Prescription Drug Insurance Coverage and Patient Health Outcomes: A Systematic Review

Previous reviews have shown that changes in prescription drug insurance benefits can affect medication use and adherence. We conducted a systematic review of the literature to identify studies addressing the association between prescription drug coverage and health outcomes. Studies were included if they collected empirical data on expansions or restrictions of prescription drug coverage and if they reported clinical outcomes.

We found 23 studies demonstrating that broader prescription drug insurance reduces use of other health care services and has a positive impact on patient outcomes. Coverage gaps or caps on drug insurance generally led to worse outcomes. States should consider implementing the Affordable Care Act expansions in drug coverage to improve the health of low-income patients receiving state-based health insurance. (*Am J Public Health*. Published online ahead of print December 18, 2014: e1–e14. doi:10.2105/AJPH.2014.302240)

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HEALTH CARE COSTS ARE one of the most important modern-day health policy issues. The United States spends more per capita on health care than any other country, with the percentage of gross domestic product dedicated to health care doubling from 9% in 1980 to 18% in 2011.[1] Costs related to implementation of the federal Medicare health insurance program are considered one of the key contributors to slowed US economic expansion.[2]

Prescription drugs have been substantial contributors to health care inflation. Pharmaceuticals account for about 10% of total health care costs, and although spending on pharmaceuticals has recently slowed, it is poised to swell in upcoming years as a result of the increasing prices of complex specialty medicines.[3] One response to this trend from public and private insurers has been to place firm restrictions on the availability of prescription drugs or to exclude certain drugs from coverage altogether. In 2009, Medicaid, the federal- and state-funded health care insurance program for the poor, spent about $25 billion on pharmaceuticals, making it one of the largest single purchasers of prescription drugs in the United States.[4] From 2010 to 2012, 7 states imposed new limits or tightened existing limits on the number of prescription drugs routinely covered by their Medicaid programs. Currently, 16 different states have such limits; in Illinois, for example, Medicaid recipients' insurance plans now cover a maximum of only 4 prescription drugs per month without prior authorization.[5]

Collateral effects will emerge from insurance changes that restrict the availability of prescription drugs or exclude patients from accessing them. One predictable effect will be on spending. Numerous previous studies have shown that expenses related to broader insurance coverage of essential prescription drugs result in lower or the same level of overall health care spending.[6–11] For example, in their randomized study of prescription drug coverage expansion, Choudhry et al. found that increased spending by one large insurer on prescription drugs in the form of reduced enrollee copays on certain categories of drugs did not lead to overall increases in health costs.[12] Another expected collateral effect will be on medication adherence. A recent systematic review of value-based insurance design programs, in which patient copayments were reduced for medications used to treat chronic diseases, showed that reduced out-of-pocket patient spending was consistently associated with improved medication adherence.[13]

Although the effects of drug insurance design changes on health care spending and medication adherence have been demonstrated, the effects on patient morbidity and mortality are less well understood. With the recent limits in drug coverage enacted by certain state Medicaid programs and the possibility of substantial expansion of drug insurance benefits offered by the implementation of the Affordable Care Act (Pub L No. 111-148), we conducted a systematic review to determine how expansions or restrictions in prescription drug insurance have affected patients' health outcomes or their use of health care services.

METHODS

We first searched the MEDLINE database via the OvidSP gateway in May 2014. Literature reviews in related subject areas and the abstracts of known studies helped us formulate the search strategy and identify a comprehensive list of search terms. We settled on 3 main subject heading domains: terms focusing on prescription drug insurance (for example, "insurance" or "coverage"), terms relating to pharmaceuticals or prescription drugs (for example, "drug" or "pharmaceutical"), and terms indicating our outcomes of interest (for example, "outcome assessment" or "health status"). Articles containing at least one search term in each of the 3 main categories met the criteria for our title and abstract review. Searches were limited to human studies and English-language studies; we did not include any date restrictions.

The following Boolean search terms were used: ("prescription drugs" or "prescription" or "drugs" or "drug utilization/economics" or "drug utilization/statistics & numerical data" or "pharmaceutical services" or "pharmacy services" or "drug utilization") and ("reimbursement mechanisms" or

"insurance coverage" or "insurance" or "cost sharing" or "medically uninsured" or "health care costs" or "insurance benefits" or "drug prescriptions/economics" or "uninsured") and ("outcome assessment [health care]" or "health services research" or "risk assessment" or "patient satisfaction" or "patient admission/statistics & numerical data" or "activities of daily living" or "health status" or "hospitalization" or "treatment outcome" or "emergency service" or "hospital utilization" or "health services accessibility") and ("humans" and "United States" and "English") but not ("literature reviews" or "systematic review" or "editorial" or "commentary" or "comment" or "interview" or "guideline" or "case reports" or "newspaper article" or "biography" or "news" or "directory" or "video audio media" or "legal case" or "news" or "clinical trial" or "autobiography" or "letter"). Similar searches were conducted in EMBASE, EconLit, and Business Source Complete, but no additional studies meeting our inclusion criteria were found.

Study Selection

Our review focused on populations of patients who had prescription drug insurance coverage. We excluded studies of patients with health insurance in which the prescription drug insurance component was not separately analyzed. The intervention or exposure of interest was expansion or restriction of prescription drug coverage. Studies were included if they collected empirical data comparing outcomes of patients before and after the expansion or restriction or if they compared patients with prescription drug insurance with a comparator population of patients without such insurance. We included only studies reporting clinical outcomes, which included use of health care services but not simply measurements of costs or health care spending related to service use. We excluded studies of prescription drug insurance benefit design changes that evaluated only effects on drug prescribing,[14,15] expenditure patterns,[16] or medication adherence alone.[17] Although these measures are of key public health importance, we chose to focus on studies that directly evaluated patient health outcomes.

