MC(60-79):$4938 ($6905.53), MC(80-100):$3124 ($4368.75), CHF: TC(1-19):$9841 ($13762.12), TC(20-39):$7733 ($10814.19), TC(40-59):$11378 ($15911.53), TC(60-79):$13924 ($19471.98), TC(80-100):$12698 ($17787.48), PC(1-19):$15 ($20.98), PC(20-39):$90 ($125.86), PC(40-59):$134 ($187.39), PC(60-79):$158 ($220.95), PC(80-100):$437 ($611.12), MC(1-19):$9826 ($13741.14), MC(20-39):$7643 ($10688.33), MC(40-59):$11244 ($15724.14), MC(60-79):$13766 ($19251.02), MC(80-100):$12261 ($17146.36)	
*Stroupe et al**[10]*** 2006 US	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 Classification: MPR<80 = undersupply, MPR >120 = oversupply Method of Assessment: pharmacy claims data	Total Healthcare Costs Inpatient Costs Outpatient Costs Pharmacy Costs	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.	Design: Retrospective cohort study Follow Up: 1 year Sample Size: 1705 (A:624, NA:1081)	Measure: MPR Classification: MPR≥80 = adherent, MPR <80 = nonadherent Method of Assessment: pharmacy claims data	Total Healthcare Costs Pharmacy Costs Medical Costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2005 Cost of Nonadherence: all cause: THC:$17807 ($21370.30), PC:$4915 ($5898.52) MC:$12892 ($15471.77) Disease state specific: THC:$2789 ($3347.10), PC:$489($586.85) MC:$2300 ($2760.25)	Quality: medium Classification: cost description
*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.	Design: Retrospective cohort study Follow Up: 1 year Sample Size: 10312 (96-100: 2453, 90-95: 1496, 85-89: 584, 80-84: 768, 70-79: 960, 60-69: 777, 40-59: 1687, <40:1587)	Measure: MPR Classification: <40%, 40-59%, 60-69%, 70-79%, 80-84%, 85-89%, 90-95%, 96-100% Method of Assessment: pharmacy claims data, census data	Total Healthcare Costs Pharmacy Costs Medical Costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 2010 Cost of Nonadherence: all cause: 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(<40):$1749.18 ($1907.97) Disease state specific: THC(96-100):$6536.05 ($7129.40), THC(90-95):$6493.80 ($7083.31), THC(85-89):$6459.40 ($7045.79),	Quality: medium Classification: cost description

					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(85-89):$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(40-59):$279.21 ($304.56), PC(<40):$133.92 ($146.08), 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(40-59):$3663.65 ($3996.24), MC(<40):$3499.95 ($3817.68)	
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	Total Costs Short term disability cost Workers compensation cost Paid time off cost	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

2007 US	outcomes and costs associated with adherence rates by antipsychotic medication class for Medicaid beneficiaries.	cohort study Follow Up: 2 years Sample Size: 10330 (>75%:6609, 50-74%:1276, 25-49%:1940, <25%:505)	prescription refill rate Classification: 75-100% = maximal adherence, 50-74.9% = moderate adherence, 25-49.9% = minimal adherence, <25% = negligible adherence Method of Assessment: pharmacy claims data		Classification: disease state specific Currency Year: USD, 2006 Cost of Nonadherence*: TC(75-100):$13564 ($15792.91), TC(50-74):$13772 ($16035.09), TC(25-49):$15792 ($18387.03), TC(<25):$16156 ($18810.84)	Classification: cost description
*Eaddy et al**[15]*** 2005 US	To evaluate the effect of partial compliance of patients with prescribed oral atypical and conventional antipsychotic agents and the corresponding impact on resource utilisation.	Design: Retrospective database analysis Follow Up: 1 year Sample Size: 7864 (<80%:2655, 80-125%:5065, >125%:144)	Measure: continuous multiple interval medications available Classification: <80% = partially compliant, 80-125% = compliant, >125% = overly compliant Method of Assessment: pharmacy claims data	Inpatient costs Outpatient costs Pharmacy costs Medical costs Physician office visit costs Other costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2002 Cost of Nonadherence*: IC:$3780 ($4906.39), OC:$504 ($654.19), PC:$1872 ($2429.83), MC:$6228 ($8083.86), POC:$1944 ($2523.29) OtC:$12 ($15.58)	Quality: medium Classification: cost description
*Gilmer et al**[16]*** 2004 US	To evaluate the relationship between adherence to	Design: Retrospective database analysis Follow Up: 1 year	Measure: cumulative possession ratio	Total costs Outpatient costs	Type of Costs: adjusted Classification: disease state specific Currency Year: USD, 1999	Quality: medium Classification: cost description

	treatment with antipsychotic medication and health expenditures. Secondary objective was to identify risk factors predictive of non-adherence.	Sample Size: 1619 (<49%:388, 50-79%:259, 80-100%:664, >110%:308)	Classification: <49% = nonadherent, 50-79% = partially adherent, 80-100% = adherent, >110% = excess medication fillers Method of Assessment: pharmacy claims data	Pharmacy costs Hospitalization costs	Cost of Nonadherence: TC:$8168 ($11261.74), OC:$3464 ($4776.04), PC:$1542 ($2126.05), HC:$3413 ($4705.72)	
*Hong et al**[17]*** 2011 UK	To investigate clinical and economic consequences of medication non-adherence in the treatment of bipolar disorder following a manic or mixed episode.	Design: Prospective observational study Follow Up: 21 months Sample Size: 1341(A:1024, NA:317)	Measure: assessed by treating psychiatrist Classification: adherent vs. nonadherent Method of Assessment: observational assessment	Total costs Inpatient costs Outpatient costs Pharmacy costs Hospitalization costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: GBP, 2008 Cost of Nonadherence*: all cause: PC:£55.43 ($94.47) Disease state specific: TC:£5846.29 ($9964.10) IC:£2740.57 ($4670.88), OC:£1082.86 ($1845.57), PC:£1630.29 ($2778.58), HC:£337.14 ($574.60)	Quality: medium Classification: cost description
*Jiang et al**[18]*** 2015 US	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	Design: Retrospective cohort study Follow Up: 2 years Sample Size: 32374 (A:11642, NA:20732)	Measure: PDC Classification: (PDC≥80% = adherent, PDC<80% = nonadherent) Method of Assessment: medical and	Total costs Pharmacy costs Medical services costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2011 Cost of Nonadherence: Disease state specific: TC:$14141 ($14517.37) PC:$3971 ($4076.69), MSC:$10170 ($10440.68)	Quality: low Classification: cost description

