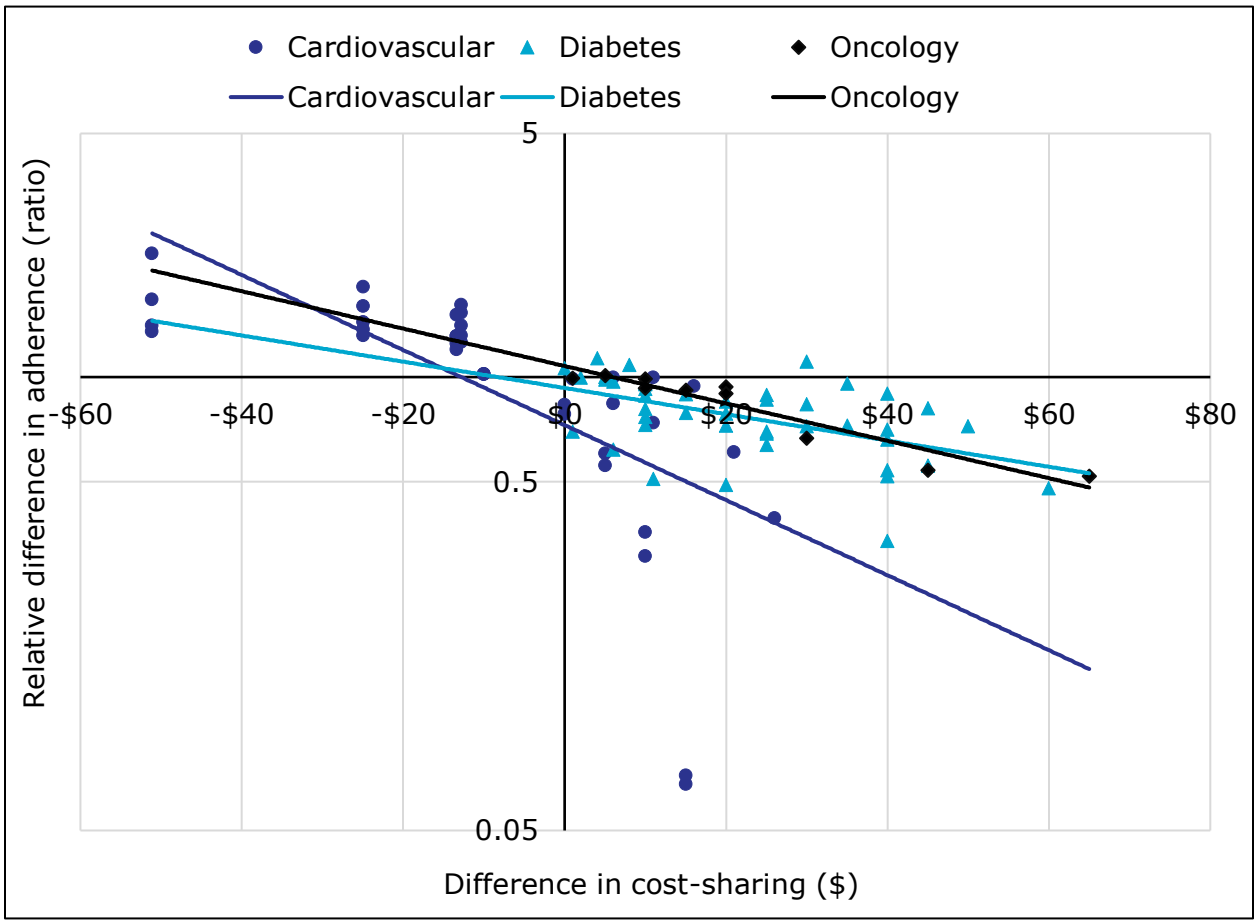
SUPPLEMENTARY MATERIALS

Cost-sharing and adherence, clinical outcomes, health care utilization, and costs: A systematic literature review

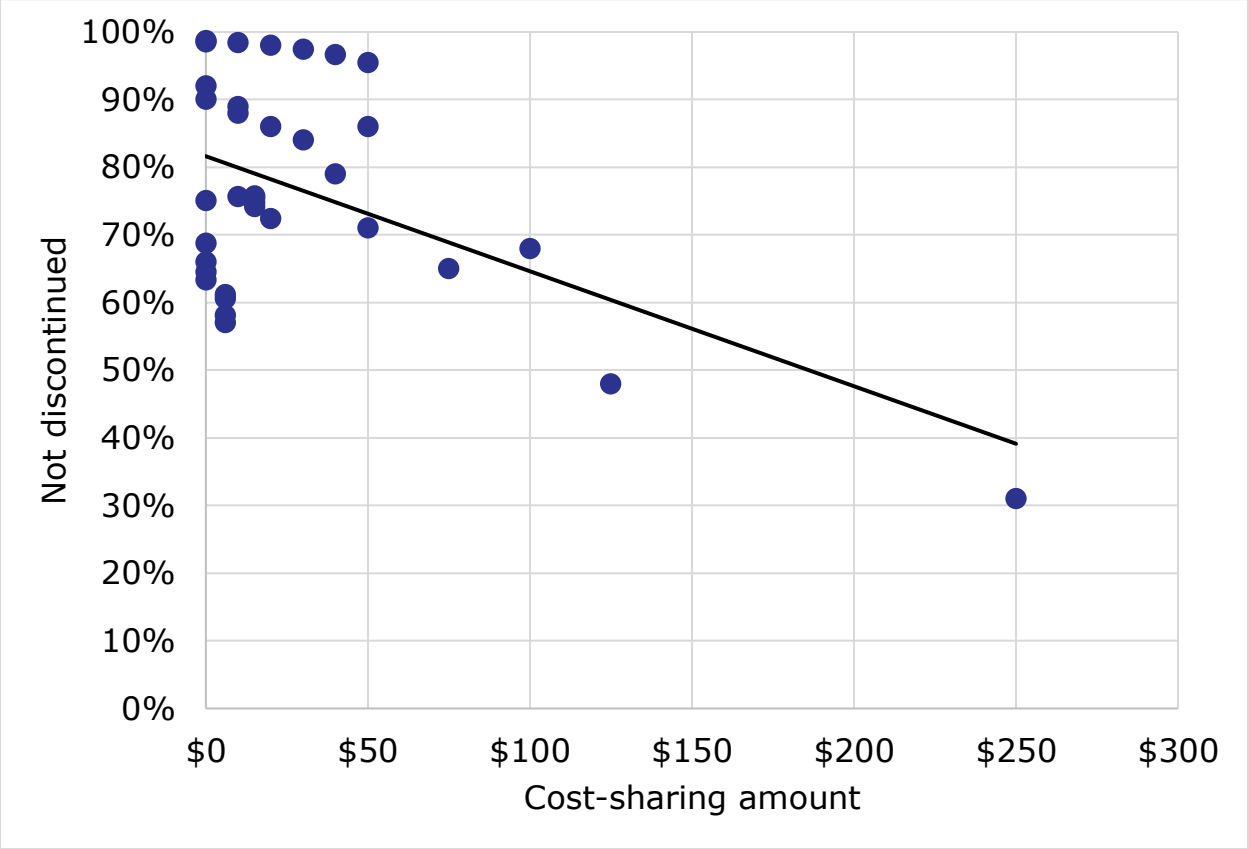
Nicole Fusco, ScD; Brian Sils, MMP; Jennifer S Graff, PharmD; Kristin Kistler, PhD; Kimberly Ruiz, EdM