These inclusion criteria did not allow for condition-specific formulary alterations such as those characteristic of value-based insurance designs,[13] nor did they allow for alterations in drug insurance benefit features such as changes in copayments or institution of prior authorization requirements.[18] Even though such programs may affect patient outcomes, we chose to focus on broader drug coverage expansions or restrictions. Studies available for inclusion could have randomized, nonrandomized, controlled, prospective, retrospective, or natural experiment designs. Policy reviews that were not data driven and economic simulations were excluded.

Two of the authors (Aaron S. Kesselheim and Lisa A. Fulchino) reviewed all of the abstracts in the search results independently and compared their results; disagreements were resolved by consensus ($\kappa = 0.52$). Manual reference mining of studies and other reviews supplemented our search results.

Data Extraction, Risk of Bias Determination, and Analysis

Data were extracted and checked by 2 abstractors (Krista F. Huybrechts and Lisa A. Fulchino), with disagreements resolved by consensus. Variables included study design, the nature of the intervention related to prescription drug insurance, study population and size, outcomes, and the funding source or sources for the trial.

We used the guidelines outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* to evaluate all studies according to their methodological qualities and to assess the studies with respect to bias. These guidelines incorporate 6 parameters: generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias.[19] The handbook outlines suggestions for determining low and high risk in each category.[19] After extraction of data, 2 of the authors (Lisa A. Fulchino and Danielle L. Isaman) independently assessed the studies for possible bias. The reviewers' results were compared, and discrepancies were resolved via consensus among all of the authors. We defined low risk as "plausible bias unlikely to seriously alter the results," unclear risk status as "plausible bias that raises some doubt about the results," and high risk as "plausible bias that seriously weakens confidence in the results." We also included a domain that would capture any additional sources of bias other than those already specified. We then determined overall bias on the basis of assessments of aggregate bias and the potential of sources of bias to affect the magnitude or direction of the results (in accordance with the *Cochrane Handbook*).

Next, we separated the studies into 3 relevant categories to facilitate our evaluation: studies comparing outcomes between patients with and without drug insurance coverage, studies evaluating expansions of drug insurance, and studies evaluating restrictions on drug insurance. Because of the heterogeneity among studies (e.g., in populations, interventions, and outcomes evaluated), a meta-analysis was not possible.

RESULTS

Our search identified 1918 unique publications, of which 40 appeared to meet our inclusion criteria. Nineteen of these articles were excluded after a full-text review, and 2 were added after mining of references in reviewed articles (Figure 1). The 23 articles forming our review sample were published between 1990 and 2013, and nearly all (22) investigated insurance changes in the United States. Patients receiving government-sponsored drug insurance were the primary population studied.

We found no randomized controlled trials among these studies. Rather, most were designed as pre-observational/post-observational studies. Study sample sizes ranged from as low as 36 to as high as 157 275 (the median sample size was 2369), with larger study populations associated with analyses of large insurer claims databases. Most populations were health insurance enrollees for whom the presence or absence of prescription drug insurance coverage could be used as a distinguishing variable.

Outcomes Among Patients With and Without Drug Insurance

We found 7 studies that evaluated the impact of drug insurance on patients' health by comparing cohorts of patients with and without coverage (Table 1). The study with the largest number of participants (Khan et al.[20]) examined the impact of reported initiation of prescription drug insurance coverage in a sample of 22 741

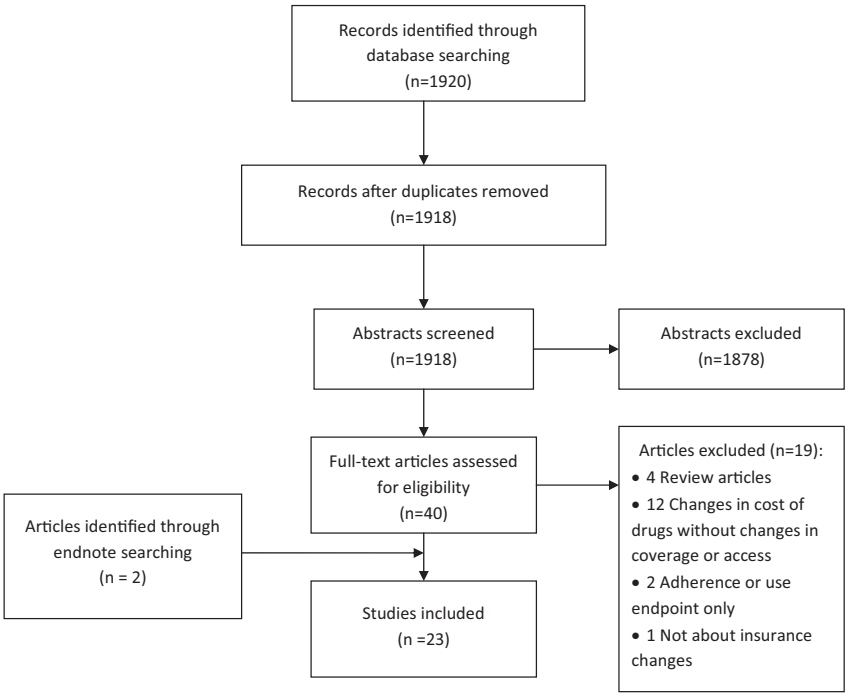

FIGURE 1—Flow chart detailing the derivation of the systematic review sample.

Medicare Current Beneficiary Survey respondents from 1992 to 2000. The authors found that, in a fixed effects regression model accounting for the number of reported chronic conditions and doctor visits, there was no relationship between drug coverage and self-reported measures of general health status, functional disability, or hospitalizations. However, 2 other smaller studies involving survey data did reveal evidence of disparities in health outcomes among participants with and without drug coverage.[8,21] These survey studies were limited in their analysis of patient-reported outcomes, which could have been affected by recall and other biases.