			pharmacy claims data			
*Joe et al**[19]*** 2016 South Korea	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 (A:2774, NA:2774, P:1956, NP:1956)	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 outcome description
*Knapp et al**[20]*** 2004 UK	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:	Total costs Inpatient costs External services 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

			survey			
*Offord et al**[21]*** 2013 US	To quantify early nonadherence to antipsychotic medications in patients with schizophrenia and its impact on short-term antipsychotic adherence, healthcare utilisation and costs.	Design: Retrospective cohort study Follow Up: 1 year Sample Size: 1462 (A:589, NA:873)	Measure: time to discontinuation Classification: adherent vs. nonadherent Method of Assessment: pharmacy claims data	Total costs Outpatient costs Pharmacy costs Hospitalization costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2008 Cost of Nonadherence: all cause: TC:$15400 ($17132.34) OC:$5773 ($6422.40), PC:$3777 ($4201.87), HC:$5850 ($6508.06) Disease state specific: TC:$5358 ($5960.72) OC:$858 ($954.52), PC:$1549 ($1723.25), HC:$2952 ($3284.07)	Quality: medium Classification: cost description
*Offord et al**[22]*** 2013 US	To examine the impact of medication adherence on healthcare utilisation among Medicare insured schizophrenia patients.	Design: Retrospective cohort study Follow Up: 1 year Sample Size: 354 (A:126, NA:228)	Measure: MPR Classification: MPR ≥ 70= high adherence, MPR < 70 = low adherence Method of Assessment: pharmacy claims data	Inpatient costs Pharmacy costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2008 Cost of Nonadherence: all cause: IC:$9053 ($10071.37), PC:$4267 ($4746.99), Disease state specific: IC:$2468 ($2745.62), PC:$1085 ($1207.05)	Quality: low Classification: cost description
*Robertson et al[**23**]* *2014* *US*	To examine the impact of the combination of treatment utilization and medication possession on arrest and incarceration outcomes and on costs.	Design: Retrospective cohort study Follow Up:90 days Sample Size:1376 (90/90:637, 60/90:240, 30/90:174, 0/90:316)	Measure: MPR Classification: MPR ≥80% = adherent Method of Assessment: Medicaid claims data	Total costs Inpatient costs Outpatient costs Emergency department costs Pharmacy	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD,2005 Cost of Nonadherence*: TC(90/90):$28068 ($33495.65), TC(60/90):$21720 ($25920.11), TC(30/90):$21084 ($25161.12), TC(0/90):$12516 ($14936.28),	Quality: medium Classification: cost description

				costs Target case management costs Psychiatric assessment costs Arrest costs Incarceration costs	IC(90/90):$12168 ($14520.99), IC(60/90):$10068 ($12014.90), IC(30/90):$11376 ($13575.84), IC(0/90):$5592 ($6673.35), OC(90/90):$6468 ($7718.75), OC(60/90):$4152 ($4954.89), OC(30/90):$2916 ($3479.88), OC(0/90):$2136 ($2549.05), EDC(90/90):$96 ($114.56), EDC(60/90):$108 ($128.88), EDC(30/90):$144 ($171.85), EDC(0/90):$84 ($100.24), PC(90/90):$5316 ($6343.98), PC(60/90):$3468 ($4138.63), PC(30/90):$2232 ($2663.61), PC(0/90):$984 ($1174.28), TCMC(90/90):$2100 ($2506.09), TCMC(60/90):$1404 ($1675.50), TCMC(30/90):$1596 ($1904.63), TCMC(0/90):$516 ($615.78), PAC(90/90):$240 ($286.41), PAC(60/90):$228 ($272.09), PAC(30/90):$204 ($243.45), PAC(0/90):$156 ($186.17), ArC(90/90):$780 ($930.83), ArC(60/90):$1032 ($1231.56), ArC(30/90):$1140 ($1360.45), ArC(0/90):$1200 ($1432.05), InC(90/90):$888 ($1059.72), InC(60/90):$1272 ($1517.97), InC(30/90):$1476 ($1761.42), InC(0/90):$1860 ($2219.68)	
*Robinson et al**[24]***	To determine if the	<u>Design:</u> Retrospective	<u>Measure:</u>	Total costs	<u>Type of Costs:</u> unadjusted	<u>Quality:</u> medium

2006 US	type of antidepressant drug is related to adherence and assess the 6 month health care costs among newly diagnosed patients.	claims analysis Follow Up: 6 months Sample Size: 60386 (A:11526, NA:8860)	Antidepressant medication management measures Classification: meeting less than <3 medication management measures = nonadherent Method of Assessment: pharmacy claims data, Medicaid data, observational assessment	Inpatient costs Outpatient costs ED visit costs Pharmacy costs Physician office visit costs	Classification: all cause and disease state specific Currency Year: USD, 2004 Cost of Nonadherence*: all cause: TC:$12658 ($15678.21) IC:$3006 ($3723.24), OC:$6118 ($7577.76), EDC:$334 ($413.69) PC:$3200 ($3963.52), POC:$178 ($220.47) Disease state specific: TC:$2028 ($2511.88) IC:$102 ($126.34), OC:$734 ($909.13), EDC:$18 ($22.29) PC:$1174 ($1454.12), POC:$120 ($148.63)	Classification: cost description
*Svarstad et al**[25]*** 2001 US	To examine the relationship of medication non-adherence to hospital use and costs among severely mentally ill clients.	Design: Retrospective database analysis Follow Up: 1 year Sample Size: 619 (A:413, NA:206)	Measure: quarter pharmacy claims Classification: one or more quarters without a claim = nonadherent Method of Assessment: pharmacy claims data, previous study data	Hospitalization costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 1990 Cost of Nonadherence: all cause: HC:$3992 ($6593.06) Disease state specific: Schizophrenia/schizoaffective disorder: HC:$3421 ($5650.01) Bipolar disorder: HC:$9701 ($16021.85), Other severe mental illness: HCD:$3024 ($4994.34)	Quality: medium Classification: cost description
*White et al**[26]*** 2003 US	To evaluate the economic impact of antidepressant	Design: Retrospective database analysis Follow Up: 6 months	Measure: MPR Classification: MPR≥70% =	Total costs Pharmacy costs	Type of Costs: adjusted Classification: disease state specific Currency Year: USD, 1999	Quality: medium Classification: cost description

