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Effect of Managed Care Pharmacy Tools: A Review of the Literature

Literature Summary Tables

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Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Berger (2007) *Objective:* Summary of Mahoney (2005) that examined change in diabetes prescription drug adherence, pt diabetes prescription drug costs, pt pharmacy costs, company's total pharm cost, short term disability, and ER visits after reducing coinsurance of diabetes rx *Quality Rating:* Poor	*Plan Type:* Self-insured and fully-insured med plan at Pitney Bowes *PBM?* No *Region:* D/K *SAMPLE Size:* 23,000 Pitney Bowes employees *Age:* Ave age=41 yrs	*Design:* Descriptive study of change diabetes prescription drug costs, adherence after Pitney Bowes implemented change to benefits *Statistics:* None reported *Timeframe:* D/K, but sometime after 2000, and from Table p.S57, appears to have been in 2002-2004? *Intervention:* • Pre intervention, Pitney Bowes used 3-tier system: 10%, 30%, and 50% coinsurance • Post intervention, Pitney Bowes moved all medications for asthma, diabetes, and hypertension to tier 1 (10% coinsurance). *Drugs/classes:* • diabetes (main focus), but Pitney Bowes also reduced coinsurance for asthma & hypertension *Strengths:*	Cost for patient with diabetes • ave cost of 30-day rx supply decreased by 50% Rates of adherence • increases significantly in response to intervention • suboptimal adherence to insulin therapy decreased by two-thirds • usage of blood glucose meter test strips increased from 28% to 55% • members adhering to single-pill combination oral anti-diabetic agents • increased from 9% to 22% Company's total annual pharm costs • increased from about $26 per month to $35 per month. Patient pharmacy costs • pharmacy costs for individuals with diabetes decreased by 7% ER visits • "Diabetes-related emergency department visit rates also decreased" (D/K significant or magnitude) Short-term disability (STD) • # active STD cases/100 employees, average duration of STD case days, & STD costs decreased (Table; D/K significant)	• Descriptive summary of another article (Mahoney 2005) • Very little detail of study and no significance of findings • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? YES o Drug utilization? ▪ Adherence YES ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other o Medical utilization? ▪ ER YES ▪ Hospitalization NO ▪ (spillover) NO • Health outcomes? NO
Briesacher et al (2004)	*Plan Type:* HMO, POS, PPO, capitated	*Design:* Retrospective claims based	Use of COX2 inhibitor among all pts with arthritis • compared to 1-tier, odds of using COX-2–inhibitors	• patients in our study had generous drug coverage provided by current employers

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Objective: to assess how 3-tier formularies influence the use of NSAIDs in an arthritis patient population as well as sub-popn of arthritic patients at risk for GI complications and COX-2–inhibitors *Quality Rating:* Fair	POS, and comprehensive *PBM?* N/A so assume no *Region:* N/A *SAMPLE Size:* 20868 pts: • 1-tier: 12225 pts, 16 plans • 2-tier: 4152 pts, 10 plans • 3-tier: 4491 pts, 13 plans (7 plans switched for 2 to 3 tier in 2000) *Age:* N/A, but 45% were aged 55-64 yrs old *Other characteristics:* From 45 large employers *Selection Criteria:* Patients treated for osteoarthritis or rheumatoid arthritis and using prescribed NSAIDs while enrolled in tiered drug plans during 2000 and had drug coverage	analysis (Medstat's Market Scan) *Statistics:* Estimated odds of any use of COX-2 inhibitors as function of tiered plan coverage, w/ robust clusters to account for correlation of enrollees w/in plan *Timeframe:* 2000 *Intervention:* • Comparison of 1-tier, 2-tier, and 3-tier plans Drug copayment ranges: • 1-24 1-tier • 4-10/8-20 2 tier • 5-10/10-16/20-31 3 tier *Drugs/classes:* Nonsteroidal anti-inflammatory drugs (NSAIDS), particularly COX 2 inhibitors *Strengths:* • findings are among the first to suggest that tiered-copayment drug plans may be influencing selection of medications beyond generic and branded	were significantly lower ([OR], 0.36; 95% [CI], 0.26-0.49) in 3-tier that designated COX-2–inhibitors as only nonpreferred products • copayments for COX-2 prescriptions exceeding $15 lowered odds of any use (OR, 0.42; 95% CI, 0.25-0.71) relative to copayments of $5 or less Use of COX2 inhibitor among pts with arthritis w/ GI comorbids • trends reported above hold for this smaller group N=2977 • compared to 1-tier, odds of using COX-2–inhibitors were about half (OR, 0.51; 95% CI, 0.40-0.66) in 3-tier that designated COX-2–inhibitors as only nonpreferred products • copayments for COX-2 prescriptions exceeding $15 lowered odds of any use (OR, 0.49; 95% CI, 0.25-0.96) relative to copayments of $5 or less	or retiree benefits → may not be generalizable to lower-income groups • cross-sectional study design does not permit us to determine whether tiered benefit design features are responsible for less use of COX-2–selective inhibitors or whether plans with lower use of COX-2–selective inhibitors are more likely to adopt 3-tier formularies. (i.e., causality) • cannot rule out selection bias (i.e., 3-tier plans may be attracting enrollees with less severe arthritis); but doesn't explain differences in COX-2–use in patients w/ GI comorb • did not consider use of other gastroprotective agents • did not capture OTC NSAIDS • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? YES o Drug utilization? YES ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other NO o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Brixner et al (2007) *Objective:* To assess the effects of benefit design	*Plan Type:* Integrated non profit healthcare system – Intermountain Healthcare (IHC)	*Design:* Pre/post analysis of comparison vs. intervention group *Statistics:*	Prescription status- same • Significant decrease in # pts who stayed on same therapy with a BDC vs. comparison for allergic rhinitis, asthma, hypertension, and osteoarthritis (9.6%, 12.8%, 18.0%, 22.1%; P < .001 for all).	• Do not take into acct SES of patients • Only 1 year of follow up • Absence of any disease severity, although tried to address by limiting to monotherapy • Drug util and cost measured at disease-

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change (BDC) on medication adherence and persistence (including switch in therapy), drug costs, and total healthcare costs. *Quality Rating:* Good	*PBM?* YES – provided internally by SelectHealth *Region:* Salt Lake City, UT *SAMPLE* *Size:* 7939 total patients among 672 IHC employer groups BDC N=2922: • 671 allergic rhinitis, • 459 asthma, • 483 diabetes mellitus • 1267 hypertension • 322 osteoarthritis Comparison N=5017: • 909 allergic rhinitis, • 690 asthma, • 1007 diabetes mellitus • 2302 hypertension • 738 osteoarthritis 909 patients had 2 or more diseases; categorized into more than 1 disease condition *Age:* N/A but all employer groups *Other characteristics:* Only patients receiving drug monotherapy were included in	• Chisq test • Multivariate analysis for MPR and medical care costs: diff between 2001 and 2002 med care costs and MPR were used as depend var • *Timeframe:* 1/1/2001-12/31/2002; looked at last 100 days in 2001 and last 100 days in 2002 *Intervention:* intervention AKA BDC • BDC defined as defined BDC as a copayment increase in 2-tier or 3-tier of $5 or greater or as a change from a flat copayment to a percentage coinsurance. • I.e., increasing co-payment differentials between tiers Comparison group - no BDC on 1/1/02 *Drugs/classes:* Drugs commonly prescribed for 5 diseases: • allergic rhinitis, • asthma, • diabetes mellitus • hypertension • osteoarthritis *Strengths:*	Compliance (measured by MPR) • medication compliance not affected by BDC EXCEPT for allergic rhinitis: MPR= -0.02 vs. +0.04 (P < .05) Differences in pharm costs • significant decrease in pharm costs for allergic rhinitis, asthma, hypertension, and osteoarthritis ($95, $269, $180, $305; P =.03 for all). Differences in TOTAL costs • no significant diff between BDC and no BDC for all 5 diseases Differences in total healthcare costs, including ER, inpt, outpt, pharmacy • no significant diff between BDC and no BDC on overall healthcare costs for all 5 diseases Persistence w/ original therapy (i.e., taking same chemical entity) aka Prescription status- discontinue • Significant increase in rates of discontinuation with a BDC vs. comparison for allergic rhinitis, asthma, hypertension, and osteoarthritis (13%, 17%, 21%, 25%; P < .001 for all).	treatment level • no attempt to assess drug therapy changes for patients with multiple drug therapies (i.e., polypharmacy) or to assess the effects of copayment changes for patients taking multiple medications to treat a single disease. • No adjustments for changes in drug formulary or in tier co-payment status of indiv drugs • No adjustments for std errors between or across employer groups w/in each comparison group • Sample May not be representative/generalizable to other popns since IHC "leader in progressive approaches to wellness/disease mgmt" • Limited sample to monotherapy pts only, so may not be generalizable to pts w/ worse health • Fairly simple analysis • No detail on what the exact co-payment amts or tiers for the intervention • Rebate $ included? NO • Patient cost? NO • Plan cost? YES • Utilization? o Drug utilization? ▪ Adherence YES ▪ Medication Possession Ratio YES ▪ Discontinuation YES ▪ Other NO o Medical utilization? YES ▪ ER YES ▪ Hospitalization YES ▪ (spillover) YES

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	the analysis in an attempt to reduce the potential confounding of compliance and cost results. *Selection Criteria:* Pts selected if they had drug claims for at least 1 of 5 diseases listed above See p. 371 for reason why authors chose these 5 diseases	• 5 diseases selected provide a mix of chronic and episodic conditions		• Health outcomes? NO
Fairman et al (2003) *Objective:* This study examined the effect of a 3-tier copayment system for chronic med therapy on pharmaceutical and medical utilization and cost for 30 months after implementation in a population of commercially insured, preferred-provider organization members *Quality Rating:* Good	*Plan Type:* PPO *PBM?* Yes – Express Scripts *Region:* Midwestern US *SAMPLE* *Size:* Intervention: 3577 Comparison: 4132 *Age:* N/A, mean age early 30's *Other characteristics:* *Selection Criteria:*	*Design:* 12 mo pre and 24 mo post design *Statistics:* 2 stage multivariate regression – 1st - Logistic reg to predict odds of util of service in each of the 2 f/u yrs 2nd – among users, linear regression analysis to predict volume (cost/claims log transformed) *Timeframe:* Intervention: 1/97-12/00; intervention occurred between 1/1/98 & 9/1/98 Comparison: 1/97-12/00 *Intervention:* intervention (2-tier to 3-tier) and comparison (2-tier constant) • 2-tier: $7, 12 for 30 day at	Total drug cost • n.s. diff in drug costs Net insurer cost (drug cost minus copayment) • intervention had slower growth vs. comparison: 6% vs. 22% for 1st year post-intervention. • From pre-intervention to 24 mo post-intervention, net insurer's cost increased by 30% vs. 57% for intervention vs. comparison (p<.001) Number of prescription claims • background: 14% pre-intervention claims were for drugs in 3rd tier • no significant diff in # total prescriptions, 1st tier, or 2nd tier drugs • intervention had significant fewer 3rd tier scripts than comparison in both 1st and 2nd year post intervention Numbers of office visits, inpatient hospitalizations, and ER visits • No diff in these between comparison and intervention groups Rates of continuation by class • Intervention had lower med continuation rates for oral	• no rebate • only examines 1 health plan • can't address how patient's income might affect their sensitivity to prices • Insurance coverage might influence employment decision • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? o Drug utilization? ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other NO o Medical utilization? ▪ ER YES ▪ Hospitalization YES ▪ (spillover) NO • Health outcomes? NO

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		retail; double for 90-day @ mail • 3-tier: 8, 15, 25 for 30-day @ retail; double for 90-day @ mail *Drugs/classes:* For persistency analysis only, analysis limited to following chronic medication therapy: • estrogens, • oral contraceptives, • antihypertensives • antihyperlipidemics *Strengths:* longer follow up periods than other studies	contraceptives 6 mo post intervention; no diff after 6 mo • no diff for other 3 chronic meds at any time	
Ganther-Urmie et al (2004) Objective: To examine patient attitudes related to formulary medications and medication-related decision making in multitier copayment prescription drug plans to identify the factors that affect plan members willingness to switch from nonformulary to formulary drug	*Plan Type:* large managed care organization including HMO, PPO or Medicare + Choice *PBM?* *Region:* Western United States *SAMPLE* *Size:* 25008 members (3816 usable responses (15.2%) from all surveyed and 35.8% (10663) responses from continuously enrolled *Age:* Mean 57.7. Standard	*Design:* Retrospective cross-sectional design using a survey *Statistics:* Paired T-Tests, OLS Regressions, and logistic regressions *Timeframe:* Survey sent in November 2000 and was retrospective *Intervention:* Not Applicable *Drugs/classes:* For the conditions listed in selection criteria *Strengths:*	Plan Member Experience/Attitudes Toward Formulary Medications • Half respondents had been told prescriptions were not on plans formulary • 53% paid extra to purchase nonformulary medication, 26% switched to formulary, 13% did not get any medication, 9.9% got permission to use nonformulary and 7.4% did not respond. • 8.8% agreed that formulary drugs are safer and than nonformulary drugs – 9.1% agreed that formulary drugs were more effective and 5.6% agreed that formulary drugs had fewer side effects than nonformulary drugs. 39.7% agreed that formulary drugs were less expensive. Willingness to Switch to Formulary Medication • For new medications – individuals in 3 tier plan were more willing to switch to formulary than a 2 tier plan – the only significant variable in the regression model	• Low response rate • Potential lack of generalizability to other plans • Plan members who had faced switching decisions were more likely to respond to the survey • Rebate $ included? No • Patient cost? Not directly considered but evaluated through patient opinions on switching • Plan cost? Not Directly Considered • Utilization? o Drug utilization? NO o Medical utilization? NO • Health outcomes? No

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Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Quality Rating: Fair	Deviation 13.2 *Other characteristics:* *Selection Criteria:* Individuals enrolled in 2 or 3 tier copayment plan with at least 2 prescription claims for arthritis, diabetes, dyslipidemia, gastrointestinal reflux disease, and hypertension		was side effects of formulary medications • For prescription refills – Only safety of formulary medications was the statistically significant predictor Factors Affecting the Switching Decision • Doctor's opinion bout switching was the most important factor in considering switching to formularies • Effectiveness of medication, specific condition, and cost were other key factors	
Gilman et al (2007) Objective: To identify the impact of absolute and relative price effects of multitier formularies on total payments, enrollee payments, number of prescriptions filled and percentage of prescriptions filled with generics. *Quality Rating:* Fair	*Plan Type:* Medicare with Supplemental Benefits – employer sponsored *PBM?* *Region:* *SAMPLE Size:* 352760 *Age:* >65 *Other characteristics:* *Selection Criteria:* >65 and dependents >65 who were retired and received Medicare+ Supplemental	*Design:* Cross sectional analysis at enrollee level comparing 1-tier plans with 3 tier plans. Data included 2 plans that were 1 tier and 3 plans that were 3 tier. *Statistics:* multivariate regression with generalized least squares. *Timeframe:* 2002 *Intervention: Not applicable* *Drugs/classes: Not specified* *Strengths:* This is an interesting study focusing on copayment differentials instead of just considering a shift in tier systems.	Total Payments • Increase in the absolute and relative copayment amount decreases the total payments Enrollee Payments • Increase in the absolute and relative copayment amounts increases the enrollee payment amounts Number of Prescriptions Filled • Increase in absolute and relative payment amount both lead to a decrease in the number of prescriptions filled Percentage of Prescriptions Filled with Generics • Increase in absolute copayment amounts leads to a small and *not statistically significant* difference in this percentage • Increase in relative copayment amounts leads to a statistically significant difference in the percentage filled with generics	• Plans offered alternative cost-sharing options for mail order and out-of-network purchases • The sample is drawn from large unionized firms in manufacturing in a few states • Firms are likely to design health plans based on retiree need and there is unobservable firm-level selection causing underestimation of effect • Sample was drawn before Medicare Part D was implemented • Rebate $ included? No • Patient cost? Extensive discussion of overall patient costs but not by drug classes or conditions • Plan cost? Yes considerable discussion in reduction in costs to plan. • Utilization? o Drug utilization? No o Medical utilization? No • Health outcomes? No
Goldman et al (2004)	*Plan Type:* 52 health plans entered the study across 30	*Design:* Retrospective observational study	Change in Spending measured in Drug Days • Decreases across all categories in full sample and	• Sample drawn from insured working-age

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Objective: To determine how changes in cost-sharing affect use of the most commonly used drug classes among the privately insured and chronically ill. *Quality Rating:* Good	large US employers – they had 1,2, and 3-tier plans *PBM?* *Region:* *SAMPLE* *Size:* 528,969 beneficiaries over 4 years (n=960,791 person years) *Age:* *18 -64 years* *Other characteristics:* *Selection Criteria:*	*Statistics:* Two stage model – first identified probability of using drugs using probit, then used GLM with log-link to estimate drug spending in terms of days supplied *Timeframe:* 1997-2000 *Intervention:* Impact on drug days when copayments double *Drugs/classes:* antihyperlipidemics, antidepressants, antiulcerants, NSAIDs, antihisthamines, antidiabetic agents, calcium channel blockers, ACEIs, Beta blockers, H2 antagonists, *Strengths:*	those who were chronically ill • Largest decreases occurred with NSAIDs (45%) and antihistamines (44%) • Antidepressants decreased least in Depressed patients (8%) • Medications with OTC substitutes had the highest reduction in use with doubling of copayments.	population and might not be generalizable • Chronically ill patients identified from claims data – risk of false positives if rule-out diagnoses are recorded on claims. • In most companies beneficiaries did not have a choice of drug benefits. • Rebate $ included? No • Patient cost? Yes in terms of drug days • Plan cost? Yes in terms of sharing • Utilization? o Drug utilization? ▪ Drug possession in terms of drug days is considered but not utilization o Medical utilization? NO • Health outcomes? NO
Harris et al (2004) *Objective:* To evaluate the financial effects in a state employee health plan of a change in the drug coverage policy to include over-the-counter (OTC) omeprazole (prilosec) in a tier-copayment drug benefit design	*Plan Type:* State employee health plan *PBM?* no *Region:* Arkansas *SAMPLE* *Size:* approx 129,500 benes; 14,295 prescriptions in study period *Age:* N/A	*Design:* Examine ave cost and util pre/post intervention *Statistics:* None – descriptive only *Timeframe:* 1/1/04-4/30/04 2 mo pre/post intervention; intervention occurred 3/1/04 *Intervention:* • Added PPI OTC to formulary with low copayment ($5)	Beneficiary utilization • 17.2% increase in util of OTC, but largely due to fact that OTC was on 42-day supply vs. all other PPIs on 30-day supply • 60% of benes shifted to OTC by end of 2 months post intervention • Figure 1: decrease in all non OTC PPIs Beneficiary cost • Ave copayment saving=4.20 (16.5%) per PPI claim Plan cost • Ave savings of 40.86 (40.55%) per PPI claim • reduced net costs of PPIs by 2.11 PMPM (38.9%) in	• only 2 mo time frame – very short • did not address satisfaction • Weak/non existent statistics – purely descriptive • Can't say what util of OTC was pre-intervention since don't have claims data on it • Rebate $ included? no • Patient cost? On average only • Plan cost? yes • Utilization?