Supplemental Figure 1. Relative Change in Adherence by Change in Cost-Sharing by Disease



Caption: When the cost-sharing amount was reported as a range, the change in cost-sharing was determined by calculating the difference in the minimums of the 2 categories. For example, when comparing $6–$15 with $0–$5, the change in cost-sharing would be $6. Similar trends were identified when the change in cost-sharing was calculated using the difference in the maximums of the 2 categories. The relative change in adherence is the odds ratio, relative risk, or hazard ratio reported in the original study. Adjusted estimates were used when they were reported in the original study. If the study reported nonadherence, the inverse of the ratio is plotted here. The observations on this graph are not all independent; several studies provided multiple data points (e.g., compared several different levels of cost-sharing to a single reference category).

Supplemental Figure 2. Prescription Discontinuation by Cost-Sharing



Caption: When cost-sharing was reported as a range, the minimum cost-sharing value was used for this graph. Similar trends were identified when cost-sharing was plotted using the maximum of the cost range. The observations on this graph are not all independent; several studies provided multiple data points (e.g., compared discontinuation for several different levels of cost-sharing). “Discontinuation” includes both patients who began a treatment but stopped picking up prescriptions and patients who were prescribed a medication but never initiated it.

Supplemental Table 1. Search Strategy

Database	Embase and MEDLINE (via Embase.com)	
Date	May 13, 2020 and (updated) August 18, 2020 [a]	
Search	Query	Number of records found
#1 (cost-sharing)	'capitation fee'/exp OR 'co-pay*':ti,ab OR 'copay*':ti,ab OR 'cost-shar*':ti,ab OR 'cost shar*':ti,ab OR 'coinsur*':ti,ab OR 'co-insur*':ti,ab OR 'out-of-pocket':ti,ab OR 'out of pocket':ab,ti OR oop:ab,ti OR 'patient payment*':ab,ti OR 'insurance coverage':ab,ti OR ‘deductible*’:ab,ti	27, 562
#2 (adherence/persistence, discontinuation/ abandonment)	'patient compliance'/exp OR 'patient compliance' OR 'medication compliance'/exp OR 'medication compliance' OR 'treatment refusal'/exp OR 'treatment refusal' OR 'adherence'/exp OR 'adherence' OR 'persistence'/exp OR 'persistence' OR ((patient NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence)):ti,ab) OR ((treatment NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence OR persistence OR abandonment)):ti,ab) OR ((therap* NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence OR persistence OR abandonment)):ti,ab) OR ((regimen NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence OR persistence OR abandonment)):ti,ab) OR ((medication NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence OR persistence	452,981

Database	Embase and MEDLINE (via Embase.com)	
Date	**May 13, 2020 and (updated) August 18, 2020** [a]	
Search	**Query**	**Number of records found**
	OR abandonment)):ti,ab) OR ((drug NEAR/2 (compliance OR adherence OR noncompliance OR nonadherence OR persistence OR abandonment)):ti,ab)	
#3 (clinical outcome)	((clinical NEAR/5 burden):ab,ti) OR 'clinical outcome*':ab,ti OR 'short term':ab,ti OR 'long term':ab,ti	1,507,770
#4 (HRU and costs)	'resource use':ti,ab OR 'resource utilization':ti,ab OR 'resource utilisation':ti,ab OR 'healthcare use':ti,ab OR 'healthcare utilization':ti,ab OR 'healthcare utilisation':ti,ab OR 'healthcare use':ti,ab OR 'healthcare utilization':ti,ab OR 'healthcare utilisation':ti,ab OR 'resource consumption':ti,ab OR 'healthcare consumption':ti,ab OR 'healthcare consumption':ti,ab OR cost:ti,ab OR costs:ti,ab OR costing:ti,ab OR fee:ti,ab OR fees:ti,ab OR budget:ti,ab OR budgets:ti,ab OR budgeting:ti,ab OR expenditure:ti,ab OR expenditures:ti,ab OR expense:ti,ab OR expenses:ti,ab OR spending:ti,ab OR spendings:ti,ab OR economic:ti,ab OR economics:ti,ab OR economical:ti,ab OR pharmacoeconomic:ti,ab OR pharmacoeconomics:ti,ab OR pharmacoeconomical:ti,ab	1,107,751
#5	#2 OR #3 OR #4	2,897,996
#6	#1 AND #5	17,308

Database	Embase and MEDLINE (via Embase.com)	
Date	**May 13, 2020 and (updated) August 18, 2020** [a]	
Search	**Query**	**Number of records found**
#7 (real-world studies)[a]	'longitudinal study'/exp OR 'retrospective study'/exp OR ('prospective study'/exp NOT 'randomized controlled trial'/exp) OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR ((epidemiolog* NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR ((observational NEAR/1 (study OR studies)):ab,ti) OR 'real-world':ab,ti OR database:ab,ti OR registy:ab,ti OR registries:ab,ti OR ((chart NEAR/1 (review OR reviews)):ab,ti) OR 'real world evidence'/exp OR 'real world data'/exp OR 'real world':ab,ti	2,680,318
#8	#6 AND #7	3,703
#9	#8 NOT ([review]/lim NOT (systematic OR (meta AND analy*)))	3,640
#10	#9 AND [humans]/lim	3,457
#11	#10 AND [2010-2020]/py	3,022
#12	#11 NOT 'conference abstract'/it	**1,584**

[a] A protocol amendment was made to update the search strategy to include randomized controlled trials; the following string was added to search #7: 'randomized controlled trial'/exp

OR 'randomized controlled trial' OR 'randomized controlled trial':ab,ti OR 'clinical trial' OR 'randomized trial'

Supplemental Table 2. Study Result Categorization

	Increased Cost-Sharing = Worse Outcome		Increased Cost-Sharing = No Difference in Outcome		Increased Cost-Sharing = Better Outcome	
	Original Study Reported Effect of Increased Cost-Sharing	**Original Study Reported Effect of Decreased Cost-Sharing**	**Original Study Reported Effect of Increased Cost-Sharing**	**Original Study Reported Effect of Decreased Cost-Sharing**	**Original Study Reported Effect of Increased Cost-Sharing**	**Original Study Reported Effect of Decreased Cost-Sharing**
Adherence						
Adherence	↓ Significantly lower adherence	↑ Significantly higher adherence	No statistically significant difference	No statistically significant difference	↑ Significantly higher adherence	↓ Significantly lower adherence
Persistence	↓ Significantly lower persistence	↑ Significantly higher persistence	No statistically significant difference	No statistically significant difference	↑ Significantly higher persistence	↓ Significantly lower persistence
Discontinuation	↑ Significantl	↓ Significantl	No statistica	No statistica	↓ Significantl	↑ Significantl

	y higher discontinuation	y lower discontinuation	lly significant difference	lly significant difference	y lower discontinuation	y higher discontinuation
Clinical Outcomes						
Clinical outcomes	Patients had significantly worse clinical outcomes	Patients had significantly better clinical outcomes	No statistically significant difference	No statistically significant difference	Patients had significantly better clinical outcomes	Patients had significantly worse clinical outcomes

Some studies reported both significant and non-significant results within an outcome category. If at least one result within a category was significant, the study was classified as significant. For adherence, persistence, and discontinuation outcomes, where this issue was the most common, these were consistently in the form of assessing multiple levels of cost-sharing where higher levels of cost-sharing reached significance and lower levels did not; these were categorized as significant associations. In figures that display specific results, significant and non-significant results are stratified.