	treatment adherence among patients treated for depression	Sample Size: 14190 (A:5638, NA:8552)	adherent, MPR<70% = nonadherent Method of Assessment: pharmacy claims data	Medical costs	Cost of Nonadherence: TC:$11815 ($16290.09) PC:$1123 ($1548.35), MC:$10692 ($14741.74)	
Diabetes						
*An et al**[27]*** 2014 Korea	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 3 year period.	Design: Prospective cohort study Follow Up: 3 years Sample Size: 608 (A:472, NA:136)	Measure: MPR Classification: MPR≥90% = adherent, MPR<90% = nonadherent Method of Assessment: pharmacy claims data	Total costs Outpatient costs Hospitalization costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2007 Cost of Nonadherence*: TC:$1657.11 ($1884.14) OC: $1413.99 ($1608.20), HC: $243.11 ($276.12)	Quality: medium Classification: cost description
Buysman et al[28] *2017* *US*	To examine the impact of real world adherence on glycaemic control in type 2 diabetes patients treated with canagliflozin.	Design: Retrospective database analysis Follow Up: 12 months Sample Size: 2261 (A:1215, NA:1046)	Measure: PDC Classification: PDC≥80% = highly adherent, PDC<80% = less than highly adherent Method of Assessment: healthcare claims data	Pharmacy costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 2014 Cost of Nonadherence: all cause: PC: $7225 ($7297.39) Disease state specific: PC: $4660 ($4706.69)	Quality: low Classification: cost description
Curtis et al[29] *2017* *US*	Examine the association between adherence to glucose lowering agents and	Design: Retrospective analysis Follow Up: 3 years Sample Size: 228074	Measure: PDC Classification: PDC≥80% = adherent,	Total costs Outpatient costs Pharmacy	Type of Costs: adjusted Classification: all cause Currency Year: USD, 2014 Cost of Nonadherence:	Quality: medium Classification: cost description

	patient outcomes in an adult type 2 diabetes population	(A:117864, NA:110210)	PDC<80% = nonadherent Method of Assessment: healthcare claims data	costs Acute care costs	TC:$38633 ($39020.09) OC: $16964 ($17134), PC: $9390 ($9484.08), ACC:$12153 ($12274.77)	
*Egede et al**[30]*** 2012 US	To examine the longitudinal effects of medication nonadherence on key costs and estimate potential savings from increased adherence using novel methodology that accounts for shared correlation among cost categories.	Design: Retrospective cohort study Follow Up: 5 years Sample Size: 740195 (A:427390, NA:312805)	Measure: MPR Classification: MPR≥80% = adherent, MPR<80% = nonadherent Method of Assessment: pharmacy claims data	Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2006 Cost of Nonadherence*: IC:$14515.24 ($17886.40) OC: $3599.27 ($4434.16), PC: $1073.12 ($1322.42)	Quality: high Classification: cost outcome description
Gentil et al**[31]** 2015 Canada	To examine healthcare costs associated with adherence to oral antihyperglycemic agents and the effects of depression and anxiety disorders on these in older adults with type 2 diabetes	Design: Retrospective, observational cohort analysis Follow Up: 1 year Sample Size: 301 (A:224, NA:77)	Measure: MPR Classification: MPR≥80% = adherent, MPR<80% = nonadherent Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs Physician office visit costs	Type of Costs: adjusted and unadjusted Classification: all cause and disease state specific Currency Year: CAD, 2010 Cost of Nonadherence: Adjusted all cause: TC:$11124 ($9818.67), IC:$7419 ($6548.43) OC: $2687 ($2371.70), PC: $504 ($444.86), POC:$513 ($452.80) Adjusted disease state specific: TC:$4477 ($3951.65), IC:$2836 ($2503.21) OC: $1518 ($1339.87),	Quality: medium Classification: cost description

					PC[###]: $-444 ($-391.90), POC:$568 ($517.24) Unadjusted all cause: TC:$14979 ($13221.30), IC:$6351 ($5605.75) OC: $4058 ($3581.82), PC: $3503 ($3091.94), POC:$1066 ($940.91) Unadjusted disease state specific: TC:$9008 ($7950.97), IC:$2854 ($2519.10) OC: $2654 ($2342.57), PC: $2498 ($2204.87), POC:$1002 ($884.42)	
*Hagen et al**[32]*** 2014 US	To evaluate the relationships between compliance with oral hypoglycemic agents and healthcare/ short term disability costs	Design: Retrospective, observational cohort analysis Follow Up: 1 year Sample Size: 4978 (A:2820, NA:2158)	Measure: PDC Classification: PDC≥80% = compliant, PDC<80% = noncompliant Method of Assessment: pharmacy claims data	Healthcare costs Pharmacy costs Medical costs Short term disability costs	Type of Costs: adjusted and unadjusted Classification: all cause and disease state specific Currency Year: USD, 2003 Cost of Nonadherence: Adjusted all cause: PC: $1668 ($2065.99), Adjusted disease state specific: HC:$7642 ($9465.39), PC:$614 ($760.50), MC:$5974 ($7399.40), STDC:$1840 ($2279.03) Unadjusted all cause: PC:$1727 ($2139.06) Unadjusted disease state specific: HC:$6919 ($8569.88), PC:$785 ($972.30), MC:$5192 ($6430.82), STDC:$1717 ($2126.68)	Quality: medium Classification: cost description
*Hansen et al**[33]*** 2010	To compare all cause total health care costs	Design: Retrospective, cohort study	Measure: MPR Classification:	Total Healthcare	Type of Costs: adjusted and unadjusted Classification: all cause and disease	Quality: medium Classification: cost