We found 3 other studies that reported associations between drug coverage and objective reports of health outcomes. The largest (Bhattacharya et al.[22]) compared the effects of public and private insurance coverage on mortality among patients with HIV during the years 1996 to 1998. The study authors found that, relative to absence of coverage, private insurance was associated with a greater survival advantage (79%) than public insurance (66%; $P<.05$). This difference was attributable to increased use of highly active antiretroviral therapy among patients in private insurance plans; 50% of patients in private insurance plans received therapy early in their care, as compared with 34% of patients with public insurance and 32% of patients with no insurance. Piette et al.[23] found similar results in their analysis of patients with Veterans Affairs–based health insurance and uninsured patients. Uninsured patients had greater odds of cost-related medication underuse (odds ratio [OR] = 5.6; 95% confidence interval [CI] = 2.7, 11.8), which was in turn linked to worse diabetes control and patient-reported health.

In the only non-US-focused study in our review, Bleich et al.[24] surveyed patients in different areas of Mexico. They found that patients with drug insurance and hypertension had higher odds of receiving a prescription for an antihypertensive drug and receiving antihypertensive treatment than a propensity-score-matched sample of hypertensive patients without drug insurance. A fourth study that examined the association between health insurance and smoking cessation outcomes (quitting attempts and rates) showed no significant difference in quitting attempts or rates; however, this study involved a high risk of bias.[25]

Drug Insurance Expansions and Patient Health Outcomes

Eight studies reviewed the effects of extending drug coverage to patients on their health outcomes (Table 2). In 3 of these studies, initiation of Medicare Part D drug insurance in 2006 was the key policy intervention. Afendulis et al.,[26] studying adults across 23 states with at least one "medication-sensitive condition" (a condition that can be improved by drug adherence, such as congestive heart failure or stroke), found that initiation of Part D coverage was associated with a significant reduction from baseline in hospitalizations for such conditions. They estimated that the introduction of Part D was responsible for half of the reduction in admissions occurring in those states during the 2005–2007 time period.

Donohue et al. found enrollment in Medicare Part D to be associated with a reduction (from approximately 3% to 2%; $P=.03$) in the percentage of prescriptions for a set of high-risk drugs previously defined by the National Committee for Quality Assurance as drugs that should be avoided in elderly patients.[27] By contrast, Liu et al.[28] studied community-dwelling patients in the year before and year after Part D coverage was initiated. Part D coverage was associated with an overall decrease in out-of-pocket drug costs (from $854 to $599; $P<.001$) but was not associated with changes in use of health services, including emergency department visits and hospitalizations. This study was limited by its small sample size and the use of a near-elderly (rather than an age-matched) comparison group.

Another 2 studies evaluated loosening of previously strict drug insurance caps. Kozma et al.[29]

TABLE 1—Comparison of Health Outcomes Among Patients With and Without Prescription Drug Insurance Coverage: Summary of Studies Conducted Between 1990 and 2013

Study	Design	Sample Type	Study Years	Participant Details	Exposure/Intervention	Main Outcomes	Findings	Funding Sources
Stuart et al.[8] (2004)	Observational; survey	Medicare participants with COPD	2000	384 beneficiaries with drug coverage; 78 beneficiaries without drug coverage	Drug insurance status	Hospital and physician costs	Drug coverage associated with 61% higher spending by patients on all drugs ($P < .05$) and 47% higher spending on COPD drugs; drug coverage associated with 29% lower spending on all physician services ($P < .05$) and 22% lower spending on COPD-related physician services; drug coverage associated with 23% lower hospital costs overall and 45% lower hospital costs related to COPD	Commonwealth Fund and Centers for Medicare & Medicaid Services
Khan et al.[20] (2008)	Observational; survey	Medicare Current Beneficiary Survey sample	1992–2000	22 741 unique individuals (66 905 person-years of observation), 63% with drug insurance (public, employer sponsored, Medicare HMO, Medigap) and 37% without drug insurance	Drug insurance status	Health outcomes	Prescription drug insurance not associated with significant (statistical or clinical) changes in self-reported health, functional disability, or hospitalization; drug insurance might offer health benefits (decreased functional disability) for chronically ill or elderly individuals	No funding source listed
Mojtabai and Olfson[21] (2003)	Observational; longitudinal survey	Health and Retirement Study sample of Medicare beneficiaries	2000	1320 beneficiaries with full drug insurance; 5132 beneficiaries with partial drug insurance; 2218 beneficiaries without drug insurance	Drug insurance status	Adherence and health outcomes	7% reported cost-related poor drug adherence, associated with no or partial drug coverage ($P < .001$); beneficiaries with poor adherence were 86% more likely to report poor health ($P < .001$); beneficiaries with poor adherence were 49% more likely to report hospitalizations in past 2 years ($P < .001$)	National Institute of Mental Health