Supplemental Table 3. Characteristics of the n=79 Included Studies

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
10	Adams 2013[21]	RC	KPNC	Adults who were new users of antihypertensive therapy	2008	Adherence	44,167	<50: 41% 50-64: 43% 65-74: 11% ≥75: 5%	51%
161	Bibeau 2016[22]	RC	IMS/Amundsen database	Patients with T2D aged 18-85 who initiated ≥1 branded antihyperglycemic products within selected Uniform System of Classification categories	2011-2014	Adherence	15,416	Mean range: 47 to 62 years across the 4 strata	NR
257	Cheng 2012[23]	RC	MEPS	Patients ≥65 years with ≥1 diagnosis for arthritis or	2005-2008	Adherence Costs	2,484	76	2005: 4%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				another rheumatic condition who had completed all 5 rounds of the Medical expenditure Panel Survey over 2.5 years					2008: 35%
265	Chin 2019[24]	RC	Clinformatics Data Mart Database (OptumInsight)	Female patients who lived in states that enacted oral parity legislation between 2008 and 2013 and who initiated oral endocrine therapy for breast cancer with an index claim 12 months prior to the year the law was enacted	2007-2014	Adherence	6,900	18-44: 13% 45-54: ~43% 55-59: ~23% 60- 64: ~21%	0%
281	Clark 2014[25]	RC	A major employer's employee	Employees, dependents, and retired plan participants who had	2008-2011	Adherence Costs	4,596	~56	50%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			benefits program	coronary artery disease, hyperlipidemia, and/or diabetes participating in disease management and wellness programs addressing diabetes, cardiac conditions, weight management, stress management, exercise, and nutrition (and a matched non-participating control group)					
293	Conwell 2011[26]	RC	Medco Health Solutions Medicare beneficiaries database	Women ≥65 with 2 teriparatide fills (and match controls: 2 fills for other osteoporosis medication, or drugs to treat other chronic conditions)	2007	Adherence	39,599	Teriparatide users: 65-<70: 14% 70-<75: 21% 75-	0%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
								<80: 25% ≥80: 40%	
303	Coy 2019[27]	RC	One national chain pharmacy database	≥18 with ≥60-day supply of tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) in 2015 and antiretroviral monotherapy with 2 years of viable data	2015 to 2017	Adherence	7,148	18-24: 11% 25-29: 22% 30-39: 35% 40-49: 20% ≥50: 12%	97%
319	Darkow 2012[28]	RC	Administrative health insurance claims	Aged ≥18 yrs with a diagnosis of chronic	1997-2009	Adherence	995	62	54%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			database covering 45 large employers	myeloid leukemia during 1997 to 2009					
324	Daubresse 2017[29]	RC	IMS Health LRx LifeLink database	Incident statin users who initiated branded atorvastatin or rosuvastatin between June 2006 and February 2013	2006-2013	Adherence, Costs	1.1 mil	~50	~45
327	Davis 2017[30]	RC	Walgreens Enterprise Data	Patients on new statin therapy during the first 3 months of 2012	2012	Adherence	326,171	58-60 depending on strata	41%-53% depending on strata
367	Doshi 2018[31]	RC	Symphony Health Solutions'	Patients with a new, adjudicated pharmacy claim for an oral anticancer agent with prescription	2014-2015	Adherence	38,111	68	58%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			Integrated DataVerse	drug coverage through a Medicare Part D or a commercial insurance plan					
400	Elliott 2013[32]	PC	Christiana Care Health System; the largest healthcare provider and the largest private employer in Delaware	Employees and dependents with diabetes	2009-2010	All 3 Clinical HRU Costs	188	48	36%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
407	Engel-Nitz 2012[33]	RC	OptumInsight	Adults with lung cancer and erlotinib prescriptions filled from November 1, 2004, through December 31, 2008	2004-2009	Adherence	1,460	~60	NR
427	Farias 2017[34]	RC	National Cancer Institute's SEER-Medicare linked database	Women ≥65 with stage I to III hormone receptor-positive breast cancer enrolled in Medicare for at least 12 months before and after they filled their first endocrine therapy prescription	2007-2009	Adherence	8,688	Median ~75	0
429	Farias 2018[35]	RC	Truven Health Analytics MarketScan database	Women <64 with at least 1 prescription claim for aromatase inhibitors or tamoxifen, who were diagnosed and surgically	2007-2011	Adherence	6,863	18-39: 8% 40-49: 33% 50-59:	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				treated for breast cancer within 12 months before the index claim				41% 60-64: 17%	
438	Fendrick 2019[36]	RC	IBM MarketScan database	Patients with T2D	2013-2014	Adherence	2,980	53	65%
457	Fowler 2013[37]	RC	A large health insurer in Pennsylvania	Community-dwelling Medicare beneficiaries ≥65 and continuously enrolled from 2004 to 2007 who filled at least 1 prescription for any drug in 1 of several thousand pharmacies in the insurer's network, where patients received a 15% discount	2004-2007	Adherence	35,102	65 to 74: 47%-61% 75 to 84: 34%-44% ≥85 years: 5%-10% Depending on strata	37%-47% depending on strata