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.	Follow Up: 2 years Sample Size: 108592 (A:63830, NA:44762)	MPR≥80% = adherent, MPR<80% = nonadherent Method of Assessment: pharmacy claims data	costs Inpatient costs Outpatient costs Pharmacy costs	state specific Currency Year: USD, 2005 Cost of Nonadherence[#]: Adjusted all cause: THC:$13258 ($15911.01) Adjusted disease state specific: THC:$2284 ($2741.04) Unadjusted all cause: THC:$15448.50 ($18539.90), IC:$4242.33 ($5091.25), OC:$ 7377.83, PC:$3828 ($4594.01) Unadjusted disease state specific: THC:$3232.33 ($3879.15), IC:$873.50 ($1048.29), OC:$1545.67($1854.96), PC:$812.67 ($975.29)	description
*Hong et al**[34]*** 2011 South Korea	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)	Measure: MPR Classification: MPR≥80% = adherent, MPR<80% = nonadherent Method of Assessment: pharmacy claims data	Total costs Hospitalization costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: KRW, 2007 Cost of Nonadherence: TC:₩765453 ($1142.31), HC:₩397549 ($593.28)	Quality: medium Classification: cost description
*Jha et al**[35]*** 2012 US	How often do previously non-adherent patients become adherent and vice versa? Are changes in adherence associated with increased or	Design: Retrospective, observational claims analysis Follow Up: unclear Sample Size: 135639 (A:99976, NA:36553)	Measure: MPR Classification: MPR≥80% = adherent, MPR<80% = nonadherent Method of Assessment:	Total costs ED costs Hospitalization costs	Type of Costs: adjusted Classification: disease state specific Currency Year: USD, 2011 Cost of Nonadherence[***]: TC:$4680000000 ($5006563305.49), EDC:$735000000 ($786287185.80), HC:$3950000000 ($4225625012.11)	Quality: high Classification: cost outcome description

	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?		pharmacy claims data			
*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	Total costs Pharmacy costs Non-pharmacy costs	Type of Costs: adjusted and unadjusted Classification: disease state specific Currency Year: USD, 2000 Cost of Nonadherence: adjusted: TC(≥95):$4835 ($6518.17), TC(75-95):$5314 ($7163.92), TC(<75):$5706 ($7692.38), PC(≥95):$1429 ($1926.47), PC(75-95):$1157 ($1559.78), PC(<75):$762 ($1027.27), NPC(≥95):$3406 ($4591.70), NPC(75-95):$4157 ($5604.14), NPC(<75):$4944 ($6665.11) Unadjusted: TC(≥95):$4809 ($6483.12), TC(75-95):$5333 ($7189.53), TC(<75):$5605 ($7556.22),	Quality: low Classification: cost analysis

					PC(≥95):$1402 ($1890.07), PC(75-95):$1153 ($1554.38), PC(<75):$766 ($1032.66), NPC(≥95):$3407 ($4593.05), NPC(75-95):$4180 ($5635.15), NPC(<75):$4839 ($6523.56)	
*Wu et al**[37]*** 2009 US	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 and Medicare supplemental Method of Assessment: pharmacy claims data	Total healthcare costs Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2006 Cost of Nonadherence: adjusted all cause: THC(com):$32407 ($37732.29), THC(med):$24622 ($28668.02), IC(com):$ 12851($14692.74), IC(med):$ 6754 ($7863.85), OC(com):$11888 ($13841.50), OC(med):$10598 ($12339.52), PC(com):$7667 ($8926.88), PC(med):$7270 ($8464.65) Adjusted disease state specific: Diabetes: 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 Classification: cost description

					IC(com):$1739 ($2024.76), IC(med):$1048 ($1220.21), OC(com):$362 ($421.49), OC(med):$181 ($210.74), PC(com):$1464 ($1704.57) PC(med):$1155 ($1344.80)	
Osteoporosis						
*Briesacher et al**[38]*** 2007 US	To assess rates of osteoporotic fractures and health care utilisation as a function of bisphosphonate compliance in usual clinical practice.	Design: Retrospective, cohort study Follow Up: 3 years Sample Size: 17988 (not specified)	Measure: MPR Classification: 80-100% = adherent, 60-79% = moderate adherence, 40-59% = moderate adherence, 20-39% = nonadherent, 0-19% = nonadherent Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: adjusted and unadjusted Classification: disease state specific Currency Year: USD, 2004 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

					IC(60-79):-$384 (-$475.62), IC(40-59):-$597 (-$739.44), IC(20-39):-$93 (-$115.19), OC(80-100):-$774 (-$958.68), OC(60-79):-$193 (-$239.05), OC(40-59):-$145 (-$179.60), OC(20-39):$148 ($183.31), PC(80-100):$384 ($475.62), PC(60-79):$284 ($351.76), PC(40-59):$170 ($210.56), PC(20-39):$48 ($59.45)	
*Eisenberg et a**[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)	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		MC(≥80):$4295 ($5000.78), MC(50-80):$4697 ($5468.84), MC(<50):$5596 ($6515.56) Medicare: MC(≥80):$4590 ($5344.25), MC(50-80):$5536 ($6445.71), MC(<50):$5801 ($6754.25)	
*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)	Measure: PDC Classification: (≥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 Currency Year: USD, 2010 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

					IC(≥80):$366 ($399.23), IC(50-80):$830 ($905.35), IC(<50):$1325 ($1445.28), OC(≥80):$1048 ($1143.14), OC(50-80):$955 ($1041.70), OC(<50):$767 ($836.63), EDC(≥80):$6 ($6.54), EDC(50-80):$9 ($9.82), EDC(<50):$44 ($47.99), PC(≥80):$10810 ($11791.34), PC(50-80):$7420 ($8093.59), PC(<50):$2068 ($2255.73)	
*Huybrechts et al**[42]*** 2006 US	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)	Measure: MPR Classification: (≥80% = compliant, <50% = noncompliant) Method of Assessment: pharmacy claims data	Total costs Medical costs Institutional costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2000 Cost of Nonadherence: TC:$7200 ($9706.44), MC:$1476 ($1989.84), InstC:$5736 ($7732.80)	Quality: low Classification: cost description
*Kjellberge al**[43]*** 2016 Denmark	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)	Measure: MPR Classification: (≥70% = compliant, <70% = noncompliant) Method of Assessment: pharmacy claims data	Total costs Medical costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: Euro, 2011 Cost of Nonadherence: all cause: TC:€4933 ($6209.58), MC:€3471 ($4369.20), Disease state specific: TC:€754 ($949.12), MC:€426 ($536.24),	Quality: high Classification: cost outcome description
*Modi et al**[44]*** 2015	To evaluate compliance with	Design: Retrospective cohort study	Measure: MPR Classification:	Total costs Inpatient costs	Type of Costs: unadjusted Classification: all cause and disease	Quality: medium Classification: cost