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TABLE 1—*Continued*

Bhattacharya et al.[22] (2003)	Observational; longitudinal survey	Nationally representative sample of HIV patients	1996–1998	718 privately insured patients; 1295 publicly insured patients; 453 uninsured patients	Health insurance status (private vs public vs none)	HIV-related mortality	Private insurance associated with 79% improvement in mortality, as compared with 66% from public insurance ($P < .05$); greater availability of highly active antiretroviral therapy among patients with private insurance	Agency for Healthcare Research and Quality
Piette et al.[23] (2004)	Observational; survey	Adults with diabetes recruited from 3 different US health care systems	Not specified	339 VA patients; 204 patients with private insurance; 95 Medicare patients; 65 Medicaid patients; 63 uninsured patients	Health insurance status	Adherence and health outcomes	Fewer VA patients reported cost-related drug underuse than patients with private insurance (OR = 1.9; 95% CI = 1.0, 3.7), Medicare (OR = 2.7; 95% CI = 1.3, 5.4), Medicaid (OR = 2.7; 95% CI = 1.3, 5.9), or no insurance (OR = 5.6; 95% CI = 2.7, 11.8); patients with cost-related drug underuse had higher A1c levels (8.7 vs 7.9; $P < .0001$), more symptoms (7.3 vs 4.9; $P < .0001$), and poorer physical ($P = .0002$) and mental ($P < .0001$) functioning than those with no underuse	Department of Veterans Affairs and Agency for Healthcare Research and Quality
Bleich et al.[24] (2007)	Observational; population-based survey	Mexico Seguro Popular members	2005	1065 hypertensive adults with insurance; 1065 propensity-score-matched controls without insurance	Insurance status	Drug treatment and blood pressure control	Insured patients had 50% greater odds of receiving antihypertensive treatment (OR = 1.50; 95% CI = 1.27, 1.78); hypertension controlled in 24.1% (95% CI = 21.9%, 26.1%) of insured patients vs 19.3% (95% CI = 17.2, 21.6) of uninsured patients	Harvard Graduate School of Arts and Sciences
Boyle et al.[25] (2002)	Observational; survey with 1-year follow-up	Blue Cross Blue Shield of Minnesota and HealthPartners members	1998–1999	1560 smokers with smoking cessation benefits; 767 smokers without such benefits	Insurance coverage for smoking cessation medicines (vs no such coverage)	Smoking cessation	No significant differences in use of smoking cessation therapy (bupropion, nicotine patches); no significant differences in quitting attempts (short or long term); no significant differences in quitting rates	Robert Wood Johnson Foundation

Note. CI = confidence interval; COPD = chronic obstructive pulmonary disease; OR = odds ratio; VA = Veterans Affairs.

TABLE 2—Effects of Expansions in Prescription Drug Insurance Coverage on Patient Health Outcomes: Summary of Studies Conducted Between 1990 and 2013

Study	Design	Sample Type	Study Years	Participant Details	Drug Insurance Change/Comparison	Main Outcomes	Findings	Funding Sources
Afendulis et al.[26] (2011)	Observational; pre/post comparison	Hospital discharge data from adults in 23 states; linked to state-level data on drug coverage	2005–2007	Adults 60 years or older	Initiation of Medicare Part D in 2006	Hospitalization rates (for diabetes, chronic obstructive pulmonary disease, congestive heart failure, angina, asthma, stroke, myocardial infarction)	Increase in drug coverage from 61% to 88%; reduction in hospitalizations of 20.5 per 10 000 (42 000 admissions in total), a 4% decrease from baseline ($P = .01$)	Pharmaceutical Research and Manufacturers of America and Harvard Medical School
Donohue et al.[27] (2012)	Observational; pre/post with comparison group	Members of a Pennsylvania Medicare health insurance provider	2004–2007	34 679 elderly Medicare beneficiaries: 3499 with no coverage, 2519 with $150 cap, 18 199 with $350 cap before Part D implementation, vs 9053 with coverage throughout (comparison group)	Initiation of Medicare Part D in 2006	Inappropriate medication use	Increase in use of DAE (ROR = 1.34; 95% CI = 1.22, 1.48; $P < .001$) in no-coverage group; proportion of total drug use attributable to DAEs declined (ROR = 0.84; 95% CI = 0.72, 0.98; $P = .03$) in no-coverage group; rates of potentially harmful drug–disease interactions in the elderly remained stable (ROR = 1.06; 95% CI = 0.78, 1.44; $P = .693$) in no-coverage group	National Institutes of Health, Agency for Healthcare Research and Quality, Veterans Affairs Health Services
Liu et al.[28] (2011)	Observational; pre/post comparison	Medical Expenditure Panel Survey	2004–2006	556 eligible nonmilitary community-dwelling individuals 65 years or older without supplementary state insurance; 549 controls 55–63 years of age	Initiation of Medicare Part D in 2006	Medication use, emergency department use, hospitalizations, preference-based health utility	Out-of-pocket drug costs decreased from $854 to $599 ($P = .034$), whereas number of prescription fills increased nonsignificantly, by 2.05 per patient per year ($P = .81$); no significant differences in emergency department use (0.037 change in annual visits; $P = .565$), hospitalizations (0.0362 change in annual hospitalizations; $P = .479$), or preference-based health utility (–0.0106 change in utility; $P = .143$)	Agency for Healthcare Research and Quality and Robert Wood Johnson Foundation