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
463	Franklin 2018[38]	RC	A linked database of electronic health records	Patients ≥65 with Medicare fee-for service and part D receiving a new prescription or an oral antidiabetic, antihypertensive, statin, asthma/COPD maintenance medication or anti-osteoporosis medication	2007 to 2014	Adherence	32,586	75	37%
498	Gibson 2012[39]	RC	Thomson Reuters MarketScan CCAE Database	18-64 yrs of age at the time of the first antidepressant prescription claim and had at least 2 medical claims with a depression diagnosis	2005-2008	HRU	48,807	38-42 depending on strata	32%-46% depending on strata
499	Gibson 2010a[40]	RC	MarketScan Commercial Claims	Adults with bipolar disorder or schizophrenia during 2003-2006, with ≥1 prescription for one of five	2003-2006	Adherence	7,910	43	38%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			and Encounters Database	approved SGA medications (aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone)					
501	Gibson 2010b[41]	RC	Thomson Reuters MarketScan Database	Adults with diabetes who used OAD (sulfonylureas, meglitinides, biguanides, thiazolidinediones, or alpha-glucosidase inhibitors)	2003-2006	Adherence	96,734	52	54%
508	Goedken 2010[42]	RC	Web based surveys by Harris Interactive	Adults aged ≥65 yrs and older, US residents, and Medicare beneficiaries	2005-2007	HRU (see report footnote)	2005 = 1,220 2007 = 1,024	72	42%-46%
520	Gor 2020[43]	RC	Truven MarketScan administrat	Patients >30 years with T2D and non-dialysis chronic kidney disease who	2009 to 2015	Adherence	9,019	~57	57%-61%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			ive claims database	initiated therapy with either DPP-4 or pioglitazone					
569	Henk 2018[44]	RC	Optum's proprietary research database of medical and pharmacy claims	Adults with T2DM who filled a prescription for a specified novel T2DM medication	2010-2012	Adherence and HRU, Costs	36,475	54	55%
574	Hershman 2015[45]	RC	OptumInsight insurance claims database	Women aged ≥50 yrs who had a diagnosis of non-metastatic invasive breast cancer who had a prescription claim for hormonal therapy (AIs or tamoxifen)	2007-2011	Adherence	10,302	50-55: 29% 56-65: 51% 66-75: 14% ≥75: 7%	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
582	Hopson 2016[46]	RC	The Humana Research Database	Patients aged 18-89 yrs continuously enrolled in the Medicare Advantage and Prescription Drug plan with a primary diagnosis of rheumatoid arthritis	2007-2012	Adherence	864	64	23%
639	Johnson 2011[47]	RC	Pharmacy claims database for the Arkansas State Employee Benefits Division	Patients enrolled in a large state employee health plan with stable enrollment who were prescribed proton pump inhibitors	2004 to 2009	Adherence and HRU Costs (see footnote)	EBD = Mean 127,500 enrolled per month Control = 984,731	NR	NR
640	Johnston 2012[48]	RC	Thomson Reuters MarketSca	Patients ≥18 and initiated CAR T had no ARV claims in the 6 months prior to the	2002-2008	Adherence	3,731	41	83%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			n Commercial Database	CAR T initiation date, and had at least 1 medical claim for HIV infection at some point within the period extending from up to 12 months before to 12 months after CAR T initiation					
667	Karaca-Mandic 2012[49]	RC	Benefits consulting firm (unspecified)	<18 years with asthma	1997-2008	Adherence and HRU, Costs	8,834	7	60%
670	Karter 2018[50]	RC	KPNC Diabetes Registry	Patients with diabetes and a glucose-, lipid- or blood pressure–lowering therapy	2006-2012	Adherence	223,730	58	53%
708	Kim 2018[51]	RC	Blue Cross Blue	Women aged 18-64 years with incident early-stage	2008-2013	Adherence	627	<40: 5% 40-44:	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			Shield insurance database	breast cancer, and lumpectomy followed by radiotherapy, partial mastectomy or mastectomy				9% 45-49: 19% 50-54: 25% 55-59: 33% 60-64: 10%	
715	Kim 2011a[52]	RC	Large retail employer database	Members of a value-based disease management program with diabetes, coronary artery disease, heart failure or asthma who were over 19; compared with matched control group with the same characteristics who were	2008	Adherence and HRU, Costs	2,552	<24: 1% 25-49: 34% 50-64: 62% ≥65: 3%	56%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				contacted about the disease management program but did not enroll					
716	Kim 2011b[53]	RC	Scott & White Health Plan pharmacy and medical claims database	Adults who used anti-inflammatory, cancer, immunosuppressant, and MS specialty medications for at least 2 years	NR	Adherence	558	49 (intervention) 55 (control)	28%
779	Law 2016[54]	RC	MarketScan Commercial Claims and	Women aged 15-44 years with any contraceptive usage and pharmacy and medical coverage in years 2011, 2012, and 2013	2011-2013	HRU	2011 = 9,320,237 2012 = 9,599,891 2013 = 8,348,898	27	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			Encounters Database						
783	Lee 2016[55]	RC	One large specialty pharmacy in the US	Patients with a diagnosis of multiple myeloma with pharmacy claims for thalidomide, lenalidomide, or pomalidomide	2011-2013	Adherence	6,731	72	NR
805	Lewey 2018[56]	RC	Aetna (insurer)	Commercially insured individuals aged >18 years with medical and prescription drug insurance benefits who switched from a typical health insurance plan to an HDHP and filled ≥1 prescription for a medication to treat hypertension, high cholesterol, or diabetes	2009-2014	Adherence	HDHP cohort = 14,866 Controls = 878,414 pool used to match 1:1 to HDHP cohort	53	>50%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				mellitus in the 15-month period before their HDHP switch date					
806	Lewey 2015[57]	RC	A self-insured employer and a control group from Horizon Blue Cross Blue Shield of New Jersey	Patients with diabetes or vascular disease who filled a prescription between Jan 1, 2006 and Dec 31, 2007 plus controls	2006-2007	Adherence	39,281	Mean 53-59	56% to 67%
869	MacEwan 2017[58]	RC	CMS Medicare Research	Medicare beneficiaries ≥65 with ≥1 claim for T2D and	2006-2009	Adherence	12,305	74	36%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			Identifiable Files	at least 1 claim for an antidiabetic medication					
890	Marcus 2018[59]	RC	KPNC	Patients ≥18 with confirmed hepatitis C	2014 to 2016	HRU	14,790	Median 60	61%
891	Marcus 2016[60]	RC	KPNC	Patients initiating tenofovir/emtricitabine PrEP	2012 to 2015	Adherence and Clinical	972	38	98
895	Marshall 2018[61]	RC	KPNC	Female patients aged 19-29 years with prescription drug coverage and a new prescription dispensed for a pharmacy-dispensed contraceptive method, the oral contraceptive pill, contraceptive patch, or contraceptive ring	2011-2014	Adherence	39,142	22	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
915	McCellan 2019[62]	RC	IBM MarketScan database	Enrollees aged 12-64 years with prescription drug coverage with no evidence of cancer or palliative care, patients who filled a buprenorphine/naloxone outpatient prescription, either as a sublingual tablet or sublingual or buccal film	2011-2015	Adherence	25,901	12-17: 1% 18-24: 31% 24-44: 44% 45-64: 24%	64.80%
991	Neugut 2011[63]	RC	Medco Health Solutions pharmacy and medical claims database	Female patients aged ≥50 with early-stage breast cancer with a surgical resection (lumpectomy or mastectomy) within 12 months of the initiation of AI	2007-2008	Adherence	22,160	50-54: 8% 55-59: 15% 60-62:13% 63-69: 22%	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
								70-74:15% 75-79:14% 80-84: 9% ≥85: 4%	
1046	Pace 2016[64]	RC	Truven Health MarketScan claims data	Women 18-45 with prescription drug or medical coverage who had a prescription or medical claim for a contraceptive pill, ring, patch, depot medroxyprogesterone injection, or IUD or implant insertion during 2010-2013	2010-2013	HRU	3,794,793	~29	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
1049	Palmer 2012[65]	RC	Truven Health Analytics MarketScan Commercial and Medicare databases	Patients ≥18 with MS diagnosis enrolled in plans with nonzero cost-sharing for disease-modifying therapies (DMT)	2004-2009	Adherence and HRU	24,697	45 to 55	33% to 37%
1075	Patterson 2011[66]	RC	De-identified data originated from a proprietary database containing administrat	Patients ≥50 years with ≥3 years of continuous B-blocker use without significant treatment discontinuation	1998-2005	Adherence	2,345	67	60%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			ive claims from more than 30 different US healthcare plans across 8 different census regions						
1083	Pawaskar 2018[67]	RC	Administrative claims data from Medicare Part A, B, and D Event Files	Medicare fee-for-service beneficiaries ≥18 years with T2D and ≥1 prescription for non-insulin antihyperglycemic agent (AHA) monotherapy under Medicare Part D coverage	2012-2013	Adherence	160,250	77	48%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			and the Medicare 100% Master Beneficiary Summary File Chronic Condition Segment file						
1098	Pesa 2012[68]	RC	CHCG database	Members of the CHCG database hypertension and at least one prescription for a hypertensive medication following the diagnosis for hypertension	2006-2008	Adherence	28,688	50	54%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
1104	Phuar 2019[69]	RC	IBM MarketScan Commercial Database	Patients with chronic myeloid leukemia	2011-2014	HRU	477	~48	44% to 56%
1153	Reynolds 2016[70]	RC	Kaiser Permanente Southern California	Patients aged ≥18 yrs with diabetes and new to dual oral hyperglycemic agent therapy	2005 to 2010	Adherence	23,612	58	56%
1170	Roblin 2014[71]	RC	Kaiser Permanente Colorado and Georgia	Females aged 9-26 yrs who obtained KP insurance through a self-pay DHP or HMP selected in 2007. Patients must be HPV vaccine-naïve and enrolled in KP for at least 12-	2007 to 2009	Adherence and HRU	6,209	19-26: 48-55% 16-18: 13-15% 13-15: 13-16% 9-12:18-22%	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				months prior to 2007 plan selection					
1179	Romley 2012[72]	RC	Administrative, claims and benefit information from 33 fortune 500 employers	Patients aged ≥18 yrs with MS	2003 to 2009	Adherence	3,460	42	33%
1202	Saito 2010[73]	RC	Medical claims database from single health plan in Hawaii	Patients with T2D and first filled a prescription for a diabetes-related medication after at least 1 full year prior to enrollment	2002 to 2007	Adherence and Clinical[a]	9,260	45-64: 60%	53%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
1213	Sambamoorthi 2017[74]	RC	Humana Medicare Advantage Prescription Drug medical, pharmacy and laboratory claims	Patients ≥65 years on Medicare with T2D and 2 or more claims for basal insulin during the baseline period who newly added RAI to their regimen	2007 to 2011	Adherence	4,979	65-74: 71% ≥75: 29%	47%
1235	Schmittdiel 2015[75]	CS	SUPREME-DM Datalink from KPNC, Colorado and Northwest	Patients aged ≥65 yrs with diabetes who had 2 or more outpatient diabetes visits within a 2 year window	2010	Adherence	ACEI/ARB = 86,210 Oral diabetes drugs = 56,629	65-69: 31-32% 70-74: 27% 75-79: 20-21% 80-84:	~51%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
							Statins = 93,276	13-14% >85: 8%	
1256	Shah 2019[76]	RC	Specialty pharmacy claims and electronic medical records	Patients aged ≥18 yrs with pulmonary hypertension who received medication through a specialty pharmacy	2014-2016	Adherence	131	Median: 55	30%
1280	Shrank 2010[77]	CS	One large retail pharmacy chain and one large pharmacy benefits manager	Patients who filled a first prescription for new medications for which no prescriptions had been filled in the 6 months before the index date	2008	Adherence	5,249,380	0-17: 12% 18-34: 15% 35-49: 23% 50-64: 29% ≥65: 21%	40%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
1308	Snider 2016[78]	RC	Longitudinal database of medical and pharmacy claims from self-insured employers	Patients 18-64 years with T2D	2004-2012	Adherence and HRU, Costs	92,410	53	56%
1327	Starner 2014[79]	RC	Single pharmacy benefit manager prescription records	Privately insured patients with an adjudicated pharmacy claim for a biologic anti-inflammatory (abatacept, adalimumab, alefacept, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab,	2013	Adherence	264,801	NR	NR