US	osteoporosis treatments and determine fracture and healthcare burden associated with noncompliance	Follow Up: 1 year Sample Size: 27913 (A:23430, NA:34483)	(≥80% = compliant, <80% = noncompliant) Method of Assessment: healthcare claims data	Outpatient costs ED costs Pharmacy costs Medical costs Other costs	state specific Currency Year: USD, 2011 Cost of Nonadherence: all cause: 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) Disease state specific: TC:$630 ($669.42), IC:$443 ($470.72), OC:$158 ($167.89), EDC:$3 ($3.19), PC:$325 ($345.33), OtC:$26 ($27.63)	outcome description
*Olsen et al**[45]*** 2013 Denmark	To assess the association between refill compliance and all cause health care costs.	Design: Retrospective observational study Follow Up: 2 years Sample Size: 47176 (not specified)	Measure: MPR Classification: (≥80% = optimal compliance, >50<80% = suboptimal compliance, <50% = low compliance Method of Assessment: pharmacy claims data	Fracture costs	Type of Costs: unadjusted Classification: fracture site specific Currency Year: DKK, 2010 Cost of Nonadherence: Hip fracture: FC(50-80):kr817575.50 ($74531.41), FC(<50):kr4454954 ($549987.04) Spine fracture: FC(50-80):kr174700 ($21568.12), FC(<50):kr226472 ($27959.14) Humerus fracture: FC(50-80):kr117776.50 ($14540.12), FC(<50):kr795217.50 ($98173.70) Forearm fracture: FC(50-80):-kr463024 (-$57162.70), FC(<50):kr45072.50 ($8665.81)	Quality: medium Classification: cost analysis

					Other fracture: FC(50-80):-kr19261.50 (-$2377.93), FC(<50):kr684067.50 ($84451.66)	
*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	Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs Radiology costs	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	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):$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

					OC(≥80):$9312 ($10157.40), OC(50-80):$12816 ($13979.40), OC(<50):$13044 ($14228.16), PC(≥80):$18864 ($20576.52), PC(50-80):$13116 ($14306.64), PC(<50):$7452 ($8128.44) Unadjusted: THC(≥80):$37464 ($40865.04), THC(50-80):$35076 ($38260.20), THC(<50):$29484 ($32160.60), IC(≥80):$7092 ($7735.80), IC(50-80):$11100 ($12107.64), IC(<50):$10632 ($11597.16), OC(≥80):$9900 ($10798.68), OC(50-80):$11352 ($12382.56), OC(<50):$11988 ($13076.28), PC(≥80):$20484 ($22343.52), PC(50-80):$12624 ($13770), PC(<50):$6864 ($7487.16)	
*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 ($43404.36), OC(≥80):$12924 ($14097.24), OC(50-80):$14928 ($16283.16), OC(<50):$17568 ($19162.80),	Quality: medium Classification: cost description

					PC(≥80):$19392 ($21152.40), 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)	
Respiratory Disease						
Davis et al[49] 2017 US	To assess the association between adherence levels to different inhaled corticosteroid/long acting β_2-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) Method of Assessment: commercially insured healthcare claims data	Total costs Outpatient costs Pharmacy costs Hospitalization costs	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),	Quality: medium Classification: cost description

					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: TC(≥80):$8075.33 ($8156.24), TC(50-80):$7053 ($7123.67), TC(30-50):$6623 ($6689.36), TC(<30):$5644 ($5700.55), OC(≥80):$2194.33 ($2216.32), OC(50-80):$1947 ($1966.51), OC(30-50):$1997 ($2017.01), OC(<30):$2152 ($2173.56), PC(≥80):$4464 ($4508.73), PC(50-80):$3345 ($3378.52), PC(30-50):$2307 ($2330.12), PC(<30):$1569 ($1584.72), HC(≥80):$1074.67 ($1085.44), HC(50-80):$1155 ($1166.57), HC(30-50):$1619 ($1635.22), HC(<30):$1405 ($1419.08)	
*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	Design: Retrospective longitudinal cohort study Follow Up: 24 months Sample Size: 12907 (≥75: 2612, 50-75%: 3608, 25-50%: 5035, <25%: 1652)	Measure: MPR Classification: (≥75, 50-75%, 25-50%, <25%) Method of Assessment: pharmacy claims data	Total costs Outpatient costs ED costs Other costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2003 Cost of Nonadherence*: TC(≥75):$1564 ($1990.27), TC(50-75):$1128 ($1435.44), TC(25-50):$900 ($1145.30), TC(<25):$632 ($804.25), OC(≥75):$1272 ($1618.69),	Quality: medium Classification: cost description

	patients in typical US clinical practice				OC(50-75):$852 ($1084.21), OC(25-50):$600 ($763.53), OC(<25):$388 ($493.75), EDC(≥75):$32 ($40.72), EDC(50-75):$36 ($45.81), EDC(25-50):$60 ($76.35), EDC(<25):$48 ($61.08), OtC(≥75):$292 ($371.59), OtC(50-75):$276 ($351.22), OtC(25-50):$300 ($381.77), OtC(<25):$240 ($305.41)	
*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