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that favored the OTC drug. *Quality Rating:* Poor	*Other characteristics:* N/A *Selection Criteria:* Not specified	• Increased dispensing fee for OTC PPI to encourage pharmacists to use • Removed brand omeprazole from formulary • Increased copayment for generic omeprazole (10 to 25) • Increased copayment for Rabeprazole and Esomeprazole (25 to 50) *Drugs/classes:* PPI *Strengths:* • Unique in that looks at adding OTC PPI to formulary • Takes into account pharmacist perspective (dispensing fee); almost necessity given introducing OTCs	2004 $. • Annualized savings est=$3.9 mill Dispensing fee • Pharm reimb increase 118% (2.88/claim pre; 6.27/claim post).	o Drug utilization? YES ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO • Weak statistics – just descriptive
Hodgkin et al (2008) *Objective:* To measure the effect of a three-tier formulary on antidepressant utilization and spending, including decomposing spending allocations between patient and plan. *Quality Rating:* Good	*Plan Type:* commercially insured benes in HMO *PBM?* Yes *Region:* New England *SAMPLE* *Size:* 109,686 (77% of elig popn) 45,197 in tx; 64,489 in control *Age:* D/K. report that 8% of sample are <18 *Other characteristics:*	*Design:* pretest-posttest non equiv quasi-experimental design w/ staggered implementation across employer groups; also includes a comparison group. *Statistics:* GEE Diff-in-diff Tooze 2 part model – logistic model for the prob of use; lognormal model for spending/user *Timeframe:* 1/1/1999-12/31/2000 7 mo pre/post intervention; intervention occurred at staggered	Probability of <u>any</u> antidepressants utilization • Rx per enrollee/ decreased 11% among 3-tier, increased 5% in comparison group • Probability higher post utilization for both groups: 0.2% increase for 3-tier; 0.5% for control (table 3). This 0.3% diff between the 2 groups is Diff in Diff estimate of impact of intervention on utilization • I.e., 3-tier formulary reduced proportion of enrollees using antidepressant • Drug selection for antidepressants relatively insensitive to copayments Beneficiary expenditure (OOP) • Treatment increased OOP Plan payment • Treatment decreased plan payment	• possible that intervention coincided w/ concurrent changes unique to group (threat of selection-treatment interaction) p.70-1 • unclear if (relative) insensitivity to prices (AKA price inelasticity) are due to MD unwilling to switch pts' meds vs. pts insisting they stay on specific meds – cannot disentangle this from study • limited to continuously enrolled • lack rebate data • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? o Drug utilization? YES

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	Selection Criteria:	times but by 3/1/00. *Intervention:* • Health plan adopts 3-tier system • Specific copayment assoc w/ each tier among plans differed, but most common: 5, 10, 25 • Also had 3 transfers from tier2 to tier 3: wellbutrin 8/00, aventyl hcl 1/01, and pamelor 1/01 *Drugs/classes:* Anti-depressants *Strengths:* Control group permits some control for potentially confounding changes that could have coincided with three-tier implementation.	Total drug spending • Treatment decreased total spending	▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other NO o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO Notes some pts in comparison do eventually face 3-tier intervention, but AFTER 3/1/00, so authors only exam their 14 mo of non-intervention claims
Huskamp et al (2003) *Objective:* to compare the utilization of and spending on drugs in 3 classes in two employer-sponsored health plans that implemented changes in formulary administration with those in comparison	*Plan Type:* Two large employers that contract with a large health insurer *PBM?* YES - Medco *Region:* N/A *SAMPLE Size:* Firm 1: • Intervention: 55567 • Comparison: 55951	*Design:* Observational study using quasi-experimental design – "JMP clustering algorithm" which is similar to propensity score matching *Statistics:* Pre and post → difference in difference • 2 part model – 1st part = logit model of prob of obtaining script in a particular class in given month; 2nd part = regs estimating monthly spending	Monthly probability of use • Firm 1 intervention resulted in: 24%, 34%, 24% decrease in monthly prob of using ACE, PPI, statins (p<.001) *vs.* • Firm 2 intervention resulted in: 5%, 5%, 2% decrease in monthly prob of using ACE, PPI, statins (n.s.) Plan med spending • Firm 1 intervention resulted in: 58%, 15%, 14% decrease in plan spending of ACE, PPI, statins (all significant at p<.001) *vs.* • Firm 2 intervention resulted in: -6%, -2%, 2% change in plan spending of ACE, PPI, statins (significant at p<.001, p=.02, p=.07)	• no rebates • filling a script does not mean enrollee takes script; discontinuation may also be due to spouse's benefit • results may not be generalizable • Firm 1 has hourly workers; firm 2 has salary workers → diff sensitivity to pay increases • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? YES o Drug utilization?

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groups of enrollees covered by the same insurers. SEE ALSO HUSKAMP 2005 – similar intervention (but w/ ADHD), methods See also Rector *Quality Rating:* Good	Firm 2: • Intervention: 11653 • Comparison: 27051 Number of users in intervention/ Comparison: Firm 1: • ACE: 2231/2596 • PPI: 3547/3850 • Statins: 2608/3391 Firm 2: • ACE: 659/1087 • PPI: 837/1822 • Statins: 933/1513 *Age:* N/A, but employees or spouses of employees *Other characteristics:* *Selection Criteria:*	among those w/ use identified in 1st part • logarithmic transformation of spending to address skewness *Timeframe:* 4/1/99-12/31/01 *Intervention:* Two interventions with 2 firms: Firm 1. 1-tier to 3-tier, including across the board increase in copayments • 1-tier: $7 for 30 day at retail pharmacy; $15 for 90 day via mail • 3-tier: 8, 15, 30 for 30-day @ retail; 16, 30, 60 for 90-day @ mail Firm 2. 2-tier to 3-tier • 2-tier: $6 generic, $12 brand name (same for pharmacy & mail) • 3-tier: $6 generic, $12 brand name, $24 nonpreferred brand name (same for pharmacy & mail) *Drugs/classes:* 3 classes: • ACE inhibitors • Proton pump inhibitors • Statins *Strengths:* Examined discontinuation of drugs	enrollee med spending • Firm 1 intervention resulted in: 141%, 148%, 118% increase in enrollee spending of ACE, PPI, statins (all significant at p<.001) *vs.* • Firm 2 intervention resulted in: 8%, 5%, 0.3% increase in enrollee spending of ACE, PPI, statins (ACE & PPI significant at p<.001) total spending • Firm 1 intervention resulted in: 0.3%, 3%, 0.7% decrease in total spending of ACE, PPI, statins (PPI only significant at p<.001) *vs.* • Firm 2 intervention resulted in: 3%, -0.4%, 2% change in total spending of ACE, PPI, statins (ACE significant at p<.001; statin significant at p=0.03) Medication continuation Firm 1: • intervention resulted in: 42%, 35%, 49% of enrollees switching to lower tier ACE, PPI, statins in intervention vs. 4%, 2%, 17% of enrollees switching to lower tier ACE, PPI, statins in comparison group; all 3 diffs significant at p<.001 • significant *fewer* of intervention group continued use of 3 rx classes compared to comparison group • significant *more* of intervention group discontinued use of 3 rx classes compared to comparison group Firm 2: • intervention resulted in: 41%, 18%, 49% of enrollees switching to lower tier ACE, PPI, statins in intervention vs. 15%, 2%, 8% of enrollees switching to lower tier ACE, PPI, statins in comparison group; all 3 diffs significant at p<.001 • significant *fewer* of intervention group continued use of 3 rx classes compared to comparison group Firm 2, discontinuation in contrast to firm 1: • *more* intervention discontinued statins vs. comparison	▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other NO o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO

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Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
			(n.s.) • *fewer* intervention discontinued PPI vs. comparison (n.s.) • *fewer* intervention discontinued ACE inhibitors vs. comparison : 8% vs. 16%; p=0.03 Use of alt drug • found no evidence that enrollees in intervention group taking 3-tier drug and stopped taking after intervention switched to alt class of drugs	
Huskamp et al (2005) *Objective:* To assess the effect of copayment increases assoc w/ a 3-tier formulary adoption on use and spending patterns for ADHD meds for children. See also Huskamp 2003 – very similar intervention (diff class), methods *Quality Rating:* Good	*Plan Type:* PPOs and POS plans from a single employer *PBM?* Yes-Medco *Region:* National ?? *SAMPLE Size:* 20,326 in intervention (839 used ADHD at some point); 15776 in control (530 used ADHD at some point) *Age:* 18 and under *Other characteristics:* Large national employer *Selection Criteria:*	*Design:* Observational study using quasi-experimental design – "JMP clustering algorithm" which is similar to propensity score matching *Statistics:* Pre and post nonequivalent design → difference in difference • 2 part model – 1st part = logit model of probability of using ADHD meds in given month; 2nd part = regression estimating monthly ADHD spending for children w/ ADHD use • logarithmic transformation of spending to address skewness *Timeframe:* 4/1/99-12/31/01 *Intervention:* Two interventions	monthly probability of using ADHD med Adoption of 3-tier from 1-tier resulted in - • 17% decrease in monthly probability of using meds (p<.001) • 20% decrease in *expected* total spending per enrollee for ADHD meds Plan ADHD med spending • Adoption of 3-tier from 1-tier resulted in - monthly plan spending decreased by 43% (p<.001) relative to control group • 2nd intervention of tier change: monthly plan spending increased by 17% (p<.001) relative to control group Enrollee ADHD med spending • Adoption of 3-tier from 1-tier resulted in - monthly enrollee spending increased by 46% (p<.001) relative to control group • 2nd intervention of tier change: monthly enrollee spending decreased by 7% (p<.001) relative to control group Total ADHD med spending • Adoption of 3-tier from 1-tier resulted in no significant change in TOTAL spending • 2nd intervention of tier change: no significant change in TOTAL spending	• Did not include rebates → estimates likely to be underestimates • study lacked the statistical power to determine precise differences in patterns of use when using relatively restrictive criteria for identifying a medication user • ideally would compare ADHD meds w/ other classes of long term use meds used by children • single employer w/ primarily hourly workforce for intervention vs. group of employers for comparison → may not be generalizable • could not control for income, other unobservables that could be important • study period ended before introduction of new ADHD drug Strattera • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? o Drug utilization? YES ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other NO o Medical utilization? NO

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		1. 1-tier to 3-tier, including across the board increase in copayments • 1-tier: $7 for 30 day at retail pharmacy; $15 for 90 day via mail • 3-tier: 8, 15, 30 for 30-day @ retail; 16, 30, 60 for 90-day @ mail 2. done 16 mo later: • 3 of brand name drugs in tier 3 (Metadate ER, Methylin ER, and Concerta) move to tier 2 For comparison group: • 2-tier formulary w/ stable cost sharing throughout study from multiple employers *Drugs/classes:* ADHD meds for children *Strengths:* 1st article to look specifically at ADHD meds among children Examined discontinuation of drugs	ADHD med continuation • Adoption of 3-tier from 1-tier resulted in lower proportion of intervention group staying w/ meds in same tier as comparison group (80% vs. 85%, p=.17); higher share of intervention group changing meds as comparison group (11% vs. 6%, p=.08) • 2nd intervention of tier change: no significant change diff in intervention vs. comparison group in ADHD med continuation rates (Table 4)	▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Huskamp et al (2007) *Objective:* To assess the effect of three-tier formulary adoption on medication	*Plan Type:* 4 retiree plans among "well insured seniors" *PBM?* YES – Medco *Region:*	*Design:* Quasi-experimental, Propensity score matching between the intervention and comparison groups, and pre/post analysis (difference in difference) *Statistics:* • Logistic regression for	Drug utilization (MPR) • Depending on the plan and class found either no or small effects (-0.03 to 0.06, p <.05) of 3-tier adoption on average MPR among those with some post period use, relative to matched comparison group. • Also found small *positive* significant effects (e.g., MPR for Plan C, ACE inhibitor use increased by 0.02) Nonpersistent use	• Popn had higher than ave income, more generous rx benes, richer than Medicare popn → may not be generalizable • Limited variability in median HH income for pt zipcodes-cannot do stratification • d/k rebates -effects on plan/total spending under-estimated • only know if pt fills script; does not necessarily mean pt takes rx

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
continuation and spending among elderly members of retiree health plans. *Quality Rating:* Good	*SAMPLE* *Size:* Intervention: 128900 • Plan A: 31311 • Plan B: 47108 • Plan C: 11929 • Plan D: 38552 Comparison: 109293 • Plan E: 49395 • Plan F: 59898 *Age:* 65+; mean age=mid 70s *Other characteristics:* *Selection Criteria:*	propensity score matching; • GEE w/ robust variance estimators (to account for potential mis-specification of the error and to account for multiple obs/individual) for MPR and spending • Logistic regression for nonpersistent use, discontinuation, and med changes *Timeframe:* 7/99-12/02 *Intervention:* Intervention: switch from 2-tier to 3-tier • Plan A: $5/15 to $5/20/35 for retail; $5/15 to $10/40/70 for mail • Plan B: $5/10 to $5/15/30 for retail; $5/5 to $10/25/45 for mail • Plan C: $10/20 to $7/20/30 for retail; $7/15 to $10/30/45 for mail • Plan D: $15/20 to $5/20/35 for retail; $20/25 to $20/30/45 for mail Vs. Comparison: 2 plans w/ no change to 2-tier • Plan E: $5/10 for retail; $8/15 for mail • Plan F: $4/12 for retail; $7/15 for mail *Drugs/classes:*	• ACE, ARB, CCB, statins – 11-18% of pre period intervention users experienced a gap >90 days in post period, depending on the plan • Rate of nonpersistent use higher for NSAIDS, PPIs SSRIs • Plan A significant more likely to have nonpersistent use in post period for all classes except NSAIDs, relative to comparison users • Plan B significant more likely to have nonpersistent use in post period for ACE, PPIs, SSRIs, and statins, relative to comparison users • Plan C significantly lower nonpersistent use for SSRI relative to comparison users • Plan D significantly lower nonpersistent use for CCB users, statin & NSAID, relative to comparison users Drug discontinuation • adjusted probability of discontinuation low overall • Plan A intervention significant more likely to discontinue for all classes except SSRI • Plan B intervention significant more likely to discontinue for statins, PPIs, SSRI • Plan C no significant diff between intervention and comparison in discontinuation rates • Plan D intervention significant more likely to discontinue for statins Med changes/drug switching • Intervention pts more likely to change from 3rd tier rx switched to lower tier after intervention particularly among cardiovascular rx • However, fewer than ½ of tier-3 users did change to lower-tier drug • Change rates lower for SSRIs, (ranging from 8% for Plan D to 19% for Plan A), which was only class where tier-3 users not significant more likely to change medications in any plan.	• d/k impact of reduced med on health outcomes, med spending, OTC use, hospitalization rates • cannot control for unobservables • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? o Drug utilization? YES ▪ Adherence YES ▪ Medication Possession Ratio YES ▪ Discontinuation YES ▪ Other o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO no explanation for positive effect of 3-tier adoption on MPR or for higher rates of nonpersistent use in the comparison group for subset of cases

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		7 drug classes used commonly by elderly: • ACE, • statins, • PPIs, • SSRIs • ARBs, • CCBs, • NSAIDs *Strengths:* • Switch in $ is more modest than in non-elderly research	Drug spending – patient, plan, total • implementation resulted in a shift in distribution of spending between plan and enrollee for almost all classes and plans studied (Table 4) • ACE: 1.1 to 6.28 pt, -1.67 to -7.72 plan; -.66 to 1.44 total • Statins: 1.18 to 5.13 pt, -2.81 to -9.49 plan; -4.36 to 0.37 total • PPIs: 2.26 to 4.94 pt, -13.39 to -2.61 plan; -8.56 to 0.49 total • SSRIs: 1.64 to 4.48 pt, -8.81 to 0.63 plan; -4.33 to 4.48 total • ARBs: 1.13 to 7.65 pt, -9.21 to -2.69 plan; -1.88 to 0.42 total • CCBs: 1.00 to 4.84 pt, -6.65 to -1.76 plan; -1.88 to 0.01 total • NSAIDs: 0.32 to 2.04 pt, -5.04 to 1.06 plan; -3.17 to 2.34 total	
Joyce et al (2002) *Objective:* To examine how innovations in benefits packages, such as those that include multitier formularies and mandatory generic substitution, affect total cost to insurance providers for generic and brand drugs and out-of-pocket payments to beneficiaries. Compares against	*Plan Type:* DK, but non managed care plans also included *PBM?* DK; assume NO *Region:* DK *SAMPLE Size:* • 420,786 benes from 25 employers w/ 1K+ employees • 55 unique med/pharm bene packages *Age:* < 65 yrs old	*Design:* Retrospective claims analysis. • used estimates from the 1st part of model to predict/simulate prob of nonzero expenditures for each person under alternative benefit designs and copayments. • Assumed 1-tier plans required mandatory generic sub (MGS) *Statistics:* 2 part model: • Probit to estimate prob that bene had at least 1 pharm claim • GLM w/ log link fn to estimate level of rx spending among people with at least 1 claim.	annual TOTAL drug expenditures: all, generic, single-source brand, multi-source brand • Increasing copayments w/in particular benefit design (i.e., tiers) significant reduced spending • 1 tier: increasing from 5 to 10 reduced annual average drug spending from $725 to $563/member; similar for generic (91 to 69); single-source brand (571-448) and multisource brand (63 to 46) • 2 tier: increasing from 5/10 to 10/20 reduced annual average ALL drug spending from $678 to $455/member; similar for generic (71 to 41); single-source brand (534-367) and multisource brand (73 to 47) • 3 tier: increasing from 5/10/15 to 10/20/30 reduced annual average ALL drug spending from $666 to $436/member; similar for generic (81 to 53); single-source brand (518-343) and multisource brand (67 to 40) • From above, can also tell that changing from a 1-tier to 2-tier plan reduced average drug spending. Adding	• examined a working age • popn w/ employer-provided drug coverage; may not be generalizable • did not control for plans that imposed higher copayments/ coinsurance rates for rx dispensed at out-of-network pharmacies. • No info on OTC meds • could not assess full impact of extremely high copayments • could not control for selection of health insurance plans b/c did not know full range of choices offered to employees. • Cross sectional analysis instead of following beneficiaries who actually changed tiers, so possibly bias if didn't control for all possible confounding vars • Rebate $ included? NO • Patient cost? YES