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				tocilizumab, or ustekinumab) or MS specialty drug (fingolimod, glatiramer acetate, interferon beta-1a, interferon beta-1b, or natalizumab), newly initiating or restarting their drug and enrolled in a health plan 180 days before and after their index date					
1330	Stein 2015[80]	RC	Clinformatics DataMart Database	Patients >40 with open-angle glaucoma	2009-2012	Adherence	8,427	66	48%
1359	Taira 2017[81]	RC	Administrative claims database of	Patients with diabetes who were all taking oral antidiabetic medications,	2008-2010	Adherence	5,136	Mean 63-72	41%-59%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			members enrolled in a large health plan in Hawaii	antihypertensive medications and cholesterol lowering medications					
1371	Tao 2018[82]	RC	Humana Inc. health plan claims	Patients aged 65-90 years, enrolled in Medicare Advantage Part D or Medicare Part D only health plan, who were eligible for the herpes zoster vaccine due to age	2007-2014	Adherence	6,295,970	73	59%
1417	Vaidya 2013[83]	RC	Medstat Marketscan databases	Patients with asthma, with an inhaled corticosteroids event but no long-acting beta-2-agonist or leukotriene receptor antagonist in 6 months	2000-2001	Adherence	1,447	37	40%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				prior to the index date, but at least one inhaled corticosteroid event with a long-acting beta-2-agonist or leukotriene receptor antagonist in the post-index period					
1461	Wang 2013[84]	RC	MedImpact Healthcare Systems Database	Patients aged ≥18 yrs with at least 1 rejected prescription claim for febuxostat	2009-2010	Adherence	1,034	18-39: 7% 40-64: 52% ≥65: 41%	73.40%
1493	Wharam 2019[85]	RC	Optum claims data	Women in low-deductible plans for 1 year who were switched to HDHP for an additional 1 month to 4 years. The control group	2003-2014	HRU	1.5 mil	~45	0

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				consisted of women matched by propensity of employer to manage HDHPs, baseline OOP spending, baseline screening mammogram or breast cancer diagnosis and treatment, follow-up duration, income level, rural vs urban location, racial profile of area, health savings or reimbursement accounts who remained on low-deductible plans					
1534	Yang 2011[86]	RC	Thomson Reuters MarketScan	Patients ≥18, with a diagnosis of hypertension and were initiated on a	2006-2008	Adherence	381,661	Age by copayment group (mean):	~46

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			Commercial and Medicare Supplemental Databases	single pill combination antihypertensive treatment				Low = 58.8 years, 29.8% ≥65 years Medium = 55.6 years, 19.4% ≥65 years High = 55.8 years, 19.2% ≥65 years	