			questionnaire		AbC(>2):$474.80 ($616.28), PrC(0):$577.20 ($749.20), PrC(1-2):$819.60 ($1063.83), PrC(>2):$598.30 ($776.59)	
*Miravitlles et al**[53]*** 2013 Spain	To analyse the economic impact of non-adherence to the global initiative for obstructive lung disease (GOLD) guidelines in patients with chronic obstructive pulmonary disease (COPD).	Design: multicentre, retrospective, observational study Follow Up: 18 months Sample Size: 1365 (A:246, NA:1119)	Measure: GOLD 2007 Guidelines Classification: (adherent, nonadherent) Method of Assessment: GOLD guidelines	ED costs Pharmacy costs Physician office visit costs Hospitalization costs Primary care costs Interdisciplinary visit costs Medical test costs Radiology costs Laboratory costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: EUR, 2009 Cost of Nonadherence: EDC:€40.83 ($57.91), PC:€771.50 ($1094.27), POC:€106.29 ($150.76), HC:€101.61 ($144.12) PCC:€123.84 ($175.65), IntC:€321.44 ($455.92), MTC:€36.66 ($51.99), RC:€24.24 ($34.38), LC:€17.35 ($24.61)	Quality: medium Classification: cost description
*Quittner et al**[54]*** 2014 US	To evaluate associations of adherence to pulmonary medications, age, healthcare use and cost among cystic fibrosis patients.	Design: retrospective, cohort study Follow Up: 2 years Sample Size: 3287 (≥80%: 663, 50-80%: 949, <50%: 1675)	Measure: MPR Classification: (≥80% = high adherence, 50-80% = moderate adherence, <50% = low adherence) Method of Assessment: pharmacy claims data	Total healthcare costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 2011 Cost of Nonadherence*: All cause: THC(≥80):$35749.50 ($38244.05), THC(50-80):$45031.50 ($48173.73), THC(<50):$50284.50 ($53793.28) Disease state specific: THC(≥80):$23764 ($25422.22),	Quality: medium Classification: cost description

					THC(50-80):$33132.50 ($35444.44), THC(<50):$33894 ($36259.07)	
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	Hospitalization costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2007 Cost of Nonadherence: HC:$37783 ($42854.12)	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: Sample Size: 41837 (A:28321, NA:13516)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs Medical costs	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	Outpatient costs ED costs Pharmacy costs Medical costs Hospitalization costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 2004 Cost of Nonadherence: All cause: OC:$6679 ($8272.62), EDC:$314 ($388.92), MC:$16129 ($19977.40),	Quality: medium Classification: cost outcome description

			Assessment: health claims data		HC:$6893 ($8537.68) Disease state specific: OC:$3931 ($4868.94), EDC:$91 ($112.71), PC:$18751 ($23225.01), MC:$10243 ($12686.99), HC:$4494 ($5566.27)	
*Mitra et al**[58]*** 2012 US	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.	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	Inpatient costs Outpatient costs ED costs Pharmacy costs Ancillary costs Non-pharmacy costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2010 Cost of Nonadherence: All cause: PC:$1541.60 ($1681.55) Disease state specific: IC:$28726.65 ($31334.47), OC:$1145.67 ($1249.67), EDC:$635.95 ($693.68), AC:$4923.29 ($5370.23), NPC:$14226.32 ($15517.79)	Quality: high Classification: cost description
*Wan et al**[59]*** 2014 US	To examine the effect of adherence versus non-adherence on healthcare costs in patients with inflammatory bowel disease.	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	Total costs Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2009 Cost of Nonadherence: All cause: TC:$47411 ($52341.27), THC:$32522 ($35903.96), IC:$17634 ($19467.76), OC:$10909 ($12043.43), EDC:$458 ($505.63), PC:$18410 ($20324.46) Disease state specific:	Quality: high Classification: cost description

					TC:$33652 ($37151.47), THC:$18764 ($20715.27), IC:$12564 ($13870.53), OC:$5890 ($6502.50), EDC:$48 ($52.99), PC:$15150 ($16725.45)	
Epilepsy						
*Davis et al**[60]*** 2008 US	To assess the extent of refill non-adherence with antiepileptic drugs (AEDs) and the potential association between AED non-adherence and healthcare costs in an adult managed care population.	Design: retrospective claims analysis Follow Up: 12 months Sample Size: 10892 (A:6644, NA:4248)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Inpatient costs ED costs Pharmacy costs Other pharmacy costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2003 Cost of Nonadherence[###]: TC:$1466 ($1865.56), IC:$1799 ($2289.32), EDC:$260 ($330.86), PC:-$71 (-$90.35), OtPC:-$358 (-$455.57)	Quality: medium Classification: cost description
*Ettinger et al**[61]*** 2009 US	To assess the extent to which elderly patients diagnosed with epilepsy are non-adherent to antiepileptic drugs (AEDs) and the potential association between AED non-adherence and seizure recurrence, resource utilisation and annual direct medical costs.	Design: retrospective claims analysis Follow Up: 12 months Sample Size: 1278 (A:758, NA:520)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Inpatient costs ED costs Pharmacy costs Physician Office visit costs Ancillary costs Other pharmacy costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2003 Cost of Nonadherence: TC:$17817 ($22673.06), IC:$2714 ($3453.71), EDC:$526 ($669.36), PC:$347 ($441.58), POC:$3063 ($3897.83), AC:$8344 ($10618.18), OtPC:$2822 ($3591.14)	Quality: medium Classification: cost outcome description
*Faught et al**[62]*** 2009 US	To study the impact of non-adherence to antiepileptic drugs	Design: retrospective observational open cohort design	Measure: MPR Classification: (≥80% = adherent,	Total costs Inpatient costs Outpatient	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2002	Quality: medium Classification: cost description

	(AEDs) on healthcare utilisation and direct medical costs in a Medicaid population.	Follow Up: 4.65 years Sample Size: 33658 (A:24907, NA:8751)	<80% = nonadherent) Method of Assessment: pharmacy claims data	costs ED costs Pharmacy costs Other pharmacy costs	Cost of Nonadherence*: TC:$14417.64 ($18713.91), IC:$6682.28 ($6873.51), OC:$2172.40 ($2819.75), EDC:$405.96 ($526.93), PC:$822.40 ($1067.46), OtPC:$4334.60 ($5626.26)	
HIV/AIDS						
*Barnett et al**[63]*** 2011 US	To characterise the cost of HIV care including combination antiretroviral treatment.	Design: retrospective observational cohort study Follow Up: 1 year Sample Size: 1896 (not specified)	Measure: antiretroviral taking behaviour Classification: (85% adherence with 3 antiretroviral therapy regimen = adherent, all other use = nonadherent) Method of Assessment: pharmacy claims data	Total costs	Type of Costs: unadjusted Classification: disease state specific; viral load count Currency Year: USD, 2006 Cost of Nonadherence**: High viral load: TC:$25824 ($30067.54) Low viral load: TC:$20509.67 ($23879.92)	Quality: medium Classification: cost description
*Cooke et al**[64]*** 2014 US	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.	Design: retrospective claims analysis Follow Up: 1 year Sample Size: 3528 (A:1737, NA:640)	Measure: MPR Classification: (≥90% = adherent, <90% = nonadherent) Method of Assessment: pharmacy claims data	Total healthcare costs Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2011 Cost of Nonadherence: THC:$18868 ($20184.58), IC:$2700 ($2888.40), OC:$915 ($978.85), PC:$15253 ($16317.33)	Quality: medium Classification: cost description