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Motheral *Quality Rating:* Good	*Other characteristics:* • Excluded employers w/ fewer than 1000 employees • 2 of 25 firms had choice of drug plans *Selection Criteria:*	Done for each outcome of interest • Adjusted for clustering of pts w/in plans *Timeframe:* 1/1/97-12/31/99 *Intervention:* None per se; rather, comparison of 4 diff plan types and simulations of differences described above (Table 3): • 15 Coinsur plans: 20% or 30% for all rx. Ave=27.3% • 15 1-tier plans: ave=$6.67 (2-10; mode=6) • 36 2-tier plans: 5.47/ 12.51 • 9 3-tier plans: ave=$5.78/11.78/23.56 *Drugs/classes:* None specified *Strengths:* • Examined mandatory generic substitution (MGS); found to be alternative to adding additional level of copayment	another tier reduced spending further but by smaller % PLAN drug expenditures • Plan spending decreased within changes to benefit design PATIENT OOP drug expenditures • Patient OOP spending did not change substantially within specific benefit design → higher copayments offset by reduced drug use • Fraction of costs borne by patients rose substantially: • 1 tier: increasing from 5 to 10 → 17% to 22% of costs borne by pt • 2 tier: increasing from 5/10 to 10/20→ 18% to 26% of costs borne by pt • 3 tier: increasing from 5/10/15 to 10/20/30 → 20% to 32% of costs borne by pt • Coinsurance: 26% of costs borne by pt MGS • adding MGS in 2-tier plans significant reduced total drug spending by $36 to $52 per person (8% reduction) • Requiring MGS reduced expenditures on multisource and single source brands, but had no appreciable effect on generic drug spending • Separate analysis (not shown) found modest increase in generic rx w/ little change in total prescriptions w/ addition of MGS.	• Plan cost? YES • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Kamal Bahl et al (2004) *Objective:* To examine association between incentive-based	*Plan Type:* Employer, health plans, and public org found in Medstat Market Scan database. Can be PPO, HMO, or comprehensive plan	*Design:* • Cross-sectional analysis of 42 diff plans. • NOTE: no change took place *w/in* plans (i.e., no intervention per se); just comparison *across* static plans.	Use of hypertensive drugs Descriptive: • Multi-tier assoc w/ lower use of all antihypertensives; not seen in 1-tier • 2-tier: # of rx is constant (15.4-16) • 2-tier: ave use drops from 18.9 scripts to 14.5 w/ copayment increase of at least $5 to at least $10 for brand name products; fell to 10.8 scripts when brand	• cross-sectional study design does not permit us to differentiate between whether tiered benefit design features are responsible for lower drug spending or whether plans with lower antihypertensive drug spending are more likely to adopt multi-tier formularies • possible selection bias - selection bias.

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
formularies and antihypertensive drug selection and spending. *Quality Rating:* Good	*PBM?* N/A so assume no *Region:* D/K *SAMPLE Size:* 149,243 pts enrolled in 42 drug benefit plans. Of drug bene plans: • 18 1-tier • 20 2-tier • 4 3-tier *Age:* 18+ *Other characteristics:* Had to have diagnosis of hypertension and using anti-hypertensive meds *Selection Criteria:*	*Statistics:* Logistic regressions for use Log-transformed OLS for expenditure and change in spending *Timeframe:* 1999 *Intervention:* • None per se; see Design above for details Grouped 42 plans into 7 broad categories defined by # tiers and copayments: • 1 tier, $0.50-4 • 1 tier, $5-10 • 1 tier, $12-15 • 2 tier, $1-4/$5-8 • 2 tier, $5-10/$10-15 • 2 tier, $3-8/$14-18 • 3 tier, $5/10-15/15-25 Use $$ amt as well as copayment differential between tiers w/in category *Drugs/classes:* Anti-hypertensive, analyzed by 5 classes: • Diuretic (generic avail) • beta blocker (generic avail) • CCB (generic avail) • ACE inhibitor (NO generic avail) • ARB (NO generic avail)	name copayments increased to at least $14 • 3-tier: lowest ave use rates – 13.6 scripts and relative high generic use (28% total spending) Multivariate: • no significant diff between plans w/ higher copayments (i.e., more tiers) and diuretic or beta blocker use • 2 tier, $3-8/$14-18 group: compared to cheapest 1-tier, ARB use significant lower (0.65) and ACE use significant lower (0.86). has important implications with respect to side effects • 2 tier, $1-4/$5-8: compared to cheapest 1-tier, use of CCB significant higher • 2 tier, $5-10/$10-15: compared to cheapest 1-tier, use of ACE inhibitor significant higher • no significant diff in use of any 5 classes of drugs in 3-tier as compared to cheapest 1-tier Person-level spending (OOP) of hypertensive drugs Descriptive: • 1-tier: OOP costs rise steadily as copayments increase • 3-tier: highest OOP and share of total spending Multivariate (Predicted): • From cheapest 1-tier to other 6 plans – predicted % increase in OOP ranges from 119% to 609.5%. Highest % change is w/ 3-tier Predicted change in plan level spending of hypertensive drugs • From cheapest 1-tier to other 6 plans – predicted % decrease in health plan spending from -15% to -51.9%. Highest % change is w/ 2 tier, $3-8/$14-18 (3-tier is -51.2%) Predicted change in total spending • From cheapest 1-tier to other 6 plans – predicted %	Plans with more tiers might be attracting enrollees with less severe hypertension and thus less costly medication needs. • could not control for enrollees' income • small number of 3-tier plans • did not examine use and costs of medical services • significant differences of most characteristics across tier status and copayment levels (end note 10). • Cost estimates are "illustrative only" – hypothetical since only cross-sectional design • Cross sectional • Rebate $ included? NO • Patient cost? YES but see above note • Plan cost? • Utilization? YES o Drug utilization? ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other NO o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		Strengths: • Focusing on 1 type of drug "reduce some of the complexities" (p.228) assoc w/ single to multi-tier • 1 of 1st to examine at level of therapeutic drug class • Controlled for whether plan had mail-order pharm option (cost sharing lower)	decrease ranges from -8.9% to -38.6%. Highest % change is w/ 2 tier, $3-8/$14-18 (3-tier is -20%) Descriptive stats • significant differences of most characteristics across tier status and copayment levels (end note 10). Study sample: • 33% of study sample in 1-tier • 52% of study sample in 2-tier • 14% of study sample in 3-tier • Most enrollees had $5 copayment • Over 60% had no/modest incentive (< $5) to use generics • Ave spending: $255-485/person; lowest amts assoc w/ plans w/ highest copayments	
Landon et al (2007) *Objective:* To examine the impact of incentive formularies on prescription drug spending shifts in formulary compliance, use of generic medications and mail-order fulfillment in the year after introduction of a new pharmacy benefit strategy. *Quality Rating:* Good	*Plan Type:* HMO, POS single health plan *PBM?* N/A so assume no *Region:* 11 states in northeast and mid-Atlantic regions *SAMPLE* *Size:* ~600K members across 7 cohorts; sub samples of below in analysis • Coh1: 67001 • Coh2: 71529 • Coh3: 37277 • Coh4: 54756 • Coh5: 2835 • Coh6: 146186 • Coh7: 226703	*Design:* • Propensity score matching within cohort, then pre/post intervention comparison • Difference in difference *Statistics:* • t-test for continuous vars • chisq for dichotomous vars • paired t-test chisq for propensity score matching from generalized estimating equations for grouped (paired) binomial data. *Timeframe:* 1/1/00-12/31/01 *Intervention:* 1/1/01 change:	Formulary compliance • 1-4% decrease in use of nonformulary drugs; increase in generic and formulary drugs. i.e., not deleterious effects on health from cost sharing (unlike other studies' findings – see p.368) • increase in generic and brand formulary utilization inconsistent across groups, suggesting little generic substitution; may be b/c difference in copayments between generic and formulary preferred agents generally small ($5) Mail order fulfillment • low at baseline; ranged from 1-13%. Doubled after intervention. Significant diff in diff between control/intervention for 9 of 12 groups (table 4) Spending-health plan • changing from a 1- or 2-tier to 3-tier with concomitant higher copayments in 2nd and 3rd tier associated with decrease in PLAN spending of ~20% (higher than decrease in total spending)	• Commercially insured beneficiaries in single health plan in single region of country, so not generalizable to poor, elderly, other regions • Single year of f/u , so might be effects after 1st yr that they don't capture • Did not adjust for clustering w/in employer group, so possible underestimation of s.e. with within employer effects • Rebate $ included? YES • Patient cost? YES • Plan cost? YES • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Age: <64 years old *Other characteristics:* • 57% of benes were w/ firms w/ at least 100 employees *Selection Criteria:* • Included states w/ min of 10k enrollees • Eliminated enrollees assoc w/ firms w/ <5 enrollees	• Created 7 cohorts w/ same pharm bene in 00; part of each cohort switched on 1/1/01 (intervention) • Coh1: $5 1-tier matched to 5/10/25 & 10/15/30 • Coh2: $10 1-tier matched to 10/15/30 and 5/10/25 and 5/15/25 • Coh3: $10/15 2-tier matched to 10/15/30 • Coh4: $5/10 2-tier matched to 5/10/25 and 5/15/30 • Coh5: $5/10 2-tier matched to 5/10/25 • Coh6: 10/15/30 3-tier matched to 15/25/35 and 5/10/25 • Coh7: 5/10/25 3-tier matched to 10/15/30 *Drugs/classes:* None *Strengths:* • Accounted for rebates by using the "average" value of rebates per rx for formulary preferred products p.361-2. • Includes intervention w/ *decrease* in tier prices, too (group 6d) • Large and diverse # of tier changes • Look at mail order change • This article compares/lists limitations of several other studies (e.g., Joyce 2002; Motheral and Fairman; Gibson;	Spending – patient • changing from a 1- or 2-tier to 3-tier with concomitant higher copayments in 2nd and 3rd tier associated with increase in OOP spending between 20-100%. Magnitude related to degree of change & # tiers Drug Spending – TOTAL • changing from a 1- or 2-tier to 3-tier with concomitant higher copayments in 2nd and 3rd tier associated with decrease in total drug spending of 5-15%. For all drug spending – • results were opposite direction (lower OOP, higher plan, higher total) for intervention w/ *decrease* in tier prices (group 6d) • changes happened immediately after intervention; stable over following year	▪ (spillover) • Health outcomes? NO • Had to use average rebate values instead of actual $ amt → in realty they vary by drug class.

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Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		Thomas)		
Landsman et al (2005) Objective: To estimate responsiveness of prescription demand within 9 therapeutic classes to increased cost-sharing compared with constant cost-sharing *Quality Rating:* Fair	*Plan Type:* Studies 4 plans: 3 switched from 2 to 3 tier; 1 did not switch at all. One of the plans that switched only changed PPO and not HMO *PBM?* *Region:* Northeast, South, Southeast *SAMPLE Size:* *Age:* *Other characteristics:* *Selection Criteria:* Patients must be continuously enrolled in plan for study period and had 2 or more prescriptions in one of 9 drug classes before benefit change	*Design:* Pre-post quasi-experimental analysis *Statistics:* Wilcoxon signed-rank test used for medication adherence, switching within drug class, and discontinuation rates between pre and post periods *Timeframe:* 1999-2001 *Intervention:* Change from 2-3 tier *Drugs/classes:* ACEI, CCBs, ARBs, COX-2 inhibitors, NSAIDS, SSRIs, TCAs, Statins, Serotonin 5-HT, and triptans *Strengths:*	Drug Persistence • Statistically significant reductions among patients continuing on same meds or switching to another in same drug class after benefit change – 6.8% reduction in NSAIDs to 1.7 increase in COX-2 • For ARBs the differences in ARBs were greater for treated groups than controls. • Substitution rates increased in treatment groups but decreased in controls. Only 3 diffs were statistically significance: statins, NSAIDs, and triptans. • Changes in discontinuation rates in drug classes ranged from an increase of 25.7% among ARBs and a reduction in triptans by -1.4%. These were statistically different from controls Elasticity of Demand • Elasticity of demand varies by drug class from -0.1 for Statins to -0.6 for NSAIDs	• Discontinuation rates might have been overestimated for NSAIDs and COX inhibitors and ACE and ARRBs because patients might have switched to a different protect in a different drug class for the condition. For some cases such as triptans patients might use OTC therapy • Study was limited to retail pharmacies alone. • Elasticity estimates are conservative because enrollees were required to have 2 or more prescriptions in class before benefit change • Rebate $ included? No • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Actual adherence to medication was not examined and only prescriptions were examined o Medical utilization? NO • Health outcomes? NO
Linton et al (2009) Objective: To quantify changes in (a) the TRICARE beneficiary utilization of esomeprazole relative to other PPIs	*Plan Type:* *PBM?* *Region:* *SAMPLE Size:* 1478815	*Design:* 6 mo pre/18 mo post Intervention Design *Statistics:* Interrupted Time Series Regression Analysis w/out comparison group Bivariate analysis/ Pearson's	(Fig 1) Change in use of esomeprazole relative to other PPIs • Esomeprazole (Brand): significant increase in use pre-intervention. Significant decrease in use at intervention (25% in calendar mo post reduction); no significant decrease in f/u period from intervention • Omeprazole (Generic): significant increase in use pre-intervention. Magnitude of increase in use	• No comparison group • Did not examine spillover in other health care service utilization • Only a 24 mo period; 6 mo pre limited statistical power to detect differences pre/post • No non-rx medication usage may have inflated discontinuation rate if users

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
and (b) the pharmacy settings used for filling esomeprazole prescriptions following implementation of a copayment increase and non-preferred formulary status for esomeprazole. *Quality Rating:* Fair	• PPI users: 1242228 • esomeprazole users: 222204 *Age:* *>=18* *Other characteristics:* *Selection Criteria:*	chisq for dis-/continued use among esomeprazole users *Timeframe:* 1/1/05-12/31/2006; intervention on 7/15/05 *Intervention:* • $13 copayment increase from $9 to $22 for PPI esomeprazole • $0 copayment if obtained from military pharm w/ prior authorization (PA) *Drugs/classes:* Esomeprazole/PPIs *Strengths:* • Looked at 0% copayment when accompanied by PA • Look at mail order change	significant directly after intervention and at time after intervention • Other PPI (Brand): significant decrease in use pre-intervention. Significant increase in use at intervention; significant decrease in f/u period from intervention Outcome 2a changes in the pharmacy setting used for esomeprazole (Fig 2) • Military pharmacy: small but significant increase in % of esomeprazole users after intervention • Community pharm: significant decrease in % of esomeprazole users after intervention • Mail order: small but significant increase in % of esomeprazole users after intervention Outcome 2b changes in the pharmacy setting used for all PPIs • Military pharmacy users as a proportion of all PPI users decreased (P < 0.001) • use of community pharm and mail-order pharm increased (P < 0.001) Continued Esomeprazole Use after intervention • bivariate comparisons with gender, age group, enrollment status, and pharm setting VS. any setting used or VS different setting used. See Table 4. Discontinued Esomeprazole Use after intervention • bivariate comparisons with gender, age group, enrollment status, and pharm setting VS. switched to preferred PPI VS. switched to non-PPI therapy VS. discontinued all acid-reducing therapy. See Table 4.	elected to switch to OTCs • A ton of information, not especially well presented • Very simple statistics (bivariate I think) for dis-/continuation analysis • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? o Drug utilization? ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other YES o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Mager et al (2007) Objective: To evaluate the	*Plan Type:* *PBM? Yes*	*Design:* Cross sectional study of plan sponsors *Statistics:* Logistic Model	Generic Fill Rate • Plans with 1 step-therapy program showed average GFR that was 2.7% higher than sponsors with no step-therapy. • Compared with flat-dollar 3-tier benefit designs, flat-	• Analysis limited to retail claims only which may have biased GFR upwards for clients with a higher proportion of home delivery claims.