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
1564	Zheng 2011[87]	RC	MedImpact Healthcare Systems Database	Patients aged ≥18 years naïve to varenicline who had a full drug benefit and a reversed varenicline claim, continuous enrollment in the same health plan 1 year before and 183 days after reversed claim, and with coverage for over the counter smoking cessation medications	2007-2008	Adherence	20,451	48	43%
1565	Zheng 2012[88]	RC	MedImpact Healthcare Systems Database	Patients aged 18-64 yrs in commercial home maintenance organizations who started an atypical antipsychotic and were	2003-2008	Adherence	15,898	42	~40

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				previously naïve to antipsychotics					
2002	Choudry 2011[89]	RCT (MI FREEE)	Aetna (insurer)	Patients receiving both medical and prescription drug benefits through Aetna, discharged from the hospital with a principal or secondary diagnosis of MI and a length of stay of 3 to 180 days	2007-2010	Adherence Clinical Costs	5,855	54	75%
2003	Choudry 2014[90]	RCT (MI FREEE)	Aetna (insurer)	As Choudhry 2011 #2002	2007-2010	Adherence Clinical Costs	5,855	54	75%
2004	Fanaroff 2020[91]	RCT (ARTEMIS)	ARTEMIS trial	Aged ≥18 yrs old, diagnosed with ST-segment elevation MI or non–ST-segment elevation	2015-2016	Adherence	10,102	As Wang 2019 #2008	As Wang

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
				MI, discharged on a P2Y inhibitor (clopidogrel, prasugrel, or ticagrelor), had US-based health insurance coverage with a prescription drug benefit,					2019 #2008
2006	Kulik 2013[92]	RCT (MI FREEE)	MI FREEE trial population	NR: Secondary analysis of MIFREE trial	Unclear	Adherence Clinical Costs	5,855	Mean: 53-55	75%
2007	Ross-Degan 2020[93]	RC	Commercial and Medicare Advantage Claims database	Patients aged 12-64 yrs with diabetes and commercial insurance on HDHP through their employer or parent's employer (HDHP defined as annual deductibles of ≥$1,000)	2005-2014	Adherence	HDHP with PDL = 1,744 Matched controls = 3,349	51	57%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
2008	Wang 2019[94]	Cluster RCT	ARTEMIS trial	Aged ≥18 yrs, diagnosed with ST-segment elevation MI or non–ST-segment elevation MI, discharged on a P2Y inhibitor (clopidogrel, prasugrel, or ticagrelor), had US-based health insurance coverage with a prescription drug benefit, and were able to provide written informed consent for longitudinal follow-up	1-year follow-up after discharge	Adherence and Clinical	10,102	Median: 62	69%
IQVIA-9	IQVIA-9[95]	RC	IQVIA Formulary Analyzer Dataset	Commercially insured patients newly accessing branded medications	2013 to 2017	Adherence	NR	NR	NR

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
186	Brixner, 2019[96]	RC	AbbVie patient support program linked medical and pharmacy claims database	Patients aged ≥18 yrs with a first adalimumab claim, with a diagnosis of an autoimmune disease (Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing, spondylitis, hidradenitis, suppurativa or uveitis)	2015-2017	Adherence	17,371	Patient support program = 45.6 ± 13.3 Non-patient support program = 46.4 ± 13.9	Patient support program = 38.7% Non-patient support program = 39%
199	Burton, 2014[97]	RC	Administrative claims database affiliated with large US managed	Patients aged ≥18 yrs with ≥2 claims for either metoprolol or carvedilol, with ≥1 medical claim for atrial fibrillation during baseline. Metoprolol group had ≥1 claim for acute MI,	2008-2010	Adherence	16,014	Metoprolol= 70.2 ± 12.1 Carvedilol = 70.4 ± 11.7	Metoprolol = 58.9% Carvedilol = 68.7%

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
			care health plan	angina, heart failure or hypertension; carvedilol group had ≥1 claim for heart failure or hypertension					
203	Buxbaum, 2018[98]	RC	MarketScan Commercial Claims and Encounters Database	Patients with major depressive disorder and 1 claim for a generic antidepressant	2012-2014	Adherence	2012: 674,468 2013: 583,455 2014: 644,254 Total: 1,902,177	Mean age = 44.2 ± 12.7 yrs	2012 = 31% 2013 = 30% 2014 =30%
1430	VanderBeek, 2020[99]	RC	Clinformatics Data Mart Database	Patients aged ≥18 yrs with a new diagnosis of diabetic macular edema	2013-2016	HRU	6,220	Mean age range (categorized by treatment	Range (categorized by gender):

RefID	First Author, Date	Study Design	Data Source	Sample Description	Study Time Period	Outcomes	Number of Subjects	Mean Age	% Male
								): 62.5-65.9 yrs	48%-62%

Note: Goedken 2010, reporting HRU data and Johnson 2011, reporting cost data met the PICOS criteria for inclusion; however, the reported data did not conceptually align with the other summarized in the respective sections and are therefore only included as footnotes, these 2 studies are included in the n=23 reporting clinical outcomes, HRU, and/or costs.

[a] Saito was originally categorized under "clinical outcomes" but was subsequently removed from category; study found that switches to drugs of equal or lesser copay cost differed significantly by glycemic control status ($P<0.001$), suggesting that patients with A1C >7% (i.e., poorer glycemic control) were less affected by increases in copayment than patients with A1C <7%. For each $5 difference in OOP costs, patients with A1C <7% were 7% more likely to switch to drugs with ≤ copayments. Effect was magnified as copayment increased. Patients with a $20 higher copayment were 28% more likely to switch to a drug of equal or lesser cost. Authors posit that "results may reflect differences in the willingness of patients with less controlled disease to disrupt their existing therapy by switching to a new drug, even within an essential class of medications. Conversely, the findings also may suggest that patients with well-controlled diabetes are considering factors such as long-term costs and exploring less expensive alternatives."

Key: AI – aromatase inhibitor; ARC – antiretroviral; CCAE – Commercial Claims and Encounters; CHCG – Consolidated Health Cost Guidelines; CAR T – Chimeric antigen receptor T-cell; CS – cross-sectional; DHP – deductible health plan; HMP – HMO plan; KPNC – Kaiser Permanente Northern California; MEPS – Medical Expenditure Panel Survey; MI – myocardial infarction; MS – multiple sclerosis; OAD – oral antidiabetic; PICOS – population, intervention, comparator, study design; PC – prospective cohort; RC – retrospective cohort; RCT – randomized controlled trial; SG – second-generation antipsychotics; SUPREME-DM – Surveillance,

Prevention, and Management of Diabetes Mellitus; T2D – type 2 diabetes; HRU – healthcare resource utilization; SEER – Surveillance, Epidemiology, and End Results; IMS – Intercontinental Medical Statistics; US – United States; CMS – Centers for Medicare & Medicaid Services; NR – not recorded; yrs – years.