*Pruitt et al**[65]*** 2015 US	To examine Medicaid insured HIV positive and AIDS diagnosed patient groups separately to determine association of ART adherence to mean monthly total healthcare expenditures in the 24 month measurement period.	Design: retrospective cohort study Follow Up: 2 years Sample Size: 502 (A:56, NA:176)	Measure: MPR Classification: (≥90% = adherent, <90% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs Other pharmacy costs Behavioural health inpatient costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2009 Cost of Nonadherence*: HIV: TC:$15360 ($16957.32), IC:$3864 ($4265.76), OC:$3948 ($4358.52), PC:$4956 ($5471.40), OtPC:$1764 ($1947.48), BHIC:$840 ($927.36) AIDS: TC:$27648 ($30523.08), IC:$13008 ($14360.76), OC:$5880 ($6491.52), PC:$5640 ($6226.56), OtPC:$2580 ($2848.32), BHIC:$528 ($582.96)	Quality: medium Classification: cost description
Parkinson's Disease						
*Davis et al**[66]*** 2010 US	To assess the extent to which patients diagnosed with Parkinson's disease are non-adherent with antiparkinson therapy and the potential association between non-adherence and all cause medical costs.	Design: retrospective administrative claims study Follow Up: 12 months Sample Size: 3119 (A:1211, NA:1908)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Pharmacy costs Medical costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2001 Cost of Nonadherence: TC:$18511 ($24262.36), PC:$2684 ($3537.36), MC:$15827 ($20859.12)	Quality: medium Classification: cost outcome description
*Delea et al**[67]*** 2011 US	To assess the associations between adherence to	Design: retrospective historical cohort study Follow Up: 12 months	Measure: PDC Classification: (≥80% =	Total costs Inpatient costs Pharmacy	Type of Costs: adjusted and unadjusted Classification: all cause and disease state specific	Quality: high Classification: cost description

	levodopa/carbidopa/entacapone therapy and healthcare utilisation and costs.	Sample Size: 1215 (A:617, NA:598)	satisfactory, <80% = unsatisfactory) Method of Assessment: pharmacy claims data	costs Other costs	Currency Year: USD, 2005 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)	
*Wei et al**[68]*** 2014 US	To examine the associations of adherence to antiparkinson drugs with healthcare utilisation and economic outcomes.	Design: retrospective cross-sectional study Follow Up: 19 months Sample Size: 7583 (90-100%:3948, 80-89%:1456, ≤79%:2179)	Measure: MPR Classification: (>90<100% = high, >80<89% = moderate, ≤79% = low) Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2007 Cost of Nonadherence: TC(90-100):$36407 ($41293.43), TC(80-89):$43417 ($49244.29), TC(≤79):$45867 ($52023.13), IC(90-100):$15294 ($17346.71), IC(80-89):$21603 ($24502.49), IC(≤79):$24727 ($28045.78), OC(90-100):$10155 ($11517.97),	Quality: medium Classification: cost description

					OC(80-89):$11838 ($13426.86), OC(≤79):$12889 ($14618.92), PC(90-100):$10957 ($12427.61), PC(80-89):$9976 ($11314.95), PC(≤79):$8251 ($9358.42)	
Musculoskeletal						
*Ivanova et al**[69]*** 2012 US	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 Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs Medical costs Short term disability costs Absenteeism cost	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), AbC:$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% =	Medical costs	Type of Costs: adjusted and unadjusted Classification: disease state specific Currency Year: USD, 2007 Cost of Nonadherence:	Quality: medium Classification: cost description

	(inpatient), ER visits, MS relapses and medical costs.	(A:1459, NA:987)	nonadherent) Method of Assessment: pharmacy claims data		Adjusted: MC:$4348 ($5062.49) Unadjusted: MC:$5179 ($6030.04)	
*Zhao et al**[71]*** 2011 US	To examine predictors associated with duloxetine adherence and its association with healthcare costs among fibromyalgia patients.	Design: retrospective cohort analysis Follow Up: 12 months Sample Size: 5435 (A:1744, NA:3691)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total costs Inpatient costs Outpatient costs Pharmacy costs	Type of Costs: adjusted Classification: disease state specific Currency Year: USD, 2008 Cost of Nonadherence: commercial: TC:$20323 ($22609.12), IC:$4808 ($5348.85), OC:$9822 ($10926.87), PC:$5693 ($6333.40) Medicare: TC:$25282 ($28125.96), IC:$8604 ($9571.86), OC:$10068 ($11200.54), PC:$6611 ($7354.67)	Quality: medium Classification: cost analysis
Cancer						
*Darkow et al**[72]*** 2007 US	Estimate the association between treatment interruptions and non-adherence with imatinib and healthcare costs for US managed care patients.	Design: retrospective observational cohort analysis Follow Up: 12 months Sample Size: 267 (≥95%:120, 90-95%:25, 50-90%:69, <50%:53)	Measure: MPR Classification: (≥95% = very high, >90<95% = high, >50<90% = intermediate, <50% = low) Method of Assessment: pharmacy claims data	Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs Medical costs Other pharmacy costs Other costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2004 Cost of Nonadherence: THC(≥95):$42250 ($52330.90), THC(90-95):$39236 ($48597.76), THC(50-90):$54770 ($67838.19), THC(<50):$131357 ($162698.93), IC(≥95):$1156 ($1431.82), IC(90-95):$1362 ($1686.97), IC(50-90):$19096 ($23652.33), IC(<50):$81572 ($101035.18), OC(≥95):$9299 ($11517.75), OC(90-95):$11148 ($13807.93),	Quality: high Classification: cost description