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Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
relationship between generic and brand copayment differentials and generic fill rate *Quality Rating:* Fair	*Region:* *SAMPLE* *Size:* 3979 *Age:* *Study at level of plan sponsor not patient* *Selection Criteria:* Eligible if sponsor was with ESI for year 2005 and did not experience a benefit design change during the year, represented a commercially insured plan, offered a subsidized benefit to members, adopted 1 of 2 standard ESI formularies and had at least 100 members	*Timeframe:* *Intervention:* *Drugs/classes:* *Strengths:*	dollar 2-tier benefit designs flat coinsurance, and tiered coinsurance had est. GFRs that were 2.0, 1.5, and 1.2 points lower. • Compared with plans with $0-$5 copayment differential – those with diffs between $11 and $15 had an increase in GFR of 1.9%, whiles those with $16 to $20 increase had a 2.9% GFR increase and diffs >=$21 had a GFR increase of 5.2%	• Rebate $ included? no • Patient cost? Yes in terms of tier changes but not overall costs. • Plan cost? • Utilization? o Drug utilization? NO o Medical utilization? NO • Health outcomes? NO
Mahoney (2005) *Objective:* In response to a 13% cost surge in 2000, Pitney Bowes redesigned their pharmacy benefits for diabetes drugs to help reduce pharmaceutical non-adherence. *Quality Rating:* Poor	*Plan Type:* Self-insured and fully-insured health plans at Pitney Bowes *PBM?* No *Region:* Does not specify, but approximately 25% of employees are in NY, NJ, CT; remaining employees are dispersed across the other states *SAMPLE* *Size:* 23,000 (all US) Pitney Bowes	*Design:* Descriptive study of how a tier change in brand name drugs for diabetes affects adherence, costs, and healthcare utilization *Statistics:* Descriptive analysis *Timeframe:* 1/2001-12/2004 *Intervention:* • Pre intervention, Pitney Bowes used 3-tier system: 10% (most generics), 30% (most preferred brand name drugs), and 50%	Cost for patient with diabetes • Average cost of 30-day prescription supply decreased by 50%. Many patients were paying 80% less than previous drug costs Rates of adherence • Suboptimal adherence to insulin therapy decreased by two-thirds • Members adhering to fixed-combination oral hypoglycemics increased from 9% to 22% • Usage of blood glucose meter test strips increased from 28% to 55% Company's pharmacy costs • Total pharmacy costs increased from about $26 per month to $35 per month between 2002 and 2004	• No comparison group • Very little detail given about sample, number of patients with diabetes, etc. • Pitney Bowes was also enhancing its diabetes disease management and wellness efforts in parallel with pharmacy benefit changes (e.g., glucometers were supplied free of charge to employees with diabetes), which could be a confounder • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? YES o Drug utilization? ▪ Adherence YES ▪ Medication Possession Ratio NO ▪ Discontinuation NO

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	employees *Age:* Not specified, but average age=41 yrs	(non-preferred brand name drugs) coinsurance. • Post intervention, Pitney Bowes moved all medications (i.e., including brand name) for asthma, diabetes, and hypertension to tier 1 (10% coinsurance). • Intervention occurred 1/2002 *Drugs/classes:* • Diabetes is focus of article, but intervention also decreased cost-sharing for asthma & hypertension *Strengths:*	Patient pharmacy costs among members with diabetes • Pharmacy costs decreased by 7% among members with diabetes Overall per-patient cost of care for members with diabetes • Decreased by 6% among members with diabetes between 2001-2003 ER visits among members with diabetes • Rate of ER visits dropped by 26% for members with diabetes Hospital admissions among members with diabetes • Hospital admission rates increased by 19% among members with diabetes Annual employee healthcare costs • On average, increased 8.1 from 2000-2003 vs. composite annual of 12-15% for benchmark companies	▪ Other o Medical utilization? ▪ ER YES ▪ Hospitalization YES ▪ (spillover) NO • Health outcomes? NO
Meissner et al (2004) *Objective:* To assess the impact of a $10 increase in prescription copayment in a public employer health plan for 3 classes of drugs used for allergic rhinitis *Quality Rating:* Fair	*Plan Type:* Public employer health plan run by private managed care org *PBM?* *Region:* *SAMPLE* *Size:* 2150 patients who received NS or LSA prescription *Age:*	*Design:* Before and after intervention time-series design *Statistics:* t- and chi-square tests to assess differences in mean age, mean prescriptions per patient per month, mean number of study prescriptions, and chi square to test gender differences and percent of new versus refill prescription *Timeframe:* 1998 and 1999	Outcomes • No statistically significant difference in the average number of prescriptions dispensed per patient. • Number of patients receiving LSA increased by 11.8% with 41% increase in a average copayment • number receiving NS decreased by 10.2% with 71% increase in average copayment • Arc elasticity for LSA was 0.39 and for NS was -0.22. • No effect on combined utilization measures.	• T-tests on non-independent samples and this could produce bias • No control group • Are these drugs substitutes for each other? • There are tests for non-independent samples – I don't know why they didn't use them. • Rebate $ included? No • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Costs only considered actual

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Other characteristics: *Selection Criteria:*	*Intervention:* $10 increase in copayment *Drugs/classes:* Low sedating antihistamines (LSA) and Nasal Steroids (NS) *Strengths:*		utilization or non-filling of prescriptions not considered o Medical utilization? ▪ Not considered • Health outcomes? NO
Nair et al (2002) Objective: To evaluate the effects of 2- and 3-tiered pharmacy benefit plans on member attitudes regarding their pharmacy benefits *Quality Rating:* Fair	*Plan Type:* large managed care organization in Western US – with HMO, PPO, and Medicare+Choice *PBM?* *Region:* *SAMPLE Size:* *Age:* *Selection Criteria:* 5 chronic disease: hypertension, diabetes, dyslipidemia, GERD, and arthritis	*Design:* Cross sectional mail survey design *Statistics:* Chi-Square and T-tests combined with OLS and Ordinal regression models. *Timeframe:* *Intervention:* *Drugs/classes:* *Strengths:*	Note: Only discussing relevant outcomes Member Satisfaction and Loyalty • 3 tier plan members were 10.% less satisfied than 2 tier members with prescription drug coverage. • 3-tier plan members were 9.6% less likely to recommend their prescription drug coverage than 2-tier plans • No differences in type in likelihood of members selecting a plan based on availability of meds on formulary. Willingness to Pay Extra to purchase higher priced Medications • No statistically significant differences observed between tier types	• Respondents appear to be self-selected who are older, sicker, with greater cost-sharing and hence eager to respond. • Unmeasured differences between 2 and 3 tier plans • Survey data was cross-sectional and long term predictions may vary • Other covars might exist. • Rebate $ included? No • Patient cost? Yes • Plan cost? • Utilization? o Drug utilization? No o Medical utilization? No • Health outcomes?
Nair et al (2003) Objective: To evaluate impact of 3-tier copayment pharmacy benefit structure on	*Plan Type:* large managed care plan in Western US including HMO, PPO, and Medicare+Choice *PBM?*	*Design:* Pretest-Posttest quasi-experimental with comparison group. 2 tier moving to 3 tier, 2 tier remaining 2 tier and 3 tier remaining 3 tier. *Statistics:* Bivariate tests, ML	Formulary Compliance Rates – (Formulary Prescription Claims/total claims) • The formulary compliance rates in the treatment group was lower in the postperiod compared to the preperiod – the comparison groups remained the same. • These differ by disease – diabetics are more	• Did not include actions individuals took after discontinuing medication • Groups were not homogenous in demographic characteristics • The study only looked at overall changes in copayments but not the actual difference in cost sharing at various

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
medication utilization behavior *Quality Rating:* Good	*Region:* Western US *SAMPLE* *Size:* 8132 members *Age:* *Other characteristics:* *Selection Criteria:* One of 5 chronic diseases: hypertension, diabetes, dyslipidemia, gastroesophageal reflux disease, and arthritis with 2 prescriptions for the diseases from Jan 1 to May 31 2000.	repeated-measures model, and logistic regression for discontinuation of nonforumulary medications *Timeframe:* June 1,2000 – July 31,2001 *Intervention:* Moving from 2 to 3 Tier copayments *Drugs/classes:* *Strengths:*	formulary compliant than those not taking prescriptions for diabetes- individuals with GERD are less compliant than others. Generic Use Rates • All 3 groups saw an increase in generic use in the post period – the increase was highest in the treatment group (4.9%) compared to 4.8% and 3.3% Discontinuation Rates for Nonformulary medications • Pharmacy benefit structure was significantly associated with discontinuation behavior for nonformulary meds • Individuals in converting group were 1.76 times more likely to discontinue than in 2 tier comparison group and 1.49 times more likely than the 3-tier comparison group.	phases of payment. • Study period might not be long enough to capture full impact of change • Using claims as a proxy for diagnosis is a problem because of the off-label use of drugs. • Rebate $ included? NO • Patient cost? NO • Plan cost? • Utilization? o Drug utilization? ▪ The study mentions MPR briefly but doesn't appear to discuss its usage in detail. ▪ Also the study only focuses on claims and not actual utilization o Medical utilization? ▪ ER and spillover costs are not discussed at all • Health outcomes? NO
Rector et al (2003) *Objective:* To estimate the effect of tiered copayments on the choice between preferred and nonpreferred brand medications *Quality Rating:* Good	*Plan Type:* 4 health plans in state and use same list of preferred drugs *PBM?* Yes *Region:* One state *SAMPLE* *Size:* Unit of analysis was prescription claim by drug class ACEI: 4585 (NT), 1690 (T) PPI: 7177 (NT) 886(T) STATIN: 13475(NT) 1637(T)	*Design:* Longitudinal time-series comparing concurrent groups that were exposed or not exposed to tiered copayments (really a DID design) *Statistics:* Logistic regression analysis *Timeframe:* 1998-1999 *Intervention:* adoption of tiered copayments *Drugs/classes:* ACEI, PPI and	(Change in Percentage of Prescription Claims for Preferred Brands) • Average 6%-13% increase in relative use of preferred brands during 21 month observation period • Size of copayment differential $18 v. $15 does id not have a significantly greater effect	• Study could have underestimated the effect if the tiered copayments were adopted before the period of observation • Not a representative sample and had non exclusive contracts with practices that prescribed medications. • State law required coverage of nonpreferred drugs at preferred copayment when the physician felt the drug was medically necessary • Rebate $ included? NO • Patient cost? Total patient costs effect equation this was not considered • Plan cost? Plan switching because of premium costs and/or copayments not

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Age: Not specified *Other characteristics:* *Selection Criteria:*	Statins *Strengths:*		considered • Utilization? o Drug utilization? NO ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Roblin et al (2005) *Objective:* Estimate the effects of small, moderate and large increases in medication cost-sharing on 12 month trend in oral hypoglycemic usage among adults with type 2 diabetes *Quality Rating:* Good	*Plan Type:* 5 Managed Care Orgs *PBM?* *Region:* Northeast, Southeast, Midwest, West *SAMPLE* *Size:* 26220 episodes in 20933 enrollees *Age:* >=19 *Other characteristics:* *Selection Criteria:* Should have received at least one OH dispensing between 04/01/1997-06/30/1999 and had outpatient pharmacy benefit. Episodes of OH for several medications were excluded	*Design:* longitudinal time series comparison with pre-intervention 6 months, intervention month, and post intervention 6 months. Compared to group with no change in cost sharing. *Statistics:* Segmented time-series regressions *Timeframe:* 04/01/1997-06/30/1999 *Intervention:* Small, Medium, or Large Increase in Cost Sharing – primary indep var measured in $ *Drugs/classes:* *Strengths:*	(Standardized Oral Hypoglycemic [OH] Average Daily Dose per month) • Large cost sharing increases in the intervention month led to a 3.6% decrease in OH use during episodes. This was not different from 0.0000 but was significantly different from the 5.6% increase in OH in the no-cost increase group. • 6 months after cost increase the OH ADD was down by 18.5%	• The OH episodes were 12 months duration • Length of time series might not be long enough to capture effects of moderate cost sharing increases because of the increase adds up over refills. • This could limit generalizability. • Rebate $ included? No • Patient cost – Total patient costs with other drugs not considered • Plan cost? - Unclear • Utilization? o Drug utilization? ▪ Drug utilization is the focus but spillover and ER costs are not considered. ▪ Issues that could help diabetes control such as exercise and nutrition not considered o Medical utilization? ▪ Not discussed • Health outcomes? Study does not consider the overall health outcomes

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
				from increase or decrease in hypoglycemic utilization – also unclear if improvement in condition is considered
Shrank et al (2007) *Objective:* To determine if physician, patient, pharmacy benefit design, or pharmacy chars influence the likelihood of patient using generic drugs *Quality Rating:* Fair	*Plan Type:* Anthem BCBS and Anthem Prescription Management *PBM?* Yes *Region:* Colorado & Nevada *SAMPLE* *Size:* 5,399 *Age:* *Other characteristics:* *Selection Criteria:* Continuously enrolled in plan 01-03 and filled new prescription in one of the 6 classes	*Design:* Observational study *Statistics:* GEE models to account for physician clustering *Timeframe:* 2001-3 *Intervention:* *Drugs/classes:* 6 drug classes Calcium Channel Blockers, Statins, Oral Contraceptives, ACE-1s, H2RA and PPIs *Strengths:*	(Patient Initiated on Generic Medication) • Income proxies affect initiation on generics – low income least likely to start on generics • Tiers had no impact (Patient Switched from Branded to Generic only on subsample starting with branded) • Plans with 3 tiers of copayment but relatively low copayments were 2.61 times more likely to switch than patients in 1 or 2 tier plan • Patients in 3 or 4 tier were almost 4 times more likely to switch • Mail orders were 65% more likely to switch • Age gender and OB-GYN had an effect.	• Only filled prescriptions were assessed and not prescriptions written • Prescriptions changed before fill not considered • Low income patients not prescribed generics might not have filled brand prescriptions leading to inflated estimates. • Perceived efficacy of branded v. generic not considered. • About 20% of records did not have DEA # and this affects data quality • Rebate $ included? NO • Plan cost? • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Spence et al (2006) *Objective:* To compare likelihood of choosing strategies to reduce out of pocket expenses in generic only elderly COPD patients v.	*Plan Type:* Kaiser Permanente Generic Only, 1 tier and 2 tier copayments *PBM?* *Region:* California *SAMPLE*	*Design:* Study group was patients with generic only benefit with member discounts for brand medications. Comparison groups with single tier benefit against 2 tier benefit *Statistics:* Logistic regression	Discuss OOP costs with Physician • Generics only were 9 times more likely to discuss costs with physician than in single tier Purchase from another country • 7 times more likely Reduce spending on food and clothing • 4 times more likely	• Findings based on self-reported surveys and subject to recall bias and socially desirable response bias • Only half the survey sample responded • Might not be generalizable • Clinical variables in COPD population not considered and comorbidities not considered

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
those in 1 and 2 tier plans *Quality Rating:* Fair	*Size:* 3000 surveys sent to individuals with COPD – 1624 surveys returned *Age:* >65 *Other characteristics:* *Selection Criteria:* COPD diagnosis, no asthma diagnosis, at least 1 COPD prescription from Jan 2003-Dec 2004 – Members Excluded if dual coverage	*Timeframe:* 2003-2004 *Intervention:* None – Observational study *Drugs/classes:* COPD Medications *Strengths:*	Took less than prescribed amount • 1.7 times more likely Stopped taking Medication • 1.77 times more likely Shopped Around • 1.53 times more likely 2-tier v. single tier on these outcomes did not achieve statistical significance	• Rebate $ included? • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes?
Taira et al (2006) *Objective:* To measure impact of medication copayment level and other predictors on compliance with antihypertensive meds measured by medication possession ratio *Quality Rating:* Fair	*Plan Type:* HMO/PPO/Medicare Cost *PBM?* *Region:* Hawaii *SAMPLE* *Size:* 114232 drawn from pop of 650k members. *Age:* 18-107 years *Other characteristics:* Race/Ethnicity, Age sex, morbidity level, insurance type and therapeutic classes of meds were included.	*Design:* Members of a single plan with hypertension were retrospectively analyzed for compliance with medication *Statistics:* Logistic Regression *Timeframe:* 5 years (1999-2004) *Intervention:* Use of prescriptions at higher level of formulary tier *Drugs/classes:* Antihypertensive medications in all therapeutic classes *Strengths:* All members of plan used same	(Medication Possession Ratio) • Sum of total days of compliance per year across all prescriptions divided by # of days of drug coverage (0.8 = compliant) • Overall compliance was 66.8% in T1, 66.1% in T2 and 54.6% in T3. Angiotensin receptor blockers had highest compliance. • Relative to Tier 1 odds ratio for T2 compliance was 0.76 and for T3 was 0.48 • Adjusted odds ratio increases with other predictors. Patients >65 were most likely to remain compliant and patients 40-64 were 2x as likely to be compliant as <40. Patient sex had negligible effect. • High morbidity led to lower compliance. Ethnicity appeared to support compliance	• Study population from Hawaii and might not be generalizable • Outcome based on pharma claims and not actual medication consumption and did not consider free medication samples. • Could double count compliance for hospital days • Info on BP levels unavailable so goals not evaluated • All potential cofounders were not accounted for • Unobserved characteristics not included • Rebate $ included? NO • Patient cost? – Tier 3 drug copayments vary from $20-165 this variability could impact the result • Utilization? o Drug utilization?