Supplemental Table 4. Relationship Between Increased Cost-Sharing and Adherence, Persistence, and Discontinuation by Disease Area

	Adherence, n (%) N=63 studies		Persistence, n (%) N=19 studies		Discontinuation, n (%) N=19 studies	
	Number of Articles	Number (%) Reporting Worse Adherence	Number of Articles	Number (%) Reporting Worse Persistence	Number of Articles	Number (%) Reporting Worse Discontinuation
Diabetes	13	12 (92)	4	4 (100)	5	4 (80)
Cardiovascular	12	9 (75)	3	3 (100)	3	1 (33)
Oncology	10	8 (80)	5	2 (40)	4	1 (25)
Mixed/No restriction	6	6 (100)	1	0 (0)	2	1 (50)
Infectious Diseases	4	4 (100)	2	2 (100)	1	0 (0)
Mental Health	4	3 (75)	2	2 (100)	1	1 (100)
Arthritis	2	2 (100)	1	1 (100)	1	1 (100)
Multiple Sclerosis	2	2 (100)	1	1 (100)	2	2 (100)
Respiratory	2	2 (100)	0	N/A	0	N/A
Autoimmune	1	1 (100)	0	N/A	0	N/A
Reproductive Health	1	1 (100)	0	N/A	0	N/A
Dementia	1	1 (100)	0	N/A	0	N/A

	Adherence, n (%) N=63 studies		Persistence, n (%) N=19 studies		Discontinuation, n (%) N=19 studies	
Eyes and Vision	1	1 (100)	0	N/A	0	N/A
Smoking Cessation	1	1 (100)	0	N/A	0	N/A
Gastrointestinal	1	0 (0)	0	N/A	0	N/A
Gout	1	0 (0)	0	N/A	0	N/A
Osteoporosis	1	0 (0)	0	N/A	0	N/A

Supplemental Table 5. Cost-Sharing and Clinical Outcomes

First Author and Year	Clinical Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
Copay Difference						
Marcus 2016	eGFR among HIV pre-exposure prophylaxis	Low copay	<$50	High copay	≥$50	No statistically significant difference
Cost-Sharing Eliminated						
Elliott 2013[32]	Hypoglycemic control among patients with diabetes	Pre-implementation of copay elimination	$10 – generics[a] $25 – preferred brand[a] $50 – nonformulary[a]	1-years post-implementation of copay elimination	$0 copays	No statistically significant difference in HbA1c
Wang 2019	MACE (death, recurrent heart attack, or stroke)	Usual care patients without copay vouchers	No voucher	Copay vouchers for clopidogrel or ticagrelor	Median monthly voucher: $137 ($20-$339)	No significant difference in MACE at 1 year

First Author and Year	Clinical Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
Choudhry 2011 (*same study as Choudry 2014 and Kulik 2013*)	Heart attack, angina, stroke, heart failure, revascularization or death	Usual prescription coverage	ACE inhibitor/ARB: $13.35 Beta-blocker: $12.83 Statin: $24.92	Full prescription coverage	$0 cost-sharing	Fewer major vascular events, stroke; other outcomes non-significant
Choudhry 2014 (*same study as Choudry 2011 and Kulik 2013*)	Readmission for heart attack, angina, stroke, heart failure, revascularization or death	Usual prescription coverage	ACE inhibitor/ARB: $13.35 Beta-blocker: $12.83 Statin: $24.92	Full prescription coverage	$0 cost-sharing	Reduced major vascular events or revascularization in nonwhite patients; no effect in white patients
Kulik 2013 (*same study as Choudry 2011*	Heart attack, angina, stroke, revascularization	Usual prescription coverage	ACE inhibitor/ARB: $13.35	Full prescription coverage	$0 cost-sharing	Nonsignificant reductions

First Author and Year	Clinical Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
and Choudry 2014)			Beta-blocker: $12.83 Statin: $24.92			

[a] For 30-day supply; 90-day, costs were $25, $63, and $125, respectively; the proportion of participants with > $200 in monthly OOP costs decreased from 35.1% to 20.2%, and those reporting < $100/ month increased from 22.9% to 48.4%.

Key: ACE – angiotensin-converting enzyme; ARB – angiotensin-receptor blocker; eGFR – estimated glomerular filtration rate; MACE – major adverse cardiac event; OOP – out-of-pocket.

Supplemental Table 6. Cost-Sharing and Healthcare Resource Utilization

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
Karaca-Manic 2012[49]	Medication and hospital use among children with asthma	Lowest quartile of OOP asthma medication costs (comparator)	$100	Highest quartile of asthma medication costs (intervention)	$190	**Significant increase in asthma-related hospitalizations** for children 5–18 years; no significant difference for children <5; no significant differences in ED use; non-asthma	**X**	NR	Not Sig

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
						hospitalizations; (*Higher OOP = lower med use*)			
Henk 2018[44]	Inpatient stay, ER and ambulatory visits among patients with diabetes	Fixed copay Or Coinsurance (comparator)	$30 coinsurance mean	Highest copay in fixed 3-tier copay plan (intervention)	$54.54 copay	Higher 3-tier copay **significantly fewer ambulatory visits;** no significant difference in hospitalizations or ED visits	Not Sig	**X**	Not Sig

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
Elliot 2013[32]	HRU among patients with diabetes	1-year post-implementation of copay elimination (intervention)	$0 copays	Pre-implementation of copay elimination (comparator)	Copays: $10 – generic medications $25 – preferred brand medications $50 – nonformulary brand medications	Non-significant increase in hospitalizations and ED visits	Not Sig	NR	Not Sig

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
Kim 2011a[52]	Medical utilization among employees offered copayment waivers (VBID)	1.5 years post-VBID (intervention)	Copays: Tier 1: $0 Tier 2: $8 Tier 3: $25 Tier 4: $45-$105	Pre-VBID introduction (comparator)	Copays: Tier 1: $8 Tier 2: $25 Tier 3: $35-$40 Tier 4: $70-$140	**Significant increase in hospitalizations[a]** ED visits not significantly different	**X**	NR	Not Sig
Roblin 2014[71]	Initiation or completion of the HPV vaccine series and primary care visits	Traditional HMO plan (comparator)	<$5,000 annual deductible	High-deductible health plan (intervention)	≥$5,000 annual deductible	**Significant association with a lower likelihood of having primary care visits** among	NR	**X**	NR

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
						females aged 9 to 26 years			
Phuar 2019[69]	Hospital, ER, outpatient use oral chemotherapy after initial chronic myeloid leukemia diagnosis	Early initiation of TKIs (≤1 month of diagnosis) (intervention)	Mean cost $190	Late initiation of TKIs (>1 month to 12 months of diagnosis) (comparator)	Mean cost $231 *(adjusted analyses found no significant association between mean OOP costs for first 30-day*	**Significant increase in hospitalizations**; no significant differences in ED or outpatient visits	**X**	Not Sig	Not Sig

Study	HRU Outcome	Lower Cost-Sharing Group	Lower Cost-Sharing	Higher Cost-Sharing Group	Higher Cost-Sharing	Result	Hospitalizations	Outpatient	ED Visits
					supply and initiation)				
Snider 2016[78]	Days in hospital among patients with diabetes	Low cost-sharing plan (comparator)	$10 copay	High cost-sharing plan (intervention)	$50 copay	Higher copays = **significant reductions in adherence; lower adherence = significant increase in hospitalizations**	**X**	NR	NR

[a] Significant decrease in hospitalizations among the diabetes patients who received the nurse counseling along with reduced copays (these patients were considered high-risk based on risk stratification score); the diabetes patients given health education mailers along

with reduced copays (these patients were considered low-risk based on risk stratification score) had significant increase in hospitalizations.