					OC(50-90):$14631 ($18121.97), OC(<50):$33956 ($42057.94), EDC(≥95):$36 ($44.59), EDC(90-95):$568 ($703.53), EDC(50-90):$104 ($128.81), EDC(<50):$183 ($226.66), PC(≥95):$29056 ($35988.80), PC(90-95):$23693 ($29346.18), PC(50-90):$18330 ($22703.56), PC(<50):$8733 ($10816.70), MC(≥95):$10731 ($13291.43), MC(90-95):$13452 ($16661.66), MC(50-90):$34202 ($42362.64), MC(<50):$116892 ($144782.57),OtPC(≥95):$2462 ($3049.44), OtPC(90-95):$2091 ($2589.92), OtPC(50-90):$2238 ($2771.99), OtPC(<50):$5732 ($7099.66), OtC(≥95):$241 ($298.50), OtC(90-95):$374 ($463.24), OtC(50-90):$371 ($459.52), OtC(<50):$1181 ($1462.79)	
*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 Inpatient costs Outpatient costs ED costs Pharmacy costs Other pharmacy costs	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

Addiction						
*Leider et al**[74]*** 2011 US	To assess the economic burden of chronic opioid users and to determine whether opioid regimen non-adherence contributes to increased healthcare costs.	Design: retrospective claims based analysis Follow Up: 12 months Sample Size: 2100 (A:442, NA:1658)	Measure: urine testing Classification: (positive test = nonadherent, negative test = adherent) Method of Assessment: health claims data	Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs Medical costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2008 Cost of Nonadherence: THC:$26433 ($29406.43), IC:$6361 ($7076.55), OC:$9734 ($10828.97), EDC:$421 ($468.36), PC:$7960 ($8855.42), MC:$1957 ($2177.14)	Quality: medium Classification: cost analysis
Ruetsch et al[75] 2017 US	To examine patient characteristics and outcomes associated with nonadherence to buprenorphine and to identify specific patterns of nonadherent behaviour.	Design: cross sectional, retrospective analysis health claims data Follow Up: 12 months Sample Size: 477 (A:172, NA:305)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: health claims data	Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs Physician office visit costs Medical costs	Type of Costs: unadjusted Classification: disease state specific Currency Year: USD, 2013 Cost of Nonadherence: 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)	Quality: medium Classification: cost description
*Tkacz et al**[76]*** 2014 US	To estimate the healthcare service utilisation and costs associated with buprenorphine medication assisted therapy adherence among a sample of opioid dependent	Design: retrospective cohort analysis Follow Up: 12 months Sample Size: 455 (A:146, NA:309)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment: pharmacy claims data	Total healthcare costs Inpatient costs Outpatient costs ED costs Pharmacy costs	Type of Costs: adjusted and unadjusted Classification: disease state specific Currency Year: USD, 2010 Cost of Nonadherence: Adjusted: THC:$49051 ($53503.88), IC:$26470 ($28872.96), OC:$14570 ($15892.67), EDC:$4439 ($4841.98),	Quality: medium Classification: cost description

	members.				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)	
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 Inpatient costs Outpatient costs ED costs Pharmacy costs Other pharmacy costs	Type of Costs: unadjusted Classification: all cause and disease state specific Currency Year: USD, 2010 Cost of Nonadherence: All cause: PC:$5556 ($6060.38) Disease state specific: TC:$126996 ($138524.78), IC:$14844 ($16191.55), OC:$101854 ($111100.37), EDC:$734 ($800.63), PC:$3244 ($3538.49), OtPC:$9564 ($10432.23)	Quality: medium Classification: cost description
Blood						
*Candrilli et al**[78]*** 2011 US	To investigate the relationships among hydroxyurea adherence, healthcare utilisation and healthcare costs.	Design: retrospective longitudinal study Follow Up: 12 months Sample Size: 312 (A:110, NA:202)	Measure: MPR Classification: (≥80% = adherent, <80% = nonadherent) Method of Assessment:	Total costs Inpatient costs ED costs Pharmacy costs Physician office visit	Type of Costs: adjusted Classification: all cause and disease state specific Currency Year: USD, 2008 Cost of Nonadherence: All cause: TC:$ 20436 ($22734.83),	Quality: medium Classification: cost description

			pharmacy claims data	costs Ancillary costs	IC:$9780 ($10880.15), EDC:$837 ($931.15), PC:$2579 ($2869.11), POC:$3483 ($3874.80), AC:$3911 ($4350.95) Disease state specific: TC:$12097 ($13457.78), IC:$7315 ($8137.86), EDC:$552 ($614.09), PC:$158 ($175.77), POC:$1865 ($2074.79), AC:$2466 ($2743.40)	
All						
*Alvarez Payero et al**[79]*** 2014 Spain	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[####]: All cause: HC:€6275.80 ($8893.94)	Quality: low Classification: cost outcome description

A: adherent, NA: nonadherent, MA: moderate adherence, LA: low adherence, NC: noncompliance, NP: nonpersistent, P: persistent, T: turbulent, NE: no exposure, CHF: chronic heart failure, THC: total healthcare costs, TC: total costs, IC: inpatient costs, OC: outpatient costs, EDC: emergency department visit costs, PC: pharmacy costs, MC: medical costs, HC: hospitalization costs, POC: physician office visit costs, NPC: non-pharmacy costs, AC: ancillary costs, OtPC: other pharmacy costs, PAC: psychiatric assessment costs, TCMC: targeted case management costs, ArC: arrest costs, InC: incarceration costs, RC: radiology costs, SC: services costs, InstC: institutional costs, ESC: external services costs, MSC: medical services costs, PCC: primary care costs, MTC: medical test costs, FC: fracture costs, LC: laboratory costs, IntC: interdisciplinary costs, BHIC: behavioural health inpatient costs, STDC: short term disability costs, WCC: workers compensation costs, PTOC: paid time off costs, TPC: total productivity costs, AbC: absenteeism costs, PrC: presenteeism costs, ACC: acute care

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

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