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TABLE 2—*Continued*

Kozma et al.[29] (1990)	Observational; 1-year pre/post comparison	South Carolina Medicaid sample	1983–1986	12 139 beneficiaries with 1 or more prescription claims	In October 1984, change from restrictive to nonrestrictive drug formulary	Medical service use and expenditures	Formulary expansion associated with increase in prescriptions, physician visits, and outpatient hospital services and decrease in inpatient hospital admissions	National Pharmaceutical Council
Balkrishnan et al.[30] (2001)	Observational; 1-year pre/post comparison	Medicare HMO sample	1998–1999	2411 older adults continuously enrolled for 2 years	In January 1999, change from generic/brand tier copay ($7/$15) and $200 total per quarter to unlimited generics ($5 copay) and $25 per month brand limit ($15 copay)	Medical service use and expenditures	Policy change associated with 27% decrease in prescription costs ($P < .05$), but no significant change in other costs; total costs decreased by 6% ($P < .05$); policy change associated with 4% decrease in office visits ($P < .05$), but no significant change in inpatient visits	Wake Forest University
Shaw and Carrozza[31] (2008)	Telephone survey	Cincinnati MedShare patients	2003	928 participants in Medshare program; 259 were propensity score matched to external comparison group.	Enhanced access to prescription drugs for indigent patients through subsidies	Quality of life	No statistically significant differences in either physical or mental quality of life among patients themselves or vs external comparison group	Funding source not listed
Spiker et al.[32] (2003)	Telephone survey	Prescription assistance pharmacy service patients in Ohio	2002	104 patients lacking health insurance who were near or below the federal poverty level	Enhanced access to prescription drugs ($7 copay for short-term drugs, free 3-month supplies for long-term therapies) for indigent patients through subsidies	Medication adherence, medication safety, health care use, health outcomes	69% reported drug adherence; 24% reported adverse effects; 49% made unscheduled health care visits (59% of nonadherent patients vs 44% of adherent patients); 79% reported improvement in health care–related quality of life; 89% planned to skip drugs, give up necessities if not enrolled	Funding source not listed

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TABLE 2—Continued

Chisholm et al.[33] (2007)	Observational; pre/post comparison	Patients enrolled in Medical College of Georgia medication access program	1999–2005	36 adult renal transplant recipients enrolled in medication access program for 1 year or more	Medication assistance program providing full access for enrolled patients along with medication therapy oversight to evaluate adherence and adverse events	Medication access, clinical outcomes, health-related quality of life	Significant increase in use of antihypertensives ($P < .001$), antidiabetics ($P = .004$), and antilipemics ($P = .001$); significant decrease in fasting blood glucose, glycosylated hemoglobin, LDL cholesterol, total cholesterol, triglycerides, blood pressure, and graft rejections ($P < .01$); significant increase in number of patients reaching target serum cyclosporine levels ($P = .007$) but not serum tacrolimus levels ($P = .343$); significant increase in health-related quality of life ($P < .01$)	Carlos and Marguerite Mason Trust Fund (partial funding)

Note. CI = confidence interval; DAE = drugs to avoid in the elderly; ROR = relative odds ratio.

reviewed the effects of a 1984 policy change in South Carolina Medicaid; as a result of this policy change, a drug formulary that provided coverage for only a subset of prescription drugs was replaced with a program in which the state offered reimbursements for all prescription drugs and some over-the-counter drugs without restrictions. The formulary expansion was associated with increases in outpatient-focused variables (e.g., outpatient hospital services and physician visits) and reductions in inpatient-focused variables (e.g., hospitalizations). Balkrishnan et al.[30] examined a similar change at a southeastern Medicare health maintenance organization that altered its policy from a tiered copay system for brand-name ($15) and generic ($7) drugs and a $200 quarterly drug expenditure cap to unlimited coverage of generic drugs (with a $5 copay) with a high copay ($25) and a cap on brand-name drugs ($25 per month). They found that the policy change was associated with a 4% decrease in patient office visits ($P < .05$) and a 6% decrease in total health care costs.

The final 3 studies examined the extension of specific drug coverage via state subsidies to indigent patients[31,32] and renal transplant recipients.[33] Examining the perceptions of indigent patients in a cross-sectional survey, Spiker et al.[32] reported substantial perceived improvements after initiation of medication coverage, including a 79% reported increase in health-related quality of life. By contrast, Shaw and Carrozza[31] found no statistically significant difference in either physical or mental quality of life among patients who received a subsidy for prescription drugs. In their study of renal transplant recipients, Chisholm et al.[33] concluded through preenrollment/postenrollment comparisons that a medical assistance program was associated with improvements in key clinical outcomes, including blood sugar control, target blood levels of cyclosporine antirejection therapy (although tacrolimus levels were unchanged), and a reduction in the number of graft rejections ($P = .008$).

Drug Insurance Restrictions and Patient Health Outcomes

Eight studies evaluated the effects of drug insurance restrictions on health outcomes (Table 3). Only one study (Fuller et al.[34]) examined complete withdrawal of drug insurance. That study assessed the impact of the Oregon Medicaid program's elimination of its methadone benefit program, which had previously been available to patients with opioid addiction. The authors found that enrollees who left the program after the elimination of coverage had a 75% rate of self-reported heroin use over the next year, as compared with a rate of approximately 33% among patients who paid for the methadone themselves or did not lose their coverage benefits. However, this study was uncontrolled and was methodologically the weakest in our review.

Five of the studies in this category examined the effects of firm caps on drug benefits that arose after patients expended a certain baseline amount of resources on prescription drugs. Four assessed the impact of reaching the coverage limitation built into the Part D benefit. Raebel et al.[35] found that, among patients who had recently obtained insurance through Medicare Part D, reaching the coverage limitation was associated with increases in emergency

TABLE 3—Effects of Restrictions in Prescription Drug Insurance Coverage on Patient Health Outcomes: Summary of Studies Conducted Between 1990 and 2013