“X”: Indicates increased cost-sharing was associated with statistically significant increased hospitalization and HRU.

“Not Sig”: A statistically significant association not found between cost-sharing and HRU outcome.

“NR”: association between cost-sharing and specific HRU outcome was not assessed.

Key: ED – emergency department; HRU – healthcare resource utilization; HPV – human papillomavirus; HMO – health maintenance organization; OOP – out-of-pocket; TKI – tyrosine kinase inhibitor; VBID – value-based insurance design.

Supplemental Table 7. Cost-Sharing and Healthcare Medication Initiation/Uptake

First Author and Year	HRU Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
Palmer 2012[65]	Filling DMT prescription	High copay	>$29	Low copay	≤$29	**Statistically significant decreased odds of filling prescription**
Gibson 2012[39]	Augmenting therapy for depression	Copay increase	$10	No increase	$0	**Statistically significant decreased odds of augmenting therapy**
VanderBeek 2020[99]	Filling initial prescription for DME	Copay	≥$1	No copay	$0	**Statistically significant decreased odds of filling prescription**

First Author and Year	HRU Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
		HDHP	NA	Not HDHP	NA	No significant association
Phuar 2019[69]	TKI initiation	Copay	>$0–$50, >$50–$100, >$100	No copay	$0	No significant association
Marcus 2018[59]	Initiating DAA among HCV patients	High maximum OOP costs	>$3,000	Low maximum OOP costs	≤$3,000	**Statistically significant decreased RR of filling prescription**
Roblin 2014[71]	Initiation and completion of HPV vaccine series	HDHP	≥$5,000 annual deductible	Traditional HMO	<$5,000 annual deductible	**Among females 9-26: statistically significant decreased odds of initiating or**

First Author and Year	HRU Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Result
						completing series
Law 2016[54]	Contraception utilization rates	Pre-ACA		Post-ACA	$0 copay	No significant difference
Pace 2016[64]	LARC utilization rates				$0 copay	No significant difference
Wharam 2019[85]	Time in receiving a mammogram, having a diagnosis of breast cancer, or starting chemotherapy	Women who remained on LDHP	LDHP (≤$500)	Women switched to from LDHP to HDHP	HDHP (>$1,000)	**Significantly longer for HDHP women**

[a] Unclear if "higher" is the result of an analysis that evaluated a $10 increase in copayment, or if it refers to categorical comparisons across the maximum third-tier fixed copayment amounts ($25, $50, $75, $100).

[b] among 5-18 year-olds; NS among <5 year-olds.

Key: DMT – disease modifying therapies; HDHP – high-deductible health plan; DAA – direct-acting antiviral agents; HCV – hepatitis C virus; HMO – health maintenance organization; ACA

– Affordable Care Act; LARC – long-acting reversible contraceptives; LDHP – low-deductible health plan; OOP – out-of-pocket.

Supplemental Table 8. Cost-Sharing and Healthcare Costs

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
Karaca-Manic 2012[49]	Total (OOP + plan-paid) asthma-related hospitalization costs; asthma-related hospitalization and medication costs (among 5-18 year olds)	Lowest quartile of OOP asthma medication costs	$100	Highest quartile of asthma medication costs	$190	Not Sig (OOP+plan paid hospitalizations & medications)	Not Sig (Hospitalization costs)	**X** Increased OOP=**significantly lower** asthma medication expenditures (OOP + plan paid)

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
Henk 2018[44]	Mean total healthcare costs	Fixed Copay		Coinsurance		**X** Fixed = greater adjusted mean total healthcare costs (No sig difference between $25 vs. $100 copay increase for OOP+plan paid; higher cost sharing = lower health plan	NR	NR

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
						and higher OOP)		
Choudry 2011[89]; Choudry 2014[90]; Kulik 2013[92]	Total healthcare costs	Usual copay		No copay	$0	Not Sig (Insurer paid or insurer + OOP)	Not Sig No copay = reduction in patient nondrug payments no increase in insurer spending for nondrug medical services	**X** Reduced OOP pharmacy costs and significantly increased insurer-paid pharmacy costs (no significant difference in insurer paid or insurer + OOP pharmacy costs)

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
Cheng 2012[23]		Pre-Medicare Part D		Medicare Part D		Not Sig Total medical [a] OOP significantly reduced; Medicare-paid significantly increased for median (no sig change for 75th, 90th percentile); no significant change for	NR	**X** 3 years following Medicare Part D coverage, significant reductions in OOP prescription costs; Medicare-paid drug expenditures increased; total Medicare-paid + OOP prescription spending significantly

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
						OOP + Medicare-paid		increased in 75th and 90th percentile (not for median)
Elliot 2013[32]	total medical costs (assuming this is hospitalizations, ED visits & pharmacy; OOP + plan-paid)	Pre-implementation of copay elimination	Copays: $10 – generic medications $25 – preferred brand medications $50 – nonformulary brand	1-year post-implementation of copay elimination	$0 copays	NR	Not Sig	Not Sig

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
			medications					
Kim 2011a[52]	Medical utilization among employees offered copayment waivers (VBID)	Pre VBID introduction	Copays: Tier 1: $8 Tier 2: $25 Tier 3: $35-$40 Tier 4: $70-$140	1.5 years post VBID	Copays: Tier 1: $0 Tier 2: $8 Tier 3: $25 Tier 4: $45-$105	NR	**X** Reduced copay = lower total medical costs; statistically significantly lower inpatient costs and professional costs;	**X** Reduced copay = higher pharmacy costs

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
							Outpatient costs not statistically significantly different	
Snider 2016[78]	Days in hospital among patients with diabetes	Low cost-sharing plan	$10 copay	High cost-sharing plan	$50 copay	NR	**X** $342 per person increase in payer hospitalization costs. higher overall payer costs (combined drug and	**X** High cost-sharing = $242 reduction in per-person payer costs for T2D prescriptions

Study	Cost Outcome	Comparator Group	Comparator Cost-Sharing	Intervention Group	Intervention Cost-Sharing	Total Healthcare	Medical Care	Pharmacy costs
							hospitalization costs)	
Daubresse 2017[29]	Pharmacy costs	No Coupon		Coupon		NR	NR	Not Sig OOP + plan paid
Clark 2014[25]	Pharmacy costs	to propensity matched non-VBID participants	Usual copay	No copay (VBID)	$0	NR	NR	**X** Savings to employers of $24 per member per year

KEY: NR – not reported; T2D – type 2 diabetes; VBID – value based insurance design