Appendix I: Summary of Studies that Examined the Effect of Tiered Formularies				
Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Selection Criteria: (1) diagnosis of hypertension and (2) have filled at least 1antihypertensive prescription between Jan 1999 and June 2004	formulary – this eliminated plan selection bias		▪ Discontinuation does not appear to be specifically addressed ▪ Other o Medical utilization? • ER costs not considered in compliance

Appendix II: Features of Reviewed Prior Authorization Studies

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Adams et al. (2009) *Objective:* The purpose of the study was to evaluate the impact of the Michigan PA for nonpreferred antidepressants among nonelderly disabled dual (Medicaid and Medicare) enrollees. *Quality Rating:* Good	*Plan Type:* Medicaid & Medicare FFS *PBM?* Not mentioned so assume no *Region:* Michigan (treatment) and Indiana (comparator) *SAMPLE Size:* Continuously enrolled: Michigan, n=28 798; Indiana, n=21 769. Newly treated: Michigan, n=3671; Indiana, n=2400. *Age:* 18-64 years old *Other characteristics:* • Conducted sub-analysis of dual enrollees with depression, serious mental illness • Grandfathered prior users *Selection Criteria:* • Excluded patients with	*Design:* Interrupted time-series and longitudinal data analysis *Statistics:* • Patient-level effects assessed using generalized estimating equation (GEE) and survival analysis (Cox proportional hazard model). • Covariates included sex, age, race, ethnicity, level of comorbidity (as measured by count of total number of anti-depressants used at baseline), interaction term between state and post-intervention time segments. • Model fit was assessed using a Durbin-Watson statistic. Tested for autocorrelation and nonlinearity of the outcomes of interest. For parsimony, non-significant terms (P<.05) were excluded from final time-series models. *Timeframe:* 1/1/00-12/31/03 *Intervention:* • March 2002, when the MI Medicaid program began	Rate of antidepressant medication use by preferred status Among continuously enrolled dual enrollees: • MI: 1% point absolute decrease in use of nonpreferred SSRI/SNRI agents, accompanied by declining trend post policy (P<.001), which were largely offset by an increase in the use of preferred SSRI agents. Changes in MI were driven by a shift away from nonpreferred agents among newly treated patients. More than 50% of newly treated patients initiated on these agents pre-policy, fewer than 20% did so post-policy. • IN: 2% (P<.01) absolute increase in use of nonpreferred SSRI/SNRI agents, accompanied by declining trend post policy (P<.001). Rate of therapy initiation • Slight decrease in number of MI dual enrollees starting any antidepressant therapy immediately following PA policy (P=.02), but no change in level or rate of antidepressant therapy initiation among IN dual enrollees. • For subgroup of dual enrollees with depression, there was a slight declining trend in rates of antidepressant initiation in MI post-policy vs. stable trends in IN. Switching from Current Therapy • Found a 2-fold higher risk of switching during implementation among MI dual enrollees relative to IN overall (RR=2.07; 95% CI=1.48-2.88) and among those with depression (1.53; 1.01-2.32) • Dual enrollees taking nonpreferred agents (approx 49% of established users) had highest odds of switching	• Did not require patients to have a depression diagnosis (but performed sub-analysis of patients with depression). • Requirement of continuous enrollment may have reduced generalizability of findings. • Did not have explicit justification for definition of new users. • measure of discontinuation may have been imprecise. • • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? YES o Drug utilization? ▪ Adherence YES ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other YES o Medical utilization? ▪ ER YES ▪ Hospitalization YES ▪ (spillover) NO • Health outcomes? NO

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	managed care	requiring PA for new prescriptions of nonpreferred antidepressants, including commonly used SSRIs (removed the PA policy in late June 2003). *Drugs/classes:* SSRIs *Strengths:* • Engaged an expert panel of clinical psychiatrists to provide internal review of study methods and interpretation of key findings.	therapy (overall, 2.88; 1.87-4.42; depression, 2.04; 1.22-3.42), but no evidence of increased risk during remainder of follow-up period Discontinuities in Therapy Among Newly Treated Patients • No evidence of greater risk of treatment disruptions in MI overall or among those with depression • Persistence with therapy was slightly higher in MI post-policy but not statistically significant Hospitalization and Emergency Visits Among Newly Treated Patients • No statistically significant differences in risk of hospitalization or ER visits in overall cohort, depression diagnosis, or serious mental illness • No statistically significant *changes* in rates of hospitalization or ER visits	
Delate et al. (2005) *Objective:* To examine clinical and financial outcomes associated with a proton-pump inhibitor (PPI) prior authorization (PA) policy *Quality Rating:* Good	*Plan Type:* Medicaid *PBM?* Not specified. *Region:* Not specified. *SAMPLE* *Size:* 1.2 million Medicaid enrollees – all enrollees *Age:* *Other characteristics:* All Medicaid enrollees *Selection Criteria:* Continuously eligible patients	*Design:* Interrupted time series analyses; separate 6-month retrospective cohort analyses *Statistics:* Interrupted time series with adjustment for time trend and effect of policy implementation; logistic regression controlling for: sex, age, race, Chronic Disease Score *Timeframe:* Preperiod -12 months pre 2/1/02; Postperiod – 12 months post 2/1/02 *Intervention:* PA required for all PPI prescriptions on 2/1/02 (prescribers and pharmacists were	Drug Expenditures (antisecretory drugs) • PPI drug expenditures decreased; H2A drug expenditures increased • Rate of PPI PMPM claims and expenditures decreased, and increased for H2A PMPM claims and expenditures in month immediately following PA policy • PMPM expenditures for antisecretory drugs decreased nearly 50% equal to a net expenditure decreased of $23.4 million for the Medicaid program Drug Use • Of the nearly 8000 enrollees who attempted to fill a PPI approximately 50% did not attempt to go through the PA process and of those over 50% had an H2A claim. Medical Utilization • PPI users were more likely to have had at least 1 GI-related ambulatory service in follow-up compared with nonusers (p<.05) • No increase for non-users and H2A users	• Did not measure effect of PA policy on prescribers' time • Did not include patient cost (but is Medicaid - low cost to patients?)

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		notified of change in advance). Because of prescriber/patient advocate complaints modified PA program on 4/1/02. PA valid 6 months. *Drugs/classes:* PPIs *Strengths:* • Sensitivity analysis excluding dual eligibles, and found similar results. • Included administrative costs of PA program in analysis	Medical Expenditures • [increases in mean net payments for GI-related and total medical service costs were not found for H2A or nonusers] • [H2A and nonusers no more likely to have had greater GI-related and medical service use or expenditures]	
Fischer et al. (2004) *Objective:* To evaluate the effect of PA policy on use of coxibs by Medicaid beneficiaries *Quality Rating:* Fair	*Plan Type:* Medicaid *PBM?* *Region:* 49 states (excludes Arizona) and DC *SAMPLE* N/A state-level *Size:* *Age:* *Other characteristics:* *Selection Criteria:*	*Design:* CMS state-level data, and survey of states on PA programs for coxibs *Statistics:* -Interrupted time series analysis - general linear models adjusting for repeated observations by using generalized estimating equations *Timeframe:* 1999 -2003 - 6 months pre and 6 months post *Intervention:* state PA programs - 22 states PA program between 2000 & 2003 - 20 states no PA programs control data *Drugs/classes:* Coxibs	NSAID Use • Use of NSAIDs increased driven by increased use of coxibs Drug Spending • Annual spending on NSAIDs increased by nearly $600M, almost all due to coxibs Prescription Drug Use • In states with PA programs, the proportion of coxib use decreased by average of 11.1% [CI 95%; 5.7 – 16.6] • PA program was associated with initial decrease in coxib use, followed by much smaller increase in use in subsequent use • PA program reduced the proportion of NSAID doses made up by coxibs by 15% [95% CI; 10.9 – 19.2] Coxib Use by Restrictiveness of PA • Similar reductions in coxib prescribing after implementation of PA programs in more restrictive and less restrictive states • States with more restrictive PA programs has lower levels of coxib use before implementation of program	• Couldn't examine clinical appropriateness of PA program • States with PA programs may differ from those without program • Unable to evaluate clinical appropriateness of PA program implementation • Unknown whether there were other benefit changes at time PA program initiated • 8 states excluded from time-series because implemented PA policies immediately after coxibs introduced to market • State-level data so no patient data or patient-level outcomes – costs, utilization, etc.

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
			than less restrictive Drug Spending $10.28 [95% CI; $7.56 - $113.00] reduction in spending per prescription corresponding with PA program; representing an 18% decreased in the cost per NSAID prescription.	
Gleason et al. (2005) *Objective:* To evaluate effects of COX-2 Inhibitor PA on direct medical and pharmacy costs *Quality Rating:* Fair	*Plan Type:* Large employer group's health plan & PBM *PBM?* Yes. *Region:* Midwest *SAMPLE* *Size:* Of 26,375 continuously enrolled members, 737 used COX-2 Inhibitor in the 3-months before the PA program *Age:* *Other characteristics:* *Selection Criteria:*	*Design:* Prospective, pre-post-implementation cohort study with reference group. *Statistics:* Student t-test, chi-square, b/c right-skewedness log-transformed and geometric means with SDs were used; $p < 0.01$ *Timeframe:* 3 month pre, and 3-month post; total 1 year follow-up after implementation *Intervention:* PA program began on January 1, 2003 for members not at high risk for a GI event *Drugs/classes:* COX-2 Inhibitors *Strengths:* ?? Electronic claim edit for patients with high risk of GI event to continue COX-2 w/o contacting doctor • included admin costs	For members who had no COX-2 inhibitor claims after PA program implementation: • Per member total pharmacy costs decreased a significant $126 (40%) and remained significantly lower during the year of follow-up • Medical costs declined 18.7% and remained significantly lower For members who tried to fill a COX-2 inhibitor prescription but were denied: • Pharmacy costs declined 48% and remained significantly lower • Medical costs initially declined 10.3%, but overall medical costs increased in the 2nd and 3rd quarter and seem to be associated with an increase in ER visits and hospitalizations, though none were associated with a gastrointestinal bleed, ulcer, or perforation in the diagnosis. • No change observed in physician office visits through follow-up • Per member pharmacy utilization and costs declined and remained significantly lower Net Plan Savings • >$78,000 for 1 quarter	• Lacks comparison group • Changes in disease status were not assessed, and eligibility for COX-2 Inhibitor was not adjusted for in follow-up • Potential regional variation in prescribing • One group's experience • 12-month follow-up limits probability of observing changes in GI adverse-events • Members paying out-of-pocket not captured in data • No patient costs • No patient health outcomes • No patient drug utilization and adherence
Hartung et al. (2004)	*Plan Type:* Medicaid MCO *PBM?*	*Design:* Retrospective, interrupted time services of 22 monthly health-related utilization	Utilization of Celecoxib • Reduced from 1.07 to 0.53 days' supply per person-year (58.9%; 95% CI; 50% - 67.9%)	• Potential selection bias given differences between intervention and control group, and FFS patients were generally older

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Objective: To evaluate the intended and unintended effects of a PA policy for celecoxib on pharmacy and medical-service utilization in a Medicaid MCO. *Quality Rating:* Fair	*Region:* Oregon *SAMPLE* *Size:* *Age:* *Other characteristics:*	rates; included reference group Control was Medicaid FFS *Statistics:* Linear regression *Timeframe:* 1/1/99 -10/31/00 *Intervention:* PA policy *Drugs/classes:* celecoxib	Utilization in Other Drug Classes • Changes in utilization were not observed for other drug classes. ER Visits • An 18% non-significant increase in ER visits was observed in entire sample; however, a similar change was not observed for prior NSAID users	and more likely to be more severely ill. • Insufficient sample size to detect impact of PA on medical claims for GI-related conditions • Did not evaluate individual changes • No HRQOL, functional status, or patients satisfaction measures • Instituted other formulary restrictions????
Law et al (2008) *Objective:* To examine the impact of prior authorization on antipsychotic medications in two state Medicaid populations. *Quality Rating:* Good	*Plan Type:* Medicaid *PBM?* Not mentioned so assume no *Region:* West Virginia and Texas *SAMPLE* *Size:* Not listed *Age:* Not listed *Other characteristics:* Grandfathered prior users *Selection Criteria:*	*Design:* interrupted time-series analysis of quarterly, publicly available aggregated state-level drug utilization data *Statistics:* • generalized least squares model and allowed for autoregressive structure with a one quarter lag to control for correlation between consecutive quarters. *Timeframe:* WV: 8 quarters before and 11 quarters post 4/9/03 TX: 8 quarters before & 7 quarters post 3/28/04 *Intervention:* • PA required for all second	Medicaid Market Share for non-preferred agents • WV: After implementation of PA, immediate drop of 3.5% (p=.003) in market share and a subsequent drop of 1.3% (p<.001) per quarter. This led to estimated market share reduction of 13.8% (p<.001). • TX: After implementation of PA, immediate drop of 2.6% (p=.055), but trend n.s. • No significant increase in market share of first-generation agents in either state post-PA Total Medicaid reimbursement of all antipsychotic medications • WV: no significant change in reimbursement level or trend. • TX: no significant change in reimbursement level. Reimbursement trend appeared to increase after PA by $441 per quarter (p<.01), but a decrease in costs in the control series of $360 per quarter (p<.01) largely explained this result (n.s. when a model was fit with TX data alone and controlled for the preexisting trend in the state). Reimbursement per defined daily dose to Medicaid of all	• Data quality concerns for total reimbursement in WV. • PA policies in WV and TX may not be representative of experience in other states and may differ in their authorization criteria, drugs covered, and implementation. • Does not include rebates, but provide discussion of how rebates likely to affect results • Rebate $ included? NO • Patient cost? NO • Plan cost? YES • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		generation antipsychotic prescriptions on 4/9/03 for WV (PA criteria: 14-day trial of preferred agent); 3/28/04 for TX (PA criteria: treatment failure, contraindication, or allergic reaction to preferred agent). • Constructed a control series using a weighted average of the 38 states that did not implement a PA policy for particular second- generation antipsychotic agents *Drugs/classes:* second- generation antipsychotic agents *Strengths:* Performed sensitivity analyses with 2 comparison groups: • Compared 2 policy states with 27 states without PA policies for any dosage form • Compared each state with three states in a similar geographic region or of similar size (OH, MD & VA for WV; AL, CA & LA for TX)	antipsychotic medications • No evidence of important changes in reimbursement per defined daily dose in either TX or WV post PA.	▪ (spillover) • Health outcomes? NO
McCombs et al. (2002) *Objective:* Effect of revocation of PA policy on patient	*Plan Type:* Medicaid (FFS or MCO?) *PBM?* *Region:* California	*Design:* ???? *Statistics:* Logistic regression models *Timeframe:* 9/94 – 1/99	Drug Therapy Completion • Aggregate rate of drug therapy completion dropped from 23.2% before the formulary change to 20.5% • Odds ratio for completing therapy relative to tricyclic antidepressant treated patients dropped from 3.916 to 1.706 in open access for fluoxetine-treated patients, and 1.591 and 0.726 in paroxetine-treated patients.	• Inconsistent findings (likelihood of completing therapy and likelihood of adding 2nd antidepressant decreased after change) may be due to exogenous factors • Claims data used for compliance

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
compliance *Quality Rating:* Fair	*SAMPLE* *Size:* 6409 patient treatment episodes	*Intervention:* Revocation of PA restrictions on SSRIs (fluoxetine and paroxetine) in 5/96 *Drugs/classes:* SSRIs	Switching • No change in likelihood of switching therapies	
Stacy et al. (2003) *Objective:* To determine from a health plan perspective the cost-effectiveness of COX-2 inhibitors, with and without a PA process. *Quality Rating:* Fair	*Plan Type:* Health plan with 3.8 million HMO and PPO members *PBM?* *Region:* *SAMPLE* *Size:* 96,154 members (3% of plan membership with a drug benefit) *Other characteristics:* All NSAID users and potential NSAID users (members who tried to get a COX-2 inhibitor but claim was rejected)	*Design:* Cost-effectiveness analysis using a decision tree Probabilities of serious GI event were obtained from literature. Health plan data were used for utilization and prescribing patterns *Statistics:* *Timeframe:* 1-year model *Intervention:* PA program *Drugs/classes:* COX-2 Inhibitor	Average Cost per Successful Treatment (no serious GI event) • Cost per success with PA was $278 versus $422 without PA	• Probabilities of GI events were obtained from published literature not actual events • Assumed 100% compliance rate • Did not examine effect of tiered copayments • Examined classes of drugs • CEA model, not actual costs or occurrences
Zhang et al (2009) *Objective:* To examine the impact of a PA policy in Maine on second-generation antipsychotic and anticonvulsant utilization, discontinuations	*Plan Type:* Medicaid (and Medicare, if dual enrollees) *PBM?* Not mentioned so assume no *Region:* Maine (study state) and New Hampshire (comparison state). *SAMPLE* *Size:* 5,336 patients in Maine (study	*Design:* Interrupted time-series and comparison group design, survival analysis, Kaplan-Meier survival curves. Examined newly treated for 8 months pre and post first prescription filled. *Statistics:* • Segmented time-series regression models, using three 8-month periods: pre, policy period, & post	Effects of prior authorization on use of medications • Prior to PA: prevalence of use of all nonpreferred medications was 30% in ME; 34% in NH with upward trend in both states • During PA: upward trend in ME reversed (PA associated with 8 point decrease); stayed unchanged in NH • Post PA: downward trend of antipsychotics in ME remained stable, but downward trend of anticonvulsants persisted (note that PA was still in effect for anticonvulsants) Pharmacy spending by Medicaid for bipolar medications	• Did not assess PA's impact on use of medical care. • Could not measure whether patients in either state obtained care in the other state's Medicaid program. • Did not account for possible savings from rebate • Rebate $ included? NO • Patient cost? NO • Plan cost? YES • Utilization? o Drug utilization? YES

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
in therapy, and pharmacy costs among Medicaid beneficiaries with bipolar disorder. *Quality Rating:* Good	state) and 1,376 in New Hampshire (comparison state). *Age:* 18 years or older *Other characteristics:* • Must have had at least one inpatient or two outpatient diagnoses of bipolar disorder (identified via ICD-9 code) during study period. • Patients were newly treated with any bipolar medications (i.e., no use of bipolar medications in 90 days prior to initial prescription). • Two newly treated cohorts: "policy cohort" initiated any bipolar medication between 7/1/03 and 2/29/04; "pre-policy cohort" initiated bipolar medication 7/1/02 and 2/28/03 (same calendar period 1 year before implementation of PA) *Selection Criteria:*	• Controlled for all significant autocorrelation terms and excluded n.s. (p≥.10) time-series terms step by step • Extended Cox regression models to examine impact of PA policy on hazard rates of treatment discontinuation & medication switching or augmentation in newly treated pre-policy and policy cohorts. • Cox hazard model included indicators for policy, state, and the policy-state interaction term ("difference-in-difference"). Also controlled for age, gender, dual enrollment, and two comorbidity measures (number of non-bipolar medications dispensed and number of inpatient admissions) *Timeframe:* 2001-2004 *Intervention:* • July 1, 2003, when ME Medicaid program began requiring PA for new prescriptions for nonpreferred agents used to treat bipolar disorder • PA discontinued 8 months later (March 2004) for antipsychotics but remained in effect for anticonvulsants.	• Prior to PA: $167/patient/mo with monthly increase of $3.60 in ME; $232/patient/mo with monthly increase of $2.80 in NH • During PA: ME trend leveled off, and upward trend continued in NH. • PA associated with downward trend in pharmacy costs of $3.40 pppm with estimated overall medication savings during 8-month period of about $27 per patient; for 5,336 continuously enrolled ME patients, total savings in drug spending was $144,072. • When PA ended, spending trend in ME was similar to that seen in NH during same period. Changes in rates of bipolar drug treatment discontinuations • Controlling for relative hazard ratios between pre-policy and policy cohorts in comparison group, PA associated with 2.28 significantly higher adjusted hazard of discontinuation of all bipolar medications 30 days after therapy initiation, compared with pre-policy cohort (not observed for treatment discontinuation within 30 days of initiation). • In policy cohort in ME, percentages of patients who discontinued treatment at any given point in follow-up were consistently higher than in pre-policy cohort, representing increased risk. Changes in rates of switching and augmentation • No differences in hazard rates of switching or augmentation of initial medication regimen between policy and pre-policy cohorts observed in both states, which suggests PA did not affect switching or augmentation rates of initial regimen of bipolar medication.	▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO

Appendix II: Summary of Studies that Examined the Effect of Prior Authorization				
Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		Drugs/classes: • Two second-generation antipsychotics: olanzapine and aripiprazole • Seven anticonvulsants: lamotrigine, topiramate, gabapentin, brand-name carbamazepine, brand-name valproic acid, oxcarbazepine, & levetiracetam *Strengths:*		

Appendix III: Features of Reviewed Step-therapy Studies

Appendix III: Summary of Studies that Examined the Effect of Step-therapy

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Cox et al. (2004) *Objective:* To understand health plan member experiences with point-of-service step-therapy edits and outcomes in terms of drug received. *Quality Rating:* Fair	*Plan Type:* Managed care plan with 33 groups *PBM?* Yes. *Region:* Northeastern U.S. *SAMPLE Size:* 1) 1000 members 2) 617 members *Age:* *Other characteristics:* *Selection Criteria:* 1) Members with no use of brand (target) drugs in the previous 180 days for NSAIDs or 130 days for PPIs 2) Members who received no medication after the edit	*Design:* 1) A mailed, self-administered survey (23% response rate), and 2) a follow-up telephone survey (33% response rate) *Statistics:* Descriptive statistics, chi-square test, and logistic regression *Timeframe:* 1) 9/1/02 – 1/31/03; 2) 1/1/03 – 4/25/03 *Intervention:* Point-of-service step-therapy edit; Required try generic H2 antagonist prior to PPI. Required first try 2 generic NSAIDs prior to COX-2 therapy. Medical exceptions were granted (e.g., previously tried generic, or stabilized on brand drug previously but not in PBM data) *Drugs/classes:* PPIs and NSAIDs *Strengths:* • response bias assessed – those responded were older,	Contact to Physicians to Pursue PA • 67% reported contacted physician directly • 40% reported pharmacist contacted physician Drug Received • 44% received a different drug than was originally prescribed • 15% obtained PA for brand • 11% received no medication • 11% paid full price for brand • 8% got an over-the-counter medication Likelihood of Receiving Medication • Members who contacted their physician were approximately 3 times more likely to obtain a first-line drug, and 2.5 times more likely when the pharmacist contact the physician Reasons Why Did Not Receive Medication • 12% indicated receiving no medication • 32% indicated had received, but some time after step-therapy edit • 28% indicated affordability • 20% were unclear or misunderstood	• 1 health plan • 13% respondents didn't remember – poor recall given time lag (2.5 months) • Low response rate • Response bias given those with prescription claims prior to the edit were more likely to respond • Low response rate • 13% didn't remember event occurred – excluded – implications?