Study	Design	Sample Type	Study Years	Participant Details	Drug Insurance Change/ Comparison	Main Outcomes	Findings	Funding Sources
Fuller et al.[34] (2006)	12-month prospective survey	Oregon Medicaid enrollees	2003–2004	149 clients at a methadone program: 33 left care after benefit elimination, 68 self-paid after benefit elimination, 48 did not lose benefits	Elimination of methadone benefits	Treatment discontinuations and associated problems	66% of those in self-pay group and 82% of those who did not lose benefits remained in treatment at 1 year; 75% in left-care group reported heroin use in next year, vs 37% in self-pay group and 38% of those who did not lose benefits; left-care group had greater legal and psychiatric problems	Center for Substance Abuse Treatment, Oregon Practice Improvement Collaboration, National Institute on Drug Abuse, and Robert Wood Johnson Foundation
Raebel et al.[35] (2008)	Observational; retrospective cohort	Kaiser Permanente Colorado members	2005–2006	21 349 Kaiser Permanente Colorado beneficiaries with Medicare Part D and a drug insurance threshold; 9088 Medicare beneficiaries with nonthreshold employer drug insurance plans	Medicare Part D coverage gap (vs no gap)	Health care and medication use	1237 (6%) Part D beneficiaries reached the threshold; reaching the threshold was associated with more inpatient care use (RR = 1.85; 95% CI = 1.64, 2.09) and ED use (RR = 1.60; 95% CI = 1.40, 1.83); reaching the threshold was associated with fewer primary care visits vs Part D beneficiaries who did not reach the threshold (RR = 0.86; 95% CI = 0.79, 0.93) and matched group with no threshold (RR = 0.88; 95% CI = 0.84, 0.92); the adherence decline was greater for those who reached the threshold	Kaiser Permanente Colorado and Agency for Healthcare Research and Quality
Fung et al.[36] (2013)	Observational; pre/post comparison with comparator group	Patients in Medicare Advantage plan offered by national sponsor	2006–2007	10 190 noninstitutionalized Medicare Advantage beneficiaries on antipsychotics with schizophrenia, bipolar disorder, or no mental health diagnosis; 5054 with coverage gap, 5136 without gap	Medicare Part D coverage gap (vs no gap)	APM spending, adherence, and clinical events	With cost-sharing increases in the gap, total monthly expenditures on APM decreased (schizophrenia: $–123; 95% CI = $–138, $–108), out-of-pocket spending increased (schizophrenia: $104; 95% CI = $98, $110), adherence (proportion of days covered) decreased (schizophrenia: –20.6%; 95% CI = –22.3%, –18.9%), and hospitalization and ED visit rates increased for schizophrenia and bipolar patients but not for individuals without mental health diagnoses; increases were largely ascribed to mental health diagnoses	National Institute on Aging and National Institute of Mental Health

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TABLE 3—*Continued*

Polinski et al.[37] (2012)	Observational; prospective cohort	Medicare beneficiaries with prescription drug coverage administered by Caremark	2005–2007	3980 Medicare beneficiaries 65 years or older with cardiovascular disease who reached gap spending threshold and received no financial assistance (exposed group), propensity score matched to 3980 beneficiaries with financial assistance (unexposed group)	Medicare Part D coverage gap (vs no gap)	Cardiovascular drug use, risk of death or hospitalization owing to cardiovascular outcomes	Beneficiaries without assistance were more likely to discontinue cardiovascular drugs (HR = 1.57; 95% CI = 1.39, 1.79) but not to switch drugs (HR = 1.04; 95% CI = 0.88, 1.23); no significant differences in rates of death (HR = 1.23; 95% CI = 0.89, 1.71) or other outcomes	National Institute on Aging; National Institute of Mental Health; National Heart, Lung and Blood Institute; Robert Wood Johnson Foundation, and CVS Caremark
Polinski et al.[38] (2012)	Observational; prospective cohort	Medicare beneficiaries with prescription drug coverage administered by Caremark	2006–2007	9383 Medicare beneficiaries 65 years or older enrolled in stand-alone Part D or retiree drug plans who reached the gap spending threshold and received no financial assistance (exposed group), propensity score matched to 9383 beneficiaries with financial assistance (unexposed group)	Medicare Part D coverage gap (vs no gap)	Risk of death or hospitalization owing to cardiovascular outcomes	Beneficiaries without financial assistance had higher risk of death (HR = 1.25; 95% CI = 0.98, 1.59) and acute coronary syndrome (HR = 1.16; 95% CI = 0.83–1.62) than unexposed patients; effects were further attenuated in propensity-score-matched cohort; no differences in other cardiovascular outcomes	National Institutes of Health, Robert Wood Johnson Foundation, and CVS Caremark
Hsu et al.[39] (2006)	Observational; prospective cohort	Kaiser Permanente Northern California members	2003	157 275 Medicare + Choice beneficiaries with annual $1000 drug benefit cap; 41 904 beneficiaries with unlimited drug benefits because of employer supplements	Cap on Medicare drug benefits (vs no cap)	Clinical and economic outcomes	Capped insurance resulted in higher rates of ED visits (RR = 1.09; 95% CI = 1.04, 1.14); higher rates of nonelective hospitalizations (RR = 1.13; 95% CI = 1.05, 1.21); higher rates of death (RR = 1.22; 95% CI = 1.07, 1.38); higher odds of nonadherence to antihypertensive drugs (RR = 1.30; 95% CI = 1.23, 1.38), lipid lowering drugs (RR = 1.27; 95% CI = 1.19, 1.34), and antidiabetics (RR = 1.33; 95% CI = 1.18, 1.48); greater likelihood of systolic blood pressure of 140 mmHg or above (OR = 1.05; 95% CI = 1.00, 1.09), LDL cholesterol of 130 mg/dL or above (OR = 1.13; 95% CI = 1.03, 1.25), and A1c of 8% or above (OR = 1.23; 95% CI = 1.03, 1.46); and lower costs of drugs that applied to cap (RR = 0.69; 95% CI = 0.67, 0.71) but not total medical costs (RR = 0.99; 95% CI = 0.94, 1.04)	Agency for Healthcare Research and Quality and Alfred P. Sloan Foundation

Continued

TABLE 3—*Continued*

Soumerai et al.[40] (1991)	Observational; time-series analyses	New Hampshire and New Jersey Medicaid program enrollees	1981–1983 (cap implemented from September 1981 to July 1982)	411 New Hampshire Medicaid recipients 60 years or older with at least 3 prescriptions per month (with 1 or more prescriptions being for a chronic medication), compared with identically defined cohort of 1375 enrollees in New Jersey (no cap)	3-drug reimbursement cap (vs no cap)	Admissions to hospitals and nursing homes	Cap resulted in 35% decline in use of study drugs ($P < .001$); cap increased rates of admission to nursing homes (RR = 2.2; 95% CI = 1.2, 4.1); cap did not increase risk of hospitalization (RR = 1.2; 95% CI = 0.8, 1.6)	Agency for Healthcare Research and Quality, John A. Hartford Foundation, and National Institute on Aging
Soumerai et al.[41] (1994)	Observational; time-series analyses	New Hampshire and New Jersey Medicaid program enrollees	1980–1983 (cap implemented from September 1981 to July 1982)	268 (New Hampshire) and 1958 (New Jersey) permanently disabled, noninstitutionalized patients with schizophrenia (19-60 years of age) covered by Medicaid	3-drug reimbursement cap (vs no cap)	Use of psychotropic drugs and acute mental health care	Implementation of cap led to 15%–49% drop in use of psychotropics (antipsychotics, antidepressants, lithium, anxiolytics, hypnotics), 43%–57% increase in outpatient mental health visits ($P < .001$), increased emergency mental health service use and partial hospitalizations (1.2–1.4 episodes per patient month), no change in hospital admissions, and average increase in mental health care costs of $1530	Agency for Healthcare Research and Quality, National Institute of Mental Health, Robert Wood Johnson Foundation, and Harvard Community Health Plan Foundation

Note. APM = antipsychotic medication; CI = confidence interval; ED = emergency department; HR = hazard ratio; OR = odds ratio; RR = relative risk.

department use (relative risk [RR] = 1.60; 95% CI = 1.40, 1.83) and hospitalizations (RR = 1.85; 95% CI = 1.64, 2.09). Fung et al. observed a positive association between reaching the Part D coverage gap and worse outcomes among patients in psychiatric institutions with schizophrenia and bipolar disorder, including hospitalizations (schizophrenia: hazard ratio [HR] = 1.32; 99.5% CI = 1.06, 1.65; bipolar disorder: HR = 1.45; 99.5% CI = 1.16, 1.82).[36]

Two studies conducted by Polinski et al. also evaluated the effects of reaching the Part D beneficiary limit. One showed that beneficiaries reaching the coverage limitation were more likely to discontinue prescribed medications[37]; however, after control for numerous demographic factors and comorbidities, there were no significant differences in rates of death, hospitalizations related to acute coronary syndrome, or other clinical outcomes.[38] The other Polinski et al. study, the only investigation not relating to the Part D coverage gap, assessed the impact of a $1000 annual drug benefit cap imposed by Medicare + Choice prescription drug coverage plans.[39] Patients with the capped insurance plan, as compared with another cohort of enrollees in the same health plan with unlimited supplemental drug coverage, were more likely to have worse control of their blood pressure, cholesterol, and diabetes.

Finally, 2 studies conducted by Soumerai et al. examined how a strict 3-drug coverage benefit cap imposed by the state of New Hampshire in 1981 affected health outcomes. The study patients were compared with a matched cohort in New Jersey, where a cap was not imposed. In the first study, the authors found that the 3-drug cap in the context

TABLE 4—Risk of Bias Summary Table

Study	Sequence Generation	Allocation Concealment	Provider Blinding	Assessor Blinding	Incomplete Outcome Data	Selective Reporting	Other	Overall
Studies comparing health outcomes among patients with and without prescription drug insurance coverage								
Stuart et al.[8]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Mojtabai and Olfson[21]	Low	N/A	N/A	N/A	Low	Unclear	High	Unclear
Bhattacharya et al.[22]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Piette et al.[23]	Low	N/A	N/A	N/A	Low	Unclear	High	Low
Bleich et al.[24]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Boyle et al.[25]	High	N/A	N/A	N/A	Low	Unclear	High	High
Khan et al.[49]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Studies evaluating effects of expansions in prescription drug insurance coverage on patient health outcomes								
Afendulis et al.[26]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Donohue et al.[27]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Liu et al.[28]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Kozma et al.[29]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Balkrishnan et al.[30]	Low	Low	Low	Low	Low	Unclear	Low	Low
Shaw and Carrozza[31]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Spiker et al.[32]	Low	N/A	Low	Low	Low	Unclear	High	Low
Chisholm et al.[33]	Low	Low	Low	Low	Low	Unclear	Low	Low
Studies evaluating effects of restrictions in prescription drug insurance coverage on patient health outcomes								
Fuller et al.[34]	High	N/A	Low	Low	Low	Unclear	High	Unclear
Raebel et al.[35]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Fung et al.[36]	High	N/A	N/A	N/A	Low	Unclear	Low	Low
Polinski et al.[37]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Polinski et al.[38]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Hsu et al.[39]	Low	N/A	N/A	N/A	Low	Unclear	Low	Low
Soumerai et al.[40]	Low	N/A	N/A	N/A	Low	Unclear	High	Unclear
Soumerai et al.[41]	Low	N/A	N/A	N/A	Low	Unclear	High	Unclear

Note. N/A = not applicable.

of elderly patients led to a more than doubling of the relative risk of nursing home admissions (RR = 2.2; 95% CI = 1.2, 4.1).[40] In the second study, they found that the cap led to a 43% to 57% increase in outpatient mental health visits among patients with psychiatric conditions ($P < .001$) as well as an increase in use of emergency mental health services.[41]

Risk of Bias Assessment

Our risk of bias assessment (Table 4) showed that most studies were of high quality, and overall the risk of bias was low. Because many of the studies were not randomized prospective trials, some of the quality assessment tools did not apply, and it was particularly difficult to determine the presence or absence of selective reporting. All of the studies consistently ranked highly with respect to reports of full outcome data.