Appendix III: Summary of Studies that Examined the Effect of Step-therapy

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		received prescription for 1st or 2nd line drug, and differed based on month.		
Dunn et al. (2006) *Objective:* Evaluate the impact on utilization and costs of a generic step-therapy edit for antidepressant drugs excluding TCAs in an HMO in an HIS. *Quality Rating:* Fair	*Plan Type:* HMO IHS *PBM?* (as comparison group) *Region:* Unspecified *SAMPLE Size:*440,000 members *Age:* *Other characteristics:* *Selection Criteria:*	*Design:* pre-post *Statistics:* t-test *Timeframe:* 1/4/04 – 12/31/05 12-month pre; 12-month post *Intervention:* step-therapy edit for patients new to antidepressant therapy; Also generic anti-dep moved to tier-1 copayment with the 1st fill copayment waived… *Drugs/classes:* Antidepressants (except TCAs); required generic step-therapy edit	Generic Dispensing Rate • Increased by 20 points in intervention group versus 7.4 points in comparison group Drug Cost per Day of Therapy • Decreased 11.7% for INT, versus 2.7% decrease in comparison group Days of Drug Therapy PMPM • Dropped by 1.5% in INT, versus 5.0% in COMP Plan Savings • $0.36 PMPM savings; or $1.8M	• Effect on medical costs was not measured • Effect on humanistic outcomes were not measured • Other change (dose optimization) may have impact cost measured • Did not assess effect on adherence / persistence • Administrative costs of program not included • Did not assess effect on pharmacists
Mager et al. (2007) [Also Examined in Appendix I: Tiered Formularies] *Quality Rating:* Fair	*SAMPLE Size:* 3979 *Selection Criteria:* Eligible if sponsor was with ESI for year 2005 and did not experience a benefit design change during the year, represented a commercially insured plan, offered a subsidized benefit to members, adopted 1 of 2 standard ESI formularies and had at least 100 members	*Design:* Cross sectional study of plan sponsors *Statistics:* Logistic Model	Generic Fill Rate • Plans with 1 step-therapy program showed average GFR that was 2.7% higher than sponsors with no step-therapy.	• Analysis limited to retail claims only which may have biased GFR upwards for clients with a higher proportion of home delivery claims. • Rebate $ included? no • Patient cost? Yes in terms of tier changes but not overall costs. • Plan cost? • Utilization? o Drug utilization? NO o Medical utilization? NO • Health outcomes? NO
Mark et al. (2009)	*Plan Type:* Employer-	*Design:* Pre/post design with	Days Supplied Per Year	• Step-therapy is implemented in various

Appendix III: Summary of Studies that Examined the Effect of Step-therapy

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Objective: To examine the effects of antihypertensive step-therapy on prescription drug utilization and spending, and other medical care utilization and spending. *Quality Rating:* Good	sponsored health plans – 2 firms selected that recently implemented step-therapy *PBM?* *Region:* *SAMPLE Size:* 269,561: 66,308 in step-therapy of which 11,851 were antihypertensive users *Age:* <65 years old; not eligible for Medicare *Other characteristics:* *Selection Criteria:*	control group *Statistics:* t-test, chi-square, and multivariate generalized estimating equation models *Timeframe:* Implemented step-therapy from 2003 – 2005; 2003 – 3rd quarter 2006 *Intervention:* Step-therapy required certain ACE inhibitors or ARBs *Drugs/classes:* Anti-hypertensive drugs: ACE inhibitors & ARBs *Strengths:* • examined medical utilization & spending	• Lower in the step-therapy group (224.5) versus comparison (252.4) • Effects of step-therapy has immediate 7.9% drop in days supplied after implementation, however, the number increased with time and after 5 quarters the days supplied began to exceed comparison. Discontinuation Rate • Higher for step-therapy group (0.13) versus comparison group (0.10) • Step-therapy was associated with a higher rate of discontinuation Prescription Drug Utilization & Spending • Lower in the step-therapy group • While prescription drug spending declined 3.1% after implementation of step-therapy, spending on prescription drugs in step-therapy plans grew over time closer to that in non-step-therapy plans. Emergency Room Utilization & Spending • Higher for step-therapy group • Step-therapy was positively associated with an increase in ER visits and increase in ER visits grew with time elapsed from step-therapy implementation Outpatient Visits Utilization & Spending • Higher for step-therapy group • Step-therapy was associated with increase in outpatient visits Inpatient Admissions • Step-therapy was associated with increase in inpatient admissions	ways • Utilization and cost measures were comprehensive, and didn't examine cardiac-specific measures • effects measured at different times for different plans • Authors do not include mail order pharmacy for the step therapy versus comparison groups. • Treatment and control groups may not be comparable (e.g., total medical expenditures higher in comparison group) • Rebate $ included? • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes?
Motheral et al. (2004)	*Plan Type:* An employer *PBM?* Yes.	*Design:* Pharmacy claims data; survey of members	Prescription Drug Expenditures • Employer experienced decrease of $0.83 in next costs after step-therapy while comparison group has	• 1 employer • Small sample size at drug class • No medical costs

Appendix III: Summary of Studies that Examined the Effect of Step-therapy

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Objective: To examine the effect of step-therapy programs in terms of plan sponsor savings and member experience at the point of service. *Quality Rating:* Fair	*Region:* Midwest *SAMPLE* *Size:* 20,000 *Age:* *Other characteristics:* Grandfathered prior users *Selection Criteria:*	*Statistics:* Univariate and bivariate statistics; logistic regression to assess predictors of outcomes; interrupted time series *Timeframe:* 9/1/01 – 6/30/03; step-therapy edit between 9/1/02 – 12/31/02 *Intervention:* 3 step-therapy programs • PPI – required H2A • NSAID – required trial of 2 generic NSAIDs • SSRI required use of fluoxetine or fluvoxamine before brand SSRIs *Drugs/classes:* PPIs, NSAIDs, and SSRIs *Strengths:* • Examined plan sponsor savings and member effects? • Excluded members with more than 1 edit • Had medical exceptions	an upward trend of $0.10 PMPM. Contacts to Physician re: Step-therapy • 43% reported pharmacist contacted physician • 62% of members contacted physician • If pharmacist versus the patient contacted the physician, members were 8x more likely to receive a covered medication Outcome of Step-therapy Edit • 29% had prescription switched to generic • 23% reported a medical exception • 16% paid out-of-pocket for prescription • 17% reported getting no medication Medication Satisfaction • Was greater for brand users versus generic users (95% vs. 53%). Pharmacy Benefit Satisfaction • Paying OOP for the brand and receiving no medication were associated with significantly lower pharmacy benefit satisfaction compared with those who received a generic	• No HRQOL • Did not examine administrative burden to pharmacists or physicians • Patient cost? NO • Utilization, adherence? NO • Medical utilization? NO • Health outcomes? NO
Panzer et al. (2005) *Objective:* To determine the economic impact of a generic step-therapy formulary compared with an open formulary for SSRIs in patients with anxiety	*Plan Type:* Health plan population with 1 million covered lives (hypothetical *PBM?* *Region:* *SAMPLE* *Size:* 40,120 treated with SSRI (4% of plan population) of which 32,096 (80%) estimated seeking treatment for anxiety-	*Design:* Economic model using literature and market data; with sensitivity analysis *Statistics:* *Timeframe:* *Intervention:*	Discontinuation or Therapy Change • Generic step-therapy resulted in a higher number of patients discontinuing therapy or requiring a therapy change before 6 months, and a lower number of patients who have continuous therapy for at least 6 months. Total Number of Prescriptions Filled • Total number of prescriptions filled during 1-year period rises for the generic step-therapy formulary	• Patterns of utilization and cost of treatment were derived from published literature • Model assumed 100% of patients who received SSRI were treated for anxiety with or without depression (80%) or depression along (20%), whereas SSRIs are used for migraines and other illnesses • Model assumed 100% conversion from branded products to generics

Appendix III: Summary of Studies that Examined the Effect of Step-therapy

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
disorder. *Quality Rating:* Fair	related illness *Age:* *Other characteristics:* *Selection Criteria:* Patients with anxiety disorder	*Drugs/classes:* *Strengths:*	Pharmacy Costs • Total cost of SSRIs is lower because of the decreased use of higher-cost brand drugs. • Net reduction of $0.26PMPM for the generic step-therapy formulary Medical Costs • Significant increase in medical costs associated with implementing the generic step-therapy formulary • Net increase of $0.32 PMPM for the generic step-therapy formulary Total Costs • An additional cost of $0.06 PMPM for the total health plan population	• Prescription costs derived from WAC • Excluded variables on: costs of implementation, administrative costs, patient outcomes, satisfaction
Yokoyama et al. (2007) *Objective:* To assess the effectiveness of a step-therapy intervention for ARBs as measured by prescription use patterns and antihypertensive drug ingredient costs. *Quality Rating:* Fair	*Plan Type:* 3 health plans (INT) compared with 1 health plan *PBM?* Yes. *Region:* Midwest & Northeast (INT), and West (comparison) *SAMPLE* *Size:* INT: 6,758 COMP: 33,709 *Age:* >18 yrs *Other characteristics:* *Selection Criteria:* INT: Patients with claim rejects for ARB or had a paid claim for	*Design:* Retrospective cohort study *Statistics:* Descriptive statistics, Chi-square, and t-test. Ordinary least squares regression analysis was used controlling for potentially confounding variables. *Timeframe:* *Intervention:* ARB step-therapy intervention *Drugs/classes:* ARBs *Strengths:*	Rate of Initiation • In the step-therapy plans a smaller proportion of ARB/ACEI patients attempted to obtain an ARB compared with health plan • Of the 1,296 patients who attempted to obtain an ARB and were rejected: o 44.6% went through PA and received an ARB as initial therapy o 48.8% received other anti-hypertensive therapy o 6.6% didn't receive any anti-hypertensive therapy within the 12 month f/u period Switch Rate • In the 12 months of follow-up, 51.1% of patients in the intervention group who received other antihypertensives as index therapy switched to or added an ARB Prescription Drug Costs • Mean antihypertensive drug cost per day was 35.9%	• Only pharmacy claims data • No medical service outcomes • No satisfaction • Unable to assess why prescribing patterns were different between intervention and comparison group • Did not measure pharmacy and prescriber costs • No administrative costs included • Did not include rebate contacts on drugs costs

Appendix III: Summary of Studies that Examined the Effect of Step-therapy				
Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	an ACEI over the 6-month identification period and had no ARB or ACEI claim in the previous 3 months (new starts) were followed for 1 year.		lower in the intervention group than in the comparison group • Average cost per day of anti-hypertensive drug therapy was 12.8% lower in the step-therapy group than the comparison • ARB step-therapy was associated with $43.91 in antihypertensive drug cost savings per patients over 12 month	

Appendix IV: Features of Reviewed Therapeutic Interchange Studies

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Andrade et al. (2000) *Objective:* To evaluate the impact of a formulary switch from conjugated to esterified estrogen tables *Quality Rating:* Fair	*Plan Type:* A mixed-model HMO. *PBM?* *Region:* Massachusetts *SAMPLE* *Size:* 7,778 with HRT; 2,984 with conjugated estrogen *Age:* *Other characteristics:* All members dispensed in timeframe estrogen replacement product; cohort of users of conjugated estrogen *Selection Criteria:*	*Design:* Retrospective, cohort *Statistics:* Paired t test *Timeframe:* 5/1/95 – 12/31/97 *Intervention:* 3-stage intervention to achieve switch: 1) in Nov. 95 informational newsletter to physicians, 2) in May 96 physicians provided list of patients on conjugated estrogen, and pharmacy staff telephoned physicians to encourage switch 3) in May 97, physicians were required to complete a form to justify need for conjugated estrogen for patients. *Drugs/classes:* Estrogen replacement therapy *Strengths:*	Prescribing Rates • Frequency of dispensing conjugated estrogen tablets steadily declined from 3,139 prescriptions in May 1995 to 413 prescription in December 1997, with a corresponding rise in dispensing esterified estrogen tablets from 53 to 3,719. Switch Rates • During intervention period (11/95 – 12/97) 72% switched to esterified estrogens, 3% switched to another HRT, 20% discontinued therapy without a switch, and 5% remained on conjugated estrogen therapy. Physician Visits • Among users who switched to esterified estrogen the number of physician visits was significantly greater in the period after the switch than pre-switch, though there wasn't a difference in HRT-related visits. Switching Back Rates • Among those who switched to	• Did not evaluate effect on patient outcomes, satisfaction, quality of life • Did not include time spent by health care providers on telephone contacts to the patient or health care provider • Did not evaluate patient adherence/persistence • Rebate $ included? • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes?

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
			esterified estrogens, the probability of switching back to conjugated estrogens was 12% (95% CI, 11% to 13%) by 6 months and was 15% (95% CI, 14% to 17%) by 2 years. Discontinuation of Esterified Estrogen • Overall probability of discontinuing esterified estrogen was 16% (95% CI, 14% to 17%) and was 32% (95% CI, 29% to 35%) by 2 years after initiation of therapy. Prescription Drug Savings • $5,222 ($2.43 per patient) for this cohort, assuming patients were compliant	
Benedetto et al. (2000) *Objective:* To assess the impact of interventions designed to shift prescribing from loratadine to fexofenadine at HMOs. *Quality Rating:* Fair	*Plan Type:* Four HMOs (3 intervention, 1 control) HMO A – 60,000 member; in Northeast HMO B – 250,000 members; in Midwest HMO C – 230,000 member; on West Coast HMO D – 430,000 members; in Northeast *PBM?* Yes. *Region:* Northeast, Midwest, West Coast *SAMPLE* *Size:* *Age:*	*Design:* Retrospective analysis *Statistics:* *Timeframe:* 6-month pre and 6-months post-period *Intervention:* HMO A: mandatory lockout; letter notified patients, physicians, and pharmacists in advance. Also had coverage limits – one dose per day, and evening does had to be chlorpheniramine or diphenhydramine, but no copayment. One month later changed to allow 2 doses/day. Also, letter to patients included a $10 off first prescription.	Market Share • All HMOs had similar market share of the antihistamines, and all had significant shifts in prescribing patterns after the intervention (p<0.001) although the magnitude of shifts varied greatly. • HMO A had the largest increase in market share for fexofenadine (18.9% to 65.2%), and largest decrease in loratadine's market share (62.3% to 8.7%) • Market share increased for fexofenadine for HMOs B & C, and declined for loratadine, but greater differences for HMO B than HMO C.	• Multi-faceted interventions • Didn't assess effect on medical utilization and costs • Did not assess impact on patients health outcomes, QOL, and satisfaction • Did not include rebates in the cost • Did not look at patient adherence or persistence • (+) Did include costs for administering the program • Did not examine burden on physicians/pharmacists

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Other characteristics: *Selection Criteria:*	HMO B: voluntary switch; letters to physicians informational and listing patients; members received letter and a $10 manufacturer coupon. HMO C: voluntary switch; letters to physicians only. Letter included information and list of patients. Also enclosed $10 manufacturer coupons. HMO D: had not restrictions on member benefits for antihistamines. *Drugs/classes:* Antihistamines	Prescribing Patterns • Paralleled market share changes with HMO A having a significant increase in fexofenadine prescribing and a decrease in loratadine prescribing. Member Behavior – Switched to Fexofenadine • 39.7% in HMO A switched, and 13% of them switched back to loratadine • 4.5% in HMO B switched, and 69% of them switched back to loratadine • 2.5% in HMO C switched, and 69% of them switched back to loratadine • 0.08% in HMO D switched, and 63.7% of them switched back to loratadine Cost Analysis • HMO A has an estimated total costs savings of $37,185 • HMOs B & C the cost of antihistamines continued to rise (8.7% and 5.4% respectively) • HMO D average cost of prescription increased 4.2% (in line with inflation)	
Fugit et al. (2000) *Objective:* To determine the effects of a therapeutic interchange conversion on clinical outcome measures	*Plan Type:* *PBM?* *Region:* Albuquerque VAMC	*Design:* Prospective, descriptive study *Statistics:* Differences between the mean values was performed with two-tailed t-test; level of significance	Conversion Outcome • Of 210 patients, 114 were excluded from analysis of therapeutic effectiveness= 96 patients	• Only assessed patients receiving low-dose simvastatin • Subjective compliance data • Effect of therapy change may also have been result of switching patient to pharmacist-