DISCUSSION

Our systematic review of studies evaluating patient health status and health care service use related to possession of prescription drug insurance shows that such programs can have significant effects on both outcomes. Benefits were demonstrated in a variety of clinical circumstances, geographic regions, and temporal settings.

The link between drug insurance expansion and patient health outcomes might be mediated by a number of different mechanisms. One contributor is the improved access to prescription drug therapies offered by enhanced insurance coverage. Patients without insurance may obtain episodic care in an emergency department, but the health effects derived from most prescription therapeutics accrue after ongoing treatment. Consistent access is a key feature of stable insurance coverage. For example, in the Bhattacharya et al. study of outcomes among patients with HIV, the observed improvements in health were a direct result of the life-saving antiretroviral therapy made available to patients through their prescription drug insurance. Clearly, by reducing financial strain on patients, prescription drug insurance helps insulate them from cost-related medication nonadherence and helps advance their health outcomes.

Whether insurance coverage has a positive or negative effect on health care outcomes has become particularly controversial[42] because the Affordable Care Act now authorizes the federal government to offer substantial resources to states for the purposes of expanding Medicaid. Although the federal government plans to cover the full cost of the expansion

for the first 3 years and 90% of the cost thereafter, Medicaid expansion has been rejected by some states as too expensive, with state governors expressing worry about excessive spending on Medicaid necessitating cuts to other parts of the government budget.[43] Such perceptions have been buoyed by economic calculations of Medicaid expansion that predict the costs of additional individual enrollees[44] without considering the reductions in costs accruing from the prevention of morbidity associated with use of medications among millions of Americans previously without drug insurance. A key question is whether there would be benefits from the expansion in terms of reduced mortality, and we found limited data addressing mortality directly.

The results of our review are consistent with retrospective studies showing that state-driven Medicaid expansions since 2000 in Wisconsin, New York, Arizona, and Maine have led to reduced mortality and improved coverage, access to care, and self-reported health.[45,46] A prospective randomized study conducted in Oregon, where a Medicaid expansion was implemented through a lottery process in 2008, also demonstrated better self-reported physical and mental health among those who received health insurance.[47] After 2 years of observation, the experience in Oregon has shown inconsistent effects on health promotion, with significant improvements in access to care and reductions in financial strain from medical costs but insignificant changes in clinical markers of hypertension and diabetes control (however, the study was underpowered for these clinical outcomes).[48]

Notably, effects on health care outcomes or health service use were not observed in all of the studies we identified. In some cases, the effects seen might be explained by the short-term time windows assessed. For example, studying a population sample after only 1 year of coverage, Liu et al. found reductions in out-of-pocket medication costs and increases in prescription drug use but no impact on outcomes. In other cases, negative outcomes may have been consequences of the study designs. For example, Khan and Kaestner found no statistically significant evidence of health benefits in a survey of elderly patients who self-reported changes in health and disability status, in part because their sample also reported limited changes in their use of prescription drugs after obtaining insurance.[49] Their study showed a nonsignificant trend toward beneficial outcomes among a chronically ill subgroup of the population.

Limitations

Our results should be interpreted with caution given that many of the studies reviewed were conducted during years when costly brand-name drugs were more likely to be prescribed than is the case today, allowing for a greater impact of drug insurance programs. Recently the percentage of prescriptions filled with generic drugs has reached nearly 80% owing to patent expirations of top-selling drugs for a range of different medical conditions. As a result, patients now can be prescribed a wide variety of generic alternatives for many common medication-responsive diseases, such as hypertension and diabetes, offered at prices as low as $4 per month. Use of generic drugs helps address many issues that account for the health benefits of drug insurance, such as cost-related medication nonadherence. Thus, the effect of insurance may be less pronounced in the present-day market, in which generic products are more widely available. Moreover, insurance for generic medications should be rather inexpensive and should promote adherence, which in turn reduces morbidity and its associated costs.

Our conclusions are also limited by the heterogeneity of the studies we identified, many of them examining different aspects of health care delivery and incorporating a variety of methodological approaches and outcome definitions. This heterogeneity prevented us from conducting a quantitative meta-analysis of the results, which would have given greater weight to the findings of the larger studies. To account for heterogeneity, we focused our interpretation on the studies with the largest sample sizes. Another major limitation of our study is the possibility of publication bias. Most of the studies in our sample were retrospective observational investigations, which are not required to be prospectively registered with a trial disclosure database such as ClinicalTrials.gov. Thus, we cannot exclude the possibility that studies were conducted but not completed or published.

Conclusions

Despite the limitations just described, we believe our systematic review shows that substantial evidence supports the central role effective prescription drug insurance can play as policymakers seek mechanisms to reduce the rising health care costs in the United States. Expanding insurance benefits may lead to initial costs in administration, but these costs should be offset by reductions in spending associated with preventable patient morbidity and mortality. Other strategies aimed at increasing the accessibility of essential prescription drugs, such as timely availability of generic alternatives and policies designed to improve medication adherence, will help augment the salutary effects of prescription drug insurance on patient health outcomes. ■

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Contributors

A. S. Kesselheim, N. K. Choudhry, and T. A. Brennan originated the study. A. S. Kesselheim designed the protocol and wrote the first draft of the article. A. S. Kesselheim, L. A. Fulchino, D. L. Isaman, and M. K. Kowal conducted the systematic review. A. S. Kesselheim, K. F. Huybrechts, L. A. Fulchino, D. L. Isaman, and M. K. Kowal extracted the data. A. S. Kesselheim, K. F. Huybrechts, N. K. Choudhry, and T. A. Brennan reviewed and revised drafts of the article.

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