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Quality Rating: Fair	*SAMPLE* *Size:* 210 eligible patients of which 96 were included for evaluation of conversion *Age:* *Other characteristics:* Patients who had received simvastatin 5 or 10mg/day for at least 2 months, lived within 60 miles, *Selection Criteria:*	(0.05) *Timeframe:* *Intervention:* Conversion of patients receiving low dose simvastatin (5 & 10mg) to lovastatin (10 & 20mg/day) Patients scheduled for initial clinic visit to determine acceptability for conversion (e.g., risk of CHD) and assessed by pharmacist *Drugs/classes:* HMG-CoA (statins)	Lipid and Liver Function Tests • No statistically-significant differences between the conversion group(simvastatin 5mg to lovastatin 10mg or simvastatin 10mg to lovastatin 20mg) Weight • No significant weight changes in either conversion group Results of Pharmacist Intervention • Of 157 patients, of which 52% were not at LDL goals at initial assessment, by 1st follow-up 38% were not at goal, and by 2nd follow-up 26% were not at goal Cost of Conversion • The net costs of the program for 1 year was $15,792 including the cost of pharmacist salary, laboratory monitoring,	management • Small sample (n=96), over ½ eligible were excluded • No comparison group
Nelson et al. (2000) *Objective:* To measure the clinical and humanistic outcomes in patients with GERD converted from omeprazole to lansoprazole in managed care plan. *Quality Rating:* Fair	*Plan Type:* 80,000-member group/independent practice association-model MCO *PBM?* *Region:* Wisconsin *SAMPLE* *Size:* 339 patients met criteria; 105 completed both surveys *Age:* >18 years old *Other characteristics:*	*Design:* Prospective, observational outcomes study; and 2 telephone surveys – pre and post-conversion (response rate of 31%) *Statistics:* t-test, 2-sample z-test, chi-square, Wilcoxon signed rank test, and Whitney rank sum test, Pearson correlation *Timeframe:* *Intervention:* Patients were converted from omeprazole to lansoprazole	Satisfaction • Post-conversion overall satisfaction was significantly lower than per-conversion • Patients were less satisfied with therapeutic interchange program if symptoms worsened Symptom Severity • Post-conversion symptom severity measured by severity score was significantly higher than before conversion • Nighttime symptoms differed less when comparing pre and post-conversion survey results	• Did not control for some patient characteristics (e.g., baseline symptom severity) • Surveys subject to self-report bias • Perceived coercion may have exacerbated frustration • Short post-conversion period, symptoms may have stabilized • Did not examine hospitalization, clinic visits, ER visits, etc. • Didn't examine cost of program • Small sample sizes made difficult to detect significance in some groups • Severity score change may not be clinically significant

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Patients with GERD on long-term or high-dose omeprazole; >18yoa; received omeprazole >30 days,	*Drugs/classes:* PPIs *Strengths:*	• Increase of symptom severity correlates with decease in overall satisfaction OTC Heartburn medication use • 33% (n=35) of patients consumed more OTC heartburn meds after conversion Diet Changes • 13% (14) had increased freq. diet changes due to heartburn symptoms after conversion Worsened Symptoms • Patients with worsened heartburn outcomes were significantly younger, mean daytime severity score change and mean overall satisfaction score were significantly different	• Selection bias – members who agreed to participate different than others? • Small sample size
Witt et al. (2003) *Objective:* To provide additional information on the clinical and economic impact of warfarin product conversion *Quality Rating:* Fair	*Plan Type:* Group-model HMO *PBM?* *Region:* Colorado region *SAMPLE* *Size:* 2299 patients of the Clinical Pharmacy Anticoagulation Service *Other characteristics:* Patients taking warfarin for 180 days uninterrupted for 90days pre and 90-days post switch	*Design:* retrospective, pharmacoeconomic study from the HMO perspective. *Statistics:* Cost-minimization analysis, generalized linear model of INR *Timeframe:* 10/1/98 *Intervention:* Conversion on 10/1/98 to generic warfarin. *Drugs/classes:* Warfarin	INR values • Overall difference in INR values were below (22.6% before vs. 26.1% after switch) and within the therapeutic range (65.9% before vs. 63.3% after switch) was statistically, but not clinically significant • A significant proportion of patients (72.0%) experienced a 10% or greater change in therapeutic INR control after switch (consisting of 33.1% control that improved and 38.9% control worsened) Cost • Difference in total treatment costs	• Analysis excluded patients who had adverse events that necessitated withdrawal of warfarin • Sample size difficult to detect differences in adverse events

Appendix IV: Summary of Studies that Examined the Effect of Therapeutic Interchange				
Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
		Strengths:	associated with brand name and generic warfarin was $3128/100 patient-years. • Economic impact of warfarin conversion was highly dependent on costs associated with treating nonfatal adverse events.	

Appendix V: Features of Reviewed Drug Utilization Review Studies

Appendix V: Summary of Studies that Examined the Effect of DUR

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Gleason et al (2004) *Objective:* To assess the impact of a DUR alert letter program on metformin discontinuation rates in patients with a metformin claim and an absolute contraindication to metformin therapy. *Quality Rating:* Fair	*Plan Type:* Members enrolled in a large Blue Cross plan and their affiliated PBM *PBM?* Yes, but does not state name of PBM *Region:* US Midwest *SAMPLE Size:* Treatment: 566 members (metformin claim with an absolute contraindication to metformin therapy) Control: 16,575 members with a metformin claim *Age:* Not specified. *Other characteristics:* *Selection Criteria:* To be included in sample, members had to have a claim submitted for metformin	*Design:* • Retrospective administrative medical and pharmacy claims *Statistics:* • Kaplan-Meier to compare discontinuation rates between treatment and controls 9-months post-intervention *Timeframe:* • Script for metformin: 1/1/02-5/22/02; intervention: 6/1/02; follow-up: 9-months post-intervention *Intervention:* • One page letter sent to physician prescriber of patients who had a metformin claim and an absolute contraindication to metformin therapy. *Drugs/classes:* • metformin (oral anti-diabetic drug in the biguanide class) *Strengths:* • uses both medical and pharmacy claims	Metformin discontinuation rates at 9 months • 533/566 of treatment and 15,280/16,575 of controls still enrolled at 9 months follow-up • Metformin discontinuation rate at 9-months follow-up for intervention group vs. comparison group was 37.3% vs. 20.0%, respectively ($p<0.001$) • Rate of discontinuation was 84% higher in intervention group ($p<0.001$) with the largest divergence between the group seen during initial 60-days post intervention Administrative cost associated with the metformin alert letter • $1,436.40, which included cost for creating the letter, administering the program, and materials Potential cost avoidance of metformin alert letter for control group • Authors estimate $6,122.77/year for 566 intervention patients	• Assumed that treatment and control groups had comparable discontinuation rates prior to intervention, but not verified • Publication of inappropriate metformin prescriptions within 1 month of intervention could be a confounder • Lack of randomization precludes drawing direct cause-effect conclusion • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO

Appendix V: Summary of Studies that Examined the Effect of DUR

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	between 1/1/02-5/22/02. To identify treatment arm, members were screened for diagnoses that are absolute contraindication for metformin: heart failure, renal insufficiency, or metabolic acidosis 5/01-4/02.			
Moore et al (2000) *Objective:* to estimate the system wide effects of retrospective drug utilization review programs on Medicaid drug and nondrug outcomes *Quality Rating:* Fair	*Plan Type:* State Medicaid plans *PBM?* Not mentioned so assume NO *Region:* All state Medicaid plans *SAMPLE* *Size:* Not reported *Age:* Not reported *Other characteristics:* *Selection Criteria:*	*Design:* Pooled cross-sectional and time-series *Statistics:* OLS Used the log of the outcome variables based on a box and Cox analysis *Timeframe:* 1985-1992 *Intervention:* State Medicaid programs that use a DUR compared to those that do not use a DUR *Drugs/classes:* None reported *Strengths:* • Considered spillover in MD services, inpt hosp, outpt hosp, SNF, and intermediate facility services	# prescriptions/recipient • No significant diff between DUR and non-DUR states # of drug recipients • No significant diff between DUR and non-DUR states (DUR measured as binary) • Older DURs programs reduce the number of drug recipients by 4.4% average prescriptions costs • No significant diff between DUR and non-DUR states drug expenditures/recipient • 4.9% lower in DUR states vs. non-DUR states total drug expenditures/state • 6.5% lower in DUR states than in non-DUR states • Older DURs programs reduce expenditures by 5.4% Outcome 6-10: also looked at 3 measures (# recipients, expenditures/recipient, total expenditures) for physician, inpt hosp, outpt hosp, SNF, and intermediate facility services • we find that DUR programs have no significant (positive or negative) spillover effects on nondrug expenditures. • SNF/intermediate - generally not significant, so not reported in main text– see FN13 • Authors also look at restrictive formulary (instead of DUR), which did have significant spillover effects; see	• Highly aggregated data does not permit direct analysis of individual outcomes (e.g., good and bad clinical outcomes could offset each other, yielding n.s. aggregate results) • unable to distinguish between individual DUR programs although we know they are not all the same • could not conducted benefit/cost analysis since do not have cost data on DUR programs • Rebate $ included? NO • Patient cost? YES • Plan cost? YES • Utilization? o Drug utilization? ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation NO ▪ Other NO o Medical utilization? ▪ ER NO ▪ Hospitalization YES ▪ (spillover) YES • Health outcomes? NO

Appendix V: Summary of Studies that Examined the Effect of DUR

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
			Table 3 for details. Not reporting specifics here since outside main scope of paper (seems to have been done in response to an earlier publication of authors').	
Seltzer et al (2000) *Objective:* To assess the use of sedative/ hypnotic agents in TX Medicaid patients and evaluate practitioner receptiveness to intervention letters concerning sedative/ hypnotic prescribing generated by the TX Medicaid DUR Board. *Quality Rating:* Poor	*Plan Type:* Medicaid *PBM?* Not mentioned so assume NO *Region:* TX *SAMPLE Size:* 244 patient claims of 89,158 sedative/ hypnotic claims (0.27%) 291 prescribers/ physicians *Age:* 7-95 yrs old *Other characteristics:* *Selection Criteria:* Had to have at least 1 of 3 diff issues w/ sedative/ hypnotic: • Excessive dosage (N=46) • Prolonged treatment (>4 months) (N=188) • Concurrent therapy w/ 2 or more sedative/ hypnotics (N=10)	*Design:* Retrospective administrative pharmacy claims *Statistics:* *Timeframe:* 7 month evaluation: 1/1998-7/1998; follow-up Jan-Oct 1999 (approx 1 yr after intervention letter) *Intervention:* Letter sent to physician prescriber with 6 responses; MDs replying with "agree" were re-evaluated Jan-Oct 1999 to monitor whether treatment recommendations were actually made *Drugs/classes:* sedative/ hypnotics: Benzodiazepine, barbiturates, misc non-barbiturates *Strengths:*	Change in rx use 71.5% response rate for MDs (208/291). Of these, • 84 (40.4%) agreed that sedative/ hypnotic dose was excessive – this is the sample size for the 1 yr follow up • 55 (26%) disagreed that sedative/ hypnotic dose was excessive 78/84 patients were avail for re-evaluation: • 37 (47%) no longer receiving sedative/ hypnotic. Translates to "favorable response in approximately 20% of 208 physicians who responded" • 41 (53%) still using sedative/ hypnotic "on an extended basis"	• May not be applicable to other patient populations • Did not include possible seasonal differences in fall/holiday season • MDs may have prescribed anti-depressants/anti-anxiety agents as sedatives, which was not measured, so magnitude of results may be under-stated • No control group • Length of time for prolonged treatment 'arbitrary' • Very small sample size • No break down by age of patients – may have different implications? • Don't know if person actually taking the drug – prescription does not equal use • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? NO o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO
Starner et al (2009)	*Plan Type:* BCBS 3 Medicare Part D plans	*Design:* • Retrospective administrative pharmacy claims.	Discontinued script for DAE • 5403 (48.8%) of DAE claims were discontinued 6 mo post analysis	• Unable to capture claims for benzodiazepines • Did not include amitriptyline or digoxin

Appendix V: Summary of Studies that Examined the Effect of DUR

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Objective: Identify members aged 65 and over participating in a Medicare Part D BCBS benefit plan who are receiving medications that may be inappropriate for use in older adults and, through a retrospective DUR, to notify their prescribers of the possible safety concerns with continued use. *Quality Rating:* Poor	*PBM?* Not mentioned so assume NO *Region:* 4 states – IL, NM, OK, TX *SAMPLE* *Size:* 328K eligible members; 16973 (5.2%) w/ DAE claim. final sample: 10,364 members with 11,062 DAE claims (7963 prescribers) *Age:* 65+ *Other characteristics:* *Selection Criteria:* To be included in sample, had to have a claim for a 7 day script for at least one Drug to be Avoided in the Elderly (DAE)	• Used NCQA HEDIS list as means of identifying inappropriate prescribing *Statistics:* None *Timeframe:* 7-day script for DAE between 8/15/07-9/14/07, and with drug supply avail on/after 10/1/07; follow-up at 6 mo (3/28/08) *Intervention:* Mail letter to prescribers with patients who had at least 1 DAE *Drugs/classes:* Defined by NCQA HEDIS guidelines; 87.5% of DAE claims comprised of Estrogens, propoxyphene, nitrofurantoin, muscle relaxants, antihistamines, anticholinergics *Strengths:* Letter to prescriber included patient-specific information	• Discontinuation ranged from 31.3% (estrogens) to 66.7% (anticholinergics) Cost of mailing intervention letter • Cost $9830 to mail letter; 6050 due to printing, rest for postage	• no control group – direct cause/effect link cannot be made • limited to Medicare popn; may not be generalizable to commercial popn • relied solely on claims to determine discontinuation; no additional methods to validate findings used • drugs used in study could be used for short-term therapy, and reason for discontinuation could be that course of therapy completed → major weakness • Unable to evaluate health care outcomes • Rebate $ included? NO • Patient cost? NO • Plan cost? NO • Utilization? o Drug utilization? YES ▪ Adherence NO ▪ Medication Possession Ratio NO ▪ Discontinuation YES ▪ Other NO o Medical utilization? NO ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes? NO

Appendix VI: Features of Reviewed Medication Therapy Management Studies

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
Barnett et al. (2007) *Objective:* To describe changes over 7-year period in MTM services, and quantify potential MTM-related cost savings based on pharmacists' self-assessments of the likely effects of their interventions on health care utilization *Quality Rating:* Poor	*Plan Type:* Multiple payers *PBM?* MTM Vendor *Region:* National; 47 states *SAMPLE* *Size:* *Age:* *Other characteristics:* *Selection Criteria:*	*Design:* Retrospective descriptive analysis *Statistics:* Descriptive statistics from MTM claims database and documentation system Convenience sample of 50 MTM programs representing 90% of drug plan sponsors 76,148 claims for 23,798 patients *Timeframe:* 1/1/00 – 12/31/06	Pharmacy Reimbursement • >60% increase in mean(SD) payment from $7.65 ($3.03) in 2000 to $12.28 ($6.65) in 2006. Estimated Cost Avoidance (ECA) • ECA mean $ (SD) per claim increased from $24.18 ($139) to $429 ($2,421) from 2000 to 2006, but the significant change is the result of a few high-cost, high-impact claims. MTM Interventions • Over time period changed from mostly education and monitoring to prescriber consultations regarding cost efficacy • Over time period shifted from acute meds to chronic meds, resulting in significant changes in therapeutic classes associated with MTM claims and increase of older patients	• Self-reported estimates of ECA • No comparison group; unable to attribute outcomes to MTM • Sample of plans; convenience sample used • Plans dropped and were added over time • No clinical outcomes • No medical utilization outcomes • MTM interventions are not necessarily indicative of desired outcomes. • No patient perspectives • Largely descriptive, on
Borenstein et al. (2003) *Objective:* To compare the effectiveness of an evidence-based systematic approach to hypertension care involving PCPs and	*Plan Type:* Staff model medical group *PBM?* *Region:* *SAMPLE* *Size:* 197 patients *Age:* 18 years or older	*Design:* Randomized trial *Statistics:* Chi-square and t-test, intent-to-treat analysis, analysis of covariance *Timeframe:* 12 months follow-up. *Intervention:* All physicians received group and individual education and participated in	Reductions in Systolic Blood Pressure (SBP) • INT: reduction of 22mmHg (p<0.01) • UC: reduction of 11mmHg (p<0.01) • Greater reduction of SBP in INT versus UC was statistically significant, and persisted after adjustment for baseline Reductions in Diastolic Blood Pressure (DBP) • INT: reduction of 7mmHg (p<0.01) • UC: reduction of 8mmHg (p<0.01) • Non-significant difference between INT and UC Blood Pressure Goals Achieved	• Exclusion of patients after randomization, though found no diff in baseline characteristics • Selection bias • Did not assess other clinical outcomes (e.g., stroke, MI) • Drug costs calculated using AWP no actual costs • Actual savings would only occur if physician workload was offset by pharmacist's role

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
clinical pharmacists vs. usual care in patients with uncontrolled hypertension *Quality Rating:* Good	*Other characteristics:* Uncontrolled hypertension *Selection Criteria:* Usual Care (UC) and intervention group (INT)	development of evidence-based treatment algorithm. The intervention group patients were comanaged by their PCP and a clinical pharmacist who provided patient education, made treatment recommendations, and provided follow-up.	• 60% of INT, and 43% of UC, respectively (p<0.02) Evidence-Based Drug Use • % of patients receiving at least 1 1st-line therapy per algorithm increased significantly from baseline in both groups. Provider Visit Costs per Patient • Lower for INT than UC patients ($160 vs. $195, p=0.04) resulting from lower # of visits to PCP during study by INT than UC patients (3.4 vs. 6.6, P<0.01). Although also a trend to more total provider visits in INT vs. UC. Drug Costs • Not significant, but greater increase for INT in drug costs from baseline vs. UC ($11.31 vs. $4.25, p=0.12).	• No humanistic outcomes • Part of intervention (education and treatment algorithm) provided to all PCPs • Only examined costs separately • Small sample size may have affected ability to detect differences due to limited power
Etemand et al. (2003) *Objective:* To evaluate the effect that community pharmacists could have on medication-related morbidity and mortality in elderly if comprehensive pharmaceutical care were included in Medicare Part D *Quality Rating:* Fair	*Plan Type:* *PBM?* *Region:* *SAMPLE Size:* *Age:* *Other characteristics:* *Selection Criteria:*	*Design:* Cost-effectiveness model from a societal perspective using relevant literature, data sources, and model parameters. *Statistics:* *Timeframe:* *Intervention:* *Drugs/classes:* *Strengths:*	• A pharmaceutical care benefit in the elderly population would cost $2100 (year 2000 prices) per life-year saved, which is highly cost-effective. Reasonable changes in model parameters did not raise the cost-effectiveness ratio above $13,000 per life-year saved.	• Rebate $ included? • Patient cost? • Plan cost? • Utilization? o Drug utilization? ▪ Adherence ▪ Medication Possession Ratio ▪ Discontinuation ▪ Other o Medical utilization? ▪ ER ▪ Hospitalization ▪ (spillover) • Health outcomes?
Fischer et al. (2002) *Objective:* To	*Plan Type:* Large HMO *PBM?*	*Design:* Non-randomized, controlled trial *Statistics:* Bivariate analyses,	Drug Therapy Problems • Pharmacists identified at least 1 DTP for 69% of patients Pharmacist Intervention	• Still may be unmeasured differences between INT and control sites • Selected sites, did not randomize • Did not account for group randomization in analysis

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
assess whether a pharmaceutical care program decreases health utilization, medication use, or charges *Quality Rating:* Fair	*Region:* Greater Minneapolis-St. Paul region *SAMPLE* *Size:* 231 HMO enrollees (48% participation rate) from 6 pharmacies – 3 located with staff clinics, 3 free-standing (volunteered) *Age:* Adult *Other characteristics:* *Selection Criteria:*	multiple linear regression, performed an intention-to-treat analysis *Timeframe:* 1-year follow-up *Intervention:* Pharmaceutical care: pharmacist assessment of drug therapy problem and goals of therapy, initial visit with patient, contact doctor as necessary, and follow-ups with patients *Drugs/classes:* *Strengths:*	• Pharmacists provided some form of intervention for a large majority of patients (87%) • For 70% patients, pharmacist contacted physician Number of Unique Medications • After adjustment the average increase in # of meds was 0.6 higher for the INT group than control (p=0.03) Number of Prescriptions • No significant difference Hospital Outcome • No significant difference with proportion with 1+ hospital admissions • No significant difference with mean number of hospital days Adherence Analysis (compared subset of INT patients with control) • INT patients had a statistically significant increase in numbers of clinic visits and unique medications compared with patients in control group • No statistical difference in total charges	• Only half of those invited to participate in PC chose to do so • Unable to assess how many follow-up visits • Selection bias – pharmacies • Limited specificity on the MTM interventions and services provided
Fox et al. (2009) *Objective:* to determine a MTM service's impact on HEDIS, and use and cost expenditures *Quality Rating:* Fair	*Plan Type:* Mixed-staff model HMO Medicare Advantage Plan *PBM?* *Region:* Florida *SAMPLE* *Size:* 2,114 enrollees with diabetes, 311 targeted for MTM and 255 participated *Age:* Medicare enrollees	*Design:* non-equivalent group, quasi-experimental study *Statistics:* Descriptive statistics, chi-square, t-test, ANOVA, least squares regression Pharmacy and claims data *Timeframe:* intervention occurred from 1/1/06 – 12/30/07 with study data for evaluation collected 1/1/07 – 12/31/07 using most recent values	Mean LDL Levels • Significantly higher in control groups than MTM group (93.6 ± 30.5 mg/dL and 90.8± 31.0 vs. 83.4 ± 31.1) • Significant differences between MTM group and comprehensive diabetes care control group, but not significantly different compared with MTM non-participant control group or between control groups. LDL Values < 100mg/dL • 69% of MTM group had LDL < 100, and higher proportion compared with nonparticipant control (50.0%), and CDC only (54.1%) X^2=20.9, p<0.001) LDL Screened	• Claims re: cost benefit cannot be confirmed, did not do cost-benefit analysis • Findings of non-significance may be due to lack of power • Lack of baseline measures on outcome variables • Control group consisted, in part, of individuals who self-selecting to opt-out • One of control groups was older than intervention group • Did not examine medical utilization and costs

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	Other characteristics: 3+ chronic diseases, 4+ medications, and >$4000/year drug costs *Selection Criteria:*	*Intervention:* MTM provided in-house by staff clinical pharmacists – med review and evaluation and sent to physician. RPh conducted patient interview and reviews of pharmacy history, lab data, medical notes. Took 1- 3 hours total for each person served during intervention period. 2 control groups: 1) part of comprehensive diabetes care population but not eligible for MTM, 2) MTM non-participant control group (e.g., self-selected not participate, unreachable, not reviewed) before end of measurement year.	• Of 311 eligible, all but 9 screened PMPM Use & Costs • Overall PMPM use and drug costs differed from 2007 to 2008 - average # of 30-days equivalents dispensed, Medicare Part D costs, Medicare Part D copayments, and all copayments were significantly different although they did no improve in every case for the MTM eligible participants	
Isetts et al. (2008) *Objective:* To measure differences in clinical and economic outcomes over a 1-year period in a group of patients with health insurance benefits after receiving MTM services. *Quality Rating:* Fair	*Plan Type:* BCBS health plan *PBM?* *Region:* Minnesota *SAMPLE* *Size:* 285 intervention group patients *Age:* 18 years or older *Other selection criteria:* At least 1 of 12 conditions continuously enrolled in BCBS received care in 1 of 6 clinics with MTM, had 2+ claims related to 1 of 12 conditions	*Design:* 1-year prospective *Statistics:* t-tests with p<0.05 *Timeframe:* 8/1/01 to 7/31/02 *Intervention:* MTM; consistent, systematic process to help achieve goals of therapy and resolve DTPs. RPhs completed intensive certificate program training (120hr, 50-patient). Use MTM documentation system.	Process Measures • Total of 285 patients receive 684 encounters (2.4/patient) in 1 year period • Total of 1,827 conditions (6.4/patient) • Total of 2,252 drug therapies (7.9/pt) % of Patients' Goals of Therapy Achieved • Increased from 76% at first encounter to 90% at final MTM encounter Drug Therapy Problems (DTPs) • 637 DTPs resolved for 285 patients (2.2/patient): 78% resolved without direct involvement of physician HEDIS Measures • 71% of MTM patients compared with 59% of comparison group patients met HEDIS 2001 hypertension goal (p=0.03)	• Selection bias: i) Patients with more pressing medical issues may be more likely to use MTM services, ii) Drs may have induced selection bias by encouraging pt. participation • Baseline expenditures of comparison group were about ½ amount of intervention group – may be due to clinics encouraged to participate if had complex patients • Economic results could be affected by regression to the mean b/c high-resource patients were selected • Patients enrolled b/c Dr, RPh, or patient thought had DTPs so may no represent general pop. • Did not include health care costs paid by patient • Based on face-to-face MTM

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	(highest resource-use group)		• 52% of MTM patients compared with 30% of comparison group patients met HEDIS 2001 hyperlipidemia goal (p=0.001) Total Health Expenditures • Decreased from $11,965 to $8,197 per person (n=186, p<0.0001), and exceeded cost of providing MTM by more than 12 to 1.	• Patients self-selected or volunteered to receive MTM – selection bias likely • Patients not billed for MTM • MTM services provided via research grants, demo projects, support of health system • Site selection bias
Okamoto et al (2001) *Objective:* To measure clinical, economic, and humanistic outcomes associated with a pharmacist-managed hypertension clinic compared with physician-managed clinics. *Quality Rating:* Good	*Plan Type:* Managed care organization *PBM?* No *Region:* Not mentioned *SAMPLE* *Size:* 330 patients (164 treatment; 166 control) with mild-to-moderate essential hypertension *Age:* 18 years or older *Other characteristics:* • Diagnosed with essential hypertension, be a member of the managed care organization for at least 1 year, fill prescriptions at the managed care organization's pharmacies • taking the targeted antihypertensive drugs	*Design:* • Prospective, randomized, comparative study *Statistics:* • Wilk's test for normality, student t-test, Wilcoxon rank sum test (nonparametric), Welch's test (heterscedasticity), paired-t test, chi-square analysis *Timeframe:* • Two evaluations were required for all patients: one at baseline and one at the final visit 6 months later *Intervention:* • Hypertension care provided by either the pharmacist-managed hypertension clinic (treatment) or physician-managed general medical clinics (control). *Drugs/classes:* • antihypertensive drugs (nifedipine, verapamil, captopril, diltiazem, clonidine,	Blood pressure • Within the treatment group, statistically significant decreases in both systolic and diastolic blood pressure between baseline and final visit; no significant change in control group • Between-group comparisons showed mean systolic blood pressure decreases statistically lower for treatment vs. control group after 6 months Quality of life • Statistically significant higher score for role-physical domain for control vs. treatment after 6 months • Within group comparison: no significant changes in treatment group from baseline to final visit. In control group, significant reductions in physical functioning and general health domains. Health care utilization • No patients hospitalized for reasons related to blood pressure • 4 ER visits in control group; 0 ER visits in treatment group. • ER visits cost $439/patient. • Average number of clinic visits significantly higher in the treatment group vs. control group (5.25 vs. 1.41) Drug utilization • No significant difference in average number of antihypertensive drugs/patient between treatment and control groups at baseline or follow-up	• Study not restricted to only patients newly diagnosed with hypertension (i.e., previous treatment could affect outcome). • Sample included only those patients taking certain antihypertensive drugs, which are typically the more costly, so results may not be generalizable to patients who take other commonly used (less expensive) antihypertensive drugs • Only analyzed costs that could be attributed to blood pressure or its treatment instead of analyzing all costs incurred by patients • Used only two blood pressure readings to determine effectiveness (baseline and 6 months later); numerous blood pressure readings may improve quality of the data • Physicians in control group were internists or family practitioners, and results may not be generalizable to other physicians. • SF-36 may not be sufficiently responsive in assessing patients with essential hypertension or who are asymptomatic. • MCO would not allow for dissemination of itemized costs of goods and services, so results may have been different if study conducted at an institution with significantly different cost structures for drugs and other health care resources. • Effectiveness determined only by

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	nifedipine, verapamil, captopril, diltiazem, clonidine, terazosin, propranolol, or lisinopril, or be taking at least three prescription antihypertensive drugs. • Patients excluded if had secondary hypertension, significant end organ disease, or had baseline blood pressure higher than 200 mm Hg (systolic) or 105 mm Hg (diastolic). *Selection Criteria:* • Interested physicians gave consent for patients to be enrolled, patients sent letter and prescreened over the phone.	terazosin, propranolol, lisinopril) *Strengths:* • Includes medical utilization	Cost-effectiveness • No statistically significant differences in mean drug cost/patient, cost of hospitalization, or total costs/patient between groups. • Clinic visit costs were significantly higher in treatment group vs. control group • Average cost/patient for ER visits was significantly lower in the treatment group vs. control group	reductions in blood pressure (rather than reduced morbidity/mortality).
Planas et al. (2009) *Objective:* To evaluate effect of 9-month community pharmacy-based MTM program on quality of care in patients with diabetes and hypertension *Quality Rating:* Good	*Plan Type:* *PBM?* *Region:* Tulsa, OK *SAMPLE* *Size:* 52 patients with diabetes and hypertension in an MCO at 5 regional chain pharmacies *Age:* 18 years or older 3 recruitment approaches: mailed recruitment letters from	*Design:* Randomized, controlled trial *Statistics:* descriptive statistics, t-test, intention-to-treat analysis, Pearson chi-square; and $p<0.05$ *Timeframe:* Nov. 05 – July 07 *Intervention:* During monthly visits patients received MTM for hypertension (HTN) and diabetes (DM) CONT: visits at 3,6, 9 BP was recorded and were informed of	Systolic Blood Pressure (SBP) • INT group mean SBP decreased 17.32mmHg vs. CONT group mean SBP increased 2.73mmHg (P=0.003) % Patients At Goal Blood Pressure (BP) • % of patients at goal BP increased from 16% to 48% in INT, vs. decreased from 20% to 6.67% in CONT group • INT patients 12.92 times more likely to achieve goal BP (p=0.021) Adherence Rate • Mean adherence rate in INT group increased 7.0% while remaining fairly constant in CONT group, but difference wasn't statistically significant	• Small sample size, limiting power • Selection bias – participants may be more highly motivated than average patient • Site effects of pharmacies • Nested within another study – effect? • Didn't examine costs • Didn't examine medical utilization or costs

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	MCO, screening at health fair, faxing patient referral requests to physicians	BP goals for patients with diabetes (study nested within a larger study of patients with uncontrolled diabetes)		
Stebbins et al. (2005) *Objective:* To measure changes in generic drug use, document savings in OOP drug costs, and measure patients access to drugs that had been, or would have been, discontinued due to cost. *Quality Rating:* Fair	*Plan Type:* *PBM?* *Region:* Pennsylvania *SAMPLE* *Size:* 520 study patients INT: Medicare-eligible, low-income elderly with multiple diseases, medications, and high drug costs Comparison: PACE program for generic drug use patterns, and MEPS data for OOP	*Design:* Non-controlled, retrospective pilot study; analysis of clinic database *Timeframe:* 2002 *Intervention:* PRICE clinic: Pharmacist-directed program serving Medicare patients about half of whom are MA HMO plan patients – thorough medication review	Process Measures • 1297 interventions among 520 patients (2.5/patient) – all accepted by physicians • Most common interventions were pharma-industry sponsored patient assistance programs, generic substitution and therapeutic interchange Generic Drug Use Rates • Average ratio of generic drug use to total prescriptions for PRICE clinic patients increased from 51% to 56% • Total of 122 patients (23%) increased their use of generic drugs Savings in OOP Drug Costs • After implementation, the average OOP expense was reduced to $60 / patient month, a 68% decrease, representing an average of $1,500 per member per year in OOP savings Access to Medications • 215 patients (41%) reported that they had discontinued or would soon discontinue use of a prescribed drug because of cost – among those 186 (87%) were able to continue indicated drugs after PRICE clinic interventions	• No direct control group, but used a comp group for OOP • Used self-reported data for income level and whether patients discontinued or planned to discontinue med • Did not examine medical utilization • Did not examine medication adherence
Stockl et al. (2008) *Objective:* To measure increase in new users of statins due to intervention aimed at prescribers for Part D MTM	*Plan Type:* PDP & MA-PD of a PBM *PBM?* Yes *Region:* Several states (AZ, CA, TX, others)	*Design:* comparison *Statistics:* Means were compared by t-tests and percentages by chi-square; Logistic regression to eval effectiveness. Used pharmacy and health plan	Initiated Statin Medication • 12.1% of the INT members started a statin med compared with 7.3% of COMP (p=0.001) • After covariate adjustment, odds of initiating a statin were 65% higher (OR=1.65'95% CI=1.15-2.36; p=0.006) in INT than comparison Cardiovascular Events	• Comp group had diff clinical characteristics than INT • Comp group only has MA-PD members, while INT had MA-PD and PDP • Comp group had fewer with CAD and more with diabetes than INT group – though post-hoc analysis shows lower rate of initiating statin not result of COMP group consisting of greater proportion of

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
members with diabetes or CAD and estimate potential cost savings associated with project reduction in CV events based on published controlled trials. *Quality Rating:* Fair	*SAMPLE* *Size:* 1,340 members of MA-PD and PDP Medicare Part D plans' MTMPs *Selection Criteria:* MTMP criteria: >$4000 drugs; 10+ part D meds; at least 3 of 5 diagnoses of interest COMP: MA-PD members who met MTMP criteria except at least 3 of 5 conditions of interest	claims. *Timeframe:* 4/1/05 -12/31/06; 4 month f/u period *Intervention:* On 8/18/06 prescribers mailed a patient-specific report that highlighted members under his/her care that could benefit from statin. Mailing also included section for prescriber feedback, and educational booklet. *Drug/Class:* statins	• Estimated number of members requiring interventions to prevent 1 major CV event was 220 • Estimated coronary event cost avoidance is $12,323 per 220 members who receive intervention, after subtraction of program admin costs and cost of drug therapy.	members with diabetes; and level of comorbidity between groups not significantly different • 4-month follow-up may be too short to observe effects (e.g., patient only visits doctor every 6 months) • Did not measure actual costs of coronary event – so may be higher or lower • Did not include additional costs like labs, physician visits which may result from initiating tx • Did not examine dual eligibility of members
Welch et al. (2009) *Objective:* To assess impact of MTMP on mortality, health care utilization, and medication costs and to quantify drug-related problems identified. *Quality Rating:* Good	*Plan Type:* Group-model, not-for-profit HMO with approx. 470,000 members *PBM?* *Region:* Denver/Boulder region *SAMPLE* *Size:* 539 accepted of the 1231 home-based members targeted for MTM *Age:* *Selection Criteria:* 2+ conditions (1 of which was high-risk), 5+ Part D drugs, >$4000 drug costs Voluntary participation;	*Design:* non-randomized controlled study. Data from electronic medical, pharmacy and admin databases and manual medical chart review to assess those opted-out. *Statistics:* Wilcoxon rank-sum and chi-square tests for continuous and categorical variables; multivariate logistic regression (unadjusted and adjusted) performed on binary outcome variables (e.g., ER visits) *Timeframe:* 12 months *Intervention:* Received a thorough medication review by pharmacist to identify DRPs, telephone consult also provided. Frequency depended on clinical	Drug-related Problems Identified • At least 1 DRP was identified in more than 83% of beneficiaries in both groups, most common of which was drug-drug interaction All Cause Mortality • Beneficiaries who opted-in were less likely to die compared with beneficiaries who opted out (adj OR 0.5; 95% CI 0.3 to 0.9) during follow-up Hospitalization • Beneficiaries who opted-in were more likely to have had a hospitalization (adj OR 1.4; 95% CI 1.1. to 2.0) during follow-up Medication Costs • Beneficiaries who opted-in were more likely to have an increase in medication costs (adj OR 1.4; 95% CI 1.1 to 1.9) during follow-up ER Visits • No difference.	• Did not assess patients reaching Part D gap • Control group was those who declined participation • Small sample size may have affected ability to detect differences due to limited power • Impacts may not be due wholly to MTM

Appendix VI: Summary of Studies that Examined the Effect of Medication Therapy Management

Study	Plan & Sample	Research Design	Outcomes Measured & Results	Limitations
	pharmacist contacted via telephone to invite to participate, a letter mailed after calls	situation – 1 time with recommendations to physician or intensive, short-term INT: those who opted-in COMP: those who declined; received "mock MTM" review of medication list for DRPs		